Locally Induced Hyperthermia Using Microwave for Cancer Thermotherapy

Varadharaju G. (ME), Mohanraj V. (ME), Velusamy M. (ME)

Akshaya College of Engineering and Technology, Kinathukadavu
Coimbatore-642109

Abstract

India is ranked the top spot in terms of overall death in various types of cancer. The chemotherapy is used for the therapies for cancer but many side effects are seen. These side effects are mostly lifelong or long term effects. Hyperthermia is emerging as a prominent promising adjunct for conventional cancer therapies. For oral cancer doctors mostly recommend chemotherapy, because of the moisture in the saliva. The proposed technique will be helpful in thermotherapy in both the extremes that is in high water content body parts and low water content body parts. Here a needle like phased array microwave antenna is designed for the treatment of the localized hyperthermia by passing about 50 microampere current. This reduces the size of the tumour. The paper provides an introductory overview of the thermotherapy.

Keywords: Chemotherapy, thermotherapy, hyperthermia, phased array antenna, microwaves.

1. Introduction

Physiology of cancer: Cancer or tumour is the uncontrolled proliferation of the cells. The cells divide irregularly and grow uncontrollably, forming onus malignant tumour and invade the nearby organs of the body. The cancer also spread to the more distant organs through lymphatic system and blood stream. It is found that the hydration in the cancerous cells is high due to the increased rate of cell proliferation and cell living activity. It is estimated that the water content of the cell cancerous cell is more than 80 per cent than any other cells. It is confirmed that the normal living cell has 20 per cent low water content in tissues. Also the fat reduction and sugar cycle in the cancerous cycle is very high hence it forms high water and carbon dioxide in the cells. As the water content is far high than the normal cells, H-bonding is also far high than the normal cells or tissue. The cancer process is clearly described in the figure 1.

The carcinogenesis, the transformation of normal cell into a cancerous cell by mutation or epimutation, is the principal cost for the ransom amount of energy spent in abnormal cell proliferation and cell death. The net result is the increased rate of cell activity and hence this leads to high water content in the cancerous tissue. The tumours are of two types, they are benign tumours and malignant tumours, or cancer. Benign tumour do not invade other tissues, but malignant tumours are turn to the cancer tissue which invade other organs and can become life threatening.

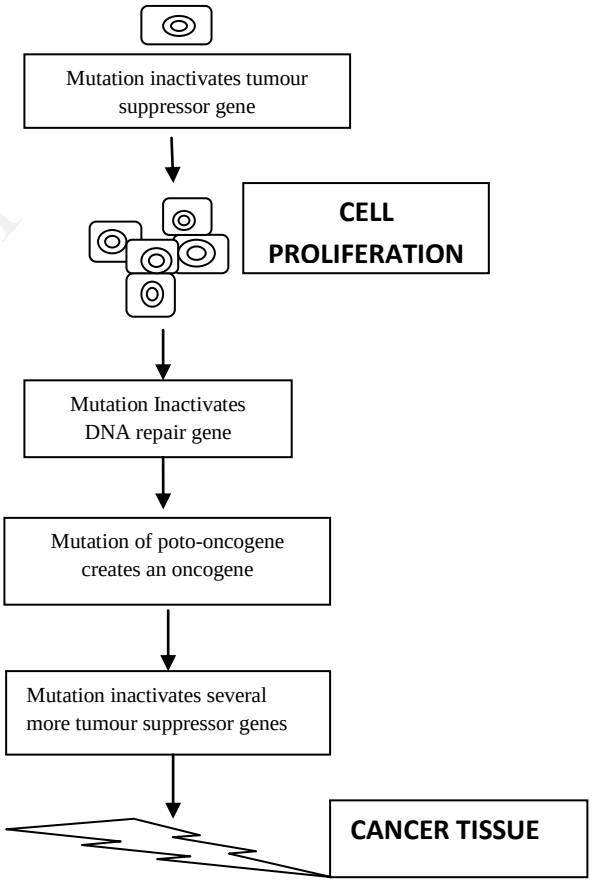

Figure 1: Cancer Proliferation

2. Effect of Microwave on Water Dipole

Two equal and opposite charges separated by a very small distance constitute an electric dipole. Water, ammonia, carbon−dioxide molecules are some examples of permanent electric dipoles. These molecules behave like electric dipole, because the centre of positive and negative charge do not

coincide and are separated by a small distance. A typical dipole is shown in the figure 2.

