A PROJECT REPORT ON

ADVANCEMENTS IN GOLD NANOPARTICLE FOR CANCER DETECTION AND PHOTOTHERMAL THERAPY-BASED TREATMENT

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Guided By:-
Dr. Binaya ku. Sahu
Asst. Professor in Physics
Panchayat Degree College,
Bargarh

Submitted By:-
Name - Saraswat Meher
Roll No - S04521PHY022
Class - BSc 6th Semester

Advancements in AuNPs for Cancer Detection and Photothermal Therapy-Based Treatment:

by

Saraswat Meher
Roll No – S04521PHY022

A Project Report Submitted to
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NAME: SARASWAT MEHER

ROLL NO: S04521PHY022

SIGN:

ABSTRACT:

Gold is a multifunctional material that has been utilized in medicinal applications for centuries because it has been recognized for its bacteriostatic, anticorrosive, and antioxidative properties. **Gold nanoparticles (AuNPs)** are attractive photothermal agents for cancer therapy because they show efficient local heating upon excitation of surface plasmon oscillations. The strong absorption, efficient heat conversion, high photostability, inherent low toxicity and well-defined surface chemistry of AuNPs contribute to the growing interest in their photothermal therapy (PTT) applications. **Photothermal therapy (PTT**), in which nanoparticles embedded within tumours generate heat in response to exogenously applied laser light, has been well documented as an independent strategy for highly selective cancer treatment. Gold-based nanoparticles are the main mediators of PTT because they offer:

1. Biocompatibility
2. Small diameters that enable tumour penetration upon systemic delivery,
3. Simple gold-thiol bioconjugation chemistry for the attachment of desired molecules
4. Efficient light-to-heat conversion
5. The ability to be tuned to absorb near-infrared light

Which penetrates tissue more deeply than other wavelengths of light. Gold NPs-mediated PTT has recently been evaluated in combination with other therapies, such as chemotherapy, gene regulation, and immunotherapy, for enhanced anti-tumour effects. It can enhance the therapeutic success of both PTT and the secondary treatment while lowering the required doses of the individual agents, leading to fewer off-target effects. Given the benefits of combining gold nanoparticle-mediated PTT with other treatment strategies, many exciting opportunities for multimodal cancer treatment are emerging that will ultimately lead to improved patient outcomes.

Keywords: Cancer, Photothermal Therapy (PTT), Detection, Tumor, AuNPs.

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1. INTRODUCTION:

An imperative and burgeoning worldwide problem, **Cancer** is a leading cause of morbidity and mortality and is currently responsible for one in six global deaths. In 2018, there were 18.1 million new cases and 9.6 million deaths, figures that are expected to increase in the next few decades. The ICMR-NCDIR-NCRP pulls the data through 36 PBCRs (Population-based cancer registry) and 236 HBCRs (Hospital-based cancer registry). The approximate projected cases of cancer in India were 1,392,179 (~1.4 million) in the year 2020, leading to 850,000 (~0.85 million) deaths due to cancers. The five leading cancers in India, as per reported data, were breast, lung, mouth, cervix uteri, and tongue. The sex-based incidences reported were 679,421 male patients and 712,758 female patients. **Breast** and **Cervix uteri** cancers were the most common cancer types in females in India.

1.1 OVERVIEW OF TRADITIONAL METHODS OF CANCER DETECTION AND TREATMENT:

Cancer remains one of the most significant health challenges globally, with millions of new cases diagnosed each year. Traditional methods of detection primarily rely on invasive procedures such as biopsies and imaging techniques like X-rays and MRI scans. While these methods have been essential in diagnosing cancer, they often come with limitations such as invasiveness and limited sensitivity.

Treatment modalities for cancer include surgery, chemotherapy, radiation therapy, immunotherapy, targeted therapy, and hormone therapy. However, these treatments can be associated with significant side effects and may not always effectively eradicate cancer cells, especially in advanced stages.

1.2 IMPORTANCE AND SIGNIFICANCE OF GOLD NANOPARTICLE TECHNOLOGY:

In the field of cancer detection and treatment has experienced significant advancements with the introduction of gold nanoparticle (AuNP) technology. In the realm of cancer detection, AuNPs provide heightened sensitivity and specificity, enabling the precise identification of cancer biomarkers. Consequently, novel diagnostic techniques have been developed, capable of detecting cancer at its early stages when treatment is most effective. Moreover, Advances in gold nanoparticle (AuNP) technology have revolutionized cancer treatment by offering novel and targeted therapeutic approaches.

Gold nanoparticles possess unique properties that make them well-suited for use in cancer therapy. Furthermore, gold nanoparticles can be functionalized with targeting ligands or therapeutic payloads, allowing for precise delivery of drugs or genes to cancer cells. This targeted drug delivery approach enhances the efficacy of chemotherapy and reduces off-target effects, thereby improving patient tolerance to treatment and overall quality of life.

1.3 OBJECTIVE AND SCOPE OF THIS PROJECT:

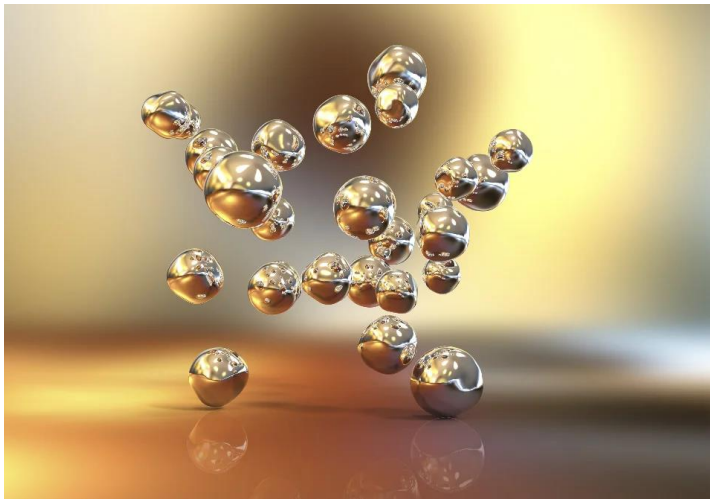
The objective of this project is to explore the advancements in gold nanoparticles (AuNPs) technology and their significance in cancer detection and treatment.

The project aims to:

a) Investigate the latest developments in AuNP synthesis methods, functionalization techniques, and targeting strategies.
b) Evaluate the efficacy of AuNP-based approaches in cancer detection through various diagnostic modalities.
c) Assess the role of AuNPs in photothermal therapy (PTT) and their potential as targeted therapeutic agents in cancer treatment.
d) Explore the challenges and future directions in the field of AuNP-based cancer detection and treatment.
e) Provide insights into the significance of AuNP technology in improving early detection rates, treatment outcomes, and patient quality of life in cancer care.

The scope of this project encompasses a comprehensive review of the literature, including research articles, review papers, and clinical studies, to gather insights into the current state-of-the-art in AuNP-based cancer detection and treatment

2. FUNDAMENTALS OF GOLD NANOPARTICLES (AuNPs):



Gold nanoparticles (AuNPs) are nanoscale particles composed of gold atoms arranged in various shapes and sizes. Their unique physical, chemical, and optical properties have garnered significant attention in biomedical research, particularly in the field of cancer detection and treatment. AuNPs exhibit surface plasmon resonance, a phenomenon that allows them to absorb and scatter light, making them highly suitable for imaging and sensing applications. Additionally, AuNPs can be easily functionalized with targeting ligands and therapeutic agents, enabling precise delivery to specific cellular targets. Their biocompatibility and tuneable surface chemistry further enhance their utility in biomedicine. As a result, AuNPs hold immense potential for revolutionizing cancer detection and treatment, offering personalized and targeted approaches for improved patient outcomes.

