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RESONANCE INDUCED ALTERATIONS OF INTRACELLULAR BIOPHYSICAL PROPERTIES

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ABSTRACT

A treatment of cancer by the application of external electromagnetic energy at a resonant frequency capable of the generation of heat intracellularly to induce selective thermal death of cancer cells is described. This process also allows for the detection of cancer cells by the use of differential resonant frequencies including nuclear magnetic resonance and electron spin resonance techniques. This process permits the selective treatment of cancer cells by the compartmentalized alteration of biophysical properties in the cancer cells and the detection of cancer cells by determination of their biophysical properties.

The process comprises an ability to determine the respective resonant frequencies of cancer cells and normal cells at a cellular level. An external alternating electromagnetic field is then applied at the resonant frequency of the cancer cells which differs from the resonant frequency of the normal cells. The cancer cells absorb significant energy at this resonant frequency whereas the normal cells absorb minimal energy at this frequency. Generating the heat intracellularly instead of extracellularly results in the cell's membrane, which is an effective thermal barrier, enhancing the process by keeping the heat within the cell instead of outside of the cell.

This process is enhanced by the nuclear differences between cancer cells and normal cells and by the energy changes characteristic of structural and conformational changes in the deoxyribonucleic acid and the histones of the nucleus including their interrelationship. This process promises great efficacy in the diagnosis and the treatment of neoplastic and also perhaps of atherosclerotic diseases.

Intracellular
Hyperthermia
Biophysical
Magnetic Resonance
Electromagnetic
Deoxyribonucleic Acids
Selective
Cancer
Cell
Atherosclerosis

1. Hyperthermia
2. Neoplasms
3. Magnetics
4. Electromagnetics
5. Nuclear Magnetic Resonance
6. Neoplasm Circulating Cells
7. Cell Transformation Neoplastic
8. Deoxyribonucleic Acids

INTRODUCTION

There are presently a number of methods and techniques for the treatment of cancer, among which may be included: radiation therapy, chemotherapy, immunotherapy, and surgery. The common characteristic for all of these techniques as well as any other presently known technique is that they are extracellular in scope; that is, the means of inducing cancer cell death are applied from outside the cell.

This extracellular approach is found to be less effective and less efficient because of the difficulties of penetrating the outer membrane of the cancer cell that is composed of two protein layers with an intervening lipid layer. Of even greater significance is that to overcome the protection afforded the cell by the cell membrane in any extracellular techniques, the attack on the cancer cells must be of such intensity that considerable damage is caused to the normal cells resulting in severe side effects upon the patient. These side effects have been found to limit considerably the effectiveness and the usefulness of these treatments.

A safe and effective cancer treatment has been the goal of investigators for a substantial period of time. Such a technique, to be successful in the destruction of the cancer cells, must be selective in effect upon the cancer cells and produce no irreversible damage to the normal cells. In sum, cancer treatment must selectively differentiate cancer cells from normal cells and must selectively weaken or destroy the cancer cells without affecting the normal cells.

It has been known that there are certain physical differences which exist between cancer cells and normal cells. One primary physical difference that exists is in the temperature differential characteristics between the cancer cells and the normal cells. Cancer cells, because of their higher rates of metabolism, have slightly higher resting temperatures compared to normal cells. In the living cell, the normal temperature of the cancer cell can be 37.5° Centigrade or higher, while that of the normal cell is 37.0° Centigrade. Another physical characteristic that differentiates the cancer cells from the normal cells is that cancer cells undergo cell death at lower temperatures than do normal cells (45.5° Centigrade as compared to 46.5° Centigrade and often the differential in temperature cell death is more than 1.0° Centigrade). Therefore, the temperature elevation increment necessary to cause death in the cancer cell is determined to be approximately 8.0° Centigrade as compared to an increment of 9.5° Centigrade for the normal cell.

It follows, therefore, that with an appropriate controlled increment of heat, the cancer cells can be selectively destroyed. On the basis of this known differential in temperature characteristics, a number of extracellular attempts have been made to treat cancer by heating the cancer cells in the body. This concept of treatment is referred to as "hyperthermia." To achieve these higher temperatures in the cancer cells, researchers have attempted a number of methods, including inducing high fevers, utilizing hot baths, diathermy, applying hot wax, and even the implantation of various heating devices in the area of the cancer.

Thus far, the above described approaches to treat cancer, have had limited effectiveness and all have the common characteristic of approaching the problem by treating the cancer cell extracellularly. The outer membrane of the cancer cell being composed of lipids and proteins, is a poor thermal conductor, thus making it difficult for the application of heat by external means to penetrate into the interior of the cell where the intracellular temperature must be raised to effect the death of the cancer cell. If, through the extracellular approaches of prior hyperthermia techniques, the temperatures were raised sufficiently to effect an adequate intracellular temperature to kill the cancer cells, many of the normal cells adjacent the application of heat could very well be destroyed.

