Effect of Arterial flow on Heat Transfer during Hyperthermia Applications

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BY

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DECLARATION

I declare that the dissertation work entitled "**Effect of Arterial flow on Heat Transfer during Hyperthermia Applications**" represents my idea in my own words where other's words that have been included are adequately cited and referenced to the original sources. I also declare that I have adhered to all academic honesty and integrity principles. I have not mis-presented/falsified any idea/data/fact in any submission.

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DECLARATION

I, Subeg Singh, hereby declare that the Project work entitled“EFFECT OF ARTERIAL FLOW ON HEAT TRANSFER DURING HYPERTHERMIA APPLICATIONS” is an authentic record of my own work carried out at Thapar Institute of Engineering and Technology as a part of the my final year dissertation.

I declare that I have successfully completed my dissertation, under the guidance of my mentor Dr. Neeraj Kumar and Dr. Kundan Lal.No part of the matter embodied in this report has been submitted to any other university or institute for the award of any degree.

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ABSTRACT

Hyperthermia is a heat treatment that basically refers to the application of heat to treat a disease by using heat. Heat treatment as a therapy method is not new, but it is becoming more popular as a tumour treatment. Magnetic fluid hyperthermia (MFH) which has been used to treat cancer for decades, involves injecting magnetic nanoparticles into tumours and then heating them in an alternating magnetic field. The concept is to insert magnetic particles into a malignant tumour and use alternating magnetic fields to raise the interstitial temperature, so eliminating the tumour. In present work the effect of magnetic hyperthermia in the arteries on different positions is analysed by creating a three dimensional model and using computational methods with the help of COMSOL Multiphysics software. In this computational study the effect of variation in distance from artery is studied by giving a specific blood flow rate. In this work different artery positions x=3mm, 6mm, 9mm, 12mm are considered on the basis of configurations namely near tumour center, mid tumour, tumour boundary and outside tumour configuration respectively. In other part of this study maximum temperature in the tumour domain have been analysed on different locations or artery configurations. Results find that position of artery plays a key role in heat dissipation through artery. The final conclusion of this work suggested that therapeutic temperature decreases when arteries are closer to the tumour due to convective heat transfer effect and same temperature starts to increase when arteries are away from the tumour.

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NOMENCLATURE

Symbols	**Description**
k_t	Tumour Conductivity (W/m·K)
wb_{ti}	Perfusion rate healthy tissue (1/s)
wb_{tu}	Perfusion rate tumour (1/s)
T_a	Artery temperature (K)
cp_b	Blood heat capacity (J/kg·K)
cp_t	Tissue heat capacity(J/kg·K)
q_{art}	Flow rate in hepatic arterym^3/s
ρ	Density of the fluid (kg/ m^3)
u	Velocity space vector(m/s)
n	Unit vector
T	Temperature vector
Q	Heat Source
q	Heat flux
F_i	Body force per unit volume
P_i	Surface force per unit volume
g_i	Gravitational acceleration
Q_{ext}	External heat source
Q_{met}	Metabolic heat source

Greek Letters

ρ	Density of the fluid (kg/ m^3)
μ	Dynamic viscosity of blood
∇	Del operator
∇^2	Laplace operator

Subscripts

b	Blood
ti	Tissue
tu	Tumour

ABBREVIATIONS

MRI	Magnetic Resonance Imaging
CT	Computerised Tomography
DNA	Deoxyribonucleic Acid
MRT	Magnetic Resonance Tomography
WBH	Whole body hyperthermia
RF	Radio Frequency
EM	Electromagnetic
SAR	Specific Absorption Rate
MFH	Magnetic Fluid Hyperthermia
HTP	Hyperthermia Treatment Planning
PD	Power Density
AEH	Arterial Embolization Hyperthermia
MDT	Magnetic Drug Targeting
MNP	Magnetic Nanoparticles
AMF	Alternating Magnetic Fields
PBHTE	Pennes Bioheat Transfer Equation
SLP	Specific Loss Power
BNF	Bionized Nanoferrite

CHAPTER 1 -INTRODUCTION

1.1 History of Cancer treatment

In earlier times cancer treatment was all about the causes and effects of the disease. Along with this it also meant to continue the research and discoveries regarding disease’s structure, treatments, developing new methods of diagnosis. Most common therapies available for cancer treatment includes Chemotherapy, surgery, radiotherapy, stereotactic body radiation therapy, irreversible electroporation therapy etc.

Chemotherapy is the chemical treatment of cancer disease. It began in the early 20th century but it came into practice around 1930s. This therapy was actually discovered and used during First and Second World War due the use of Mustard gas which decreased the levels of leukocytes in the human body (1). So due to this Nitrogen Mustard was being used as the first chemical agent during Chemotherapy. During late 1960s cancers like choriocarcinoma and hematologic begin to originate and chemotherapy was used to treat these diseases. Hodgkin's disease was also made curable using chemotherapy in the late 1970s. In late 1950s solid tumour treatment using surgery and radiotherapy were also popular. At that time some of the scientists also published their works to use these therapies after chemotherapy in case of advanced stages of cancer. This integrated therapy approach was first used successfully during breast cancer treatment and was also became a good example of multimodality treatment which is currently being used for cure of many cases of malignant cancer.

1.2 Types of Cancer Treatments

Cancer can now be treated with a variety of methods, including surgery, chemotherapy and radiation therapy. New methods like interventional radiology and immunotherapy are also getting used and evolving day by day. Common cancer treatment options will be discussed further:-

1.2.1 Blood & marrow stem cell transplantation

In this treatment new blood forming fresh cells is added to the person’s body to replace the old unhealthy cells. Stem cells are actually made in the bone marrow and then these get transformed into three different types of blood cells in our human body. Many common blood cancers like leukaemia, lymphoma and multiple myeloma can be treated using this technique. This technique is also used to treat certain genetic disorders and some other diseases also.

One of the main advantages of this treatment is that it is applicable on both old and young age patients. Disadvantages of stem cell transplantation include improper functioning of body for several days after the treatment due to many infections which can cause diseases like diarrhoea, nausea and fatigue. Due to these disadvantages cell transplantation treatment is not suitable to every person infected.

1.2.2 Chemotherapy

It is the chemical treatment of cancer disease using drugs. These drugs can be given through blood and mouth of the affected patient. Several drugs are used as a mixture for cancer treatment. Chemotherapy can be used for reducing the total number of cancer cells in the body, containment of cancer affected area, shrinking the tumour present. Chemotherapy has the potential to harm cells in areas such as blood, hair, skin, lining of intestinal tract. Chemotherapy drugs work by destroying cancer cells that are developing quickly. These medicines are distributed throughout the body, but they can also destroy normal, healthy, rapidly proliferating cells. Unintended repercussions can result from harming healthy cells. It is reasonable to worry about this element of cancer therapy, even though adverse effects are typically not as serious as you might anticipate. Chemotherapy is more likely to kill healthy cells, such as those found in the mouth, digestive tract, hair follicles, bone marrow, and reproductive system. Some chemotherapy medications have the potential to harm cells in the heart, kidneys, bladder, lungs, and neurological system. You may be able to take medications along with the chemo to help safeguard your body's natural cells. There are additional medications available to aid with adverse effects.

1.2.3 Immunotherapy Cancer Treatment

Utilizing the immunity to combat cancer cells, immunotherapy is a cutting-edge cancer treatment. Cancer treatment known as immunotherapy makes use of the body's innate ability to fight off infections (immune system). In order to aid the immune system in combating cancer, it uses substances created either by body or in a lab to make it work harder or more precisely. This helps to eliminate cancerous cells from your body. Immunotherapy works by:

- Boosting the immune system's capacity to eliminate cancerous cells
- Preventing the spread of cancer to different regions
- Slowing the growth of cancer cells

1.2.4 Interventional Radiology

Interventional radiology is a medical specialty that uses various imaging techniques to obtain images of internal organs (2). These pictures are carefully interpreted by an interventional radiologist in order to detect damage and illness, as well as to execute a variety of interventional medical treatments. X-rays, MRI scans, fluoroscopy, CT scans, and ultrasounds are all used by interventional radiologists.

These imaging techniques are used by interventional radiologists for treating tumours, performing biopsies of internal organs, placing stents and catheters into the area being treated. This significantly decreases the importance of open surgeries in these types of cases where interventional radiology can be performed using a thin pipe or straw like apparatus.

There are several advantages of interventional radiology over other treatments like it causes less pain, low risk, very less recovery period, light sedation is needed during treatment and minimal hospital stay.

1.2.5 Radiation Therapy

Radiation therapy kills cancer by destroying tumours with the help of high doses of radiation. It can be used as the only treatment or in combination with chemotherapy, surgery, etc. Radiation therapy uses high energy radiations for the treatment of cancer. It works on the principle that cancerous cells are destroyed by high energy radiations that cease them to reproduce by destroying their DNA, thus naturally eliminating these cells from the body. They most effectively kill actively dividing cells. At low amount of radiation doses X- Rays are used to see inside the body of a patient. At high amount of radiation doses it is very high possibility that cancer cells are damaged or their growth becomes very slow due to damaged DNA. These cancer cells whose DNA is damaged stop to multiply and finally ejected by the body.

Main advantage of radiation therapy is that it eases the pain after the treatment and it also prevent the cancer from returning or it ceases the cancer cells from growing further. Side effects of radiation therapy include diarrhoea, tiredness and sickness.

1.2.6 Surgery

Cancer surgery is the traditional and oldest kind of treatment of cancer (2). It is an invasive procedure of taking out cancerous tissue from the body surgically. Doctors follow the basic practice of not removing the tumour at primitive stages due to risk factor involved in the incision process. In the early stages of cancer surgical treatment is advised by doctors and oncologists to avoid the cancer cells from spreading further in body. There are different types of cancer surgical treatments available such as laproscopic surgery, laser surgery, cryosurgery, mohs surgery and endoscopy.

1.3 Hyperthermia

Hyperthermia is a treatment process that essentially refers to the use of heat to cure a disease (3, 4). Heat treatment as a therapy method is not new, but it is becoming more popular as a tumour treatment. Currently, tumour treatment is a fast evolving method. Physicians in Greece and Rome believed that they could cure anything if they just controlled the body temperature. The range of temperature rise is a little over usual temperature of the human body temperature (41-45 degrees). Temperatures in this range are dangerous to cancerous cells, while causing no harm to healthy cells. The hyperthermia has a therapeutic impact on both malignant and non-malignant tumours, depending on the vascular properties of the tissue; it may vary the cancerous growth. The severity of hyperthermia is determined by the rise in range of temperature and the length of time that a high temperature is maintained. The first is physiological hyperthermia, a therapy that treats pain, strain and sprain physiologically. This is conducted in a series of sessions, with low temperatures. With each 1°C rise in temperature above 42.5-43.0°C, the exposure duration can be cut in half to achieve similar cell damage. Most normal tissues are unaffected by a one-hour treatment at temperatures up to 44°C.

1.4 Types of Clinical Hyperthermia

There are three categories in which clinical studies are divided. Clinical study in Phase I is a study that evaluates the treatment's toxicity. Clinical study in Phase II is that evaluates the therapy's efficacy. In Phase III one treatment technique is compared against another. A novel treatment approach is usually compared to a standard therapy, which serves as a control. Within the research, the control group might be historical, randomised, or non-randomized.

On a clinical basis there are three types of hyperthermia namely local, regional and whole body hyperthermia.

1.4.1 Local Hyperthermia

By using either internal or external methods, the primary objective of local hyperthermia is to elevate the temperature of the cancerous cells while preserving surrounding normal tissue. The portion of volume that can be heated is entirely dependent on the heat source used and the instrument used. It is done for superficial tumors. It is done by means of applicators and antennas emitting radiowaves or microwaves. As shown in Fig1.1 applicators used can be waveguide, spiral, horn, currentsheet etc. Temperature of the tumor and surrounding tissues can be adjusted by positioning of the applicator.

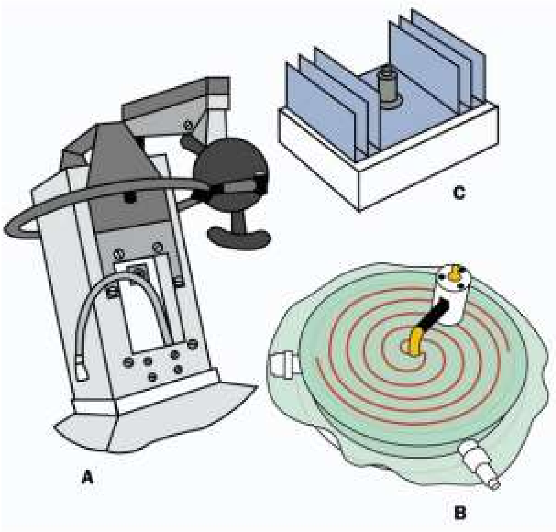

Fig 1.1: Different types of applicator used for local hyperthermia (A) waveguide applicator; (B) spiral applicator; and (C) current sheet applicator (5)

External, intraluminal, or interstitial hyperthermia can be used as a therapy. Tumours near the skin are generally treated by using external methods. They can be used alone or in combination with radiation therapy to treat people with superficial cutaneous, primary or metastatic cancer, or subcutaneous tumours, and also cervical lymphovascular attack metastases from throat and head cancer.. An external heat and energy source like a microwave or ultrasonic source, an applicator, and a method of application determining tumour temperature is used in this technique. Currently, magnetic fields can be used to interface with hyperthermia systems that allow the monitoring through noninvasive magnetic resonance imaging (MRI) systems. As shown in Fig1.2 local hyperthermia can be of different types such as Interstitial, Intraluminal, Superficial, Electroporation, High-Intensity focused ultrasound (HIFU) etc.