2.1 CHARACTERISTICS OF GOLD NANOPARTICLES (AuNPs):

Gold nanoparticles (AuNPs) possess unique characteristics that make them highly valuable for various applications in science and technology, which make them versatile and valuable materials for a diverse range of scientific and technological applications. These characteristics include:

a) **Size and Shape Control:** AuNPs can be synthesized with precise control over their size and shape, ranging from a few nanometres to several hundred nanometres. This tunability allows for customization of their properties for specific applications.
b) **Surface Plasmon Resonance (SPR):** AuNPs exhibit a phenomenon called surface plasmon resonance, where oscillations of conduction electrons on the nanoparticle surface interact with incident light, leading to strong absorption and scattering in the visible and near-infrared regions of the electromagnetic spectrum.

c) **Stability:** Gold nanoparticles are inherently stable due to the strong covalent bonds between gold atoms. Surface functionalization with various ligands or coatings further enhances their stability and dispersibility in different solvents and biological environments.

d) **Biocompatibility:** AuNPs are generally considered biocompatible and non-toxic, making them suitable for biomedical applications such as drug delivery, imaging, and therapy. Their biocompatibility stems from the inert nature of gold and the ease of functionalization with biocompatible molecules.

e) **Optical Properties:** The optical properties of AuNPs, including their colour, intensity, and wavelength of absorption and scattering, can be finely tuned by adjusting their size, shape, and surface chemistry. These optical properties are exploited in various applications such as biosensing, imaging, and photothermal therapy.

f) **Surface Chemistry:** The surface of gold nanoparticles can be functionalized with a wide range of molecules, including ligands, polymers, and biomolecules, to impart specific properties or functionalities. This versatility enables the design of AuNPs with tailored surface properties for targeted applications.

Figure 1: Desirable properties of Gold Nano-particles (AuNPs).

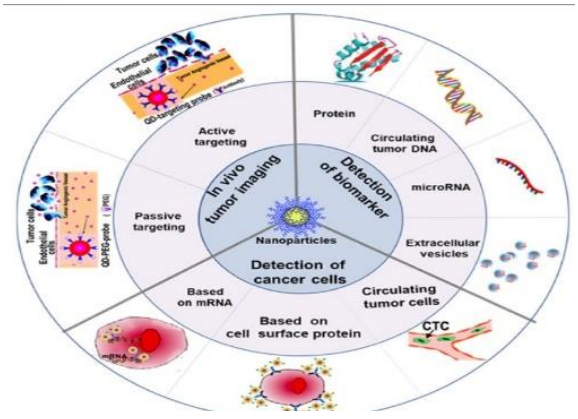


Figure 2: Schematic illustration of GNPs in cancer detection & treatment

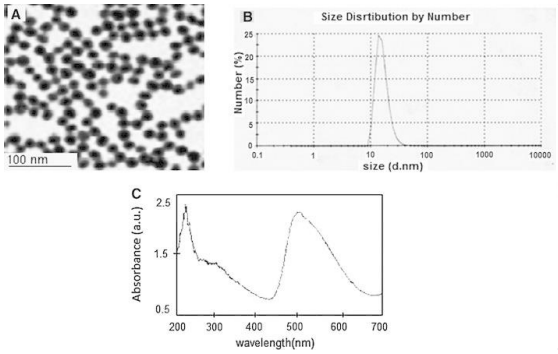


Figure 3: Characteristics of gold nanoparticles. a TEM image of gold nanoparticle, b the size distribution of GNPs determined by DLS instrument, c light-absorbance spectrum of Glu-GNPs recorded by an UV–visible spectrophotometer

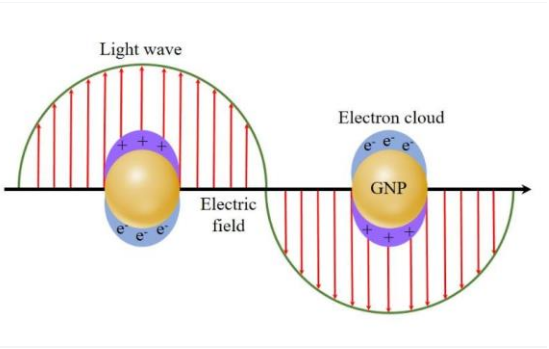


Figure 4: The Surface Plasmon Resonance (SPR) property of AuNPs. The spectrum shows the characteristic absorption peak indicative of SPR, typically observed in the UV-visible spectrum.

2.2 SYNTHESIS OF GOLD NANO PARTICLES:

Synthesis Methods and Characteristics of Gold Nanoparticles (AuNPs):

I. Synthesis Approaches:

a. Chemical Reduction: The reduction of gold ions utilizing a reducing agent in the presence of a stabilizing agent to produce AuNPs.
b. Physical Techniques: Various techniques like laser ablation, sputtering, and evaporation for generating AuNPs physically without chemical reagents.
c. Bio Synthesis: Employing biological agents like bacteria, fungi, plants in the reduction of gold ions and producing stable and biocompatible AuNPs.
d. Microwave-Assisted Synthesis: Fast and efficient method using microwave irradiation to synthesize AuNPs, enhancing control over size and shape.

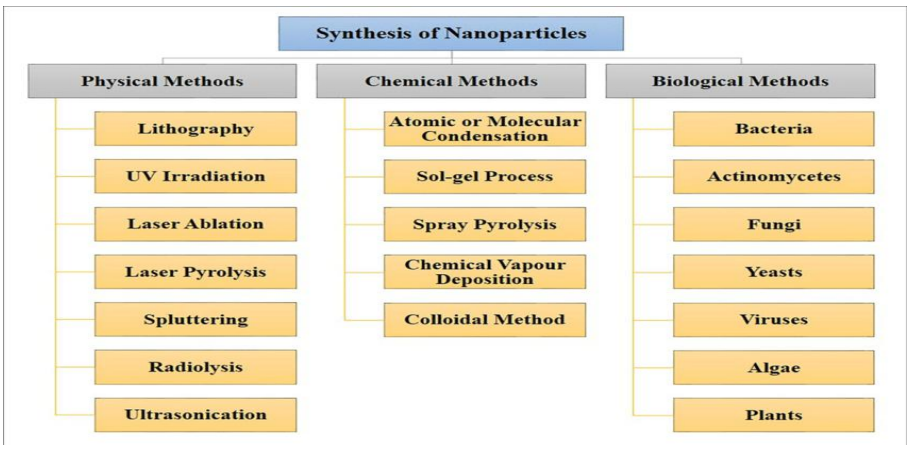


Figure 5: Different methods of Nano-particles (NPs) synthesis.

3. CANCER DETECTION USING GOLD NANOPARTICLES (AuNPs):

Gold nanoparticles (AuNPs) have gained significant attention in the field of cancer detection due to their unique optical, electronic, and chemical properties. The principles and mechanisms of AuNP-based cancer detection involve several strategies, including their use in imaging, sensing, and therapeutic applications.

3.1 PRINCIPLES OF GOLD NANOPARTICLE-BASED CANCER DETECTION:

Here are some key principles and mechanisms:

I. **Surface Plasmon Resonance (SPR):** AuNPs exhibit a phenomenon called surface plasmon resonance (SPR), which arises from the collective oscillation of electrons on the nanoparticle surface when excited by light. This property results in strong absorbance and scattering of light at specific wavelengths, making AuNPs highly suitable for optical detection methods.

II. **Surface Functionalization:** AuNPs can be functionalized with various biomolecules such as antibodies, peptides, aptamers, or small molecules that specifically target cancer cells or biomarkers associated with cancer. These functionalized AuNPs enable selective binding and detection of cancer-related molecules, enhancing the sensitivity and specificity of detection.

III. **Colorimetric Detection:** AuNPs exhibit a distinctive colour change in response to alterations in their local environment, such as aggregation or dispersion. This property is exploited in colorimetric assays for cancer detection, where the presence of target molecules leads to aggregation or dispersion of AuNPs, resulting in a visible colour change that can be detected with the naked eye or spectrophotometrically.

IV. **Surface-Enhanced Raman Scattering (SERS):** AuNPs can significantly enhance the Raman scattering signal of nearby molecules through the electromagnetic field enhancement effect, known as surface-enhanced Raman scattering (SERS).

V. **Photothermal Therapy (PTT):** AuNPs can absorb light energy and convert it into heat, leading to localized hyperthermia that can selectively destroy cancer cells while sparing surrounding healthy tissues. This photothermal therapy (PTT) approach relies on the passive accumulation of AuNPs in tumour tissues via the enhanced permeability and retention (EPR) effect or active targeting strategies.

