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Application of Hyperthermia for Cancer Treatment: Various Techniques and Recent Advancements

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Abstract: ***Cancer is a disease characterised by uncontrollable cell division in a specific area of the body. It is a leading cause of death, and its prevalence is increasing. There are numerous techniques and protocols employed, including as chemotherapy, radiography, surgical tumor removal, etc. However, these procedures have several adverse side effects that cause excruciating pain and intense anxiety in the patients. Over the past few decades, it has become increasingly challenging to discover new cancer-fighting strategies. One of the best cancer treatment choices is hyperthermia, an ancient form of therapy that offers fresh hope when paired with engineering methods. This study examines the crucial data for coupling various engineering techniques with hyperthermia, carefully organised according to the methods used, such as hyperthermic perfusion, frequency enhancers, ultrasonic hyperthermia, external radio-frequency devices, microwave hyperthermia, and the use of a catheter to heat the target area before injecting superparamagnetic and magnetic nanoparticles.***

Key words: Cancer, Hyperthermia, Ultrasonic, Radio Frequency Devices, Hyperthermic Perfusion, Microwave, Magnetic Nanoparticles

I. INTRODUCTION

Cancer is one of many diseases characterised by the growth of abnormal cells that can invade and damage healthy human tissue [1]. Cancer spreads quickly throughout your body. Survival rates for many cancer types are increasing, thanks to advances in cancer detection, therapy, and control [2].

Cancer is still the second leading cause of death. Numerous novel tactics have been developed to combat cancer. These treatments include thermal therapy, also known as hyperthermia, as well as biological therapies such as photodynamic therapy, gene therapy, immunotherapy, laser treatment, and angiogenesis inhibitors. However, most of these methods still require optimisation. One of the most widely used research approaches, hyperthermia, is being used as a possible alternative therapy for cancer patients when combined with engineering. Hyperthermia has been used as a supplement to chemotherapy and radiation therapy for the past 20 years, and it has the advantage of killing tumor cells that are resistant to both drugs and radiation [3].

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Clinical studies that focus on the treatment of various cancers, such as melanoma, sarcoma, cervix, brain, esophagus, lung, breast, bladder, rectum, liver, etc., have examined hyperthermia in conjunction with radiation or chemotherapy. There are numerous techniques for treating hyperthermia, including regional, local, and total body cooling, as indicated in Figure 1. This essay examines the various approaches employed in these three distinct hyperthermia procedures [4].

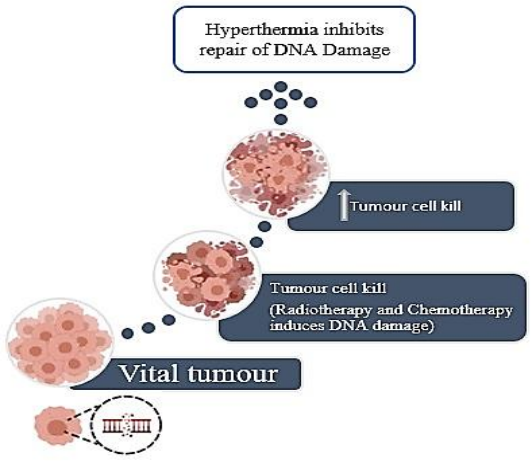


Figure 1: Hyperthermia for Tumor Cell Death

II. TYPES OF HYPERTHERMIA TREATMENT

The term "hyperthermia" typically refers to an elevated body temperature. High body temperatures are often a symptom of diseases such as fever or heat stroke. However, heat treatment, which is the carefully supervised application of heat for medicinal purposes, can also be referred to as hyperthermia. Different methods of hyperthermia are shown in Table 1**.** The entire body, large portions, or small areas can be treated with it. A Physician applies heat to a tiny region to cause local hyperthermia. The location of the tumour determines the kind of local hyperthermia that is used, as shown in Figure 2 [5].

