

# Systematic Review of Nanotheranostics in Cancer Pharmacology: Multi-Organ Insights from Liver to Brain Tumors

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## Abstract:

Cancer remains a leading cause of global morbidity and mortality, with liver, lung, pancreatic, breast, and brain tumors posing significant therapeutic challenges. Conventional pharmacological approaches are limited by systemic toxicity, poor tumor specificity, and therapeutic resistance. **Nanotheranostics**, integrating diagnostic imaging and targeted therapy within a single platform, offers a promising solution to these limitations. This systematic review (2019–2024) synthesizes recent preclinical and clinical advances in organ-specific nanotheranostic systems, highlighting mechanisms of targeted drug delivery, imaging-guided therapy, and multifunctional nanoparticles. Comparative analysis reveals shared strategies such as ligand-functionalization and stimuli-responsive drug release, alongside organ-specific barriers including the blood–brain barrier, dense stromal matrices, and molecular heterogeneity. Emerging trends emphasize AI-integrated, bioinspired, and multi-omics-enabled nanosystems, paving the way for personalized oncology. Despite regulatory, safety, and manufacturing challenges, nanotheranostics represents a paradigm shift toward precise, safer, and more effective cancer therapies.

**Keywords:** Nanotheranostics; Cancer Pharmacology; Liver Cancer; Lung Cancer; Pancreatic Cancer; Breast Cancer; Brain Tumors; Targeted Drug Delivery; Imaging-Guided Therapy; Precision Oncology

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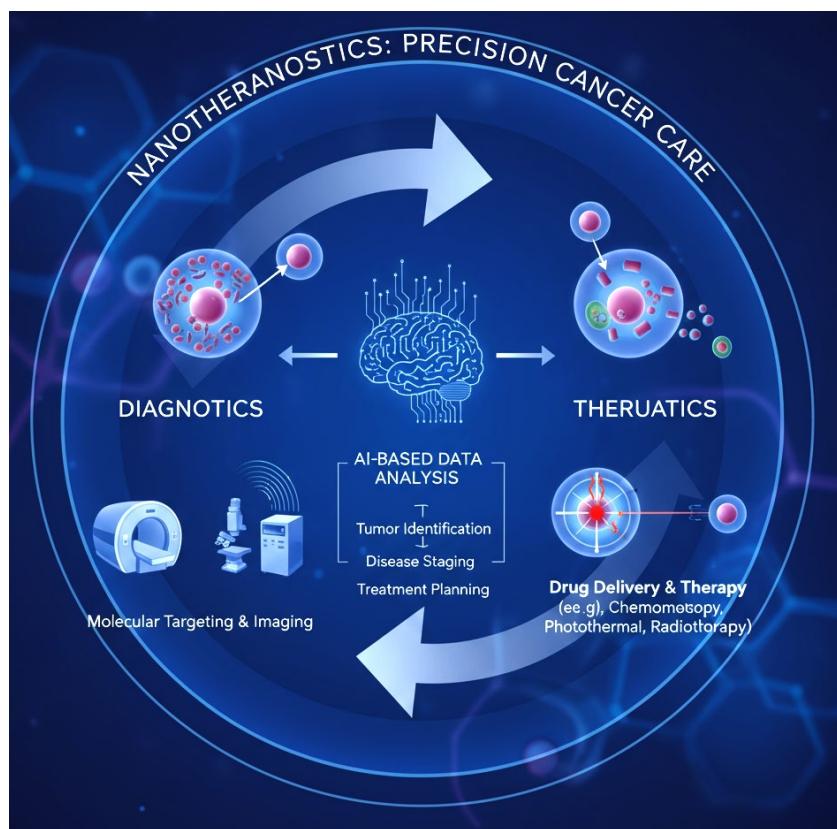
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## 1. Introduction

Cancer continues to represent one of the most formidable challenges in global health, with liver, lung, pancreatic, breast, and brain tumors accounting for a substantial proportion of

mortality and morbidity. Conventional pharmacological strategies, while foundational in oncology, are hindered by systemic toxicity, poor tumor specificity, limited penetration into tumor microenvironments, and the emergence of therapeutic resistance. These limitations have prompted the exploration of advanced, multifunctional approaches such as nanotheranostics a paradigm that integrates diagnostic imaging and targeted therapy into a single nanoparticle. (Figure 1) Nanotheranostics offers the potential to improve early detection, enable real-time monitoring of therapeutic response, and enhance drug delivery precision, thereby addressing many shortcomings of traditional cancer pharmacology <sup>1-2</sup>.

