

Nanotheranostics in Multi-Organ Oncology: A Systematic Review of Pharmacological Advances Integrating Omics and Artificial Intelligence

Shahaji Shivaji Chandanshive^{1*}

¹Department of Zoology, Shikshan Maharshi Gurusvaya R G Shinde Mahavidyalaya, Paranda District, Dharashiv, Maharashtra State, India, Pin. 413502

*Corresponding Author E-mail: chandanshive75@gmail.com

Abstract:

Background: Cancer continues to pose a major global health challenge, with liver, lung, pancreatic, breast, and brain tumors contributing substantially to morbidity and mortality. Conventional pharmacological approaches are limited by systemic toxicity, poor tumor specificity, and therapeutic resistance. **Objective:** This review systematically evaluates advances in nanotheranostics for multi-organ oncology between 2019 and 2025, emphasizing integration with omics technologies and AI-driven approaches. **Methods:** A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science. Studies reporting preclinical and clinical nanotheranostic interventions were included, with data extracted on nanoparticle platforms, therapeutic and diagnostic mechanisms, omics integration, and AI applications. **Results:** Across all organs, multifunctional nanoparticles enabled simultaneous imaging and targeted therapy, with enhanced tumor specificity and reduced systemic toxicity. Integration of multi-omics data and AI-guided analytics facilitated patient-specific targeting, predictive modeling of therapeutic response, and adaptive treatment strategies. Organ-specific challenges, including the blood-brain barrier, dense stromal matrices, and molecular heterogeneity, necessitate tailored nanotheranostic designs. Emerging approaches such as stimuli-responsive and bioinspired nanoparticles show promise for precision oncology. **Conclusion:** Nanotheranostics, when integrated with omics and AI technologies, represent a powerful paradigm shift in multi-organ cancer therapy, offering personalized, adaptive, and precise interventions. Overcoming translational barriers and optimizing clinical implementation will be to realizing their full therapeutic potential.

Key words: Nanotheranostics, Multi-organ oncology, Targeted drug delivery, Imaging-guided therapy, Multi-omics integration, Artificial intelligence, personalized cancer therapy, Stimuli-responsive nanoparticles, Bioinspired nanoplateforms, Precision oncology

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1. Introduction

Cancer remains one of the foremost challenges in global health, accounting for significant morbidity and mortality across multiple organ systems, including the liver, lung, pancreas, breast, and brain. Liver cancer, particularly hepatocellular carcinoma, is characterized by late detection, high recurrence rates, and limited responsiveness to conventional therapies. Lung cancer, dominated by non-small cell lung carcinoma, continues to be the leading cause of cancer-related deaths due to delayed diagnosis and therapeutic resistance ¹. Pancreatic cancer presents with dense stromal barriers and poor vascularization, which restrict drug delivery and compromise treatment efficacy. Breast cancer exhibits substantial molecular heterogeneity, including hormone receptor-positive, triple-negative, and HER2-positive subtypes, often limiting the effectiveness of standard chemotherapeutics. Brain tumors, notably glioblastoma, pose the additional challenge of the blood–brain barrier, which significantly restricts drug penetration and therapeutic concentrations in the tumor microenvironment. Collectively, these multi-organ challenges highlight the urgent need for advanced, precision-guided interventions in oncology ².

Conventional pharmacological approaches, while foundational in cancer management, suffer from systemic toxicity, poor tumor specificity, suboptimal pharmacokinetics, and the emergence of therapeutic resistance. These limitations often result in reduced efficacy and adverse patient outcomes, underscoring the necessity for innovative strategies that can simultaneously diagnose and treat malignancies with high precision ³.

Nanotheranostics has emerged as a transformative approach in this context, integrating diagnostic imaging with targeted therapy within a single nanoscale platform. By combining real-time imaging, tumor-targeted drug delivery, and multi-modal therapeutic functions, nanotheranostics has the potential to enhance treatment efficacy, minimize off-target effects, and provide dynamic feedback for adaptive therapy ⁴.