VI. **Nanoparticle-Based Imaging:** AuNPs can serve as contrast agents for various imaging modalities, including computed tomography (CT), magnetic resonance imaging (MRI), and photoacoustic imaging. Their high X-ray attenuation coefficient and tuneable optical properties make them valuable tools for non-invasive cancer imaging with high spatial resolution and sensitivity.

VII. **Biosensing Platforms:** AuNPs can be integrated into biosensing platforms such as electrochemical, piezoelectric, or surface plasmon resonance-based sensors for the detection of cancer biomarkers in bodily fluids like blood or urine. These sensors offer rapid, sensitive, and portable detection capabilities suitable for point-of-care diagnostics.

AuNPs offer versatile platforms for cancer detection through a combination of their unique physicochemical properties, surface functionalization strategies, and integration into various detection and imaging modalities. These approaches hold promise for early cancer diagnosis, personalized medicine, and monitoring of therapeutic responses.

3.2 TYPES OF CANCER BIOMARKERS TARGETED BY GOLD NANOPARTICLES (AuNPs):

Gold nanoparticles (AuNPs) have garnered significant attention in the field of cancer detection due to their unique optical, electronic, and surface chemistry properties. They can be functionalized with various biomolecules, enabling specific targeting of cancer biomarkers. Some types of cancer biomarkers targeted for detection using gold nanoparticles include:

I. **Proteins:**
   a. PSA (Prostate-Specific Antigen): Elevated levels of PSA are associated with prostate cancer. AuNPs functionalized with antibodies against PSA can selectively bind to PSA, leading to a change in their optical properties, which can be detected.
   b. CEA (Carcinoembryonic Antigen): Increased levels of CEA are found in various cancers, including colorectal, pancreatic, and lung cancers. AuNPs conjugated with anti-CEA antibodies can detect CEA levels in biological samples.

II. **Nucleic Acids:**
   a. miRNA (MicroRNA): Dysregulated expression of miRNAs is implicated in cancer development and progression. AuNPs functionalized with complementary DNA sequences can hybridize with target miRNAs, causing aggregation of nanoparticles, which can be detected by changes in absorbance or colour.
   b. DNA mutations: Specific DNA mutations are associated with certain cancers. AuNPs can be functionalized with DNA probes complementary to mutated sequences, allowing for the detection of mutated DNA fragments.

III. **Cell Surface Receptors:**
   a. Epidermal Growth Factor Receptor (EGFR): Overexpression of EGFR is observed in various cancers. AuNPs conjugated with EGFR-targeting ligands can bind to cancer cells expressing EGFR, facilitating cancer cell detection.
   b. HER2/neu: Amplification of the HER2/neu gene is found in breast and ovarian cancers. AuNPs functionalized with anti-HER2 antibodies can specifically bind to HER2/neu receptors on cancer cells.

IV. **Exosomes:** Exosomal proteins and nucleic acids: Exosomes, small extracellular vesicles released by cells, carry biomolecules indicative of the parent cell's physiological state, including cancer cells. AuNPs can be modified to bind to specific proteins or nucleic acids enriched in cancer-derived exosomes, enabling the detection of cancer-specific exosomes.

V. **Metabolites:** Small molecule metabolites: Altered metabolic pathways are a hallmark of cancer. AuNPs functionalized with receptors or ligands specific to cancer-associated metabolites can be used for detecting these metabolites in biological samples.

VI. **Tumour-Associated Antigens:** CA125: Elevated levels of CA125 are associated with ovarian cancer. AuNPs functionalized with anti-CA125 antibodies can selectively bind to CA125, aiding in the detection of ovarian cancer.

More few examples of cancer biomarkers targeted for detection using gold nanoparticles are: Hormones, Glycoproteins, Angiogenesis Markers, Transcription Factors, Circulating Tumour Cells (CTCs), Oncogenes, Tumour Suppressor Genes, Apoptosis Markers. The versatility of AuNPs allows for the development of various detection assays with high sensitivity and specificity, holding promise for early cancer diagnosis and personalized medicine.

3.3 TECHNIQUES EMPLOYED FOR DETECTION:

Gold nanoparticles (AuNPs) have gained significant attention in the field of cancer detection due to their unique optical, electronic, and surface properties. Various techniques are employed for detecting cancer using AuNPs, they are as follows:

I. **Surface-enhanced Raman spectroscopy (SERS):** It is a powerful analytical technique that enhances the Raman scattering signal of molecules adsorbed on or near nanostructured metallic surfaces, such as gold nanoparticles (AuNPs). In the context of cancer detection, SERS-based techniques utilize AuNPs functionalized with specific targeting molecules (e.g., antibodies, aptamers) to selectively bind to cancer biomarkers, enabling sensitive and specific detection of cancer cells or biomolecules associated with cancer.

   Here's how SERS works in cancer detection:

   a. Functionalization of AuNPs: AuNPs are functionalized with molecules that have affinity towards cancer-specific biomarkers. This functionalization ensures the selective binding of AuNPs to cancer cells or biomolecules.
   b. Targeting Cancer Biomarkers: The functionalized AuNPs are introduced to biological samples (e.g., blood, tissue), where they specifically bind to cancer biomarkers present in the sample.

c. SERS Detection: The presence of the bound AuNPs is detected using SERS. When illuminated with a laser, the AuNPs produce intense Raman scattering signals due to the localized surface plasmon resonance (LSPR) effect. This enhanced signal provides sensitive detection of the cancer biomarkers.
d. Signal Analysis: The Raman spectra obtained from the SERS measurements are analysed to identify the presence and concentration of cancer biomarkers, allowing for the diagnosis and monitoring of cancer.

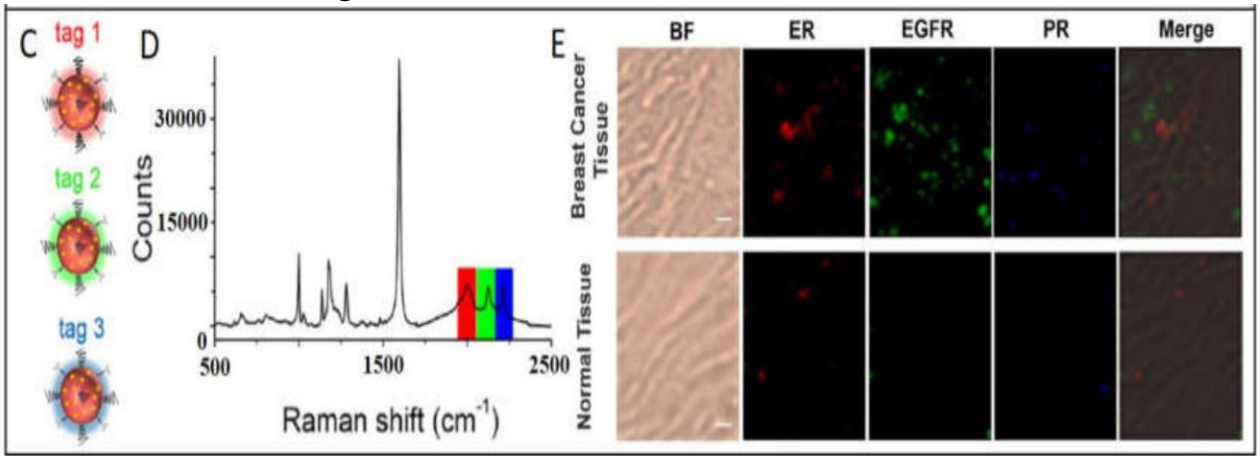


Figure 6: (**C**) Au NPs 60 nm in size are functionalized with three different SERS tags/antibodies. (**D**) The SERS spectrum of the mixture of tag1, tag2, and tag3. (**E**) Multiplex profiling of ER, EGFR, and PR expression in breast cancer tissue and normal tissue sections after treatment with a mixture of tag 1, tag 2, tag 3.