This systematic review synthesizes the progress in nanotheranostic applications across major organ-specific cancers between 2019 and 2024, with a particular emphasis on liver, lung, pancreatic, breast, and brain tumors. By collating recent preclinical and clinical evidence, the review aims to evaluate how nanotheranostic systems are reshaping cancer pharmacology and identify both the translational opportunities and persistent barriers to clinical implementation <sup>3</sup>. The core research questions guiding this review are: How effective have nanotheranostic systems been in advancing organ-specific cancer therapy? What unique pharmacological challenges exist across different tumor types? And what emerging trends suggest pathways for future breakthroughs in precision oncology?



**Figure 1:** illustrates the conceptual framework of nanotheranostics in oncology, highlighting the dual diagnostic-therapeutic cycle,

## 2 Methodology of the Systematic Review

The present systematic review was conducted in alignment with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, ensuring transparency and reproducibility in study selection and analysis. A comprehensive literature search strategy was designed to capture publications from January 2019 to June 2024, focusing on nanotheranostic applications in five major cancer types: liver, lung, pancreatic, breast, and brain tumors. Major databases including PubMed, Scopus, Web of Science, and Google Scholar were systematically searched using combinations of controlled vocabulary (MeSH terms) and free-text words such as nanotheranostics, cancer pharmacology, liver cancer, lung cancer, pancreatic cancer, breast cancer, brain tumor, drug delivery, and diagnostic imaging. Boolean operators (AND, OR, NOT) and filters (human, animal, English language, and peer-reviewed full-text articles) were applied to refine the search.

Study selection and screening were conducted in two stages: first, titles and abstracts were screened independently by two reviewers to exclude irrelevant or duplicate records; second, full texts of potentially eligible studies were assessed against predefined inclusion and exclusion criteria. Only studies that reported either preclinical or clinical evidence of nanotheranostic interventions in the specified cancer types were included. Reviews, commentaries, conference abstracts, and studies unrelated to oncology were excluded. The overall process of identification, screening, eligibility assessment, and inclusion is depicted.

Data extraction and synthesis were carried out using a standardized form capturing study characteristics (authors, year, country), cancer type, nanotheranostic platform, therapeutic/diagnostic modality, study model (cell line, animal, or clinical), and reported outcomes. Extracted data were synthesized narratively, and where feasible, comparative insights across different cancer types were generated.

Quality assessment of the included studies was performed using validated tools appropriate to study design: the SYRCLE risk-of-bias tool for animal studies and the Newcastle–Ottawa Scale (NOS) for clinical studies. This evaluation ensured that only robust and methodologically sound evidence informed the review's conclusions.

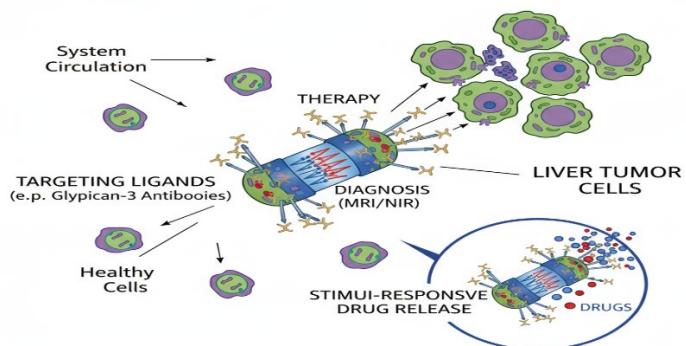
## 3. Nanotheranostics in Liver Cancer

Hepatocellular carcinoma (HCC) remains one of the deadliest malignancies worldwide, largely due to late diagnosis, high recurrence rates, and limited efficacy of conventional pharmacological regimens. In recent years, emerging nano-platforms have been engineered to overcome these barriers, offering dual diagnostic and therapeutic functions within a single construct. Notable advances include lipid-based nanoparticles, polymeric micelles, inorganic nanosystems (e.g., gold, iron oxide, silica), and hybrid bioinspired nanocarriers, all designed to enhance drug solubility, prolong circulation, and preferentially accumulate within hepatic

tumors <sup>4</sup>. Many of these nano-formulations also incorporate imaging agents, enabling simultaneous monitoring of drug delivery and therapeutic response.

