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REVIEW ON ELECTROMAGNETICS OF CANCER CELLS: MODELING TO TREATMENT

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Article Info

Abstract

cancer is a world fear and second leading cause of death. Cancer cause about 16% of worldwide deaths according to world health organization. The treatment of cancer by the use of electromagnetic radiations is well practiced in the field of oncology now a day. Many therapeutic techniques are in practice by oncologists for the cure of cancer. Having benefits and cure rate, each cancer therapy technique has some limitations and adverse effects on healthy cells in the surroundings of cancer cells and sometimes on the entire human body. To overcome these limitations and side effects, the low energy electromagnetic methods have been proposed by the scientific community. In this review article we are discussing few electromagnetic cancer therapeutic techniques and modeling of cancer cells. Hyperthermia, terahertz radiations, magnetic field and radio frequency treatment technologies are studied based on the literature survey. One of the important ways of killing the cancer cells is to rise their temperature above 40°C i.e., therapeutic level. This is the basic principle of hyperthermia. The use of magnetic fields aids in increasing the tumor temperature that further becomes the cause of death of tumor. Terahertz pulsed spectroscopy can be used to differentiate between normal and malignant tissues. Radio frequency radiation is becoming a favorable new defense against cancer. It's not only having advantageous therapeutic effects in different types of cancer patients, but also has no severe side effects. The main focus of using a therapy is to generate cell necrosis/apoptosis. The mentioned techniques are playing their premier role in the cancer diagnostics as well as in the cancer treatment, with the benefit of very less damage to the healthy cells surrounding the malignant cells

Keywords: *Cancer, Oncology, Hyperthermia therapy, Electromagnetic radiation therapy, Terahertz radiation, Magnetic field therapy, Radio frequency treatment*

Introduction

Cancer is a world fear and second dominant element of death across the world [1]. It caused by the uncontrolled division of dead cells which is called tumor if it just swells up the original tissue and do not spread but when spread from the origin tissue it is than called cancer [2]. The main cause of cancer is still unknown, there are many reasons that can cause this disease but all are not confirmed that they will cause cancer. The so far studies revealed that the cause of cancer are tobacco (smoked or un-smoked), radiations like sunlight, X-rays, chemicals and materials used in construction like benzene, air and water pollution, use of specific chemical for long like alcohol, very less use of vegetables and fruits, no physical activity and due to some bacteria's (all these mentioned causes do not confirm the cancer but they have found as most common symptoms in cancer patients). Cancer cause about 16% of worldwide deaths according to world health organization [3]. The death rate due to cancer in developed countries is greater than undeveloped ones. A question that usually arises in our minds, why our immune system does not cure the cancer by itself? As cancer is a deadly disease and immune system is meant to fight against the disease. The answer to this question is quite weird, it is quit shocking that our immune system perceives the cancerous cells as normal dividing cells, therefore instead of working against those rapidly dividing cells, immune system starts protecting them from viruses etc. Therefore, these uncontrolled rapidly dividing cells need to be treated externally. There are many therapeutic techniques are being used for cancer treatment and each has some beneficial as well as some adverse effects.

There are many different types of cancer such as lungs cancer, ovarian cancer, throat cancer, colon cancer, stomach cancer, bone cancer, skin cancer, brain cancer and breast cancer [4]. Breast cancer is also a major cause of death especially in women. Today the field of oncology is dealing with both electromagnetic and non-electromagnetic ways of cancer cure. The oncologists are adopting the below mentioned therapeutic techniques such as, radiation therapy, chemotherapy, immunotherapy, Harmon therapy, photodynamic therapy and consolidation of these techniques such as radiosurgery [5]. The main focus of using a therapy is to generate cell necrosis/apoptosis. Therapeutic results can be obtained as the cell necrosis or apoptosis which is the cell death [2]. In general wording cancer cells are first killed using specific technique then they are removed from the body by surgery. Each therapeutic technique while working for the cure has some limitations and adverse effects also i.e., they kill healthy cells or can cause the new type of cancer (bone marrow transplant technique) [6]. There are number of therapeutic techniques working for the cure

