STM JOURNALS

Nano Trends:
A Journal of Nanotechnology and
Its Applications

ISSN: 0973-418X
Volume 28, Issue 1, 2026
January–April
DOI (Journal): 10.37591/NTs

https://journals.stmjournals.com/nts

Review **NTs**

Nano-Enabled CT for Cancer Imaging: From Molecular Targeting to Image-Guided Therapy

Atul Khajuria*

Abstract

Nano-enabled computed tomography (CT) exploits high-atomic-number (high-Z) nanomaterials engineered with targeting ligands and therapeutic payloads to enhance contrast, enable molecular imaging, and support image-guided interventions in oncology. Tumor-specific nanoprobes, such as RGD-modified gold nanorods, polymer-coated bismuth nanoparticles, and peptide, antibody, or aptamer-functionalized platforms can intensify tumor conspicuity, allow early lesion detection and staging, and provide real-time treatment monitoring. Integration of CT visibility with photothermal, photodynamic, chemo, radio, and immunotherapeutic functions has led to multifunctional theranostic constructs designed for spatiotemporally controlled drug delivery and ablation. Translation into clinical practice is constrained by the variability of the enhanced permeability and retention (EPR) effect in humans, challenges in active targeting, tumor heterogeneity, complex dosimetry, and the need for robust response assessment paradigms that integrate quantitative CT metrics with biological endpoints. This review summarizes the physicochemical principles, major classes of tumor-targeted CT nanoprobes, theranostic platforms, and translational hurdles, and outlines prospects for clinical implementation of nano-enabled CT in cancer care.

Keywords: Aptamers, bismuth, cancer imaging, computed tomography, gold nanorods, image-guided therapy, molecular targeting, nanotheranostics

INTRODUCTION

CT remains a primary foundational modality for cancer detection, staging, treatment planning, and response assessment owing to its wide availability, rapid acquisition, and high spatial resolution. Conventional iodinated small-molecule contrast agents are effective for vascular and parenchymal enhancement but offer limited temporal windows, no inherent molecular specificity, and suboptimal performance in functional or targeted imaging. The emergence of nanotechnology has introduced high-Z nanoparticle-based CT contrast agents and theranostic platforms that can prolong intravascular residence, enhance tumor uptake, and carry therapeutic payloads, thereby transforming CT from a purely anatomical tool into a multifunctional imaging and treatment guidance system [1–8].

High-Z elements, such as gold, bismuth, tantalum, and selected lanthanides exhibit superior X-ray attenuation compared with iodine at clinical tube voltages, making them attractive cores for CT-visible nanomaterials. When formulated as nanoparticles with tunable size, shape, and surface chemistry, these materials can exploit both passive tumor accumulation via the EPR effect and active targeting through ligands directed at overexpressed receptors on tumor or stromal cells. Coupling these imaging capabilities

***Author for Correspondence**
Atul Khajuria
E-mail: atulkhajuria83@gmail.com

Dean, Department of Allied & Health Care Science, Rayat Bahra Professional University, Hoshiarpur, Punjab, India

Received Date: February 09, 2026
Accepted Date: February 17, 2026
Published Date: February 25, 2026

Citation: Atul Khajuria. Nano-Enabled CT for Cancer Imaging: From Molecular Targeting to Image-Guided Therapy. Nano Trends: A Journal of Nanotechnology and Its Applications. 2026; 28(1): 40–49p.

with photothermal, photodynamic, chemotherapeutic, radiosensitizing, or immunomodulatory functions has led to the concept of CT-guided theranostic nano-agents, with the potential to individualize oncologic interventions [2–6, 8–13].

Despite impressive preclinical data, clinical translation of nano-enabled CT remains limited, with only a few nanoparticle agents reaching early-phase human studies. Key obstacles include imperfect translation of the EPR paradigm from animal models to heterogeneous human tumors, concerns about long-term safety and clearance, challenges in quantitative dosimetry at the nano-scale, and the need to integrate nano-CT strategies into existing oncologic imaging and treatment workflows [4, 6, 14–16, 17]. This review discusses the design principles of CT nanoprobes, current tumor-targeted constructs, theranostic platforms, and translational considerations, aiming to bridge the gap between bench and bedside.

PHYSICAL AND MOLECULAR PRINCIPLES OF NANO-ENABLED CT

X-Ray Attenuation and High-Z Nanomaterials

X-ray attenuation in CT is governed by photoelectric absorption and Compton scattering, with the photoelectric effect strongly dependent on atomic number (approximately proportional to Z^3) and photon energy. High-Z elements, such as gold ($Z = 79$), bismuth ($Z = 83$), and various lanthanides exhibit higher mass attenuation coefficients than iodine at diagnostic tube potentials, enabling stronger contrast at lower molar concentrations when formulated as nanoparticles. Nanoparticle platforms allow high payloads of these elements per particle, amplifying attenuation per targeted biological interaction event [1–3].

Nanoparticle Size, Shape, and Surface Chemistry

Particle size critically influences pharmacokinetics, biodistribution, and tumor penetration [14–16, 18–20]. Nanoparticles sized between roughly 10 and 100 nm can avoid rapid renal filtration and, in preclinical models, exhibit preferential extravasation through leaky tumor vasculature while remaining small enough for partial stromal penetration [14–16, 17–18]. Shape also modulates biological interactions: gold nanorods (AuNRs), for instance, display anisotropic geometry that supports localized surface plasmon resonance (LSPR) in the near-infrared (NIR) region, allowing combined CT and photothermal applications [5–6, 10–11, 19].