Intraluminal or endocavitary methods are mostly used for treatment of tumours inside or near the cavities in human body. There are four types of cavities in human body namely: gastrointestinal, gynecological, genitourinary and pulmonary (trachea, bronchus). This technology allows to heat very target specifically by inserting an electrode called endotract into the human body's lumens to provide energy and heat directly to the location. Depending on the location and size of the lesion, several types of electrodes are available. Interstitial treatments are basically those treatments which used to treat cancers which are in verge of spreading throughout the body, such as brain tumours. Ultrasound imaging methods can be utilized to ensure that the probe is appropriately positioned within the tumours.

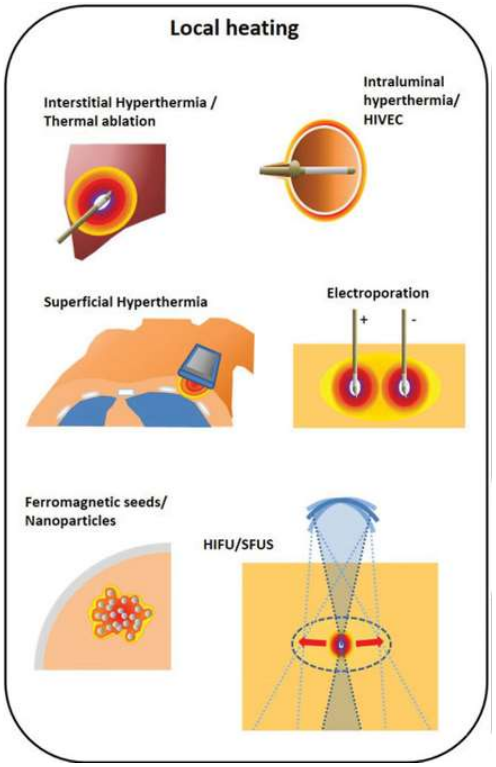

Fig 1.2 Different types of Local hyperthermia (6)

1.4.2 Regional Hyperthermia

Regional hyperthermia is mainly used for patients having later stage malignant cancers like in pelvis or abdomen. Methods such as deep tissue may be commonly used to treat internal tumours like vertebral or bladder cancer. Due to the considerable difference in physical and physiological features, regional hyperthermia is much more difficult to apply than local heating. It necessitates more complex planning, thermometry, and quality control (2). Because in regional hyperthermia, heat due to given energy harm the nearby malignant cancerous cells and energy is also provided to the adjacent normal tissues. As shown in Fig1.3 there are many applicator types for Regional hyperthermia namely hybrid system applicator, Magnetic Resonance Tomography(MRT) applicator. Regional hyperthermia has been employed in the majority of clinical research in combination with radiotherapy. Advanced tumors in pelvis or abdomen regions are major indications which include prostate, cervical, bladder and rectal carcinoma.

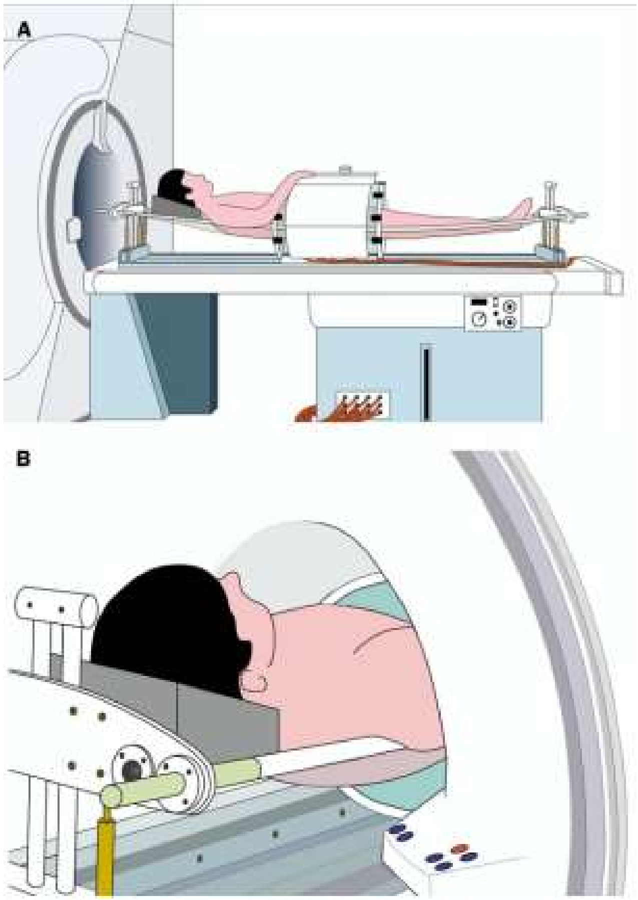

Fig 1.3: Different types of applicators used for Regional hyperthermia (A) hybrid system applicator; (B) Magnetic Resonance Tomography (MRT) applicator (5)

Cancer in specific organs, such as the liver or lungs, as well as arm and leg malignancies like melanoma, can be treated with regional perfusion techniques. A portion of the patient's blood is extracted during this procedure, heated, and then reinfused (perfused) into the affected limb or organ. During this procedure's treatment, anticancer medications are usually used. Warm fluids perfused into a body cavity, organ, or limb can cause regional hyperthermia. There are different types of Regional hyperthermia such as radiative, capacitive, isolated etc.

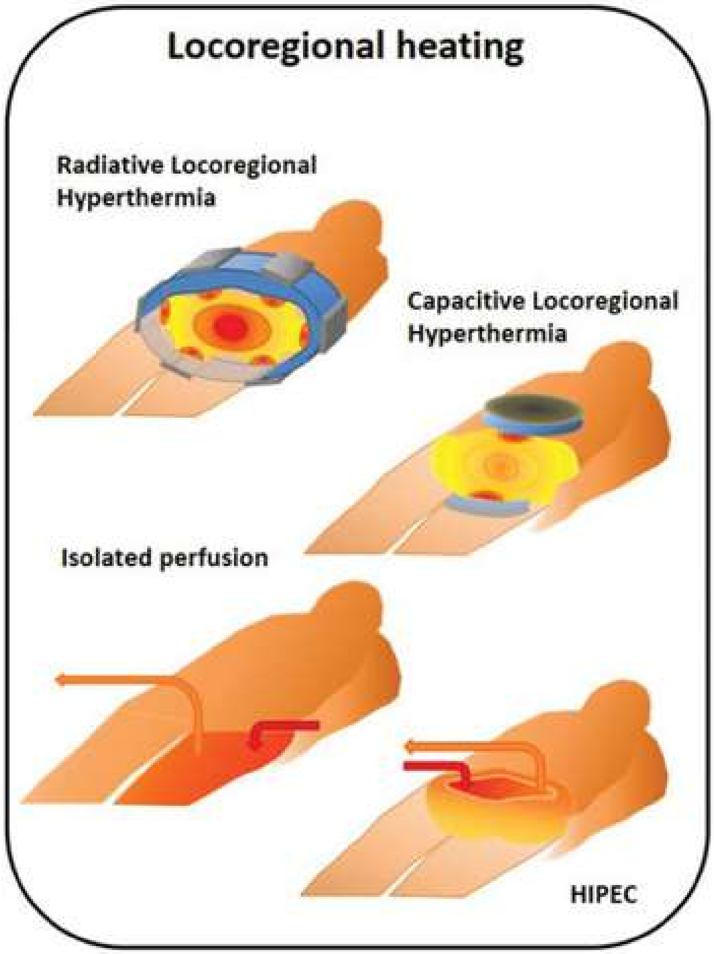

Fig 1.4: Different types of Regional hyperthermia (6)

1.4.3 Whole Body Hyperthermia

At temperatures that exceed 42°C, whole-body hyperthermia is a distinct pathophysiological condition with significant effects on metabolic activities, blood circulation, organ function, and tissue repair. WBH is distinguished by the fact that energy is injected into the body while energy losses are reduced (2). Many applicators can be used in WBH but one such known as Iratherm is given below in Fig1.5. It is done using There are presently three primary strategies for achieving regulated Whole Body Hyperthermia namely thermal conduction (surface heating), additional induction and EM induction. In liver and brain tissue the maximum temperature tolerance ranges from 41.8°C to 42°C, but this can be controlled for a certain time.

Fig 1.5: Iratherm applicator for whole body hyperthermia (5)

1.5 Devices used in Hyperthermia Treatment

In hyperthermia treatment selection of devices used for treatment plays a very important role. Devices used in particular treatment should be such that it doesn't overheat the specific target location. Controlling heat transmission deep into and within the body is a difficult issue that is totally dependent on the operation of the tissue heating and thermometry equipment, which includes heat applicators like external, intracavitary, interstitial and temperature sensing systems.

1.5.1 Capacitive Inductive Applicator

Capacitive hyperthermia equipment has RF generator, RF power meter and set of electrodes, temperature measuring and controlling system (5). The interactions of electric fields created by parallel-opposed electrodes transmit RF energy locally or regionally. The electrodes' changeable placements allow for heating at various angles and treatment areas. Numerous body parts where displacement currents are in between two capacitor plates might heat tissues easily and treats those tissues using RF capacitive devices.

For greater penetration of more than 5 cm overheating is possible when an alternating current (AC) carrying coil encloses a biological tissue via air. This is accomplished by inductive coupling. Radiofrequency induction heating uses magnetic fields to penetrate tissues like subcutaneous fat without overheating them. Eddy currents are produced by these magnetic fields inside tissues. Heating occurs because of the induced electric fields. When fields are parallel to the tissue contact, heating is very high in muscular mass rather than fat. Inductive applicators do not appear to bind as firmly to the body and reasonably strong currents as capacitive applicators as high current intensity is required frequently to obtain appropriate heat. In below given Fig1.6 capacitive inductive applicator for whole body hyperthermia is shown.

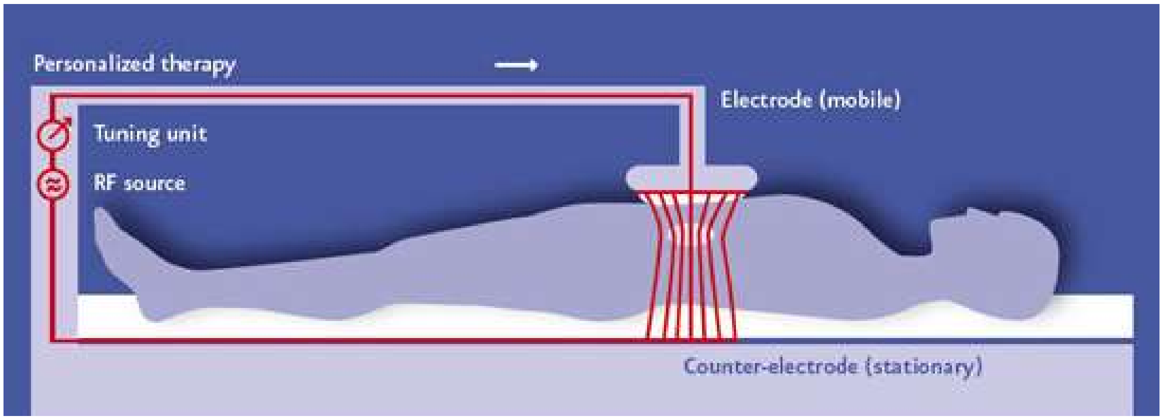

Fig 1.6: Capacitive Inductive applicator for whole body hyperthermia

1.5.2 EM radiation devices

These devices use Electromagnetic radiation to treat cancer tumors. One main disadvantage of these devices are very less penetration about 2-3cm from the skin surface (5). Different antennas are used for different type of intensities depending on the malignancy of the cancer tumors. Single-element applicators can give appropriate heat dosages to relatively tiny superficial areas safely and effectively. The employment of antennas with a power distribution that is as even as feasible throughout the area of the skin is required as a result. A variety of applicators must be used to increase the value of Specific Absorption Rate (SAR) at a sharp focal depth in comparison to the surface SAR during hyperthermia treatment.

1.5.3 Magnetic Fluid Hyperthermia

A growing number of therapeutic uses for magnetic fluids are emerging, including magnetic fluid hyperthermia, magnetic resonance imaging (MRI), and administering medication doses (MFH). The latter method involves introducing magnetic nanoparticles into cancer tumours and then heating them in an oscillating magnetic field. This technique has been used to cure cancer patients for decades. The main concept is to insert magnetic nanoparticles into a malignant tumour and use alternating magnetic fields to elevate the interstitial temperature, so eliminating the tumour. This approach satisfies the demand for maximum heat deposition within the targeted location while protecting the surrounding healthy tissue to the greatest extent possible.

