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Nanotheranostics in Multi-Organ Cancer Management: From Liver to Brain Tumors via Omics and Artificial Intelligence

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Abstract:

Background: From 2019 to 2024, **nanotheranostics** multifunctional nanosystems combining therapeutic and diagnostic capabilities have emerged as a transformative approach in oncology. The integration of **artificial intelligence (AI)** and **multi-omics technologies** enables precise tumor targeting, patient-specific therapy personalization, and real-time monitoring of treatment response across major solid tumors. **Objectives:** This review provides a comprehensive update on recent advances in nanotheranostics for liver, breast, kidney, and brain cancers, highlighting cancer-specific strategies, multi-omics-guided targeting, AI-assisted optimization, and translational progress. **Methods:** Literature from 2019–2024 was systematically evaluated, focusing on nanocarrier types, therapeutic and diagnostic payloads, functionalization strategies, and integration with AI and multi-omics. Cancer-specific applications, translational barriers, and regulatory considerations were analyzed comparatively. **Results:** Advances in liposomes, lipid nanoparticles, polymeric carriers, biomimetic nanoparticles, and exosomes have enabled multifunctional delivery of chemotherapeutics, RNA therapeutics, immunomodulators, and CRISPR-Cas systems. Diagnostic payloads, including MRI, CT, PET agents, and biosensors, allow real-time monitoring of therapeutic response. Multi-omics insights guide patient stratification and payload selection, while AI predicts nanoparticle behavior and optimizes design. Preclinical and early clinical studies demonstrate promising efficacy, although challenges remain in manufacturing, safety, and regulatory compliance. **Conclusions:** The convergence of nanotheranostics, AI, and multi-omics represents a paradigm shift in precision oncology. Future directions include AI-guided adaptive nanocarriers, omics-informed patient personalization, and adaptive clinical trial frameworks. Addressing translational and regulatory challenges will be key to realizing the full clinical potential of these integrated strategies, improving outcomes across liver, breast, kidney, and brain tumors.

Keywords: Nanotheranostics; AI; multi-omics; precision oncology; liver cancer; breast cancer; kidney cancer; brain tumors; smart nanocarriers; RNA therapeutics; immunotherapy; theranostics

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1. Introduction

The past five years (2019–2024) have witnessed a remarkable evolution in oncology with the emergence of **nanotheranostics** multifunctional nanosystems that integrate both therapeutic and diagnostic capabilities. Unlike traditional approaches that treat and monitor cancer as separate processes, nanotheranostics enable real-time imaging, targeted drug delivery, and therapy monitoring within a single platform. This convergence has significantly enhanced the precision, efficacy, and safety of interventions across various tumor types [1-2]. Central to the effectiveness of nanotheranostics is the integration of **artificial intelligence (AI)** and **multi-omics technologies.** AI-driven algorithms facilitate predictive modeling for nanoparticle design, optimize payload delivery, and enable adaptive therapy planning. Meanwhile, genomics, transcriptomics, proteomics, and metabolomics provide a comprehensive molecular map of tumor heterogeneity, guiding both therapeutic selection and diagnostic targeting [3]. The synergy of these technologies allows for highly personalized cancer interventions, where therapy can be tailored to the unique molecular profile of each patient's tumor [4]. This review focuses on the application of nanotheranostics across major solid tumors, specifically **liver, breast, kidney, and brain cancers**, highlighting advances from 2019 to 2024. By examining cancer-specific strategies, multi-omics-guided targeting, AI-assisted design, and translational progress, this article aims to provide a comprehensive perspective on the current state and future potential of integrated nanotheranostic platforms. *(Figure 1)*