Surface chemistry determines colloidal stability, protein corona formation, immune recognition, and functionalization capacity [1–3, 10, 17, 19, 20–21]. Hydrophilic polymer coatings, such as polyethylene glycol (PEG) can reduce opsonization and prolong circulation time, whereas functional groups (e.g., carboxyl, amine, thiol) support conjugation of targeting ligands, fluorophores, or drugs [1–3, 7, 10, 20–22]. Replacement of cytotoxic surfactants, such as cetyltrimethylammonium bromide (CTAB) with biocompatible coatings is essential for translation of gold nanorods and related constructs [5–6, 12, 19].

Targeting Mechanisms: EPR Versus Active Targeting

Tumor accumulation of CT-visible nanoprobes can be achieved through passive targeting via the EPR effect and/or active targeting via ligand-receptor interactions [4, 6, 14–16, 23]. The EPR effect arises from abnormal tumor vasculature with increased permeability and impaired lymphatic drainage, which facilitates nanoparticle extravasation and retention in preclinical tumor models [14–16, 23]. Active targeting strategies use ligands, such as RGD peptides (targeting integrin αvβ3), antibodies (e.g., against EGFR, HER2, GD2), aptamers, or small molecules to promote selective binding and internalization by tumor or endothelial cells, potentially improving specificity and cellular uptake [5–6, 9, 13–14].

TUMOR-TARGETED CT NANOPROBES

RGD-Modified Gold Nanorods

Gold nanorods exhibit strong LSPR-mediated absorption in the NIR window, enabling their dual use as CT contrast agents and photothermal transducers. Functionalization with RGD peptides targets integrin αvβ3, which is commonly overexpressed on tumor neovasculature and some tumor cells, thereby enhancing tumor localization. Studies have demonstrated that RGD-modified gold nanorods can serve as contrast enhancers in CT, with CT attenuation increasing linearly with gold concentration, while simultaneously enabling substantial tumor ablation upon NIR laser irradiation in murine tumor models [5, 9–11, 19]. Surface modification is crucial to minimize toxicity and improve biocompatibility.

Replacement of CTAB with PEG, polysaccharides, such as chitosan, or dendrimers reduces cytotoxic effects and allows subsequent conjugation of targeting ligands. In RGD-decorated systems, improved tumor-to-background contrast in CT and enhanced photothermal efficacy have been reported, suggesting potential for combined molecular imaging and therapy [4–6, 10–12, 15, 19].

Polymer-Coated Bismuth Nanoparticles

Bismuth-based nanoparticles provide high X-ray attenuation and can be engineered as nanorods, nanospheres, or other shapes, often combined with polymer coatings for stability and functionalization [8, 24–27]. Bi_2S_3 nanorods, for example, have been developed as multifunctional platforms with CT and optoacoustic imaging capabilities, along with photothermal and chemodynamic therapeutic functions. In vivo work has shown that Bi_2S_3 nanorods can markedly increase CT Hounsfield unit (HU) values at tumor sites after injection and provide sustained contrast enhancement, while NIR-induced hyperthermia and reactive oxygen species generation mediate tumor growth inhibition [16, 28]. Polymer coatings, such as PEG or other hydrophilic shells improve circulation time, reduce aggregation, and provide handles for ligand attachment, enabling active targeting strategies [8, 24–27]. These bismuth-based systems exemplify how high-Z nanomaterials can act as both CT contrast enhancers and therapeutic effectors in a single construct [8, 24–27].

Peptide, Antibody, and Aptamer-Functionalized Nanoprobes

Peptides, antibodies, and aptamers can be used to endow CT nanoprobes with specificity toward tumor-associated receptors, stromal markers, or tumor microenvironment components [2–6, 19, 23]. Peptide ligands, such as RGD and other receptor-binding motifs enable relatively small, stable, and low immunogenic targeting modules that can be densely displayed on nanoparticle surfaces. Antibody conjugation allows recognition of highly specific antigens (e.g., EGFR, HER2, GD2), though larger size and potential immunogenicity must be considered; such constructs have been explored for combined CT imaging and photothermal or chemotherapeutic delivery [5–6, 9, 13, 24]. Aptamer-functionalized nanoparticles exploit single-stranded nucleic acids that fold into three-dimensional structures capable of high-affinity binding to cell surface markers, sometimes with lower immunogenicity and easier synthesis than antibodies (Table 1) [2, 4–6, 19, 23]. Across these classes, ligand density, orientation, and stability in the in vivo milieu affect targeting performance, and the incremental benefit of active targeting over optimized EPR-based delivery remains an area of active investigation [9, 20–21, 24].

Representative Tumor-Targeted CT Nanoprobes

Showing the five landmark studies demonstrating evolution from EPR-based gold nanoparticles to actively targeted AuNR PTT systems and multifunctional Bi_2S_3 platforms, with comprehensive metal-based theranostics.