Recent advances further expand the capabilities of nanotheranostics through the integration of omics technologies including genomics, proteomics, and metabolomics which enable patient-specific profiling of tumor heterogeneity, predictive biomarker identification, and optimization of therapeutic regimens. Coupled with artificial intelligence (AI)-driven approaches, these systems can leverage large-scale multi-omics datasets to predict treatment outcomes, optimize nanoparticle design, and guide personalized therapy in a clinically actionable manner ⁵.

The primary objectives of this systematic review are to:

1. Evaluate recent preclinical and clinical advances in multi-organ nanotheranostics between 2019 and 2025.
2. Examine the integration of omics and AI technologies in enhancing the efficacy and precision of nanotheranostic interventions.

3. Identify organ-specific challenges and translational barriers that may influence clinical implementation.
4. Highlight emerging trends and propose directions for future research in precision oncology.

The scope of this review spans liver, lung, pancreatic, breast, and brain cancers, with a focus on studies that incorporate diagnostic–therapeutic nanoplateforms, multi-omics integration, and AI-assisted optimization. By synthesizing evidence across multiple organs, this work aims to provide a comprehensive overview of current capabilities, translational hurdles, and future prospects in nanotheranostic cancer pharmacology. (Figure 1)

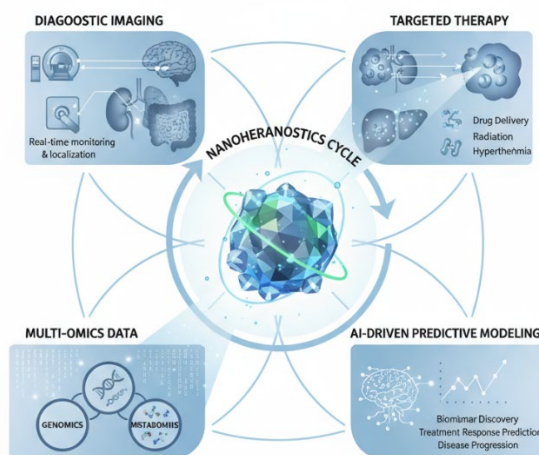


Figure 1: Conceptual framework of AI and omics-integrated nanotheranostics, illustrating the convergence of diagnostic imaging, targeted therapy, multi-omics data, and AI-driven predictive modeling in multi-organ oncology.

2. Methodology

This systematic review was conducted following the PRISMA 2020 guidelines, ensuring a rigorous, transparent, and reproducible approach to study selection and analysis. A comprehensive literature search was performed to identify studies published between January 2019 and June 2025, focusing on multi-organ nanotheranostic applications in liver, lung, pancreatic, breast, and brain cancers, with particular attention to omics and AI integration. Major databases including PubMed, Scopus, Web of Science, and Google Scholar were systematically searched using a combination of controlled vocabulary (MeSH terms) and free-text words such as nanotheranostics, cancer pharmacology, targeted drug delivery, diagnostic imaging, multi-omics, genomics, proteomics, metabolomics, *and* artificial intelligence. Boolean operators (AND, OR, NOT) were applied to refine the results, and filters were used to restrict studies to peer-reviewed, full-text articles in English. Both preclinical (in vitro and animal studies) and clinical studies were included, while review articles,

commentaries, conference abstracts, and studies not directly related to oncology or nanotheranostics were excluded.

Study selection was performed in two stages. First, titles and abstracts of all retrieved records were independently screened by two reviewers to exclude irrelevant or duplicate studies. Second, full-text articles of potentially eligible studies were assessed against predefined inclusion and exclusion criteria. Any disagreements were resolved through discussion or consultation with a third reviewer. The overall study selection process, including identification, screening, eligibility assessment, and final inclusion, is summarized.

