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Gold Nanoparticle Platforms Enabling Targeted Cancer Imaging and Treatment

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Abstract. Gold nanoparticles (AuNPs) combine a high atomic number with tunable surface plasmon resonance, enabling both diagnostic and therapeutic applications in cancer. Their strong X-ray attenuation provides excellent contrast for computed tomography, while near-infrared (NIR) plasmonic absorption allows efficient photothermal conversion for tumour ablation. Versatile surface chemistry supports precise control over size, shape and ligand functionalisation, which governs biodistribution, cellular uptake and therapeutic performance. Clinical pilot studies have shown promising outcomes in focal tumour imaging and minimally invasive photothermal therapy (PTT), and nucleic acid–grafted AuNPs have demonstrated the ability to cross the blood–brain barrier for gene regulation. Despite these advances, key translational challenges remain, including the need for predictable long-term clearance, scalable synthesis with consistent quality, and well-defined regulatory standards. This review summarises current synthesis strategies, critical physicochemical properties and representative biomedical applications of AuNPs, and highlights design principles that will be essential for achieving safe and reproducible clinical deployment.

Keywords: Gold nanoparticles; cancer theranostics; computed tomography imaging; photothermal therapy; clinical translation.

1. Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide, and its management continues to face significant obstacles. Early diagnosis is often hampered by low sensitivity and specificity of conventional imaging modalities, while standard therapies such as chemotherapy and radiotherapy suffer from systemic toxicity and off-target damage to healthy tissues [1]. These limitations have stimulated the exploration of nanotechnology as a means to improve precision in both detection and treatment. Nanomaterials can be engineered with tunable size, shape, and surface chemistry, enabling preferential tumour accumulation through the enhanced permeability and retention effect and allowing multifunctional integration of imaging and therapy within a single platform.

Among the diverse nanomaterials investigated, AuNPs stand out for their unique combination of physicochemical and biological properties. Their high atomic number confers strong X-ray attenuation, providing superior contrast for computed tomography, while localized surface plasmon resonance enables efficient conversion of light into heat for PTT and enhancement of optical imaging signals. The strong affinity between gold and thiol groups facilitates straightforward surface functionalisation with antibodies, peptides, nucleic acids or drugs, granting both colloidal stability and molecular targeting capacity. Importantly, gold exhibits relatively low intrinsic toxicity compared with many other inorganic nanomaterials when properly coated and dosed, which supports its clinical translation [2]. While the enhanced permeability and retention effect facilitates passive accumulation in many preclinical models, its magnitude varies markedly across human tumours and patient populations, motivating designs that combine passive deposition with active targeting or image-guided delivery.

This article provides an updated overview of gold nanoparticle platforms designed for targeted cancer imaging and therapy. Key synthesis strategies and physicochemical characteristics are first summarised, followed by a discussion of their applications in computed tomography, PTT and gene

delivery, and finally an examination of current challenges and future directions toward clinical implementation.

2. Synthesis of Gold Nanoparticles

Gold nanoparticles can be prepared through either top-down or bottom-up routes (Figure 1a). Top-down strategies, including laser ablation and sputtering, fragment bulk gold into nanoscale pieces but generally lack precise control over morphology. As a result, these methods are less relevant for biomedical use and are mainly employed in material science. In contrast, bottom-up synthesis, where nanoparticles are assembled from molecular precursors, is dominant in nanomedicine because it provides tunable size, shape and surface chemistry [3].

Among bottom-up approaches, the Turkevich citrate reduction is the most classical method (Figure 1b). In this process, trisodium citrate reduces chloroauric acid under heating, generating stable colloidal dispersions of nearly spherical AuNPs. The particle size can be adjusted by varying the citrate-to-gold ratio or the reaction temperature. The simplicity, scalability and biocompatibility of this method make it particularly suitable for imaging probes and drug delivery carriers that require monodisperse and functionalizable nanoparticles [3, 4].