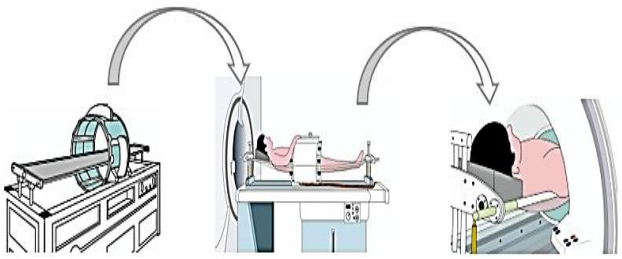


Figure 2: Hyperthermia Treatment

III. LOCAL HYPERTHERMIA

Tumors on or near the skin can be treated with local hyperthermia. Doctors set up heating equipment within or around the treatment area for this kind of hyperthermia [6].

A. Intraluminal or Endo Cavitary Hyperthermia:

It is used to treat cancers located inside or near body cavities, such as the oesophagus or rectum. In this form of hyperthermia, medical professionals introduce heat-producing probes into the tumour cavity [7].

B. Interstitial Hyperthermia:

Deep-lying cancers in the body, such as those in the brain, are treated with interstitial hyperthermia. The tumour can be heated to higher degrees than with external methods using this type of hyperthermia. While you are unconscious, the physician will use probes or needles to enter your tumour. It may be possible to employ imaging methods, such as ultrasound, to help ensure the probe is positioned correctly. The probe is then put inside the heat source [8].

C. Radiofrequency Ablation (RFA):

The most popular kind of thermal ablation is most likely this one. RFA treats patients by using high-energy radio waves. Typically, between 10 and 30 minutes, a tiny, needle-like probe is introduced into the tumour for this procedure. Images from CT, MRI, or ultrasound are used to guide the probe into its proper position. The probe's tip emits a high-frequency current, generating intense heat that kills the cells in its vicinity. Instead of being eliminated, dead cells form scar tissue that eventually shrinks and disappears over time. RFA is typically used to treat tumours that cannot be removed surgically or for patients who are unable to cope with the trauma of surgery. Usually, it is an outpatient procedure. RFA can be used again for malignancies that recur or develop. Additionally, it may be used in conjunction with other therapies such as surgery, hepatic arterial infusion therapy, radiation therapy, chemotherapy, alcohol ablation, or chemoembolization. RFA can cure tumours that are up to 2 inches (5 cm) in diameter. It is currently being researched for use in other parts of the body, but is most frequently used to treat malignancies in the liver, lungs, and kidneys. Although the long-term effects of RFA treatment are not yet understood, the preliminary findings are promising [6,8]

IV. REGIONAL HYPERTHERMIA

Regional hyperthermia occurs when medical professionals apply heat to large areas of the body, such as a cavity or limb, or an organ. Regional hyperthermia is achieved through deep tissue procedures, continuous hyperthermic peritoneal perfusion, and regional perfusion [9].

A. Deep Tissue Techniques:

These techniques are used to treat internal tumours such as bladder and cervix cancer. During this operation, energy is directed there to raise the temperature of the area, and heat-delivery equipment is placed around the cavity or organ to be treated [10].

B. Regional Perfusion Techniques:

These methods are used to treat tumours of the arms, legs, and some organs, such as the lung and liver, including melanoma. A portion of your blood is drawn during this surgery, heated, and then pumped back into the affected organ or limb. Chemotherapy is frequently used as part of this therapy [11].