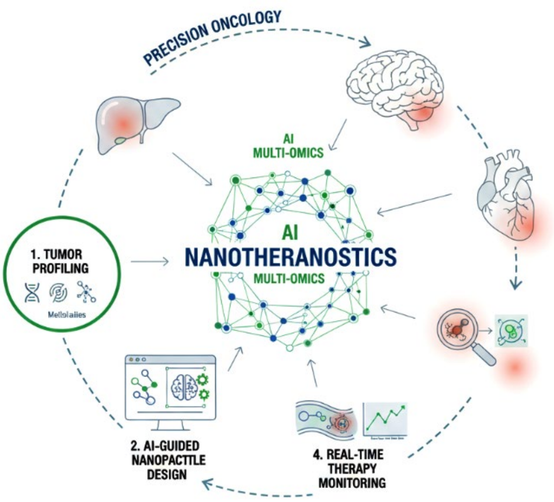

Figure 1: *Conceptual schematic of nanotheranostics illustrating AI and multi-omics integration across multiple organs, showing tumor profiling → AI-guided nanoparticle design → theranostic delivery → real-time monitoring.*

2. Nanotheranostic Platforms

Over the past five years, **nanotheranostic platforms** have evolved into sophisticated systems that combine therapy and diagnostics within a single nanoscale entity. Central to these platforms are diverse **nanocarrier types,** each offering unique advantages [5]. Liposomes and lipid nanoparticles (LNPs) remain widely employed due to their biocompatibility and ability to encapsulate both hydrophilic and hydrophobic agents. Polymeric nanoparticles provide tunable physicochemical properties for controlled drug release, while **biomimetic carriers** including cell membrane-coated nanoparticles exploit natural homing mechanisms for improved tumor targeting. Exosomes, as endogenous nanoscale vesicles, have emerged as highly selective and minimally immunogenic delivery vehicles [6.]Equally important are the **therapeutic payloads** that these carriers transport. Conventional chemotherapeutics are now combined with **RNA-based therapeutics** (siRNA, miRNA, mRNA) to modulate gene expression in tumors, as well as **immunomodulators** that reprogram the tumor microenvironment for enhanced immune response. Cutting-edge **CRISPR-Cas systems** have also been incorporated into nanocarriers, enabling precise genome editing to target oncogenic pathways [7].

On the diagnostic front, **imaging agents** such as MRI contrast molecules, CT and PET tracers, fluorescent tags, and nanoscale biosensors are integrated into these platforms to facilitate real-time tumor visualization, therapeutic monitoring, and early response assessment. By combining these therapeutic and diagnostic functionalities, nanotheranostics allow clinicians to tailor interventions dynamically, improving efficacy while reducing systemic toxicity.Finally, **smart functionalization** enhances the precision and stability of these platforms [8]. Stimuli-responsive linkers (pH, redox, or enzyme-sensitive) enable site-specific payload release, while surface ligands (antibodies, peptides, or aptamers) provide active targeting to tumor-specific markers. Stealth coatings, such as polyethylene glycol (PEG), prolong systemic circulation and reduce immune clearance, ensuring that nanocarriers reach their intended site of action effectively [9]. *(Table 1)*

Table 1: *Classification of nanotheranostic platforms with therapeutic and diagnostic functions, highlighting carrier type, payload, targeting strategy, and functionalization.*

Nanocarrier Type	Therapeutic Payloads	Diagnostic Payloads	Functionalization / Smart Features	Advantages	Reference
Liposomes	Chemotherapy, RNA therapeutics	MRI, fluorescent dyes	Ligand-targeting, pH-sensitive release, PEGylation	Biocompatible, high encapsulation, clinically validated	10

Lipid Nanoparticles (LNPs)	mRNA, siRNA, chemotherapeutics	PET tracers, fluorescent tags	PEGylation, ligand-conjugation, stimuli-responsive linkers	Efficient RNA delivery, scalable production	11
Polymeric Nanoparticles	Chemotherapy, immunomodulators, CRISPR	MRI contrast agents, biosensors	Biodegradable polymers, pH/redox-sensitive release	Controlled release, tunable size and surface properties	12
Biomimetic Carriers	Chemotherapy, RNA therapeutics, immunomodulators	Fluorescent dyes, imaging probes	Cell membrane coating, ligand-targeting	Immune evasion, tumor-homing ability	13
Exosomes	RNA therapeutics, immunomodulators	Fluorescent tags, molecular sensors	Surface modification, ligand-targeting	Endogenous vesicles, minimal immunogenicity, high specificity	14

