



Original Research

Radioactive Gold Nanoparticles for Tumor Therapy: Colloidal Radioactive Gold and Applications of Radiation in Cancer Imaging and Treatment

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Abstract:

It is becoming more and more apparent that gold nanoparticles (GNPs) have the ability to be used in cancer diagnostics and treatment. These biocompatible particles can be readily produced, tailored to suit specific needs, and conjugated to a wide range of biologically relevant compounds to enhance their functionality. Then, either by directly targeting tumor-specific biomarkers or by passively accumulating in leaky tumour arteries and tissue, precise and effective delivery to tumour tissue can be achieved. In addition to boosting the efficacy of radiation therapy, tumor-localized GNPs can be used as contrast agents for several imaging modalities. The current state of GNP as a radiosensitizer and imaging contrast agent, as well as its possible future uses, are the topics of this review. Nanoparticles made of gold have the potential to be a new theranostic adjuvant for use in cancer treatment by radiation because of their biocompatibility and adaptability. About half of all cancer therapies now employ radiotherapy, which involves putting radiation directly into tumour tissue. While it is successful in most cases, photon radiation (gamma and X-rays) in particular can damage healthy tissue outside the tumour region. The use of ion beams in radiation therapy improves results because of their unique energy deposition curve, which produces a concentrated dosage of radiation (a Bragg peak) in a specific area. Nanoparticles and other innovative sensitizers have demonstrated to enhance the localised destructive effects of photon and ion radiation when administered to tumour areas, complementing ion radiotherapy. Because of their biocompatibility, the fact that they can be synthesised using well-established methods in a wide range of sizes, and the fact that they can be coated with a large number of different molecules to partially control things like surface charge or interaction with serum proteins, gold nanoparticles have become one of the most popular nanoparticle systems available.

Keywords: Radioactive Gold Nanoparticles, Colloidal Radioactive, radiation, cancer imaging, tumor therapy

Introduction:

In order to help with cancer detection and treatment, this research will go over some of the latest developments in the field of radioactive gold nanoparticles (NPs) as imaging and therapeutic agents. To improve delivery and retention for effective therapy, nanomedicine makes use of particulate matter with sizes [1] that are comparable to or smaller than cellular components. This allows NPs to pass through various biological barriers. Nanoparticles (NPs) are promising therapeutic possibilities for cellular-level functional disorders because of their size resemblance to cellular components. Delivery and retention have been significant obstacles in cancer treatment [2]. Unfortunately, the current methods have major drawbacks that make it difficult, if not impossible, to deliver enough therapeutic molecules to the tumour site, leading to ineffective treatment. It is critical to enhance the therapeutic payload in order to kill cancer cells for tumour treatment to be effective. Oncologists are able to provide cancer patients with the most effective treatment possible since they have control over the therapeutic payload supply. Nanoparticulates carrying radioactive isotopes offer a chance to adjust the radioactive therapeutic dose given to tumour cells, which is a significant consideration in this context [3]. Type A and type B NP-based radiopharmaceuticals are the two main categories. Biodegradable NPs of organic matrices contain radioisotopes in type A nanoradiopharmaceuticals. One example is the incorporation of dirhenium decacarbonyl [Re₂(CO)₁₀] into biocompatible poly-L-lactide (PLLA) NPs, as demonstrated by Hamoudeh and colleagues. Radioactive rhenium can be produced by neutron irradiation of PLLA NPs laden with rhenium; this radioactive rhenium can then be utilised in cancer treatments (Hamoudeh et al. 2007, 2008). Their research shows that rhenium carbonyl's structural integrity is preserved even after neutron irradiation [4-6]. Direct radioisotope doping into an inorganic NP matrix is the source of Type B NPs. Nanoparticulate matter of this sort incorporates radioisotopes. The radioisotopes in Type B nanoparticulates are created in an

inorganic nanomatrix and can then be attached to antibodies, peptides, or proteins by surface conjugation [7-10]. One possible example is the incorporation of Actinium-225 into a LaPO₄ NP matrix. The discharge of four α -particles and the formation of stable ²⁰⁹Bi are the outcomes of ²²⁵Ac decay. Over the course of one month, the investigation reveals that the La(²²⁵Ac)PO₄ NPs retained around 50% of the daughter nuclides. Another approach is to combine therapeutic ¹⁹⁸Au NPs with a nonradioactive gold nanoparticle (AuNP) matrix to create [¹⁹⁸AuAuNP] NPs [11]. Several animal studies have demonstrated the remarkable therapeutic effects of these radioactive gold NPs. The use of radioactive gold NPs in cancer treatment has recently been the subject of a plethora of research published in journals all around the world.

