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## RESEARCH ARTICLE

# Nanomedicine: Treatment of Chronic Disease Using Gold Nano Thermo Robot (GNTR) Empowered With Nanotechnology Approaches

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**ABSTRACT** Nanotechnologists and medical researchers are working hard to develop new and innovative ways to use nanorobots as nanomedicine to improve healthcare outcomes and revolutionize the field of therapeutics. Nanotechnology has the potential to revolutionize healthcare by providing new ways of treating chronic diseases in the field of medicine. A “Gold Nano Thermo Robot” (GNTR) model has been proposed in this research article, which can be considered a nanomedicine that will deliver controlled thermal therapy to targeted malignant tissues without damaging healthy tissues. The proposed nanotherapeutic system, empowered with a nano sensor network, interbody body communication network, and Internet of nanomedical things, has been used to normalize and control hyperthermal waves in real-time that have been used to eliminate breast cancer cells using the “SEE and TREAT” technique. To generate hyperthermia, which has been irradiated by laser pulses to propose GNTR, a Coulomb explosion took place, and a huge amount of dispersed hyperthermia waves were produced. To convert the intensity of dispersed and irregular hyperthermia into a regulated and disciplined format, a Finite Difference Method has been used to develop a “Heat Control System.” A comparative analysis has been provided of the intricate relationship between the required radius of Gold Nano Thermo Robots and the volume depth of the tumor for penetration, with a keen focus on evaluating how different GNTR sizes fit or do not fit for the task of effectively treating tumors at various depths within cancer tumors. Furthermore, the effectiveness of treatment has multifaceted outcomes that have been acquired by the interplay between two critical factors, the temperature limit and therapy duration. By examining a comprehensive matrix of thermal therapy durations (ranging from 25 minutes to 60 minutes) alongside various temperature limits (ranging from 33°C to 60°C). The best fit and the best

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response therapy session have been verified with a temperature limit of 42 °C for 30 minutes, achieving near-complete tumor ablation with minimum harm to the healthy tissues. The complex physical effects on the Gold Nano Robots surfaces due to the Coulomb explosion procedure are also provided in the form of simulation analysis, and an explanation is given in nine panels.

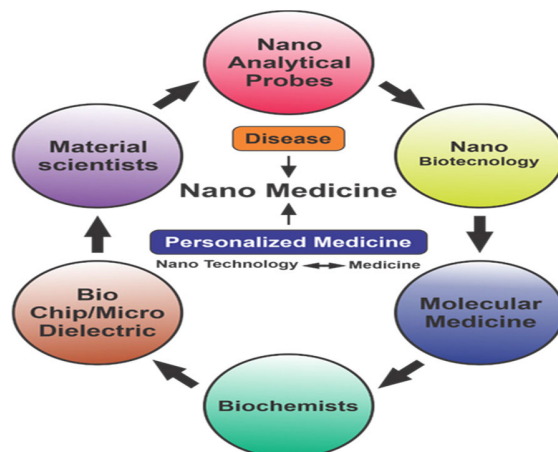
**INDEX TERMS** Coulomb explosion, nanotherapeutic system, nano sensor network, hyperthermia, nanomedicine, interbody body communication network, internet of nanomedical things, finite difference method, see and treat technique.

## I. INTRODUCTION

Nanotechnology has made tremendous progress in the pharmaceutical domain in recent years, and many devices have been developed for complex medical treatment approaches. Nanotechnology has the potential to revolutionize cancer treatment by providing targeted, minimally invasive, and efficient methods for hyperthermia, photothermal therapy, magnetic hyperthermia, combination treatments, image-guided therapy, and personalized medicine. Improvements in patient outcomes and quality of life in the battle against chronic illness of cancer are highly anticipated from further research and development in this field of study [1].

### A. NANO MEDICINE

Nanomedicine has revolutionized the field of pharmaceuticals in several ways. It is a key part of nanotechnology and a rapidly evolving field that combines nanotechnology with medicine to improve the application of nanoscale materials and devices to diagnose, treat, and prevent diseases, reducing the potential side effects associated with traditional chemotherapy or radiation therapy [1]. Nanomedicine has enabled the development of new diagnostic techniques, such as biosensors and imaging agents that can detect diseases early stage with high sensitivity and specificity. Nano medicine has revolutionized and has opened new possibilities for regenerative medicine in the pharmaceutical domain, and drug delivery by enabling the targeted and controlled release of therapeutic agents, reducing side effects, and improving Therapeutic efficacy [2]. Nano medicine is an interdisciplinary field of research that combines the fields of nanotechnology such as Nanobiotechnology, Molecular medicine, biochemist, material scientist, Nano Analytical probe Bio chip and medicine to develop new diagnostic and therapeutic approaches as described in Fig. 1 [3]. Nano medicine offers a promising alternative to more accurate and efficient treatment of chronic diseases like breast cancer. Breast cancer remains a major global health challenge, millions of women are affected by this chronic disease each year [4]. However, researchers and physicians continue to explore state-of-the-art techniques to improve treatment effectiveness while reducing adverse effects. In this context Nano medicine, an emerging discipline in the modern, high-tech era, can overcome numerous medical challenges and potentially revolutionize the field of cancer therapy by providing cutting-edge methods for fighting against chronic illnesses [5].



**FIGURE 1.** The potential of Nano medicine to achieve innovation in healthcare.

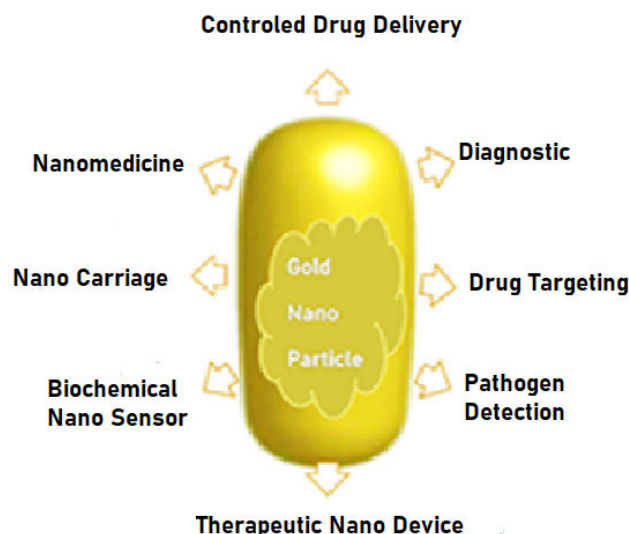
### B. NANO SMART MEDICAL DEVICES

The creation of Nano smart medical devices is the main challenge of medical sciences that can be securely transported to the location of the disease. To go through the body and reach the desired tissue or tumor, the Nano medical devices must be tiny enough. They must have characteristics that enable precision.

Targeting, such as surface alterations with ligands that recognize cancer-specific signals [6]. To achieve effective and regulated dispersion of the Nanodevices throughout the body, the delivery mechanism itself must also be optimized. Even though the fields of nanotechnology and Nanomedicine have made tremendous strides, it is crucial to recognize that creating a truly secure and efficient Nano device for heat-based treatments is a challenging undertaking that calls for more study, development, and rigorous testing [7]. This cooperative strategy makes it easier to design safer and more effective Nano medical devices such as ECG, Pulse Oximetry, and blood pressure devices, as shown in Fig. 9, for heat-based treatments by bridging the gap between basic research and clinical applications.

### C. APPLICATIONS OF GOLD NANO PARTICLES

Gold nanoparticles (GNPs) have demonstrated tremendous potential in the field of cancer therapy due to their special qualities. They are appealing prospects for a variety of cancer treatments due to their tiny size (1-100 nanometers) and biocompatibility [8].



**FIGURE 2.** Applications of gold nano particles.

Drug delivery, photothermal therapy, photodynamic therapy, radiation therapy development, diagnostic imaging, gene therapy, and immunotherapy are a few uses for gold nanoparticles in the treatment of cancer [9]. The applications of gold nanoparticles in medical sciences are described in Fig 2. However, the clinical translation of these agents is continuing, and further study is required to fully understand their safety, effectiveness, and long-term implications in human patients [10].

#### D. COULOMB EXPLOSION PROCEDURE

When highly charged particles, such as ions or molecules, are exposed to a strong electric field, a phenomenon known as a coulomb explosion takes place [11]. The term “explosion” denotes a rapid and violent disruption of the particles that results from the electrostatic force between charged particles, which is referred to as a “Coulomb” force [23]. The charged particles gain energy from the laser as they interact with the sample solid, increasing their kinetic energy. The temperature rise is correlated with this rise in kinetic energy. The substance can be locally heated because of the converted thermal energy from the absorbed laser energy. Strongly repelling forces keep highly charged ions apart from one another. The ions may ultimately recombine as they divide [24].

#### E. HEAT THERAPY

Heat therapy is one of the promising therapeutic modalities that apply raised temperatures to selectively target and kill cancer cells [13]. In current years, the integration of gold nanoparticles (AuNPs) has emerged as a ground-breaking strategy to enhance the strength of heat in breast cancer treatment. Heat can be rapidly released because of the Coulomb explosion effect [10]. The heat energy from the radiation is transmitted to the medium around the GNPs as they absorb it, leading to a localized heating effect. The radiation’s prop-

erties, such as strength, duration, and wavelength, may be changed to precisely control and target this heat. Heat-based treatments have become a viable cancer therapy option by using the special qualities of nanoscale materials. Heat treatment may be precisely targeted to cancer cells by harnessing the power of nanotechnology, resulting in localized destruction while minimizing harm to healthy tissues. Innovative heat-based medicines, particularly for the treatment of breast cancer, have been made possible by nanotechnology [25]. Hyperthermia (HT) is a clinical treatment for cancer that extraneously and intrinsically heats malignant cells to a temperature of  $33C^0$ -  $45C^0$  for suitable period [26]. Heat delivered to tumor tissues can act as a cytotoxic or sensitizing agent to enhance their remission or at least regression by utilizing several biological mechanisms and pleiotropic effects when combined with other conventional cancer treatment techniques, such as radiotherapy (RT) or chemotherapy (CT) [9].

#### F. NANO ROBOTS

Nanorobots are tiny machines that are designed to perform specific tasks at the nanoscale [14]. The downscaling of robotic programs holds considerable promise for advancing medical treatment and diagnosis. These tiny robotic surgeons can navigate and operate in remote and challenging-to-access areas within the human body. [16]. These nanorobots are made up of biocompatible materials, such as gold nanoparticles, that can be easily absorbed by the body. It is designed to be injected directly into the bloodstream, where it can travel to the site of the cancer cells [15]. Once it reaches the cancer cells, it is activated by an external heat source, such as a laser, which heats the robot by coulomb explosion and destroys the cancer cells by controlling the intensity of heat. Nanorobots are extremely small. These tiny robots are also known as nanobots as small as billionths of meters in size [22]. These nanorobots are being researched and developed for several medical applications, including the treatment of breast cancer. This kind of cancer therapy has the potential to be considerably more accurate and successful than conventional chemotherapy or radiation therapy, which can harm both healthy and malignant cells. Although they are still in the experimental stage and have not been given human use approval, nanorobots show promise for the future of cancer therapy [27].

#### G. INTERNET OF NANO MEDICAL THINGS (ION MT)

The term “Ion MT” describes the integration of nano-sized devices into a network that can communicate and interact with one another, allowing for real-time data collection, analysis, and decision-making [20]. A multifaceted and patient-centered strategy is offered using the Internet of Nano Things in the treatment of breast cancer, ranging from early detection and precise diagnosis to individualized treatment plans and on-going monitoring [21]. Ion MT has the potential to greatly enhance breast cancer management by leveraging the power of nanotechnology and networked devices,

improving patient outcomes, and enhancing the effectiveness of the healthcare system [22]. In the field of medicine, Ion MT can be applied in several ways to improve the treatment of breast cancer patients [23].

Breast cancer remains the most common cancer affecting women worldwide, underscoring the importance of understanding and addressing this frightening health challenge. In 2020 alone, the medical world observed an unbelievable 2.26 million new cases of breast cancer reported in women, highlighting the shocking scale of its occurrence. This disease not only poses a significant danger to women’s health but also requires combined efforts in terms of awareness, early detection, and advanced medical research to enhance treatment outcomes.

The local breast cancer data has been taken from the Shaukat Khanum Memorial Cancer Hospital and Research Center (“SKMCH& RC”) trust and its affiliated centers from December 1994 to December 2021, [78]. The graphic representation of the distribution of malignancies in all provinces of Pakistan, including Afghanistan, Azad Kashmir, and other neighboring countries, is shown in the pie diagram in Fig.1 below.

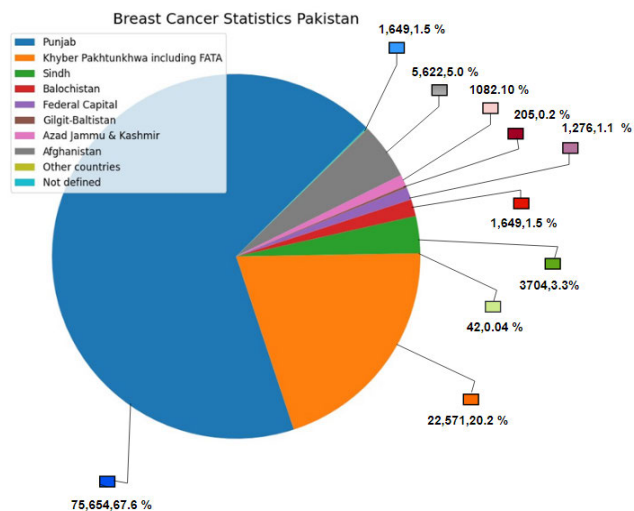


FIGURE 3. Distribution of malignancies according to the geographic area of residence of the patients in Pakistan. Dec.1994 to Dec.2020.

The global breast cancer data has been taken from “World Cancer Research Fund International [79]. The statistics of the top ten countries worldwide with the highest rates of breast cancer in women in 2020 are represented graphically in the pie diagram in Fig. 4.

A novel approach has been introduced, designed by the combination of nanomedical devices, Ion MT, and precise heat control, which holds immense promise for revolutionizing breast cancer treatment [18]. It can administer therapy in real-time, tailored to the patient’s needs and tumor characteristics, and has the potential to minimize side effects and enhance overall treatment outcomes. In this study, current key medical challenges and considerations have been addressed.

Breast Cancer Statistics Worldwide

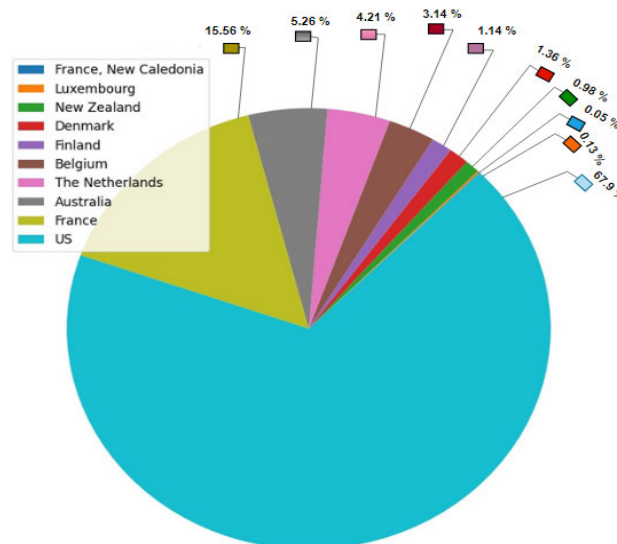


FIGURE 4. Distribution of malignancies in the top 10 countries with the highest rates of breast cancer worldwide in women in 2020.

The safety and biocompatibility of GNTRs in human bodies require rigorous evaluation [19]. Ensuring that they do not elicit adverse immune responses or toxicity is paramount. Scalability and manufacturing processes have been optimized for clinical practices. Clinical trials have validated the efficacy and safety of this approach in patients. After several studies about nanodevices, we have come to know that there is not yet a single nanodevice available that can provide a harmless and effective safe treatment mode using a heat control system for complex operations that have been delivered [17]. There is a serious need to develop a nanodevice, that is small enough to easily reach the site of disease and can kill the cancer cells with controlled thermal therapy without damaging the neighboring healthy cells. In response to this challenge, we proposed an efficient nanomedicine treatment approach in the shape of GNTRs.

The main contributions of this research are as follows.

- The key object of the present research is to design a novel Gold Nano Thermos Robot (GNTR) made of gold nanoparticles that is small enough to penetrate cells and deliver medication directly to the affected, minimizing the risk of side effects associated with traditional treatments.
- The key objective of this research is to ensure the safe treatment of ‘breast cancer patients and to kill the cancer tumor without damaging the surrounding healthy tissues of the organ using proposed novel nontherapeutic.
- The proposed nanotherapeutic system GNTRs, is designed to be entangled with IonMT devices and an inter-body communication network co-working with a medical network A novel “See and Treat” technique for

<b>Introduction</b>	Section I
<ul style="list-style-type: none"> <li>▪ The paper set with an introductory discussion with some important definitions.</li> </ul>	
<b>Literature review</b>	Section II
<ul style="list-style-type: none"> <li>▪ Literature review and previous related studied is discussed.</li> </ul>	
<b>Design methodology of proposed GNTR</b>	Section III
<ul style="list-style-type: none"> <li>▪ Morphology of proposed GNTRs, key components and their functions are discussed.</li> </ul>	
<b>Discrete mesh process</b>	Section IV
<ul style="list-style-type: none"> <li>▪ Physical domain of proposed GNTRs is divides in finite number nodes is discussed.</li> </ul>	
<b>Proposed mechanism of action of proposed GNTR</b>	Section V
<ul style="list-style-type: none"> <li>▪ The proposed mechanism of actions of proposed GNTR is presented.</li> </ul>	
<b>Inter body communication of network.</b>	Section VI
<ul style="list-style-type: none"> <li>▪ The applications of inter body communication network are discussed.</li> </ul>	
<b>Role of Ion MT for nano therapeutic system</b>	Section VII
<ul style="list-style-type: none"> <li>▪ The role of Ion MT for healthcare system is presented.</li> </ul>	
<b>Coulomb explosion procedure</b>	Section VIII
<ul style="list-style-type: none"> <li>▪ The procedure of how heat generated by gold nanoparticles is discussed.</li> </ul>	
<b>Scheme of heat control system</b>	Section IX
<ul style="list-style-type: none"> <li>▪ By using Mat Lab software, the scheme of heat control system is discussed.</li> </ul>	
<b>Mathematical model</b>	Section X
<ul style="list-style-type: none"> <li>▪ Governing the mathematical heat equations and related advance algorithms is discussed.</li> </ul>	
<b>Simulation results analysis</b>	Section XI
<ul style="list-style-type: none"> <li>▪ The results analysis is presented in this section.</li> </ul>	
<b>Discussion</b>	Section XII
<ul style="list-style-type: none"> <li>▪ Whole paper its outputs, limitations and its significations are discussed in detail.</li> </ul>	
<b>Conclusion</b>	Section XIII
<ul style="list-style-type: none"> <li>▪ The paper is concluded with brief and future applications of proposed GNTRs for</li> </ul>	

**FIGURE 5.** Highlights and organization of the paper.

safer and more secure real-time treatment procedures is provided.

- To improve the treatment effectiveness of the Nano Therapeutic System, we have implemented a heat control system strategy to strengthen the treatment process and ensure that the system is carried out effectively. The proposed GNTRs can store heat, transfer heat, and control the intensity of heat in the range of  $38C^0$  to  $45C^0$ , have a targeted approach to treating cancer cells without affecting neighboring cells, and offer an opportunity to save precious lives and reduce costs too.

The breakdown of the paper's structure and organization has been explained in Fig. 5 above.

## II. LITERATURE REVIEW

In this section, several studies have been reported on the mechanisms related to nanorobots, Nanorobots which involve a comprehensive analysis of the basic parameters involved in their functioning and applications in the pharmaceutical domain. The objective is to understand how robots can be used for various complex medical situations that have brought to the forefront aspects of chemotherapy and radiation-based therapies. While these conventional cancer treatments are frequently successful, they do have certain drawbacks.

The nano research has not only developed various models of nanorobots at the nanoscale, tailored for a range of biomedical applications [6] but has also created robotic nanomanipulators capable of handling nano-objects, achieving significant milestones in biomedicine. These amazing accomplishments within nanorobotics have not only extended the domain of medical robotics but have also presented fresh insights into the intricate mechanisms governing life procedures. This progress holds great promise, offering an emerging and impactful avenue for advancing diagnostic and treatment capabilities in the forthcoming era of individualized precision medicine [30].

Jonathan M. Voss, et al. have explained the employ of in situ electron microscopy to drop light on one such process concerning Coulomb fission of plasmonic nanoparticles when subjected to femtosecond laser irradiation. Their observations reveal that gold nanoparticles, enclosed in a silica shell, undergo fission by releasing smaller droplets consisting of about 10–500 atoms. Mysteriously, these droplets are ejected in a preferential direction along the laser polarization. With sustained laser exposure, the released droplets coalesce into a second core within the silica shell, finally transforming the system into a dual-core particle. These findings are associated with a mechanism where electrons are selectively emitted from the gold core by laser polarization [11].