The mechanisms of action underpinning these liver-specific nanotheranostics revolve around tumor-targeted drug delivery, real-time imaging, and stimuli-responsive drug release. Nanocarriers functionalized with ligands such as glypican-3 antibodies, galactose derivatives, or transferrin exploit the overexpression of specific receptors on HCC cells to achieve precise targeting. Dual-function systems often combine chemotherapeutic payloads (e.g., doxorubicin, sorafenib) with imaging moieties such as MRI contrast agents or near-infrared fluorophores, creating platforms that both visualize and treat tumors. Advanced designs have also integrated photothermal or photodynamic elements, amplifying cytotoxic effects while sparing surrounding healthy tissue <sup>5-6</sup>.

Findings between 2019 and 2024 highlight significant strides in both preclinical and early clinical research. Preclinical studies have demonstrated that multifunctional nanoparticles can enhance intratumoral accumulation up to 3–5 times compared to free drugs, while reducing systemic toxicity. For example, gold nanorods conjugated with sorafenib exhibited superior tumor regression in murine HCC models under near-infrared irradiation. Clinically, early-phase trials of liposomal and polymeric nanocarriers in liver cancer patients have reported improved safety profiles and prolonged progression-free survival, though large-scale validation remains pending <sup>7</sup>. Despite these advances, several limitations and translational challenges persist. The heterogeneity of the liver tumor microenvironment including variable vascularization and hypoxia can compromise nanoparticle accumulation and therapeutic efficacy. Potential hepatotoxicity, immunogenic responses, and off-target accumulation remain significant safety concerns. Furthermore, the regulatory pathway for clinical approval of nanotheranostic systems is complex, given their dual diagnostic–therapeutic functions. Manufacturing scalability, reproducibility, and cost-effectiveness also hinder clinical translation <sup>8-9</sup>. To overcome these barriers, future research must focus on optimizing bioinspired designs, refining patient-specific targeting strategies, and integrating multi-omics data to personalize nanotheranostic interventions in liver cancer. (Figure 2).



**Figure 2:** Schematic representation of nanotheranostic mechanisms in liver cancer.

#### 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 detection and resistance to standard chemotherapy and targeted therapies. In recent years, advances in nano-imaging and drug delivery systems have provided powerful tools to address these shortcomings. Lipid-based nanoparticles, dendrimers, mesoporous silica, and metallic nanostructures have been functionalized with ligands targeting overexpressed receptors such as EGFR and PD-L1<sup>10</sup>. These nanoplatforms not only deliver chemotherapeutics like paclitaxel or cisplatin more selectively to tumor tissues but also integrate imaging modalities including MRI, PET, and near-infrared fluorescence, enabling real-time visualization of drug biodistribution and treatment response<sup>11</sup>.

A particularly promising development has been the emergence of synergistic strategies combining immunotherapy with nanotheranostics. Nanoparticles have been used to co-deliver immune checkpoint inhibitors (e.g., anti-PD-1/PD-L1 antibodies) alongside chemotherapeutics or siRNAs, enhancing tumor immunogenicity while simultaneously suppressing resistance pathways. Additionally, nanotheranostic constructs incorporating photothermal or photodynamic therapy have been shown to remodel the tumor microenvironment, thereby improving T-cell infiltration and amplifying immunotherapy efficacy. These multi-modal strategies represent a step toward overcoming the immunosuppressive landscape that characterizes lung tumors<sup>12</sup>.

Between 2019 and 2024, several clinical trial updates have underscored the translational potential of nanotheranostics in lung cancer. For example, early-phase studies of liposomal doxorubicin and polymeric micelle-based paclitaxel formulations demonstrated improved therapeutic indices and reduced cardiotoxicity compared to conventional delivery methods. Trials integrating diagnostic components, such as nanoparticles tagged with PET tracers, have shown promise for monitoring drug accumulation and predicting patient outcomes. However, large-scale phase III trials remain limited, and most evidence to date comes from small cohorts or preclinical models<sup>13</sup>.

Despite encouraging progress, safety, toxicity, and resistance issues remain hurdles. Nanoparticles can trigger off-target effects, oxidative stress, and long-term accumulation in reticuloendothelial organs such as the liver and spleen. Concerns also arise around immune-related adverse events when nanotheranostics are combined with checkpoint inhibitors. Moreover, the adaptive resistance of lung tumors driven by genetic heterogeneity and dynamic microenvironmental factors continues to limit the long-term efficacy of nanoparticle-based therapies<sup>14</sup>. Future directions must focus on refining nanoparticle biocompatibility, integrating precision biomarkers for patient stratification, and developing scalable, cost-effective systems that can progress smoothly into routine clinical oncology.