of cancer. Some of them basically the electromagnetic techniques are discussed in this review paper. The treatment of cancer by the use of electromagnetic radiations is well practiced now a day. The electromagnetic therapeutic techniques provide better cure with very less damage to the nearby healthy cells. So far, many effective techniques have been working for the detection of cancer cells. For the effective implementation of these techniques' exact knowledge of dielectric properties of human malignant tissues at microwave frequencies is essential. Previously published papers showed the dielectric properties of normal and cancerous tissues. The properties of dispersion for cancerous and normal tissues were different [7]. It had been confirmed that the normal and cancerous tissues can be characterized using their dielectric properties and inevitable water content. The electromagnetic cancer treatments can overcome the problems like infections, wound formation due to surgery; can minimize the overdose side effects using the non-invasive technique. These kinds of treatments use physical impetuses like; heat, light, electric fields, magnetic fields and ultrasounds. And these techniques showed enhanced treatment abilities, low wound formation due to surgery, economically affordable and eradicated infections. The technique of using ultrasound enhances the reactive oxygen species production in the mice helping the nanoparticles and terminating the tumor growth. The use of magnetic fields aids in increasing the tumor temperature that further becomes the cause of death of tumor. Preeminent lump temperature, or tumor hyperthermia, is a scheme used in the dealing of cancer based on a significant amount of good experimental data. The number of human polyps that can be cured with hyperthermia rises as we go deeper inside the human tissue. The important deliberation in hyperthermia method is how deeper the incident beam is going? Noninvasiveness of the technique is the basic feature. Electromagnetic and ultrasound are two foremost techniques that are useful for noninvasive heating [8]. THz pulsed imaging provides broadband (0.1 – 4 THz) evidence on samples making it possible to discriminate between areas with diverse optical characteristics over the THz frequency range. THz waves have longer wavelengths than that of visible and infrared. The shorter wavelength of THz as compare to the microwaves make them capable of higher special resolution. These radiations are sensitive to water, this property make them useful for many biomedical applications and cancer treatment is one of them i.e., Terahertz pulsed spectroscopy can be used to differentiate between normal and malignant breast tissues [9]. One of the important ways of killing the cancer cells is to rise their temperature above 40°C i.e., therapeutic level. For this purpose, radio frequency hyperthermia is one of the heating methods. Radio frequency radiation is becoming a favorable new defense against cancer. RF-induced localized hyperthermia not only has advantageous therapeutic effects in different types of cancer patients, but also has no severe side effects. RF radiations can go deeper in fat layers without much loss in strength even if the tumor is in several centimeters deep in the muscle, when applied under controlled environment. In the form of exponentially decomposing waves the RF waves travel through the body, giving dielectric heating to the tissues when they cross them. This type of dielectric heating gives confined hyperthermia to the breast cancer cells and the cancer of any type on the body. Moreover, oncology is casting a chemical process of converting infrared light to visible as the effective cancer treatment [10].

1. Historical Background

When in 1890s electricity was generated in controlled way, it was assumed that the biological tissues could be impacted through radiations [11]. Arsène d'Arsonval was the first to indicate rise in temperature and digestion of the bacteriological cell in contact with electricity, and, he reported with Albert Charrin, the diminution of diphtheria and pyocyanin venoms by radiation at a 200 kHz frequency, regardless a noteworthy rise in temperature [12]. Later in 1924 it was reported that the cancerous when subjected to very short wavelengths it was first grown rapidly and then end up (necrosis of cell) selectively. Later it was reported that the cancer in mice can be removed by the application of current of very high frequency [13]. Light therapy was in function by the ancient Greeks, Egyptians and Rome. From the end of 19th century to the start 1930s, light therapy was painstaking an operational and conventional medical therapy in the United Kingdom for circumstances such as swollen ulcer, 'sickly children' and a wide range of various circumstances. Niels Ryberg Finsen is considered the founder of modern phototherapy. He established 1st synthetic gadget for phototherapy. Radiations can be categorized in two forms i.e., ionizing and non-ionizing radiations. Ionizing radiations which in general are high frequency radiations ionize the cells and tissues when they pass through them. DNA changes and destructions occur as the result of passing the ionizing radiations. The non-ionizing radiations that are low frequency radiations do not damage the DNA when pass through the cells as they have not enough energy. Photons and particle radiations are ionizing and ultraviolet, visible, IR rays radio waves and low frequency radio frequency waves are non-ionizing radiations [14]. The use of mentioned types of radiations in history is described below. Cancer therapy through radiations is in practice over 100 years. It was started just after the discovery of X-rays. Radiation therapy started growing in 1900s, when the radioactive elements was discovered by Marie Curie (News of Science 1957). Radiation therapy then applied to many diseases using Radium only with very less precautionary measures at that time its toxicity was not very well understood. Radium was the only used source of radiations for the therapy before the World War II, along with x-rays tubes and radon gas. The x- ray machines with less voltage were the innovation in the technique at that time. Its use was, only the cancerous cells that are less penetrated in the skin can be treated with low voltage x-rays but for deeper penetrations higher voltages were required. In the era of 1920s and later higher voltage x-ray machines were begun to use with voltage ranging from 200 to 500 kilovolt. For the deeper penetration of radiations, the x-rays needed to have 1MV energy in order to avoiding the damage to the normal surrounding skin tissues. For the production of such high energy the machines have to be equipped with expensive installations. Megavolts installations were begun in 1930s and due to expensive set up the machines were limited to few organizations. Terahertz radiations being non-ionizing can penetrate deeper in the skin and can target the cancer tissues, these radiations are safe to use for humans. Approximately three spans ago, the spectrum range of Terahertz were complex of its impending for use, basically due to the trouble in providing proper foundations and sensors. But in the recent few decades Terahertz have shown fast development. And now they are being used in research worldwide. In the electromagnetic radiation spectrum terahertz has frequency ranging from 0.1 to 10THz. Later in 1960s THz radiations were begun to use in medicine. The imaging applications of terahertz were started in 1970s, now a day a lot of researches are in THz and spectroscopy are using time-domain spectroscopy techniques [15].