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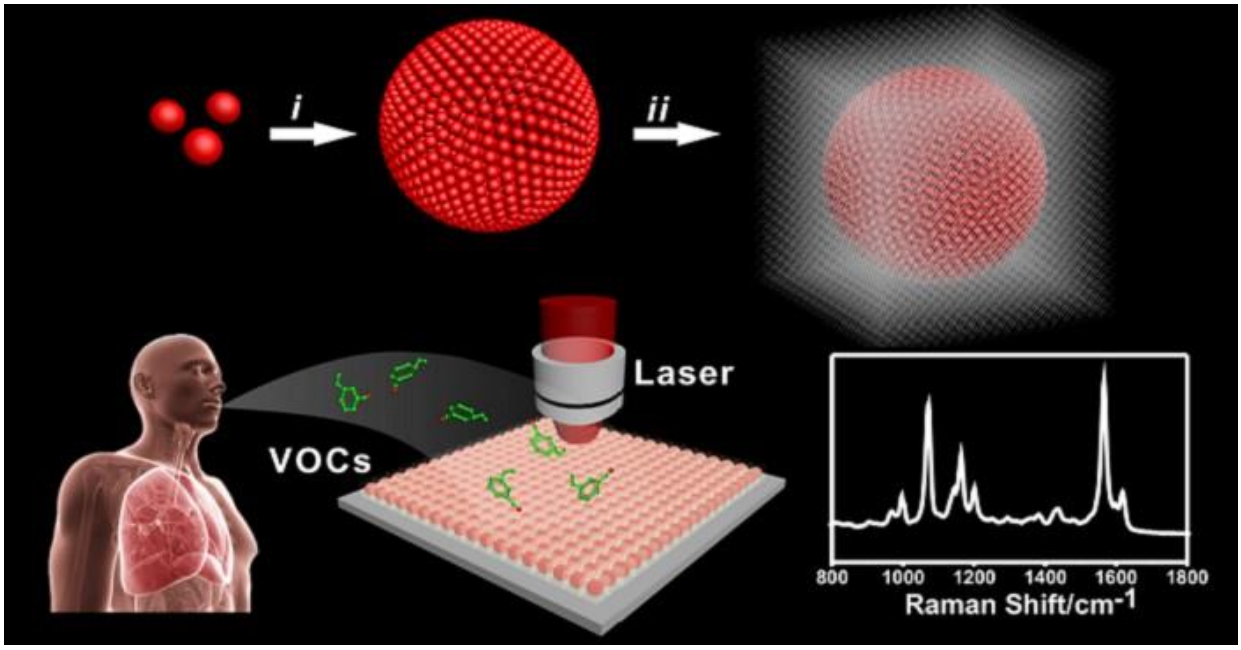


Figure 7: A biosensor based on SERS to detect lung cancer volatile organic compound (VOC) from exhaled breath

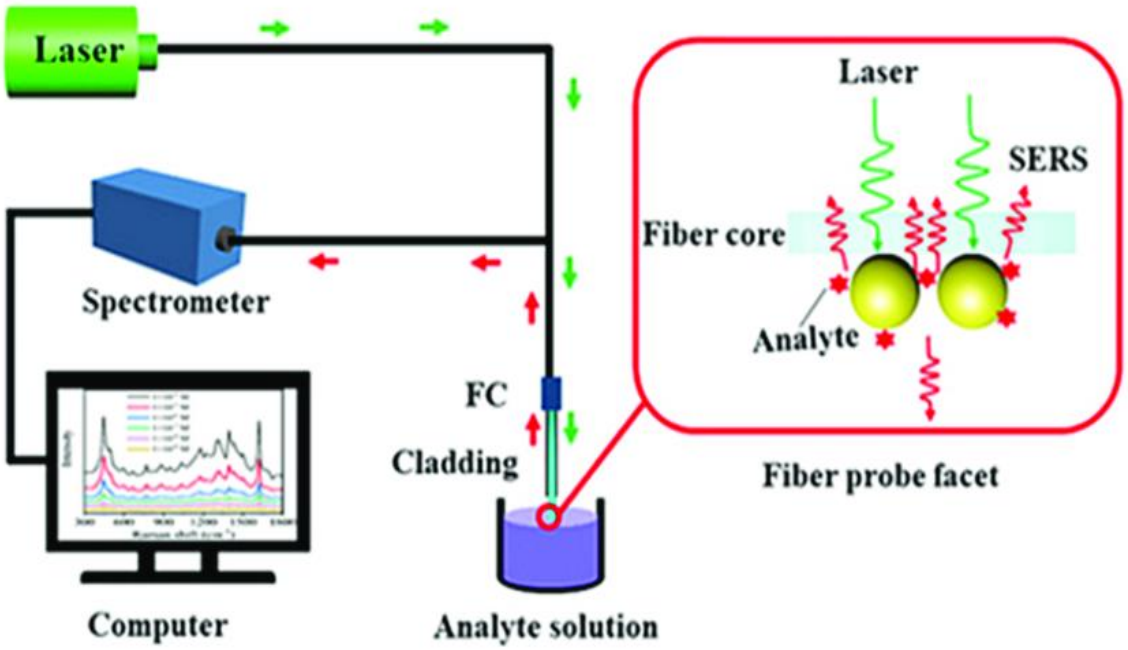


Figure 8: Schematic of experimental set up of SERS sensor based on reflection mode using Analyte solution

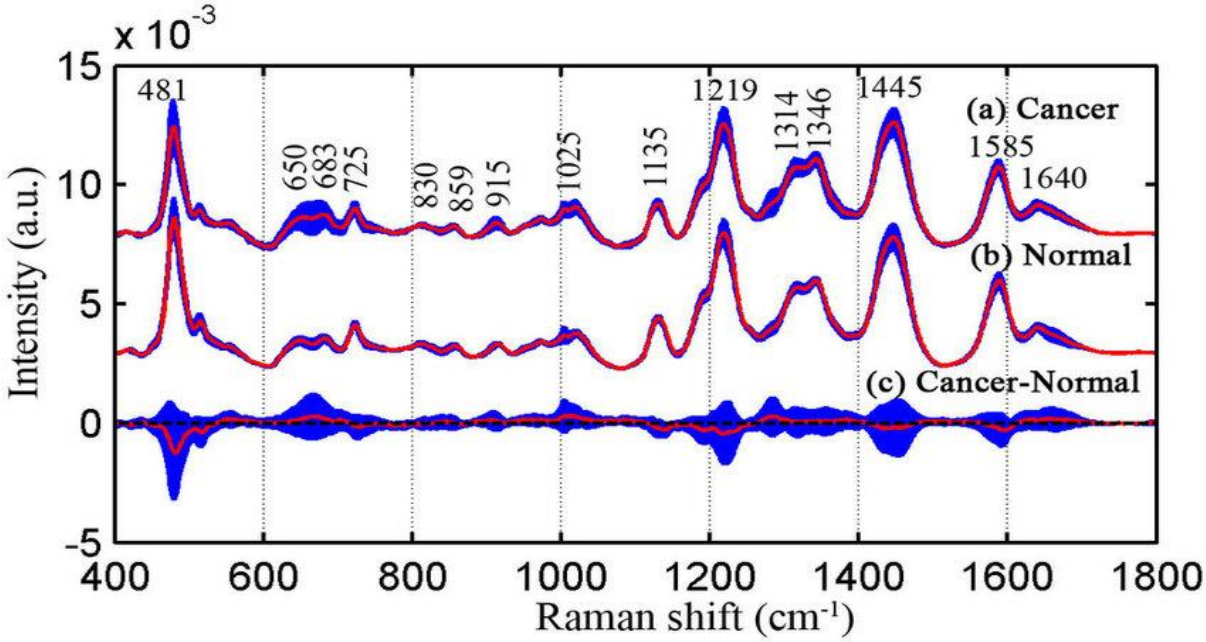


Figure 9: Normalized average SERS spectra of 55 cancer and 36 normal serum samples. (a) Cancer, (b) normal, (c) difference spectra of cancer-normal, shade area represents the standard deviations

Advantages of SERS-based cancer detection using AuNPs include high sensitivity, specificity, and multiplexing capability. Additionally, it enables label-free detection of biomolecules and can be performed in complex biological samples.