According to the study, these therapies may have several negative impacts on patients, including immune system suppression and long-term health difficulties. Furthermore, patients' quality of life during treatment may be negatively impacted by the severe side effects of chemotherapy and radiation, which frequently include nausea, exhaustion, and

hair loss. Although Nanorobots are controllable machines that can be easily identified and controlled due to their small size, their lack of precision makes them difficult to integrate [38]. The literature review provides a detailed analysis of the uses of Nanorobots in the medical field, including their potential applications, limitations, and challenges. Despite this, Nanorobots can be used in various biomedical applications, and their speed of identification is faster than wearable devices and can be achieved at a lower cost [39]. By evaluating different parameters, the researchers aim to provide a comprehensive understanding of how Nanorobots can be used to treat various medical conditions. Anzar [39] have described in their study the integration of Nano robots in medical applications, particularly in fast real-time arrangements for disease detection and treatment. Alexandre Lukyanov [3] have highlighted in their article that the implementation of Nanorobots requires the integration of artificial intelligence techniques and analysis of the results in real-time. This integration can be achieved through a media access control (MAC) design, which enables online analysis and improves the accuracy of the outcomes, The article emphasizes the potential of Nanorobots in revolutionizing the treatment of chronic diseases such as breast cancer is their ability to target specific areas and perform tasks with greater precision than traditional treatment tools. This can result in less invasive procedures, faster healing times, and improved patient outcomes. Hamdi and Ferreira [56] have explained the highlights of the challenges associated with using magnetic control systems and robotic technology in the medical field. While technology shows great promise, some limitations must be addressed before it can be used for widespread biomedical applications. The innovative formulation for magnetic radiation and mechanical designs presented in the paragraph provide potential solutions to some of these challenges. He highlighted the importance of careful consideration and evaluation of the chemical parameters used in the development of Nanorobots, especially when implementing the technology in real-life environments. By integrating sensing devices and leveraging real-time simulations, researchers can test and refine Nanorobots to ensure their safety and efficacy in medical applications. Loscri [33] introduced a complete study and design of an in-body system, describing the characteristics of each stage: emission, diffusion, and reception. Their methodology engaged in developing a realistic model to correctly represent these processes. The primary objective was to extract crucial insights regarding the potential toxicity of the system within the human body. Through this characterization, they targeted to obtain a systematic understanding of how the released substances disperse, diffuse, and are received inside the body, providing precious information about their influence on human health and safety. Pramanik [35] discussed a contrivance that involves a communication system of IoNT including the network architecture and layers system with the coordination of the Internet of nano things to save lives from epidemic diseases. The system used Nanorobots that move inside blood vessels and are observed using an

adaptive control algorithm to reach their destination with high accuracy. However, the installation of Nanorobots is difficult, and they cannot be kept in neighboring nodes, making the system unsuitable for real-time applications. To address this issue, several basic parameters have been evaluated using rigid body trajectory paths, which provide a highly intelligent system for the precise design of controllers. The robots are co-constructed with constructed with sup and require high-speed power line communication. Overall, he emphasized the challenges associated with using Nanorobots for surveillance and the need for sophisticated control systems to ensure their precise movement. Huang [57] explained advanced developments in medical diagnosis through the implementation of nanorobots. They also discussed the applications of Nanorobots in the medical field can minimize the risks of operations and allow for complex tasks to be performed at small-scale operations. They also mentioned the high technological implications of Nanorobots and their potential to create better opportunities for future medical treatments. Li [62] have discussed the current advancements in Nano robotic technology, particularly its applications in detecting and treating diseases in the human body. In their article, they highlighted the potential of Nanorobots in checking the DNA of individuals and treating cancer with high radiation. Hyperthermia (HT) can be applied to the tumor tissue directly or indirectly through the surrounding tissues. The use of HT in cancer treatment has shown several benefits, including its ability to enhance the effectiveness of other cancer treatment modalities such as radiotherapy (RT) and chemotherapy (CT). Santhakumar elaborated in their study that hyperthermia (HT) is a cancer treatment method that involves heating malignant tissues to a temperature range of  $40C^0$  to  $43C^0$  [28]. This temperature range is typically higher than the normal body temperature and can cause cancer cells to die. HT can be applied to the tumor tissue directly or indirectly through the surroundings. Onal introduced an alternate approach to breast cancer treatment that involves combining different modalities to increase effectiveness [12]. They suggested that elevated temperature levels can be used to attract temperature-sensitive drugs used in chemotherapy and increase their effectiveness on the target area while minimizing toxicity in healthy tissues. The main goal of hyperthermia studies is to increase the temperature in body tissues from  $40 C^0$  to  $43C^0$ . As the temperature is further increased, it can cause the denaturation of proteins in malignant cells, leading to a cytotoxic effect on the cancerous cells. This process is known as thermal ablation and can be used as a standalone treatment technique if the temperature threshold of  $43C^0$  is exceeded. McNabb [23], mentioned another method of treatment of breast cancer by hyperthermia that involves raising the temperature of cancerous tissues to  $40C^0$  to  $43C^0$ . Wang et al. [47], have investigated in their study the effects of hyperthermia on human breast carcinoma cell lines. It was found that cell viability was highly influenced by the temperature and duration of hyperthermia

exposure. When the temperature was increased from  $38 C^0$  to  $42C^0$ , more cancer cells were killed during the same period of heat exposure compared to normal cells. Bakker et al. have used Microwave hyperthermia for the treatment of cancerous tissues. They used microwave energy to raise the temperature of breast cancer cells to a therapeutic level [45]. In the literature, linear antenna arrays have been used for microwave hyperthermia treatments. Bellizzi et al. [48], described in their work an invasive method using an electric diode was used to monitor the temperature, which is not feasible for use in human breasts. Microwave hyperthermia has shown promise as a cancer treatment, it is noted during the literature review that these technologies are still in the testing phase, have limitations, and have several drawbacks. These methods have more disadvantages as compared to benefits. Therefore, there is a need to introduce new techniques to overcome previous disadvantage strategies. Through the applications of nanotechnology approaches, it has become possible for the immediately safe treatment of breast cancer with control thermal therapy without any side effects through real-time monitoring using See-and-Treat procedures along with the Internet of Nanomedical Things (Ion MT) approaches [33]. The article emphasizes the importance of delivering thermotherapy at a suitable time with exact heat intensity using noninvasive techniques to effectively eradicate tumors. The combined use of nanorobotic technology along with heat control systems is a promising area of research that has the potential to revolutionize the ways medical complexity is treated. Through the literature review, researchers hope to identify areas where further research is needed to improve the efficacy and safety of Nanorobotic technology. The goal of this work is to provide a novel nanotechnology-based treatment system that can perform effectively. We propose a Gold Nano Thermo Robot for the management treatment procedure. This work summarizes the evidence underlying the use of thermometric parameters in breast cancer treatment, particularly in the context of heat therapy [49]. It shows promise for improving treatment outcomes as compared to previous efforts. Further research is needed to determine the optimal use of thermal parameters such as thermal doses and temperature timing to the tumors in breast cancer treatment and to identify the most effective strategies for incorporating them into clinical practices, the research work being referred to in the previous context are related to the field of nanotechnology, which is the study of materials and devices that are extremely small, typically at the scale of atoms and molecules, all interventions are tested with some limitations.

To the best of our knowledge, there has not been a working report for treating breast cancer with a Gold Nano Thermo Robot designed by gold nanoparticles empowered with sensor technologies and a comparative analysis of heat intensity generated by the coulomb explosion process. Moreover, to control the heat intensity develop a heat control system by governing mathematical equations so that heat can

**TABLE 1. Comparative analysis of previous published and our proposed study.**

Study [Refs.]	Nature of Study Therapy	Nano Smart Sensors	Nano Medical Devices	Coulomb Explosion Procedure	Heat Control System	Ion MT	Gold Nanoparticles Properties	Domain of Applications
Ashiq. et al.2013 [21]	Laser Induced Therapy	No	No	Yes	Yes	No	Yes	Breast Cancer
Aggarwal et al. 2022 [22]	Laser Therapy	No	No	Yes	No	No	Yes	Breast Cancer
McNabb et.al.2023 [23]	Radiation Therapy	No	No	Yes	No	No	No	Breast Cancer
Eversole et al. 2020 [24]	Laser Therapy	No	No	Yes	No	No	No	Breast Cancer
Sogomon yan et al.2023 [25]	Photothermal Therapy	No	No	Yes	No	No	Yes	Breast Cancer
O Dion et. al.2023 [9]	Photothermal Therapy	No	No	Yes	No	No	Yes	Breast Cancer
Santhakumar et al.2023 [28]	Photothermal Therapy	No	No	Yes	No	No	Yes	Breast Cancer
<b>Our Proposed Study</b>	Thermal Therapy	Yes	Yes	Yes	Yes	Yes	Yes	Breast Cancer

be maintained at 35 C<sup>0</sup> to 45 C<sup>0</sup> [23], [31]. This range of temperature can be used to kill cancer cells without damaging the neighboring healthy cells and it has been verified in many research studies in different unsaved ways. We have not found this in the whole literature. This research work is aimed at addressing this research gap. The comparative analysis of our

proposed study and those previously published are shown in Table 1.

Finally, accurate results of the proposed nanotherapeutic system showed, that control thermal therapy for breast cancer disease employing the proposed heat control system monitoring by **See and Treat** technique using an interbody



networking system proved to be more accurate and safer with cancer patient treatment as compared to traditional approaches mentioned in the literature.

### III. DESIGN METHODOLOGY OF THE PROPOSED GOLD NANO THERMO ROBOT

#### A. MORPHOLOGY OF PROPOSED GOLD NANO THERMO ROBOT

The proposed Gold Nano Thermo Robots (GNTRs) are made of gold metal. Gold is a key element in the transmittal of electrical signals throughout the body and can absorb heat and then release it in a controlled manner [24]. Gold compounds have attracted considerable interest as anti-cancer drugs. Gold nanoparticles (AuNPs) are widely used in the research of cancer diagnosis and therapy due to their excellent properties such as surface-enhanced Raman spectroscopy, surface plasma resonance, controlled synthesis, the plasticity of surface morphology, biological safety, and stability [24]. The structure of the proposed nanorobots is designed after inspiration from the unicellular biological organism's Chlamydomonas structures that help complete their tasks promptly, as depicted in Fig. 6.

#### B. COMPONENTS OF GOLD NANO ROBOTS

The proposed Gold Nano Thermo Robot (GNTR) consists of dynamic control of nanomotors for effective cancer treatment that carries out predetermined tasks and includes a departure from conventional tumor-directing nanoplatforms in favor of nanomotors, showing improved abilities for deep tumor penetration due to their self-propelled technique. This modification towards nanomotors represents a state-of-the-art approach to cancer therapy, harnessing their unique capabilities to attain more effective penetration into tumor tissues, potentially enhancing the precision and efficiency of therapeutic involvement. devices [57]. The navigational network installed inside the patient's body keeps track of all moving nanorobots to provide them with accurate topographical data. This proposed novel nanodevice is empowered with nano sensors including a nano camera, heat sensor, heat storage, photo sensor, a location sensor, biochemical sensors, timer sensors, heat transducer device and heat storage devices, a camera that can pinpoint exactly the position where the Nano robots are located inside the body. Actuators, sensors, power, control, communications, and interfacial components are used in the assembly of proposed nanorobots [38], the proposed model of GNTR is shown in Fig. 6.

#### IV. DISCRETE MESH PROCESS

Gold is a good conductor of heat because its nodes (atoms) are arranged in a way that facilitates rapid and efficient transfer of thermal energy. There are three means of transfer of heat, Radiation, Convection, and Conduction. In our study, we have been focused on the conduction technique. Through conduction, heat can transfer from one place to the other place of gold nano rod due to direct contact of nodes (atoms) as shown in Fig.8. In the discretization process [8], the physical

domain is divided into a finite number of discrete points or nodes, one of which is the gold rod of the Gold Nano Thermo Robot, as shown in Fig. 8 and the PDE is replaced by a set of equations that relate the values of the unknown quantity at these discrete points. These equations are called difference equations because they express the difference between the value of the unknown quantity at one point and its value at a neighboring point. In the case of a 1D heat equation, a Gold Nano Rod, which behaves like a straight line, is used as the physical domain, and the discretization process involves dividing this line into a finite number of points or nodes as described in Fig. 8. Each node is assigned a value of the unknown temperature, and the heat equation is replaced by a set of differential equations that relate the temperatures at neighboring nodes [72].

#### A. COMPLEX INTERNAL DISCRETIZE MESH STRUCTURE OF GNTRS

The proposed Gold Nano Thermo Robot (GNTR) may be thought of as a hierarchical arrangement of building blocks, assuming its internal structure is made up of several horizontal rods of gold, each of which is composed of mesh-discretized nanoparticles, or, as said, tiny atoms [72]. The Internal structure of a Gold Nano Robot may be built using a flexible and scalable method that allows for fine control and manipulation at the nanoscale, mesh-discretized nanoparticles, or atoms [8]. It is assumed, that the entire internal area of a Gold Nano Thermal Robot is divided into several equal lengths of gold nanorods. Each nanorod consists of an  $n + 1$  node, as shown in Fig. 7. In the discretization process, the physical domain is divided into a finite number of discrete points, or nodes. One of the gold rods is taken, as shown in Fig. 8, and the PDE is replaced by a set of equations that relate the values of the unknown quantity at these discrete points. These equations are called difference equations because they express the difference between the value of the unknown quantity at one point and its value is a neighboring point [8].

#### V. MECHANISM OF ACTION OF PROPOSED GNTR

The proposed GNTR is a novel nano-therapeutic system that works through a complicated system of advanced technologies. It applies nano sensors, heat sensors, and nano cameras to gather precise interior data such as biomarkers, temperature, and images. ECG nanosensors and pulse oximetry monitor heart activity and blood oxygen levels [33]. The temperature storage device stores a specific amount of heat and controls the intensity of heat to maintain in range between  $38\text{ }^{\circ}\text{C}$  to  $45\text{ }^{\circ}\text{C}$  [20]. When a GNTRs cluster with a radius of 10 nm is exposed to a laser pulse with a duration of 10 ns, a coulomb explosion technique occurs [42]. During this wonderful procedure, at once a huge amount of heat waves and numerous micro bullets are created inside the environment of treatment with a radius of  $5\text{ }\mu\text{m}$  Fig. 10., illustrates how the intensity of heat and nano bullets radius increases from 5 to 10 nm with an increase in pulse duration in the range of 10 to 40 ns [37]. The proposed Nano therapeutic device also has the

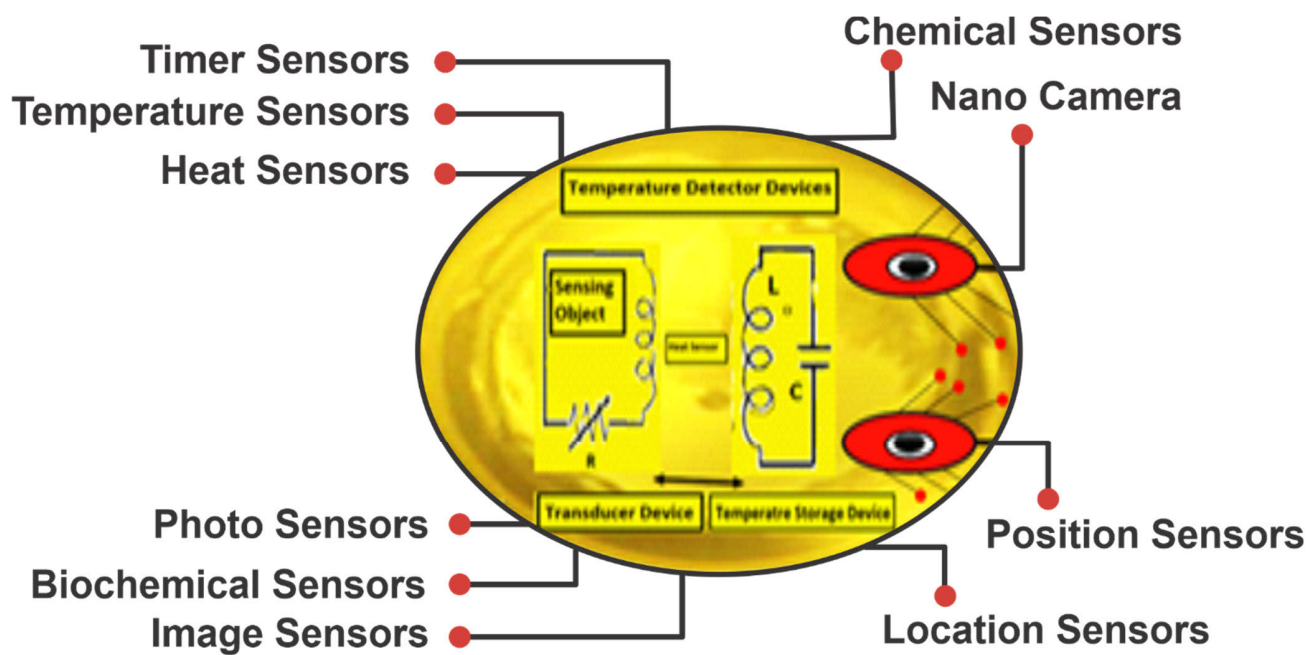


FIGURE 6. Design of the proposed Gold Nano Thermo Robot.

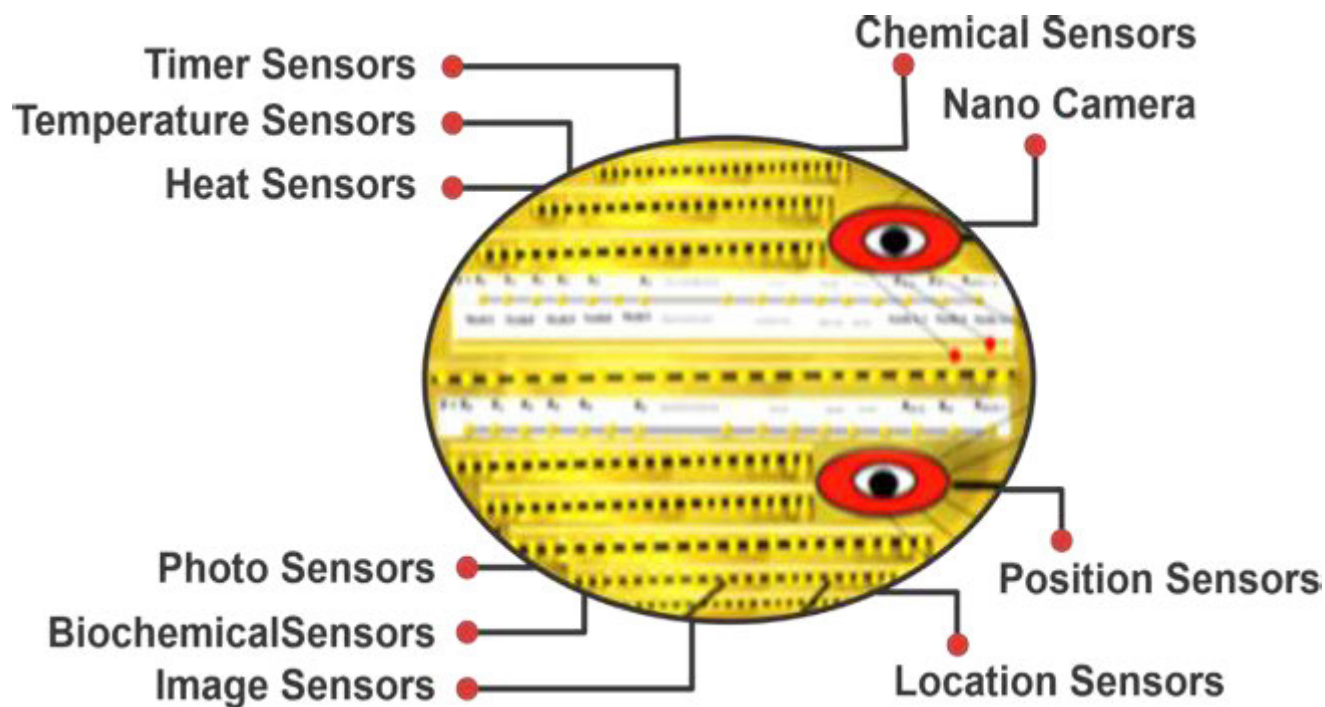


FIGURE 7. Discretization mesh of proposed Gold Nano Thermo Robot (GNTR).

aptitude to control the intensity of heat by using the proposed heat control system at  $33\text{ }C^0$  to  $45\text{ }C^0$  [31]. This range of heat is sufficient to damage the cancerous cells with a radius of 8 to  $13\text{ }\mu\text{ m}$  of proposed GNTRs [31], [34]. A Transducer device is used to transfer the store heat to the tumor. A Temperature detector device is used to detect the temperature. By using

the novel **See and Treat** technique, inside the body, nano sensors and nano cameras monitor vital signs and collect detailed health data [33]. This information is transmitted through in-body networks and gateways, ensuring real-time data flow. Implantable devices enhance monitoring capabilities. External Body Area Network devices, such as wearables,

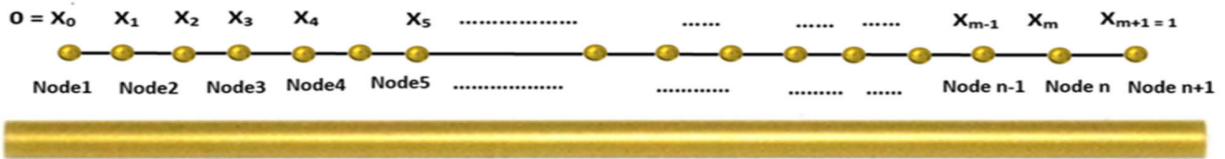


FIGURE 8. Gold nano rod is divided into discrete finite nodes.