## 5. Nanotheranostics in Pancreatic Cancer

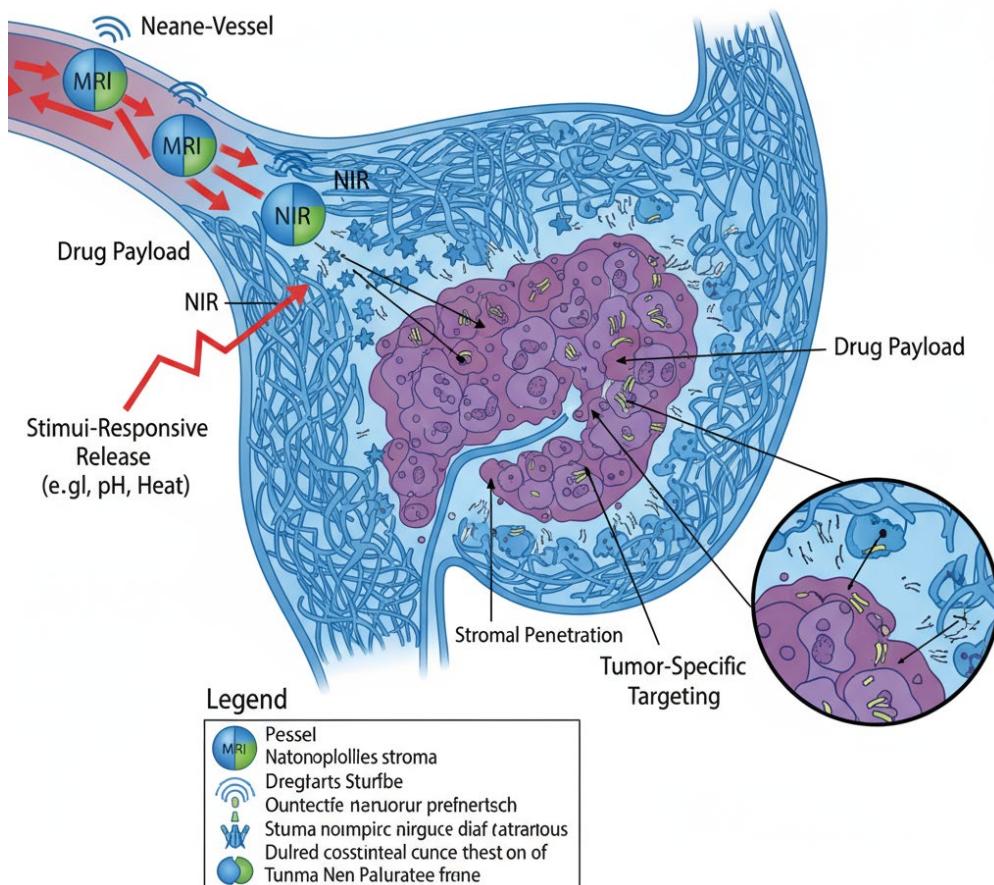
Pancreatic cancer, especially pancreatic ductal adenocarcinoma (PDAC), is among the most aggressive malignancies, characterized by late presentation, poor prognosis, and high resistance to conventional chemotherapy. Standard drugs such as gemcitabine and nab-paclitaxel often face barriers from the dense stromal matrix and hypovascular tumor microenvironment, which restrict drug penetration<sup>15</sup>. In response, nano-enabled drug delivery systems have emerged as a powerful strategy to overcome chemoresistance. Liposomal, polymeric, and exosome-mimetic nanoparticles have been engineered to improve drug bioavailability, enhance tumor penetration, and bypass multidrug resistance mechanisms. Importantly, many of these platforms encapsulate multiple agents, such as gemcitabine plus siRNA, providing combinatorial action at both genetic and pharmacological levels<sup>16</sup>.