II. **Colorimetric Assays:** Colorimetric assays utilize the change in colour or absorbance of AuNPs upon interaction with specific cancer biomarkers. This change can be visually observed or quantified using spectrophotometry, offering a simple and rapid detection method.

III. **Lateral Flow Assays (LFAs):** LFAs employ AuNPs conjugated with cancer-specific antibodies or aptamers to capture target biomarkers present in biological samples. The formation of antibody-antigen or aptamer-target complexes results in visible colour changes on the test strip, enabling rapid and point-of-care cancer detection.

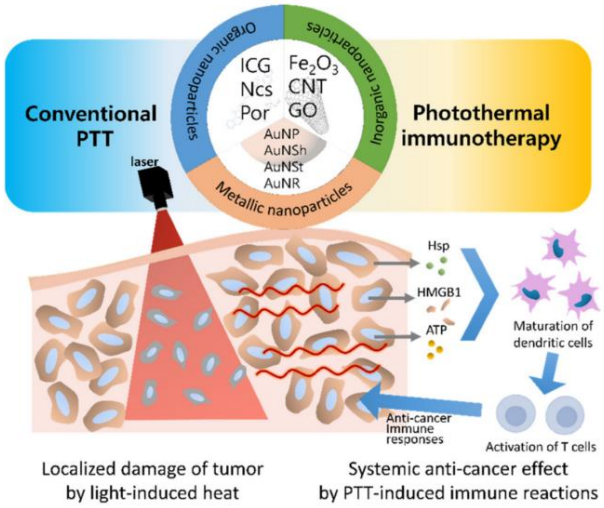
IV. **Fluorescence Resonance Energy Transfer (FRET**): FRET involves the transfer of energy between fluorophores and AuNPs when they are in close proximity. By conjugating fluorophores with cancer-specific probes and AuNPs, FRET-based assays can detect cancer biomarkers with high sensitivity and multiplexing capability.

V. **Electrochemical Detection:** AuNPs can serve as excellent substrates for electrode modification, facilitating sensitive and selective electrochemical detection of cancer biomarkers. This label-free technique offers advantages in terms of simplicity, portability, and cost-effectiveness.

VI. **Magnetic Resonance Imaging (MRI) Contrast Agents**: AuNPs can be functionalized with MRI contrast agents to enhance the imaging contrast between cancerous and healthy tissues. By targeting specific cancer biomarkers, AuNP-based MRI contrast agents enable early cancer detection and precise tumor localization.

These techniques, often combined with AuNPs' unique properties and functionalization strategies, contribute to the development of highly sensitive, specific, and versatile platforms for cancer detection and diagnosis.

4. PHOTOTHERMAL THERAPY (PTT)- BASED CANCER TREATMENT USING GOLD NANOPARTICLES (AuNPs):



Plasmonic photothermal therapy (PPTT), a type of treatment involving the intravenous or intertumoral injection to introduce gold nanoparticles to cancerous cells and the subsequent exposure to heat generating near-infrared (NIR) light, is a potentially favourable alternative to traditional treatments of localized tumors such as chemotherapy, radio therapy, and surgery. The current main concern of PPTT, however, is the feasibility of the treatment in clinical settings. Since PPTT's initial use 15 years ago, thousands of studies have been published. In this feature article, we summarize the most recent scientific progress, including the efficacy, molecular mechanism, toxicity, and pharmacokinetics of PPTT in vitro with cancer cells and in vivo through mouse/rat model testing, animal clinical cases (such as dogs and cats), and human clinical trials. Given the benefits of PPTT, we believe that it will ultimately become a human clinical treatment that can aid in our ultimate goal of beating cancer

4.1 PRINCIPLES OF PHOTOTHERMAL THERAPY (PTT):

PTT based cancer treatment using AuNPs exploits the selective absorption of NIR light by AuNPs to induce localized hyperthermia and selective destruction of cancer cells, offering a promising approach for precise and minimally invasive cancer therapy. The principles of photothermal therapy (PTT) based cancer treatment using gold nanoparticles (AuNPs) involve several key aspects:

I. **Selective Absorption:** AuNPs are designed to selectively absorb near-infrared (NIR) light due to their surface plasmon resonance (SPR) properties. This absorption leads to efficient conversion of light energy into heat.

II. **Localized Heating:** Upon NIR irradiation, AuNPs generate heat, resulting in localized hyperthermia in the tumor region. This heat selectively damages cancer cells while sparing surrounding healthy tissue.

III. **Targeted Delivery**: AuNPs can be functionalized with targeting ligands or antibodies to specifically accumulate in cancer cells or tumors, enhancing the specificity of treatment and minimizing off-target effects.

IV. **Thermal Damage Mechanisms:** The heat generated by AuNPs induces various cellular damage mechanisms within cancer cells, including protein denaturation, membrane disruption, and induction of apoptosis, leading to cell death.

V. **Real-Time Monitoring:** The temperature increase induced by PTT can be monitored in real-time using imaging techniques, allowing for precise control of the treatment parameters and optimization of therapeutic outcomes.

4.2 MECHANISM OF PTT USING GOLD NANO PARTICLES (AuNPs):

Photothermal therapy (PTT) is a promising approach for cancer treatment that involves the use of light-absorbing agents to generate localized heat and induce tumor cell death. The multifaceted mechanisms of action of GNPs in PTT-based cancer treatment make them attractive candidates for improving therapeutic outcomes and minimizing side effects in cancer patients. The mechanisms of action of GNPs in PTT-based cancer treatment include:

I. **Synthesis and functionalization of AuNPs:** Gold nanoparticles are synthesized and then functionalized with specific ligands or antibodies that can target cancer cells. This allows for the selective accumulation of AuNPs in the tumor site while minimizing damage to healthy tissues.

II. **Accumulation of AuNPs in the tumor:** The functionalized AuNPs are delivered to the tumor site either via systemic circulation or through direct injection into the tumor. The targeting ligands or antibodies on the AuNPs help them bind to specific receptors overexpressed on cancer cells, enhancing their accumulation in the tumor tissue.

III. **Laser irradiation:** After the AuNPs have accumulated in the tumor tissue, a laser with a specific wavelength is applied to the area. The laser is chosen to match the absorption peak of the AuNPs, which allows them to efficiently absorb the light.

The Finite-Difference Time-Domain (FDTD) method is invaluable for enhancing photothermal therapy (PTT) effectiveness in cancer treatment. By simulating the interaction between laser light and gold nanoparticles (AuNPs), FDTD enables precise optimization of treatment parameters. It accurately predicts how AuNPs absorb and scatter light, facilitating the design of nanoparticles with optimal shapes, sizes, and configurations for efficient heat generation. Additionally, FDTD simulations help identify the most effective laser settings, such as wavelength, intensity, and polarization, to maximize heat delivery to cancer cells while minimizing damage to healthy tissue. Through detailed analysis, FDTD provides insights into temperature distributions, hotspot formation, and heat dissipation around AuNPs, crucial for understanding and improving PTT outcomes. By leveraging FDTD simulations, researchers can refine treatment strategies, accelerate nanoparticle development, and ultimately enhance the efficacy of PTT as a targeted and minimally invasive approach for cancer therapy.

Using FDTD simulations, comparing nanospheres and Nano polygons elucidates their photothermal properties. Understanding how these shapes interact with laser light aids in optimizing cancer treatment. Insights gained guide nanoparticle design and laser parameters for enhanced efficacy in photothermal therapy.

IV. **Photothermal effect:** When the AuNPs absorb the laser light, they undergo a process called surface plasmon resonance. This process results in the conversion of light energy into heat, generating localized hyperthermia in the tumor tissue.

V. **Thermal ablation of cancer cells:** The heat generated by the AuNPs induces a rapid increase in temperature in the tumor tissue. The high temperatures cause thermal damage to the cancer cells, leading to their destruction. The heat can also disrupt the tumor microenvironment, damaging blood vessels that supply nutrients to the tumor.

VI. **Immune response:** The destruction of cancer cells releases tumor-associated antigens, stimulating an immune response. This immune response can help in the recognition and elimination of remaining cancer cells and provide long-term protection against tumor.