The nuclei of cancer cells and the nuclei of normal cells possess some differences structurally as well as morphologically.(1) The alterations which occur in a cell to produce malignancy either take place in, or are transmitted to the nucleus. This is evident by the very fact that the cells produced by tumor cell multiplication often possess the same characteristics as the original tumor cell. These alterations may very well exist in the structural and conformational relationship of the deoxyribonucleic acids and the histones in the nucleus.

Extensive work has been done in vitro concerning the nuclear magnetic resonance of cancer tissues as opposed to normal tissues.(2,3) Differences in T_1 and T_2 relaxation times have been attributed to differences in the amount of water present in the cancer cells and the way in which the water molecules are ordered.(4) Similarly, much work has been done to establish the dielectric properties of DNA and histones in the human and their interrelationships.(5-9) However, the key to this new process lies in the nuclear changes in the cancer cell, both conformational and structural, which allows the cancer cell to resonate at frequencies different from the normal cells.

DISCUSSION

The purpose of the process herein presented is to destroy the cancer cells selectively by intracellularly generating a temperature and by changing biophysical characteristics that will destroy the cancer cells with no harmful effects upon the normal cells. This work represents a portion of our research into the intracellular alteration of biophysical properties for the past ten years as introduced in previous published work.(10-12) The method herein presented also provides a means for the diagnosis of cancer cells wherever they exist in the body.

Utilizing this method, a precise increment of heat rise is achieved within the cancer cell and within the cytoplasm. The thermal barrier that characteristically exists as the outer membrane or cell wall of the cell is now utilized as a means of retaining the heat produced within the cell, rather than, as in previous attempts by others, preventing any heat build-up within the cell. On the basis of the cell resting temperature and the temperature required to produce cell death, the increment that the cell temperature must be raised to effect cell death is critical. For the cancer cell, the temperature rise is approximately 8.0° Centigrade. Thus, any temperature rise in the cancer cell or in the normal cell that is at least 8.0° Centigrade and not greater than 9.5° Centigrade above the normal cell temperature, will result in the selective destruction of the cancer cell without any harmful effects to the normal cell.

This intracellular heat rise and intracellular destruction of the cancer cell is achieved through the use of the differential resonance frequencies of cancer cells and normal cells to pump energy into the cancer cells at their specific resonance frequency whil allowing very little energy into the normal cells.

Nuclear magnetic resonance has been utilized to study many facets of hemoglobin, creatine kinase, conformational changes in ribonuclease, the distance in biological systems, ligand-enzyme relationships and hydrogen bonds; this latter subject being of special interest relative to this discussion.

Nuclear magnetic resonance studies have been done utilizing ^{1}H, ^{13}C, ^{31}P and ^{15}N.(13) Much work has also been done using nuclear magnetic resonance to investigate the conformation and structure of histones relative to the chromosome and DNA.(14) The nuclei of cancer cells (the deoxyribonucleic acids, histones and their interrelationship) besides often being different in content, are also usually different in conformation and binding when compared to the nuclei of normal cells (the deoxyribonucleic acids, histones, etc.).(15) These differences provide the difference in the resonance frequencies of the nuclear material in cancer cells and in normal cells. This difference between the cancer cells and normal cells being nuclear in origin is transmitted to the daughter cancer cells formed by cell division and explains the daughter cells' propensity towards malignancy.

When energy is pumped into a system at a given frequency, those elements of the system which resonate at that given frequency will absorb a significant portion of the energy. Therefore, by pumping energy into the subject at the specific resonant frequency of the cancer cells, the cancer cells' intracellular temperature and biophysical properties are affected which selectively destroys the cancer cells without affecting the normal cells.

Similarly, proton magnetic resonance has been utilized to study nucleic acid conformation.(13) Electron spin resonance has been used to investigate free radical and paramagnetic species in both malignant and normal tissues.(14,15) Electron spin resonance has also been utilized to investigate the effects of radiation on DNA, nucleic acids, nucleosides and nucleotides with regard to the formation of free radicals.(16-20) This approach may be useful in determining the sensitivity of a tumor to radiation.

A linear energy beam which allows electromagnetic energy to be transmitted at a given frequency in a straight line focused by a surrounding stream of ionized gases is utilized. This beam is projected on the living tissue and the amount of resonance measured as in nuclear magnetic resonance. The measurement is made by either series of coils whose axis is at 90° to the transmitted energy or by crystals which act as small coils. The frequency is varied over a wide range and a plot of resonance versus frequency is made. The beam is then rotated over an arc of 180° as is the detector. The data is fed into a computer to allow a three-dimensional mapping of the resonance spectrum of all points in the subject.(21)

The cancer cells having a different resonance spectrum will be located. Each cancer cell can be detected.

The subject is then placed within a large coil and the entire subject receives energy at a frequency preset by the computer. This frequency being the frequency of resonance closest to that of the cancer cells and furthest from that of the

normal cells. The cancer cells therefore absorb the energy at their respective resonant frequency and are destroyed intracellularly (actually from within the nucleus) while the normal cells are unharmed.

This destruction of the cancer cells can be monitored by repeating the first part after completion of the second in order to follow the destruction of the cancer cells. This destruction of the cancer cells can be followed by observing the disappearance of cells which resonate at the cancer cells' resonant frequency.