Imaging-guided drug release and theranostic models have further transformed the treatment paradigm for pancreatic cancer. Smart nanocarriers incorporating MRI or near-infrared probes enable real-time visualization of drug delivery and tumor localization, ensuring more precise dosing and reducing systemic toxicity<sup>17</sup>. Stimuli-responsive nanoparticles activated by pH, enzymatic activity, or external triggers like ultrasound have been applied to pancreatic models, allowing on-demand drug release within the tumor site. Such systems exemplify the theranostic approach, merging diagnostics with therapy in a single intervention. Figure 3 conceptually depicts these imaging-guided, dual-functional nanosystems in pancreatic cancer<sup>18</sup>.

Recent research has also focused on combination strategies to amplify therapeutic efficacy. Photothermal nanoplatforms, often gold- or carbon-based, have been combined with chemotherapeutics to induce localized hyperthermia, weakening tumor stroma and improving drug uptake. Gene therapy approaches using nanocarriers to deliver KRAS-targeted siRNAs or microRNAs have shown potential in reprogramming tumor biology. Additionally, immuno-nanotheranostics leveraging nanoparticles to deliver tumor antigens or checkpoint inhibitors have demonstrated enhanced antitumor immunity in preclinical PDAC models. These integrative strategies reflect a shift toward multi-pronged approaches capable of tackling the disease's multifaceted resistance mechanisms.

Breakthroughs reported between 2019 and 2024 highlight the translational potential of nanotheranostics in pancreatic cancer. Preclinical studies show that nanoparticle-mediated co-delivery of gemcitabine and photothermal agents results in synergistic tumor regression and extended survival in murine PDAC models. Early-phase clinical evaluations of liposomal irinotecan (nal-IRI) combined with imaging components indicate improved therapeutic monitoring and tolerability. Meanwhile, CRISPR/Cas9-loaded nanocarriers represent a frontier direction, offering gene-editing capabilities alongside real-time imaging to track therapeutic progress<sup>19</sup>.

Despite these advancements, challenges remain in translating nanotheranostic platforms to the clinic. Pancreatic tumors' dense fibrotic stroma and immunosuppressive microenvironment still limit nanoparticle distribution, while issues of systemic toxicity, regulatory hurdles, and production scalability persist. Nonetheless, the integration of imaging, gene modulation, and immune activation into nanotheranostic systems offers unprecedented opportunities for precision pharmacology in pancreatic cancer<sup>20</sup>.



**Figure 3:** Schematic of imaging-guided nanotheranostic drug delivery systems in pancreatic cancer.

## 6. Nanotheranostics in Breast Cancer

Breast cancer remains the most frequently diagnosed cancer in women worldwide and is highly heterogeneous, encompassing hormone receptor-positive, triple-negative, and HER2-positive subtypes. Traditional treatment strategies chemotherapy, endocrine therapy, and HER2-targeted drugs are often limited by toxicity, late-stage detection, and the rapid onset of therapeutic resistance<sup>21</sup>. Against this backdrop, nanotheranostics have emerged as a versatile platform that integrates advanced diagnostics with targeted therapy, providing a precision medicine approach tailored to breast cancer's molecular complexity<sup>22</sup>.

One advance lies in the development of nano-biomarkers and targeted imaging platforms. Nanoparticles conjugated with fluorescent dyes, MRI contrast agents, or radionuclides have been designed to identify circulating tumor cells (CTCs), exosomes, and molecular signatures such as estrogen receptor (ER) expression. These nano-enabled diagnostics allow for early disease detection and noninvasive monitoring of therapeutic response. For instance, iron oxide nanoparticles functionalized with folate ligands have demonstrated enhanced imaging of ER-positive tumors while simultaneously serving as drug carriers, thereby bridging diagnosis with therapy<sup>23</sup>.

HER2-targeted nanotheranostics represent a particularly promising frontier. HER2-positive breast cancers, although responsive to trastuzumab and pertuzumab, frequently develop resistance. To address this, nanosystems functionalized with HER2 antibodies or aptamers have been designed to deliver both chemotherapeutics and siRNAs directly to HER2-overexpressing tumor cells. Multifunctional liposomes and polymeric nanoparticles have shown significant potential in preclinical studies, enabling simultaneous HER2-targeted imaging via PET or MRI and therapeutic delivery of agents such as doxorubicin or paclitaxel. Figure 4 illustrates the mechanism of HER2-targeted nanotheranostics in breast cancer<sup>24</sup>.