Another widely used protocol is the seed-mediated growth method (Figure 1c). Here, tiny gold seeds are first generated with a strong reductant and then transferred into a growth solution containing chloroauric acid, cetyltrimethyl ammonium bromide (CTAB), silver ions and ascorbic acid. Controlled deposition of gold onto these seeds produces anisotropic structures such as nanorods with aspect ratios that can be tuned to shift their longitudinal plasmon resonance into the NIR region [4]. This optical property is crucial for PTT and photoacoustic imaging, where deeper tissue penetration is required. For biomedical use, residual CTAB requires rigorous removal and surface exchange (e.g., PEGylation) to minimise cytotoxicity and improve serum stability.

The Turkevich method is well suited for applications that demand stable spherical nanoparticles for drug and gene delivery, whereas the seed-mediated strategy is advantageous for cancer theranostics that rely on strong optical absorption in the NIR region. These methods provide complementary options for tailoring gold nanoparticles to specific clinical needs.

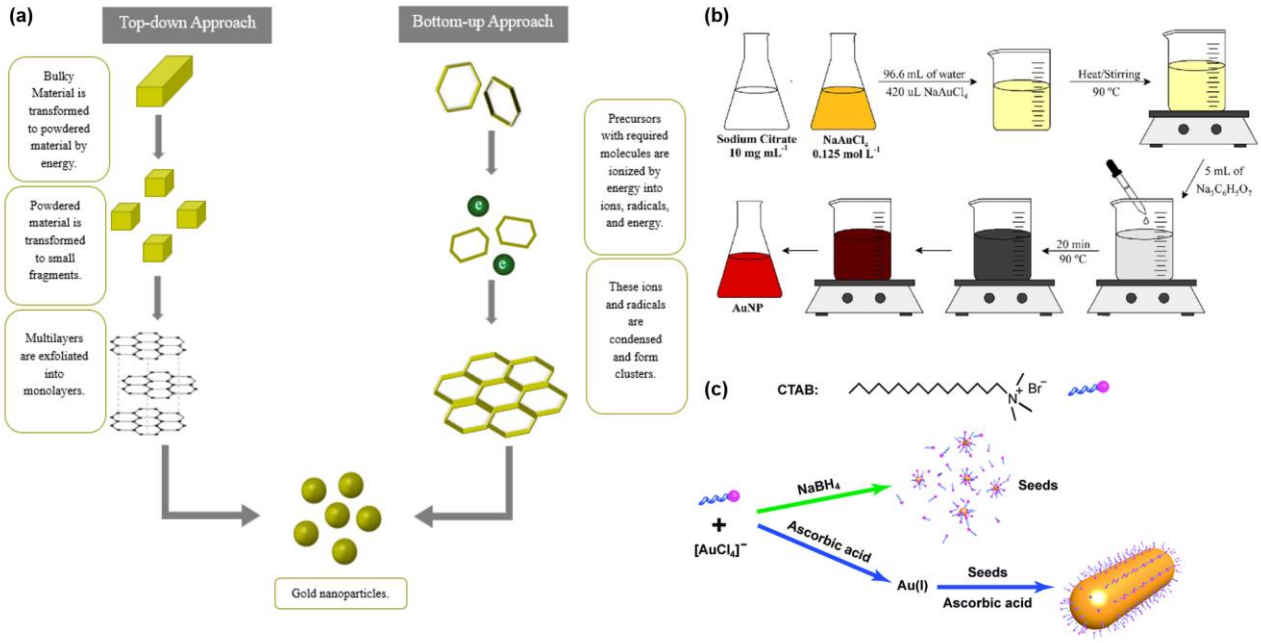

Fig. 1 Synthesis of Gold Nanoparticles (a) Top-down and bottom-up approaches; (b) Turkevich citrate reduction method; (c) Seed-mediated growth method [4, 5, 6]

3. Key Properties of Gold Nanoparticles for Biomedical Use

AuNPs possess distinctive physicochemical features that make them valuable in cancer diagnosis and therapy. A central attribute is their localized surface plasmon resonance (LSPR), generated by collective oscillations of conduction electrons when excited by light. By adjusting particle size and morphology, the LSPR band can be shifted from the visible into the NIR region, which is advantageous for PTT and deep-tissue optical imaging [6].