Experimental findings showing that almost 90 percent of the iron infused in the human body was identifiable by CT scan on tissue samples provided for this. One particular benefit of MFH is the capability to anticipate the permanent magnet fluid spread prospectively and calculate the heat distribution to a highly reliable degree afterward because of the distribution of density of the nanoparticles in post-instillation computerised tomography (CT). Experimental findings showing that almost 90 percent of the iron infused in the human body was identifiable by CT scan on tissue samples provided for this.Another advantage of the approach is the stability of nanoparticle deposits.A schematic diagram for MNPs-induced hyperthermia planning for cancer therapy is shown below in Fig1.7.

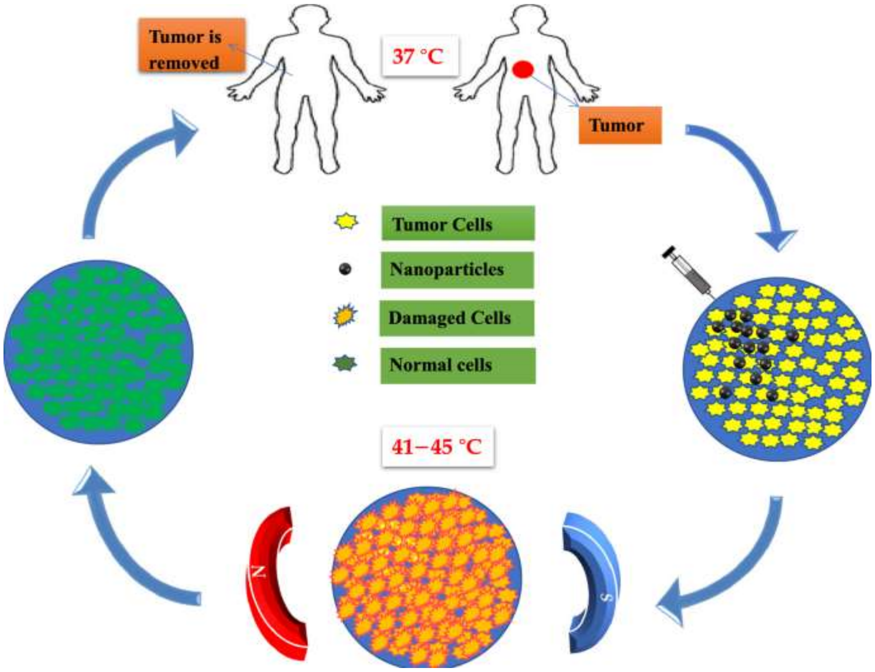

Fig 1.7: A schematic for MNPs-induced hyperthermia planning for cancer therapy(7)

1.6 Hyperthermia and its combination treatments

Hyperthermia treatment is more effective when it is used as a combination with other therapies like chemotherapy, radiotherapy, radiochemotherapy and gene therapy (8). So, all these combinational treatments are shown in Fig1.8 and will be discussed further.

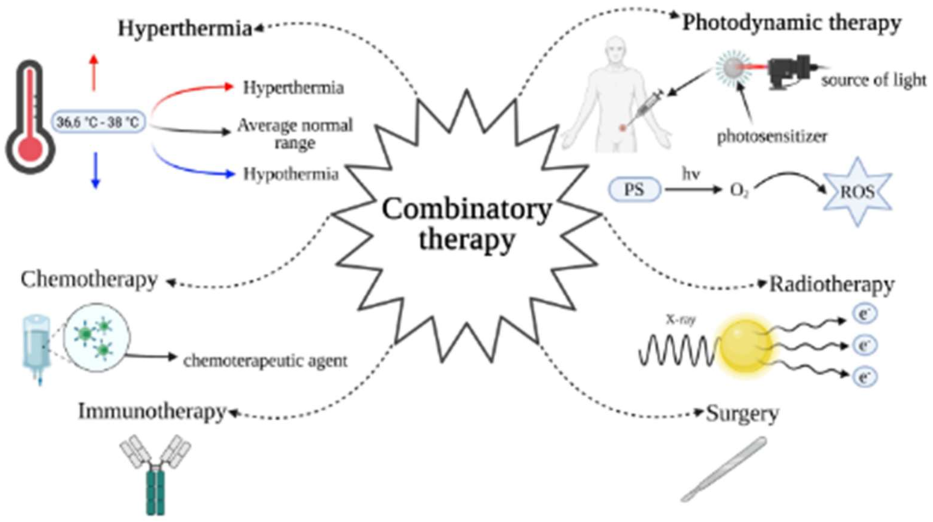

Fig 1.8: Hyperthermia and its combination treatments (8)

1.6.1 Hyperthermia and chemotherapy

The main benefit of hyperthermia over chemotherapy is that it works in conjunction with some drugs that fight cancer cells. Hyperthermia may be useful in avoiding or delaying the development of tumour resistance to a certain chemotherapeutic treatment, or in reversing acquired tumour resistance to a specific therapeutic agent (2, 8). Due to a net increase in DNA damage following hyperthermia and chemotherapy exposure, the interaction of hyperthermia and chemotherapy appears to enhance cell toxicity. Without raising the dosage of medication administered, the increased cell tissue temperature brought on by EM energy absorption considerably enhances the effectiveness of chemotherapy in the treatment of human malignant tumours. Numerous researches have noted enhancements in local administration and therapeutic efficacy of chemotherapy and heat combinations.

1.6.2 Hyperthermia and radiotherapy

In comparison to radiation alone, the combinations of hyperthermia and radiation have been able to produce more thorough and durable responses in surface tumours. There are several factors that contribute to the cumulative effects of radiation and hyperthermia. Hyperthermia may result in increased blood flow, which may improve tissue oxygenation, resulting in temporarily increased radio sensitivity. As a result, this combination treatment may be regarded successful, particularly for individuals who are unable to take chemotherapy (2). According to Franckena et al. the combined treatment of hyperthermia and radiotherapy is more effective than chemoradiotherapy in case of advanced cervix cancer.

1.6.3 Hyperthermia and radiochemotherapy

Radiochemotherapy is a popular therapeutic option for people with primary, locally progressed, or reoccurring rectal cancer. The inclusion of localised hyperthermia to this standard therapy can improve treatment success. Recent publications have reported on the possibility and efficacy of combination treatment of hyperthermia with radiochemotherapy in the treatment of a wide variety of cancer (5, 8). The use of hyperthermia to radiochemotherapy may improve patients' quality of life without raising the risk of problems. In controlled clinical studies, further study is needed to evaluate radiochemotherapy compared to radiochemotherapy with hyperthermia.

1.7 Advantages of Hyperthermia

There are some advantages to hyperthermia. The physiology of tissues is altered by heat in a number of ways, including an increase in local blood flow, vascular permeability, and metabolic activity. The most crucial physiological parameter in this case is blood flow. The majority of the physiological changes occur when tissues and cells are heated with variations in blood flow. Because most enzymes increase their activity when the temperature rises, hyperthermia causes a general increase in metabolic rate. As a result, tissue consumes more oxygen locally, and hyperthermia increases oxygen contribution towards the heated location. Blood flow to these tissues will have a significant influence on their ability to heat the corresponding tissues since blood flow is one of the main ways that removes the heat from tissues. Takahashi et al. (9) proposed that hyperthermia, as a less-invasive and less-expensive conservative therapy, can successfully treat osteoarthritis.

1.8 Risks during Hyperthermia treatment

Heat generated during hyperthermia is often not hazardous. Pain and burn are common hyperthermia dangers that may be reduced or prevented by using proper heating procedures. The principal dangers of hyperthermia are caused by either a rise in core body temperature or an increase in temperature of some specific organs. The body's thermal equilibrium is often restored when the temperature increases by the increase in blood flow towards the skin and sweat. These reactions increase the heartbeat and cause the body to drain salt and fluids. It reduces functioning efficiency and can overwhelm the heart, causing it to fail haemoglobin concentration, which can cause brain thrombosis, particularly in the older age people with atherosclerotic arteries. The majority of healthy persons can withstand body core temperature fluctuations of up to 40^{o}C only when they are properly hydrated. When body core temperatures reach 42 to 43^{o}C cell damage starts to occur.

Hyperthermia may increase the growth of tumours by ionising the developing radiations or by chemical substances (7). Both the general press and the biological journals continue to be very concerned in the argument about whether EM radiation prevents or encourages the development of cancer. According to conflicting findings, depending on the treatment protocol, hyperthermia therapy can either be an anti-promoter or a promoter.

The neural tissues appear to be extremely heat sensitive, with the likelihood of nerve injury and changes in neural morphology affecting nerve transmission and function.

CHAPTER 2 - LITERATURE REVIEW

2.1 International Status

In this paper Behnaz et al. (11) used nanostructures to accumulate exclusively in cancerous cells and act as energy providing sources of heat. The main aim of this paper was to investigate the non-uniform distribution of gold nanoparticles used within a cancer tumour and the heat transfer of large blood vessels taken in geometrical model. In this study 3D, the mass equation was utilised to predict the nanoparticle dispersion by assuming a predetermined beginning position of nanoparticles at the core of the tumour. Author used Beer-Lambert's Law to compute laser heating as a volumetric source of heat. Using this numerical model best laser intensity between nanoparticles diffusion and laser irradiation can be forecast for a specific given time. By showing the distribution of nanoparticles and implanted major blood vessels in the cancer affected zone, authors wanted to prove that heat transfer and dispersion plays a very important role altogether for reduction in tissue damage. Significance of this paper was that by taking hyperthermia therapy into account their model was more accurate and thorough in forecasting the tissue damage and providing the particular methods to prevent more healthy damage.

Idir et al. (13) present a 3D Finite Element Method (FEM) approach for directed tumour removal. The suggested model demonstrates a novel way for controlling the temperature diffusion direction during thermal ablation. To eradicate the cancerous cells while protecting the surrounding healthy cells, we created a directed probe with a bent cathode as a heating source. Authors numerically modelled the ablation process using the COMSOL Multiphysics programme. Using a curved cathode, we were able to achieve directed ablation. Overheated cells were supposed to be destroyed, but surrounding healthy tissue was meant to be protected. Authors examined the necrotic tissue percentage from various angles and discovered that the cells are destroyed in the cathode direction while staying safe in the other directions. Idir et al. also measured the temperature at various sites; the findings reveal that the temperature rise in the cathode direction but remained nearly constant in the opposite direction. This research describes a novel method for controlling the direction of temperature dispersion during tumour thermal ablation. The presented model might be a useful technology for oncologists to plan for effective thermal ablation of tumours with little harm to healthy tissue.

Research by Moroz et al. (13) shows that Arterial embolization hyperthermia (AEH) is caused when ferromagnetic particles in tumours blocked region exposed to an alternating magnetic field that causes hysteretic heating. The goal of this study was to examine AEH utilising a big animal kidney as a tumour model. Three pigs' kidneys were arterially injected with 50 to 400 mg of ferromagnetic microspheres. Temperature probes were placed in kidney tissue, epidermis, and subcutaneous fat. After that, each patient was subjected to an oscillating magnetic field for 5 minutes while under general anaesthesia. The heart pulse was monitored using a femoral artery catheter. The iron concentration of renal tissue was chemically measured three days after treatment and then associated with tissue heating rates.

In research paper by Khaled et al. (14) flow and heat transfer in biological tissues are performed to explore the possibility of showing transport theories in porous mediums. Porous media in heat transfer applications is considered to be more accurate due to fewer assumptions than bioheat transfer models.

Javidi et al. (15) follows the trend for one of the main challenges in cancer treatment which is the rise of body temperature for a long time during hyperthermia or some other treatment therapy. Heating configuration in the tumour treatment using magnetic nanoparticles mainly depends on frequency, intensity of magnetic field, dispersion of particles & properties of biological tissues. In this research paper numerical results were compared with experimental results in order to show the accuracy of the model. In second part a specific gel was used in different concentrations and at different inlet velocities to see the temperature and power distribution throughout the tumour part. Results show that by enhancing the inlet velocity average temperature in the domain decreases and semi spherical magnetic nanoparticles have lower temperature than gel with 2% concentration.

Pavel et al. (16) discussed Magnetic fluid hyperthermia (MFH) and cancer treatments have seen a spike in popularity in recent years. At the moment, certain unresolved issues are impeding the proper implementation of this multidisciplinary study. The motive of this study is to figure out how much magnetic nanoparticles to be injected into the tumour to help it reach an ideal temperature of 42oC, resulting in increased sensitivity to apoptosis in tumour cells. We developed a computer model in COMSOL Multiphysics to investigate heat dissipation within tumour tissue, as well as the amount of heat produced by Brownian rotation and Neel relaxation. Simulations of a spherical tumour in a cubical area with a volume of specific number were performed in order to explore this research area further.

Pavel et al. (18) in this paper points out a few unresolved issues now stand in the way of the magnetic fluid hyperthermia (MFH) treatment being successfully implemented. The selection of the proper particle concentration to generate a certain temperature increase in the tumour tissue is one of these issues. It involves taking into consideration the physiological characteristics of various tissue types. It is feasible to gauge the effectiveness of this treatment approach by using the appropriate nanoparticle dosage and taking into account their unique loss power. If the cancer's exact location is obtained using CT scan and MRI images computational simulation like these could help the oncologists to decide the specific dose and we can also see their particle distribution in the tumour.