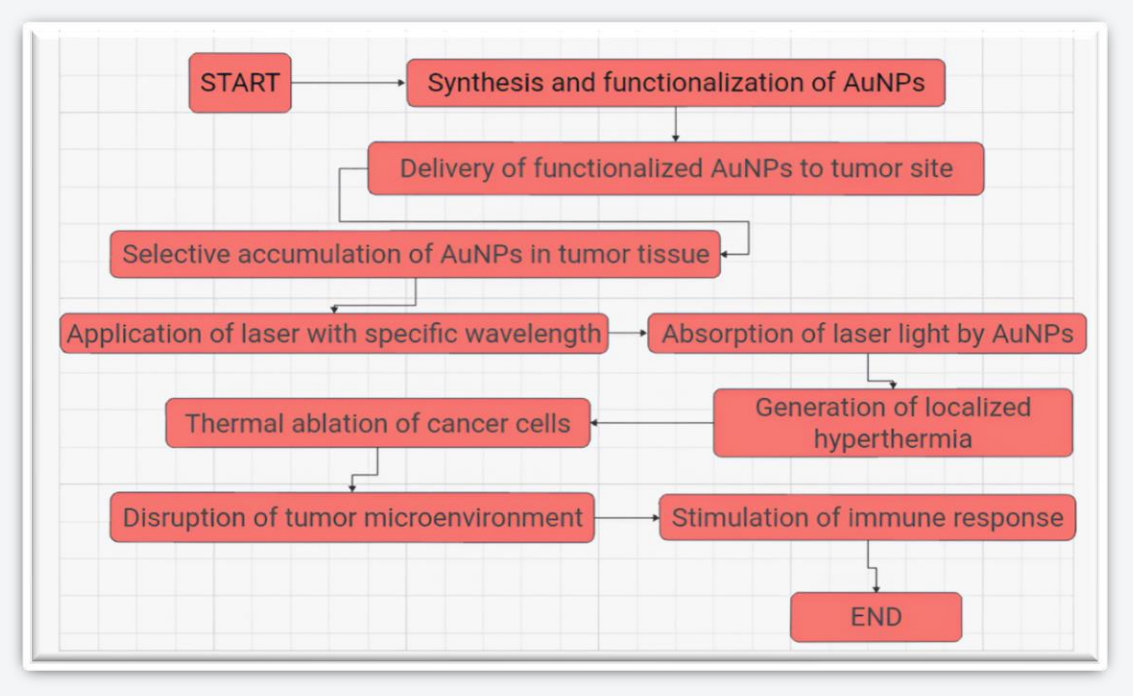


Figure 10: Schematic Flowchart of the complete mechanism of the PTT- based Cancer Treatment and all the methodologies associated in this therapy.

4.3 EFFICACY OF PTT IN CANCER TREATMENT:

The efficacy of PTT-based (Photothermal Therapy) cancer treatment using GNPs (Gold Nanoparticles) has been demonstrated in various preclinical and clinical studies. Here are some key points regarding the efficacy of this treatment approach:

I. **Selective Cancer Cell Targeting:** GNPs can be functionalized with targeting ligands or antibodies to specifically bind to cancer cells or tumor tissues. This selective targeting allows for the accumulation of GNPs in the tumor area, enhancing the treatment's efficacy by focusing on cancer cells while minimizing damage to healthy tissues.

II. **Efficient Photothermal Conversion:** GNPs have unique optical properties that enable efficient photothermal conversion. They can absorb near-infrared (NIR) light and convert it into heat through surface plasmon resonance. This results in localized heating and thermal damage to cancer cells.

III. **Enhanced Tumor Cell Destruction:** The heat generated by GNPs upon NIR irradiation leads to the destruction of tumor cells. The

elevated temperature causes damage to cellular structures, proteins, and induces cell death, thereby effectively reducing or eliminating the tumor.

IV. **Potential for Combination Therapy:** PTT-based cancer treatment using GNPs can be combined with other therapies like chemotherapy, radiotherapy, or immunotherapy to achieve enhanced treatment outcomes. This combination approach can have synergistic effects, leading to improved tumor regression and long-term control.

V. **Precise Localization and Minimized Side Effects:** The selective accumulation of GNPs in tumor tissues allows for a more targeted treatment approach. This targeted delivery reduces the impact on healthy tissues, minimizing side effects and preserving the surrounding normal cells.

Further research and clinical trials are necessary to optimize the treatment approach, improve its efficacy, and establish its safety in a wider range of cancer types and patient populations.

4.4 RESULTS FROM FDTD STIMULATION:

The FDTD simulations revealed distinct photothermal properties between nanospheres and Nano sized polygons. Nano sized polygons exhibited a higher absorption efficiency of laser light compared to nanospheres, leading to more localized and intense hotspot formation. This suggests that Nano sized polygon have a greater potential for inducing thermal effects within the targeted tissue region. Additionally, the simulations showed that Nano sized polygon displayed a more pronounced scattering effect, which could contribute to enhanced light absorption and distribution around the nanoparticle. Additionally, it includes:

I. FDTD simulations reveal temperature distribution around gold nanoparticles (AuNPs) under laser irradiation.
II. Hotspot formation is identified, guiding efficient heat generation for cancer cell destruction.
III. Light absorption efficiency of AuNPs is quantified, aiding nanoparticle design optimization.

IV. Scattering effects are assessed to ensure uniform light distribution within tissues.

V. Insights from FDTD simulations optimize treatment protocols for better clinical outcomes.

VI. FDTD results validate experimental data and predict AuNP behaviour in biological environments.

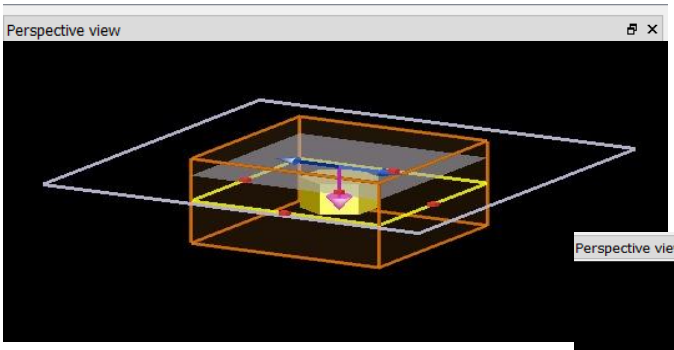


Figure 11: Perspective View of the Gold Nano sized polygon taken

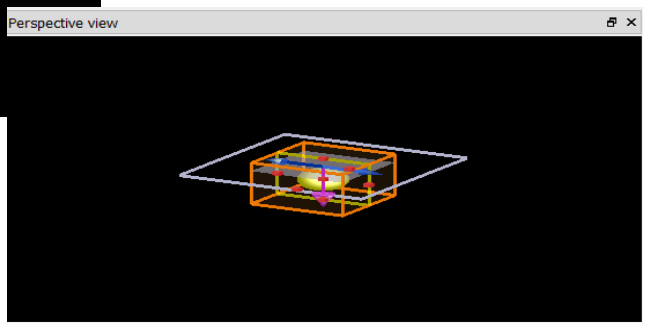


Figure 12: Perspective View of the Gold Nanosphere taken

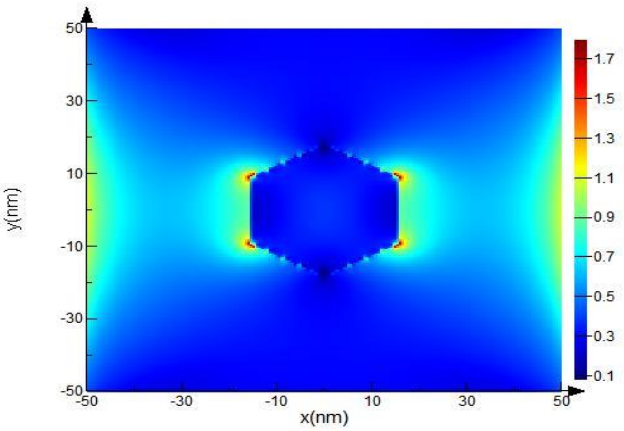


Figure 13: FDTD simulation results for the Nano sized polygon taken

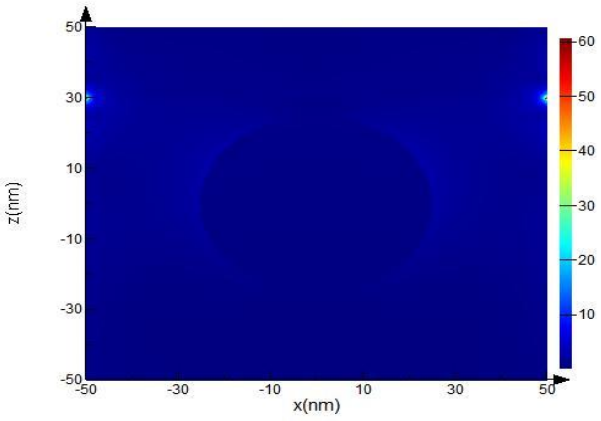


Figure 14: FDTD simulation results for the nanosphere taken

These results highlight the importance of nanoparticle shape in dictating photothermal therapy efficacy. Understanding these differences enables the optimization of nanoparticle design and laser parameters for improved treatment outcomes in cancer therapy.