The gold–thiol affinity enables straightforward functionalization with antibodies, peptides, nucleic acids or drugs, thereby providing targeting ability and enhancing colloidal stability in biological environments. Surface coatings such as polyethylene glycol (PEG) further prolong circulation and reduce immune clearance, improving in vivo performance [2].

Gold is generally biocompatible when appropriately coated, but biological effects remain size- and dose-dependent. Particle diameter strongly influences biodistribution and cellular uptake: spherical AuNPs in the 10–50 nm range are efficiently internalised by cells, while anisotropic structures such as nanorods or hollow particles offer larger surface areas and tunable LSPR for drug delivery and photothermal conversion [4].

Together, the unique optical response, versatile surface chemistry and morphology-dependent biological behaviour establish AuNPs as highly adaptable platforms for precision oncology.

4. Applications in Cancer Diagnosis and Therapy

AuNPs possess tunable plasmon resonance, easily addressable surface chemistry and a high atomic number, enabling both diagnostic and therapeutic functions in cancer theranostics. Their physicochemical versatility allows precise control of size, shape and ligand decoration, which in turn governs circulation half-life, tumour accumulation and multimodal imaging performance.

4.1. Computed tomography imaging

Because gold (Z = 79) exhibits a much higher photoelectric absorption coefficient than iodine in the diagnostic X-ray energy range, AuNPs provide strong and persistent CT contrast when appropriately surface-stabilised [4]. In a representative blood-pool study, PEGylated AuNPs produced bright vascular enhancement that remained visible for more than 24 hours, substantially outlasting iodinated agents [7]. Beyond conventional CT, the high K-edge of gold at 80.7 keV enables photon-counting CT to spectrally separate gold signal from background tissue, allowing sensitive detection of small lesions and quantitative mapping of particle distribution [8]. These capabilities improve pre-operative delineation of tumour margins and longitudinal monitoring of therapeutic response. In practice, achievable sensitivity depends on particle dose, scan protocol and spectral calibration, so quantitative maps should be interpreted alongside pharmacokinetic context. Typical preclinical protocols use gold concentrations in the tens of mg Au per kg range, while human trials to date have remained below this threshold for safety.

4.2. Photothermal therapy

PTT uses AuNP-mediated plasmonic heating to induce local hyperthermia sufficient to kill cancer cells while sparing adjacent structures. Photothermal efficiency can be tuned by particle geometry and surface chemistry, which is why shells, rods and branched structures remain the dominant designs for in vivo applications [8]. Systemic or intralesional administration is followed by image-guided NIR irradiation with temperature-guided titration (e.g., thermal dose metrics such as CEM43) to balance efficacy and safety in heterogeneous tissue.

The therapeutic process is illustrated in Figure 2, which shows tumour-level accumulation, laser activation, cell- and tissue-level injury patterns, and real-time monitoring by ultrasound or photoacoustic imaging [9]. Such intrinsic optical–acoustic signals allow confirmation of nanoparticle localisation and titration of energy delivery. Preclinical studies continue to demonstrate durable

tumour control when NIR exposure follows AuNP administration, and alginate-coated AuNPs can further enhance efficacy when combined with radiotherapy [10]. This diagnostic–therapeutic continuity underpins the theranostic nature of AuNP-mediated PTT.