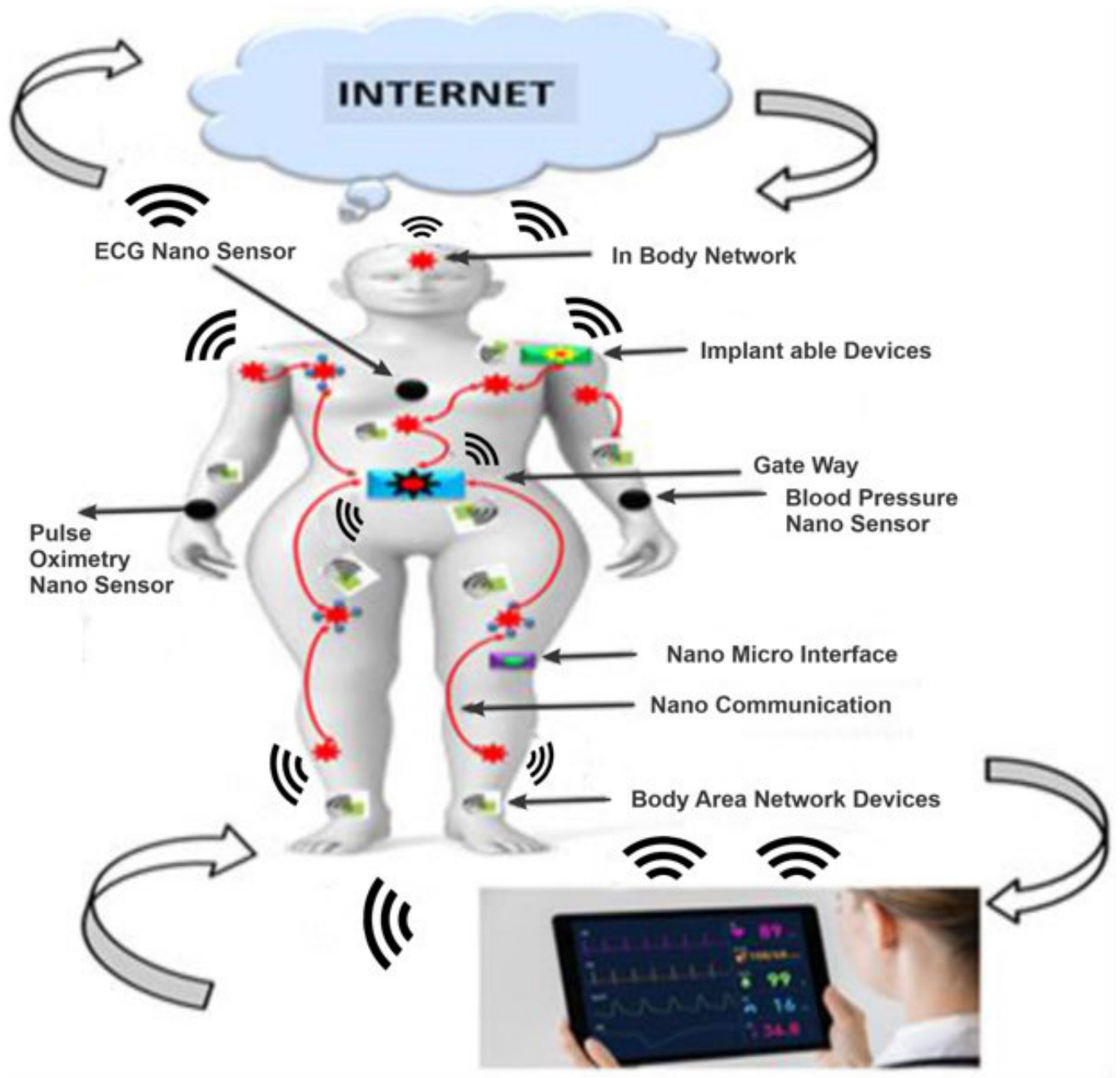


FIGURE 9. Proposed inter body communication network architecture.

enable user collaboration. Digital mobile devices provide a user-friendly interface for both patients and physicians [20].

Internet technology connects the GNTR to healthcare professionals, allowing for remote diagnosis and treatment

recommendations. This integrated system enables precise, real-time healthcare monitoring and improves access to medical expertise, revolutionizing nanomedicine [19]. Patients access their information through digital devices like mobile phones and tablets, actively engaging in their healthcare. This innovative system enables accurate real-time diagnostics and remote medical assistance, improving patient care and convenience for medical specialists [34].

## VI. INTER BODY COMMUNICATION NETWORK

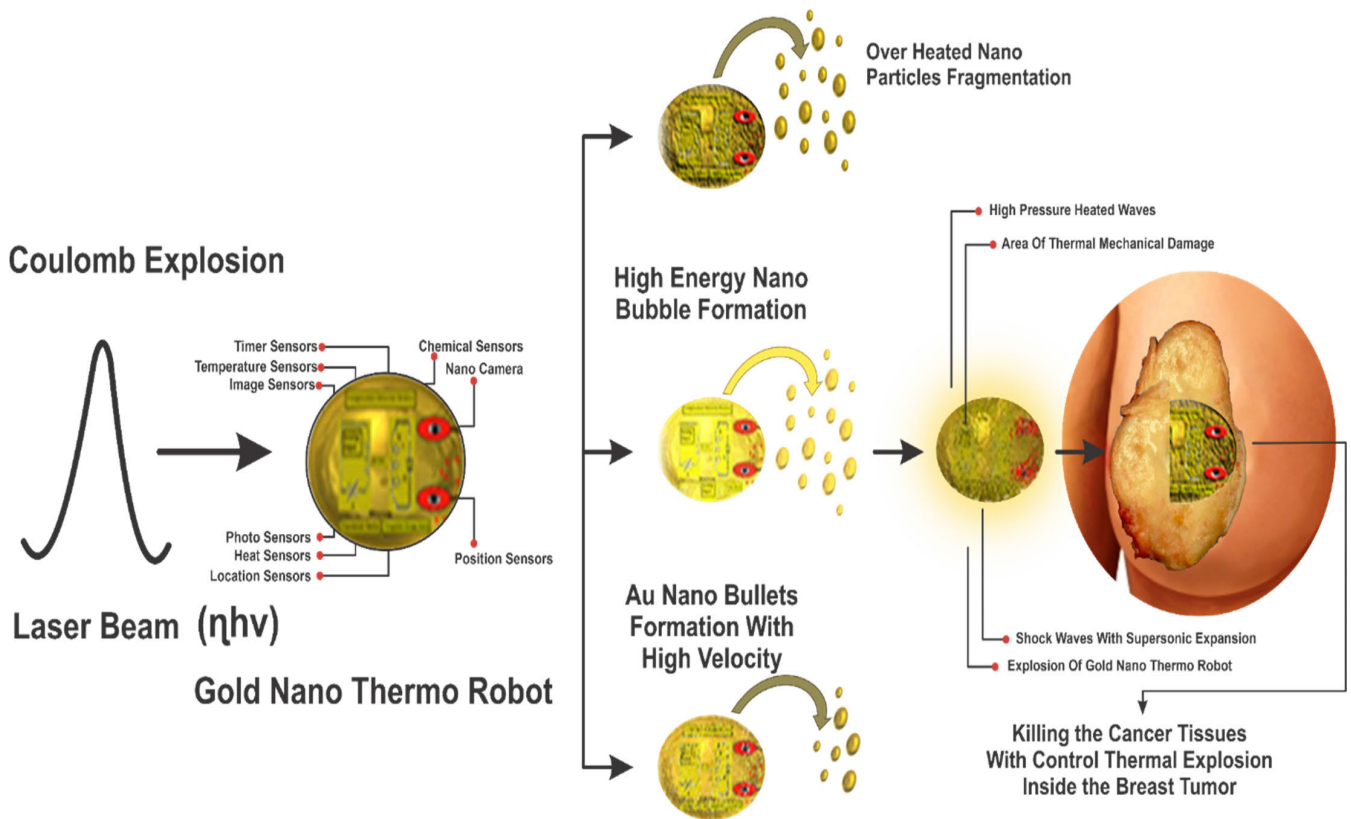
The Inter-Body Communication Network (IBCN) architecture for breast cancer treatment is a novel paradigm in oncology [34]. The concept has the potential to dramatically alter how breast cancer is treated because of its improved precision, efficacy, and results for patients. Real-time monitoring, individualized therapy changes, and enhanced patient interaction are made possible by this comprehensive approach, utilizing a synergy of innovative technologies to offer highly customized, real-time services [35]. Monitoring the hyperthermia during treatment choices for patients with breast cancer [12]. This sophisticated system combines several different components, including blood pressure nano sensors, heat sensors, nano cameras, ECG nano sensors, pulse oximetry, nano micro interfaces, in-body networks, gateways, body area network (BAN) devices, implantable devices, internet connectivity, and digital mobile phones and tablets nano sensors are one type of these sensors [35]. They carefully document the electrical activity of the heart to provide important information about cardiovascular health. Additionally, vascular dynamics are monitored by blood pressure nano sensors, allowing for a thorough evaluation of the patient's general health [20]. Heat sensors that are built into the design act as sentinels for localized inflammation or aberrant tissue activity. Nano cameras are used when abnormalities are found. These powerful imaging tools provide a thorough picture of the afflicted area by collecting real-time visual information [20].

## VII. ROLE OF ION MT FOR NANO THERAPEUTIC SYSTEM

The integration of an innovative nano robot device within the Ion MT framework, incorporating a wide array of sensors and devices, along with an accurate temperature control system, represents a groundbreaking leap in breast cancer treatment [20]. This approach combines accuracy, personalization, and real-time sensitivity to provide a highly effective means of fighting breast cancer with localized heat therapy [35]. When combined with information from other sensors, such examinations create an accurate representation of the patient's health state, assisting physicians in making acceptable decisions. Using nano-microscopic interfaces, the complex network of sensors and cameras inside the body is connected, enabling error-free information transfer [37]. Effective collection of information and transmission is made possible by these interactions, which are equipped with innovative digital signal processing capabilities. When directed towards the architectural main hub, the gateways, this unpro-

cessed data is transmitted through in-body networks, which serve as a circulatory system for information [41]. In this kind of architecture, gateways are essential because they serve as an interface that links in-body networks and the outside world [37]. To preserve data integrity and confidentiality for patients, they aggregate, manipulate, and then encrypt the data. The data is communicated to external devices, such as body area network devices after it has been prepared. Body area network devices serve as extensions of the inter-body network that are frequently incorporated into wearable technology or smart clothes [42]. These tools enable patients to interact with their health findings in an accessible manner by transmitting real-time health data to external interfaces like digital mobile phones and tablets [20]. Patients are empowered to take an active role in their medical treatment due to the accessibility and convenience of these devices [17]. In the global age of internet technology, architecture makes use of connectivity's capacity to bridge the gap between patients and medical professionals. The information collected by the nano sensors and other devices is easily communicated to distant medical specialists and data centers by cure internet channels [65]. The approach to breast cancer care is changing from a static, appointment-based procedure to a dynamic, data-driven one thanks to this real-time transmission, which enables ongoing evaluation and monitoring. The structure incorporates pulse oximetry sensors for continuous monitoring of oxygen saturation levels. This information is essential for evaluating general respiratory wellness as well as for individuals receiving cancer treatment [59]. Similarly, devices that are inserted are useful, particularly for individuals who need to receive treatments like chemotherapy [51]. These tools provide perceptions of the effectiveness of the treatment, allowing for prompt modifications and minimizing any adverse consequences. An approach to treating breast cancer that is focused on the patient results from the collaboration of various technologies. Patients may effortlessly communicate information with their physicians through wearable body area network devices [68]. Medical professionals might simultaneously examine data patterns, remotely monitor the patient's development, and make defensible decisions [19].

9. A phenomenological picture of these complex physical effects is schematically shown in Fig.9. These technologies serve as user interfaces, provide a practical method of remote monitoring and control, and help decision-makers make well-informed choices [37]. They provide a practical method for remote monitoring and control, improving overall effectiveness and efficacy, and may provide a thorough and synergistic approach to the treatment of breast cancer. A Nano camera is a key component of our proposed “**See-and-Treat**” approach. In the context of breast cancer treatment, A Nano camera has the potential to be used to guide treatment procedures, improve the accuracy and precision of cancer treatment, and have the potential to monitor the efficacy of treatment in real-time by visualizing the uptake of Nano robot in cancer cells during thermal therapy. Time consumption can be



**FIGURE 10.** Schematic coulomb explosion procedure. Conventional laser induced into the elliptical shape of GNTRs for the formation of shock waves and thermal expansion in the specific location of breast cancer.

reduced between diagnosis and treatment procedure by using the “See and Treat” technique.

### VIII. COULOMB EXPLOSION PROCEDURE

In this section, a coulomb explosion model is proposed to get the heat that will work as heat therapy for the treatment of fatal cancer cells at the molecular and nano atomic level [41]. The elliptical geometry shape of GNTR, consisting magical properties of gold, can deliver ephemeral and powerful thermal pulses by occurring coulomb explosion [41]. The coulomb explosion occurs when the proposed GNTRs are by short laser pulses, the energy of the laser is absorbed by the GNTRs, causing its temperature to rapidly increase [42]. This process is known as photo thermal heating, and it occurs because the laser energy is converted into heat energy when it interacts with the nanorobots. The rate at which the temperature of the Nano robots increases depends on the laser pulse duration, intensity, and absorption properties of the nanorobots [37]. When the temperature of the nanorobots reaches a certain threshold, nonlinear effects can occur. This results in the formation of micro bubbles, which are small gas-filled cavities that can form on the surface of the nano robots. These bubbles can grow rapidly due to the high temperature and pressure, and they can eventually burst, creating acoustic waves that can be detected using ultrasound [37]. A phenomenological picture of these

complex physical bubble’s formation procedure, high energy shockwaves, and generation of huge amounts of temperature thermotherapy is schematically described in Fig. 10. This temperature can be used to damage cell cells and lead to their destruction by controlling the intensity of heat- induce heat therapy, which involves heating the cancerous tissue to a temperature range between  $38\text{ }^{\circ}\text{C}$  to  $45\text{ }^{\circ}\text{C}$  to selectively kill the cancer cells [37]. In thermal expansion mode, the Gold Nano Robot absorbs the radiation energy, and the surface temperature increases rapidly, leading to a local expansion of the material. This expansion causes a transient modulation of the nanorobot’s thermal conductivity, which in turn affects the heat transfer within the nanorobot. Under the action of short laser pulses in the spectral range of the Surface Plasmon Resonance (for a solid rod Gold Nano Robots the maximum absorption is  $\sim 520\text{ nm}$ ), gold Nano robots are excited to upper electronic states owing to absorption of many photons [24]. Through rapid (picosecond time scale) relaxation, Gold Nano Robots atoms decay to their ground state with effective electron -phonon conversion of the absorbed photon energy into thermal energy [24]. This heat energy is then managed by using a heat control system in the required target range [79]. The Whole coulomb explosion procedure is described in the given below flowchart in Fig. 11. Depending on the Gold Nano Robots temperature,  $U$ , the following effects can occur. Expansion of a single gold Nano robot

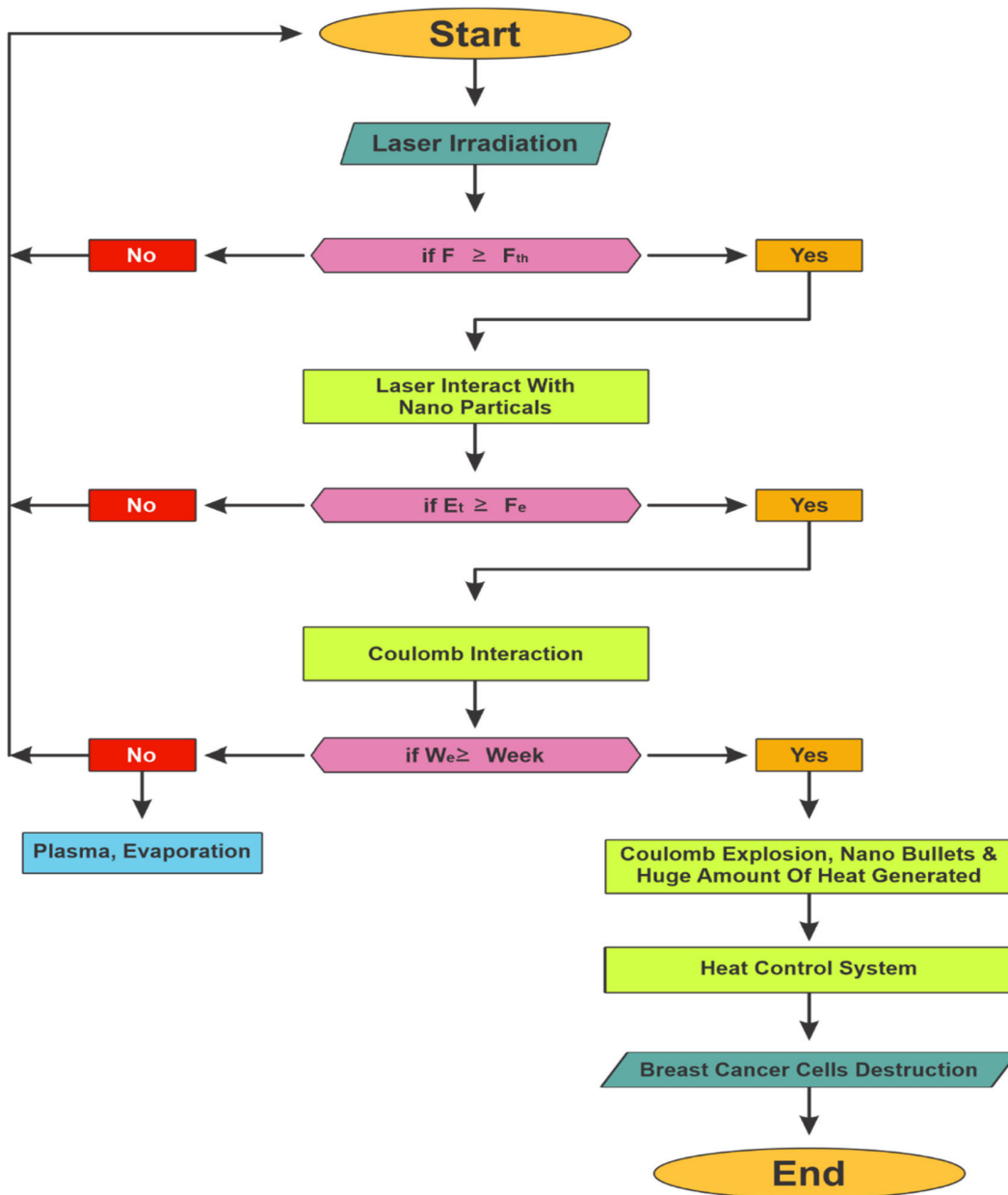


FIGURE 11. Schematic coulomb explosion procedure flowchart.

and surrounding thin liquid layer, which is accompanied by the generation of linear acoustic waves known as the ‘classic’ photo acoustic (PA) effect,  $U_{LV} \leq U < U_{GNRM}$ . Where  $U_{GNRM}$  is the Gold Nano Robot melting point,  $\sim 1063 \text{ C}^0$  [10]. This bubble formation with expansion and collapse, which is accompanied by the production of acoustic and shock waves  $U_{GNRM} \leq U < U_{GNRB}$ . Where  $U_{GNRM}$  is the Gold Nano Robot boiling point of  $\sim 2719 \text{ C}^0$  [9], with Gold Nano Robot melting;  $U \geq U_{GNRM}$ , Gold Nano Robot is boiling with the formation of gold vapor around liquid gold drops.

1) **Time Scale Approximations** The goal of the theoretical modeling is to estimate the threshold laser energy

density  $E_{exp} \rho$  required for the realization of thermal expansion mode, which is realized through the rapid overheating of a strongly absorbing target during a short laser pulse when the influence of heat diffusion is minimal [10]. Let us first estimate the time scale for thermal relaxation due to heat diffusion from the surface of the nanorobot. Near Gold Nano Robot  $GNR \leq 5R$ , where R is the Nano robot radius, the thermal relaxation time for an elliptical GNTR can be estimated as  $e_T = \frac{R^2}{6.75K}$ , where k is the thermal diffusivity [24]. For  $R = 50, 100, \text{ and } 200\text{nm}$ , estimates are approximately 2.6, 10, and 41 ns, respectively. For a laser pulse duration  $e_p \leq e_T$  heat is generated within the GNTR more

rapidly than can be diffused away, thus we can neglect heat losses from the surface of GNTR due to heat diffusion into the surrounding medium. This condition for smaller gold Nano robots is valid with picosecond and femtosecond laser pulses. However, Consider here nanosecond pulse durations because most of the experimental results (ours and others) have been obtained with lasers generally used in the biomedical field ( $e_P \sim 5\text{-}12$  ns), which are less expensive and less harmful to normal tissue (compared with picosecond and femtosecond lasers) and still satisfy the condition  $e_P \leq e_T$  for relatively large gold nano robots. With this assumption, the probability of a non-PT mechanism of explosion is very low because multi-photon ionization usually occurs more effectively under super-short femtosecond pulses [41].

#### A. THRESHOLD INTENSITY FOR LASER -INDUCED THERMAL EXPLOSION

The threshold intensity for laser-induced thermal explosion during coulomb explosion is important in this technique because it helps to determine the laser parameters needed to produce the desired thermal effect without causing excessive damage to the surrounding healthy tissue [50]. By carefully controlling the intensity of the laser, clinicians can ensure that. Laser energy is sufficient to induce thermal damage to the tumor while avoiding the potentially damaging effects of a full coulomb explosion [37].