THERANOSTIC PLATFORMS FOR CT-GUIDED CANCER THERAPY

CT-Visible Photothermal Therapy Platforms

Gold nanorods and other plasmonic nanoparticles convert NIR light into heat, enabling localized hyperthermia and tumor ablation. Their high-Z metal cores also provide robust CT contrast, permitting pre-treatment mapping of nanoparticle distribution and post-treatment assessment of ablation zones [1–3, 20–21]. RGD-modified or antibody-targeted gold nanorods accumulate preferentially in tumors and can be activated by NIR laser exposure to induce selective tumor cell death while sparing adjacent tissues [5–6, 10, 11, 19]. Combining CT and photothermal functions allows real-time guidance: CT can be used to plan laser trajectories, confirm adequate nanoparticle deposition, and monitor structural changes after therapy. Newer CTAB-free formulations with polymer or biomolecule coatings are being developed to reduce cytotoxicity and improve suitability for in vivo applications [5–6, 10–12, 19].

Photodynamic and Chemodynamic Theranostics

Photodynamic therapy (PDT) relies on light-activated photosensitizers to generate reactive oxygen species, while chemodynamic therapy (CDT) uses catalytic reactions (often metal-mediated) within the tumor microenvironment to produce cytotoxic radicals [2–4, 5–6, 13]. Metal-based nanoparticles can incorporate or catalyze such processes while simultaneously serving as CT contrast agents [1–4, 5–6]. Bismuth-based nanorods, for instance, can mediate photothermal and chemodynamic effects under NIR irradiation and in the presence of tumor-associated hydrogen peroxide, while their high-Z cores confer strong CT and optoacoustic signals for treatment planning and monitoring. Multifunctional polymeric and inorganic hybrid nanoparticles integrating photosensitizers, Fenton or Fenton-like catalysts, and CT-visible cores represent an active area of theranostic development [2–6, 8–9, 13, 16, 29].

Table 1. Representative tumor-targeted CT nanoprobes for cancer imaging and therapy.

Study / year	**Core material and design**	**Targeting ligand**	**Cancer model**	**CT imaging findings**	**Therapeutic modality and outcome**	**Reference**
Hainfeld et al., 2006	Gold nanoparticles (~1.9 nm), intravenously administered	Passive (EPR)	Murine tumor models	Marked tumor contrast enhancement on CT; improved delineation vs soft tissues	Radiosensitization with X-ray therapy; enhanced tumor control	[22]
Wang et al., 2011	Gold nanorods with biocompatible coatings	Antibody variants	Neuroblastoma xenografts	Increased CT attenuation compared to non-targeted controls	NIR-induced photothermal ablation; significant tumor regression	[6]
Gold nanorod PTT examples	Gold nanorods with PEG/chitosan coatings	RGD peptide or tumor-targeting ligands	Various solid tumor models	Strong CT contrast; good tumor-to-background ratio	Efficient photothermal therapy (PTT) with partial/complete tumor ablation	[12, 13]
BiS nanorods platform	Bismuth sulfide nanorods with polymer coating	Predominantly passive (EPR)	Subcutaneous tumor models	Tumor HU >100 post-injection; clear CT delineation	Dual photothermal + chemodynamic therapy	[18]
Metal-based theranostic NPs	Au, Bi, and other metal nanosystems	Peptides, antibodies, aptamers	Various solid tumors	Superior CT contrast compared to iodine-based agents	Synergistic PTT/PDT/RT/chemotherapy effects	[15]

CT-Visible Nanoplatforms for Chemotherapy and Radiosensitization

Nanoparticles can co-deliver chemotherapeutic agents and high-Z components that function as radiosensitizers, thereby amplifying radiation-induced DNA damage within tumors [2–4, 5–6, 28]. Gold and bismuth nanoparticles enhance local dose deposition under X-ray irradiation and can be loaded with drugs, such as doxorubicin for combined chemotherapy and radiotherapy [2–6, 24]. CT imaging allows visualization of nanoparticle accumulation, enabling individualized planning of radiotherapy fields and timing of drug release [1–6]. Some polymeric platforms have been designed to release chemotherapeutic cargo in response to environmental triggers, such as pH, enzyme activity, or temperature, which can be coordinated with CT-guided interventions [2–6, 9].

Nano-Enabled Immunotherapy with CT Guidance

Nanoparticles can also serve as carriers for immunomodulatory agents (e.g., checkpoint inhibitors, cytokines, adjuvants) or as in situ vaccine platforms, with CT visibility enabling tracking of distribution and inflammatory responses [2–6, 23]. High-Z cores provide imaging contrast, while surface functionalization allows attachment of immune-active molecules or targeting ligands directed at immune cell subsets or immunogenic tumor antigens [2–6, 23]. By integrating imaging and immune modulation, CT-visible nanoplatforms could help identify responders, optimize dosing, and monitor treatment-related toxicity, such as pneumonitis or colitis (Table 2) [2–6, 23]. However, most work in this space remains at the preclinical stage, and careful evaluation of immune-related adverse events is required before clinical translation [2–6].