Thodsaphon et al. (19) provided some insights about the intensity of an external magnetic field, which weakens with increasing distance, is the main drawback of magnetic drug targeting (MDT). To avoid blockage in the artery, small nanoparticles (NPs) with superparamagnetic properties are also necessary. However, due to their tiny size, small NPs are challenging to vector and maintain at the intended area. The objectives of this study were to look at factors that affected how well drug carriers were captured in an arterial flow model. In this study, researchers used COMSOL Multiphysics to computationally simulate and assess capture efficiency in MDT. The non-magnetic coating materials' thickness had no discernible impact on how well MDT captured particles. Small drug carriers 200 nm in diameter in the vascular flow were challenging to collect. We contend that tiny blood arteries with low blood velocities, such as micro-capillary vessels, can produce the MDT with high capture efficiency.

Paulides et al. (20) through his clinical studies have demonstrated that hyperthermia (HT), or raising temperature of the body to 39–44^{o}C, greatly improves the efficacy of chemotherapy and radiation. Personalized hyperthermia treatment planning (HTP) has developed into a strong tool for enhancing treatment quality, driven by advancements in computational methods and processing capacity. To optimise patient-specific therapy, electromagnetic, ultrasonic, and thermal simulations are currently being carried out using accurate clinical setups. Extensive studies that try to evaluate the quality of HT and correctly apply new HT tools and approaches are also becoming increasingly prevalent. In this article, researchers discussed the simulation tools and methodologies created for clinical hyperthermia and assessed their progress from "model" to "clinic" at present time. Additionally, authors provide explanations of the main methods that are used to validate the paper. In this paper authors had shown the importance of HTP for treatment quality and in for hyperthermia as a combinational treatment.

Q Wang et al. (20) discussed about large blood arteries enclosing the tumour would act as a considerable heat sink, severely reducing the thermal ablative surface when the tumour is heated up. Recently, magnetic nanoparticles (MNP) have been recognised as a crucial heating enhancer to increase therapy effectiveness. It can hinder blood flow, which in turn lessens the ability of big vessels to act as a heat sink and absorb more energy when exposed to an external magnetic field. These two crucial parameters, which in principle were supposed to remain a secret, were thoroughly examined in this work using three-dimensional numerical modelling. According to the findings, the factor of blood flow obstruction is more effective than the factor of energy absorption in terms of contributing to temperature rise in tissues around large vessels.

Seotaert et al. (21) discussed that alternating magnetic fields (AMFs) are used with Magnetic nanoparticles (MNPs) to deposit localised energy for cancer hyperthermia therapy. Hyperthermia can be used in combination with radiation or chemotherapy to improve disease management without increasing toxicity and damage caused to the healthy tissues. The distinct properties of heat deposition and transfer with MNPs have sparked tremendous interest and have been the focus of many researchers to understand processes and maximise performance. MNPs were shown to have a normal distribution in a model liver tumour. Furthermore, estimated spatial and temporal temperature changes were compared between no modulation, sinusoidal, rectangular, and triangular modulation of a base 150-kHz sinusoidal waveform and magnetic field amplitude frequency modulation. When the amplitude modulation and tissue damage-related perfusion profiles were changed, complex connections between nanoparticle heating and cancer tissue damage were discovered. These findings are intriguing and encourage additional research into amplitude modulation as a technique of improving efficiency and overcoming technical hurdles connected with magnetic nanoparticle hyperthermia (MNH).

2.2 National Status

Mital et al. (22) showed us that cancer cells are damaged locally during the treatment of tumours with hyperthermia, which can also be used to boost the effectiveness of other therapies like chemotherapy. The least intrusive method of providing heat is magnetic nanoparticle hyperthermia. It is based on exposing magnetic nanoparticles to an oscillating magnetic field after injecting them into the tumour. The method aims to harm the tumour while sparing the healthy tissue around it. In this exploratory investigation, we consider a basic model that is composed of two concentric spheres to represent the tumour and its surrounding tissues and is based on numerical results from the Pennes bioheat model. In this model, the spatial variation of thermal ablation is represented by a Gaussian distribution, and the time variation is represented by an exponential decay function. The focus of the research is to maximise the factors that affect how thermal energy changes by changing in space and time. The ultimate goal of this study is to provide a way for treating hyperthermia in a clinical setting.

Koustav et al. (23) worked by carefully selecting the magnetic absorption characteristics of the MNPs the thermal effect caused by heating magnetic nanoparticles (MNPs) in the presence of an external magnetic field can be controlled. In this study, a thermo fluidic model created with ANSYS FLUENT is used to numerically simulate the temperature field that develops within or outside of the tumour when it is exposed to an external oscillating magnetic field. The volumetric distribution's linear pattern dominates the other two in a significant way. To find the temperature in the tumour domain many other factors like intensity of magnetic field, frequency of magnetic field, vascular congestion, and different type of MNP material used. Proper selection of these parameters plays a very effective role and it is very important from efficacy or efficiency point of view.

The purpose of this study conducted by G. Singh et al. (24) was to research, assess, and contrasting the effectiveness of various intra-tumoural magnetic nanoparticle (MNP) administration methods (single-site and multi-site injection). The comparison is done in light of a hypothetical case of uniform MNP distribution within the tumour volume. The Gaussian spatial distribution of MNPs was taken into consideration while modelling the injection strategies in a 3D tumour surrounded by healthy tissues. In a multi-site injection technique, the tumour is segmented and MNPs are injected at nine different sites rather than just the tumour centre as in a single-site injection method. The temperature field in tissues is calculated during and after thermotherapy by solving Pennes' Bio-heat model with the finite volume approach. The efficacy of each injection approach is calculated using the temperature field. The multi-site injection method's thermal damage is remarkably comparable to the damage brought on by uniform MNP distribution. On the other hand, a multi-site injection technique that results in increased MNP dispersion affects a greater amount of healthy tissue. Conclusion of this research study is that multi-site injection strategies outperform single-site injection strategies. However, for optimum treatment the number, location, and quantity of injection sites must be chosen carefully.

Amritpal et al. (25) explored the effects of different shapes of tumour models during magnetic nanoparticles hyperthermia treatment. These tumours have the same volume, but varied surface areas due to their various forms. Tumour shape is assessed using the form factor (f). MNPH simulations are performed using a physical model of tumour tissue encased within healthy tissue. MNP distribution following injection is assumed to be Gaussian. Results indicate that a tumour's form has a substantial impact on the therapeutic benefits of MNPH. In compared to tumours with lower form factors, those with greater shape factors experience fewer treatment outcomes. To evaluate the effectiveness of MNPH in actual complex-shaped tumours, an empirical thermal damage model is also constructed.

2.3 Conclusion from Literature Review

Above given research and literature review shows that present work is more inclined towards numerical and computational approach in cancer treatment using magnetic hyperthermia. Effect of large blood vessels near tumour, effect of different shapes of tumour and new innovative multi-site injection strategies have also been explored slightly. In many studies distribution of magnetic nanoparticles on tumour site is given importance due to the fact that the intensity of heat generated also depends upon the volume distribution inside the tumour. Researchers are also working on superparamagnetic properties of magnetic nanoparticles to avoid blockage and reduction in intensity of magnetic field strength inside any tumour. Some researchers are working on treating hyperthermia clinically and others are predominantly working on figuring out the proper optimized dose given for tumour treatment. For all these research works hyperthermia treatment planning was followed as a very common practice.

2.4 Scope of present work

- Many researchers had worked on topics like concentration of MNPs, suitable dose of MNPs, different shape and size of tumour, different clinical methods, and different injection strategies but very few of them worked on the heat transfer and dissipation effects to reduce thermal damage to healthy tissues inside human body.
- So present study will be able to cover these challenges by showing the heat dissipation effect with an artery present near the tumour domain. In this study computational approach will be used to observe the effect by varying certain critical parameters of cancer tumour.

2.5 Objective of the project

The objectives of this thesis work are as follows:

- The effect of varying locations of artery from center of the tumour will be studied during magnetic hyperthermia.
- Study of temperature distribution of the tumour and artery model with the help of temperature contours and graphs.

CHAPTER 3 - METHODOLOGY

To investigate the current problem, basic geometry has been constructed in COMSOL software. After that geometry has been build material properties was assigned to the model. Then, physics is chosen and boundary conditions are applied. Then physics controlled mesh is chosen and critical region is given importance for choosing element shape for more accuracy. Then stationary or time dependent study is chosen as per requirement. Then various solutions are obtained and plotted with the help of graphs and contours.

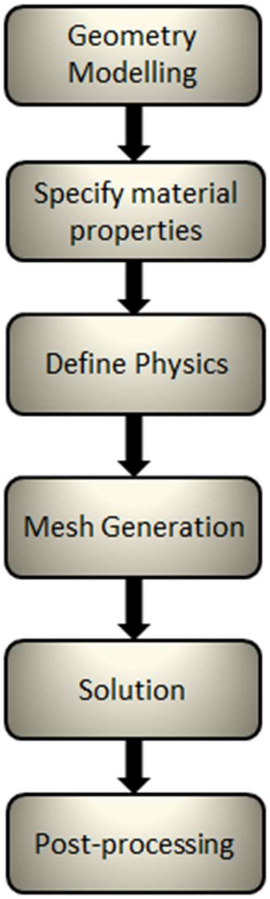

Fig 3.1: Flow chart for numerical simulation

3.1 Physical Model

For physical model many shapes were considered as tumour shape. But 3D spherical tumour shape was taken as final tumour and healthy tissue domain shape due to common results available for validation of final results. The outer healthy tissue domain was also taken as spherical. Generally, tumours are very irregular in shape and due to which non-uniform three dimensional variations are produced. Therefore, spherical domain and spherical tumour is preferred over other shapes. Also, physics in case of spherical domain and tumour can be explained and other revealing information can also be easy to understand. Moreover, the focus of this study is finding concrete information of effect of an artery present near the tumour not the complexity of the tumour shape. This artery is taken near tumour to study the effect of heat transfer due to heat source present in the whole tissue domain. The physical model shown in the Fig3.2 consists of spherical tumour, surrounded by the spherical healthy tissue domain along with cylindrical artery passing through the tumour. The healthy tissue domain is of 60mm in diameter, tumour size is 10mm which is considered as normal dimension and cylindrical artery is 4mm in diameter and for a basic case it is placed through and through tumour so that later on effects of varying distance can be seen and analysed. This 3D geometry model given above has been created in COMSOL 5.5

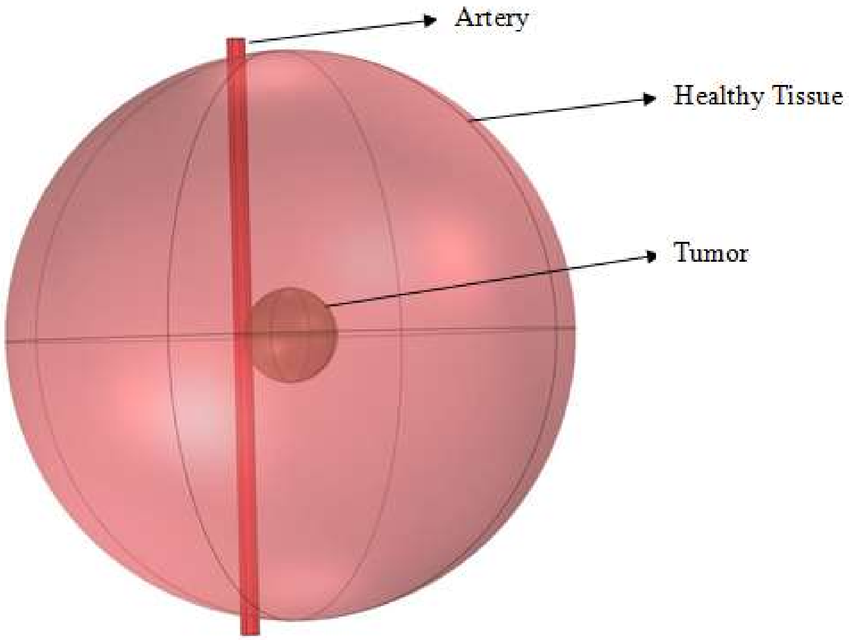

Fig 3.2: Physical model

3.2 Material used for Numerical Simulation

These are the thermophysical properties of the material used.

Table 1: Thermophysical properties

S. No.	Thermo physical property	Symbol	Value
1	Tumour Conductivity	k_t	0.53 W/(m·K)
2	Perfusion rate healthy tissue	wb_{ti}	0.0064 1/s
3	Perfusion rate tumour	wb_{tu}	0.025 1/s
4	Blood Density	rho_b	1000 kg/m³
5	Tissue Density	rho_t	1060 kg/m³
6	Artery temperature	T_a	310.15 K
7	Blood heat capacity	cp_b	4180 J/(kg·K)
8	Tissue heat capacity	cp_t	3500 J/(kg·K)
9	Flow rate in hepatic artery	q_{art}	3.53E−7 m³/s

3.3 Mesh generation

The mesh you select for your COMSOL Multiphysics simulation has a significant impact on your modelling needs. In reality, when it comes to setting up and resolving a finite element issue, meshing is one of the memory-intensive phases. Selecting the appropriate element types and sizes is frequently necessary to determine which mesh is most appropriate for your specific model. Tetrahedral, hexahedra, triangular prisms, and pyramids are the four distinct element types that are used in COMSOL Multiphysics for meshing. Additionally, there are nine pre-set element size options, ranging from extremely fine to coarse.