Data from eligible studies were extracted using a standardized form capturing details such as authors, year, country, cancer type, nanotheranostic platform design, diagnostic and therapeutic modalities, integration of omics and AI approaches, study models (cell line, animal, or clinical trial), and reported outcomes. Extracted data were synthesized narratively to provide organ-specific insights, with quantitative summaries included where feasible to highlight therapeutic efficacy, imaging performance, and translational potential.

The methodological quality of included studies was evaluated using validated tools appropriate to study design. The SYRCLE risk-of-bias tool was applied to preclinical studies, the Newcastle Ottawa Scale (NOS) was used for clinical studies, and AI-based studies were assessed based on dataset quality, model validation, and reproducibility. Only studies meeting acceptable quality thresholds were included in the final synthesis to ensure robust and reliable conclusions.

3. Nanotheranostics in Liver Cancer

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality globally, primarily due to late-stage diagnosis, high recurrence rates, and the limited effectiveness of conventional therapies. To overcome these challenges, nanotheranostic platforms have emerged as a versatile solution, integrating targeted therapy and diagnostic imaging within a single nanostructure ⁶. Common platforms include lipid-based nanoparticles, polymeric micelles, inorganic nanoparticles (gold, iron oxide, silica), and bioinspired hybrid carriers. These systems are engineered to enhance drug solubility, prolong systemic circulation, and achieve tumor-specific accumulation, while simultaneously incorporating imaging agents for real-time monitoring of drug delivery and therapeutic response. Dual-function systems, combining chemotherapeutic payloads with MRI or near-infrared fluorophores, and stimuli-responsive carriers activated by pH, enzymatic activity, or external triggers, exemplify the multifunctional potential of liver nanotheranostics ⁷.

The integration of omics technologies has added a new dimension to precision nanotherapy. Genomic, transcriptomic, and proteomic analyses facilitate identification of tumor-specific biomarkers and heterogeneity, which guide nanoparticle functionalization with ligands such as

glypican-3 antibodies, galactose derivatives, or transferrin for patient-specific targeting. By tailoring nanocarriers to the molecular profile of each tumor, these approaches enhance therapeutic efficacy while minimizing off-target toxicity. Additionally, artificial intelligence (AI) has been applied to predict therapeutic outcomes, optimize nanoparticle design, and model drug–tumor interactions, enabling adaptive, personalized treatment strategies and informed decision-making ⁸.

From 2019 to 2025, preclinical and clinical studies have highlighted the potential of these integrated approaches. Preclinical data show that multifunctional nanoparticles can achieve 3–5-fold higher intratumoral drug accumulation compared to conventional formulations, reducing systemic toxicity. For example, gold nanorods loaded with sorafenib and functionalized with targeting ligands demonstrated enhanced tumor regression in murine HCC models, particularly under near-infrared irradiation ⁹. Early-phase clinical trials of liposomal and polymeric nanocarriers incorporating imaging agents have reported improved safety, prolonged progression-free survival, and the ability to monitor treatment response in real time.

Despite these advancements, translational challenges persist. Tumor heterogeneity, variability in vascularization, potential hepatotoxicity, immunogenic responses, and off-target nanoparticle accumulation complicate clinical translation. Furthermore, dual diagnostic–therapeutic platforms face regulatory complexities, while large-scale manufacturing, reproducibility, and cost-effectiveness remain hurdles ¹⁰. Future efforts should focus on optimizing bioinspired designs, incorporating multi-omics data for personalized therapy, and leveraging AI-driven predictive modeling to facilitate the clinical implementation of liver cancer nanotheranostics ¹¹. (Figure 2)