Another method of monitoring the destruction of the cancer cells is to place the subject within a large coil with the subject on a large number of small coils whose axis is at 90° to the original coil. Then the same frequency range is explored and the resonance frequencies at the different points in the subject are recorded. Once again, the specific resonance frequencies of the tumor cells are noted. The large coil is then set at this frequency and energy is specifically delivered to the cancer cells without affecting the normal cells.

As an example, the subject is placed on a table with the linear energy beam transmitter on one side and the detection on the opposite side. The transmitter and the detection are on a moveable axis which can swing through an arc of 180° . The frequency is varied from 1 Kilohertz to 50 megahertz at each point on the 180° arc. Studies have shown that the discrimination between malignant and normal tissue may increase as the frequency decreases.(22) A number of frequencies is necessary in order to avoid overlap in frequencies of some abnormal but not malignant tissues; i.e. at certain frequencies the T_1 of some abnormal tissues may be increased similar to the malignant tissues.(4) The input from the detection is fed into the computer which composes a three-dimensional picture of the resonance frequencies of all points in the subject. The distribution of cancer cells is noted as is their resonance frequency.

The subject is then placed in a large coil approximately 3-6 feet in diameter. The coil is set at the frequency determined by the computer. The subject is treated for an appropriate time period. At the end of this time, the patient is placed back on the original table and the procedure of detection repeated. Should any cancer cells with their specific resonance frequency be detected, then the patient would be treated again, etc.

As another example, the subject is placed in a large coil approximately 3-6 feet in diameter. The subject lies on a table containing a number of small coils (or crystals) whose axis is perpendicular to that of the large coil. Applying an external electromagnetic field, the frequency is varied from 1 kilohertz to 50 megahertz. The resonance points at various frequencies are noted in the subject, especially for the cancer cells.

Two dimensional studies of nuclear magnetic resonance have been performed with scanning by the selective irradiation of the specimen in switched magnetic field gradients.(23) This technique may be helpful in this process as well.

The coil is then set at the frequency of the cancer cells and energy delivered for an appropriate time period to destroy the cancer cells at their resonance frequency without affecting the normal cells. Once again the subject is scanned at the range of frequency to determine if any cancer cells remain and if further treatments are necessary.

ADDITIONAL APPLICATIONS

This concept may be carried one step further to the treatment of Atherosclerosis. Based upon research work by our group and studies in the literature, it is suggested that the development of atherosclerotic lesions is in many ways similar to tumor formation with the multiplication of a single cell line and the proliferation of smooth muscle cells (the monoclonal theory). These proliferating smooth muscle cells along with the deposition of cholesterol allow the components of the atherosclerotic plaque to have resonant frequencies different from those of the normal intimal wall. A number of investigations have been performed into the nuclear magnetic resonance of cholesterol and lipids.(25)

The nuclear magnetic resonance of lipids in bilayers and membranes as well as of phospholipids in relation to membrane permeability (which of course is very important to our present discussion of atherosclerosis), have been studied.(26) Membrane pertubations by physical agents can actually be followed using electron spin probe analysis.(27) Using selective irradiation of the specimen in switched magnetic field gradients, blood flow in a vessel can be measured due to the different spin characteristics of the new polarized blood entering a specific region of the vessel.(24) Studies by our group, along with others found in the literature, illustrate the changes in the newly formed atherosclerotic plaques.

Therefore by performing a three-dimensional scan utilizing nuclear magnetic resonance or proton resonance, the areas of atherosclerotic lesions may be identified. Subsequently by subjecting the individual to the frequency closest to the resonant frequency of the atherosclerotic lesions, the lesions may be destroyed due to the absorption of energy, without affecting the normal vessel wall whose cells respond to a different set of frequencies.

The uptake of particles by tumors and atherosclerotic plaques in certain stages of their formation has been demonstrated experimentally by our group (10-12) Nuclear magnetic resonance

may be utilized to characterize the magnetic parameters of metal ions.(28) Electron spin probe analysis has been used to detect membrane perturbation by physical agents.(29) By allowing the tumor or atherosclerotic plaque to take up the particles, be they ferromagnetic, paramagnetic, or diamagnetic, the process of determining the resonant frequencies of the cancer cells or the atherosclerotic lesions and of pumping in energy at the desired resonant frequency, may be enhanced.

SUMMARY

There are numerous studies and investigations which demonstrate the difference in nuclear morphology, structure, content and conformation between normal and neoplastic cells. These nuclear changes may be related to the passage of neoplastic characteristics to the daughter cells; i.e. DNA - histone composition and conformation.

Nuclear magnetic resonance depends on the nuclear morphology, structure, content and formation. Utilizing the difference in resonance frequencies between the cancer cells and the normal cells, energy can be "pumped" into the system close to the resonant frequency of the cancer cells, yet far from the resonant frequency of the normal cells, thereby destroying the cancer cells without affecting the normal cells. The concept described in this paper represents another segment of our approach to the treatment of cancer and other diseases through the intracellular alteration of biophysical properties.

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