5 RECENT ADVANCEMENT IN GNPs FOR CANCER DETECTION AND PTT-BASED TREATMENT:

The recent advancements in gold nanoparticles (GNPs) for cancer detection and PTT-based treatment, specifically focusing on novel synthesis techniques, enhanced targeting strategies, integration of imaging modalities, and combination therapies:

5.1 NOVEL SYNTHESIS TECHNIQUES FOR GNPS:

I. **Seed-mediated growth:** This technique allows for precise control over the size and shape of GNPs by using pre-formed seed nanoparticles as templates for growth.
II. **Green synthesis:** Researchers are exploring environmentally-friendly methods using plant extracts or microorganisms to synthesize GNPs. These methods offer advantages such as reduced toxicity and eco-friendliness.
III. **Microfluidic synthesis:** Microfluidic-based approaches provide a controlled and reproducible environment for synthesizing GNPs with precise size and shape control.

5.2 ENHANCED TARGETING STRATEGIES FOR CANCER CELLS:

I. **Functionalization with targeting ligands:** GNPs can be functionalized with specific ligands, antibodies, or peptides that can selectively bind to cancer cell receptors or biomarkers. This enhances their affinity for cancer cells while minimizing interactions with healthy cells.

II. **Active targeting:** Researchers are exploring active targeting strategies by incorporating stimuli-responsive components into the GNPs. These components can respond to specific conditions within the tumor microenvironment, leading to enhanced tumor penetration and cellular uptake.

III. **Precision Medicine:** Tailoring treatment regimens based on the unique genetic, molecular, and cellular characteristics of individual patients and their tumors. This approach enables the selection of therapies that are most likely to be effective and minimizes unnecessary treatment-related toxicity.

5.3 COMBINATIONAL THERAPIES UTILIGING GNPS:

I. **Chemo-photothermal therapy:** GNPs can be loaded with chemotherapy drugs and used in combination with photothermal therapy. The heat generated by GNPs upon NIR irradiation not only induces photothermal cell death but also enhances the efficacy of chemotherapy drugs by increasing their cellular uptake and improving drug release kinetics.

II. **Immunotherapy combination:** GNPs can be utilized to enhance the efficacy of immunotherapies such as immune checkpoint inhibitors or vaccines. GNPs can act as adjuvants, promoting immune system activation and improving the immune response elicited by the therapy.

5.4 INTEGRATING IMAGING FOR ENHANCED CANCER DETECTION:

I. **Multimodal imaging:**

GNPs can be combined with other contrast agents or imaging probes such as fluorescent dyes or radioactive tracers. This allows for the integration of multiple imaging modalities, such as fluorescence imaging, positron emission tomography (PET), or magnetic resonance imaging (MRI), to provide comprehensive detecting information.

II. **Artificial Intelligence (AI) and Machine Learning:**

Employing AI algorithms and machine learning models to analyse large volumes of imaging data and assist radiologists in detecting, characterizing, and classifying cancerous lesions. AI-based image interpretation can improve diagnostic accuracy, reduce interpretation variability, and enable automated image segmentation and tumor quantification

III. **Photoacoustic imaging**:

GNPs possess strong light absorption properties, making them ideal agents for photoacoustic imaging. This imaging technique combines laser-induced ultrasound waves with light absorption by GNPs, enabling highly sensitive and specific tumor imaging.

6 APPLICATIONS OF CANCER DETECTION AND TREATMENT USING GNPs:

Some applications of cancer detection and treatment using AuNPs, excluding PTT and combinational therapies:

I. **Early Diagnostic Markers:** AuNPs can be modified to bear specific biomolecules, such as peptides and antibodies, which target cancer cells and biomarkers. They offer advantages over traditional diagnostic markers by providing improved sensitivity and specificity for early cancer detection.

II. **Prognostic Markers:** AuNPs can be used to monitor treatment response by observing biomarker expression or cellular behaviour over time. For example, they can track the expression of tumor markers that are associated with cancer recurrence.

III. **Drug Delivery Systems:** AuNPs can be used to deliver therapeutics directly to cancer cells. They can be modified with different functional groups to improve their stability, bioavailability, half-life, and biodistribution.

IV. **Radiation Enhancement:** AuNPs can increase the effectiveness of ionizing radiation therapy by increasing the local dose of radiation delivered to cancer cells.

V. **Personalized Medicine:** AuNPs can be used to deliver drugs in a targeted manner. By considering the patient's genetic and molecular profile, oncologists can develop a personalized treatment plan that is tailored to the patient's specific needs.

Overall, AuNPs have vast potential not only in PTT and combinational therapies, but also in cancer detection and treatment without these therapies. They offer a wide range of applications in the field of cancer research, improving our understanding of the disease and paving the way for innovative therapies that can improve patient outcomes.

7 CHALLENGES AND FUTURE DIRECTIONS

Challenges:

There are several challenges associated with AuNPs cancer detection and PTT-based treatment. Some of the main challenges are:

I. **Limited Targeting Efficiency**: AuNPs face challenges in selectively targeting cancer cells in vivo, especially in the presence of healthy cells. This reduces their efficacy and specificity in detecting and treating cancer.

II. **Low Tissue Penetration:** AuNPs have limited tissue penetration due to their larger size, making it difficult to access deep-seated tumors and affecting their effectiveness in cancer therapeutics.

III. **Biocompatibility and Safety:** AuNPs, like any nanomaterial, can cause potential biological toxicity, which needs to be carefully addressed to ensure their safety and efficacy.

IV. **Biological Barriers:** Biological barriers, including blood-brain barrier and tumor cell membrane, may hinder AuNPs transport and hinder their functionalization, affecting their targeting, and therapeutic efficacy.

V. **Regulatory Approval:** The regulatory approval process for clinical translation of AuNPs cancer detection and PTT-based treatment is still a challenge and needs to meet biological efficacy and safety criteria for approval.

VI. **Manufacturing and Scaleup:** Large-scale manufacturing of AuNPs is still quite challenging and requires a more cost-effective strategy to achieve reasonable production costs.

VII. **Photothermal and Photoacoustic Integration:** Photothermal and photoacoustic imaging methods due to their limited tissue penetration depth could benefit from combinational imaging techniques.

VIII. **Limited Stability:** AuNPs needs proper storage and proper handling to avoid damage and maintain their stability, which influences their biological activity.

Future Directions:

There are multiple future directions of AuNPs cancer detection and PTT-based treatment which has the potential to revolutionize cancer diagnosis and treatment. Some of the main future directions include:

I. **Multifunctional AuNPs:** Development of multifunctional AuNPs with capabilities of target recognition, multi-modal imaging, drug delivery, and photothermal therapy could enhance cancer-specific targeting, detection, and treatment.

II. **Personalized Medicine:** AuNPs in personalized medicine is an emerging area that involves tailoring treatment to an individual's unique genetic and molecular characteristics, giving an edge to more effective targeted-screening and targeted treatment.

III. **Intra-Operative Detection:** Intra-operative detection with multifunctional AuNPs, allowing immediate detection of residual and invasive tumors during surgery, which enhances the complete removal of the tumor.