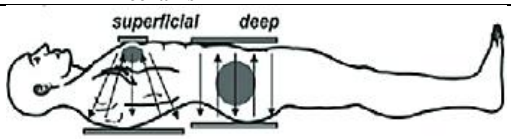
C. Continuous Hyperthermic Peritoneal Perfusion:

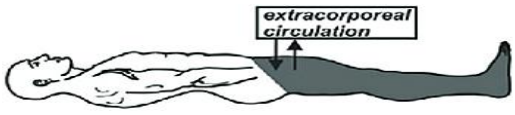
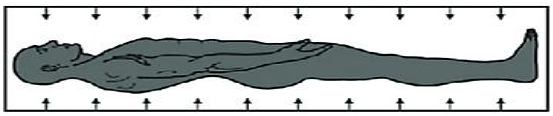
These treatments deal with cancer that has spread to the peritoneal cavity, the area of the abdomen that houses the intestines, liver, and stomach. During surgery, this therapy is administered. Your peritoneal cavity heats up to 106 to 108°F while you are asleep due to heated chemotherapy medications flowing into it via a warming device [12].

V. WHOLE-BODY HYPERTHERMIA

Chemotherapy for the treatment of cancer that has spread is being researched as a potential treatment option that could improve with whole-body heating (metastatic cancer). Body temperature can be raised using thermal chambers, warm-water immersion therapy, heating blankets, and other methods (much like large incubators). Patients undergoing whole-body hyperthermia may occasionally be given sedatives or even light anaesthesia. Fever range: When a person's body temperature rises, as if they have a fever, this is referred to as whole-body hyperthermia. According to research, this may activate a few immune cells and raise blood levels of cell-destroying materials for a few hours. For brief periods, some researchers raise the temperature of the body to around 107° F. Additional research is being conducted on hyperthermia, chemotherapy, and other therapies aimed at strengthening a person's immune system to fight cancer [13-15].

Table 1: Different Methods of Hyperthermia

Hyperthermia	Methods	Mechanism
Regional	External Applicator	

	Regional perfusion	
Local	Intraluminal methods	
	Interstitial methods	
Whole body	Whole body [Heat exchange of perfusion blood]	

VI. TECHNIQUES USED

A. Ultrasonic Hyperthermia:

The transmission of sound waves with a frequency between 2 and 20 MHz via soft tissues constitutes ultrasonic waves, and their absorption results in the heating of the medium. The most useful technology is ultrasonic, which has a short wavelength and the ability to concentrate electricity into small places. The suggested ultrasonic therapy system is cylindrical, with a stack of rings, each of which includes up to 48 transducers mounted inside and oriented inward. The penetration that may be accomplished by driving tiny cylindrical transducers with an outside diameter of about 1 mm at 6–10 MHZ is adequately approximated in simulations utilizing interstitial ultrasonic transducers [16]. One of the two frequency bands, which are symmetrically separated, is used by the design (1.8-2.8 MHZ and 4.3-40.8 MHZ). The 3D simulations show that it is possible to produce temperature dispersion between 41.5 and 440C with reasonable accuracy [17]. Utilizing inhalable perfluorochemical liquids as the acoustic coupling medium in the lung, it is examined if deep localized lung hyperthermia with therapeutic ultrasound is feasible. The use of both liquid-filled lung ultrasonic hyperthermia and convective lung hyperthermia for the treatment of lung cancer allows for a variety of heating patterns [18]. The outcomes of a technique have allowed for the use of the phantom for targeted therapy and MRI-based temperature distribution for interstitial ultrasonic low dose radiation treatment of the brain [19].