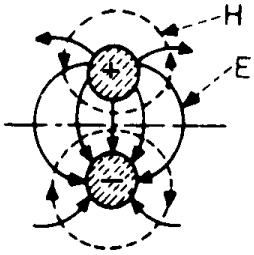

Figure 2: A Typical Dipole

In figure 2 'H' is the magnetic field and 'E' is the electric field. Both electrical and magnetic fields are perpendicular to one another. The magnetic field encircles the charges and the electric field lines starts from the positive charge and ends in the negative charge.

Microwave refers to electromagnetic waves with frequencies between 300MHz (3×10^8 Hz) and 300 GHz (3×10^{11}), with a corresponding wavelength from 1m and 1mm. Signals with wavelengths on the order of millimetres are called millimetre waves. The dipoles may be in ions or in charged molecules.

In case of a water molecule, the scissors molecule forms a 3D infinite network of hydrogen bond between the highly electronegative oxygen atom and highly electropositive hydrogen atom of adjacent water molecule. The hydrogen bond network or H-bond network is shown in the figure 3.

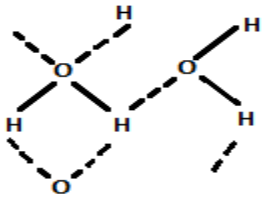

Figure 3: H-bond network in water molecule

The hydrogen and oxygen are highly electropositive and highly electronegative atoms they easily acquire partial charges and are separated by small distance and naturally said to constitute a dipole. This is not limited to the same molecule it also extends to the adjacent neighbour molecules in 3D network pattern.

When an external electric field or magnetic field is applied or electromagnetic waves with very high frequency is passed through water the molecular shape or angle between oxygen and hydrogen gets distorted hence free negative and positive charges are created this forms a free dipole in the liquid. The above process is discussed below in detail.

Electric effect of microwave on water molecule:

Water being dipolar, partly can be aligned by an external electric field and this may be easily shown by the movement of a stream of water by an electrostatic field. Very high field strengths ($5x10^9$ Vm^{-1}) is required to reorient water in ice such that freezing is inhibited, while lower fields,(10^5 Vm^{-1}) encouraging ice formation in supercooled water by weakening the hydrogen bonding. As said in above a partial alignment of the electric field will cause the water molecules to bend or break the H-bonding. The balance between H-bonding and Vander Waals attractions giving rise to less cyclic hydrogen bonded clustering. An electric field also changes the molecular covalent bond lengths and H-O-H bond angle (25×10^9 V m^{-1} causing approximately ±6% change in a lone water O-H length and 0.2% to 1% H-O-H angle) vibrational frequencies, dissociation energy depending on the orientation of the molecule to the field, which affects the H-bond network in an anisotropic manner.

High field might affect hydrogen bonding in anisotropic manner, hydrogen bonding being strengthened along the field but weakened orthogonal to the field. At low fields, both transitional and rotational motion gets reduced, hence ortho and para- forms of water properties starts changing. Electric fields also lower the dielectric constant due to the complete or partial destruction of H-bonded network.

Even pure water is not a pure insulator due to the presence of self ionizing property, when passing current through electrodes in electrolysis produce O_2 at anode and H_2 at cathode, hence the ions or charges stored in the water for hours. A -0.23 V orients water hydrogen atoms towards the metal electrode whereas +0.52V reverse this, hence some of the H-bonds are broken and localized density increases. Also ions are repelled or attracted in accord to their charges.