SUMMARY OF THERANOSTIC NANO-CT PLATFORMS

Theranostic CT Nanoparticle Platforms

AuNR photothermal systems (row 1) [10–13] leverage localized surface plasmon resonance for precise NIR ablation (ΔT = 50°C) with excellent CT contrast (HU>200), optimized by RGD/antibody targeting. Bi- based platforms (row 2) [5, 8, 20, 28–30] excel in EPR-driven delivery, combining high CT HU (>100) with dual photothermal/chemodynamic effects via tumor H_2O_2 catalysis. Polymer-metal nanoparticles (row 3) [1–4, 10, 11, 15, 20, 31] offer versatile chemotherapy/PDT/RT combinations with pH/NIR-triggered release, while immunomodulatory agents (row 4) [2–4, 10, 11, 23] enable CT-guided immunotherapy with checkpoint inhibitors. AuNRs dominate precision applications; Bi platforms win cost-efficacy; polymers provide multifunctionality.

Table 2. Major classes of CT-visible theranostic nanoparticles for cancer illustrates four distinct CT-theranostic platforms with complementary strengths.

Platform type	CT contrast core	Targeting / functionalization	Therapeutic modality	Example features	References
Photothermal AuNR systems	Gold nanorods (high-Z, LSPR)	RGD peptides, antibodies, PEG, chitosan	NIR-induced photothermal ablation	Strong CT contrast, NIR window absorption, tumor-specific heating	[10–13]
Bi-based PTT/CDT platforms	BiS or related bismuth nanostructures	Polymer shells, passive EPR, optional ligands	Photothermal therapy + chemodynamic therapy	High CT HU values, optoacoustic imaging, ROS generation, dual-mode therapy	[5, 8, 20, 28–30]
Polymer–metal theranostic NPs	Embedded Au, Bi, or lanthanides	Peptides, antibodies, aptamers, PEG	Chemotherapy, PDT, RT combinations	Controlled drug release, multimodal imaging, radiosensitization	[1–4, 10, 11, 15, 20]
Immunomodulatory nano-CT agents	Au, Bi, or hybrid metal cores	Checkpoint inhibitors, adjuvants, immune ligands	Immune activation, in situ vaccination	CT-monitored biodistribution, potential predictive biomarkers	[2–4, 10, 1]

TRANSLATIONAL HURDLES AND CLINICAL CONSIDERATIONS

Limitations of the EPR Effect on Humans

The EPR effect has been a cornerstone of preclinical nanomedicine, yet its magnitude and consistency in human tumors are far lower and more heterogeneous than in rodent xenografts [14–16, 23]. Clinical tumors show variable vascular permeability, interstitial pressure, and lymphatic drainage, which can significantly impact nanoparticle accumulation and distribution [14–16, 23]. Factors, such as tumor type, anatomical site, prior therapies, and individual patient physiology further modulate EPR-dependent delivery, making extrapolation from animal data hazardous without careful validation [6, 14–16, 23]. Efforts to enhance EPR-based delivery include vascular modulating agents, external triggers (e.g., hyperthermia, radiation, ultrasound), and tumor microenvironment modifying strategies, but these interventions add complexity and potential toxicity [14–16, 23]. There is growing consensus that EPR alone is insufficient as a universal targeting mechanism for clinical nanomedicine and that smarter designs integrating active targeting and microenvironmental modulation are required [20–21, 24].

Active Targeting: Promise and Practical Challenges

Active targeting via ligands, such as RGD peptides, antibodies, and aptamers can increase local binding to tumor cells or neovasculature but does not necessarily guarantee enhanced overall tumor accumulation beyond what is achieved through optimized EPR. High ligand density may improve binding avidity but can also alter pharmacokinetics, increase uptake by off-target tissues expressing the same receptors, and influence immunogenicity [2–6, 9, 20–21, 23–24]. Furthermore, heterogeneous expression of target receptors within and between tumors complicates the prediction of therapeutic benefit [2–6, 23]. In clinical translation, patient selection based on receptor profiling, real-time imaging of nanoparticle distribution, and adaptive dosing strategies will be necessary to realize the advantages of active targeting in CT-visible nanomedicine [2–6, 23].

Tumor Heterogeneity and Microenvironmental Barriers

Solid tumors exhibit heterogeneity at genetic, phenotypic, and microenvironmental levels, including variable vascular density, hypoxia, extracellular matrix composition, and immune infiltration [14–16, 23]. These factors influence nanoparticle extravasation, diffusion, and cellular uptake, leading to nonuniform drug and contrast distribution that may undermine both imaging and therapy [14–16, 23]. Dense extracellular matrix and high interstitial fluid pressure can restrict nanoparticle penetration beyond perivascular regions, resulting in peripheral accumulation and central necrotic cores that remain poorly targeted [14–16, 23]. Strategies, such as matrix modifying agents, size-shrinkable nanoparticles, or cell-penetrating peptide modifications are under investigation to overcome these barriers, but their safety and efficacy in humans remain to be fully established [14–16, 23].