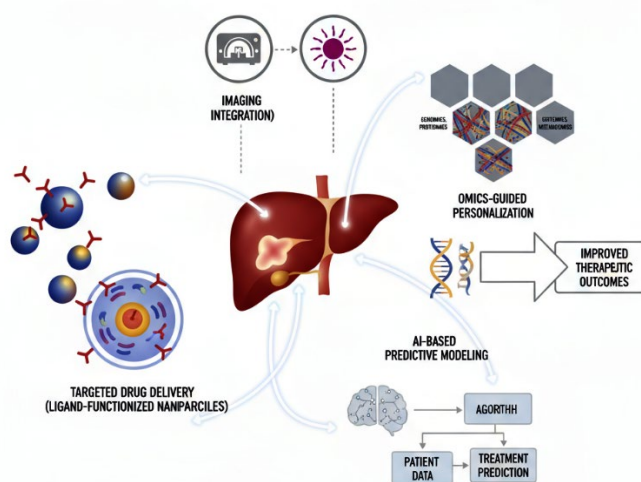


Figure 2: Conceptual schematic of liver cancer nanotheranostic strategies integrating targeted drug delivery, imaging, omics-guided personalization, and AI-based predictive modeling.

4. Nanotheranostics in Lung Cancer

Lung cancer, particularly non-small cell lung carcinoma (NSCLC), remains the leading cause of cancer-related deaths worldwide, largely due to late diagnosis, high metastatic potential, and the emergence of therapeutic resistance. Recent advances in nano-imaging and drug delivery systems have offered promising solutions to these challenges ¹². Lipid-based nanoparticles, dendrimers, mesoporous silica, and metallic nanostructures have been engineered to target overexpressed receptors such as EGFR and PD-L1, allowing for precise drug delivery while simultaneously integrating imaging modalities including MRI, PET, and near-infrared fluorescence. These multifunctional nanoplatforms enable real-time visualization of drug biodistribution and therapeutic response, enhancing the efficiency and safety of treatment strategies ¹³(Figure 3).

Synergistic strategies have emerged by combining nanotheranostics with immunotherapy, where nanoparticles co-deliver chemotherapeutics or siRNAs along with immune checkpoint inhibitors, such as anti-PD-1/PD-L1 antibodies. These approaches not only enhance tumor immunogenicity but also counteract resistance mechanisms. AI-guided predictive modeling further refines treatment by analyzing patient-specific tumor characteristics, predicting drug response, and optimizing nanocarrier design to maximize therapeutic outcomes ¹⁴.

The integration of omics-driven precision targeting adds another layer of sophistication. Genomic, proteomic, and metabolomic profiling of lung tumors guides the selection of molecular targets for nanoparticle functionalization, improving the specificity of therapy and reducing off-target effects. Personalized nanocarriers, informed by patient-specific omics data, have demonstrated improved tumor penetration and enhanced therapeutic efficacy in preclinical and early clinical studies ¹⁵.

From 2019 to 2025, preclinical and clinical findings highlight the translational potential of these strategies. Early-phase trials of liposomal doxorubicin, polymeric micelle-based paclitaxel, and other nanotherapeutics incorporating imaging components have shown improved pharmacokinetics, reduced systemic toxicity, and enhanced monitoring of drug accumulation. Nanotheranostic constructs combined with AI-guided treatment planning have also demonstrated promising outcomes in modeling and predicting patient responses ¹⁶.

Despite these advances, safety, toxicity, and resistance remain significant concerns. Nanoparticles may accumulate in the liver, spleen, or lungs, causing off-target effects, oxidative stress, or immunogenic responses. Adaptive tumor resistance driven by genetic heterogeneity continues to challenge long-term efficacy, and combining nanotheranostics with immunotherapy introduces additional immune-related adverse events ¹⁷. Future research should focus on optimizing biocompatibility, refining AI- and omics-guided patient stratification, and developing scalable, cost-effective nanotheranostic platforms for clinical application.