B. Hyperthermia with External Radio Frequency Devices:

The calculation of the specific absorption rate (SAR) in hyperthermia treatment and tumor planning is shown using three-dimensional electromagnetic field modelling [20]. Many waveguide structures are used in the 100-2000 MHz frequency range. The SAR in a tumor is calculated experimentally using three-dimensional (3D) numerical models created with the electric field integral equation (EFIE) and the magnetic field integral equation (MFIE) (MFIE). The Gaussian beam model is the precise source model that demonstrates how aperture and incident fields can be established (GBM). The findings demonstrate the effectiveness of GDM in classifying the applicators used in hyperthermia cancer treatment. The use of simulations using a one-dimensional, one-point model of a tumor to provide thermal dose for hyperthermia cancer treatment is demonstrated in a model predictive controller (MPC) [21]. Hyperthermia aims to increase the temperature in the targeted area by about 43 °C for up to an hour without heating or harming the neighbouring healthy tissue. Instead of using increased temperatures for therapeutic application, this approach directly controls the thermal dose. A feedback pulse is used to adjust the thermal dose directly. The simulations are run with various blood flow rates at a single point or dimension within the tumor. When heat is applied to a cancer, there is a chance that some of the tumor will remain active because the central and peripheral regions of the tumor can have different temperatures. This is demonstrated in an experimental setup for soft heating in hyperthermia. Therefore, a heater with a drive mechanism is created to provide a precise temperature range at each place. In this design, a body heated by an external high-frequency magnetic field is filled with delicate magnetic materials. The rotating field also acts as a propellant for it. Due to its ability to penetrate tumors, this heater may thoroughly heat a tumor in 40 minutes, reaching a heating surface temperature of450C [22]. Breast cancer is treated with a conformal microwave array (CMA) applicator that employs a temperature-controlled water bolus [23]. The finite difference time domain (FDTD) method-based 3D solver SEMCAD, a simulation tool, performs calculations. Results are compared at frequencies of 915 MHZ and 2450 MHZ. An eight-element circular annular phase array (APA) with either 915 MHz or 2450 MHz half-wavelength dipole elements, positioned 1 mm from a cylindrical phantom, is used to interact with electromagnetic fields and human body tissues. Cervical, prostate, and esophageal cancers are all treated with a single endoscopic probe. It offers a combination process of hyperthermia treatment and 3D visualization of the target tissues.

A real-time 3D gadget with a 1 cm diameter and 504 active channels, operating at a frequency of 5 MHz, is the endoscopic probe. A finite element mesh with more than 128000 components is constructed to result in a temperature rise of 4°C in 5 minutes and a hyperthermia zone of 41°C.Heating must be consistent throughout the entire targeted region for the treatment to be successful. However, the most excellent heating achieved with this probe is only inside a 1mm diameter, which is insufficient for treatment. To improve transmission efficiency and achieve stability, the model will need to be modified. It is possible to successfully treat early-stage breast cancer by designing an antenna array with optimal constrained power focusing (OCPF), where the focusing is carried out at microwave frequency [24]. It has been demonstrated that the OCPF approach is more effective in attaining maximal power deposition at a target position while maintaining power levels below a safe threshold for healthy tissues. The focusing is carried out between 1 and 3 GHZ. Some of commercial RF medical devices used in clinical trials combining adjuvant hyperthermia and chemotherapy as shown in table 2 [25].

Table 2: List of Commercial RF Medical Devices Used in Clinical Trials Combining Adjuvant Hyperthermia and Chemotherapy.

Device	Manufacturer, country	Applicator	Frequency (MHz)
Alba 4D	Medlogix, IT	Alba 4D	70
Alba ON4000		Alfa, Beta, Gamma, Delta	434
BSD-500	Pyrexar Medical, US	MA-151, MA-100	915
BSD-2000		Σ-30, Σ-60, Σ-Ellipse	75-140
BSD-2000 3D		Σ-Eye	100
BSD-2000 3D/MR		Σ-30-MR, Σ-Eye-MR	100
Synergo® RITE	Medical Enterprises, NL	SB-TS 101	915
Yacht-3	JSC MC SEZ Istok, Fryazino, RU	4 rectangular applicators	915