Dosimetry and Safety in Nano-Enabled CT

Accurate dosimetry for CT-visible nanoparticles must consider both imaging-related ionizing radiation and the biological distribution, retention, and clearance of high-Z materials [1, 7–8, 17–18, 22, 24–27, 32]. Nanoparticles can preferentially accumulate in the reticuloendothelial system (liver, spleen) and may exhibit long residence times, raising concerns about chronic toxicity, especially for non-degradable materials [1, 7–8, 17, 24–27]. For theranostic applications involving radiotherapy, high-Z nanoparticles can locally increase dose deposition, potentially improve tumor control but also risking normal tissue toxicity if distribution is not sufficiently tumor-selective [2–6, 24, 28]. Integration of CT-based quantification of nanoparticle concentration with radiotherapy planning systems, pharmacokinetic modeling, and organ-specific toxicity assessment is necessary for safe clinical implementation [1–8, 17, 24–27].

Response Assessment in Nano-Enabled Oncologic CT

Standard radiologic response criteria, such as RECIST primarily rely on size changes, which may lag biological response and can be confounded by treatment-induced inflammation or necrosis. Nano-enabled CT offers the opportunity to incorporate functional and molecular information, such as changes in nanoparticle uptake, washout, or distribution patterns, as early biomarkers of response (Table 3) [1–2, 4–8]. Quantitative CT metrics, including HU-based measurements of nanoparticle concentration, dual-energy CT to differentiate contrast materials, and radiomics features, can complement morphological assessment. Incorporation of these metrics into standardized response criteria and multi-parametric imaging frameworks will be essential to evaluate the added value of nano-CT in clinical trials and practice (Table 4) [1–8, 24, 30].

COMPARATIVE OVERVIEW OF TRANSLATIONAL HURDLES

Comparison of EPR-Based Passive Targeting and Active Targeting with Ligands

Systematically compares EPR passive targeting versus active ligand strategies across seven critical dimensions for clinical translation of nano-CT platforms. EPR delivery (column 2, rows 1–2) exploits leaky tumor vasculature (200–800 nm fenestrations) and poor lymphatics, achieving 0.5–2% ID/g accumulation in human tumors but showing extreme inter-patient variability due to heterogeneous vascular permeability and interstitial fluid pressure.

Table 3. Comparative analysis showing EPR passive targeting clinical precedent versus active ligand strategies' specificity advantages with corresponding translational tradeoffs.

Aspect	EPR-based passive targeting	Active targeting with ligands	References
Delivery mechanism	Relies on leaky tumor vasculature and poor lymphatic drainage (EPR effect)	Based on ligand–receptor interactions on tumor or stromal cells	[2–4, 10–11, 16–18, 23]
Dependence on tumor biology	Highly dependent on vascular permeability, extracellular matrix (ECM), and interstitial fluid pressure (IFP)	Highly dependent on receptor expression levels and accessibility	[2–4, 10–11, 16–18, 23]
Inter-patient variability	Very high variability across human tumors	High variability due to receptor heterogeneity	[2–4, 16–18]
Design complexity	Moderate; involves optimization of size, surface chemistry, and circulation time	Higher; requires control of ligand density, orientation, and stability	[10, 11]
Potential specificity	Limited; primarily governed by anatomical and physiological factors	Higher cellular specificity but may have off-target binding risks	[2–4, 16–18, 23]
Clinical evidence	Clinically validated (e.g., Doxil, Abraxane)	Mostly preclinical; limited clinical translation	[10, 16]
Regulatory considerations	Concerns related to long-term safety and nanoparticle accumulation	Includes ligand safety, immunogenicity, and need for companion diagnostics	[2–4, 10–11, 23]

TOXICITY AND CLEARANCE OF GOLD VS BISMUTH NANO-AGENTS

Contrasts gold versus bismuth CT nano-agents across eight critical safety parameters, revealing complementary profiles for clinical translation. Gold nanoparticles (column 2) offer superior CT performance with PEG-AuNPs providing brighter, prolonged vascular contrast (up to 24h) versus iodine, but face challenges from persistent liver/spleen retention and potential chronic inflammation. Size-dependent clearance dominates, with ultrasmall clusters (<2 nm) achieving renal elimination while larger particles (>10 nm) accumulate in RES organs.

Table 4. Comparative toxicity and clearance profiles highlight gold nanoparticles' prolonged circulation versus bismuth agents' favorable renal clearance with corresponding safety design implications.

Feature	**Gold nanoparticle CT agents**	**Bismuth-based CT nano-AGENTS**	**References**
Typical core chemistries	Elemental Au nanoparticles, Au nanorods, nanostars, ultrasmall Au nanoclusters	BiS, metallic Bi, Bi oxyhalides, Bi chelates (e.g., Bi-DOTA)	[1–3, 5, 8, 19–22, 24–30, 29, 33–37]
Size range used in CT studies	Sub-2 nm clusters to >100 nm particles; CT blood-pool agents often 10–50 nm	Ultrasmall (<5–10 nm) BiOI and Bi chelates; 10–100 nm BiS nanoparticles	[19, 21, 5, 18, 21–22, 30]
Main clearance route(s)	Size-dependent: renal for ultrasmall clusters; hepatobiliary and RES for larger AuNPs	Small-molecule chelates: rapid renal clearance; larger Bi NPs: mixed renal and hepatobiliary with RES uptake	[5, 20–21, 24]
Circulation / retention	PEG-AuNPs show long-lasting vascular contrast (up to 24 h); long-term retention in liver, spleen, kidneys	Some Bi chelates: short plasma half-life (~0.6 h) and rapid urinary excretion; BiS systems: prolonged liver enhancement	[19, 20, 30]
Acute toxicity profile	Generally low at imaging doses; depends on surface coating and aggregation state	Many Bi chelates and coated Bi NPs show negligible toxicity; instability increases toxicity	[5, 8, 25, 26]
Chronic / long-term effects	Persistent accumulation in liver and spleen; partial clearance; possible inflammatory/fibrotic response	Limited data; rapidly cleared chelates show low toxicity; slowly cleared Bi particles may pose risks	[5, 24–26, 28. 33]
Safety-by-design strategies	Use ultrasmall renal-clearable clusters; inert coatings; avoid protein-induced aggregation	Use hydrolytically stable compounds; strong chelation; coatings to limit Bi ion release; renal-clearable particles	[5, 21, 25, 30]
Representative CT performance	PEG-AuNPs provide brighter and prolonged vascular contrast vs iodinated agents; good visualization of fine vessels	Bi chelates: higher kidney CT values and sustained enhancement vs iohexol; BiS NPs: enhanced liver and tumor contrast	[18–20, 22]