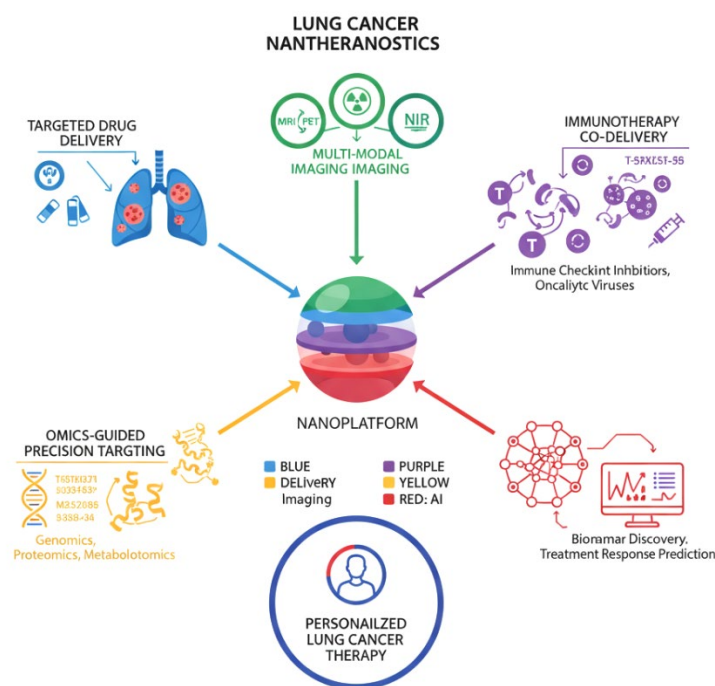


Figure 3: Lung cancer nanotheranostic platforms integrating targeted drug delivery, multi-modal imaging, immunotherapy, omics-guided precision targeting, and AI-driven predictive modeling.

5. Nanotheranostics in Pancreatic Cancer

Pancreatic cancer, particularly pancreatic ductal adenocarcinoma (PDAC), is one of the most aggressive malignancies, characterized by late-stage detection, poor prognosis, and profound chemoresistance. Traditional therapies, including gemcitabine and nab-paclitaxel, are often hindered by the dense stromal matrix and hypovascular tumor microenvironment, which limit drug penetration¹⁸. To address these challenges, nano-enabled strategies have been developed to improve drug delivery, enhance tumor specificity, and overcome chemoresistance. Liposomal, polymeric, dendrimer-based, and exosome-mimetic nanoparticles have been engineered to encapsulate chemotherapeutics, siRNAs, or gene-editing agents, enabling multimodal therapy while minimizing off-target toxicity¹⁹.

Imaging-guided drug release and AI-assisted therapeutic planning further enhance precision in pancreatic cancer treatment. Nanocarriers incorporating MRI or near-infrared probes allow real-time visualization of drug localization, tumor penetration, and therapeutic response. AI-driven models optimize nanoparticle design, predict patient-specific drug responses, and guide adaptive treatment strategies, maximizing efficacy while reducing adverse effects²⁰.

Combination strategies have also been explored extensively. Photothermal and photodynamic nanoplateforms, often gold- or carbon-based, induce localized hyperthermia to weaken tumor

stroma and improve chemotherapeutic uptake. Gene therapy via siRNA, microRNA, or CRISPR/Cas9-loaded nanocarriers allows modulation of oncogenic pathways such as KRAS, while immuno-nanotheranostics integrate immune checkpoint inhibitors or tumor antigen delivery with nanoplateforms to enhance antitumor immunity²¹. These approaches reflect a shift toward multi-pronged, personalized interventions that tackle PDAC's intrinsic resistance mechanisms.

The integration of omics technologies enables patient-specific tailoring of nanotheranostics. Genomic, transcriptomic, and proteomic profiling identifies molecular signatures and biomarkers that guide the selection of therapeutic targets, nanoparticle functionalization, and drug combinations, facilitating personalized therapy²².