C. Hyperthermic Perfusion:

A physical portion, such as a limb or an organ, is heated up during regional hyperthermia. It is a method that is frequently used in conjunction with chemotherapy or radiation therapy. Surgery is used to isolate the blood supply to a specific portion during regional perfusion. The blood is pumped into a heater and then returned to the artwork that is being heated. The process of perfusion hyperthermia is automatically monitored and controlled by a computer system. A fluid channel persists between a patient and an outer fluid treatment subsystem, and it is controlled by a feedback signal from the patient's sensor [26]. The effects of administering a drug while also delivering heat are beneficial because they increase the drug's uptake by the cell, increase tumor cell death at a given level of intracellular drug, and reduce microvascular density. The experiment also suggests that there will be reduced drug diffusion to nearby tissues that are very small, such as those measuring 0.48 millimeters or less [27]. The survival rates of hyperthermic intraperitoneal chemotherapy (HIPEC) at various time points are provided for the treatment of ovarian cancer, and the findings indicate possible survival benefits [28]. This article describes Continuous Hyperthermic Peritoneal Perfusion Chemotherapy (CHPPC) as a treatment for malignant peritoneal mesothelioma. The peritoneal malignant mesothelioma is a sporadic tumor, and even identifying it can be difficult, therefore there are no set treatments for it. The results show that following CHPPC, the patient's health and survival rate were satisfactory [29].

D. Hyperthermia uses Frequency Enhancer:

Living tissues exhibit a lower absorption limit in the KHz range. However, 20 kHz ultrasound mixed with intravenously administered polystyrene nanoparticles will improve the administration of the chemotherapy drug 5-fluorouracil. When nanoparticles and medication injections are used in conjunction with ultrasound irradiation, the results include both total tumor regression and a decrease in tumor volume. The use of local hyperthermia to treat cancers that are both localized and metastatic is suggested [30Using biocompatible fluids and solutions can enhance the absorption of RF energy and microwave radiation in live tissues. In sufficient concentrations, dissolved salts of Fe, Mg, and Cr, as well as alkali metals, can accelerate the solution's heating. When two different processes, such as resistive heating and ion cyclotron resonance, are combined, they significantly increase RF absorption [31]. The target area is connected to the RF energy using a transceiver. The transceiver is made up of the following components: the receiving inductor, the receiving head, two tuned circuits, the RF generator, the RF absorption enhancer, the transmission head, and the transmission inductor. In this system, RF absorption is enhanced by supplying an aqueous solution with colloidal particles of electrically conductive material [32]. The patient's body is injected with RF-absorbing particles in a newly developed frequency-modulated hyperthermia procedure. These antibodies are improving the effects of hyperthermia as well as RF absorption. Frequency-modulated RF signals are produced using multi-frequency heating. The frequency that FM hyperthermia modulates depends on the size tolerance of the particles, which are used to boost energy absorption and are the source of the centre frequency of FM hyperthermia [33]. To heat citrate-coated gold nanoparticles for cancer therapy, a technique for generating a 13.56 MHz radio frequency electromagnetic field has been developed. The findings indicate that the introduction of gold nanoparticles significantly increases the mortality of cancer cells. It has also been shown that heating is concentration and size dependent, with 5 nm particles causing a temperature rise of 50.60.2°C for 25 g/mL gold (125 W input) in 30 s [34].

E. Hyperthermia using a Catheter:

An apparatus has been developed that incorporates a catheter with fluid-free channels, allowing for the introduction of temperature sensors and microwave antenna applicators to measure prostate tissue temperature. The electromagnetic generator powers the applicator.

A comparator is connected to the other terminal of the temperature sensor using a temperature reference potentiometer to compare the tissue's current temperature with the goal temperature to calculate the heating impact [35]. A device is presented that transmits electromagnetic energy (EM) at a frequency between 0.3 and 10 GHz and a power level between approximately 100 mW and 150 W. This device uses microwave energy. The device also has directional parts with radiating components to increase energy, a temperature sensor to determine a location's temperature, and a catheter with a balloon made of a substance that transmits electromagnetic energy at the distal end [36]. The utilisation of catheter-based ultrasonic applicators, an enhanced thermal therapy platform, improves the delivery of hyperthermia treatment. These treatments provide feedback on the best starting power setting, the best angle or orientation to place the applicator, and the applicator selection [37].