3. Multi-Omics in Nanotheranostics

The integration of **multi-omics technologies** has been pivotal in advancing nanotheranostic strategies for precision oncology. **Genomics and transcriptomics** provide comprehensive insights into tumor-specific mutations, gene expression profiles, and actionable targets, guiding both therapeutic payload selection and imaging strategies [15]. By mapping mutations such as TP53, KRAS, or BRCA, nanocarriers can be tailored to deliver RNA therapeutics, chemotherapeutics, or CRISPR-Cas systems to the most relevant oncogenic pathways.**Proteomics and metabolomics** complement these insights by revealing dysregulated signaling pathways, enzymatic activities, and metabolic dependencies within tumors. This knowledge informs the design of nanotheranostics capable of modulating the tumor microenvironment (TME), targeting angiogenesis, or exploiting metabolic vulnerabilities for enhanced therapeutic efficacy [16].**Single-cell and spatial omics** have further refined precision nanotheranostics by capturing intra-tumoral heterogeneity. Understanding the distribution of distinct cell populations and their microenvironmental context enables the development of nanoparticles that can selectively target resistant subpopulations and improve overall treatment response.**AI integration** plays a critical role in synthesizing multi-omics data to optimize nanotheranostic design. Machine learning models can predict nanoparticle behavior, patient-specific drug response, and potential off-target effects. AI-driven patient stratification allows clinicians to identify individuals most likely to benefit from specific nanotheranostic interventions, enhancing treatment personalization [17-18]. *(Figure 2)*

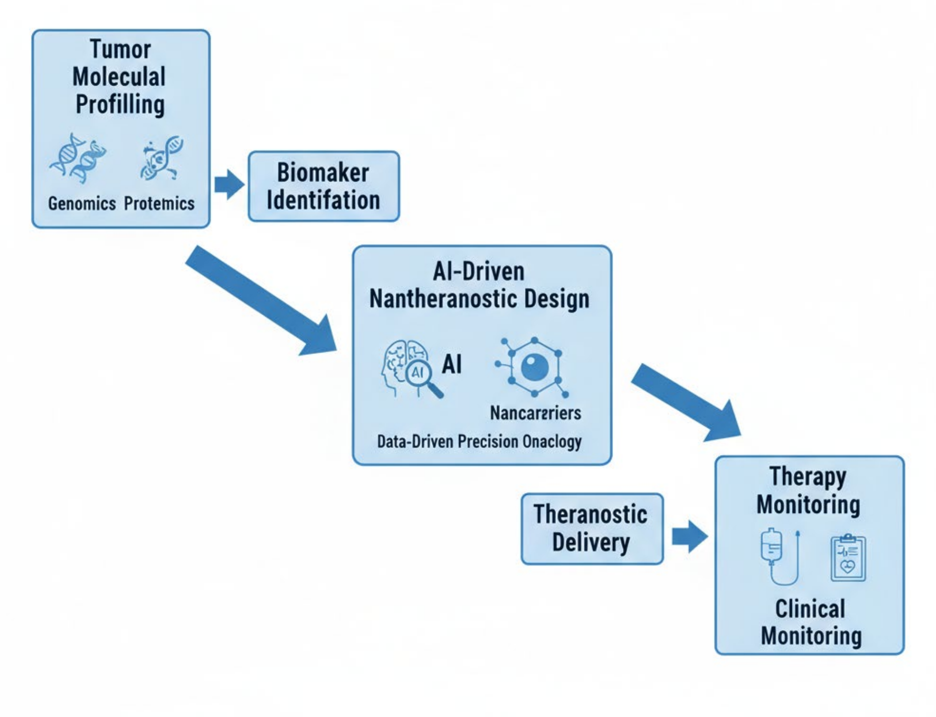

Figure 2: *Workflow of multi-omics integration with AI-driven nanotheranostic design, showing tumor profiling → biomarker identification → nanoparticle design → theranostic delivery → therapy monitoring.*