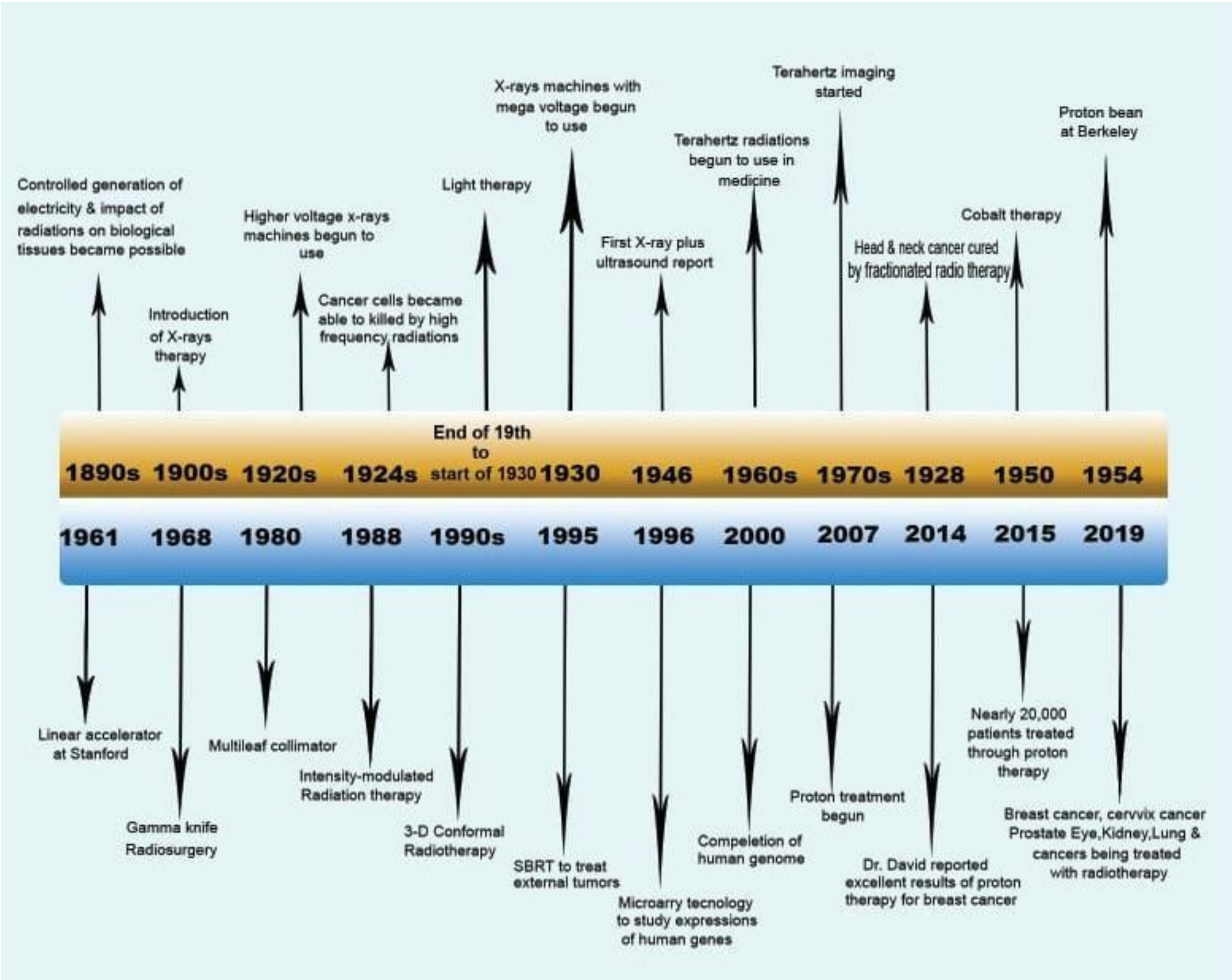

Figure 1: Chronological development in the biomedical physics for the cancer diagnosis and treatment

2. EM modeling of cancer cells and tumors

The cancerous and normal cells of same body organ show different dielectric properties [16]. Early stage cancer diagnosis could be very helpful in order to increase the patient health condition and treatment ability to that stage of cancer. But due to absence of many physical symptoms of cancer at early stages the detection is difficult. Definitely early detection of malignancy can increase survival rate and decrease the health complications that usually occur at high stages. Dielectric characterization of organs can help in the early diagnosis of malignancy as malignant and normal cells can be characterized based on their dielectric properties [17]. The dielectric properties of some normal and malignant liver tissues are listed below.

Table 1: Comparison between the malignant and normal liver tissues [18].

Frequency		**Normal**		**Malignant**	
		Relative permittivity	Conductivity (S m^{-1})	Relative permittivity	Conductivity (S m^{-1})
1	2.45GHz	57.5	1.9	62.4	2.1
2	915MHz	59.9	1.16	64.0	1.3

ii) Model of malignant liver tissues.

Table 2: Conductivity and permittivity of malignant liver tissues by [19].