Meshing is dynamic and modifiable, like many other COMSOL Multiphysics applications. Individual faces or domains can be readily meshed in a few simple steps. Furthermore, the built-in physics-controlled meshing sequences generate meshes with a variety of element kinds and size attributes that you may use as a jumping-off point for adding, moving, disabling, and deleting meshing operations. To create the final mesh, each meshing operation is constructed in the order in which it appears in the meshing sequence. By adjusting the quantity, kind, and quality of components, a customised meshing sequence can provide an accurate and effective simulation while requiring less memory. The default Physics-controlled mesh, a straightforward, unstructured tetrahedral mesh, will be used to start. The element size is set to Normal by default, and the meshing sequence, which consists of a Size and a Free Tetrahedral node, is hidden. This mesh is automatically generated and adjusted for the model's physics settings.

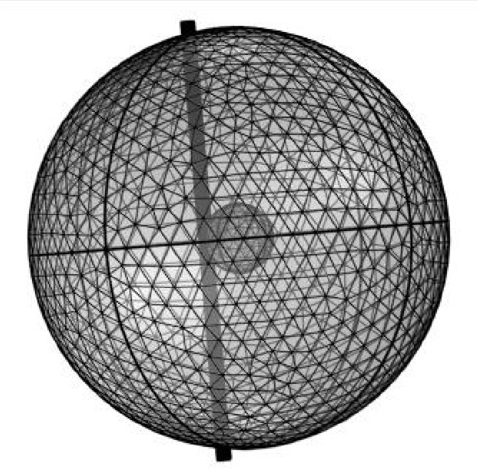

Fig 3.3: Generated mesh

Modifying the mesh to be more detailed at the spherical domains, which represent the joints, and coarser across the remainder of the geometry in order to minimise mesh elements is very benificial to obtain results more accurately. Moreover, focus on the local and global size characteristics in the meshing sequence to accomplish this. The parameters of the first global attribute feature are applied to the next Free Tetrahedral 1 node in the default meshing order. The initial size feature node used in a sequence is referred to as a global attribute feature since it has an impact on all actions that come after it. To accomplish this, we extend the Free Tetradhedral 1 procedure to include a local Size characteristic that is applicable to each domain of the solder junction. So this allows to focus more on the key elements of the model geometry. This reduces number of elements to 2,93,804 which is almost half of the previous default mesh generated. So this method makes mesh more finer on the critical points and also makes the solution more accurate due to more number of elements on that particular critical area. Example of this configuration is shown above in Fig 3.4

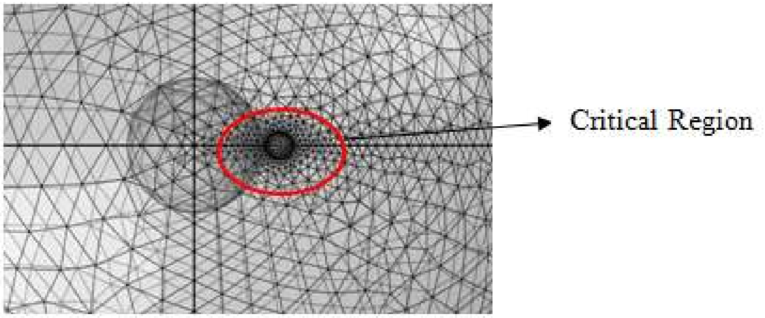

Fig 3.4: Critical region in a mesh

Some of the Mesh statistics are given below. Fine mesh is very important for good and accurate results in computational modelling. Mesh parameters like element size and number of different types of elements at critical region plays an important role .Above given Table 2 represents key parameters which will decide the quality of meshing in the geometrical model.

Table 2: Statistics of generated mesh

S. No.	Description	Value
1.	Minimum element quality	0.02976mm
2.	Average element quality	0.6416mm
3	Tetrahedron	253935
4	Prism	21780
5	Triangle	16472
6	Quad	240
7	Edge element	1346
8	Vertex element	31
9	Minimum element size	0.504mm
10	Curvature factor	0.4
11	Resolution of narrow regions	0.7
12	Maximum element growth rate	1.4
13	Predefined size	Finer

3.4 Boundary Conditions

Boundary condition plays an important role in achieving the correct set of results required. Above given Fig3.5 depicts the application of boundary conditions on geometry model more clearly.

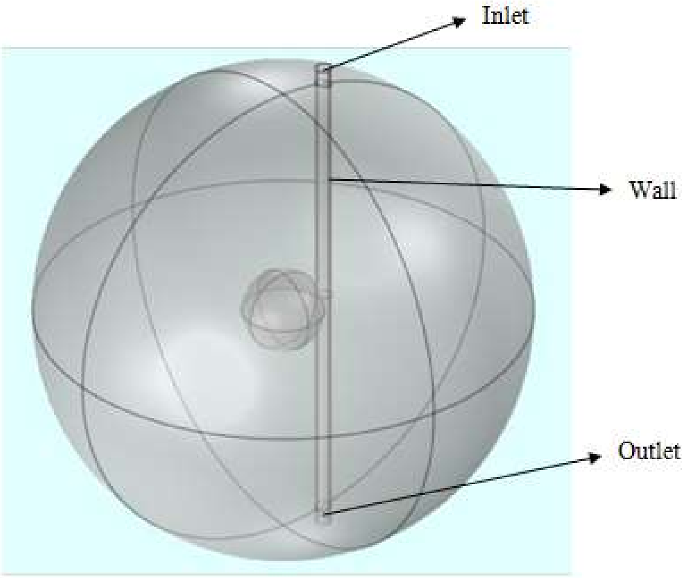

Fig 3.5: Application of boundary conditions on geometrical model

3.4.1 Boundary Conditions on Artery

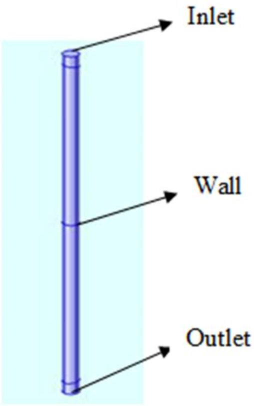

Fig 3.6: Boundary conditions on Artery

Artery plays an important role in fluid flow and showing the heat transfer using blood flow. So boundary conditions of artery must be theoretically correct. Laminar flow model is used in this simulation. For calculation of outlet velocity, mass flow rate in an artery was taken from previous research work and by help of this inlet velocity of hepatic artery is calculated and eventually Reynolds Number is calculated and cross verified in Laminar range. Inlet Boundary Condition: Mass flow boundary condition is applied on inlet of artery, equation is given below.

$$-\int_{\partial\Omega} \rho\,(u \cdot n) d_{bc} \mathrm{d}S = m \tag{1}$$

Wall Boundary Condition: No slip boundary condition is applied on wall of the artery. Equation of the boundary condition at wall is given below.

$$u=0 \tag{2}$$

Outlet Boundary Condition: Pressure boundary condition is applied on outlet of the artery. Equation of the boundary condition at wall is given below.

$$[-pI + K]n = -p_0 n \tag{3}$$

3.4.2 Boundary Conditions of Bioheat Transfer Model

This bioheat transfer model consists of two domains namely healthy tissue domain and tumour domain. In the biological healthy tissue domain user defined properties like blood perfusion rate, specific heat capacity was defined. Similarly for biological tumour domain these properties are defined separately.

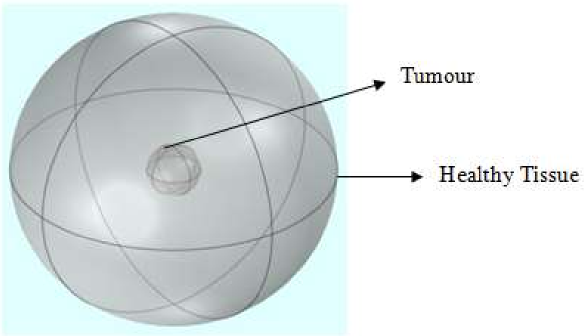

Fig 3.7: Application of boundary conditions on bioheat transfer model

For this bioheat transfer model Pennes bioheat transfer equation is applicable for calculation of heat transfer in biological tissues and tumour.

- Biological Tissue& Tumour: PBHTE
- Heat Source: $Q = Q_0$
- Temperature: $T = T_0$

Boundary Conditions on Tumour Artery Interface:

Interface is the most important part in this bioheat transfer model due to the phenomena of heat dissipation by blood flow through the artery. So, as to provide link or coupling between two different models boundary condition needs to be correct and exact for providing effect of heat transfer during fluid flow.

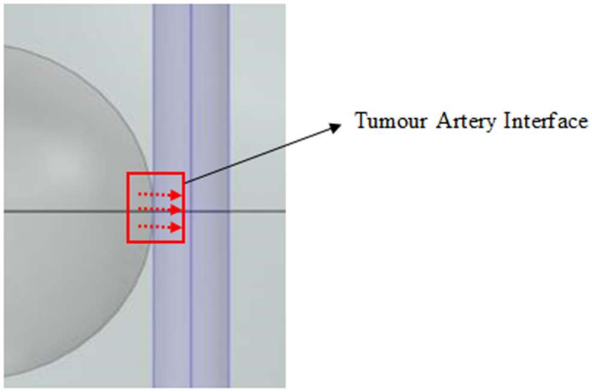

Fig 3.8: Application of boundary conditions on bioheat transfer model

- Heat Flux: General inward heat flux $-n.q = -k_t(n_x T_x + n_y T_y + n_z T_z)$

This is due to the fact that when tumour is a heat source then heat flux at the interface will be outwards. Therefore, negative sign is used in these boundary conditions. Here k_t is thermal conductivity, nx, ny & n_z are unit vectors across x, y and z axis respectively. T_x, T_y & T_z are temperature vectors across x, y and z axis respectively.

3.4.3 Boundary Conditions of Heat Transfer in Fluids Model

Artery is the main part of geometry on which heat transfer in fluids model is considered. In this convection diffusion equation is solved on artery domain which shows heat transfer by the flowing blood. Inward heat flux is also given to artery by same magnitude given at artery tumour interface.

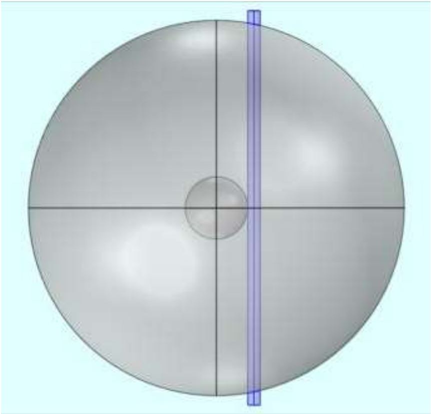

Fig 3.9: Application of boundary conditions on Heat transfer in fluids model

Boundary Conditions on Artery:

- Heat transfer in fluids: Convection-Diffusion equation
- Heat flux: $-n.q = k_t(n_xT_x + n_yT_y + n_zT_z)$

Here positive sign is used due to inward flux coming from the tumour which is heat source in bioheat transfer model.

3.5 Governing Equations

In this section majorly used equations are defined an explained thoroughly. Equations like momentum, convection diffusion and Pennes bioheat equations are defined and explained in detail to enhance the basic understanding of these equations. In this geometrical model there are different domains like artery, tumour and healthy tissue domain. Each domain is getting solved by a major governing equation. For artery domain momentum equation is solved over the whole artery by giving outlet velocity as a result. Momentum equation is solving the actual phenomena of flowing blood through an artery. Tumour and healthy tissue domain are solved by the Pennes bioheat equation.

3.5.1 Momentum Equation

Newton's second law of motion serves as the basis for the momentum equation. Additionally, two different types of forces must be taken into account when considering fluid motion: (1) body forces, which operate throughout the fluid element's mass (such as gravitational forces);

and (2) surface forces, which act at the boundary (such as pressure and friction). The above given momentum equation in indicial notation may be stated as if Fi indicates the body force per unit volume and Pi denotes the surface force per unit volume, both in direction, i.

$$\rho\left(\frac{DV_i}{Dt}\right)=F_i+P_i \qquad (4)$$

Where DV_i/Dt stands for the fluid element's instantaneous acceleration. The gravitational force is the most prevalent body force. In this instance, F is equal to pgi, where gi is the gravitational acceleration. The surface forces are dependent on how quickly the fluid is stressed by the velocity field inside it, but the body forces are thought of as provided external forces. In actuality, the stress and the surface force Pi are connected.

3.5.2 Pennes Bioheat Equation

For more than 50 years, the Pennes' bioheat transfer equation (PBHTE) (26) has been the standard used model for forecasting temperature distributions in living tissues. A series of tests monitoring the temperatures of tissue and arterial blood in a resting human forearm were used to create the equation. A unique component in the equation is used to represent the heat transfer between blood flow and solid tissues. It is assumed that the arterial blood temperature is constant. The well-known bioheat transfer equation (BHTE), often known as the classic BHTE, was developed in 1948 by Pennes through a series of studies that monitored the temperatures on volunteer participants' forearms. The PBHTE is the most generic formulation that may be used to describe tissue matrix thermal equations. It is written as follows:-

$$K\nabla^2 T = \rho\, C\left(\frac{\partial T}{\partial t}\right) - w_b C_b \rho_b (T_b - T_a) - (Q_{met} + Q_{ext}) \qquad (5)$$

Where ρ, C and K are the density, specific heat, and thermal conductivity of the tissue, respectively. Cb, wb, ρb and Tb denote the specific heat of the blood, blood perfusion rate, blood density, and blood temperature, respectively. T is the absolute temperature function. Q_{met} denotes the metabolic heat generated by the chemical reaction inside the tissue, and it is constant, and the external heat source is given by $Q_{ext} = Q_{ext}(t)$. ∇^2 is the well-known Laplace operator. The term $wc_b(T_b\text{-}T_a)$, which takes the effects of blood perfusion into consideration, may be the predominant kind of energy removal. It is presumptively true that blood enters the control volume at an arterial temperature T_a before equilibrating at tissue temperature. Therefore, the blood works as energy sink in the therapy of hyperthermia because when it leaves the control volume, it takes the energy with it.