Consider a nanoparticle delivered selectively to a targeted site, for example, a breast cancer tumor to be irradiated by a laser of intensity  $I$  [24]. The power of the absorbed electromagnetic field is.  $P = \sigma \text{ abs } I$ , where  $\sigma \text{ abs}$  as the Gold Nano Robot's cross section of absorption. If  $\sigma \text{ abs}$  is large enough, a thermal explosion of the Gold Nano Robot may occur at certain values of the threshold laser intensity  $E_{exp} \rho$  which is less than the threshold intensity for optical plasma formation in the surrounding medium [10]. Under the thermal explosion of Gold Nano Robots, The specific situation where the energy required for a complete thermal explosion of the Gold Nano Robots  $\rho q V = N_{Au} q_1 V$  and energy absorbed by the gold nanoparticles of GNTRs during the time of its inertial retention in vapor condition is  $e_{expl} = \frac{R}{u_s}$ , go beyond the energy required for the Gold Nano robot's complete desertion. Here,  $V$  is volume,  $\rho$  is density,  $N_{Au}$  is the number of Au atoms per unit volume and  $u_s$  is the sound velocity in Au vapor at the critic Temperature  $U_{cr} \sim U_{GNRB}$ ;  $q$  and  $q_1$  are the nano gold nodes of the proposed Gold Nano Robot [41]. Laser pulse duration is considered  $e_L (\sim 1\text{ons}) \gg e_{expl} = \frac{R}{u_s} (\sim 1\text{ps for } R \sim 10\text{nm})$ , where  $e_{expl}$  is an explosive evaporation time [42]. To compute  $E_{exp} \rho$  could write the following energy balance equation.  $\sigma_{abs} I_{expl} \frac{R}{u_s} \approx \rho q v$ , in terms of absorption efficiency.  $E_{abs} = \frac{\sigma_{abs}}{\pi R^2}$  the threshold strength of the laser energy for a thermal explosion of the rod-shaped gold nanoparticle is described in Fig. 10. Thus, the Gold Nano Robot in a relatively strong laser field with

intensity  $I \geq I_{(expl)}$  during the shot time  $e_{expl} \sim \frac{R}{u_s}$  convert into a gas (vapor) radius of Gold Nano Robot is  $\sim R$ , contained high-temperature  $U \sim U_{GNRB}$  and high-pressure  $P \gg P_{(\infty)}$ , where  $P_{(\infty)}$  is the ambient pressure [37]. We assumed here that a thermal explosion of a Gold Nano Robot is caused by the generation of shockwaves that increase with a supersonic velocity  $u_s = \frac{R}{e_{expl}} = \frac{I_{expl}}{4\Delta H} \approx 10^5 \text{cms}^{-1}$ , Here  $\Delta H = \Delta H_{300-vap} + \Delta H_{vap}$ , where  $\Delta H_{300-vap} +$  is the enthalpy change per unit volume for heating the Gold Nano Thermo Robot from ambient high- temperature to the vaporization high temperature and  $\Delta H_{vap}$  is the vaporization enthalpy per unit volume [23]. The shockwaves could be waves of high acoustic which spread out over long distances around an epicenter of explosion [24]. The whole procedure of coulomb explosion has been explained in flowchart Fig. 11. All this Schematic coulomb explosion procedure for shock waves and conservative bubble creation laser-induced thermal expansion of elliptical shape Gold Nano Thermo Robot is explained in Fig. 10.

#### IX. SCHEMES FOR HEAT CONTROL SYSTEM

Creating a mathematical model for a heat control system used in thermal therapy for breast cancer requires understanding the principles of heat transfer and how they can be applied to maintain a specific temperature for a set duration. To control the heat intensity at  $42^\circ\text{C}$  for 30 minutes, the proposed system can use the heat conduction equation, which is a form of the heat equation. The heat equation describes how heat diffuses through a medium over time. To maintain a constant temperature of  $42^\circ\text{C}$  for 30 minutes, the proposed nano therapeutic system needs to apply appropriate boundary conditions and initial conditions. The system will need to specify the temperature boundary conditions on the edges of the body region the proposed system is heating. These conditions will depend on the specifics of the treatment setup. In general, the proposed system would set the temperature to  $42^\circ\text{C}$  at the boundaries of the region of interest. The initial condition represents the temperature distribution at the beginning of the treatment. The system will need to set the initial temperature distribution within the treatment region and time stepping. The system will use numerical methods to solve the 2D heat equation over time. One popular approach is the finite difference method, which discretizes the spatial and temporal derivatives in the equation and iteratively updates the temperature values at each grid point. The whole scheme of the heat control system has been explained in given below in Fig. 16.

#### X. MATHEMATICAL MODEL

The following are the equations for the generic second order linear PDE with two independent variables and one dependent variable.

$$\alpha \frac{(\partial^2 U)}{\partial x^2 U} + \beta \frac{(\partial^2 U)}{\partial x \partial y} + \gamma \frac{(\partial^2 U)}{\partial y^2 U} + \delta = 0 \quad (1)$$

where  $\alpha$ ,  $\beta$ ,  $\gamma$  are functions of the independent variables,  $x$ ,  $y$ , and  $\delta$  can be a function of  $x$ ,  $y$ ,  $U$ .

$\frac{\partial U}{\partial x}$  and  $\frac{\partial U}{\partial y}$  If  $\beta^2 - 4\alpha\gamma = 0$ , Equation (1) is called parabolic partial differential equation. In our problem we take one of the gold metal rods from the proposed GNTR structure for heat conduction equation as an example for getting solution as shown in Fig. 7. One dimension of the heat equation is.

$$\alpha \frac{(\partial^2 U)}{\partial x^2} = \frac{\partial U}{\partial t}, \quad 0 \leq x \leq L, t \geq 0 \quad (2)$$

where, U is considered as a function of temperature location, x, and time, U(x, t), t Thermal diffusivity,  $\alpha$  is constant-coefficient. In  $\alpha \frac{K}{\rho}$ , here K is considered the thermal conductivity of gold metal, and the density of gold rod is represented by  $\rho$ . Equation (1) is known as a model of the heat condition of a gold rod with a thickness of L. The domain of solution is a semi-infinite strip of width that continues indefinitely in time. In practical computation, the solution is obtained only for a finite time, say  $\frac{t}{max}$ . The solution to equation (1) requires the specification of boundary conditions at  $x = 0$  and  $x = L$  and initial conditions at  $t = 0$ . Simple boundary and initial conditions are  $U(0, t) = U_0$ ,  $U(L, t)$  and  $U(x, 0) = f_0(x)$ . To find the amount of heat U everywhere in x and y, and over time t. i, j, and k are the steps for each difference for x, y, and t, respectively. We can get the solution of U by using this formula:

$$U(x, y, t) = U_{i,j}^K, \alpha \left( \frac{\partial^2 U}{\partial x^2} + \frac{\partial^2 U}{\partial y^2} \right) = \frac{\partial U}{\partial t} \quad (3)$$

K is the superscript to denote the time step for U. A heat equation of two dimensions could be written using a finite method like this:

$$\left( \frac{U_{i,j}^{K+1} - U_{i,j}^K}{\Delta t} \right) = \alpha \left( \frac{U_{i+1,j}^K - 2U_{i,j}^K + U_{i-1,j}^K}{\Delta x^2} + \frac{U_{i,j+1}^K - 2U_{i,j}^K + U_{i,j-1}^K}{\Delta y^2} \right) = 0 \quad (4)$$

If arrange the above equation by taking  $\Delta x = \Delta y$  get this equation as:

$$U_{i,j}^{K+1} = r(U_{i+1,j}^K + U_{i-1,j}^K + U_{i,j+1}^K + U_{i,j-1}^K - 4U_{i,j}^K) \quad (5)$$

where  $r = \alpha \frac{\Delta t}{\Delta x^2}$ . Here is an explicit method used for the solution of the heat equation, which will be numerically stable whenever.  $\Delta t \leq \frac{\Delta x^2}{4\alpha}$

**A. FINITE DIFFERENCE METHOD**

For the heat equation, the finite difference method [71] has been used to approximate temperature at different points in a domain as a function of time. This approach involves discretizing the domain of the gold rod into a grid of points, as shown in Fig. 8., and approximating the second-order partial derivatives has been used for temperature with finite differences [29]. For a one-dimensional heat equation, the discretization involves dividing the domain of the gold rod into a series of equally the discretization involves dividing the domain of gold rod into a series of equally speedy points along the x-axis as explained in Eq. 4. Letting U(x, t) be the

temperature at a point x and time t, we can approximate the second derivative of U with respect to x using the following finite difference approximation:

$$\frac{[U(x+h, t) - 2U(x, t) + U(x-h, t)]}{h^2} \quad (6)$$

where h is the distance between adjacent grid points. This approximation is then substituted into the heat equation, which becomes a set of ordinary differential equations (ODEs) for each grid point. The resulting ODEs can be solved numerically using an appropriate numerical method, such as Euler’s method or the Runge-Kutta method [29]. The solution is then updated at each time step, with the temperature at each grid point being computed based on the temperature at neighboring grid points of the gold nanorod. Now For a two-dimensional heat equation, the discretization involves dividing the domain into a grid of points in the x-y plane. The proposed system can be used to approximate the second partial derivatives of temperature with respect to x and y using the following finite difference approximations:

$$\frac{[U(x+h, y, t) - 2U(x, y, t) + U(x-h, y, t)]}{h^2} \quad (7)$$

(Used for x direction)

$$\frac{[U(x, y+h, t) - 2U(x, y, t) + U(x, y-h, t)]}{h^2} \quad (8)$$

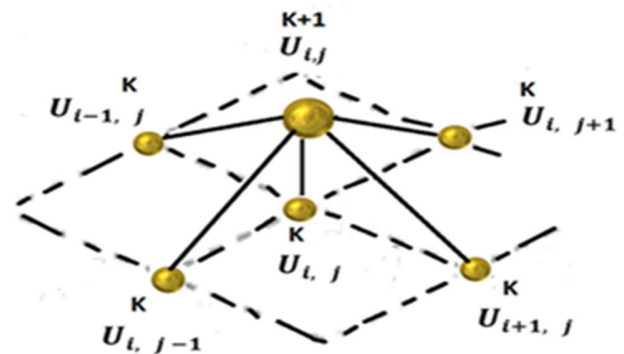
(Used for y direction)

**1) FORWARD TIME CENTRAL SPACE (FTCS) SCHEME**

FTCS is an explicit scheme [71], as explained in Fig. 13, which means  $U_i^{K+1}$  can be explicit if the values of U at the proceeding interval level n are identified. Therefore, the FTCS scheme has been used to solve our problem as described in equation (9).

$$\frac{U_i^{K+1} - U_i^K}{\Delta t} = \frac{\alpha}{\Delta x^2} (U_{i+1}^K - 2U_i^K + U_{i-1}^K) \quad (9)$$

where  $r = \frac{\alpha \Delta t}{\Delta x^2}$ , r is considered a grid Fourier number.



**FIGURE 12. Explicit method stencil.**

**2) BACKWARD TIME CENTRAL SPACE (BTCS) SCHEME**

BTCS is an implicit scheme [29], as explained in Fig. 14, which means that the temperature at each time step has been



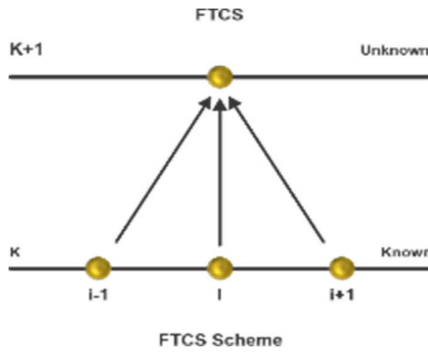


FIGURE 13. FTCS scheme.

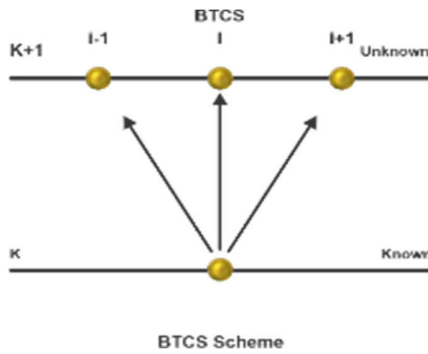


FIGURE 14. BTCS scheme.

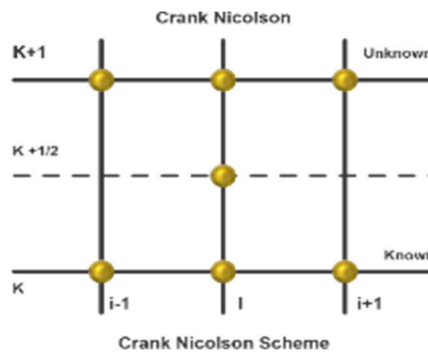


FIGURE 15. Crank Nicolson scheme.

computed using a system of linear equations that must be solved iteratively. For this goal, the BTCS scheme has been developed as described below in Eqs 11 and 12.

$$(U_t)_i^{K+\frac{1}{2}} = \alpha(U_{xx})_i^{n+\frac{1}{2}} = \frac{\alpha}{2} \left[ (U_{xx})_i^K + (U_{xx})_i^{K+1} \right] \quad (10)$$

Now the system is applied  $U_{xx}$  at  $\frac{K+1}{2}$  time level by the average of the preceding and existing time values using  $n$  and  $n+1$ , respectively. A second-order central difference rough calculation of the time derivative at the  $\frac{K+1}{2}$  time level and the space derivatives are described in equation (14).

$$\frac{U_i^{K+1} - U_i^K}{\Delta t}$$

$$= \frac{\alpha}{2} \left[ \frac{U_{i+1}^K - 2U_i^K + U_{i-1}^K}{\Delta x^2} + \frac{U_{i+1}^{K+1} - 2U_i^{K+1} + U_{i-1}^{K+1}}{\Delta x^2} \right] \quad (11)$$

$$\begin{aligned} & U_i^{K+1} \\ &= U_i^K + \frac{r}{2} \left[ \left( U_{i+1}^{K+1} 2U_i^{K+1} U_{i-1}^{K+1} \right) \right] \frac{1}{\alpha} \left[ \frac{U_i^{K+1} - U_i^K}{\Delta t} \right] \\ &= n \left[ \frac{U_{i+1}^k - 2U_i^k + U_{i-1}^k}{(\Delta x)^2} \right] \\ &+ (1-n) \left[ \frac{U_{i+1}^{k+1} - 2U_i^{k+1} + U_{i-1}^{k+1}}{(\Delta x)^2} \right] \end{aligned} \quad (12)$$

Now the system will convert into an explicit scheme [71], as shown in Fig. 12., when putting the value of  $n = 1$  and will convert into an implicit scheme [29] when putting  $n = 0$  in Eq. 17, as described in Equ. 4. and Equ.5. above respectively.

$$\frac{1}{\alpha} \left[ \frac{U_i^{t+1} - U_i^t}{\Delta t} \right] = \left[ \frac{U_{i+1}^t - 2U_i^t + U_{i-1}^t}{(\Delta x)^2} \right] \quad (13)$$

$$\frac{1}{\alpha} \left[ \frac{U_i^{t+1} - U_i^t}{\Delta t} \right] = \left[ \frac{U_{i+1}^{t+1} - 2U_i^{t+1} + U_{i-1}^{t+1}}{(\Delta x)^2} \right] \quad (14)$$

Let's choose  $n = 0.5$  in our problem between 0 and 1

$$\begin{aligned} &= \frac{1}{\alpha} \left[ \frac{U_i^{t+1} - U_i^t}{\Delta t} \right] 0.5 \left[ \frac{U_{i+1}^t - 2U_i^t + U_{i-1}^t}{(\Delta x)^2} \right] 0.5 \\ &\times \frac{U_{i+1}^{t+1} - 2U_i^{t+1} + U_{i-1}^{t+1}}{\Delta x} \end{aligned} \quad (15)$$

By applying these equations to all the nodes of selected gold Nano rode, we shall obtain a system with a tri-diagonal coefficient matrix. The Crank Nicolson Scheme is the average.

$$\begin{aligned} &-0.5 \left[ \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_{i-1}^{k+1} + \left[ 1 + 2 \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_i^{k+1} \\ &-0.5 \left[ \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_{i+1}^{k+1} = 0.5 \left[ \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_{i-1}^k \\ &+ \left[ 1 - 2 \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_i^k - \left[ \frac{\alpha \Delta t}{(\Delta x)^2} \right] U_{i+1}^k \end{aligned} \quad (16)$$

The expression  $\frac{\alpha \Delta t}{(\Delta x)^2}$  is known as the diffusion number and can be denoted by  $m$ , i.e.,  $m = \frac{\alpha \Delta t}{(\Delta x)^2}$  then Eq. 16. becomes as below:

$$\begin{aligned} &-0.5mU_{i-1}^{k+1} + (1 + 2m) U_i^{k+1} - 0.5U_{i+1}^{k+1} 0.5U_{i-1}^k \\ &+ (1 - 2m) U_i^k + mU_{i+1}^k m \left[ U_{i-1}^{k+1} + U_{i+1}^{k+1} \right] \\ &+ 2(1 + m) U_i^{k+1} = m \left[ U_{i-1}^k + U_{i+1}^k \right] \\ &+ 2[(1 - m)] U_i^k \end{aligned} \quad (17)$$

Eq. 17., is known as the Crank Nicolson scheme as has been explained in Fig.15. is related to the boundary and initial conditions, are as explained. If  $x$  interval is divided into  $0 \leq x \leq 1$  into  $h$  equal interval per row time. Then it could be possible to find  $(h-1)$  internal mesh

points per time row, for  $k = 1$  and  $i = 1, 2, 3, 4, \dots, h-1$  provided by the system of  $(h-1)$  linear-equations for the  $(h-1)$  unidentified values  $U_1^1, U_2^1, U_3^1, U_4^1, U_5^1, \dots, U_{h-1}^1$  in the first time row in terms of the initial values  $U_0^0, U_1^0, U_2^0, U_3^0, U_4^0, U_5^0, \dots, U_h^0$  and the boundary values  $U_0^1 = 0, U_k^1 = 0$ . Likewise for  $k = 1, k = 2$ , and so on that is, for each time row, to find a solution to such a system of  $(h-1)$  linear equations resultant from Eq. 9. From Eq. 9, the solution could be found by converting it into matrix form, as described below:

$$TU = tr \tag{18}$$

where the unknown  $U = U^{K+1}$  is the known concentration (19) and (20), as shown at the bottom of the next page,

By convergence, it's the condition now became as

$$q = \frac{\alpha \Delta t}{(\Delta x)^2} \leq 0.5 \text{ or } q = \frac{\alpha \Delta t}{(\Delta x)^2} \leq \frac{1}{2} \tag{21}$$

$$q = \frac{\alpha \Delta t}{(\Delta x)^2} \tag{22}$$

Condition in equation (22) is a drawback in practice. Indeed, to attain sufficient accuracy, we must choose  $\Delta x$  small, which makes  $\Delta t$  very small for equation (22). It is found to make the computation exceptionally lengthy, in this way more time durations had to require completing the project. To solve these issues, the Crank Nicolson scheme as shown in Fig.15., has been applied to overcome the issues.

### 3) THE STABILITY OF THE CRANK NICOLSON SCHEME

By using equation (9), the solution is given below:

$$q \left[ U_{i-1}^{K+1} + U_{i+1}^{K+1} + 2(1+q)U_i^{K+1} \right] = q \left[ U_{i-1}^K + U_{i+1}^K \right] + 2[1-m]U_i^K \tag{23}$$

Substituting (23) into (9), the worst-case solution is given below:

$$-qp^{(k+1)}[-1]^{i-1}[-1]^{i-1} + [-1]^{i+1} + 2(1+q)p^{k+1}[(1)]^i = q \tag{24}$$

$$p^k [1]^i [1]^{(i+1)} + [1]^{(i+1)} + 2(1+q)p^k [(-1)]^i p(-q)(-1) - 1 + 2(1+q) - r(-1) + 1 = q(-1) - 1 + 2(1-q) + q \tag{25}$$

A stability study would show that this implicit technique remains continually stable. This numerical discussion is explained step by step in the heat control system flow chart in Fig.14.

### 4) PSEUDOCODE

Pseudo-code for solving the two-dimensional heat equation using the finite difference method has been presented below:

- 1) Define the problem parameters such as the thermal diffusivity  $\alpha$ , the length and width of the domain  $L_x$  and  $L_y$ , the time interval  $T$ , the number of grid points  $N_x$  and  $N_y$  in the  $x$  and  $y$  directions and the time step size  $\Delta t$ .

Set the initial temperature distribution  $u(x, y, 0)$  for all grid points.

- 2) Compute the grid spacing's  $\Delta x = L_x/(N_x-1)$  and  $\Delta y = L_y/(N_y-1)$ .
- 3) Set the boundary conditions for the problem, such as  $u(x, 0, t)$ ,  $u(x, L_y, t)$ ,  $u(0, y, t)$ , and  $u(L_x, y, t)$ .
- 4) Define a matrix and also a vector for the system of linear equations to be solved at each time step.
- 5) Set the diagonal entries of a matrix to  $1 + 2\alpha \frac{\Delta t}{\Delta x^2} + 2\alpha \frac{\Delta t}{\Delta y^2}$  and the off-diagonal.
- 6) Entries to  $-\alpha 2\alpha \frac{\Delta t}{\Delta x^2}$  and  $-\alpha 2\alpha \frac{\Delta t}{\Delta y^2}$
- 7) For the first time step ( $t = \Delta t$ ), solve the system of linear equations to obtain the temperature distribution at  $t = \Delta t$ .
- 8) For the next time steps ( $t = 2\Delta t, 3\Delta t, \dots, T$ ), update the vector  $b$  based on the previous temperature distribution and solve the system of linear equations to obtain the new temperature distribution.
- 9) Output the final temperature distribution  $u(x, y, T)$  at the termination of the simulation.