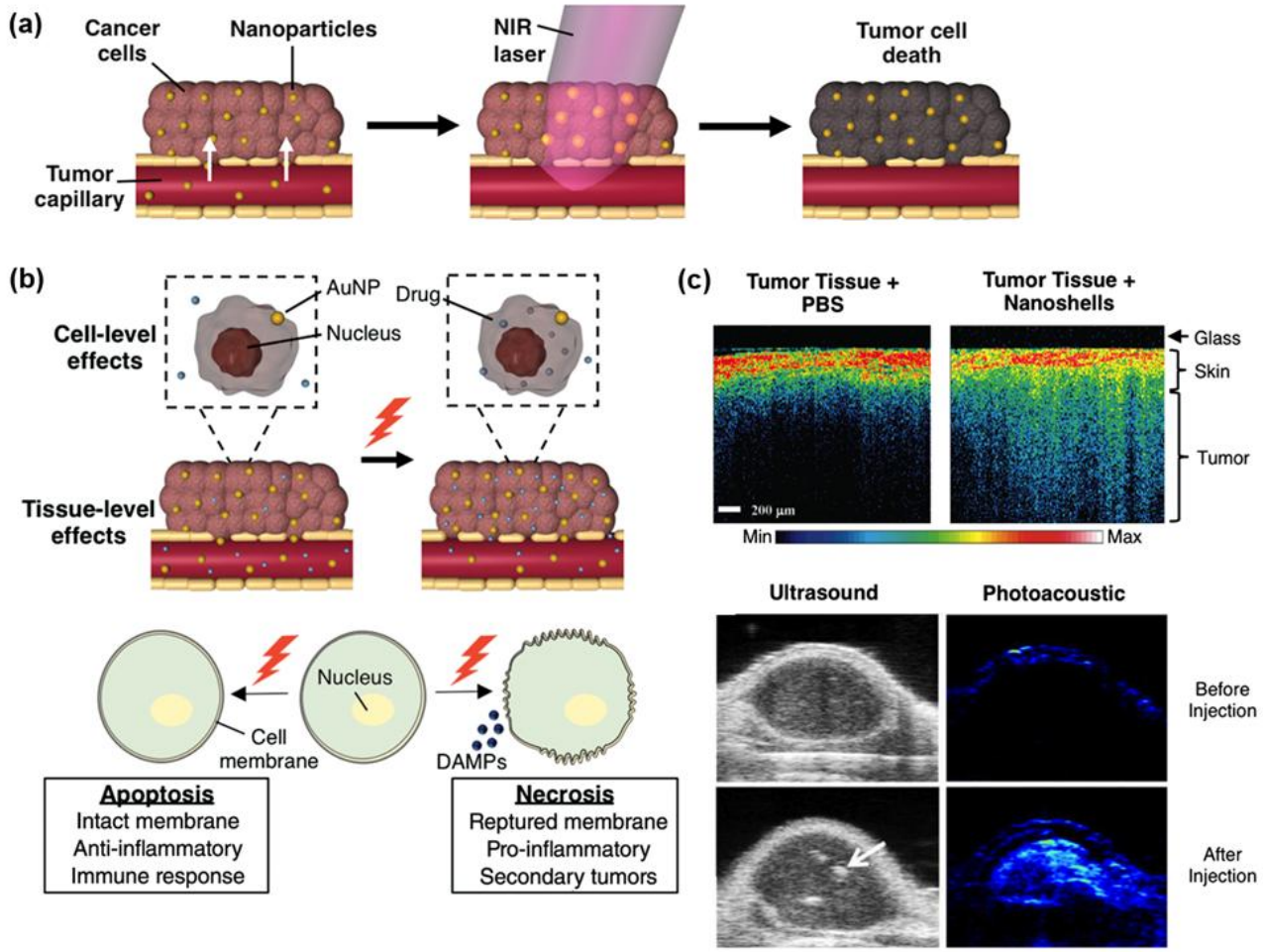

Fig. 2 Gold nanoparticle–mediated PTT (a) Nanoparticle accumulation and NIR laser–induced tumour ablation; (b) Cell- and tissue-level effects showing apoptosis or necrosis; (c) In vivo imaging confirming nanoparticle deposition and photoacoustic signal enhancement [9]

