ENHANCEMENT OF CANCER CHEMOTHERAPY BY SELECTIVE ELECTROMAGNETIC HEATING OF TUMORS

H. A. Ecker, C. P. Burns and R. L. Magin
Georgia Institute of Technology
V. P. Popovic
Emory University School of Medicine

The heating property of electromagnetic radiation has been used for many years in medical applications for various types of diathermy treatments. During the last three years the authors and their associates have been working on a new application of electromagnetic radiation: selective heating of tumors in deeply cooled animals to enhance the effectiveness of tumor chemotherapy treatment. This new type of tumor treatment (warm tumor - cold body) was first developed in Dr. Popovic's laboratory at Emory University and is called differential hypothermia.[1] In the differential hypothermia technique, the body of the whole animal is profoundly cooled to a temperature of 40-50°F. After the animal becomes hypothermic, the electromagnetic radiation is used to increase and to maintain the temperature of the tumor at approximately normal level (98°F) through selective and uniform heating. After differential hypothermia is stabilized, anticancer drugs are administered. These drugs are extremely destructive and fully unspecific; that is, they can affect every cell and every tissue in the body. However, when the drugs are administered in differential hypothermia, the cooled healthy tissues utilize very little of the drug, whereas the warm tumor which has a high metabolic rate is affected to a much higher degree. Thus, the objective of the differential hypothermia technique in the treatment of cancer is to increase susceptibility of tumor cells to a chemotherapeutic agent (anticancer drug) and at the same time to decrease the effects of the administered drug on other healthy parts of the body.

In previous research conducted by Georgia Tech and Emory University into the selective heating of tissues, we have investigated the relative permittivity and resistivity of biological tissues since these are the properties which determine the absorption of electromagnetic energy by the tissues. Relative permittivity and resistivity for various organs in the frequency range of 100 to 1000 MHz are well known.[2] The values of these parameters in the frequency range of 1 to 100 MHz were determined at Georgia Tech utilizing a new technique of measurement which allows the data to be obtained from animals <u>in vivo</u>.[3] This method is contrasted to previous techniques which utilize <u>in vitro</u> tissue samples.

The amount of electromagnetic heating produced in biological tissues is dependent on the depth of penetration of the electromagnetic energy into the tissue and on the power absorbed per unit volume. Both of these quantities can be calculated from the tissue permittivity and resistivity parameters. The penetration of electromagnetic radiation into biological tissues is the limiting process which controls the capability of selective heating.

In biological tissues, penetration depth is of the order of a wavelength of the incident electromagnetic radiation. Therefore, the longer the wavelength of the radiation, the deeper the penetration. However, power absorption per unit volume is inversely proportional to wavelength so that the shorter the wavelength, the higher the power absorbed per unit volume. In summary, short wavelength radiation provides the best heating with tissues whose dimensions are of the order of centimeters, but it is not effective for the deep heating of central body organs or the brain.

Our own experiments in differential hypothermia have indicated that microwave energy can be used to achieve selective heating in tumors in rats and mice.[4] Results of the differential hypothermia treatments while administering 5-fluorouracil to mice with spontaneous tumors verify that significant tumor regression occurs when the animal is treated for several hours. Similar results were obtained for chemically induced tumors in rats. In the rat experiments, tumor regression was observed for all cases after treatment with differential hypothermia and chemotherapy.

A technique has been developed for heating tumors deep in the brain and most other body tissues by the use of high frequency electromagnetic radiation (in the range of 3 MHz to 30 MHz) in combination with doping the tumor with high loss magnetic or ferrite material. The penetration depth (effective depth of heating) at these frequencies is much greater than at microwave frequencies and the radiation will penetrate the whole body. Of course, heating of the whole body is not desired, but by using the doping materials which are significantly more lossy than the surrounding tissue, the heating will be concentrated in the doped area, i.e., the tumor. The particle size of doping material may be as small as ten microns without significantly changing its magnetic properties, therefore, the implantation of doping material can be accomplished by injection rather than surgery. The high loss of some ferrites at 1 MHz provides a mechanism for selectively increasing the loss of biological tissues through injection of ferrite powder into the areas to be treated. The use of metallic powders or magnetic conductors as doping materials has shown that magnetic stainless steel balls one millimeter in diameter may be even more effective than ferrite for doping tumors.

This research has resulted in the development of new techniques for the treatment of cancer. Especially significant will be the potential treatment of brain tumors without the need for major surgery through the use of doping materials. Brain tumors have been emphasized because of the special problems associated with brain surgery, but the ferrite doping techniques will be useful for treatment of cancer in many of the major organs of the body, without surgery. The use of differential hypothermia with selective electromagnetic heating will improve the effectiveness of known anticancer drugs while reducing harmful effects on healthy tissues. This technique will allow a more general use of chemotherapeutic drugs on cancer tissues.

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