No.	Frequency (Hz)	Relative permittivity	Conductivity (Sm^{-1})
1	976.6	$9.9e^4$	0.166
2	1953.1	$8\ e^4$	0.169
3	3906.3	$5.8e^4$	0.173
4	7812.5	$3.9e^4$	0.179
5	9765.6	$3.4e^4$	0.181
6	15 625.0	$2.5e^4$	0.185

ii) Model of breast cancer cells.

Table 3: At 900MHz, average dielectric properties of female breast tissue measured in vivo by an active microwave imaging system [20].

No.	**Age**	**Average relative permittivity**	**Average conductivity**
1	6	17:22 ± 11:21	0.5892 ± 0.3547
2	57	31:14 ± 4:35	0.6902 ± 0. 3650
3	52	36:44 ± 6:24	0.6869 ± 0:3156
4	49	35:43 ± 3:93	0.5943 ± 0:3841
5	48	30:85 ± 7:22	0.6350 ± 0:3550

3. Electromagnetic Therapeutic Techniques

3.1 Hyperthermia

Hyperthermia is one of the most widely held research technique which in the combination with engineering brings new hope to cancer patients and assumed as an auspicious therapy amid the alternative methods. The complement of chemotherapy and radiation therapy is hyperthermia that offers the advantage of eliminating drug resistance and radio resistance tumor cells, from the last two decades [21]. Explained in fig. 1. Hyperthermia is widely used for the treatment of various types of cancers. The basic principle of this technique is; "if the body is heated to the temperature as higher as up to 104ºF for at least 60 minutes where the malignant cells located the cells will be killed" [22

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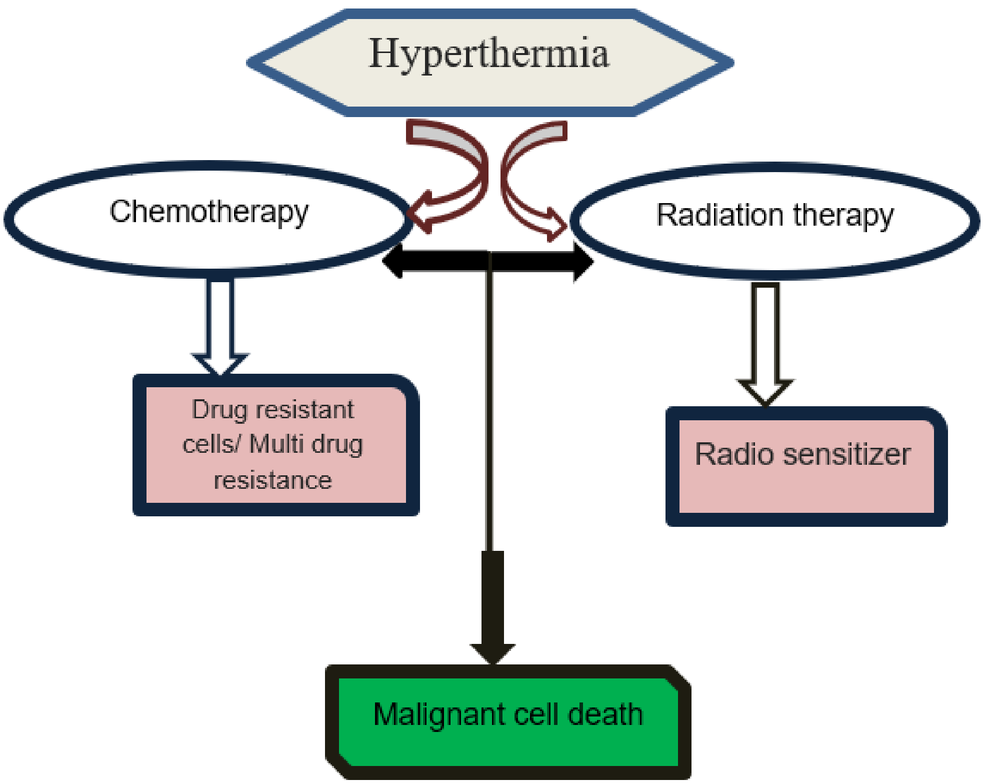

Figure 2: Hyperthermia technique for cancer cell death

3.1.1 Hyper thermic Perfusion

A part of the body like a limb or an organ is cured with heat in local hyperthermia. The motion to the limb is quarantined and blood is pumped at 43.3℃ temperature. Further in this method the anti-cancer chemotherapeutic drug is induced in the blood when the temperature is in between 38 to 40℃. The heating circulation of the blood is accomplished using circular tubes provided with controlled water bath [23].

Scientists have developed full body hyperthermia perfusion based on this technique. In this setup there are two reservoirs for blood heating and chilling separately, and their temperatures are set as 40℃ and 30℃ respectively. The circulation of blood is done through extracorporeal exchanger and mixer gadget. The temperature and the rate of blood flow through coils are carefully controlled by the aid of valves and pumps [24]. The procedure is explained in figure 2.