F. Microwave Hyperthermia:

It is one of the promising methods that has helped thousands of people with breast or prostate cancer. Cancerous tumours can be heated effectively using microwave energy because they contain a high amount of water. Depending on the size and location of the tumor, one or more microwave antennas may be used to treat it. Single waveguide microwave transmitters operating at 434,915, and 2450 MHZ have been used for microwave hyperthermia [38]. For the treatment of pathological human tissues with tumors, a 2D finite element analysis is described. The study contrasts coaxial antennas with one, two, and three air slots. In a transient state scenario, the model is based on the TM mode and Penne's equation. The antenna's operational frequency is 2.45 GHz. [39]. It is feasible to produce a uniform SAR distribution in the plane parallel to the applicator aperture when using a zero-order mode resonator (ZOR) metamaterial (MTM) structure for microwave thermotherapy. This structure emits an electromagnetic wave in the direction of the treated biological tissue. The ZOR concept is simulated using COMSOL software, and the results show perfect SAR homogeneity and a penetration depth comparable to an EM plane wave [40]. It is described how to induce microwave hyperthermia using a tiny microwave antenna buried in human tissue. The finite element method (FEM) is used for numerical simulation. The findings demonstrate a straightforward way for selecting the best model parameters for the most effective interstitial microwave hyperthermia therapy [41].

Hyperthermia with the Injection of Superparamagnetic and Magnetic Nanoparticles: Superparamagnetic nanoparticles, which are not only biocompatible with the body but also biodegradable, are used to heat tumour cells locally. High-frequency magnetic fields cause an increase in temperature, which a closed-loop temperature control and feedback system regulates. According to the results, colon cancer cells CT-26 start to lose their viability at a temperature increase of 45 °C [42]. intensely magnetic Ferro fluid is introduced into a breast tumour inside a realistic breast model, and external electromagnetic field excitation hyperthermia is used to treat it. A mathematical model describing magnetic fluid hyperthermia in an experiment on a three-layer breast simulation is developed in two steps using the Pennes Bioheat Equation. A heat exchange equation and a magnetic fluid simulation follow. According to the simulation results, the mixture model incorporating both magnetic fluid and tumour tissue is the most crucial factor to consider because it produces superior outcomes and offers precise temperature control for a tumour with little adverse effects [43]. Gelatin mixed with magnetic nanoparticles made of Fe2O3 is detailed in terms of their thermal properties to help with target potential. Calculations are performed for several variables that influence thermal characteristics, including radio wave frequency, particle concentration, applied field strength, temperature, and others. However, given the worry for the surrounding tissues, additional research is needed in this area to increase the target's and the surrounding tissue's heating efficiency and to increase the technique's acceptability in the design of hyperthermia treatments [44]. Magnetite is the magnetic nanoparticle that is directed to the tumour tissue when heat is applied using an external alternating magnetic field and magnetic nanoparticles. The findings also point to a field of study where this method will be helpful for cancers that are located far away [45].

VII. CHALLENGES

Despite significant progress in our understanding of the molecular genetics of MH, we still face several challenges. Because genetic screening on patient populations or family members with ambiguous data is frequently ineffective, a patient's phenotype must be determined before DNA analysis. The Clinical Regulations is a scoring system that links mental health clinical signs to the likelihood of an MH event, and is one tool used to help with phenotypic confirmation [61]. Another strategy is to do a detailed analysis of family history to seek clinical MH crises that have been handed down through many generations [62].

The finding that DNA mutation patterns (and possibly the functional impact of particular variations) may vary between human cultures makes assessing DNA variants even more difficult. For instance, Sambuughin et al. observed that people of African heritage may have a neutral polymorphism alteration in the RyR1 variation, associated with MH susceptibility in the Caucasian population. However, in other instances, the search for disease-causing mutations may also be facilitated by the fact that some mutations are more common groups [63,64].