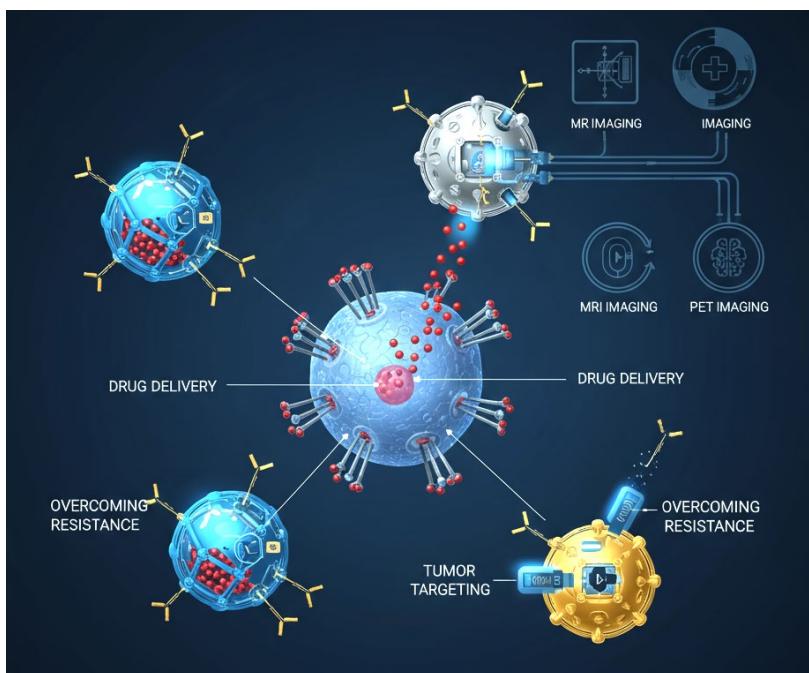
Another major application has been modulation of drug resistance using nanosystems. Nanoparticles can bypass efflux pumps (e.g., P-glycoprotein), alter tumor microenvironment acidity, and co-deliver resistance-modifying agents such as siRNAs or PI3K inhibitors. For example, polymeric nanoparticles co-loaded with paclitaxel and survivin siRNA have demonstrated strong anti-tumor activity in resistant breast cancer models by re-sensitizing tumors to chemotherapy<sup>25</sup>. Furthermore, theranostic nanoparticles capable of monitoring resistance biomarkers in real time provide dynamic feedback on therapeutic success or failure, allowing treatment regimens to be adjusted promptly. (Table 1)

From a patient-centered and clinical perspective, nanotheranostics in breast cancer show promise in improving survival outcomes, reducing off-target toxicity, and enhancing quality of life. Early clinical evaluations of nanocarriers such as albumin-bound paclitaxel and liposomal doxorubicin, now integrated with diagnostic agents, demonstrate favorable pharmacokinetics and reduced cardiotoxicity<sup>26</sup>. Importantly, personalized nanotheranostic systems guided by patient tumor profiles, receptor expression, and circulating biomarkers are moving the field closer to precision oncology in breast cancer. Nevertheless, clinical translation faces barriers, including manufacturing standardization, regulatory approval complexities, and long-term safety data.

**Table 1:** summarizes major preclinical and clinical nanotheranostic studies in breast cancer from 2019 to 2024, highlighting nano-biomarkers, HER2-targeted strategies, resistance modulation platforms, and clinical outcomes.

Nanoplatform	Target/Mechanism	Breast Cancer Subtype/Model	Outcomes	Reference
Iron oxide nanoparticles conjugated with folate ligands	Dual imaging (MRI) + drug delivery (doxorubicin)	ER-positive breast cancer (murine xenograft)	Enhanced tumor visualization; 2.5× higher intratumoral drug accumulation; reduced systemic toxicity	27
Gold nanorods coated with PEG and trastuzumab	HER2-targeted photothermal + drug delivery	HER2-positive cell lines (BT-474)	Synergistic tumor ablation under NIR irradiation; significant reduction in HER2 resistance markers	28
Polymeric nanoparticles co-loaded with paclitaxel + survivin siRNA	Overcoming drug resistance via siRNA-mediated gene silencing	Triple-negative breast cancer (TNBC, MDA-MB-231)	Re-sensitization to paclitaxel; ~60% greater tumor regression vs. paclitaxel alone	29
Liposomal doxorubicin with MRI contrast agent	Theranostic monitoring of drug accumulation	HER2-positive breast cancer (Phase I)	Safe tolerability; real-time MRI monitoring of tumor uptake; promising therapeutic signals	30
Exosome-mimetic nanoparticles loaded with miRNA-34a + paclitaxel	Gene therapy + chemotherapy combination	TNBC patient-derived xenografts	Reduced tumor growth; improved survival; minimal off-target toxicity	31
Albumin-bound paclitaxel integrated with PET tracer	Drug delivery + diagnostic tracking	Metastatic breast cancer (Phase II)	Improved pharmacokinetics; enhanced PET imaging	32