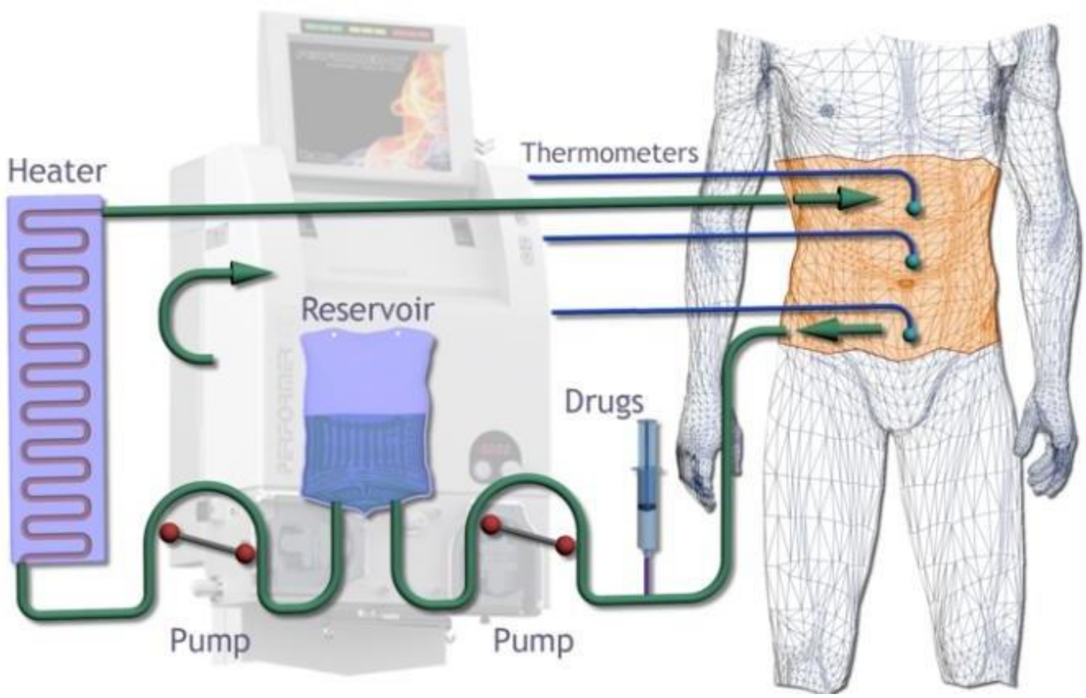

Figure 3: Schematic view of Hyper thermic perfusion

3.2 Magnetic Field for cancer treatment

There are three mechanisms the malignant cells can be treated using magnetic field (i) thermic influence (ii) cavity formation influence (iii) non-thermic and cavity formation influence [14]. To stimulate confine hyperthermia in the flesh, pulsed magnetic fields have been used where magnetic nanoparticles have been hoarded. The tissues that cannot tolerate chemotherapy the pulsed magnetic field treatment is applied there especially for the high stages of cancer (3 & 4 stage). The frequent use of this method made the cells thermo resistive and the efficiency of treatment decreases. However, the use of static magnetic field instead of pulsed field, oxidative stress can damage the malignant cell membrane leading to apoptosis. The reactive oxygen species produced as a result of interaction between static magnetic field and ionic molecules of cellular areas that restrict the growth of cancer cells. The cancer treatment in the animals using magnetic field have prospective use in the therapy as they have shown auspicious results for the treatment. Moreover, the blood vessels in the malignant cells can be expanded by joules' heating of magnetic field. The excessive oxygen therefore entre the cells and produce limitation to the subsistence of cells. The natural killers can entre to the malignant tissues due to the expansion of blood vessels and stops

survival as well as cause the proliferation of cancer cells [26]. For the growth and spread of malignant cells to the other body parts, the formation of new blood vessels is necessary which is stopped by the magnetic field.

Cancer therapy now a day uses electromagnetic field with the Nano particles, which can produce much