Liposomes, in contrast to AuNPs, spontaneously form bilayers due to the amphiphilic characteristics of phospholipids, as we discover when comparing methods for generating the two types of nanoparticles. The process of generating AuNPs is not complicated per se, but it does necessitate certain environmental factors. One major perk of AuNPs is the abundance of documented synthesis methods, many of which take environmental factors into account. Because of differences in research timetables, liposomes and auNPs both have many benefits, but they also have different uses and commercialised products. The cytotoxicity of AuNPs is a major drawback that varies with particle size, shape, production processes, and environmental factors. Liposomes, on the other hand, provide flexible targeting choices by being able to concentrate on particular tissues through active and passive methods. The size range of 400-5000 nm presents a significant hurdle for the mononuclear phagocytic system (MPS) when it comes to clearing liposomes. Reducing MPS clearance and increasing their circulatory half-life, PEGylation aids in mitigating opsonization. The most stable metal nanoparticles, gold nanoparticles (Au NPs) display characteristics not seen in larger materials. In detecting applications, where intelligent sensors make use of intrinsic nanoparticle qualities, their

nanometric shape enables a number of desirable aspects. Making your own AuNPs is easy, and you may change their size and shape by adjusting the synthesis parameters. The high surface-to-volume ratio is another striking feature of AuNPs. Because of this, large amounts of targeted functional groups can be immobilised, leading to improved sensitivity and faster reactions to the analyte of interest. By simply adjusting the plasmon resonance, AuNPs can have their optical properties fine-tuned to meet individual requirements. Nanoparticles are perfect for transport scaffolding since they are highly compatible with active molecules, both biologically and chemically. This means that they won't compromise the active coating's functional activity in any way. Multifaceted detection platforms are AuNPs because of their adaptability to colorimetric, fluorimetric, spectroscopic, and electrochemical approaches.

Nuclear Gold:

There are two radioactive isotopes of gold that have medicinal applications: ^{198}Au and ^{199}Au , which can be used to target tumour cells and kill them. ^{198}Au has a 2.7-day half-life and emits 90% β radiation with an average energy of 312 KeV and a peak of 961 KeV. The maximal penetration in soft tissue for ^{198}Au , a short-range β emitter, is 3.8 mm. As the principal cause of the radiating effect in specific regions, half of the β emissions only reach a depth of 0.38 mm. The immediate region immediately surrounding the source is where the therapeutic (or destructive) action of ^{198}Au is most concentrated [12–14]. After being transformed into ^{198}Hg , each ^{198}Au nucleus decays. In order to shift to the stable state, the excited state ^{198}Hg releases a γ -ray with an energy of 0.41 MeV. Although ^{198}Au breaks down to mercury, the nano- to picomolar amounts of mercury produced in the body after therapeutic doses of gold are significantly lower than levels of chemical toxicity. Transport and chemical synthesis are both made possible by ^{198}Au 's 2.7-day half-life, which is sufficient for medical uses. The γ -rays emitted by ^{198}Au and ^{199}Au are both appropriate for use in SPECT imaging, according

to references [15–17]. On the other hand, SPECT imaging experiments using ^{198}Au γ -rays are not ideal since their high energy cannot be collimated efficiently. Since its gamma energy is so similar to that of technetium-99m, the imaging radioisotope most often used, ^{199}Au is well suited for SPECT scans. Dosimetry evaluation of the ^{198}Au analogue and individualised dosage calculations are both made possible by imaging studies with ^{199}Au , which measure the drug's absorption, bio-distribution, and excretion [18, 19]. Since 25-60% of the time, radiation administered without imaging is either too high or too low in dose, this imaging modality leads to a more effective dose delivery.

Prior to administering the therapeutic dose of ^{198}Au -198, imaging with ^{199}Au can be utilised to acquire precise patient dosimetry. Opportunities for the creation of "matched pair" drugs for imaging-therapy are greatly enhanced by gold. In addition to streamlining the regulatory [20,21] processes that lead to FDA approval, developing such matched pairs and dual diagnostic-therapy (theranostic) trials would bring about significant consistency in therapy study follow-up. ^{198}Au and ^{199}Au isotopes are among the select few elements in the periodic table that have the unique ability to emit both therapeutic β and imaging γ ions. The neutron bombardment of pure gold (Au -197), in a research reactor, yields ^{198}Au with a high specific activity.