			sensitivity; reduced cardiotoxicity	
Multifunctional liposomes with trastuzumab + near-infrared dye	HER2-targeted imaging + drug delivery (doxorubicin)	HER2-positive orthotopic mouse model	High imaging precision; marked tumor regression; reduced recurrence risk	33



**Figure 4:** Mechanistic schematic of HER2-targeted nanotheranostic platforms in breast cancer.

## 7. Nanotheranostics in Brain Tumors

Brain tumors, particularly glioblastoma multiforme (GBM), are among the most lethal cancers due to their aggressive growth, diffuse infiltration, and the protective challenge posed by the blood-brain barrier (BBB). Conventional chemotherapeutics and targeted agents often fail to reach therapeutic concentrations in the tumor tissue, necessitating the development of nanotechnology-based delivery systems that can cross or circumvent the BBB<sup>34</sup>. Recent advances have led to the design of lipid-based nanoparticles, polymeric nanocarriers, dendrimers, and exosome-mimetic vesicles, many functionalized with BBB-penetrating ligands such as transferrin, angiopep-2, or low-density lipoprotein receptor-related peptides. These platforms improve drug bioavailability in the central nervous system while minimizing systemic toxicity<sup>35</sup>.

Imaging-guided therapies have become a cornerstone of nanotheranostics in brain tumors. Nanoparticles conjugated with MRI contrast agents, PET tracers, or near-infrared fluorescent dyes allow for real-time monitoring of tumor localization, drug delivery, and therapeutic efficacy. This imaging capability is critical for brain tumors, where precise targeting is essential to preserve surrounding healthy neural tissue. For instance, dual-functional nanoparticles delivering temozolomide alongside a fluorescent MRI probe have demonstrated enhanced tumor visualization and significant tumor suppression in orthotopic GBM models<sup>36</sup>.

Multi-functional nanoparticles further integrate diagnostics and therapy into a single system. These constructs combine chemotherapeutic payloads, gene therapy elements (siRNA or CRISPR/Cas9), and photothermal or photodynamic components, enabling simultaneous tumor eradication and monitoring of therapeutic response. For example, polymeric nanoparticles co-loaded with doxorubicin and siRNA targeting MGMT have improved chemotherapeutic sensitivity in GBM models while allowing non-invasive tracking of drug distribution. Such multifunctional designs exemplify the potential of nanotheranostics to overcome both biological and therapeutic hurdles inherent to brain cancers<sup>37</sup>.

Despite these promising advances, several translational hurdles and safety considerations remain. Nanoparticle penetration is highly variable across patients due to heterogeneity in BBB integrity and tumor vasculature. Long-term neurotoxicity, immunogenic responses, and off-target accumulation in critical brain regions are ongoing safety concerns<sup>38</sup>. Moreover, the complexity of synthesizing multifunctional nanoplatforms poses challenges for large-scale production, regulatory approval, and clinical standardization. Future research must focus on optimizing BBB-targeting strategies, improving biocompatibility, and developing scalable manufacturing approaches to facilitate the clinical translation of brain tumor nanotheranostics<sup>39</sup>.

## 8. Comparative Multi-Organ Insights

The exploration of nanotheranostics across liver, lung, pancreatic, breast, and brain tumors reveals both shared strategies and organ-specific nuances that shape therapeutic efficacy and translational potential. Across all cancer 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 drug release. These shared features underscore a common pharmacological framework for enhancing tumor specificity, reducing systemic toxicity, and enabling real-time monitoring of therapeutic response<sup>40</sup>. Despite these overarching similarities, organ-specific challenges and pharmacological barriers significantly influence the design and performance of nanotheranostic systems. In liver cancer, the heterogeneous vascularization and high metabolic activity affect nanoparticle clearance and drug bioavailability. Lung tumors present obstacles related to dynamic pulmonary physiology and immune-mediated clearance of inhaled nanoparticles. Pancreatic tumors are characterized by a

dense stromal matrix and poor vascularization, limiting nanoparticle penetration. HER2-positive and triple-negative breast cancers exhibit molecular heterogeneity, requiring subtype-specific targeting strategies. Brain tumors face the formidable blood–brain barrier, which necessitates specialized BBB-penetrating ligands and delivery modalities. Understanding these organ-specific barriers is critical for designing precision-targeted nanotheranostic interventions<sup>41</sup>.