## XI. SIMULATION RESULTS

In this section, we are providing fully verified results of proposed GNTRs, which describe the most advanced state, currently possible for a plan of action and technological advance. These results are well-validated and will be key points in any nanomedicine project for breast cancer treatment in the future. The proposed results are described below in full detail. Laser irradiation by elliptical shapes of GNTRs of different scale intensity hyperthermia exposure with tumor depth viability percentage monitoring the time duration in nanoseconds, tumor depths are taken as functions were selected. To irradiate, the established size of GNTRs is shown in the below-mentioned three panels of Fig. 18a, 18b, and 18c. The clinical heat therapy analysis results and their relationship among tumor depth, heat intensity required, size of GNTRs, laser fluency, and time duration have been described in Fig. 18a, 18b, and 18c. The proposed nanotherapeutic system acted upon the heat therapy technique for superficial cutaneous metastases (breast cancer and melanomas). After stronger verification, the proposed system provides significant treatment results and new insight into the mechanism of heat therapy in single-modal oncological (breast cancer) treatment.

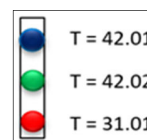


Fig. 17., describes that the proposed GNTRs have the potential to regulate the intensity of heat, and minimize & maximize it according to the requirement using the heat control system. The red, green, and blue color circles show the variation of temperature between different nodes of the proposed GNTRs. The visible 2D square block diagram in Fig. 17. represents the size in Nm of the proposed GNTRs.

While the visible 3D cubic block diagrams represent the different radii and temperature variability in percentage at different intervals of time. The temperature reached its steady state in 1800 seconds; the blue point, green point, and red point noticeable in the diagram show  $42.01C^0$ ,  $40.62 C^0$  and  $31.01C^0$  control temperatures respectively.

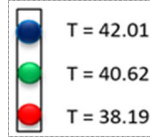
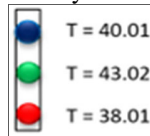


Fig. 19., describes the size of GNTR in Nm (length and width), and the temperature reached its steady state in 2520 seconds. The **red, green, and blue** circles could be noticeable in Fig.18. show  $42.01C^0$   $40.62 C^0$  and  $38.19 C^0$  control temperature respectively.



In Fig. 20., which describes the size of GNTR in Nm (length and width), the size of GNTR has been taken according to the volume of the targeted breast tumor. The temperature reached its steady state in 2700 seconds: the **red, green, and blue** circles could be noticeable in the diagram,

and  $42.01C^0$ ,  $43.02 C^0$  and  $38.01 C^0$ . The control temperature is shown in Fig. 20.

**A. COMPLEX PHYSICAL EFFECTS OF THE COULOMB EXPLOSION PROCEDURE ON THE SURFACE OF THE PROPOSED GOLD NANO THERMO ROBOT**

The Coulomb explosion is a remarkable physical phenomenon that occurs when charged particles like those within GNTRs experience rapid and explosive expansion due to the repulsive forces between them. In this description, we will provide a detailed exploration of the complex physical effects of the Coulomb explosion on GNTRs, as depicted below in nine panels, each illustrating different stages of this phenomenon. The following nine panels present a phenomenological depiction of the intricate and dynamic physical effects of the Coulomb explosion within GNTRs, as shown above in Fig. 22. These panels reveal the sequence of changes in the GNTRs’ state and behavior as they experience varying temperatures and durations.

1) PANEL (A) 33 °C FOR 30 MINUTES

In the first panel, we introduce the GNTRs at a relatively moderate temperature of 33°C, which is maintained for 30 minutes. At this stage, the GNTRs’ physical state begins

$$\begin{bmatrix} 2(1+q) & -q & 0 & 0 & 0 & 0 & 0 & 0 \\ -q & 2(1+q) & -q & 0 & 0 & 0 & 0 & 0 \\ 0 & -q & 2(1+q) & -q & 0 & 0 & 0 & 0 \\ \vdots & \vdots & -q & 2(1+q) & -q & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & -q & 2(1+q) & -q & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & -q & 2(1+q) & -q & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & -q & 2(1+q) & -q \\ 0 & 0 & 0 & 0 & 0 & 0 & -q & 2(1+q) \end{bmatrix} \begin{bmatrix} U_1^{k+1} \\ U_2^{k+1} \\ U_3^{k+1} \\ U_4^{k+1} \\ \vdots \\ \vdots \\ \vdots \\ U_{k-1}^{k+1} \end{bmatrix} \tag{19}$$

$$\begin{bmatrix} 2(1-q) & q & 0 & 0 & 0 & 0 & 0 & 0 \\ q & 2(1-q) & q & 0 & 0 & 0 & 0 & 0 \\ 0 & m & 2(1-q) & q & 0 & 0 & 0 & 0 \\ \vdots & \vdots & q & 2(1-q) & q & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & q & 2(1-q) & q & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & q & 2(1-q) & q & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & q & 2(1-q) & q \\ 0 & 0 & 0 & 0 & 0 & 0 & q & 2(1-q) \end{bmatrix} \begin{bmatrix} U_1^k \\ U_2^k \\ U_3^k \\ U_4^k \\ \vdots \\ \vdots \\ \vdots \\ U_{k-1}^k \end{bmatrix} \tag{20}$$

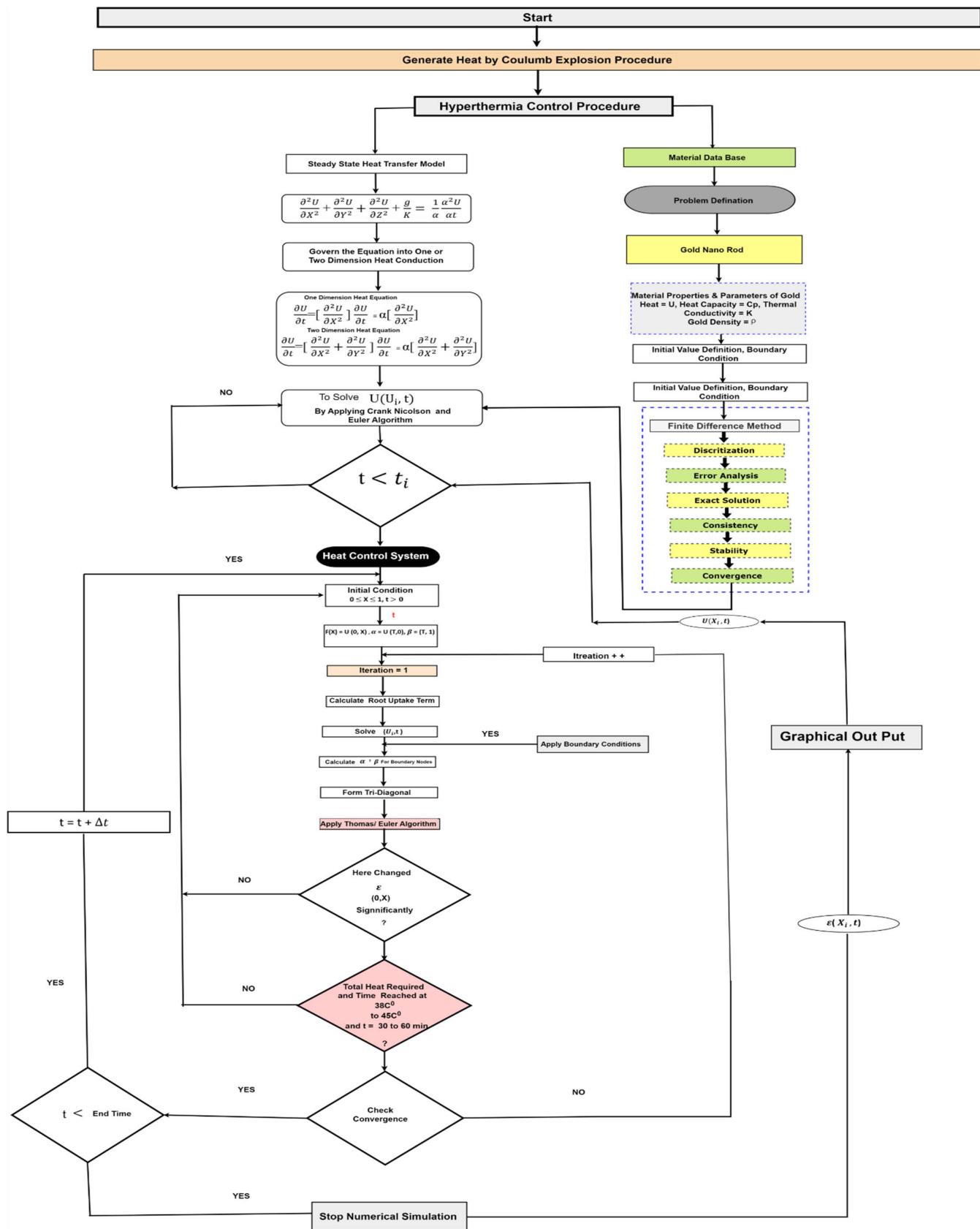


FIGURE 16. Flow chart of heat control system.

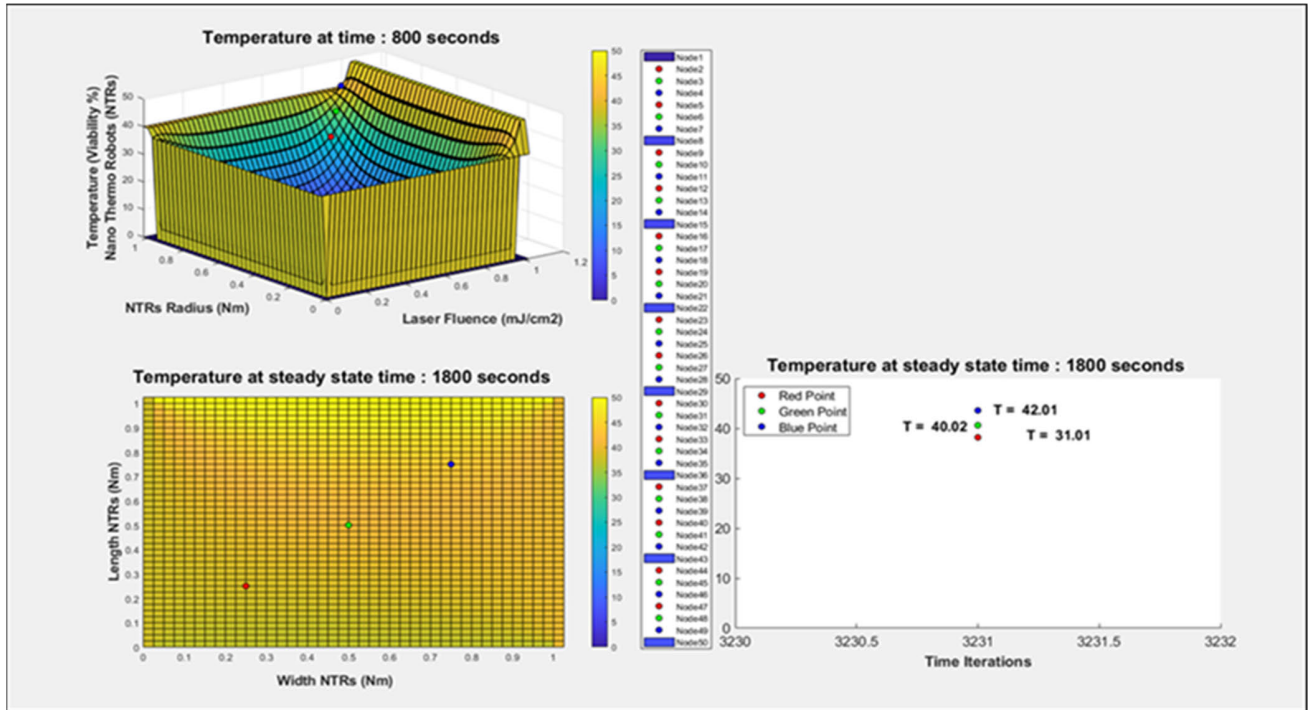


FIGURE 17. Control temperature actions between different nodes of GNTRs at steady state time 1800 s.

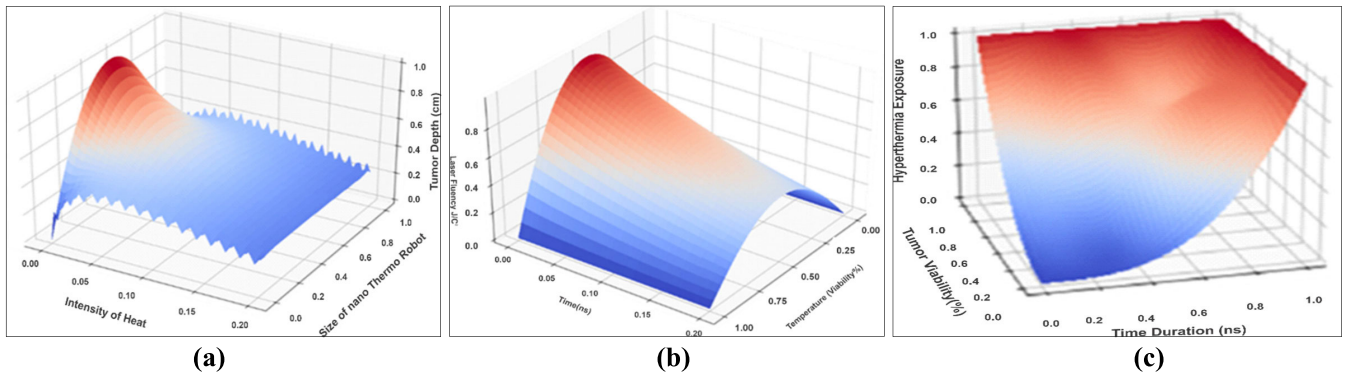


FIGURE 18. (a) Described the relationship between size of GNTR, tumor viability and hyperthermia in first panel, (b) Described the relationship between time duration temperature availability and laser fluency in second panel; (c) Described the relationship between time duration, temperature availability and laser fluency.

to change. Their original golden color starts to transition towards a darker shade, indicating alterations in their atomic structure. The temperature increase has disrupted the GNTRs, causing them to break up and lose their initial integrity.

2) PANEL (B) 35°C FOR 40 MINUTES - NANO BULLETS EMERGE

In the second panel, the temperature is raised to 35°C for 40 minutes. This elevated temperature accelerates the transformation. Nanoparticles, or “nano bullets”, emerge from the GNTRs and scatter in random directions. These nano bullets are tiny, high-velocity particles that result from the GNTRs breaking apart further under increased thermal stress.

3) PANEL (C) 38 °C FOR 42 MINUTES - ACCELERATED NANO BULLET GENERATION

The third panel introduces a temperature of 38°C, sustained for 42 minutes. This combination of higher temperatures and extended exposure time results in the accelerated generation of nano bullets or nanoparticles. These particles gain even more velocity as the GNTRs continue to disintegrate.

4) PANEL (D) 39 °C FOR 32 MINUTES - LOCAL EXPANSION

In the fourth panel, the GNTRs experience a local expansion of their material state. GNTRs absorb radiation energy, causing a rapid surface temperature to increase to 39°C within just 32 minutes. This localized expansion is a consequence of the

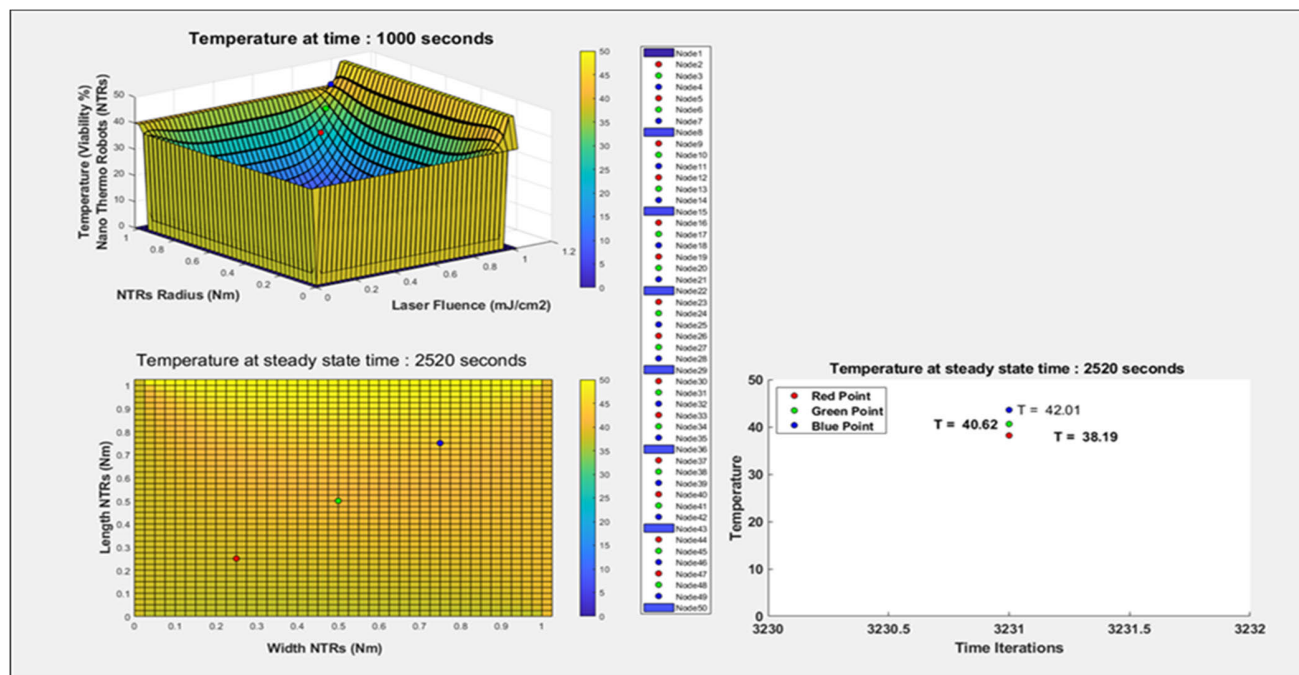


FIGURE 19. Control temperature actions between different nodes of GNTRs at steady state time 2520 s.

intense heating, leading to the GNTRs physically expanding and evolving. It’s a pivotal stage in the Coulomb explosion process.

5) PANEL (E) 42 °C FOR 30 MINUTES - PHOTOACOUSTIC EFFECT

The fifth panel delves into the impact of short laser pulses within the spectral range of the surface plasmon resonance of GNTRs. GNTRs absorb a substantial number of photons, exciting them to upper electronic states.

This excitation leads to a transient modulation of the GNTRs’ thermal conductivity, affecting heat transfer within the Nano-bubbles and nanoparticles. The expansion of a single GNTR and its surrounding thin liquid layer generates linear acoustic waves, known as the ‘classic’ photoacoustic (PA) effect. The temperature reaches 42°C in 30 minutes, representing an intense level of heating.

6) PANEL (F) 43 °C FOR 25 MINUTES - ACCELERATED DISINTEGRATION

In the sixth panel, the GNTRs enter a stage where the decay of GNTR atoms to their ground state occurs with effective electron-phonon conversion of the absorbed photon energy into thermal energy. This stage is marked by the formation, expansion, and collapse of nano bullets, which is accompanied by the production of acoustic and shock waves. The GNTRs’ physical state deteriorates significantly, with their golden color transitioning to a darker hue. They produce nano bullets, create a hot stream, generate hot scattered ion

particles, and experience a substantial increase in surface temperature, reaching 43°C in just 25 minutes.

7) PANEL (G) 40 °C FOR 45 MINUTES - ONGOING DISINTEGRATION

In the seventh panel, the GNTRs continue to disintegrate as they are exposed to a temperature of 40°C for 45 minutes. The physical transformation and generation of nano bullets persist. The surface temperature remains high, and the GNTRs’ golden color continues to darken.

8) PANEL (H) 45 °C FOR 55 MINUTES - ESCALATION OF EFFECTS

The eighth panel depicts an escalation of the effects as the GNTRs experience a temperature of 45°C sustained for 55 minutes. The Coulomb explosion process intensifies, leading to a more dramatic disintegration of the GNTRs. The temperature rise further exacerbates the production of nano bullets, hot streams, and hot scattered ion particles.

9) PANEL (I) 60 °C FOR 60 MINUTES - PEAK EXPLOSION

In the final panel, the GNTRs are exposed to the most extreme conditions, with a temperature of 60°C maintained for a full 60 minutes. At this stage, the coulomb explosion effect reaches its zenith. The GNTRs experience maximal disintegration, and their physical state is drastically altered. The surface temperature rises significantly, and the GNTRs’ color likely becomes almost entirely black. The explosion effect is at its most violent, resulting in the release of a substantial number of nano bullets and ion particles.