treatment. Fig. 3 explains the electromagnetic

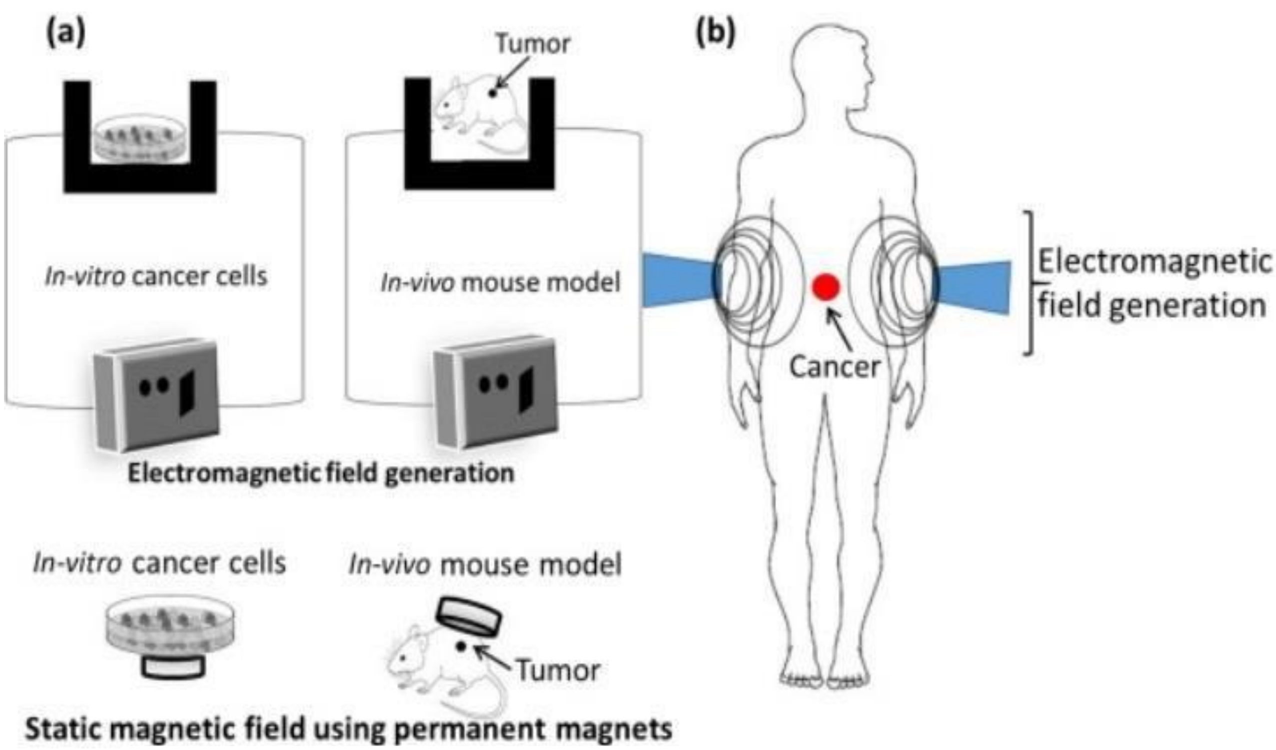

Figure 4: Schematic view of Magnetic field-based treatment of malignant tissues [27].

developed hyperthermia. In this method the selective frequencies that can heat up the malignant cells are used in the electromagnetic filed. The production of heat during hyperthermia causes the surge of membrane mutability, permeability and stimulates insusceptible system, which switches off the specific repair protein production and damage the DNA. Alternating magnetic field along with nanoparticles can also be used for cancer field generation (in *vivo* & *in vitro*).

3.3 Terahertz (THz) cancer therapy

The terahertz (THz) range of the EM spectrum ranges start of microwaves to near IR region [28]. The medical application of non-ionizing electromagnetic fields ranging from 0.1-10 Terahertz is the basic interest of scientific community from decades. Many medical applications like diagnostics and methods to cure the disease are dependent on these non-ionizing electromagnetic fields applications. In footings of the

THz impact on biomolecules, sugars, proteins, DNA, RNA, the vibrational levels are in the assortment of THz range. The high-intensity captivation of THz by biomolecules varies the conformation and function of biomolecule, when THz waves are discharged onto biomolecules or organisms, which might have a series of irregular possessions on entities [29]. Such a wide frequency band includes UV and visible light, IR radiations, microwaves, RF fields, low-frequency electromagnetic fields, and static electric and magnetic fields [30]. The main focus of using electromagnetic fields in the cancer diagnostics and therapy is to eradicate the limits of conventional therapeutic techniques [30]. The potential therapeutic mechanism of terahertz electromagnetic waves is explained. Flow chart is explaining the biomedical applications of THz radiations.