The creation of ^{198}Au is relatively efficient since natural gold has a high neutron capture cross section (100 barns). Neutron fluxes of 8×10^4 neutrons/cm²s are usually employed throughout irradiation durations ranging from a few hours to days. Approximately 100 mCi/g of radioactive gold is produced when an average of milligrammes of natural gold is irradiated. The conversion rate from gold to ^{198}Au is typically 1 in 3000, though this might vary with irradiation period and flux. Typically, ^{198}Au makes up 90% of radiogold and ^{199}Au the other 10%. This ratio, however, changes with the irradiation duration and neutron flux [22–25]. After being exposed to radiation, only a small percentage of ^{198}Pt atoms

undergo beta decay, resulting in ^{199}Au . Purification is then necessary to remove any remaining platinum from the ^{199}Au . The ^{199}Au decays through β decay, which takes 3.1 days, producing 159- and 208-keV photons with 100- and 23.42-keV relative intensities, respectively. The imaging of tumours makes use of ^{199}Au .

Radioactive Colloidal Gold:

Human patients with tumours have been treated using radioactive colloidal gold. Colloidal gold is a sluggish liquid that may be easily identified as contaminated due to its distinctive deep cherry red colour. It is easily accessible in a nonpyrogenic, sterile form. The size of the finished product, colloidal gold, is not specified. Based on electron microscope measurements, one study found that its size falls into two distinct categories: larger particles, measuring 40 to 90 nm, and smaller particles, measuring 1-1.5 nm [26, 27]. According to other sources, these colloidal particles have a size of around 60 nm, and there are around 2×10^{12} particles per millilitre. Here are the main points of the animal and human study results:

1. Interstitial irradiation with colloidal gold has been administered to prostate cancer patients. With a focus on prostate cancer, Flocks and colleagues have treated over a thousand patients. It was possible to inject the colloidal particles straight into the tumour or its bed. Survival rates of 54% after 5 years and 38% after 10 years were reported in the study, respectively. The use of radioactive gold administered intraperitoneally to treat ovarian cancer has been documented in multiple investigations. The life-saving role of colloidal gold has been established by Muller and colleagues. Patients with primary ovarian cancer who received gold treatment had a better overall survival rate, according to other research. A late recurrence of the cancer can be caused by the aberrant cells discharged by some stage I ovarian carcinomas with intact capsules. Colloidal gold was used to destroy the dangerous cells, which greatly improved overall survival rates [28, 29].

2. Stage-specific survival rates were similar to those seen in the literature in another research of 165 women with ovarian cancer who underwent

surgery and were then given intraperitoneal ^{198}Au . At the 5-year mark, 70% of patients in stage I survived tumor-free; in stages II and III, the corresponding rates were 24% and 18%, respectively [30].

3. External beam radiation and ^{198}Au have been utilised to treat cancer in humans. In a single session, the main tumour can get a high-dose local treatment, and any microscopic metastases in the tumour site can be eradicated with a lower-dose local treatment [31–33]. Patients treated with radioactive ^{198}Au colloid therapy had survival rates that were 14% to 20% greater than those treated with external radiation alone, according to a comparative research comparing ovarian cancer patients treated with the two methods. This pattern appears to be consistent throughout all three stages of patients. Microscopic metastases in the peritoneal cavity are effectively destroyed when ^{198}Au is combined with external beam therapy.

4. Multiple studies looked into the potential toxicity and side effects of treatments including colloidal gold. No research has ever found that therapeutic doses of colloidal gold were hazardous to the liver, spleen, or bone marrow. Human patients' urine or faeces did not exhibit any signs of radioactivity, according to the investigations.

Radioactive Gold in Nanoscale Form:

The design and development of well-defined ^{198}Au NPs for tumour therapeutic applications has recently attracted a lot of attention. It has been reported that two distinct synthetic techniques have resulted in NPs with therapeutic efficacies in animal models [34, 35]. The ability to house several radioactive atoms within a single nanoparticle (NP) is a huge benefit of these tiny radioactive particles. This approach successfully delivers a high therapeutic payload to tumours. Below, you will find details about the ^{198}Au NPs that are nanosized. In order to encapsulate radioisotopes, researchers Bielinska et al. (2002) and Balogh and colleagues (2003) utilised a nanocomposite device (NCD), which produced a nanoparticle with specific dimensions and surface characteristics. Incorporating radioactive ^{198}Au into NCDs has multiple uses: first, as a stabilising