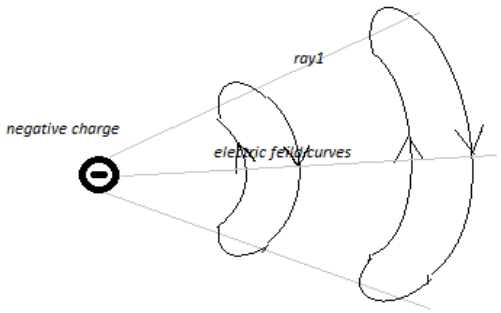

Figure 4: Electric field of a negative charge

Magnetic effect of microwave on water molecule:

Liquid water is affected by magnetic fields and such fields can assist its purification. Water is diamagnetic and may be levitated in very high magnetic fields, say 10T, and comparing earth's magnetic fields 0.2μT. One can say 0.2T is very low but it can increase the number of monomers of water molecule. Also, it is noticed that the fields increases the H-bonding at the same time. The clustering size in liquid water is caused by a magnetic field. Salt mobility is increased in strong magnetic field (1-10T), causing disruption to the H-bonding.

The increase in the magnetic field decreases the Vander Waals attraction and increases the H-bonding attraction. Hence reduces the thermal motion. Lower magnetic fields increase the evaporation rate of water. High magnetic field increases the H-bond and reduces the Vander Waal's attraction and hence increases the support of greater cycle of H-bonding in turn increases of supercooling.

Electromagnetic effect on water molecule:

It appears that electric and magnetic fields have opposite effects on the water clustering. Unstructured water with fewer H-bonding is a more reactive environment. An open more hydrogen bonded network structure slows down the reactions due to its increased viscosity, reduced diffusivity and less active participant of the reaction. Electric fields increase the reactivity due to the breakage of H-bonding or its strength, hence to say electric fields increase the reactivity in liquid water. Water clustering, even in random arrangement, has equal H-bonding in all directions. An electric or electromagnetic fields that attempt to reorient the water molecules should necessitate the break of some H-bonds. Electromagnetic waves exert its effect primarily through electrical effect rather than its magnetic effect. The increased hydration ability of the water in electromagnetic fields has shown dissociation of the enzyme dimer leading to a gel-like formation, due to the microwaves from a mobile phone.

The solubility property of the water will change in the presence of such EM fields and may result in the concentration of dissolved gases and hydrophobic molecules at surfaces followed by the reaction or phase changes. It is also possible that these processes may result in the production of low concentrations of H_2O_2 in a similar manner to mechanical vibrations. Such changes can clearly result in effects lasting for a considerable amount of time, giving rise to claims like memory effects. The important aspect to be taken to consideration is that the effect of electrical and electromagnetic field on the property of water last for long lifetime.

In addition to the breakage of the H-bonds, Electromagnetic fields may perturb in the gas or liquid interface and produce reactive oxygen species. Changes in H-bonding may affect CO_2 hydration resulting in pH changes. The role of dissolved gases in water chemistry is likely to be more important than commonly realized nanobubbles detected by light scattering experiments. Gas accumulating at hydrophobic surfaces promotes the hydrophobic effect and low density water formation. The accumulated gas molecules in such hydrophobic surfaces become supersaturated when electromagnetic effects disrupt this surface low density water.

3. Microwave Heating

The microwaves break the H-bonds and the energy is released in the form of heat. The molecular charges separated by a small distance forms a dipole. When this dipole is placed in the electric field or when microwaves are passed through it the dipole re-orient itself to the applied field or microwaves. At higher frequency this heating is caused by the rotation within the water, the dielectric.

Molecular rotation occur in water containing polar molecules, here polar molecules come to picture because of the break of the H-bonds, having an electrical dipole moment. The dipoles align themselves in the microwave field. When the electromagnetic field of the applied wave changes alternately, the dipole rotates. This rotation is called the dipole rotation. This dipole rotation creates push, pull and collide with other molecule distributing the energy to adjacent molecules and atoms in water. This distributed energy appears as the heat energy.