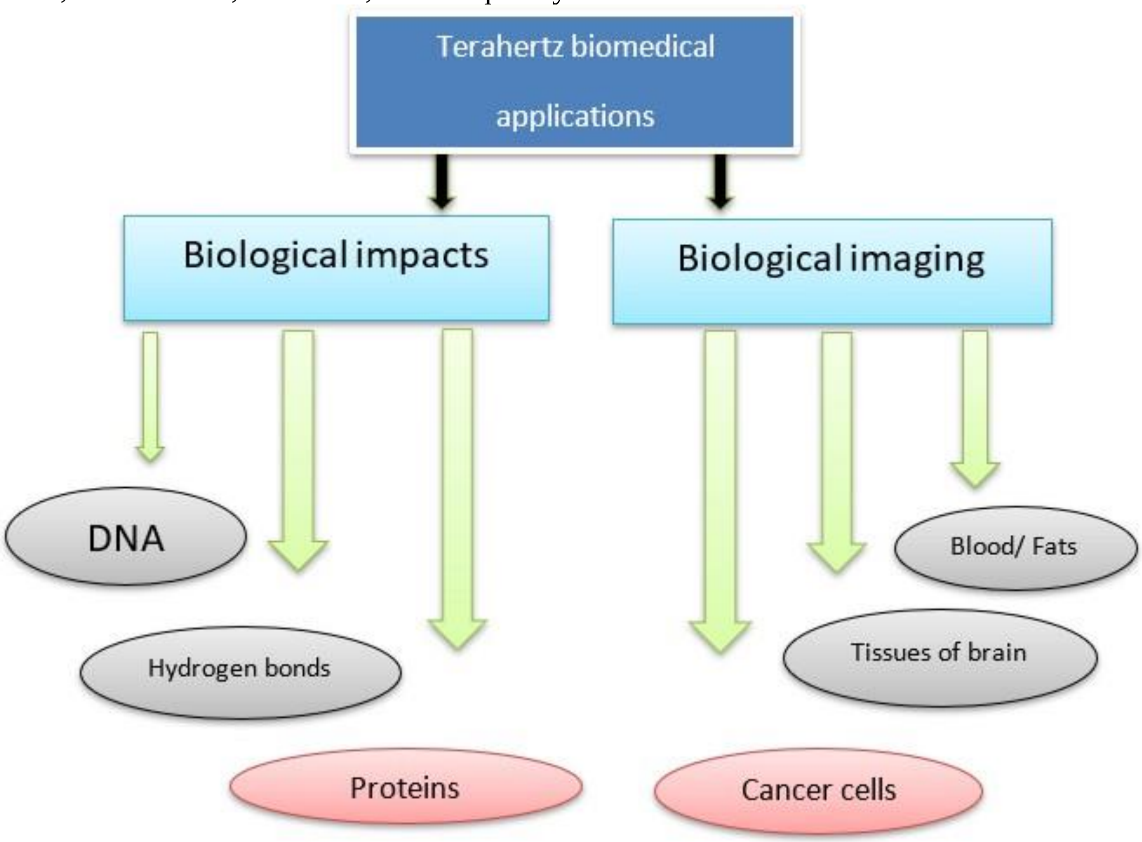

Figure 5: Flow chart regarding use of THz radiations in the biomedical applications [31]

3.3.1 Thermal effects of terahertz on biological tissues

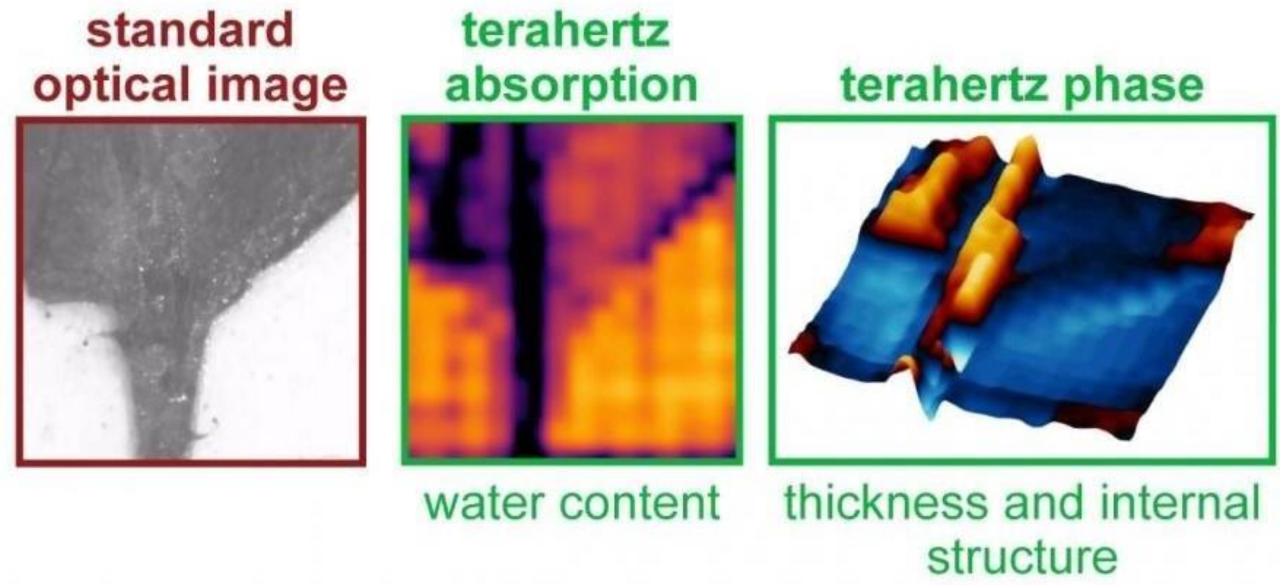

Figure 6: Terahertz radiations absorption in water and THz imaging [37].

Same like all other electromagnetic waves terahertz also have ability to heat up the biological tissues followed by the resonance mechanism of direct coherent excitation of bio tissues [32]. Previous studies explained that the terahertz radiations cannot directly heat up the tissues as they have not enough energy to dislocate the chemical bonds, unless water is used which strongly absorb the terahertz. at Ruhr University in Germany scientists evidently detected the contact between water molecules and proteins using terahertz waves [33]. Researchers discovered that the terahertz radiations with energy as high as 2.3THz are capable of diminishing DNA double standard hybridization and breaks the bonding between the focused DNA double standard. Furthermore, the results of mouse stem cells to terahertz waves revealed that the arrangement activity of thermo-sensitive genes was enhanced [34]. Researchers used Kirchhoff's heat equation to model the impact of a continuous wave terahertz beam on a sample of water; they noticed the rise in steady-state temperature of the power that was transmitted was; 1.8°C/mW. A temperature increases of 30°C for a spot diameter of 0.5mm could be accomplished, if a suitable-time introduction of terahertz beam was upheld to thermal equilibrium. Moreover, in the skin model, scientific research outcomes also signposted that by 1THz the rise in local temperature would be 5°C which is plenty much to warmness of the tissue and to kill malignant cells [35-36].