According to a recent study by Carpenter et al., RyR1 mutations in the gene's highly conserved regions may be connected to a more severe MH manifestation. The RyR1 variant type may be connected to the severity of the MH phenotype. Other factors, unrelated to changes in the DNA sequence, such as epigenetic factors, may also influence the expression of RyR1 variants. For instance, Robinson et al. recently looked at whether the RyR1 mutation's epigenetic allele silencing was a factor in the MH vulnerability's variable penetrance [65,66].

With the advent of molecular medicine, DNA analysis is advancing quickly. It is important to note that the cost of DNA sequencing has decreased 15,000-fold over the past decade and is likely to continue decreasing over the next ten years. The complete coding region of a gene, followed by the entire genome, will soon be economically possible to sequence utilizing techniques like exome sequencing [67,68]. We should have a much better knowledge of the link between genotype and phenotype if phenotypic data is accessible. More DNA variants will be found as a result, the relevance of which needs to be identified. One of the goals of these strategies is to reduce MH susceptibility through the discovery of other DNA alterations that explain phenotypic differences [69,70].

VIII. RECENT ADVANCEMENTS

A. Advanced Breast Cancers: Scope for Improvement with Hyperthermia:

In low-middle-income group countries [LMICs], locally advanced breast cancers (LABC) are a prevalent issue. Most patients arrive at the hospital in an advanced state, making it difficult to perform basic surgery. Therefore, neoadjuvant chemotherapy (NACT) is typically administered to patients to permit tumor downstaging and thereafter mastectomy. Most chemotherapy medications exhibit thermal synergism by increasing cellular drug uptake, oxygen radical generation, chemotherapeutic-induced DNA damage, and DNA damage [46]. Texans, like cyclophosphamide, 5-flurouracil, and Adriamycin, cause oxidative damage and/or strand cross linkages, as well as single and double strand DNA breaks. HT also influences a variety of DNA repair processes such as excision repair, homologous and/or non-homologous recombination [47,48].

In a phase I/II study, Vujaskovic et al investigated the safety of an NACT containing liposomal paclitaxel, doxorubicin, and HT in LABC. At the end of NACT, the cumulative response rate was 72%, with four of the 43 patients achieving a complete response (CR). The disease-free and overall survival rates after four years were 63% and 75%, respectively [49].

Oldenberg et al. recently examined the effectiveness of ReRT with HT in 196 patients with locoregionally recurrent breast cancer en cuirasse who had previously undergone 50 Gy of RT. ReRT was administered as either 12 fractions of 3 Gy or 8 fractions of 4 Gy each, once or twice weekly, in addition to locoregional radiation therapy (RT). A 30% CR and a 72% total clinical response were recorded [50].

B. Advanced Cervical Cancer: Scope for Improvement with Hyperthermia:

LMICs account for 88.1% of all cervical cancer incidences and 91.4% of all fatalities recorded globally in 2020[51]. In LMICs, the mortality/incidence ratio is therefore predicted to be 58.7%. This may be explained by the fact that most patients in LMICs present with locally advanced cervical cancer (LACC). Observing the 1992 recommendations of the National Cancer Institute [52], The most frequent therapeutic approach in LACC is chemoradiotherapy (CTRT), either alone or in conjunction with cisplatin. In a meta-analysis of 14 randomised clinical trials involving 2445 patients, CTRT was found to be superior to RT alone in terms of CR (+10.2%, p = 0.027), overall survival (+7.5%, p = 0.001), and locoregional control (+8.4%, p = 0.001). As a result, even though CTRT has been demonstrated to improve outcomes compared to RT alone, there still seems to be potential for advancement [53].

T. Ohguri and colleagues proposed a multicenter randomised clinical trial that found a link between thermal dosage parameters and the efficacy of definitive chemoradiotherapy combined with local hyperthermia in the treatment of locally advanced cervical cancer. Thermal dosage parameters and clinical outcomes showed dose-effect relationships in CC patients who got CRT plus HT [54].