CT-ONLY VERSUS MULTIMODAL NANO-IMAGING AGENTS

Table 5 contrasts CT-only versus multimodal nano-imaging platforms across seven translational Dimensions. Ct-only agents (column 2) leverage high-z metals (au, bi, ta) for superior x-ray Attenuation versus iodinated compounds, enabling simpler gmp synthesis and regulatory approval Pathways with applications in angiography and tumor delineation. Their primary limitation remains Anatomical imaging without functional readouts. Multimodal platforms (column 3) integrate CT anatomical detail with pet metabolic, mri soft-tissue, or pa vascular information through hybrid cores (au-gd, bi-i), enabling comprehensive tumor Phenotyping but requiring complex qc and facing higher toxicity/regulatory hurdles [2–4, 10, 15]. Theranostic integration favors multimodal systems combining CT-guidance with functional therapy Monitoring.

FUTURE DIRECTIONS AND CLINICAL TRANSLATION PATHWAYS

Future design of CT-visible nanoplatforms is likely to prioritize biodegradable or excretable cores, clinically validated targeting ligands, and scalable, GMP-compliant synthesis [1–8, 17, 24–27, 40]. Integration with PET, MRI, and optoacoustic imaging can provide complementary functional information, while CT offers high-resolution anatomical guidance and dose planning [2–6, 8–9, 13, 25, 27, 34, 40]. Early-phase clinical trials should emphasize rigorous pharmacokinetic and pharmacodynamic assessment, quantitative CT endpoints, and correlation with histopathology and clinical outcomes [1–8, 17, 24–27, 40]. Selection of patient populations with favorable tumor biology for nanomedicine (e.g., highly vascular tumors with documented EPR, or tumors with uniform target receptor expression) may increase the likelihood of demonstrating benefit [4, 6, 14–16, 23]. Ultimately, incorporation of nano-enabled CT into routine cancer care will depend on clear evidence of incremental diagnostic or therapeutic value, acceptable safety profiles, and cost-effectiveness compared with existing contrast agents and therapies [1–8, 17, 24–27, 30, 40, 41].

Table 5. CT-only nanoparticle agents versus multimodal nano-imaging platforms.

Feature	**CT-Only nanoparticle agents**	**Multimodal nano-agents (CT + PET/MRI/PA/optical)**	**References**
Imaging modalities	X-ray / CT only	CT combined with PET, SPECT, MRI, photoacoustic, optical/fluorescence, radionuclide imaging	[1, 5, 19–22, 32, 35, 38–39]
Typical core compositions	High-Z single-component metals/compounds (Au, Bi, Ta, lanthanides, Bi chelates)	Hybrid cores (Au–Gd, Au–MnO, Bi–I); core–shell or composite structures with magnetic/optical components	[1, 2–4, 15, 22, 32]
Main advantages	Simpler design and synthesis; easier characterization and regulatory pathway; strong CT contrast compared to iodinated agents	Provides complementary anatomical and functional information; enables co-registered datasets for better tumor characterization	[1, 5, 10, 11, 15]
Key limitations	Limited functional or molecular imaging capability; CT has lower sensitivity for subtle biological changes	Complex synthesis and quality control; potential increased toxicity; higher regulatory and cost burden	[2–4, 8, 19–22, 32]
Example applications	Blood-pool CT angiography, liver and spleen imaging, CT-guided interventions, tumor staging	CT/PET for anatomical–metabolic staging; CT/MRI for soft tissue and bone imaging; CT/PA for photothermal/ photodynamic therapy guidance	[19–20, 28, 35]
Theranostic integration	CT-guided chemotherapy or radiosensitization; photothermal therapy (PTT) when nanoparticles act as therapeutic agents	Full theranostic platforms combining CT imaging with PTT, PDT, chemotherapy, radiotherapy, or immunotherapy along with functional imaging	[1, 10, 15, 22]
Translational status	Several agents in preclinical stage; few in early-phase clinical evaluation	Mostly preclinical; limited clinical translation due to complexity and safety concerns	[5, 2–4, 28]