agent to avoid agglomeration; second, as a vehicle to deliver radioactive AuNPs to tumour locations [36]. It is possible to get precise dosing for cell death by manipulating the size of the NCD, which in turn controls the quantity of radioactivity delivered to the tumour site. The targeting ability of the NCD can be preserved while increasing the quantity of radioactive gold atoms using this technique. The production of gold NCDs involves the use of dendritic polymer hosts to immobilise radioactive guests within monodisperse hybrid NPs. Nanocomposites made of commercially accessible polymers, such as tecto dendrimers and poly(amidoamine) PAMAM dendrimers, are utilised to produce NPs. Encapsulating ^{198}Au within PAMAM dendrimers is the key step in this approach for synthesising ^{198}Au NPs. To achieve encapsulation, aqueous solutions of HAuCl_4 and PAMAM dendrimer were mixed in diluted forms. For the dendrimer matrix to successfully encapsulate gold, salt formation between the tetrachloroaurate anions and dendrimer nitrogens is essential. The dendrimer matrix transformed the elemental gold into ^{198}Au during encapsulation [37, 38]. Direct neutron irradiation was used in both the solid and solution phases to convert ^{197}Au to ^{198}Au in NCD.

In tumour models such as mouse B16 melanoma, human prostate DU 145, and human KB squamous cell carcinoma animal xenografts, biodistribution studies utilising 5-nm-sized tritium-labeled PAMAM dendrimers have been conducted. The evidence that radioactive isotope encapsulated nanodevices, like PAMAMs with ^{198}Au radiating from their β channel, could be highly beneficial in tumour therapy was given by the uptake of tritium activity in tumour tissue and the retention of activity for many weeks. Injecting $74 \mu\text{Ci}$ of 22 nm-diameter poly $\{^{198}\text{Au}\}$ into tumours in a mouse model reduced tumour volume by 45% compared to untreated mice, according to a recent study.

The use of radiation for cancer detection and therapy:

Conventional cancer diagnostic and treatment methods rely on computed tomography (CT) scans

and ionising radiation therapy. Adjuvants and complimentary agents would be a wonderful addition to these potentially life-saving procedures because of their limits and the possibility of negative effects. Radiation therapy has the ability to cause normal tissue toxicity and does not always succeed in localising the main tumour, despite substantial technological advancements in this area. When compared to radiation therapy alone, the use of radiosensitizing adjuvants, which increase the dose that is preferentially absorbed by tumour tissue [39], can lead to improved tumour killing with the same total radiation dose. Fast clearance, short imaging periods, high radiation dosage requirements, and inadequate contrast resolution are some of the imaging limitations of classic iodine-based contrast agents (1). Patients could be exposed to lower radiation doses while tumour imaging is made more sensitive and clearer with an agent that has improved X-ray attenuation capabilities. There is a lot of hope for the medicinal and diagnostic uses of gold nanoparticles (GNPs), which are presently the subject of much research.

The Functionalization and Properties of GNPs: Nanoparticles' physicochemical characteristics:

Several beneficial physicochemical features of GNPs give them the ability to fight cancer. To begin, there is strong evidence from both in vitro and in vivo studies that confirm the safety and biocompatibility of gold, which means that GNPs can be safely administered with little inflammatory activation and few systemic or local adverse effects. Second, functionalization with a wide range of biologically relevant molecules enables gold to evade immune detection, improve stability, tumor-targeting, and cross biophysical barriers like the blood-brain barrier, and the metal's easily controllable surface chemistry makes it ideal for this purpose [40]. Thirdly, imaging applications benefit greatly from gold's high atomic number ($\text{Au}, 79$), which permits excellent absorption and intensification of ionising radiation and improved X-ray attenuation. There are several non-radiation based cancer applications that have taken advantage of gold's

surface plasmon resonance and Raman scattering activity (9). These include molecular reporters, drug delivery vehicles, tumor-specific photothermal therapy agents, optical imaging and photoacoustic tomography of tumours, and antiangiogenic agents.