In the scenario of non-invasive, high resolution, low energy and penetration, it is conceivable that terahertz radiations will be broadly applied in cancer diagnostics and therapeutics.

Table 4: The non-ionizing electric fields are classified as

Field Type	Sub-Type	Frequency Range
High frequency	I. RF Fields II. Microwaves III. Terahertz frequency	I. 100kHz to 300MHz II. 300MHz to 30GHz III. 300GHz to 10-30THz
Low frequency	I. Low frequency fields II. Intermediate frequency fields	I. 1 to 300Hz II. 300Hz to 100kHz
Static field	I. Static electric fields II. Static magnetic fields	I. 0Hz II. 0Hz

Potential applications of terahertz are; as these radiations can penetrate few millimeters in the human skin that's why they are being used to identify the skin cancer up to micro levels. There are many complex chemicals that are the basic part of many explosives and absorb specific frequency of terahertz radiations produce a signature for detecting devices to decode them.

3.4 RF radiations cancer therapy

Radio frequency energy use in the tissue demolition by the production of thermal energy is the focus of research for many years. The working principle for RF technique is "from the tip of an electrode into the tissue surrounding that electrode a high frequency alternating current is moved the movement of ions in the tissue cause the resistant heating due the alternating current. As a result of this heating the tissue temperature raised above 60℃ and the cells begun to die [38]. Normally RF ablation treatment produces exceeding 100°C local tissue temperatures ensuing in glutinous necrosis of the cancerous tissue and hepatic parenchyma in the surrounding. Haptic venous branches that are less than 3 millimeters occur when the tissue vasculatures are totally diminished. The only tissues are directly heated by RF currents up to cytotoxic temperature that allow passing the currents. The proportion to the square of the distance for the electrode decreases when RF current or power is distributed thru a mono polar electrode. In the treatment of liver tumor in an open rout or laparoscopic way the radiofrequency needle is introduced. In the controlled way the needle is approached the tumorous part and other wires of electrodes are than subjected. After this setup two electrodes are employed on the patient. The tumors that are less than 2.5 in diameter are ablated when the needle of electrode is subjected in the center of the tumorous cells. For the tumors that have diameter above 2.5 are ablated by the subjection of more than one needle of electrodes. The process is controlled to ensure the complete destruction of the malignant tissues. the treatment is carried out in sequences of inner and outer parts of the liver tissues.

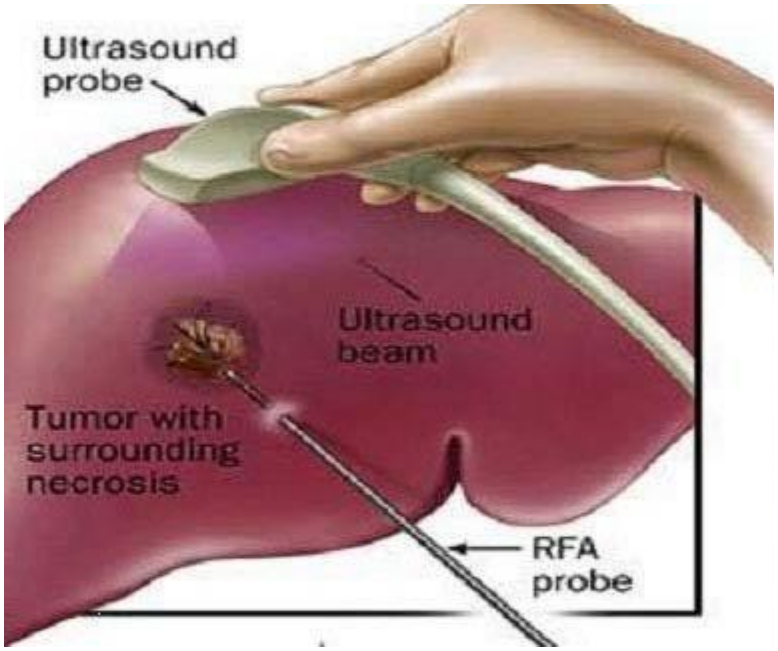

Figure 7: Radiofrequency ablation of liver tumor [39].

Concluding remarks

This paper provides the topical review on the modeling of cancer cells based on their dielectric properties as well as the cancer treatment based upon the therapeutic techniques. As cancer is the world fear and second leading cause of death round the world, the scientific community is working from centuries for its batter cure. In this paper four cancer therapy techniques have been studied. The techniques are based on electromagnetics. Hyperthermia, magnetic field, terahertz radiations and radiofrequency therapeutic techniques are studied in this paper. Though each technique has its limitations but they have benefit of providing less harm to the healthy cells in the surroundings of cancerous cells. Along with their limitations, the techniques are opening new doors to the research in the field of oncology.

Authors' Contributions: Ume Salma and M. Z. Yaqoob contributed to writing the main manuscript and data analysis. The literature review was conducted by Amna Iftikhar and Usama Ghaffar, while Abdul Ghaffar supervised the study, providing the core idea and research framework.

Availability of Data and Materials: Detail about data has been provided in the article.

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