3.5.3 Convection-Diffusion Equation

Concentration gradients will result in diffusion if we think about the mass movement of a dissolved species (solute species) or a component in a gas mixture. Convection will also contribute to the flow of chemical species if there is bulk fluid motion. As a result, we frequently try to solve for the combined impact of convection and diffusion. Above equation is called convection diffusion equation.

$$\rho(\mathrm{u}.\nabla)\mathrm{u} = \nabla.[-pI + \mu(\nabla u + (\nabla u)^T] + F \tag{6}$$

ρ is the density of blood flowing through artery, u is the velocity vector, ∇ is the del operator, μ is the dynamic viscosity of blood.

3.6 MNP Heating Mechanism

The basic purpose of nanoparticle design, given the ultimate goal of creating localised hyperthermia in a tumour, is to maximise power deposition. This will allow the nanoparticles to be heated with an AMF, resulting in direct cytotoxicity or sensitization of the tumour to radiation therapy or chemotherapy. Magnetic nanoparticles have also been employed as contrast agents in MRI scans. The nanoparticles that are easiest to photograph in vivo are not always the ones that produce the greatest heating impact. It's also likely that the MNPs with the greatest SAR values have biocompatibility issues. As shown in Fig 3.10 there are different types of biomedical hyperthermia namely magnetic imaging guided hyperthermia, magnetically actuated drug delivery, thermal cancer therapy and biofilm eradication.

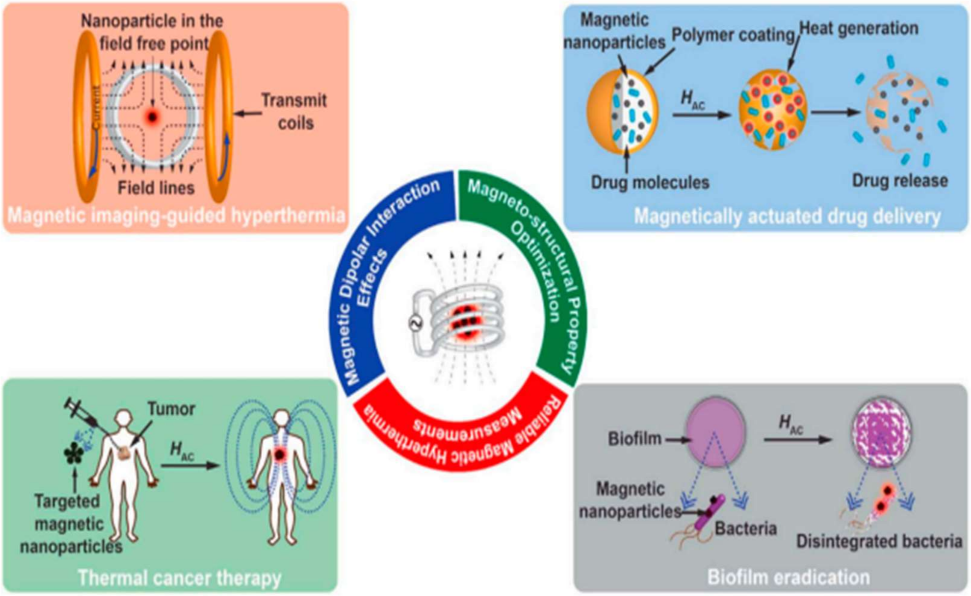

Fig 3.10: Different types of biomedical magnetic hyperthermia (27)

The SAR of magnetic nanoparticles is the parameter that must be optimised for optimal heating. Heating in an AMF can occur through four mechanisms: (1) dielectric losses in a low electrical conductivity material, (2) eddy current losses in a high electrical conductivity material, (3) frictional heating due to the physical rotation of an anisotropic magnetic particle, and (4) hysteresis losses in a magnetic material. Normal tissue heating may be caused by dielectric and eddy current losses. The three additional forms of heating for nanoparticles are discussed below. The heating effect in each scenario is determined by the particle size, shape, and coercivity as well as the frequency and amplitude of the applied AMF.

Previous experimental and theoretical studies had shown the SLP (Specific Loss Power) for MNP. For this study BNF-starch MNPs are taken. These magnetic nanoparticles act as inducers. SLP in this research is calculated using a sixth order polynomial that is given by Seotaert et al. (21) In this research work magnetic field strength and frequency of magnetic field are taken as 34 kAm^{-1}and 150 kHz respectively. Now at this constant value of frequency Seotaert provided a table through which SLP can be selected. That SLP is used for obtaining the heat flux through a formula. The value of magnetic field strength is chosen from the table provided by Seotaert et al.

1.3 Particle distribution in tumour

According to earlier studies, hepatotoxicity is caused by iron concentrations more than 4 mg per gram of wet liver weight. As a result, the MNP dosage in all tumour phantoms is 16:755 mg of MNP mass, which is comparable to 3:77 mg per gram of wet liver tumour. MNPs are injected at the tumour model's centroid. In vitro tests by Salloum et al. (17) reveal that a nearly uniform 3D Gaussian distribution of MNPs may be produced in soft tissues with a lower injection rate. As a result, the tumour's MNP distribution is Gaussian. Gaussian function which is used in this research work is given above:

$$\mathrm{m}(\mathrm{x},\ \mathrm{y},\ \mathrm{z}) = \mathrm{M}.\ \oiiint \frac{1}{\sigma_x.\sigma_y.\sigma_z\sqrt{(2\pi)^3}}\, exp\left[\frac{-1}{2}\left\{\frac{x-\bar{x}}{\sigma_x}\right\}^2 + \left\{\frac{y-\bar{y}}{\sigma_y}\right\}^2 + \left\{\frac{z-\bar{z}}{\sigma_z}\right\}^2\right] dV$$

where x, y, z are the Cartesian coordinates. $\bar{x}$, $\bar{y}$, $\bar{z}$ are coordinates of point of injection of MNPs, andσ_x, σ_y, $\sigma_z$signifies the standard deviation in x, y, and z directions. Here integration is done over a control volume and M denotes the total mass of magnetic nanoparticles present for tumour treatment.

CHAPTER 4 -VALIDATION

Validation of this research work is carried out with the help of MATLAB comparing the results with the analytical solution of Salloum et al. (17) in which a spherical tumour is taken in a cubical healthy tissue domain. In the graph shown above data1 is the temperature taken from the center of the tumour to the outermost surface of healthy tissue. This validation is done by taking all the parameters, boundary conditions of paper as same and by following the above discussed methods to obtain the result given below. Temperature at center is maximum due to the presence of heat source and slowly dissipates with increase in distance or arc length from center of tumour. Now, it can be seen that solution is exactly overlapping with the analytical solution. So, objective of this research work is successfully validated with a published paper by their matching trends.

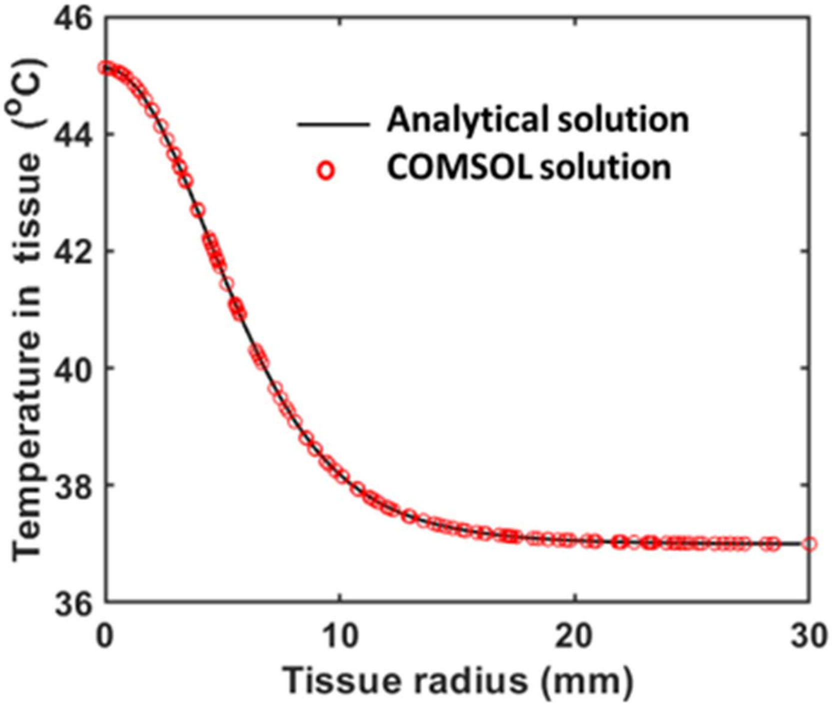

Fig. 4.1: Comparison of obtained results given in dotted line with analytical solution

CHAPTER 5 -RESULTS & DISCUSSION

In below given Fig 5.1 temperature is taken on y-axis and time is taken on x-axis in case when artery is located at x=3mm from the center of the tumour. It can be seen although x=3mm point is closer to the given heat source but still maximum temperature is less than at x=6mm So, it shows that when artery is inside the tumour and if any nearby point is taken in tumour, artery will dissipate the temperature due to flowing blood.

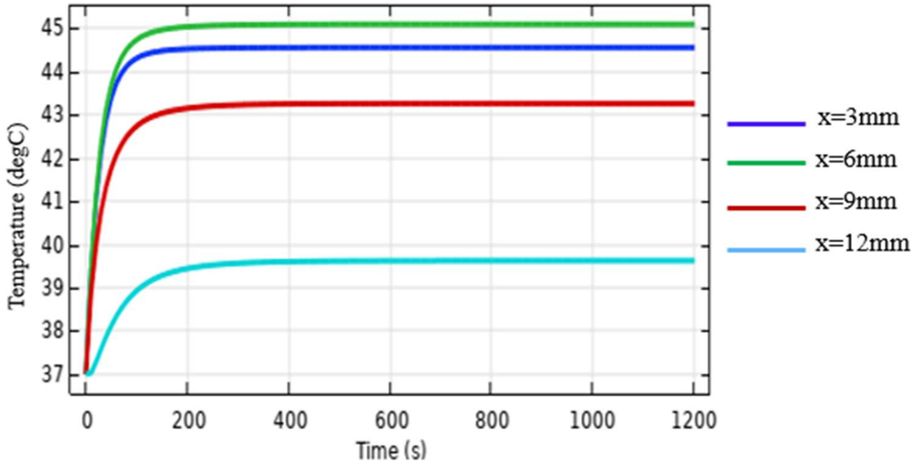

Fig 5.1: Temperature - time graph for artery at x=3mm

Below given Fig 5.2 represents the results when artery is located at x=6mm from the center of the tumour. In this figure it can be seen that maximum temperature for x=3mm rises due to the fact that artery moves away from the tumour and due to this heat transfer or heat dissipation reduces and maximum temperature rises for points near heat source.

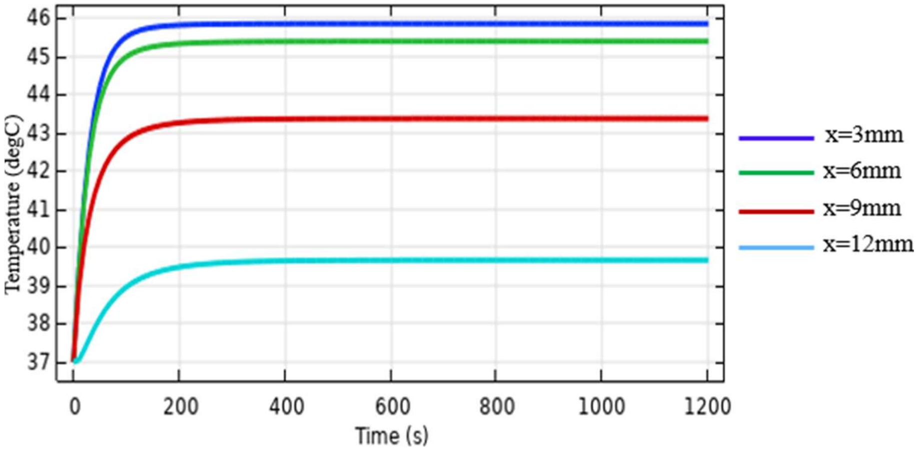

Fig 5.2: Temperature - time graph for artery at x=6mm

Below given Fig 5.3 represents the results when artery is at x=9mm from the tumour center. In this configuration artery is on the boundary of the tumour. In this figure it can be seen that maximum temperature for x=3mm and x=6mm rises from the previous figure due to the fact that artery moves away from the tumour.