Manufacturing, Functionalization, and Tumour Tissue Administration of GNPs:

The production of uniformly sized and shaped gold nanoparticles, such as nanospheres, nanorods, shells, and cages, is a straightforward process [41]. One of the most well-known ways to create gold nanospheres is via the Turkevich method, which involves reducing aqueous HAuCl₄ with citrate. Another is the Brust-Schiffrin two-phase synthesis method, which involves using NaBH₄ as a reducing agent and a binding agent that contains mercapto. Changing the gold-to-reducing-substance ratio controls the nanosphere size in both approaches. We have used other reductants to increase the yield and tunability of GNPs, and surface ligands like tumor-targeting antibodies to change the functionality and delivery of GNPs, as we will see later on. Additionally, GNPs can functionalize biological molecules like RNA and DNA. Functionalization that makes use of the electrostatic interactions between GNPs and the desired biological molecule to produce GNP bioconjugates is one of various methods for accomplishing this. One instance is the binding of positively charged GNPs to negatively charged and nucleophilic moieties; specifically, GNPs have the potential to interact with the phosphate ester backbone of nucleic acids found in DNA and RNA. There are multiple approaches to achieve the targeted delivery of GNPs to tumour tissue. For the purpose of targeting lung malignancies, direct intratumoral injection and intraperitoneal delivery have been described [42]. An improved permeability and retention (EPR) effect occurs when bare gold nanoparticles given intravenously (IV) accumulate selectively in tumour tissue as a result of the tumor's hallmark leaky fenestrated vasculature and reduced lymphatic clearance. This finding has important clinical implications. As an

illustration, Hainfeld et al. discovered that 1.9 nm GNPs accumulated up to 7 mg Au/g within tumours after a single injection (2.7 g Au/kg body weight), resulting in a selective tumor-to-normal-tissue gold concentration ratio of 8:1. However, the intrinsic heterogeneities of tumour vasculature, particularly in necrotic poorly-vascularized parts of tumour, limit the EPR-dependent passive accumulation technique for bare GNP administration. It is difficult to deliver and maintain sufficient quantities of nanoparticles at the target site due to factors such as fast renal clearance, opsonization, and nonspecific phagocytosis by the reticuloendothelial system (RES). As mentioned earlier, increased interstitial pressure within tumours can potentially act as a barrier to the EPR effect [43]. These constraints have been tackled by utilising various ligands and altering the surface of GNPs. In one example, polyethylene glycol (PEG) coatings GNPs increase their stability and circulatory persistence, which in turn increases their concentration in tumour tissue and creates a hydrophobic barrier that prevents RES phagocytosis and uptake [44]. We found that PEG-coated GNPs injected intravenously into mouse sarcoma tumours might accumulate to concentrations ten times higher than in muscle and fifty times higher than in brain (data not shown). To improve tumour targeting specificity, antibodies can be surface-conjugated to markers that are overexpressed in tumours, like EGF, HER2, and folate. Direct thiol modification of the targeting ligand or attachment of a targeting ligand to GNPs changed within a coating material (e.g., lipid, polymer, etc.) are two common methods for functionalizing gold. To enable the bioconjugation of tumor-targeting EGFR monoclonal antibodies to GNPs, Marega et al. (20) utilised a plasma-polymerized allylamine coating. Grafting thioctic acid and folic acid onto a PEG polymer chain has been used to create folic acid-conjugated GNPs; while Hainfeld et al. coated 15 nm GNPs with PEG and covalently coupled them to anti-Her2 antibodies to create Her2-targeted GNPs. To expand the functionality of GNPs, other ligands that do not target tumours have been used. For example, in a study by Kumar

et al., ultra-small GNPs were loaded with a therapeutic peptide (PMI/ p12) and a targeting peptide (neuropilin-1), allowing for regulated membrane receptor-mediated cellular internalisation [45]. In addition, there have been efforts to direct GNPs towards tumours by taking advantage of the specific tumour microenvironment, which may involve factors such as increased glucose metabolism, low pH, and matrix metalloprotease (MMP) expression. As an example, GNPs that have been 2-deoxy-D-glucose (2DG)-labeled for possible use in cancer

imaging were first described by Ayogan et al. The majority of ligands designed to target overexpressed membrane receptors also improve upon the nonspecific cellular absorption of bare GNPs by increasing receptor-mediated internalisation into tumour cells. Nanoparticle size and physical properties also have a significant impact on internalisation rates. There are a number of approaches that are currently being investigated for the purpose of modifying the geometry, surface modification, and tumor-targeting functionality of GNPs.