Temperature is the average kinetic energy of the atoms or molecules in water so agitating the molecules in this way increases the temperature rapidly. The electric potential energy of two charges is equal to the work done to assemble the charges or work done in bringing each charge.

Specific Absorption Rate:

SAR in tissue is a common parameter used to characterize the heating of tissue. It is given by the formula,

$$SAR = \frac{1}{2}\frac{\sigma|E|^2}{\rho} \quad ...1$$

Where ρ is the tissue density, σ is effective conductivity, E is the electric field.

$$\frac{dT}{dt} = \frac{SAR}{Cs} \quad ...2$$

Where T is the temperature, t is the time and Cs is the specific heat capacity of the tissue where it is employed. SAR is then can be inferred as the electromagnetic radiation energy absorbed by unit mass of a biological tissue.

Microwaves on cancer cell:

Dipole rotation is the primary mechanism normally referred as dielectric heating, and is most widely used for cancer treatment. Microwave acts good in water rather more actively in fats and sugars. This is because the fats and the sugars have far less polar than water molecules, thus less affected by the forces generated by the alternating electromagnetic fields.

Dielectric heating is different from the Joules heating of conductive media, which caused by induced electric current in the media. In high frequency $\sigma << \omega\varepsilon$, then dielectric heating is dominant mechanism of loss of energy from the electromagnetic field into the medium. Microwave frequency penetrates in living tissues, to a distance defined by the skin depth. The penetration essentially stops where all the penetrating microwave energy has been converted to heat in the tissue. For this reason it is a difficult task to have radiotherapy with antenna being outside and the waves may damage the cells all through the way to the tumor. This may damage the non-cancerous cells too, and causes severe burns to the cells.

Invasive microwave antenna:

Traditional thermotherapy used external microwave antenna. This damaged the normal cells on the way to the tumour growth and large numbers of normal cells are killed. This also damaged the cells of one or more organs and organ systems in body. This in return affected the internal biostatics of the body. The external radiation damages the skin always and it takes at least a month or two to recover. For example Radiotherapy in head is highly challenging since in is inside the hard skull, also high frequency may intervene the normal process of the Central Nervous System, CNS of the body.

The invasive radiotherapy was made a better option. Physicists use image guided radiation therapy, IGRT. This improved the better delivery of the radiation therapy to the tumours. This is very helpful since tumours can move between the treatments due to differences in organ filling or movements while breathing. IGRT involves using the conformal radiation treatment guided by specialized imaging tests like ultrasound, CT scans or X-rays. IRGT is the 2-D or 3-D imaging during a course of therapy. The positron emission tomography is one of the good imaging techniques.

Present techniques used in radiotherapy:

The radiation therapy techniques employ the process of Intensity Modulation Radiotherapy (IMRT). This process of radiation treatment uses computer and linear accelerators to sculpt a 3D radiation dose map specific to the target's location, shape and motion characteristics. Detailed data about the tumour location is recorded. This enhanced the reduction of more normal cells and also to assure for destroy of more cancerous cells. Even the invasive radiology method shows good results in destroying the cancerous cells and in tumour, it brings many side effects and other related problems for life.

4. Proposed Method

The research is going on parallel to design new methods for non-invasive thermotherapy. Many desired results are found. Now scientists propose some instrumentation methods for microwave thermotherapy using microwave array antenna.

The focused microwave radiation is the treatment which avoids heating the skin. Here needle like antennas are used to radiate the microwaves on the cancer cells. The antennas are made up of conductor like metals. Here the proposed model conductor used is the stainless steel. This is a partially invasive type of treatment for cancer. Here no catheter probe is used in all cases. In case of deep tissue exposure a probe is used. Using a probe increases the efficiency by reducing exposure area to the radiation. Here needles with thickness of a few millimetres are used. A third needle is used to increase the efficiency by varying the electric field.