From the accumulated evidence, several lessons emerge for integrating nanotheranostics into precision oncology. First, multifunctional platforms should be tailored to the tumor microenvironment of each organ to optimize accumulation, retention, and therapeutic effect. Second, real-time imaging is essential not only for monitoring treatment response but also for dynamically adjusting therapy in patient-specific contexts. Third, combining nanotheranostics with immunomodulatory or gene-targeting strategies enhances treatment efficacy across multiple tumor types. Finally, comparative evaluation of safety, pharmacokinetics, and resistance mechanisms across organs can inform rational design and accelerate clinical translation<sup>42</sup>.

## 9. Future Directions

As nanotheranostics continue to evolve, next-generation nanosystems are expected to redefine cancer pharmacology by incorporating advanced functionalities such as stimuli-responsiveness, artificial intelligence (AI)-driven optimization, and bioinspired designs. Stimuli-responsive nanoparticles, activated by pH, temperature, enzymes, or external fields, can achieve precise spatiotemporal drug release, minimizing systemic toxicity while maximizing tumor-targeted effects<sup>43</sup>. AI integration enables predictive modeling of nanoparticle behavior, optimization of drug loading, and real-time monitoring of therapeutic outcomes, allowing adaptive and personalized treatment regimens. Bioinspired designs mimicking natural vesicles, exosomes, or cellular membranes offer enhanced biocompatibility, immune evasion, and targeted delivery, further accelerating clinical applicability.

The integration of multi-omics data (genomics, transcriptomics, proteomics, metabolomics) with nanotheranostics represents another frontier in precision oncology. By mapping tumor heterogeneity at multiple molecular levels, nanotheranostic platforms can be tailored to individual patient profiles, enabling simultaneous diagnosis, targeted therapy, and response monitoring. This convergence of nanotechnology and multi-omics could facilitate early detection of resistance mechanisms, optimize combination therapies, and provide actionable insights for dynamic treatment adaptation<sup>44</sup>. Despite these technological advances, regulatory, ethical, and commercialization challenges remain significant. Dual-function nanotheranostics face complex regulatory pathways due to their combined diagnostic and therapeutic roles. Ethical considerations around personalized nanomedicine include patient data privacy, equitable access, and long-term safety monitoring. Commercialization is challenged by high manufacturing costs, reproducibility, and the need for scalable production methods.

Addressing these barriers will require coordinated efforts among researchers, clinicians, regulatory bodies, and industry stakeholders.

To accelerate clinical translation, a strategic roadmap is essential. Key steps include standardizing nanoparticle characterization and quality control, developing robust preclinical models that mimic human tumor microenvironments, conducting adaptive early-phase clinical trials with integrated imaging and biomarker endpoints, and fostering cross-disciplinary collaboration among nanotechnology, oncology, and computational biology. By following this roadmap, nanotheranostics can progress from experimental research toward routine clinical application, ultimately enabling safer, more effective, and personalized cancer therapy<sup>45</sup>.

## 10. Conclusion

Nanotheranostics has emerged as a transformative approach in cancer pharmacology, integrating diagnostic imaging with targeted therapy to overcome the limitations of conventional treatments. Across liver, lung, pancreatic, breast, and brain tumors, multifunctional nanoparticles have improved tumor targeting, enabled real-time therapeutic monitoring, and enhanced treatment outcomes in both preclinical and early clinical studies. While shared strategies such as ligand-functionalization and stimuli-responsive drug release are common, organ-specific barriers like the blood–brain barrier, dense stroma, and molecular heterogeneity require tailored designs. Future directions focus on AI-integrated, stimuli-responsive, and bioinspired nanosystems combined with multi-omics data to enable precision oncology. Despite regulatory, safety, and manufacturing challenges, nanotheranostics offers a promising pathway toward personalized, more effective, and safer cancer therapies, marking a significant step toward the convergence of diagnostics and therapeutics.

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