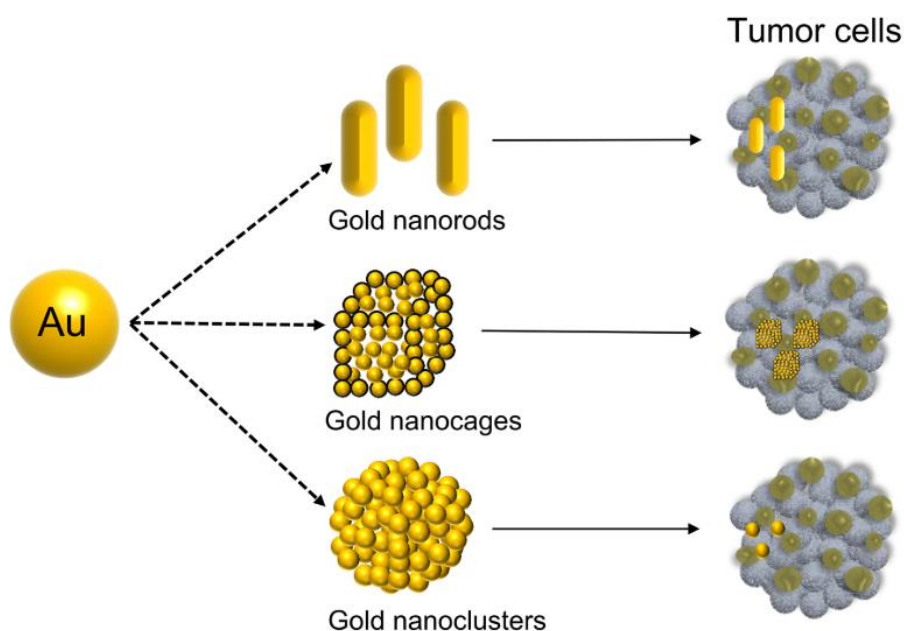


Figure 1. Different shapes of GNPs.

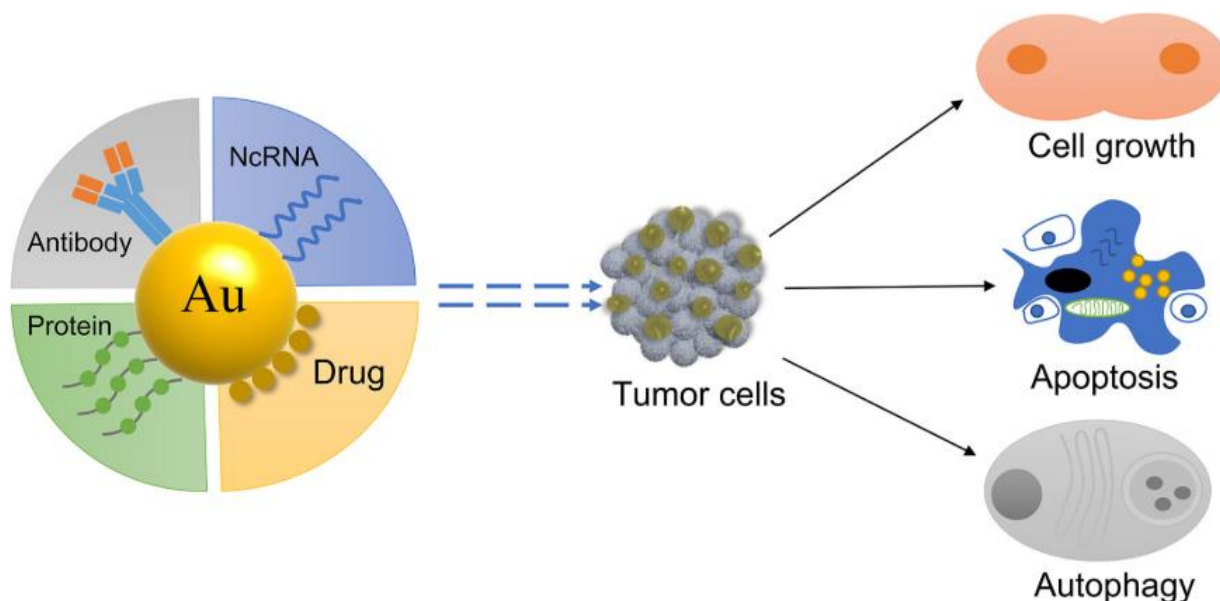


Figure 2. Delivery using GNPs to regulate tumor cell fate.