Between 2019 and 2025, notable breakthroughs include nanoparticle-mediated co-delivery of gemcitabine and photothermal agents achieving synergistic tumor regression in preclinical PDAC models, and early-phase clinical trials demonstrating improved imaging-guided monitoring and tolerability of liposomal irinotecan (nal-IRI). Despite these advances, translational hurdles remain, including poor nanoparticle penetration due to stromal barriers, systemic toxicity, regulatory complexities, and manufacturing scalability²³. Future directions focus on refining omics- and AI-integrated nanoplateforms, optimizing combination therapies, and advancing translational pipelines to accelerate clinical adoption of pancreatic cancer nanotheranostics. (Figure 4)

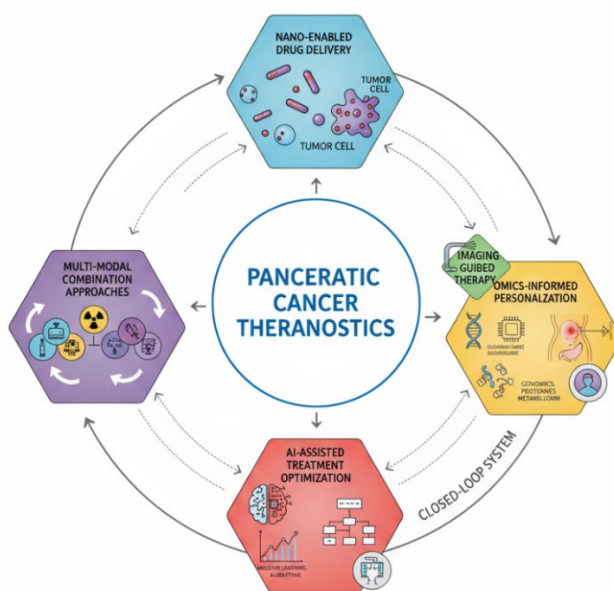


Figure 4: Pancreatic cancer theranostic models integrating nano-enabled drug delivery, imaging-guided therapy, omics-informed personalization, AI-assisted treatment optimization, and multi-modal combination strategies.

6. Nanotheranostics in Breast Cancer

Breast cancer remains the most frequently diagnosed malignancy among women worldwide, with a highly heterogeneous profile encompassing hormone receptor–positive, HER2-positive, and triple-negative breast cancer (TNBC) subtypes. Conventional therapies, including chemotherapy, endocrine therapy, and HER2-targeted treatments, are often limited by systemic toxicity, tumor heterogeneity, and acquired resistance. In this context, nanotheranostics have emerged as a versatile platform integrating advanced diagnostics with targeted therapy, enabling precision oncology approaches²⁴. Nano-biomarkers and targeted imaging systems have been developed to detect circulating tumor cells (CTCs), exosomes, and receptor-specific signatures. Nanoparticles conjugated with MRI contrast agents, fluorescent dyes, or radionuclides allow early detection, real-time monitoring of drug delivery, and evaluation of therapeutic response. HER2-targeted nanotheranostics utilize antibody- or aptamer-functionalized nanoparticles to deliver chemotherapeutics or siRNAs selectively to HER2-overexpressing cells, enabling simultaneous imaging and treatment²⁵. For TNBC, multifunctional nanoparticles co-loaded with chemotherapeutic agents and gene modulators address the challenge of limited targeted therapy options. Drug resistance modulation is further enhanced through omics-guided strategies, where genomic, transcriptomic, and proteomic analyses inform nanoparticle design and therapeutic combinations to circumvent efflux pumps, hypoxic microenvironments, or oncogenic signaling pathways. AI-assisted tools provide patient stratification, predictive modeling, and real-time therapeutic monitoring, facilitating adaptive treatment adjustments tailored to tumor subtype and molecular profile. From 2019 to 2025, and preclinical and early clinical studies demonstrate the efficacy of these approaches. For instance, polymeric nanoparticles co-delivering paclitaxel and siRNAs in TNBC models show significant tumor regression and resensitization to chemotherapy, while HER2-targeted liposomal formulations combined with imaging agents improve therapeutic precision and reduce systemic toxicity²⁶. Clinically, nanotheranostic interventions have improved patient-centered outcomes, including reduced adverse events, enhanced monitoring, and improved progression-free survival. Despite these advances, challenges such as manufacturing standardization, regulatory approval, and long-term safety remain barriers to widespread adoption. Future research should focus on integrating multi-omics and AI-driven analytics to refine personalized nanotheranostics, optimize drug resistance modulation, and improve translational efficiency in breast cancer care³⁰.