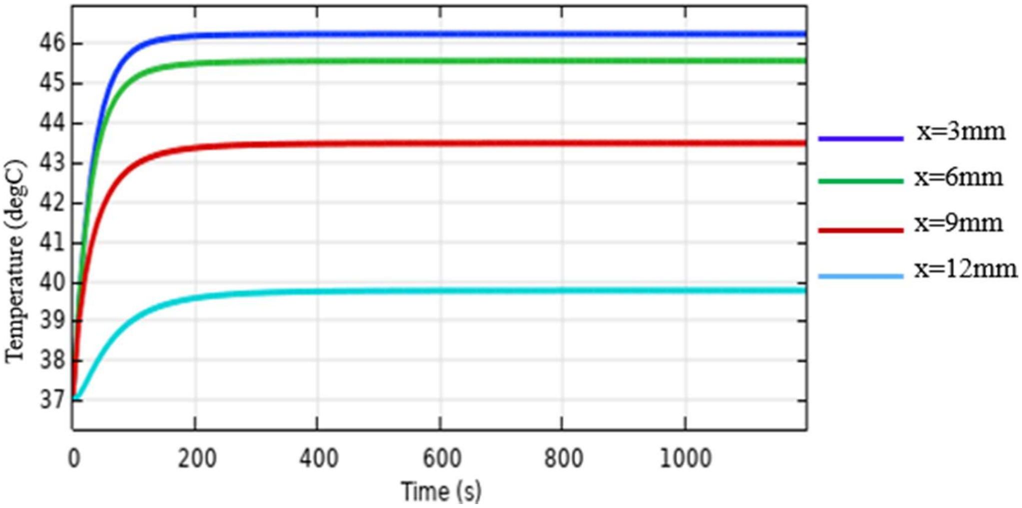

Fig 5.3: Temperature - time graph for artery at x=9mm

Below given Fig 5.4 represents the results when artery is located at x=12mm. In this configuration artery is out of the tumour. Here maximum temperature at x=3mm is slightly more than in case of artery at x=9mm.

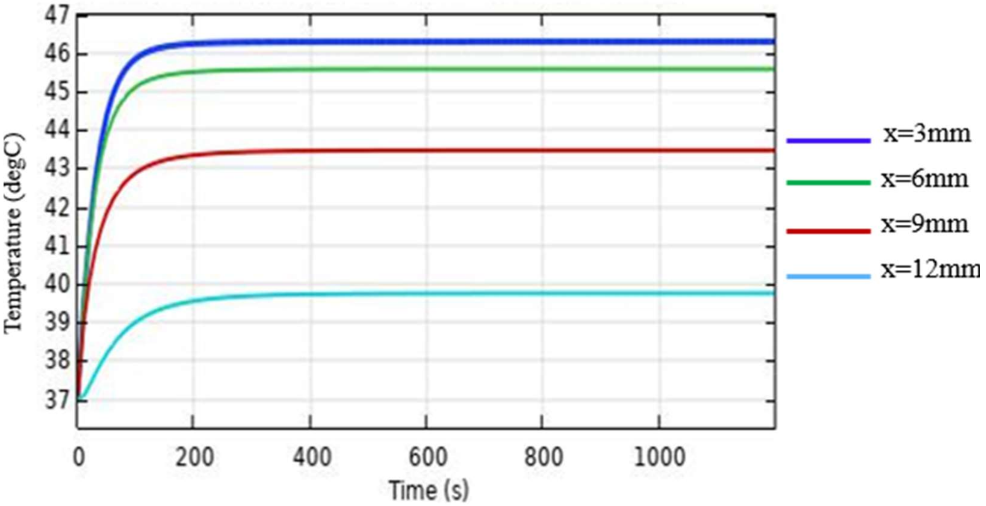

Fig 5.4: Temperature - time graph for artery at x=12mm

Below given Fig 5.5 represents the temperature contour of whole domain when artery is at x=3mm. In this contour temperature around artery is around 318 K but as moving away from the center of the tumour temperature starts to decrease and certainly drops down to 311 K in artery due to blood flow and 316 K at the boundary of the tumour.

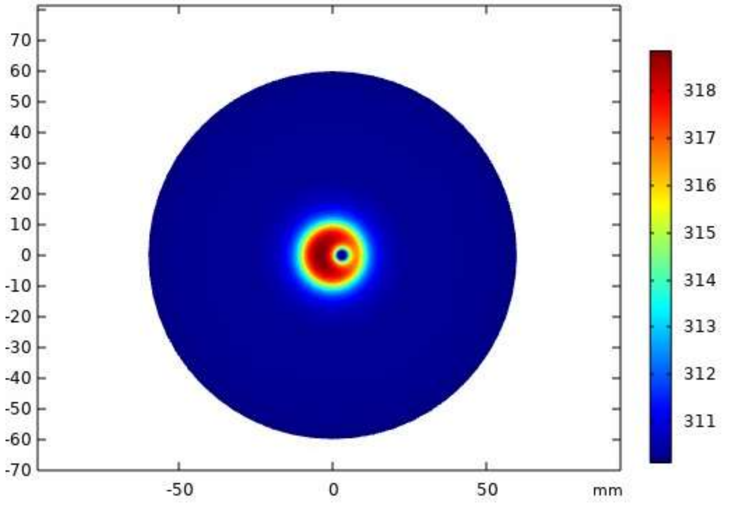

Fig 5.5: Temperature contour of whole domain with artery at x=3mm

Below given figure represents the temperature contour when artery is at x=6mm. In this contour temperature is around 319 K but as moving away from the center of the tumour temperature starts to decrease and certainly drops down to 318 K on left side of artery. This shows when artery moves away from the tumour maximum temperature increases. Maximum temperature is 319.01 K.

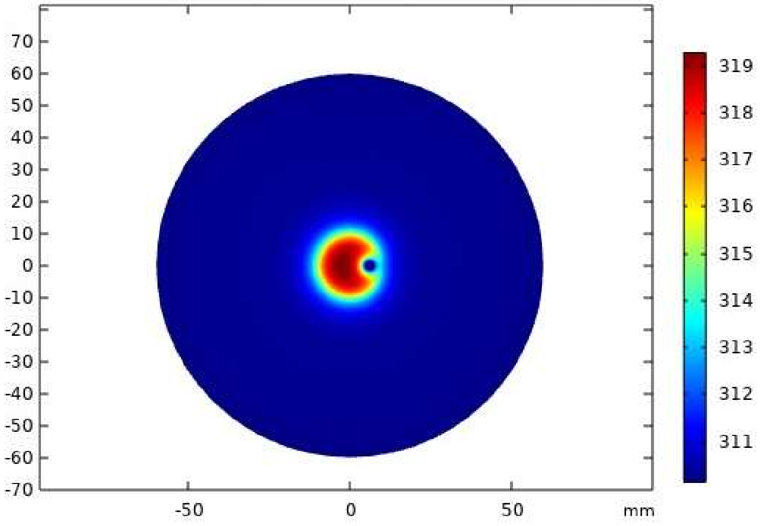

Fig 5.6: Temperature contour of whole domain with artery at x=6mm

Below given Fig 5.7 represents the temperature contour of whole domain when artery is at x=9mm. In this contour temperature is slightly more than 319 K. When moving away from the center of the tumour temperature starts to decrease and certainly drops down to 311 K on boundary of the tumour. This shows when artery moves away from the tumour maximum temperature in the tumour domain also increases. Maximum temperature is 319.55 K.

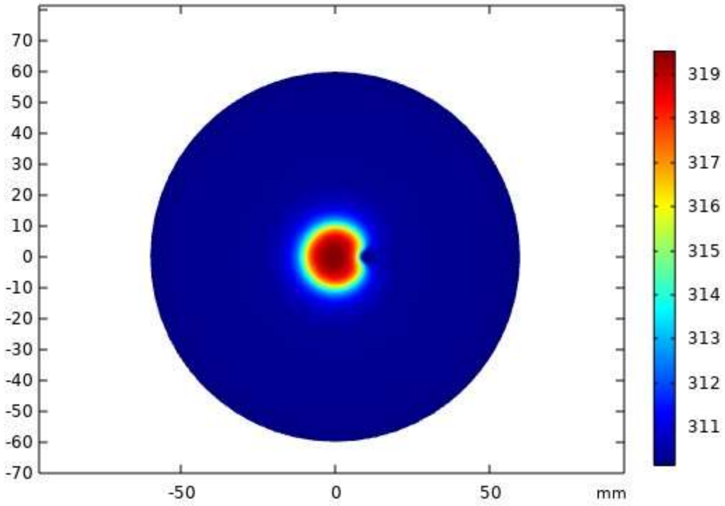

Fig 5.7: Temperature contour of whole domain with artery at x=9mm

Below given Fig 5.8 represents the temperature contour when artery is at x=12mm. In this contour temperature is slightly more than 319 K. Maximum temperature is 319.78 K. As it can be seen there is no artery inside the tumour due to which heat dissipation is very less or equal to a domain with no artery.

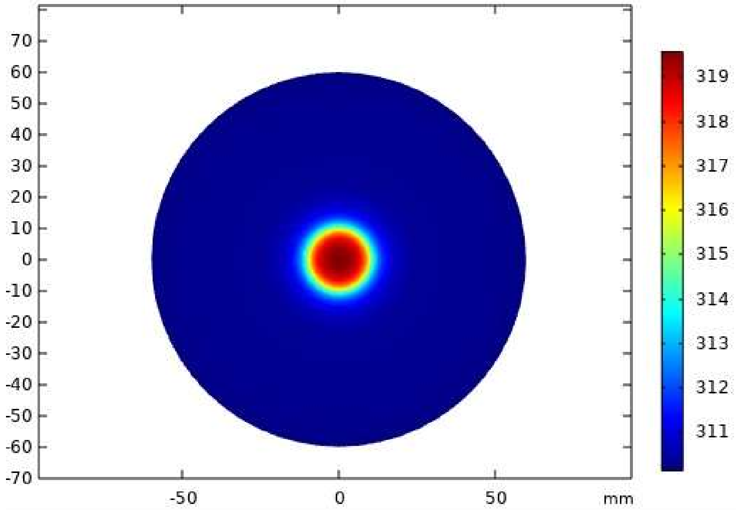

Fig 5.8: Temperature contour of whole domain with artery at x=12mm

Below given graph in Fig 5.9 shows the maximum temperature with varying distance of artery from the center of the tumour. It can be clearly seen that when artery is moving away from the tumour maximum temperature of the whole domain region is increasing. From this it can be clearly drawn that artery is improving the heat dissipation by its heat transfer through blood flow.

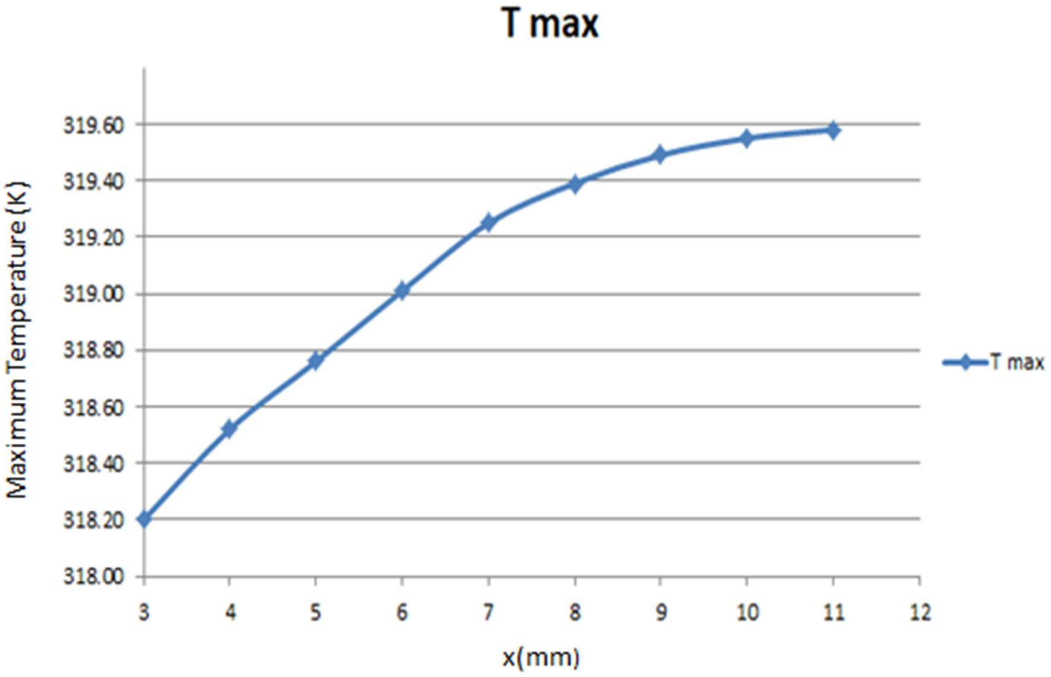

Fig 5.9: Maximum Temperature with varying artery distance

Below given graph in Fig 5.10 shows the maximum temperature with varying artery distance that with increase in distance of artery from tumour peak temperature of the shift upwards which means heat dissipation reduces with increase in distance away from tumour. This shows the critical role of artery in heat dissipation.