Radiation sensitivity

Multiple studies have demonstrated that tumour tissue treated with gold nanoparticles increases the effectiveness of radiation therapy in destroying tumour cells in a targeted manner. Radiosensitization is thought to occur due to a higher percentage of primary ionising photon energy being transferred to tumour tissue as a result of enhanced photon absorption of high-Z elements. However, the specific mechanisms behind this effect are still not fully understood. According to Monte Carlo simulations, the dosage enhancement that can be theoretically accomplished with gold radiosensitization is substantial, reaching 200% or even more. Although studies have demonstrated dose increase and radiosensitization at megavoltage (MV) energies as well, the photoelectric mechanism of radiosensitization mainly happens at kilovoltage (kV) energies, which are often less clinically relevant (apart from brachytherapy). With similar dose-enhancing ratios at kV and MV energies, Jain et al. demonstrated cell-specific radiosensitization in MDA-MB-231 cells, which are cancer cells found in breasts. By increasing the radiation dose to the tumour microvasculature and endothelial cells, GNPs can improve the tumor-killing effectiveness of 6 MV X-rays, according to Berbeco et al. Chitthrani demonstrated in vitro that 50 nm GNPs are radiosensitized to both low- and high-energy photons, with dose modification factors (DMF) of 1.66 at 105 kVp and 1.17 at 6 MVp, respectively.

To find the dose enhancement, we subtracted the pre-exposure background dose map from the post-radiation dose map. This was done in the presence of water, PEG vehicle, or PEGylated-GNP (P-GNP) solution on film, and underwent a single 2 Gy treatment. As anticipated, we showed no increase due to the PEG vehicle alone compared to water in a comparison of baseline and post-radiation dose maps of water, PEG alone, and PEG-GNPs. On the other hand, P-GNPs exhibit a notable increase in absorbed dosage in radiochromic film measurements, as depicted in an example dose map image. Using a Varian

TrueBeam system in Flattening Filter Free (FFF) mode, we measured these outcomes for 2 Gy of radiation. Compared to water or PEG alone, P-GNP significantly improves performance. All things considered, this provides preliminary evidence that GNPs can be used for radiosensitization within the MV range of radiation energy that are therapeutically important. The mechanism of higher-energy radiosensitization may be better understood in light of short-range, low-energy Auger electrons that impart a localised, precisely deadly dose. The production of low-energy secondary electrons, which are approximately three times more effective than X-rays in DNA damage, was found to be the primary cause of GNP-induced radiosensitization, according to Zheng et al., and this radiosensitizing mechanism is activated at MV photon beam energies typically employed in radiotherapy. Some have postulated that radiosensitization at MV energies is due to biological processes other than gold's inert photon-absorbing properties. Instead, gold could serve as a biologically active agent that amplifies radiation damage by triggering cellular reactions like accelerated cell cycle, cytokinesis arrest, increased apoptosis, and DNA damage caused by reactive oxygen species (ROS). Preliminary modelling and cell line results indicate that GNPs can also be effective radiosensitizers in the MV range, which has obvious implications for therapeutic radiation therapy, even if there are limited in vivo studies of radiosensitization at higher energy. Radiosensitization and tumour cell death have been studied in cell line and animal models to varying degrees. In 2004, Hainfeld et al. demonstrated for the first time that 1.9 nm GNPs given intravenously increased radiation-induced death of mammary carcinomas in mice, resulting to an 86% 1-year survival rate, compared to 20% with X-rays alone and 0% with gold alone. Subsequently, Chang et al. demonstrated that GNPs aggregate within melanoma cells, which in turn increases the effectiveness of ionising radiation, leading to tumour cell apoptosis, tumour development retardation, and a marked improvement in survival rates in mice with

tumours. Ovarian, prostate, and head and neck squamous cell carcinomas have all demonstrated comparable GNP radioenhancement. Our laboratory's research has demonstrated that brain tumours and glioma cells can be effectively radiosensitized using PEGylated GNPs. This results in increased DNA damage, tumour cell death, and better survival rates, even though these tumours are protected from the circulation by the blood-brain barrier. Interestingly, it has also been demonstrated that proton radiation has a greater impact on tumours loaded with gold, increasing their ability to kill them. Researchers Polf et al. found that compared to cells treated with proton therapy alone, prostate tumour cells that had internalised gold nanoparticles displayed a reduced surviving proportion and an enhanced ionisation density when exposed to proton beams. The relative biological effectiveness of proton therapy with gold-loaded tumour cells is estimated to be 15-20% higher than proton therapy without gold. This effect is attributed to proton-Au scatter interactions and the production of low energy delta-ray electrons, which cause intracellular damage and lower cell survival for any given proton dose [46, 47]. In a more recent study, Kim et al. utilised protons (10-41 Gy) to irradiate tumours in mice that were loaded with gold and iron nanoparticles. They observed various effects, including an increase in intracellular ROS generation, tumour regression, and mouse survival rates, all caused by particle-induced radiation and the release of secondary electrons. Radiation dosage, energy, surface coating, nanoparticle size and shape, tumour type, and the main processes and degree of GNP-induced radiosensitization are expected to be affected by a number of factors. It is possible that radiosensitization and other GNP-assisted processes, including hyperthermia and chemosensitization, operate in tandem. It is becoming more apparent that GNPs have therapeutic potential as safe and effective adjuvants in radiation therapy for cancer, but further research is required to optimise GNP surface architecture and understand the mechanisms underlying gold-enhanced tumour cell death.