7. Nanotheranostics in Brain Tumors

Brain tumors, particularly glioblastoma multiforme (GBM), remain among the most lethal cancers due to aggressive growth, diffuse infiltration, and the restrictive blood–brain barrier (BBB). Conventional pharmacological approaches often fail to achieve therapeutic concentrations within the tumor, necessitating advanced delivery strategies. Nanotheranostic platforms have emerged to overcome these limitations, utilizing lipid-based nanoparticles, polymeric nanocarriers, dendrimers, and exosome-mimetic vesicles functionalized with BBB-

penetrating ligands such as transferrin, angiopep-2, or low-density lipoprotein receptor-related peptides³¹. These multifunctional nanosystems enable targeted drug delivery while minimizing systemic toxicity and off-target accumulation. Multi-functional nanoparticles integrate chemotherapeutic payloads, gene modulators (siRNA or CRISPR/Cas9), and photothermal or photodynamic therapy components, creating platforms that combine diagnostics and therapy within a single intervention. Imaging-guided strategies leveraging MRI, PET, or near-infrared fluorescent probes provide real-time visualization of tumor localization, drug distribution, and therapeutic efficacy, which is critical for precise targeting in the complex brain microenvironment. Integration of omics data (genomic, transcriptomic, and proteomic profiles) informs patient-specific targeting and therapeutic combinations, enhancing treatment personalization³².

AI-driven prediction models complement these strategies by forecasting nanoparticle penetration across the BBB, estimating tumor-specific drug accumulation, and optimizing therapeutic regimens to maximize efficacy while minimizing adverse effects. These approaches facilitate adaptive, precision-guided treatment planning, particularly for heterogeneous tumors like GBM.

Despite these promising advances, significant translational and safety challenges remain. Variability in BBB permeability, tumor vascularization, and microenvironment heterogeneity affects nanoparticle distribution and efficacy. Potential neurotoxicity, immunogenic responses, and off-target accumulation in critical brain regions require careful evaluation. Additionally, the synthesis of multifunctional nanoplateforms poses hurdles for large-scale production, regulatory approval, and clinical standardization. Future research should focus on enhancing BBB-targeting efficiency, improving biocompatibility, integrating multi-omics with AI analytics, and developing scalable manufacturing approaches to accelerate the clinical translation of brain tumor nanotheranostics³³.

.8. Comparative Multi-Organ Insights

The systematic evaluation of nanotheranostic applications across liver, lung, pancreatic, breast, and brain tumors highlights both shared strategies and organ-specific nuances that influence therapeutic efficacy and translational potential. Across all tumor types, core similarities include the use of multifunctional nanoparticles capable of simultaneous drug delivery and imaging, surface functionalization with tumor-targeting ligands, and incorporation of stimuli-responsive mechanisms for controlled release. These shared features underscore a common pharmacological framework that enhances tumor specificity, reduces systemic toxicity, and allows real-time monitoring of treatment response³⁴.