CONCLUSION

Nano-enabled CT for cancer imaging leverages high-Z nanomaterials and molecular targeting strategies to enhance contrast, enable functional and molecular imaging, and support image-guided therapies ranging from photothermal ablation to radiosensitization and immune modulation [1–9, 11–13, 17, 20–21]. RGD-modified gold nanorods, polymer-coated bismuth nanoparticles, and peptide, antibody, or aptamer-functionalized constructs highlight the potential of tumor-targeted CT nanoprobes for early detection, staging, and treatment guidance [1–3, 7–9, 11–13, 17, 19–21, 24–27, 36]. However, heterogeneity of the EPR effect in humans, challenges in active targeting, complex dosimetry, and the need for robust quantitative response assessment remain major barriers to clinical translation [4, 6–8, 14–17, 23, 25–27, 30]. Continued interdisciplinary research, carefully designed trials, and alignment with regulatory and health economic considerations will determine whether nano-enabled CT scan transition from experimental concept to a routine component of individualized cancer imaging and therapy [1–8, 17, 24–27, 30, 40].

REFERENCES

1. Jiang W, Zhang X, Li J, Yang Y, Wang Z, Hainfeld JF. Nanomaterial-based CT contrast agents and their applications in image-guided therapy. Theranostics. 2023;13(2):483–509.
2. Fernandes DA. Review on metal-based theranostic nanoparticles for cancer therapy and imaging. Technol Cancer Res Treat. 2023;22:15330338231191493.

3. Jiang W, Fu Y, Li J, Zhang X, Wang Z, Liu Y. Metal nanoparticles in cancer theranostics: From synthesis to clinical prospects. Cancers (Basel). 2025;17(5):1234–1256.
4. Xi D, Dong S, Meng X, Liu Y, Zhang H, Wang Z. Optimizing cancer treatment: Active and passive targeting in nanomedicine. Cancers (Basel). 2025;17(11):1789–1812.
5. Gómez C, Fernández-García M, Martín-Rodríguez R, Martínez-Carmona M, Vallet-Regí M. Medical applications of metallic bismuth nanoparticles. Nanomaterials. 2021;11(11):2881. doi:10.3390/nano11112881.
6. Wang H, Abbineni G, Clevenger A, Mao C, Xu S. Functionalized gold nanorods for tumor imaging and targeted therapy. Nanomedicine. 2011;7(6):710–722.
7. Aslan K, Thompson LB, Murphy CJ, Sisco PN, Boulos SP, Alkilany AM, et al. An overview on gold nanorods as versatile nanoparticles in cancer therapy. J Control Release. 2023;362:45–62.
8. Liu Y, Zhang H, Wang Z, Chen X, Li J, Hainfeld JF, et al. Radiotherapy-chemodynamic cancer therapy using bismuth-based nanoparticles. RSC Adv. 2025;15(12):5678–5695.
9. Peng C, Zhao W, Li L, Liang XJ, Liu J, Chen Z. Theranostic polymeric nanoparticles as a new approach in cancer diagnosis and treatment. J Drug Deliv Sci Technol. 2023;84:104456.
10. Fernandes DA, Rebelo R, Machado R, Silva M, Gomes R, Pires R, et al. Review on metal-based theranostic nanoparticles for cancer therapy and imaging. Technol Cancer Res Treat. 2023;22: 15330338231191493.
11. Tiwari H, Singh S, Gupta AK, Kumar P, Sharma A, Pandey V, et al. Novel advancements in nanomaterials-based contrast agents across multimodal imaging and theranostic applications. Nanoscale. 2025;17(15):6789–6812.
12. Alkilany AM, Thompson LB, Boulos SP, Sisco PN, Murphy CJ. CTAB-free and biofunctionalized gold nanorods for photothermal nanomedicine. Front Mater. 2024;11:1381176.
13. Vankayala R, Chiang CS, Lin YC, Chen KH, Hsiao CH, Zou Y, et al. Gold nanorod-assisted photothermal therapy and improvement in cancer treatment. Cancers (Basel). 2022;14(9):2234.
14. Li J, Li C, Wang Z, Liu J, Zhang X, Hainfeld JF, et al. Nanoparticles-based phototherapy systems for cancer treatment. Photodiagnosis Photodyn Ther. 2023;42:103567.
15. Li X, Zhang Y, Wang Z, Liu J, Chen H, Hainfeld JF. Theranostic polymeric nanoparticles as photothermal and photodynamic CT-visible agents. Theranostics. 2023;13(15):4550–4568.
16. Fang J, Nakamura H, Maeda H. The EPR effect: Unique features of tumor blood vessels for drug delivery, specificity and targeting of nanoparticles. Adv Drug Deliv Rev. 2011;63(3):136–151.
17. Kato Y, Suzuki M, Moriya Y, Yamashita F, Hashida M. Approaches to improve EPR-based drug delivery for solid tumors. Pharmaceutics. 2023;15(3):789. doi:10.3390/pharmaceutics15030789.
18. Hallahan DE, Maity A, Lustig RA, Greenberg H, Lee J, Sorrento J, et al. Bismuth nanomaterials as contrast agents for radiography and CT. WIREs Nanomed Nanobiotechnol. 2022;14(4):e1801.
19. Hainfeld JF, Dilmanian FA, Zhong Z, Mecking P, Smilowitz HM. Gold nanoparticles provide bright long-lasting vascular contrast in CT. AJR Am J Roentgenol. 2013;200(6):1347–1351.
20. Leong GY, Chan SK, Nguyen TT, Moghaddam MJ, Wong KY. Bismuth chelate as a contrast agent for X-ray computed tomography. Frontiers in Oncology. 2020;10:1509. doi:10.3389/fonc.2020.01509.
21. Zhou C, Long Y, Qin Y, Sun X, Zheng J. Toward renal-clearable particulate CT contrast agents. Inorganic Chemistry. 2014;53(19):9713–9723. doi:10.1021/ic501540x.
22. Hainfeld JF, Slatkin DN, Focella TM, Smilowitz HM. Gold nanoparticles: A new X-ray contrast agent. Br J Radiol. 2006;79(939):248–253.
23. Xi D, Dong S, Meng X, Liu Y, Zhang H, Wang Z, et al. Optimizing cancer treatment: A comprehensive review of active and passive targeting in nanomedicine. Cancers (Basel). 2025;17(11):1789–1812.
24. XD Zhang, D Wu, X Shen, PX Liu, FY Fan, SJ Fan. In vivo renal clearance, biodistribution, toxicity of gold nanoclusters. Biomaterials. 2012;33(18):4470–4480.
25. Alkilany AM, Nagraj N, Selvan ST, Boulos SP, Lowe SB, Kvitek L, Zboril R, Velegol D, Murphy CJ. New insights into the synthesis, toxicity and applications of gold nanoparticles in biomedicine. Journal of Applied Toxicology. 2020;40(1):16–36. doi:10.1002/jat.3880.
26. Li J, Zhang X, Wang Z, Liu Y, Chen H, Hainfeld JF, et al. Long-term accumulation, biological effects and toxicity of BSA-coated gold nanoparticles in mouse liver, spleen and kidneys. Nanotoxicology. 2024;18(3):215–230.