4. Liver Cancer (Hepatocellular Carcinoma)

Hepatocellular carcinoma (HCC) has been at the forefront of nanotheranostic applications due to its high incidence, poor prognosis, and complex tumor microenvironment. **Targeted nanotheranostics** leveraging ASGPR (asialoglycoprotein receptor) and GPC3 (glypican-3) receptors have demonstrated enhanced tumor accumulation and selective delivery of therapeutic payloads. These platforms often integrate imaging agents such as MRI or fluorescent probes to provide real-time visualization of tumor uptake and treatment response [19-20].**RNA-based nanotherapeutics,** including siRNA, miRNA, and mRNA, have been incorporated within these platforms to modulate gene expression, silence oncogenes, or restore tumor suppressor function. When combined with **transarterial chemoembolization (TACE)** and photothermal or photodynamic therapies, these nanotheranostics enhance local tumor control while reducing systemic toxicity.Preclinical studies over 2019–2024 have shown promising results in tumor regression, gene modulation, and imaging-guided therapy. Early-phase clinical trials are now evaluating the safety, biodistribution, and efficacy of these multifunctional platforms, laying the groundwork for broader translational adoption [21-22].

5. Breast Cancer

Breast cancer management has increasingly benefited from **subtype-specific nanotheranostics** designed to target ER+, HER2+, and triple-negative breast cancers (TNBC). Nanocarriers are engineered to deliver chemotherapeutics, RNA therapeutics, or immunomodulators directly to tumor cells, improving efficacy while minimizing off-target toxicity [23]. For HER2+ tumors, antibody-conjugated nanoparticles enable precise receptor-mediated targeting, whereas TNBC interventions often combine nanocarrier-based cytotoxic drugs with immuno-modulatory payloads to overcome the lack of conventional targets.Integration with **immunotherapy** and nano-enabled vaccines has further expanded treatment options, providing synergistic activation of the immune system alongside cytotoxic therapy. Imaging-guided interventions, including MRI or fluorescence-assisted surgery, facilitate intraoperative tumor visualization, improving resection accuracy and reducing recurrence rates [24.]The **translational pipeline from 2019–2024** has seen significant progress, with multiple preclinical studies demonstrating efficacy and safety, and early-phase clinical trials evaluating combinatorial nanotheranostic approaches. These advances underscore the potential of precision-targeted strategies in breast cancer management [25-26].

6. Kidney Cancer (Renal Cell Carcinoma)

In renal cell carcinoma (RCC), **tumor microenvironment (TME)-modulating nanotheranostics** are emerging as a critical tool for addressing immunosuppressive and angiogenic barriers. Nanocarriers are engineered to deliver VEGF inhibitors, tyrosine kinase inhibitors (TKIs), and immune-modulatory agents selectively to the tumor milieu, enhancing therapeutic efficacy and minimizing systemic toxicity.Combination approaches, particularly integrating nanoparticles with **immune checkpoint inhibitors,** have demonstrated synergistic anti-tumor effects in preclinical models [27-28]. These strategies aim to modulate the TME, normalize vasculature, and activate anti-tumor immunity, providing a multifaceted approach to RCC therapy.Despite these promising results, **preclinical-to-clinical translation** faces challenges, including heterogeneity in patient response, nanoparticle biodistribution, and scalable manufacturing. Addressing these barriers is essential to move kidney cancer nanotheranostics from experimental platforms to standard-of-care therapies [29-30].