Despite these overarching similarities, each organ presents distinct pharmacological barriers. In liver cancer, heterogeneous vascularization and metabolic activity affect nanoparticle clearance and therapeutic accumulation. Lung tumors are influenced by dynamic pulmonary

physiology and immune-mediated clearance of inhaled nanocarriers. Pancreatic tumors face dense stromal matrices and poor vascularization, limiting nanoparticle penetration. Breast cancer heterogeneity, particularly in HER2-positive and TNBC subtypes, requires subtype-specific targeting strategies. Brain tumors are uniquely constrained by the blood–brain barrier, demanding specialized BBB-penetrating ligands and delivery systems³⁵. Understanding these organ-specific challenges is critical for designing precision-targeted nanotheranostic interventions. Lessons learned for AI- and omics-driven precision oncology emerge from cross-organ comparisons. First, multifunctional platforms must be tailored to tumor microenvironments to optimize accumulation, retention, and efficacy. Second, real-time imaging is essential not only for monitoring therapeutic response but also for dynamically adjusting treatment in patient-specific contexts. Third, combining nanotheranostics with immunomodulatory, gene-targeting, or AI-guided strategies enhances treatment efficacy across multiple tumor types. Finally, comparative assessment of safety, pharmacokinetics, and resistance mechanisms informs rational nanoplatform design, promoting more efficient clinical translation³⁶.

9. Future Directions

The field of nanotheranostics is poised for transformative advancements, driven by next-generation nanosystems that integrate stimuli-responsive, AI-guided, and bioinspired designs. Stimuli-responsive nanoparticles, activated by pH, temperature, enzymes, or external triggers such as light or ultrasound, enable precise spatiotemporal drug release, minimizing systemic toxicity while maximizing tumor-specific effect³⁷s. Bioinspired designs, mimicking natural vesicles, exosomes, or cellular membranes, enhance biocompatibility, immune evasion, and targeted delivery, offering promising routes toward clinical applicability.

The integration of multi-omics data (genomics, transcriptomics, proteomics, metabolomics) with AI-driven analytics represents a major frontier in precision oncology. By mapping tumor heterogeneity at multiple molecular levels, nanotheranostic platforms can be customized to individual patient profiles, allowing simultaneous diagnosis, targeted therapy, and real-time monitoring of treatment response. AI models facilitate predictive simulations, therapy optimization, and adaptive treatment planning, accelerating personalized interventions across diverse organ-specific cancers³⁸.

Despite technological advancements, significant regulatory, ethical, and commercialization challenges remain. Dual-function nanosystems face complex regulatory pathways due to their combined diagnostic and therapeutic roles. Ethical considerations include patient data privacy, equitable access, and long-term safety monitoring, while commercialization is hindered by high manufacturing costs, reproducibility issues, and the need for scalable production methods³⁹.

To accelerate clinical translation, a strategic roadmap is essential. steps include standardizing nanoparticle characterization, developing robust preclinical models that recapitulate human

tumor microenvironments, conducting adaptive early-phase clinical trials with integrated imaging and biomarker endpoints, and fostering cross-disciplinary collaboration among nanotechnology, oncology, AI, and computational biology experts. By following this roadmap, nanotheranostics can progress from experimental research to routine clinical application, ultimately enabling safer, more effective, and personalized cancer therapy ⁴⁰.

10. Conclusion

This systematic review highlights the transformative potential of nanotheranostics in multi-organ oncology, encompassing liver, lung, pancreatic, breast, and brain tumors. By integrating diagnostic imaging, targeted drug delivery, multi-omics profiling, and AI-guided analytics, nanotheranostic platforms offer unprecedented opportunities for personalized, precise, and adaptive cancer therapy. Across organ systems, multifunctional nanoparticles demonstrate enhanced tumor specificity, reduced systemic toxicity, and the capacity for real-time monitoring of therapeutic response.

However, organ-specific barriers—such as the blood–brain barrier in brain tumors, dense stromal matrices in pancreatic cancer, and molecular heterogeneity in breast cancer—highlight the need for tailored strategies. Translational challenges including safety, regulatory pathways, manufacturing scalability, and clinical validation remain critical hurdles. Looking forward, the convergence of stimuli-responsive nanosystems, bioinspired designs, multi-omics integration, and AI-driven predictive modeling is expected to redefine cancer pharmacology, advancing nanotheranostics from experimental research toward clinical reality and precision oncology implementation.

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