Clinical translation is most advanced with silica–gold nanoshell platforms for focal ablation of prostate cancer. Magnetic-resonance-guided, transperineal nanoshell infusion followed by interstitial laser exposure achieved durable lesion control with preservation of urinary continence and sexual function in a pilot trial [11]. Subsequent imaging studies have documented nanoshell retention and refined procedural parameters, while detailed case reports describe a reproducible two-day workflow and negative biopsy results at six to twelve months [12]. These findings establish PTT as a clinically feasible, image-guided focal-therapy pathway with integrated diagnostic and therapeutic capability.

Mechanistically informed optimisation remains important. Contemporary reviews emphasise that particle size, shell thickness, and polymer stealthing influence circulation time and tumour deposition, while wavelength selection and fluence determine depth and selectivity in heterogeneous tissue [8]. As institutional experience grows, the same gold constructs used for pre-procedural imaging can supply intra-procedural monitoring and the therapeutic effect itself, which positions PTT as a genuinely theranostic intervention rather than an add-on to surgery or external beam radiation [12].

4.3. Molecular and gene therapy

AuNPs can also function as carriers for therapeutic nucleic acids. Spherical nucleic acids (SNAs) protect small interfering RNA (siRNA) from degradation and promote cellular uptake without transfection agents, even enabling penetration of the blood–brain barrier in glioblastoma models [13].

Building on this platform, the first-in-human Phase 0 trial of NU-0129 demonstrated that intravenously administered SNAs reached intracranial tumours and achieved target engagement of the oncogene Bcl2L12 in patients with recurrent glioblastoma [14]. Future studies will need to define dose ceilings, immunostimulation risks and durability of target knockdown to support progression beyond proof-of-mechanism trials.

5. Challenges and Future Outlook

Despite encouraging preclinical and early clinical data, several barriers must be addressed before AuNPs can achieve broad clinical adoption. The long-term fate of AuNPs remains incompletely resolved, and issues such as chronic toxicity, immune activation, organ retention and clearance pathways require systematic and standardised evaluation to define safe exposure windows. From a manufacturing perspective, scalable synthesis with tight lot-to-lot control of size, shape and surface chemistry continues to be a bottleneck that constrains regulatory approval and commercial translation. Clinically, only a few AuNP platforms have reached human studies; for example, a Phase 0 trial of the spherical nucleic acid therapeutic NU-0129 demonstrated intracranial tumour delivery and target engagement in patients with recurrent glioblastoma [14]. In focal ablation, silica–gold nanoshell PTT has shown feasibility and safety in a clinical pilot for localised prostate cancer [11]. Integration of pharmacokinetic imaging with early-phase dose-escalation trials will be critical to link preclinical safety profiles with regulatory expectations. Looking ahead, priorities include engineering biodegradable or renal-clearable gold constructs and validating their in vivo fate with harmonised protocols. Parallel progress in regulatory science, including clear quality standards and internationally accepted characterisation methods, will be essential to accelerate the translation of AuNP-based theranostics from laboratory proof of concept to routine oncology practice [15].

6. Conclusion

AuNPs have evolved from laboratory curiosities into multifunctional platforms for precision oncology. Their high atomic number and plasmonic tunability underpin dual roles in computed tomography imaging and PTT, while nucleic acid–conjugated structures extend their utility to gene modulation. Early clinical studies provide proof-of-concept for real-world translation, demonstrating enhanced imaging sensitivity and effective local tumour ablation. Nevertheless, widespread adoption will depend on the development of biodegradable or renally clearable designs, comprehensive pharmacokinetic and toxicity assessments, and harmonised manufacturing standards. Continued collaboration between material science, molecular oncology and advanced imaging will be critical to convert AuNP-based diagnostics and therapeutics from promising pilot studies into safe, reproducible and widely accessible clinical interventions.

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