7. Brain Tumors

Brain tumors, particularly **glioblastoma (GBM),** remain among the most challenging cancers due to their aggressive nature and the presence of the **blood–brain barrier (BBB),** which restricts the delivery of therapeutic agents. Advanced nanotheranostic strategies have been developed to overcome this barrier, including **ligand-mediated transcytosis**, exosome-based carriers, and **ultrasound-assisted delivery** [31-32]**.** These approaches enhance CNS penetration while minimizing systemic exposure, thereby improving the therapeutic index. **Theranostic nanoparticles** integrate imaging and therapy, allowing real-time monitoring of tumor localization, drug release, and treatment response. RNA-based interventions, such as siRNA or mRNA therapeutics, have been delivered via nanoparticles to modulate oncogenic pathways or restore tumor suppressor activity. In parallel, **immuno-nanotherapies** aim to activate anti-tumor immune responses within the immunosuppressive brain microenvironment. Preclinical and early-phase clinical studies from 2019–2024 have evaluated these platforms for **safety, toxicity, and translational feasibility,** revealing promising biodistribution and efficacy profiles. However, challenges remain in ensuring long-term safety, optimizing dosing strategies, and translating preclinical findings into clinically effective treatments [33-34].

8. Translational and Regulatory Challenges

While nanotheranostics show significant promise, their **clinical translation** is influenced by multiple regulatory, manufacturing, and ethical considerations. **Biomarkers and companion diagnostics** are essential for patient stratification, enabling the selection of individuals most likely to benefit from specific nanotheranostic interventions. These diagnostics also provide critical real-time feedback on therapy efficacy. **Manufacturing scalability** is another major challenge. Achieving GMP/GLP-compliant production that ensures batch-to-batch reproducibility, functionalization consistency, and payload stability is complex, especially for multifunctional nanoparticles or exosome-based systems [35-36].Ethical and safety considerations further impact translation. Long-term toxicity, off-target effects, gene-editing safety, and **AI-driven decision biases** must be carefully evaluated to ensure patient safety and regulatory compliance. Addressing these barriers through robust preclinical validation, standardized protocols, and ethical oversight is essential to facilitate the clinical adoption of nanotheranostics [37].

9. Future Perspectives

The future of cancer management lies in the convergence of **AI-guided, adaptive, and multifunctional nanotheranostics** with comprehensive multi-omics insights. Machine learning algorithms will continue to optimize nanoparticle design in real time, predicting biodistribution, therapeutic efficacy, and off-target effects, while enabling dynamic adjustments based on patient-specific tumor profiles [38].

Omics-driven personalization will allow clinicians to tailor therapeutic payloads, targeting strategies, and release kinetics to the molecular characteristics of each patient's tumor. Integrated diagnostic functionalities within nanocarriers will provide **real-time therapy monitoring,** allowing early detection of resistance or adverse effects and facilitating immediate treatment adaptation [39]. Future clinical evaluation will leverage **adaptive trial designs,**

including basket, umbrella, and platform studies, to test nanotheranostic interventions efficiently across heterogeneous patient populations [40]. These designs, combined with robust biomarkers and AI-guided analytics, are expected to accelerate the translation of nanotheranostics from bench to bedside.

10. Conclusion

Over the period 2019–2024, **nanotheranostics** have demonstrated transformative potential in the management of liver, breast, kidney, and brain tumors. By integrating therapeutic and diagnostic functions, these platforms offer precise tumor targeting, RNA and immunomodulatory interventions, and real-time monitoring of treatment response. The synergistic incorporation of **AI and multi-omics technologies** has enabled patient-specific therapy personalization, optimized nanoparticle design, and adaptive clinical decision-making. Despite challenges in manufacturing, safety, ethical oversight, and regulatory approval, translational progress is evident in early-phase clinical studies and preclinical pipelines. Looking forward, the combination of AI-guided adaptive nanocarriers, omics-informed patient stratification, and next-generation clinical trial designs provides a clear roadmap for bringing nanotheranostics into routine oncology practice. These integrated strategies promise to improve outcomes across major solid tumors, marking a new era of precision cancer therapy.

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