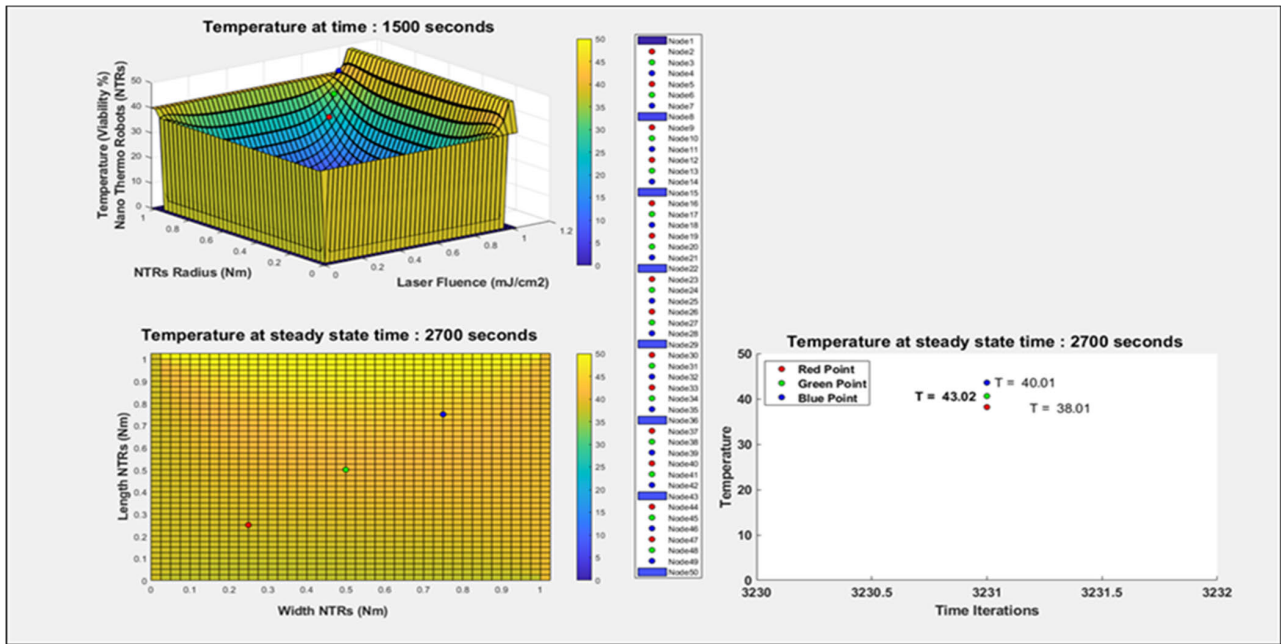


FIGURE 20. Control temperature actions between different nodes of GNTRs at steady state time 2700 s.

Temperatures in brick in deg. C =

0.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	
0.0	49.7	69.2	78.2	83.0	85.8	87.6	88.7	89.4	89.8	89.9	89.8	89.4	88.7	87.6	85.8	83.0	78.2
0.0	29.7	48.9	60.7	68.0	72.7	75.8	77.8	79.1	79.9	80.1	79.9	79.1	77.8	75.8	72.7	68.0	60.7
0.0	20.1	36.0	47.5	55.6	61.2	65.1	67.7	69.4	70.4	70.7	70.4	69.4	67.7	65.1	61.2	55.6	47.5
0.0	14.8	27.6	37.8	45.6	51.4	55.6	58.5	60.5	61.6	62.0	61.6	60.5	58.5	55.6	51.4	45.6	37.8
0.0	11.4	21.8	30.6	37.7	43.2	47.3	50.4	52.4	53.6	54.0	53.6	52.4	50.4	47.3	43.2	37.7	30.6
0.0	9.1	17.6	25.0	31.3	36.3	40.2	43.2	45.2	46.3	46.7	46.3	45.2	43.2	40.2	36.3	31.3	25.0
0.0	7.4	14.4	20.7	26.1	30.6	34.2	36.9	38.8	39.9	40.2	39.9	38.8	36.9	34.2	30.6	26.1	20.7
0.0	6.1	11.9	17.2	21.8	25.8	28.9	31.4	33.1	34.2	34.5	34.2	33.1	31.4	28.9	25.8	21.8	17.2
0.0	5.0	9.8	14.3	18.3	21.7	24.5	26.7	28.2	29.1	29.4	29.1	28.2	26.7	24.5	21.7	18.3	14.3
0.0	4.2	8.2	11.9	15.3	18.2	20.6	22.5	23.9	24.7	25.0	24.7	23.9	22.5	20.6	18.2	15.3	11.9
0.0	3.5	6.8	9.9	12.8	15.3	17.3	19.0	20.1	20.8	21.1	20.8	20.1	19.0	17.3	15.3	12.8	9.9
0.0	2.9	5.6	8.2	10.6	12.7	14.5	15.8	16.8	17.4	17.6	17.4	16.8	15.8	14.5	12.7	10.6	8.2
0.0	2.4	4.6	6.8	8.8	10.5	11.9	13.1	13.9	14.5	14.6	14.5	13.9	13.1	11.9	10.5	8.8	6.8
0.0	1.9	3.8	5.5	7.1	8.5	9.7	10.7	11.4	11.8	11.9	11.8	11.4	10.7	9.7	8.5	7.1	5.5
0.0	1.5	3.0	4.4	5.7	6.8	7.8	8.5	9.1	9.4	9.5	9.4	9.1	8.5	7.8	6.8	5.7	4.4
0.0	1.2	2.3	3.4	4.4	5.2	6.0	6.6	7.0	7.3	7.4	7.3	7.0	6.6	6.0	5.2	4.4	3.4
0.0	0.9	1.7	2.5	3.2	3.8	4.4	4.8	5.1	5.3	5.4	5.3	5.1	4.8	4.4	3.8	3.2	2.5
0.0	0.6	1.1	1.6	2.1	2.5	2.9	3.1	3.3	3.5	3.5	3.5	3.3	3.1	2.9	2.5	2.1	1.6
0.0	0.3	0.5	0.8	1.0	1.2	1.4	1.5	1.7	1.7	1.7	1.7	1.7	1.7	1.5	1.4	1.0	0.8
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

FIGURE 21. Control temperature behavior between different nodes of gold nano node of GNTR using Mat Lab software.

**B. CORRELATION BETWEEN TUMOR SIZE AND REQUIRED RADIUS OF GNTRS.**

A comparative analysis of the correlation between tumor size and the radius of the proposed GNTR is presented. We investigated the intricate relationship between the required radius of Gold Nano Thermo Robots (GNTRs) and the depth of tumor penetration, with a focus on evaluating how different GNTR sizes fit or do not fit the task of effectively treating tumors at various depths within the tissue. We explored the concept of “best fit,” “better fit,” “good fit,” and “not

fit” scenarios and provided the relationship between required radii of GNTR such as (10nm, 20nm, 30nm, 40nm, and 50nm) for volumes of tumor penetration depths such as (1.113 cm, 1.154 cm, 1.188 cm, 1.210 cm, and 1.22 cm) as shown in Tab. 2.

1) BEST FIT SCENARIO

In the context of GNTRs and tumor penetration, a “best fit” scenario occurs when the radius of the GNTR aligns optimally with the depth of the tumor. For example, if we

consider a relatively shallow tumor with a depth of 1.113 cm, GNTRs with a smaller radius, such as 10nm, would be the best fit. Smaller GNTRs can efficiently penetrate this shallower tumor depth, navigating through the tissue matrix with ease. Conversely, for a deeper tumor with a penetration depth of 1.22 cm, larger GNTRs, like those with a radius of 50nm, might be the best fit. These larger GNTRs can better reach the deeper tumor, ensuring effective therapeutic delivery. The “best fit” scenario maximizes the likelihood of successful tumor penetration and treatment.

## 2) BETTER FIT SCENARIO

A “better fit” scenario arises when the chosen GNTR radius is not a perfect match for the tumor depth but still demonstrates reasonable effectiveness. For instance, if we consider a tumor depth of 1.154 cm, GNTRs with a radius of 20nm may not be the “best fit” but can still be a “better fit.” They might not penetrate as efficiently as 10nm GNTRs, but they can navigate through the tissue to reach the tumor. Similarly, for a depth of 1.188 cm, GNTRs with a radius of 30nm may be a “better fit.” While they are not ideal for deeper tumors, they can still provide meaningful therapeutic benefits. In “better fit” scenarios, the GNTR size may not perfectly match the tumor depth, but it is still a viable option for treatment.

## 3) GOOD FIT SCENARIO

In a “good fit” scenario, the chosen GNTR size is not ideal for the tumor depth but can still offer some level of therapeutic effectiveness. For example, if we consider a tumor depth of 1.210 cm, neither smaller GNTRs (e.g., 10nm or 20nm) nor larger ones (e.g., 40nm or 50nm) are an ideal fit. However, GNTRs with a radius of 30nm may represent a “good fit.” While they might not efficiently penetrate the entire tumor depth, they can partially reach the tumor, providing localized treatment. In “good fit” scenarios, the GNTR size may not align perfectly with the tumor depth, but it can contribute to treatment, especially when combined with other therapeutic modalities.

## 4) NOT FIT SCENARIO

A “not fit” scenario occurs when the chosen GNTR size is fundamentally incompatible with the tumor depth, rendering it ineffective for treatment. For instance, if we consider a tumor depth of 1.22 cm, GNTRs with a radius of 10nm or 20nm would likely fall into the “not fit” category. Their small size makes it extremely challenging for them to penetrate the tumor at such a depth. In “not fit” scenarios, alternative treatment approaches or modifications to GNTR design are required to address the limitations posed by the size-depth mismatch.

## C. EFFECTIVE TREATMENT RESPONSES

In the realm of thermal therapy, the effectiveness of treatment is a multifaceted outcome determined by the interplay

between two critical factors: temperature limit and therapy duration. By examining a comprehensive matrix of thermal therapy durations (ranging from 25 minutes to 60 minutes) alongside various temperature limits (ranging from 33°C to 60°C), we aim to uncover the multifaceted landscape of treatment response within this dynamic interplay. At the heart of this analysis lies the categorization of treatment responses into several distinct levels: normal response, average response, satisfactory response, best response, and worst response. These gradations serve as valuable tools to evaluate the effectiveness of thermal therapy based on the selected temperature limits and therapy durations. The choice of temperature limit and therapy duration in thermal therapy is a critical decision that must consider the unique characteristics of the tumor, the patient’s overall health, and the treatment objectives [36]. It is essential to strike a balance between delivering sufficient thermal energy to destroy cancer cells and safeguarding healthy tissues. Moreover, factors such as tumor size, location, and sensitivity to heat must be considered. The comparative analysis of treatment response in thermal therapy highlights the intricate relationship between temperature limit and therapy duration [31]. It underscores the need for a nuanced approach that considers the individualized nature of each patient’s condition and treatment objectives, as described in Table 2. Achieving the “best response” is the goal, but the spectrum of responses, from “normal” to “worst,” reflects the complexities and challenges of thermal therapy in clinical practice. Ongoing research and technological advancements continue to refine our ability to optimize treatment parameters and enhance the effectiveness and safety of thermal therapies for various medical conditions, including cancer [32].

### 1) NORMAL RESPONSE

A “normal response” in thermal therapy occurs when the selected temperature limit and therapy duration are within a range that induces the desired therapeutic effects without causing excessive damage to healthy tissues. For instance, a treatment with a temperature limit of 33°C for 25 minutes might result in a normal response if it effectively targets and damages cancer cells while preserving the surrounding healthy tissue [36]. Normal responses are indicative of a well-balanced therapy regimen that achieves the treatment goals without undue adverse effects.

### 2) AVERAGE RESPONSE

An “average response” signifies a treatment outcome where the selected parameters, while not ideal, still yield some therapeutic benefit. This response often falls within a moderate range, offering a degree of tumor control without reaching the highest efficacy. An example could be a therapy session with a temperature limit of 38°C for 30 minutes, which may achieve a partial tumor response but not as effectively as a treatment in the “normal response” category [36].



### 3) SATISFACTORY RESPONSE

A “satisfactory response” indicates that the therapy has met the desired treatment goals, although not optimally. It implies that the selected temperature limit and therapy duration effectively target the tumor and deliver a significant therapeutic impact, even though there might be room for improvement. A temperature limit of 39°C for 30 minutes, for instance, might result in a satisfactory response where substantial tumor destruction occurs with manageable side effects [31].

### 4) BEST RESPONSE

The “best response” characterizes an ideal treatment outcome where the selected temperature limit and therapy duration maximize therapeutic effects while minimizing collateral damage. This scenario represents the pinnacle of treatment efficacy. An example could be a therapy session with a temperature limit of 42°C for 30 minutes, achieving near-complete tumor ablation with minimal harm to healthy tissues.

### 5) WORST RESPONSE

The “worst response” reflects a treatment outcome where the selected parameters do not achieve the desired therapeutic effects and might even exacerbate the condition or cause harm to healthy tissues. This response serves as a cautionary tale, underscoring the importance of carefully optimizing temperature and duration in thermal therapy. For instance, using a high-temperature limit like 60°C for an extended period of 60 minutes could result in extensive tissue damage and represent the worst-case scenario [36].

## XII. DISCUSSION

In this section, we have been providing a discussion about the outcomes and performance of the proposed GNTRs. The comprehensive working procedure and outcomes of proposed GNTRs have been presented in more detail in this part of the article. The treatment process begins with the insertion of the implantable, the proposed nanotherapeutic device, a marvel of modern medical technology. This tiny yet powerful device is equipped with a multifaceted array of components, such as heat sensors, heat storage devices, ECG sensors, an in-body network, gateways, blood pressure nano sensors, nano pulse oximetry body area network devices, and nano cameras, to deliver localized hyperthermia therapy. each playing a pivotal role in the “See and Treat” technique.

The proposed GNTRs are injected into the body, typically near the breast cancer tumor site, and have the ability, due to smart nanosensors, to reach the target of specific cancer cells by moving, with guiding definite nano biochemical sensors and nano cameras as described in the proposed Gold Nano Thermo Robot model in Fig. 6. Once inside, the nanorobot device deploys its nano cameras to visualize the tumor. These high-resolution images provide a precise map of the cancerous tissue, guiding the subsequent steps of the procedure. With the tumor site accurately identified,

the nanorobot device initiates hyperthermia therapy. This therapy involves the controlled delivery of heat directly to the tumor site, intending to raise its temperature to 42°C for 30 minutes. Heat therapy effectively targets and damages cancer cells while minimizing harm to surrounding healthy tissue. Throughout the procedure, the integrated system operates with a high degree of precision and personalization. The proposed nanotherapeutic system will delve into the comprehensive treatment process, which not only detects and treats breast cancer with precision but also ensures patient safety and comfort throughout the procedure. Treatment strategies for breast cancer typically include surgery, radiation therapy, chemotherapy, and targeted therapies. While these methods have been effective, they often come with side effects and can be invasive. These wearable nanosensors collected real-time data from patients, and this gathered information could be transmitted through the in-body network via the internet, which is designed to act as a communication infrastructure within the patient’s body. The proposed gateway is used to collect data from built-in devices of the therapeutic Nano system [34]. The targets, such as breast tumors, are selectively attached to the proposed GNTR and then irradiated with short laser pulses of femtosecond time scale. In this response, a coulomb explosion took place inside the surface of the GNTRs [41]. Due to multi-photon ionization and electron-electron interactions, electron-photon excitation relaxations in the spectral range of the Surface Plasmon Resonance (SPR) occurred due to a coulomb explosion [24]. The laser-induced elliptical shape of GNTRs for thermal generation in a specific location of breast cancer is shown in Fig. 10. The temperature of the proposed GNTRs increases very rapidly, which may cause them to go into the threshold range for nonlinear effects, in this way, microbubbles are formed, and acoustic and shock waves are generated [23]. The atoms of gold decay to their ground state with the process of rapid relaxation and the effective electron-photon conversion of absorbed photon energy into thermal energy (Hyperthermia) [53]. A phenomenological picture of these complex physical effects is shown schematically in nine panels (a to i) in Fig. 22. The generated heat is irregular, asymmetrical, unstructured, and uncontrolled. To address this issue, a heat control system for thermal therapy has been introduced to achieve selective killing of malignant cells while sparing healthy cells as described in the flow chart in Fig. 16. Once the GNTRs are localized to the cancer cells, they have the potential to sprinkle heat waves on breast tumors and start to kill the cancer cells slowly and gradually [12], controlling the intensity of heat waves by the proposed heat control system while sparing healthy tissue of the organ, as shown in Fig. 10. The proposed nano theopoetic device uses control hyperthermia therapy, which involves raising the temperature of the cancerous cells [74] and presents an alternative and complementary approach to treating breast cancer. Once the necessary data is collected, the implantable nanorobot device will be responsible for delivering heat therapy for breast cancer tumors. This device, controlled remotely, would navigate through the

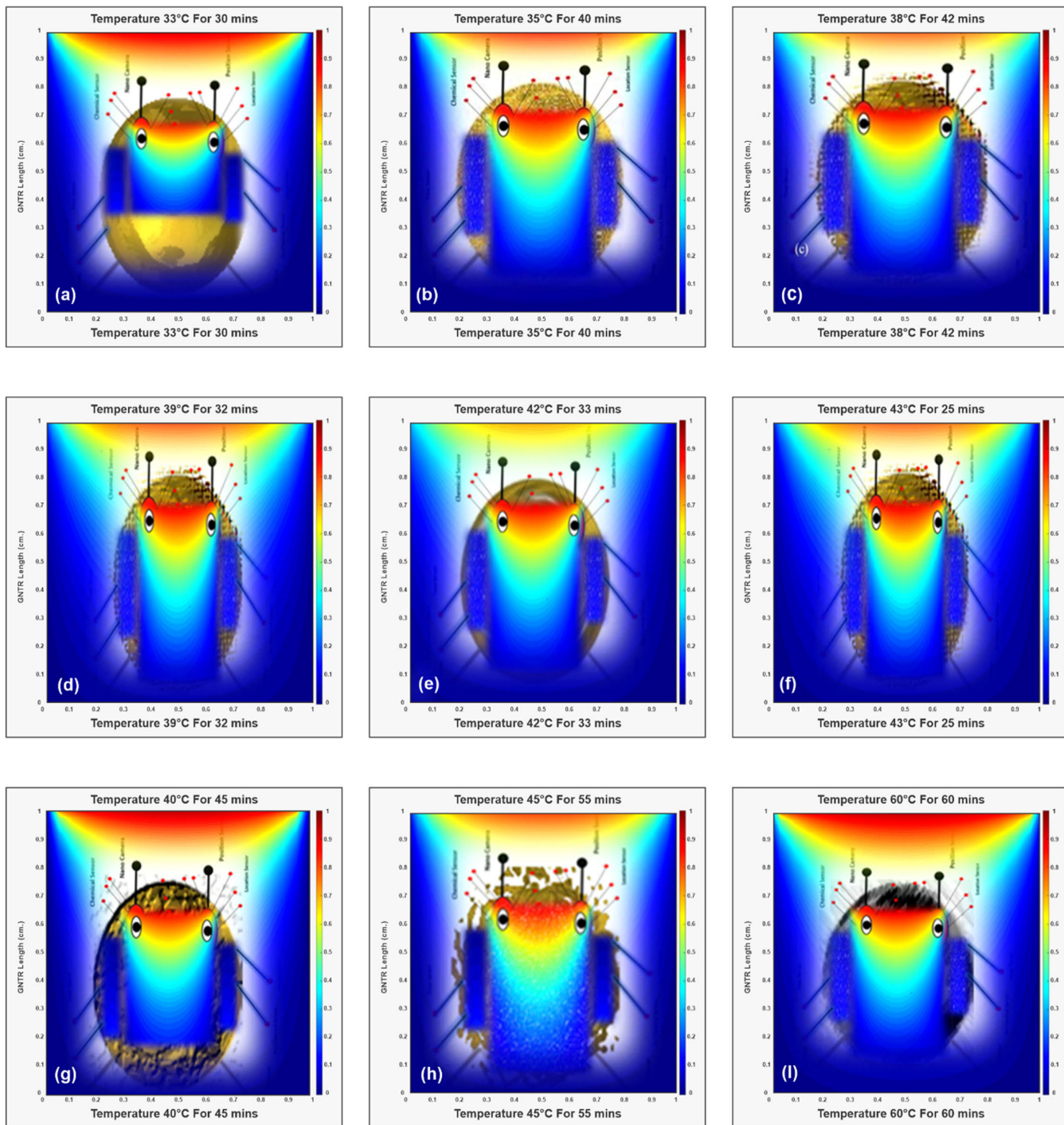
patient's body to precisely target the tumor site [32]. By incorporating heat-generating components within its structure, the nanorobot device would be able to raise the temperature at the tumor location, effectively inducing tumor cell destruction through hyperthermia. Implantable nanorobot devices represent a promising frontier in the treatment of breast cancer. These robots are designed to be small enough to navigate the human body, reaching areas that are difficult to access through traditional means. In the context of breast cancer treatment [60], implantable nanorobots can be engineered to perform several critical functions [62]. The “**See and Treat**” technique with the integrated nanorobot device, combined with the IoNMT framework and controlled heat generation, This innovative approach utilizes a sophisticated network of technologies, including ECG sensors, an in-body network, gateways, blood pressure nano sensors, nano pulse oximetry body area network devices, and nano cameras, to deliver localized hyperthermia therapy that acts with assimilate Ion MT technology along with an in-body communication network as well as ECG sensors, gateways, blood pressure nanosensors, and nano pulse oximetry body area network devices, making it powerful and holding great potential for the treatment of breast cancer [32]. This proposed technique is used as the guideline for proposed therapeutic nanomedicine devices during treatment. Its ability to precisely detect, visualize, and treat cancerous tissue while ensuring patient safety and comfort holds immense potential [75], which not only improves treatment outcomes but also redefines the standards of care in the fight against breast cancer [51]. Nano cameras are attached to the implantable proposed GNTR, providing real-time imaging of the tumor site. These cameras can capture high-resolution images, allowing precise localization of the cancerous tissue. Embedded ECG sensors continuously monitor the patient's cardiac activity throughout the procedure [32]. This ensures that the heart rate and rhythm remain stable, which is crucial for patient safety during hyperthermia therapy. The blood pressure nanosensors are responsible for monitoring the patient's blood pressure levels. Any fluctuations during the therapy can be detected promptly and managed to maintain circulatory stability. Nano pulse oximetry devices track oxygen saturation levels in the patient's blood. This real-time data ensures that respiratory health is maintained throughout the procedure [32]. The in-body network connects all these components, enabling seamless communication and data sharing among the nanorobot device, sensors, and cameras. This network serves as the foundation for real-time data collection and analysis [65]. Gateways serve as the bridge between the in-body network and external systems, including cloud-based resources. They collect and preprocess data, ensuring that it is transmitted efficiently for further analysis and intervention [34]. The ECG sensors, blood pressure nanosensors, and nano pulse oximetry devices continuously monitor the patient's vital signs. Any deviations from the norm trigger real-time alerts, enabling immediate intervention if