CA Minnaar et al. proposed Modulated Electro-Hyperthermia for Potentiation of the Abscopal Effect in Patients with Locally Advanced Cervical Cancer. He discovered that six months after treatment, the CMR of disease outside the radiation area shows signs of an abscopal effect that is strongly correlated with the addition of mEHT to treatment regimens [55].

C. Advanced Head and Neck Cancers: Scope of Improvement with Hyperthermia:

The LMICs recorded 81.5% and 71.8% of the world's incidence and fatalities of neck and head cancers in 2020[56]. In LMICs, these tumors are expected to have a 38.2% mortality rate and incidence. Most patients with locally advanced head and neck cancers (LAHNC) present, and CTRT has been the cornerstone of their management, similar to the cervix. Later research from the Meta-analysis of Chemotherapy in Head and Neck (MACH-NC) joint group found that CTRT improved outcomes. A 6.5% absolute advantage at 5 years was demonstrated in their most recent update, which included 107 randomized trials with 19,085 participants and was published in 2021 (hazard ratio: 0.83; 95% confidence interval: 0.79-0.86). However, as patients aged and their performance conditions deteriorated, this benefit diminished [57].

G. M. Verduijn and colleagues used the HYPERcollar system in conjunction with radiation therapy to provide deep hyperthermia to advanced neck and head cancer patients. The average power used during the 119 hyperthermia sessions ranged from 120 to 1007. (Median 543 W). 15 (13%) hyperthermia treatments were not completed due to pain from hyperthermia (6/15), dyspnea from sticky saliva linked to irradiation (2/15), and unidentified causes (7/15) [58].

Recently, M. Kroesen et al. investigated the clinical results, SAR distribution, and viability of reirradiation and profound hyperthermia. Based on patient acceptance and SAR deposition in the target area, he concludes that deep hyperthermia using the Hypercollar3D, in conjunction with reirradiation of recurrent and salvageable head and neck cancer (HNC), is a viable treatment option. The Hypercollar3D's introduction enhanced concentrated delivery by delivering 52 W/kg more SAR to the tumour than the preceding technology. Future studies utilizing this feature will necessitate accurate thermometry of both target and normal tissues [59,60].

IX. CONCLUSION

The experimental findings of investigations demonstrate that hyperthermia is both a powerful radiosensitizer and a potent enhancer of many cytotoxic medications, and it is considered an optimal supplementary therapy. Surface lesions, head and neck tumors, as well as deep area malignancies, can all be treated with ultrasonic hyperthermia. With this method, heating is achievable up to a depth of 20 cm with several transducers and up to a depth of 5 to 10 cm with a single transducer. Although the procedures are not tailored to target tumor cells, hyperthermia with external radio frequency devices is a suitable alternative for the treatment of prostate cancer. The techniques are extremely straightforward because they aim to send electromagnetic energy as close as possible to the tumour site. Cancer in the arms, legs, or body is treated using hyperthermic perfusion. Frequency enhancers and catheters are used to enhance therapeutic responsiveness and minimise adverse effects. The treatment of superficial cancers in the breast, leg, prostate, and brain involves microwave hyperthermia. With the use of specialised antennas, advanced technology enables the heating of vast volumes of space. Temperature measurement is challenging, nevertheless, when localized heating has a high penetration rate. By reaching precise target doses, the benefits of magnetic and paramagnetic nanoparticles can lessen or even eliminate potential adverse effects. With the benefit of specific heat deposition to tumour cells, nanotechnology-based cancer therapy is also known as interstitial thermotherapy. The whole basis of cancer diagnosis, treatment, and prevention may alter as a result of this technologically assisted thermal therapy. In the coming years, this sector is expected to be increasingly driven by research into targeted strategies, delivery tactics, and higher radiation dosages. Clinical studies still need to improve their methods to achieve more effective outcomes, which are more promising.

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Authors Contributions	I am only the sole author of the article

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