Each part of body has different Specific Absorption Rate, SAR, depending on the amount of its fat content. Different intensity of radiation is applied and radiation intensity differs from one

part to another depending on this SAR of the tissue. This reduces the time of exposure and number of sitting for thermotherapy is also reduced. The varying electric fields induce dipoles and also create rotational motion. This rotational motion is increased by passing some electromagnetic waves, here the focused microwave. The change in electric field in 3D helps to break the H-bonds and also reduces the Vander Waal's attraction between the water molecules. It should be understand that the microwaves from two antennas should be in same phase, and the electric field of the third antenna should be in same phase otherwise it may cancel with other electric fields and reduce the efficiency. The needle-like microwave antenna shall be constructed using ceramic or MEMS. They have high efficiency but they are tedious to design and construct. It is noted that magnetic field is not considered because it may strengthen the H-bonds.

5. Conclusion

The cancer treatment using microwaves is seen that they shall pass through the molecule and even disturb the bonds. The reason for choosing the microwave for cancer thermotherapy is discussed that 80 percent of increase in water content in cancer tissue, which is a supporting factor for the hyperthermia, that is the breakage of hydrogen bond release of energy. The release of energy is in the form of heat which disintegrates the cell wall and stops the cancer cell proliferation. The effect of the electric fields, magnetic fields and electromagnetic waves are also discussion shows that effect of electrical field is opposite to that of magnetic field due to the internal body biostatics. The antennas used and need for using third antenna is to reduce the effect of the magnetic field. The H-bond which plays a vital role in the locally partially invasive microwave antenna for locally –induced hyperthermia for cancer thermotherapy. The various aspects on theory and in practice are discussed and put forward for further discussions in medical view points for further advancements in various parts of the body.

The selection of any type of treatment for cancer depends on cancer staging, stage I-IV. Primitive the stage is any single therapy may be enough in such cases hyperthermia is prescribed. Doctors often prescribe radiotherapy only after chemotherapy.

7. Reference

1. Toshihito Seki, M.D., Masayuki Wakabayashi M.D., Taiichi Nakagawa, M.D.,Takayuki Itho, M.D., Tomohiro Shiuo, M.D., Kouji Kunieda, M.D., Masahiro Sato, M.D., Syouzou Uchiyama, M.D., And Kyoichi Inoue, M.D., "Ultrasonically Guided Percutaneous Microwave Coagulation Therapy For Small Hepatocellular Carcinoma" IEEE Trans. Biomed Engg, 2011.

2. Earl Zastrow, student member, IEEE, Susan C.Hagness, Fellow, IEEE, Barry D. Van Veen, and Joshua E. Medow, "Time-Multiplexed Beamforming for Noninvasive microwave Hyperthermia Treatment", IEEE Trans. Biomed Engg, vol.63. pp.1574-1583, 2012.

3. Masako Urata, Satoshi Kimura, Kikuo Wakino, Toshihide Kitazawa, "Optimization Of Three Layer Tapered Coaxial Line Applicator For Cancer Thermotherapy By Impedence Matching Of Transition Layer Sections." IEEE conference, 2011.

4. Waldemar Wlodarczyk, Peter Wust, Martin Seebass, Johanna Gellermann, and Jacek Nadobny," RF Hyperthermia: Modeling And Clinical Systems", Dept. of radiation Medicine, Charite Medical School, Humboldt University, Germany.

5. T. Michiyama, K. Asanuma, S. Kuwano, "Numerical Simulation of Heating Characteristics in A New Microwave Coaxial-Slot Antenna for Cancer Therapy" IEEE conference, 2010.

6. Federal Communication Commission (FCC), "Tissue dielectric properties," http://www.fcc.gov/fcc-bin/dielec.sh/.

7. http://www.microwave101.com/