necessary. Temperature detector devices are responsible for precisely monitoring and controlling the temperature during the therapy. Maintaining a consistent temperature of  $42^{\circ}\text{C}$  for 30 minutes is crucial for its effectiveness [12]. Transducer devices play a vital role in converting one form of energy into another. In this context, they can help convert electrical signals into thermal energy, contributing to the controlled heat generation required for hyperthermia [54]. Location sensors and position sensors enable the nanorobot device to navigate within the body with exceptional precision, ensuring it reaches the exact tumor location for treatment [58]. Chemical Sensors, Photo Sensors, Image Sensors, and Biochemical Sensors: These sensors provide a comprehensive view of the tumor site, detecting chemical and molecular markers indicative of cancer. Photo and image sensors capture high-resolution images for precise visualization [56]. Heat sensors monitor the temperature at the tumor site, ensuring that the therapy remains on track and that no overheating occurs. Timer sensors help track the duration of the therapy, precisely controlling the 30-minute treatment period. Throughout the procedure, the integrated system operates with meticulous precision and personalization [57]. Our central aim is to assess the effectiveness of these GNTRs, appropriately considered a pioneering form of nanomedicine, in the precise regulation of localized hyperthermia at varying temperature levels, ranging from  $33^{\circ}\text{C}$  to an extreme of  $60^{\circ}\text{C}$ , for different durations. We focus on understanding the physical state transitions that GNTRs undergo under these temperature regimes and their consequential impact on selectively eradicating breast cancer cells while preserving neighboring healthy tissue which reveals promising outcomes for the proposed innovative nano-therapeutic GNTRS approach. The GNTRS, equipped with IONMT, successfully localized to the target area through a combination of controlled nano-sensors network fields and surface functionalization. Once positioned, the system initiated the heat control mechanism, precisely raising the temperature within the tumor site to the therapeutic threshold of  $42^{\circ}\text{C}$  [45], [55]. This targeted hyperthermia treatment was maintained for the prescribed 30-minute duration [36]. In Fig.22., nine panels of temperature with time durations are tried to be applied for verification to get significant outcomes. These GNTRs serve as a form of nanomedicine, leveraging their unique properties for targeted therapy. The study investigates a range of temperatures:  $33^{\circ}\text{C}$  for 25 minutes,  $35^{\circ}\text{C}$  for 30 minutes,  $38^{\circ}\text{C}$  for 32 minutes,  $39^{\circ}\text{C}$  for 40 minutes,  $42^{\circ}\text{C}$  for 42 minutes,  $43^{\circ}\text{C}$  for 45 minutes, and  $60^{\circ}\text{C}$  for 60 minutes, aiming to understand their effects on GNTRs physical state transformations. These temperature variations also impact their color changes, reflecting shifts in their physical properties. As the temperature increases, the GNTRs experience phase transitions, leading to changes in their color and physical properties. At lower temperatures, such as  $33^{\circ}\text{C}$  and  $35^{\circ}\text{C}$ , the GNTRs retain their original state, indicating stability and minimal transformation. However,

at higher temperatures, beginning at 38°C and above, noticeable changes in color and structure are observed, signifying alterations in their physical states. The transition from red to black, for instance, suggests a change from a dispersed to an aggregated state, which can impact their behavior within the body. While temperatures above 42°C can lead to more efficient cancer cell death [55], there is a potential risk of damaging healthy cells. Therefore, a balance must be struck to ensure optimal treatment efficacy while minimizing collateral damage. Through the integration of Ion MT, these nano thermos robots can be remotely controlled, allowing real-time temperature adjustments to achieve optimal therapeutic outcomes [32]. This novel approach involves a heat control system to precisely regulate the temperature at various levels for different durations, aimed at eradicating breast cancer tumors while safeguarding neighboring healthy cells using the **See and Treat** technique. The simulation results we have obtained from the proposed GNTRs offer a fascinating glimpse into the dynamic relationship between temperature variations and the physical states of the proposed GNTRs. At the relatively mild temperature of 33°C, maintained for 25 minutes, these GNTRs retain their solid-state composition, exhibiting the familiar gold coloration. As the temperature is incrementally raised to 35°C for 30 minutes, minor alterations in the physical state become apparent. The GNTRs display a subtle shift in color and a slight increase in translucency, indicative of their evolving nanostructure as the temperature rises. This subtle transformation hints at the remarkable adaptability of GNTRs to environmental changes. Continuing our investigation, at 38°C for 32 minutes, the GNTRs undergo a more noticeable transformation, transitioning into a semi-solid state characterized by increased malleability. This phase change is associated with the phenomenon of ligand shell melting, a thermally induced transition that enhances the GNTRs' capacity to interact with the microenvironment of cancer cells, facilitating their therapeutic action. The increased pliability of GNTRs is advantageous for efficient drug delivery and targeted therapy. Advancing further to 39°C for 40 minutes, we observe a more pronounced change in physical state. The GNTRs transition into a gel-like state with heightened flexibility and deformability. This transition equips them with enhanced capability to penetrate deeply into tumor tissues, thereby promoting greater drug release and therapeutic efficacy. The dynamic adaptability of the GNTRs to temperature variations is becoming increasingly evident as we progress in our study. Stepping closer to the therapeutic threshold, at 42°C for 42 minutes, the GNTRs reach a pivotal phase transition. They transform into a liquid-like state while retaining their structural integrity. This critical phase change marks the commencement of hyperthermia, a mode of treatment where cancer cell membranes become disrupted, proteins undergo denaturation, and DNA damage ensues, ultimately leading to cellular death. The liquid-like state enables the GNTRs to effectively disseminate therapeutic agents, ensuring their precise delivery to cancer cells. Continuing our exploration,

at 43°C for 45 minutes, we witness a more pronounced liquid state of the GNTRs, amplifying their capacity for drug diffusion and cellular uptake. The elevated temperature accelerates the release of therapeutic agents, thereby promoting a targeted and efficient therapeutic response. Finally, at the extreme temperature of 60°C, maintained for 60 minutes, the GNTRs undergo a phase transition into a highly viscous liquid state. This transition signifies an extreme form of hyperthermia, leading to profound cellular destruction within the tumor microenvironment. The physicians can examine and monitor the patients in real-time by using their tablets and mobile phones and patients do not need to visit the hospitals, as described in the whole structure and working procedure of the proposed inter-body communication network planning in Fig. 9.

The objective is to generate control hyperthermia through a coulomb explosion. According to the volume of tumor depth adjust the size of the proposed GNTRs and control the threshold level of thermotherapy. This objective has been achieved by keeping a constant temperature of 42°C for 30 minutes, which is important for its effectiveness in killing the abnormal cells in the environment of breast therapy. In an ideal scenario, treatment planning would aim for the “best response” by carefully tailoring temperature and duration to achieve maximum therapeutic efficacy with minimal side effects. However, clinical realities often necessitate consideration of trade-offs, leading to outcomes ranging from “normal” to “worst” responses. Furthermore, advances in real-time monitoring and control during thermal therapy are crucial in optimizing treatment responses. Continuous feedback on temperature distribution within the target area and surrounding tissues can guide adjustments to therapy parameters during the procedure, potentially improving outcomes and reducing the risk of adverse responses. As we ascend the response hierarchy, we encounter the best response as the epitome of treatment success. The literature review analysis consistently demonstrates that the optimal response is achieved through a temperature limit of 42°C applied for 30 minutes. This paradigmatic approach maximizes treatment efficacy by triggering targeted cell death while preserving the integrity of adjacent healthy tissues. The convergence of findings from both the literature and our proposed research output affirms the robustness of this treatment strategy. On the opposite end of the spectrum lies the worst response, symbolizing outcomes that substantially deviate from desired therapeutic goals. This situation might arise from inadequate treatment parameters, such as employing a temperature limit of 33°C for a therapy duration of 25 minutes. Such a combination often yields limited results. Therapeutic impact and underscores the importance of meticulous parameter selection to achieve favorable outcomes. Thermal ablation is a safe and effective treatment for breast cancer. It is a minimally invasive procedure, which means that there is less risk of complications than with surgery or radiation therapy. A Thermal ablation is also a relatively short procedure which means that patients can return home the same day. The results have been



**FIGURE 22.** Comparison analysis of physical effects of coulomb explosion procedure on the surface of proposed GNTRs.

obtained from the heat control system by the Crank -Nicolson numerical method and using Mat Lab software, as shown in Fig.21. The expected high-quality results are prognostic indicators for treating breast cancer. The expected high-quality results are prognostic indicators for treating breast cancer. The proposed nano-therapeutic system has been used for thermal therapy techniques for the treatment of breast cancer

managing the temperature within the range of  $38\text{ }^{\circ}\text{C}$  to  $45\text{ }^{\circ}\text{C}$  for 30 to 32-minute intervals of time. The target infected part of the patient was heated, generated by proposed GNTRs for moderately less than  $45\text{ }^{\circ}\text{C}$  instead of whole-body hyperthermia. The results of the proposed GNTRs show that the controlled heat between the range ( $38\text{ }^{\circ}\text{C}$  to  $45\text{ }^{\circ}\text{C}$ ) towards tumor volume of the breast suggested was very good and

**TABLE 2.** Comparative analysis of treatment response between TEMPERATURE LIMIT & THERMAL THERAPY therapduration.

Thermal Therapy Duration	Temperature Limit								
	33 C <sup>0</sup>	35 C <sup>0</sup>	38 C <sup>0</sup>	39 C <sup>0</sup>	40 C <sup>0</sup>	42 C <sup>0</sup>	43 C <sup>0</sup>	45 C <sup>0</sup>	60 C <sup>0</sup>
25 mint /1500 s	Normal Response	Normal Response	Average Response	Average Response	Average Response	Satisfactory Response	Satisfactory Response	Worst Response	Worst Response
30 mint/ 1800 s	Normal Response	Normal Response	Average Response	Satisfactory Response	Best Response	Best Response	Best Response	Worst Response	Worst Response
32 mint/1920 s	Average Response	Average Response	Average Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response
40 mint/2400 s	Average Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response
42 mint/2520 s	Average Response	Average Response	Average Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response
45 mint/2700 s	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response
55 mint/3300 s	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response
60 mint/3600 s	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response	Worst Response

**TABLE 3.** Comparative analysis between the required radius of GNTRs and tumor depth during penetration.

Required tumor depth (in cm) for penetration	Required radius (in nm) of proposed GNTRs during penetration				
	10 nm	20 nm	30 nm	40 nm	50 nm
1.113 cm	Best Fit	Better Fit	Average Fit	Average Fit	Average Fit
1.154 cm	Best Fit	Better Fit	Average Fit	Not Fit	Average Fit
1.188 cm	Better Fit	Good Fit	Average Fit	Not Fit	Not Fit
1.210 cm	Good Fit	Average Fit	Not Fit	Not Fit	Not Fit
1.22 cm	Average Fit	Average Fit	Not Fit	Not Fit	Not Fit

effectively reduced the tumor size with the highest diminish rate.

In Table 3. A comparative analysis is presented between the required radius of GNTRs and tumor depth during penetration. The radius of GNTRs and tumor depth are inversely

proportional to each other. The best fit was found to be a smaller radius and a deeper tumor. When the radius of the GNTRs is held constant, the depth of the tumor begins to decrease. The performance of fitting is starting to decrease, as described in Table 3. When the radius of the Nano system

is kept at 10nm, 20 nm, 30 nm, 40 nm, and 50 nm and the tumor depth is kept at the smallest, the results are found in the form of best fit, better fit, and average fit respectively, and when the radius size is kept at a maximum of 50 nm and the tumor depth is kept at the largest 1.22 cm, the result is not fit. If the relationship between the radius of GNTRs and tumor depth is the best fit, keep the temperature at  $38\text{ }^{\circ}\text{C}$  to  $43\text{ }^{\circ}\text{C}$  and the thermotherapy duration at 1800 s. The outcomes of the proposed GNTRs will be in the best response mode. The measurement of specific temperature limits and heat periods during treatment and a comparison of this relationship are given in Table 3. The results are explained, and the normal response, average response, and worst response outcomes are also discussed using different intensities of heat and time duration. The best results were obtained using a temperature of  $42\text{ }^{\circ}\text{C}$  for 30 minutes. Repeat this procedure again and again till they cleared the tumor and should have been using the See and Treat technique side by side too till the finish.

The results have been accepted after several literature investigations of thermal treatment data in comparative and no comparative tests were also established for end cavitory extremely small invasive temperature measurements in breast cancer tumor contact. Patients dealt with the medication well, and there were no seen or observed serious adverse effects. The proposed GNTRs have successfully completely uprooted the cancer tissues. The performance of the proposed GNTRs was found to be outclassed, and a clear dependency of disease-free survival on response was found. The positive results have shown that the proposed treatment approach is effective and feasible. The results show that when the temperatures were maintained at  $43\text{ }^{\circ}\text{C}$  or above  $45\text{ }^{\circ}\text{C}$  and the thermotherapy duration was kept at 45 minutes/2700s. The proposed system showed the worst response. But when the temperature is maintained at  $33\text{ }^{\circ}\text{C}$ ,  $40\text{ }^{\circ}\text{C}$ ,  $41\text{ }^{\circ}\text{C}$  and  $42\text{ }^{\circ}\text{C}$ , and the duration is kept at 25minutes/1500 s. and 30mints/1800s.the system shows an average response.

Furthermore, if temperatures are kept at  $42\text{ }^{\circ}\text{C}$ ,  $45\text{ }^{\circ}\text{C}$ , and  $55\text{ }^{\circ}\text{C}$  and the therapy duration is kept at 42mints/2520 s, 45minutes/2700s and 55minutes/3300 s. respectively, during thermotherapy, the system provides the worst outcomes. At this high temperature, there is a risk of burning immune cells. The Nano system delivers the best response to breast cancer treatment when the temperature is maintained at  $42\text{ }^{\circ}\text{C}$  or  $45\text{ }^{\circ}\text{C}$  during the thermotherapy and the duration is kept at 30 minutes/1800 sec. This detail is described in Table 3. This type of treatment is known as thermal ablation, and it is a minimally invasive way to treat breast cancer. It is often used to treat small tumors that are not suitable for surgery or radiation therapy. The depth of penetration in the tumor expands from 1.13 to 1.23 cm as the short pulse duration increases from 4 ns to 50 ns. [21,]. This proposed technique made sure to reach the exact target site for precise and effective treatment options, [31]. The penetration rate into the depth of the tumor is described as 1.15cm, 1.55cm, 1.188cm, 1.23cm, and 1.25cm [21], [36]. The maximum penetration depth in the tumor can be obtained with GNTs of 50 nm radius. This

proposed technique made sure to reach the exact target site, for precise and effective treatment options. As the radius of GNTRs increases the penetration of hot GNTRs into the tumor goes on increasing. This is due to the increasing density of Nanorobots per unit volume. The penetration rate into the depth of the tumor is as described at 10nm, 20nm, 30nm, 40 nm, and 50nm in Table 3 [21], [36]. It is observed that, as the radius of GNTRs increases, the penetration rate of GNTRs in the tumor goes on increasing. It means the penetration rate and radius of GNTRs are directly proportional to each other. The results obtained show that an increase in laser fluency causes the generation of hyperthermia in tumor depth [48]. For a 10 nm radius of GNTRs, the penetration depth of the tumor is 1.503 cm. As the size of the Nano robot decreases, tumor depth also increases. This is due to the large density of GNTRs. An increase in the Nano robot's size requires more energy from laser irradiation. Due to it's their large size, Nanorobots will go deep inside the tumor. When a GNTR of size 10 nm is irradiated by a laser pulse duration of 10 ns, a huge amount of dispersed hyperthermia is produced inside the breast tumor region. The intensity of heat has been maintained from a limit of  $38\text{ }^{\circ}\text{C}$  to  $45\text{ }^{\circ}\text{C}$  with an increase in time duration in the range of 1800s. This relationship and the different sizes of radii of proposed GNTRs are described in Table 3. The comparison analysis between specific temperature and heat periods is given in Table 2. Therefore, a positive influence of higher thermal doses on survival is expected and has been validated by the highly accurate results of proposed GNTRs, for primary cutaneous breast cancer. The heat and time duration response relations for targeted thermal therapy indicate the clinical efficacy of the proposed control heat therapy approach. However, there were signs of skin-burning wounds or skin lesions burns after the experiment ended, which reinforced that hyperthermia as a single treatment modality had some limitations in our observation. Specific targeted heat therapy in conjunction with systemic chemotherapy for malignant tumors may be a good option that will be available for better results for the patients in the future.

### XIII. CONCLUSION

Breast cancer is a complex and heterogeneous disease and one of the major cancer types among females worldwide [75]. In this background, we have introduced a novel nanodevice (GNTRs) for selective thermal killing of abnormal cells by laser thermal explosion of GNTRs (Nano Medicine) due to coulomb explosion delivered to the cells. Heat therapy is an innovative method for various types of cancer treatments that has the potential to increase cytotoxic effects within the tumor volume [76] without increasing normal tissue harmfulness.

In the present study, it was aimed to investigate the effect of temperature and duration of heat shock on the viability of human normal tissues and breast carcinoma cell lines using control heat therapy. The simulation results, analysis, and discussion presented in this study demonstrate the significant potential of GNTRs empowered with nanotech-

nologies, IoNMT, and precise heat control for the treatment of breast cancer. These GNTRs [16] offer a promising avenue for identified medicine, combining targeted drug delivery, localized hyperthermia [9], and real-time monitoring [32]. While further research and development are needed to address safety, scalability, and long-term effectiveness, this innovative approach holds the potential to revolutionize breast cancer treatment and improve patient outcomes. The convergence of nanotechnology and medicine offers new hope in the battle against cancer, paving the way for more effective, less invasive, and better-tolerated therapies. Additionally, the effective therapeutic effect for breast cancer cell killing is achieved owing to nonlinear phenomena that accompany the thermal explosion of the GNTRs. Breast tumor-selective treatment should be the main oncological approach in the future. The Synthesis of nanomedicine with low yield but characterized by uniform size and shape could be helpful in the development of such techniques. The proposed GNTRs seem to be one of the most promising nanomedicines in oncology. GNTRs can be employed in a variety of ways, and all the suggested heat therapy-based tactics interact specifically with malignancies. Better results can be obtained in the future if a specific amount of chemotherapy (CT) is used along with a heat control system [63].