Potential avenues for theranostic

Research on GNPs has mostly concentrated on their radiosensitizing or imaging properties; efforts to integrate theranostic anticancer GNP uses have mostly targeted nonradiation based medication delivery with molecular or cellular imaging modalities. While Hainfeld et al.'s principal goal was to show that GNPs might induce radiosensitization of breast cancer, they also discovered that the gold-loaded tumour showed X-ray contrast enhancement, suggesting that GNPs could have imaging uses. Additionally, our lab work has demonstrated that PEGylated-GNPs can serve as a radiosensitizer and CT contrast agent all at once. To further explore the multifunctional theranostic potential of GNPs, future research are still necessary and are being conducted.

Diagnostic and Therapeutic Use of Gold Nanoparticles for Colorectal Cancer

China has maintained a high rate of gastrointestinal cancer-related morbidity and mortality in recent years. The early signs of cancer are sometimes difficult to detect since the gastrointestinal organs, such the stomach, are located deep within the body. Lymph node infiltration and distant metastases are common symptoms at the time of diagnosis, which makes the disease difficult to cure. This highlights the critical need for new technology that can improve the detection and treatment of gastrointestinal cancer and, in the long run, lower cancer mortality rates. By transporting medications and nucleic acids to cancer cells and tissues, gold nanoparticles (GNPs)—a form of nanocarrier with exceptional biocompatibility and distinctive optical characteristics—may impact the course of cancer. Exploring new avenues for cancer treatment, GNPs serve as a trustworthy visualisation agent that can monitor medications and precisely pinpoint the location and extent of malignancy. Further applications of GNPs include photothermal therapy and photodynamic therapy for photosensitizer delivery. For this reason, GNPs are a promising new nanomaterial for the detection and treatment of gastrointestinal cancer.

Based on the "2020 Global Cancer Report" that was recently published by the International Agency for Research on Cancer (IARC) of the World Health Organisation, the following will be the top ten cancer cases in China in 2020: cancers of the cervix, gallbladder, oesophagus, thyroid, pancreas, and lungs (the World Cancer Report 2020 was released by the World Health Organisation and the International Agency for Research on Cancer). People who are sedentary, overweight, drink excessively, smoke cigarettes, have a history of helicobacter pylori infection, eat a diet high in sugar and low in fibre, and have a high cancer risk for the gastrointestinal tract account for the majority of cases. The prognosis and quality of life of patients are greatly affected by the late diagnosis, which occurs when the disease has progressed significantly. Accelerating the diagnosis and treatment of gastrointestinal malignancies is crucial for lowering the cancer rate, fewer deaths from the disease, and better patient survival. The exceptional sensitivity and effectiveness of noble metal nanoparticles in imaging, diagnosis, and treatment have garnered considerable interest in cancer medical research in the last several years. The simplicity of manufacturing, excellent biocompatibility, unique optical features, and surface plasmon resonance (SPR) qualities of gold nanoparticles (GNPs) make them frequently used, especially in cancer research. For various malignancies, specialised GNPs have been developed. The integration of cancer diagnosis and treatment is made possible by the utilisation of surface receptor expression, tumour environment, photodynamic therapy, gene therapy, targeted therapy, photothermal therapy, immunotherapy, and a combination of other treatments. The use of GNPs in the treatment of gastrointestinal cancer is the subject of this review.

Conclusion:

The unique diagnostic and therapeutic capabilities of gold nanoparticles make them promising candidates for use in a range of cancer-related contexts. Biocompatibility, ease of synthesis and modification, and a high Z coefficient are just a

few of the appealing physicochemical features of these nanoagents. However, before they can be used in clinical settings, we still don't know enough about their safety mechanisms or how they become radiosensitive at different energy levels. While their versatility has not yet been completely investigated, GNPs show promise as a theranostic adjuvant for use in radiation-based cancer diagnostics and treatments. These prospective theranostic drugs are presently the subject of intensive investigation as we work to bring them closer to clinical deployment.

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