IV. **Advanced Surface Chemistry:** Advanced modification of AuNPs surface chemistry and leveraging of singlet oxygen generation and thermal expansion properties in a unique way to achieve Photodynamic therapy can improve cancer treatment outcome.

V. **Cutting-Edge Imaging Techniques:** Advanced techniques of AuNPs based imaging using Photoacoustic, ultrasound, and Raman technologies can improve the detection sensitivity and specificity.

VI. **Super-resolution Imaging Techniques:** Revolutionary super-resolution imaging techniques utilizing AuNPs, could lead to the high-definition visualization of cancer cells and improve our understanding of the disease at the nanoscale level.

VII. **Environmental Applications:** AuNPs can be utilized as a green alternative for environmental monitoring and remediation applications, bringing an end to pollution and environmental safety.

8 CONCLUSION:

In conclusion, the utilization of AuNPs in cancer detection and photothermal therapy (PTT) holds tremendous promise for the future of cancer treatment. The unique properties of AuNPs, such as their plasmonic nature and controllable absorption of light, make them an ideal candidate for targeted cancer detection and localized thermal therapy.

Throughout this project, we have explored the challenges associated with AuNPs in cancer detection and PTT-based treatment and discussed various future directions that can propel this field forward. Despite the challenges of limited targeting efficiency, low tissue penetration, and biocompatibility concerns, researchers are actively working towards overcoming these obstacles.

The future directions of this field include developing multifunctional AuNPs for combination therapies, advancing surface chemistry for improved treatment outcomes, and exploring personalized medicine approaches. Additionally, cutting-edge imaging techniques and super-resolution imaging offer exciting possibilities for enhanced cancer detection and understanding at the nanoscale level.

The potential impact of AuNPs in revolutionizing cancer treatment is immense. Their ability to enable precise and localized therapy with minimal damage to healthy tissues holds great promise for enhancing patient outcomes and improving overall quality of life. Moreover, AuNPs may also find applications in environmental monitoring and remediation, further expanding their potential benefits beyond cancer research.

At last I would say, the continuous exploration and development of AuNPs cancer detection and PTT-based treatment will undoubtedly contribute to advancements in the field of oncology. As researchers and scientists continue to push the boundaries of innovation, we can look forward to a future where AuNPs play a significant role in improving cancer diagnosis, treatment, and ultimately, the lives of patients affected by this devastating disease.

9 REFERENCES:

1. Hwang S, Nam J, Jung S, Song J, Doh H, Kim S. Gold nanoparticle-mediated photothermal therapy: current status and future perspective. Nanomedicine (London). 2014 Sep;9(13):2003-22. doi: 10.2217/nnm.14.147. PMID: 25343350.
2. Riley RS, Day ES. Gold nanoparticle-mediated photothermal therapy: applications and opportunities for multimodal cancer treatment. Wiley Interdisciplinary Rev Nano med Nanobiotechnology. 2017 Jul;9(4):10.1002/wnan.1449. doi: 10.1002/wnan.1449. ePub 2017 Feb 3. PMID: 28160445; PMCID: PMC5474189
3. S. Bayda, M. Adeel, T. Tuccinardi, M. Cordani, F. Rizzolio, The history of nanoscience and nanotechnology: from chemical-physical applications to nanomedicine, Molecules 25 (1) (2019), https://doi.org/10.3390/molecules25010112.
4. W. Lu, J. Yao, X. Zhu, Y. Qi, Nanomedicines: redefining traditional medicine, Biomed. Pharmacother. 134 (2021) 111103, https://doi.org/10.1016/j. biopha.2020.111103.
5. S.S. Kelkar, T.M. Reineke, Theranostics: combining imaging and therapy, Bioconjug. Chem. 22 (10) (2011) 1879–1903, https://doi.org/10.1021/bc200151q.
6. S. Wang, Z. Sun, Y. Hou, Engineering nanoparticles toward the modulation of emerging cancer immunotherapy, Adv. Healthc. Mater. 10 (5) (2021) e2000845, https://doi.org/10.1002/adhm.202000845.
7. Liu, K. Y. et al. Label-free surface-enhanced Raman spectroscopy of serum based on multivariate statistical analysis for the diagnosis and staging of lung adenocarcinoma. Vib. Spectrosc. 100, 177–184, https://doi.org/10.1016/j.vibspec.2018.12.007 (2019).
8. Wang, X. et al. Detection of circulating tumor cells in human peripheral blood using surface-enhanced Raman scattering nanoparticles. Cancer Res. 71, 1526–1532, https://doi.org/10.1158/0008-5472.CAN-10-3069 (2011).
9. Ahmad, R., Fu, J., He, N., and Li, S. (2016). Advanced gold nanomaterials for photothermal therapy of cancer. J. Nanosci. Nanotechnol. 16, 67–80. doi: 10.1166/jnn.2016.10770
10. Almeida, J. P., Chen, A.L., Foster, A., and Drezek, R. (2011). In vivo biodistribution of nanoparticles. Nanomedicine 6, 815–835. doi: 10.2217/nnm.11.79
11. Almeida, J. P., Figueroa, E. R., and Drezek, R. A. (2014). Gold nanoparticle mediated cancer immunotherapy. Nanomedicine. 10, 503–514. doi: 10.1016/j.nano.2013.09.011

12. Alric, C., Miladi, I., Kryza, D., Taleb, J., Lux, F., Bazzi, R., et al. (2013). The biodistribution of gold nanoparticles designed for renal clearance. Nanoscale. 5, 5930–5939. doi: 10.1039/c3nr00012e
13. Huang, X., El-Sayed, I. H., Qian, W., & El-Sayed, M. A. (2006). Cancer cell imaging and photothermal therapy in the near-infrared region by using gold nanorods. Journal of the American Chemical Society, 128(6), 2115-2120. DOI: [10.1021/ja057254a](https://doi.org/10.1021/ja057254a)
14. Dreaden, E. C., Mackey, M. A., Huang, X., Kang, B., El-Sayed, M. A. (2011). Beating cancer in multiple ways using nanogold. Chemical Society Reviews, 40(7), 3391-3404. DOI: [10.1039/c0cs00180j](https://doi.org/10.1039/c0cs00180j)
15. Chen, J., Wang, D., Xi, J., Au, L., Siekkinen, A., Warsen, A., ... & Li, X. (2007). Immuno gold nanocages with tailored optical properties for targeted photothermal destruction of cancer cells. Nano Letters, 7(5), 1318-1322. DOI: [10.1021/nl070345g](https://doi.org/10.1021/nl070345g)
16. Dykman, L. A., & Khlebtsov, N. G. (2012). Gold nanoparticles in biomedical applications: recent advances and perspectives. Chemical Society Reviews, 41(6), 2256-2282. DOI: [10.1039/c1cs15166e](https://doi.org/10.1039/c1cs15166e)
17. Hirsch, L. R., Stafford, R. J., Bankson, J. A., Sershen, S. R., Rivera, B., Price, R. E., ... & West, J. L. (2003). Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. Proceedings of the National Academy of Sciences, 100(23), 13549-13554. DOI: [10.1073/pnas.2232479100](https://doi.org/10.1073/pnas.2232479100)
18. Lal, S., Clare, S. E., Halas, N. J. (2008). Nanoshell-enabled photothermal cancer therapy: impending clinical impact. Accounts of Chemical Research, 41(12), 1842-1851. DOI: [10.1021/ar800150g](https://doi.org/10.1021/ar800150g)
19. Boisselier, E., & Astruc, D. (2009). Gold nanoparticles in nanomedicine: preparations, imaging, diagnostics, therapies and toxicity. Chemical Society Reviews, 38(6), 1759-1782. DOI: [10.1039/b806051g](https://doi.org/10.1039/b806051g)
20. Dreaden, E. C., Alkilany, A. M., Huang, X., Murphy, C. J., & El-Sayed, M. A. (2012). The golden age: gold nanoparticles for biomedicine. Chemical Society Reviews, 41(7), 2740-2779. DOI: [10.1039/c1cs15237h](https://doi.org/10.1039/c1cs15237h)