## REFERENCES

- [1] V. Gote, A. R. Nookala, P. K. Bolla, and D. Pal, "Drug resistance in metastatic breast cancer: Tumor targeted nanomedicine to the rescue," *Int. J. Mol. Sci.*, vol. 22, no. 9, p. 4673, Apr. 2021.
- [2] P. Boix-Montesinos, P. M. Soriano-Teruel, A. Arminan, M. Orzaez, and M. J. Vicent, "The past, present, and future of breast cancer models for nanomedicine development," *Adv. Drug Del. Rev.*, vol. 173, no. 1, pp. 306–330, 2021.
- [3] A. Loukanov, S. Nikolova, C. Filipov, and S. Nakabayashi, "Nanomaterials for cancer medication: From individual nanoparticles toward nanomachines and nanorobots," *Pharmacia*, vol. 66, no. 3, pp. 147–156, Dec. 2019.
- [4] M. Afzal, K. S. Alharbi, N. K. Alruwaili, F. A. Al-Abassi, A. A. L. Al-Malki, I. Kazmi, V. Kumar, M. A. Kamal, M. S. Nadeem, M. Aslam, and F. Anwar, "Nanomedicine in treatment of breast cancer—A challenge to conventional therapy," *Seminars Cancer Biol.*, vol. 69, pp. 279–292, Feb. 2021.
- [5] M. Li, N. Xi, Y. Wang, and L. Liu, "Atomic force microscopy in probing tumor physics for nanomedicine," *IEEE Trans. Nanotechnol.*, vol. 18, pp. 83–113, 2019.
- [6] H. O. Ammar, M. I. Tadros, N. M. Salama, and A. M. Ghoneim, "Therapeutic strategies for erectile dysfunction with emphasis on recent approaches in nanomedicine," *IEEE Trans. Nanobiosci.*, vol. 19, no. 1, pp. 11–24, Jan. 2020.
- [7] J. C. Henson, A. Brickell, J.-W. Kim, H. Jensen, J. L. Mehta, and M. Jensen, "PEGylated gold nanoparticle toxicity in cardiomyocytes: Assessment of size, concentration, and time dependency," *IEEE Trans. Nanobiosci.*, vol. 21, no. 3, pp. 387–394, Jul. 2022.
- [8] M. Sadeghi-Goughari, S. Jeon, and H.-J. Kwon, "Enhancing thermal effect of focused ultrasound therapy using gold nanoparticles," *IEEE Trans. Nanobiosci.*, vol. 18, no. 4, pp. 661–668, Oct. 2019.
- [9] R. Odion, Y. Liu, and T. Vo-Dinh, "Plasmonic gold nanostar-mediated photothermal immunotherapy," *IEEE J. Sel. Topics Quantum Electron.*, vol. 27, no. 5, pp. 1–9, Feb. 2021.
- [10] D. Li, P. Zhao, J. Feng, L. Xing, B. Chen, and D. Liao, "Theoretical and experimental investigations on the photo-thermal effect of gold nanorods irradiated by femtosecond and nanosecond laser," *Thermal Sci.*, vol. 26, no. 4, pp. 3133–3142, 2022.
- [11] J. M. Voss, P. K. Olshin, R. Charbonnier, M. Drabbels, and U. J. Lorenz, "In situ observation of Coulomb fission of individual plasmonic nanoparticles," *ACS Nano*, vol. 13, no. 11, pp. 12445–12451, Nov. 2019.
- [12] H. Onal, T. Yilmaz, and M. N. Akinci, "A BIM-based algorithm for quantitative monitoring of temperature distribution during breast hyperthermia treatments," *IEEE Access*, vol. 11, pp. 38680–38695, 2023.
- [13] A. Ademaj, E. Puric, O. Timm, D. Kurti, D. Marder, T. Kern, R. A. Hälgl, S. Rogers, and O. Riesterer, "Real world analysis of quality of life and toxicity in cancer patients treated with hyperthermia combined with radio(chemo)therapy," *Cancers*, vol. 15, no. 4, p. 1241, Feb. 2023.
- [14] J. Li, L. Dekanovsky, B. Khezri, B. Wu, H. Zhou, and Z. Sofer, "Biohybrid micro-and nanorobots for intelligent drug delivery," *Cyborg Bionic Syst.*, vol. 2022, pp. 1–13, Feb. 2022.
- [15] A. M. Muhumed, M. I. Solihin, B. H. Teh, and W. K. Ng, "A mini review on nanorobots in medical field: Applications and challenges," *Mekatronika*, vol. 5, no. 1, pp. 13–17, 2023.
- [16] F. Soto, J. Wang, R. Ahmed, and U. Demirci, "Medical robotics: Medical micro/nanorobots in precision medicine," *Adv. Sci.*, vol. 7, no. 21, Nov. 2020, Art. no. 2070117.
- [17] A. Banerjee, C. Chakraborty, and M. R. Sr, "Medical imaging, artificial intelligence, Internet of Things, wearable devices in terahertz healthcare technologies," in *Terahertz Biomedical and Healthcare Technologies*. Amsterdam, The Netherlands: Elsevier, 2020, pp. 145–165.
- [18] S. M. A. El-Atty, N. A. Arafa, A. Abouelazm, O. Alfarraj, K. A. Lizos, and F. Shawki, "Performance analysis of an artificial intelligence nanosystem with biological Internet of Nano Things," *Comput. Model. Eng. Sci.*, vol. 133, no. 1, pp. 111–131, 2022.
- [19] S. M. A. El-Atty, K. A. Lizos, O. Alfarraj, and F. Shawki, "Internet of Bio Nano Things-based FRET nanocommunications for eHealth," *Math. Biosciences Eng.*, vol. 20, no. 5, pp. 9246–9267, 2023.
- [20] H. Assi, C. Yang, E. Shaswary, M. Tam, J. Tavakkoli, M. Kolios, G. Peyman, and C. Kumaradas, "Real-time control of nanoparticle-mediated thermal therapy using photoacoustic imaging," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 7, pp. 2188–2194, Jul. 2021.
- [21] M. G. B. Ashiq, M. A. Saeed, B. A. Tahir, N. Ibrahim, and M. Nadeem, "Breast cancer therapy by laser-induced Coulomb explosion of gold nanoparticles," *Chin. J. Cancer Res.*, vol. 25, no. 6, p. 756, 2013.
- [22] M. Aggarwal and S. Kumar, "The use of nanorobotics in the treatment therapy of cancer and its future aspects: A review," *Cureus*, vol. 14, no. 9, pp. 1–8, Sep. 2022.
- [23] E. McNabb, D. Sharma, L. Sannachi, A. Giles, W. Yang, and G. J. Czarnota, "MR-guided ultrasound-stimulated microbubble therapy enhances radiation-induced tumor response," *Sci. Rep.*, vol. 13, no. 1, p. 4487, Mar. 2023.
- [24] D. Eversole, K. Subramanian, R. K. Harrison, F. Bourgeois, A. Yuksel, and A. Ben-Yakar, "Femtosecond plasmonic laser nanosurgery (fs-PLN) mediated by molecularly targeted gold nanospheres at ultra-low pulse fluences," *Sci. Rep.*, vol. 10, no. 1, p. 12387, Jul. 2020.
- [25] A. S. Sogomonyan, S. M. Deyev, and V. O. Shipunova, "Internalization-responsive poly (lactic-co-glycolic acid) nanoparticles for image-guided photodynamic therapy against HER2-positive breast cancer," *ACS Appl. Nano Mater.*, vol. 2023, pp. 1–24, Jun. 2023.
- [26] K. Bromma and D. B. Chithrani, "Advances in gold nanoparticle-based combined cancer therapy," *Nanomaterials*, vol. 10, no. 9, p. 1671, Aug. 2020.
- [27] S. Dolev, R. P. Narayanan, and M. Rosenblit, "Design of nanorobots for exposing cancer cells," *Nanotechnology*, vol. 30, no. 31, 2019, Art. no. 315501.
- [28] H. Santhakumar, R. V. Nair, D. M. Govindachar, G. Periyasamy, and R. S. Jayasree, "Engineering of tripeptide-stabilized gold nanoclusters with inherent photosensitizing property for bioimaging and photodynamic therapy," *ACS Sustain. Chem. Eng.*, vol. 11, no. 6, pp. 2102–2114, 2023.
- [29] X. Rao, Y. Liu, and H. Zhao, "An upwind generalized finite difference method for meshless solution of two-phase porous flow equations," *Eng. Anal. Boundary Elements*, vol. 137, pp. 105–118, Apr. 2022.

- [30] M. Li, N. Xi, Y. Wang, and L. Liu, "Progress in nanorobotics for advancing biomedicine," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 1, pp. 130–147, Jan. 2021.
- [31] A. Elengoe and S. Hamdan, "Heat sensitivity between human normal liver (WRL-68) and breast cancer (MCF-7) cell lines," *J. Biotechnol. Lett.*, vol. 4, no. 1, pp. 45–50, Jan. 2013.
- [32] S. Nakhla, A. Rahawy, M. A. E. Salam, T. Shalaby, M. Zaghoul, and E. El-Abd, "Radiosensitizing and phototherapeutic effects of AuNPs are mediated by differential Noxa and Bim gene expression in MCF-7 breast cancer cell line," *IEEE Trans. Nanobiosci.*, vol. 20, no. 1, pp. 20–27, Jan. 2021.
- [33] V. Loscri, L. Matekovits, I. Peter, and A. M. Vegni, "In-body network biomedical applications: From modeling to experimentation," *IEEE Trans. Nanobiosci.*, vol. 15, no. 1, pp. 53–61, Jan. 2016.
- [34] R. Asorey-Cacheda, L. M. Correia, C. Garcia-Pardo, K. Wojcik, K. Turbic, and P. Kulakowski, "Bridging nano and body area networks: A full architecture for cardiovascular health applications," *IEEE Internet Things J.*, vol. 10, no. 5, pp. 4307–4323, Mar. 2023.
- [35] P. K. D. Pramanik, A. Solanki, A. Debnath, A. Nayyar, S. El-Sappagh, and K.-S. Kwak, "Advancing modern healthcare with nanotechnology, nanobiosensors, and Internet of Nano Things: Taxonomies, applications, architecture, and challenges," *IEEE Access*, vol. 8, pp. 65230–65266, 2020.
- [36] S. Nakhla, A. Rahawy, M. A. E. Salam, T. Shalaby, M. Zaghoul, and E. El-Abd, "Radiosensitizing and phototherapeutic effects of AuNPs are mediated by differential noxa and BIM gene expression in MCF-7 breast cancer cell line," *IEEE Trans. Nanobiosci.*, vol. 20, no. 1, pp. 20–27, Jan. 2021.
- [37] V. I. Mazhukin, A. V. Shapranov, M. M. Demin, O. N. Koroleva, and A. V. Mazhukin, "Visualization analysis of the results of continuum-atomistic modeling of a Coulomb explosion in metals under the influence of ultrashort (fs, ps) laser action," *Sci. Vis.*, vol. 15, no. 1, pp. 112–126, 2023.
- [38] P. Manickam, A. Vashist, M. Sadasivam, R. Shinde, and V. Kanagavel, "10—Mobile nanorobotics for biomedical applications," in *Engineered Nanostructures for Therapeutics and Biomedical Applications*. Amsterdam, The Netherlands: Elsevier, 2023, pp. 297–311.
- [39] N. Anzar, N. Yadav, and J. Narang, "Nanorobots for improved theranostic applications," in *Advanced Nanoformulations*. Cambridge, MA, USA: Academic Press, 2023, pp. 579–603.
- [40] O. V. Dement'eva and M. E. Kartseva, "Noble metal nanoparticles in biomedical thermoplasmonics," *Colloid J.*, vol. 85, no. 4, pp. 500–519, Aug. 2023.
- [41] Z. Ning, Y. Lian, L. Jiang, J. Sun, S. Wu, and F. Wang, "Femtosecond laser-induced anisotropic structure and nonlinear optical response of yttria-stabilized zirconia single crystals with different planes," *ACS Appl. Mater. Interfaces*, vol. 14, no. 34, pp. 39591–39600, Aug. 2022.
- [42] H. H. Kristensen, L. Kranabetter, C. A. Schouder, J. Arlt, F. Jensen, and H. Stapelfeldt, "Laser-induced Coulomb explosion imaging of alkali-metal dimers on helium nanodroplets," *Phys. Rev. A, Gen. Phys.*, vol. 107, no. 2, Feb. 2023, Art. no. 023104.
- [43] A. Johnson, "Investigation of network models finite difference method," *Eurasian J. Chem., Medicinal Petroleum Res.*, vol. 2, no. 1, pp. 1–9, Jan. 2023.
- [44] H. Zhao, W. Zhan, Z. Yuhui, T. Zhang, H. Li, and X. Rao, "A connection element method: Both a new computational method and a physical data-driven framework—Take subsurface two-phase flow as an example," *Eng. Anal. Boundary Elements*, vol. 151, pp. 473–489, Jun. 2023.
- [45] A. Bakker, J. van der Zee, G. van Tienhoven, H. P. Kok, C. R. N. Rasch, and H. Crezee, "Temperature and thermal dose during radiotherapy and hyperthermia for recurrent breast cancer are related to clinical outcome and thermal toxicity: A systematic review," *Int. J. Hyperthermia*, vol. 36, no. 1, pp. 1023–1038, Jan. 2019.
- [46] K. M. Rashed, and M. M. F. Al-Halbosiy, "Silver: Gold nanoparticles medicating for phototherapy against breast cancer cell line (MCF7)," *Executive Editor*, vol. 11, no. 4, p. 392, 2020.
- [47] J. Li, B. Wang, D. Zhang, C. Li, Y. Zhu, Y. Zou, B. Chen, T. Wu, and X. Wang, "A preclinical system prototype for focused microwave breast hyperthermia guided by compressive thermoacoustic tomography," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 7, pp. 2289–2300, Jul. 2021.
- [48] G. G. Bellizzi, M. M. Paulides, T. Drizdal, G. C. van Rhooon, L. Crocco, and T. Isernia, "Selecting the optimal subset of antennas in hyperthermia treatment planning," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 3, no. 4, pp. 240–246, Dec. 2019.
- [49] G. Cappiello, M. M. Paulides, T. Drizdal, D. O'Loughlin, M. O'Halloran, M. Glavin, G. van Rhooon, and E. Jones, "Robustness of time-multiplexed hyperthermia to temperature dependent thermal tissue properties," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 4, no. 2, pp. 126–132, Jun. 2020.
- [50] D. A. Deenen, B. Maljaars, L. C. Sebeke, B. de Jager, E. Heijman, H. Grüll, and W. P. M. H. Heemels, "Offset-free model predictive temperature control for ultrasound-based hyperthermia cancer treatments," *IEEE Trans. Control Syst. Technol.*, vol. 29, no. 6, pp. 2351–2365, Nov. 2021.
- [51] A. H. Faïd, S. A. Shouman, N. A. Thabet, Y. A. Badr, and M. A. Sliem, "Laser enhanced combinatorial chemo-photothermal therapy of green synthesis gold nanoparticles loaded with 6Mercaptopurine on breast cancer model," *J. Pharmaceutical Innov.*, vol. 18, no. 1, pp. 144–148, Mar. 2023.
- [52] A. I. Fraguas-Sánchez, C. Martín-Sabroso, A. Fernández-Carballido, and A. I. Torres-Suárez, "Current status of nanomedicine in the chemotherapy of breast cancer," *Cancer Chemotherapy Pharmacol.*, vol. 84, no. 4, pp. 689–706, Jul. 2019.
- [53] H. Gamal, W. Tawfik, H. M. Fahmy, and H. H. El-Sayyad, "Breakthroughs of using photodynamic therapy and gold nanoparticles in cancer treatment," in *Proc. IEEE Int. Conf. Nanoelectronics, Nanophotonics, Nanomaterials, Nanobiosci. Nanotechnol. (5NANO)*, Apr. 2021, pp. 1–4.
- [54] C. Gani, U. Lamprecht, A. Ziegler, M. Moll, J. Gellermann, V. Heinrich, S. Wenz, F. Fend, A. Königsrainer, M. Bitzer, and D. Zips, "Deep regional hyperthermia with preoperative radiochemotherapy in locally advanced rectal cancer, a prospective phase II trial," *Radiotherapy Oncol.*, vol. 159, pp. 155–160, Jun. 2021.
- [55] Y. Gu, R. Piñol, R. Moreno-Loshuertos, C. D. S. Brites, J. Zeler, A. Martínez, G. Maurin-Pasturel, P. Fernández-Silva, J. Marco-Brualla, P. Téllez, R. Cases, R. N. Belsué, D. Bonvin, L. D. Carlos, and A. Millán, "Local temperature increments and induced cell death in intracellular magnetic hyperthermia," *ACS Nano*, vol. 17, no. 7, pp. 6822–6832, Apr. 2023.
- [56] M. Hamdi and A. Ferreira, "Guidelines for the design of magnetic nanorobots to cross the blood-brain barrier," *IEEE Trans. Robot.*, vol. 30, no. 1, pp. 81–92, Feb. 2014.
- [57] L. Huang, F. Chen, Y. Lai, Z. Xu, and H. Yu, "Engineering nanorobots for tumor-targeting drug delivery: From dynamic control to stimuli-responsive strategy," *ChemBioChem*, vol. 22, no. 24, pp. 3369–3380, Dec. 2021.
- [58] M. Nagpal, M. Kaur, and G. Aggarwal, "Nanotechnology for targeted drug delivery to treat osteoporosis," *Current Drug Targets*, vol. 24, no. 1, pp. 2–12, Jan. 2023.
- [59] J.-Y. Kim, S. Zschaecck, J. Debus, and F. Weykamp, "Combined hyperthermia and re-irradiation in non-breast cancer patients: A systematic review," *Cancers*, vol. 15, no. 3, p. 742, Jan. 2023.
- [60] L.-W. Kuo, G.-C. Dong, C.-C. Pan, S.-F. Chen, and G.-S. Chen, "An MRI-guided ring high-intensity focused ultrasound system for noninvasive breast ablation," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 67, no. 9, pp. 1839–1847, Sep. 2020.
- [61] L.-W. Kuo, L.-C. Chiu, W.-L. Lin, J.-J. Chen, G.-C. Dong, S.-F. Chen, and G.-S. Chen, "Development of an MRI-compatible high-intensity focused ultrasound phased array transducer dedicated for breast tumor treatment," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 65, no. 8, pp. 1423–1432, Aug. 2018.
- [62] J. Li, L. Dekanovsky, B. Khezri, B. Wu, H. Zhou, and Z. Sofer, "Biohybrid micro- and nanorobots for intelligent drug delivery," *Cyborg Bionic Syst.*, vol. 2022, Jan. 2022.
- [63] D. R. Löke, H. P. Kok, R. F. C. P. A. Helderman, N. A. P. Franken, A. L. Oei, J. B. Tuijnman, R. Zweije, J. Sijbrands, P. J. Tanis, and J. Crezee, "Validation of thermal dynamics during hyperthermic IntraPEritoneal chemotherapy simulations using a 3D-printed phantom," *Frontiers Oncol.*, vol. 13, Feb. 2023, Art. no. 1102242.
- [64] V. Loscri and A. M. Vegni, "An acoustic communication technique of nanorobot swarms for nanomedicine applications," *IEEE Trans. Nanobiosci.*, vol. 14, no. 6, pp. 598–607, Sep. 2015.



- [65] K. R. Mahmoud and A. M. Montaser, "Design of multiresonance flexible antenna array applicator for breast cancer hyperthermia treatment," *IEEE Access*, vol. 10, pp. 93338–93352, 2022.
- [66] P. Manickam, A. Vashist, M. Sadasivam, R. Shinde, and V. Kanagavel, "10—Mobile nanorobotics for biomedical applications," *Engineered Nanostruct. Therapeutics Biomed. Appl.*, vol. 2023, pp. 297–311, Jan. 2023.
- [67] P. Manickam, S. A. Mariappan, S. M. Murugesan, S. Hansda, A. Kaushik, R. Shinde, and S. P. Thipperudraswamy, "Artificial intelligence (AI) and Internet of Medical Things (IoMT) assisted biomedical systems for intelligent healthcare," *Biosensors*, vol. 12, no. 8, p. 562, Jul. 2022.
- [68] R. Merten, O. Ott, M. Haderlein, S. Bertz, A. Hartmann, B. Wullich, B. Keck, R. Kühn, C. M. Rödel, C. Weiss, C. Gall, W. Uter, and R. Fietkau, "Long-term experience of chemoradiotherapy combined with deep regional hyperthermia for organ preservation in high-risk bladder cancer (Ta, Tis, T1, T2)," *Oncologist*, vol. 24, no. 12, pp. 1341–1350, Dec. 2019.
- [69] N. Jabbari, E. Akbariazar, M. Feqhhi, R. Rahbarghazi, and J. Rezaie, "Breast cancer-derived exosomes: Tumor progression and therapeutic agents," *J. Cellular Physiol.*, vol. 235, no. 10, pp. 6345–6356, Mar. 2020.
- [70] O. J. Ott, C. Gani, L. H. Lindner, M. Schmidt, U. Lamprecht, S. Abdel-Rahman, A. Hinke, T. Weissmann, A. Hartmann, R. D. Issels, D. Zips, C. Belka, R. Grützmann, and R. Fietkau, "Neoadjuvant chemoradiation combined with regional hyperthermia in locally advanced or recurrent rectal cancer," *Cancers*, vol. 13, no. 6, p. 1279, Mar. 2021.
- [71] X. Rao, "An upwind generalized finite difference method (GFDM) for meshless analysis of heat and mass transfer in porous media," *Comput. Part. Mech.*, vol. 10, no. 3, pp. 533–554, Jun. 2023.
- [72] X. Shen, Q. Ouyang, H. Tan, J. Ouyang, and N. Na, "Computation-assisted design of ssDNA framework nanorobots for cancer logical recognition, toehold disintegration, visual dual-diagnosis, and synergistic therapy," *Anal. Chem.*, vol. 95, no. 14, pp. 5903–5910, Mar. 2023.
- [73] F. Soto, J. Wang, R. Ahmed, and U. Demirci, "Medical micro/nanorobots in precision medicine," *Adv. Sci.*, vol. 7, no. 21, Oct. 2020, Art. no. 2002203.
- [74] M. Srivastava, R. K. Mandal, and N. K. Prasad, "AC magnetic field dependent hyperthermia for controlled heating near therapeutic temperature," *IEEE Trans. Magn.*, vol. 58, no. 10, pp. 1–6, Oct. 2022.
- [75] A. R. Venmathi and L. Vanitha, "Performance evaluation of nanorobot drug delivery mechanism for breast cancer," in *Next Generation of Internet of Things*, vol. 201, no. 1. Singapore: Springer, Jun. 2021, pp. 233–242.
- [76] S. Zong, C. Cao, and K. Chen, "Red blood cell membrane camouflaged mesoporous silica nanorods as nanocarriers for synergistic chemo-photothermal therapy," *IEEE Trans. Nanobiosci.*, vol. 22, no. 3, pp. 655–663, Dec. 2022.
- [77] C. Kher and S. Kumar, "The application of nanotechnology and nanomaterials in cancer diagnosis and treatment: A review," *Cureus*, vol. 14, no. 9, pp. 1–6, Sep. 2022.
- [78] (May 2023). *Cancer Registry and Clinical Management (CRCMD)-Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&R) Report Based on Cancer Cases Registered at SKMCH&RC From Dec. 1994-Dec. 2022 and in 2022*. Lahore, Pakistan: Shaukat Khanum Memorial Cancer Hospital and Research Center. [Online]. Available: <https://www.shukatkhnum.org.pk>
- [79] World Cancer Research Fund International. (2020). *Breast Cancer Statistics*. London, U.K. [Online]. Available: <https://www.wcrf.org/cancer-trends/breast-cancer-statistics>

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