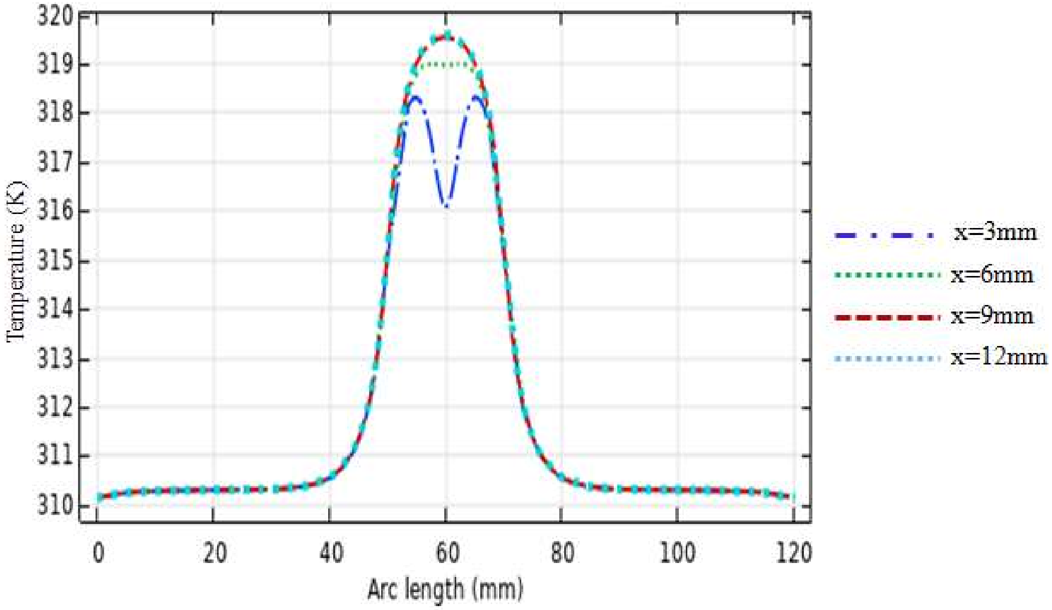

Fig 5.10: Maximum Temperature with varying artery distance

CHAPTER 6 - CONCLUSION & FUTURE SCOPE

6.1 Conclusion

In this study the effect of magnetic hyperthermia in the arteries on different positions is analysed. This is done by creating a three dimensional model and using computational methods to study the effect of artery on heat dissipation during magnetic hyperthermia. Thus we have investigated the effect of heat transfer between arteries and tumour during magnetic hyperthermia treatment. Therapeutic temperature decreases when arteries are closer to the tumour due to convective heat transfer effect and temperature starts to increase when arteries are away from the tumour. Thus the position of arteries plays an important role in heat dissipation through the malignant tumour. In this work, secondary objective was to study the maximum temperature in the tumour domain by giving different locations to the artery. The final conclusion of my work suggested that when the arteries are closer to the tumour carries heat away and the temperature in the tumour domain starts to decrease effectively but when we move arteries away from the tumour the temperature in the tumour domain starts to increase slowly.

6.2 Future scope

- Possible future works can be done on the following parameters:
- Different shapes and size of tumour can be explored by extracting the tumour using DICOM images.
- Different size and shape of artery can be studied to know the effect by varying diameter or by varying the shape or both.
- In current work steady state simulation are performed but in the near future transient flow analysis can also be done.
- In the future work arteries can also be considered as porous domain, so that wall boundary conditions can be different.
- Blood is taken as a Newtonian fluid but in future real life picture can be drawn by taking it as Non-Newtonian fluid. So all the models used will change and results can be compared.

REFERENCES

1. Habash RW, Krewski D, Bansal R, Alhafid HT. Principles, applications, risks and benefits of therapeutic hyperthermia. Frontiers in Bioscience-Elite. 2011 Jun 1;3(3):1169-81.

2. Adam A, Kenny LM. Interventional oncology in multidisciplinary cancer treatment in the 21st century. Nature Reviews Clinical Oncology. 2015 Feb;12(2):105-13.

3. Van der Zee J. Heating the patient: a promising approach?. Annals of oncology. 2002 Aug 1;13(8):1173-84.

4. Kumar CS, Mohammad F. Magnetic nanomaterials for hyperthermia-based therapy and controlled drug delivery. Advanced drug delivery reviews. 2011 Aug 14;63(9):789-808.

5. Wust P, Hildebrandt B, Sreenivasa G, Rau B, Gellermann J, Riess H, Felix R, Schlag PM. Hyperthermia in combined treatment of cancer. The lancet oncology. 2002 Aug 1;3(8):487-97.

6.Kok HP, Cressman EN, Ceelen W, Brace CL, Ivkov R, Grüll H, Ter Haar G, Wust P, Crezee J. Heating technology for malignant tumors: A review. International Journal of Hyperthermia. 2020 Jan 1;37(1):711-41.

7. Suleman M, Riaz S, Jalil R. A mathematical modeling approach toward magnetic fluid hyperthermia of cancer and unfolding heating mechanism. Journal of Thermal Analysis and Calorimetry. 2021 Nov;146(3):1193-219.

8. Bienia A, Wiecheć-Cudak O, Murzyn AA, Krzykawska-Serda M. Photodynamic therapy and hyperthermia in combination treatment—Neglected forces in the fight against cancer. Pharmaceutics. 2021 Jul 27;13(8):1147.

9. Takahashi I, Emi Y, Hasuda S, Kakeji Y, Maehara Y, Sugimachi K. Clinical application of hyperthermia combined with anticancer drugs for the treatment of solid tumors. Surgery. 2002 Jan 1;131(1):S78-84.

10. Paulides MM, Stauffer PR, Neufeld E, Maccarini PF, Kyriakou A, Canters RA, Diederich CJ, Bakker JF, Van Rhoon GC. Simulation techniques in hyperthermia treatment planning. International Journal of Hyperthermia. 2013 Jun 1;29(4):346-57.

11. Gheflati B, Naghavi N. Computational study of nanoparticle assisted hyperthermia in tumors embedded with large blood vessels. International Journal of Heat and Mass Transfer. 2020 Apr 1;151:119415.

12. Mellal I, Oukaira A, Kengene E, Lakhssassi A. Thermal therapy modalities for cancer treatment: A review and future perspectives. Appl. Sci. Res. Rev. 2017;4(02):1-1.

13. Moroz P, Jones SK, Gray BN. Arterial embolization hyperthermia in porcine renal tissue. Journal of Surgical Research. 2002 Jun 15;105(2):209-14.

14. Khaled AR, Vafai K. The role of porous media in modeling flow and heat transfer in biological tissues. International Journal of Heat and Mass Transfer. 2003 Dec 1;46(26):4989-5003.

15. Javidi M, Heydari M, Karimi A, Haghpanahi M, Navidbakhsh M, Razmkon A. Evaluation of the effects of injection velocity and different gel concentrations on nanoparticles in hyperthermia therapy. Journal of biomedical physics & engineering. 2014 Dec;4(4):151.

16. Pavel M, Stancu A. Ferromagnetic nanoparticles dose based on tumor size in magnetic fluid hyperthermia cancer therapy. IEEE transactions on magnetics. 2009 Oct 30;45(11):5251-4.

17. Salloum M, Ma R, Zhu L. Enhancement in treatment planning for magnetic nanoparticle hyperthermia: optimization of the heat absorption pattern. International Journal of Hyperthermia. 2009 Jan 1;25(4):309-21.

18. Pavel M, Gradinariu G, Stancu A. Study of the optimum dose of ferromagnetic nanoparticles suitable for cancer therapy using MFH. IEEE Transactions on Magnetics. 2008 Dec 16;44(11):3205-8.

19. Lunnoo T, Puangmali T. Capture efficiency of biocompatible magnetic nanoparticles in arterial flow: A computer simulation for magnetic drug targeting. Nanoscale research letters. 2015 Dec;10(1):1-1.

20. Wang Q, Deng ZS, Liu J. Theoretical evaluations of magnetic nanoparticle-enhanced heating on tumor embedded with large blood vessels during hyperthermia. Journal of Nanoparticle Research. 2012 Jul;14(7):1-0.

21. Soetaert F, Kandala SK, Bakuzis A, Ivkov R. Experimental estimation and analysis of variance of the measured loss power of magnetic nanoparticles. Scientific reports. 2017 Jul 27;7(1):1-5.

22. Mital M, Tafreshi HV. A methodology for determining optimal thermal damage in magnetic nanoparticle hyperthermia cancer treatment. International Journal for numerical methods in biomedical engineering. 2012 Feb;28(2):205-13.

23. Adhikary K, Banerjee M. A thermofluid analysis of the magnetic nanoparticles enhanced heating effects in tissues embedded with large blood vessel during magnetic fluid hyperthermia. Journal of Nanoparticles. 2016;2016.

24. Singh G, Kumar N, Avti PK. Computational evaluation of effectiveness for intratumoral injection strategies in magnetic nanoparticle assisted thermotherapy. International Journal of Heat and Mass Transfer. 2020 Feb 1;148:119129.

25. Singh A, Kumar N. Parameterizing the effects of tumor shape in magnetic nanoparticle thermotherapy through a computational approach. Journal of Heat Transfer. 2022 Mar 1;144(3):031201.

26. Pennes HH. Analysis of tissue and arterial blood temperatures in the resting human forearm. Journal of applied physiology. 1948 Aug 1;1(2):93-122.

27. Obaidat IM, Narayanaswamy V, Alaabed S, Sambasivam S, Muralee Gopi CV. Principles of magnetic hyperthermia: a focus on using multifunctional hybrid magnetic nanoparticles. Magnetochemistry. 2019 Dec 6;5(4):67.

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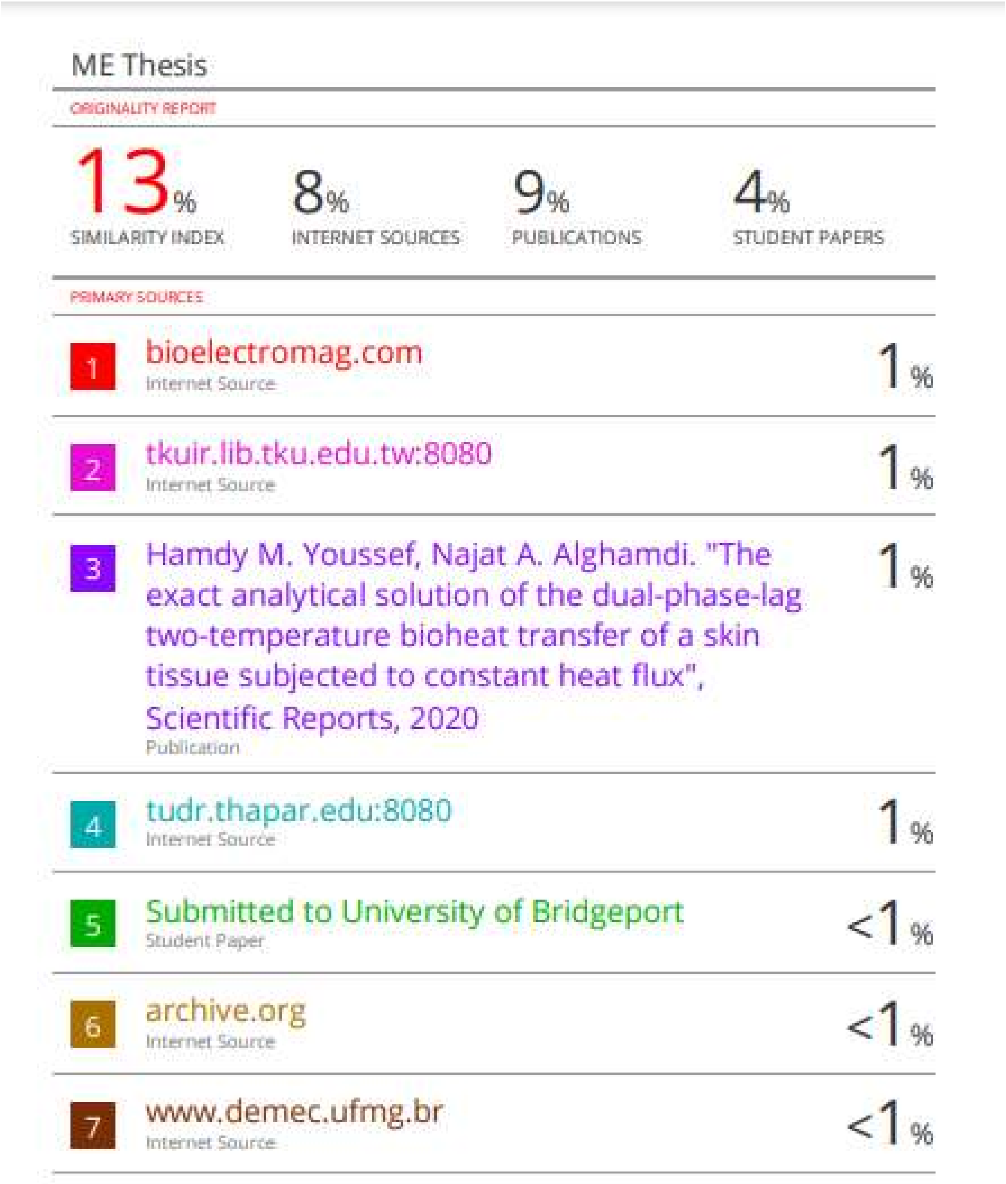

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