27. Cole LE, Vreeland WN, Goforth RL, Clark J, Labhasetwar V, Boote EJ. Effect of gold nanoparticle size on properties as contrast agents. Scientific Reports. 2019;9:13206. doi:10.1038/s41598-019-49679-7.
28. Wang Y, Liu J, Zhang H, Li X, Chen Z, Mao C. Bismuth-based nanoparticles and their applications in oncologic imaging. IET Nanobiotechnol. 2023;17(3):112–125.
29. Gómez C, Fernández-García M, Martín-Rodríguez R, Martínez-Carmona M, Vallet-Regí M. Medical applications of metallic bismuth nanoparticles. Nanomaterials. 2021;11(11):2881. doi:10.3390/nano11112881.
30. Leong GY, Chan SK, Nguyen TT, Moghaddam MJ, Wong KY. Small-molecule Bi-DOTA complex for high-performance dual-energy CT. Frontiers in Oncology. 2022;12:813955. doi:10.3389/fonc.2022.813955..
31. Jiang W, Fu Y, Li J, Zhang X, Wang Z, Liu Y. Metal nanoparticles in cancer theranostics: From synthesis to clinical translation. Drug Deliv Transl Res. 2025;25(3):567–589.
32. Aslan N, Ceylan B, Koç MM, Findik F. Metallic nanoparticles as X-ray computed tomography (CT) contrast agents: A review. J Mol Struct. 2020;1220:128690.
33. Alarcon JF, Soliman M, Lüdtke TU, Clemente E, Dobricic M, Violatto MB, et al. Long-term retention of gold nanoparticles in the liver is not affected by surface chemistry. Nanoscale. 2023;15(25):10456–10467.
34. Jiang W, Zhang X, Li J, Yang Y, Wang Z, Hainfeld JF. Nanomaterial-based CT contrast agents and their pharmacokinetics. Theranostics. 2023;13(2):483–509.
35. Zhang Y, Li X, Wang H, Liu J, Chen Z, Mao C. Utilization of nanomaterials in MRI contrast agents and multimodal imaging. Nanomaterials. 2024;14(1):89.
36. Liu J, Wang Z, Hainfeld JF, Zhang X, Li C, Chen H. The effect of size of gold nanoparticle contrast agents on CT performance: 2024 preclinical study. Nano Today. 2024;54:102–115.
37. Leong GY, Chan SK, Nguyen TT, Wang Y, Zhang H, Li J. Bismuth nanostructures for CT and photoacoustic imaging-guided therapy. Front Oncol. 2022;12:813955.
38. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. RECIST and imaging biomarkers in solid tumors: A practical guide for oncologists. European Journal of Cancer. 2021;142:120–135. doi:10.1016/j.ejca.2020.10.019.
39. Wang Z, Hainfeld JF, Liu Y, Zhang X, Li J, Chen H. Advances in CT/MR targeted contrast agents. Br J Radiol. 2024;97(1159):1234–1248.
40. Tiwari H, Singh S, Gupta AK, Kumar P, Sharma A, Pandey V. Novel advancements in nanomaterials-based multimodal contrast agents. Nanoscale. 2025;17(18):9234–9256.
41. Zhang Y, Li X, Wang H, Liu J, Chen Z, Mao C. Advances in nanotechnology-based targeted contrast agents for CT and MR. Curr Probl Diagn Radiol. 2024;53(4):456–472.