EurekAlert! InContext • Bioinformatics • Nanotechnology

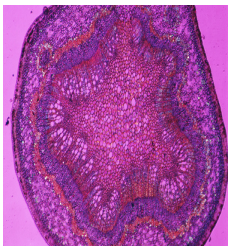
AUGUST 2002

Nanotechnology Essays

Cancer Treatment By Electromagnetic Activated Nanoheaters

Written by Yoed Rabin, *Associate Professor*, Department of Mechanical Engineering, Carnegie Mellon University, mailto:rabin@cmu.edu

Jump to: 1910, 1950s, 1970s, late1970s, and 1986 to read more about the history of using heat to treat cancer.

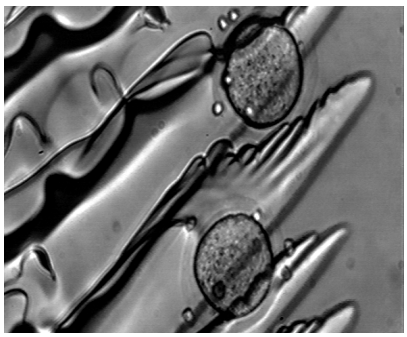


Click here for an enlarged image.

Heat Kills

Heating biological cells above normal body temperatures is destructive. Exposing cells to temperatures in the range of 41 to 46 degrees C (hyperthermia), and temperatures higher than 56 degrees C (thermal ablation), triggers different sequences of cellular and sub-cellular events that lead eventually to cell death. Cell death can be classified as either a necrotic process or an apoptotic process. Necrotic cells undergo swelling and rupture, while apoptotic cells are removed by phagocytosis (the body's "cleaning service") as they display markers on their cell surface that target them for selective elimination.

Mild hyperthermia (43 degrees C for 30 to 60 minutes) is known to enhance apoptosis in normal and cancerous cell populations. Thermal ablation also triggers the necrotic process. Evidently, the likelihood of cell death is not only associated with the elevated temperature, b also with the time of thermal exposure. The combined effect is known as the thermal dose.



Oocytes engulfed by ice dendrites during freezing, observed through cryomicroscope. Click here for an enlarged image.
For more information on Dr. Karlsson, please visit his home page.

At the early stages of hyperthermia research, it was assumed that adequately controlled therma treatment could be applied as a stand-alone treatment for certain cancers. Today, the therma treatment of cancer is not considered a stand-alone, but as a treatment in combination with radiotherapy and/or chemotherapy.

The use of heat to improve radiation response ir tumors was clinically introduced in 1910. Sporac reports demonstrated the potential improvement radiotherapy by hyperthermia, but systematic scientific exploration of this concept began in the 1970s. Today, the sensitizing effect of hyperthermia on cells prior to radiation therapy i well-recognized effect, based on clinical observations.

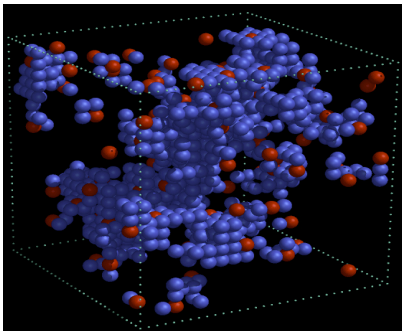
In 1986, the European Society of Hyperthermic Oncology began a multicenter randomized clinic

trial to assess the clinical success of local hyperthermia given as an adjuvant to radiotherapy in the treatment of advanced malignant melanoma (skin cancer). Over all, the treatment yielded a high response rate, and resulted i significant alleviation in most patients, irrespective of their treatment schedule.

Tumor size, radiation dosage, and the extent of heating achieved by hyperthermia were all significant factors in determining the efficacy of the treatment. Supporting results for the combination of hyperthermia with radiotherapy of a similar nature have been reported on metastatic lymph nodes in individuals with advanced stage cancer in the head and neck, locally advanced rectal cancer, brain cancer, and recurrences of breast cancer.

Send In The Nanoheaters

Heating cancer tumors in a clinical setup can be achieved by various technologies, such as focused ultrasound, radio frequency, thermal radiation, lasers, and magnetic nanoparticles. The magnetic nanoparticle size is typically in the range of five to ninety nanometers, which is about one-thousandth the size of the smallest biological cell, but also about one thousand times larger than typical molecules.



Monte Carlo simulation of intracellular ice formation (a cause of cell injury) during freezing of a three-dimensional biological tissue (8000 cells).
Click here for a complete caption and an enlarged image.

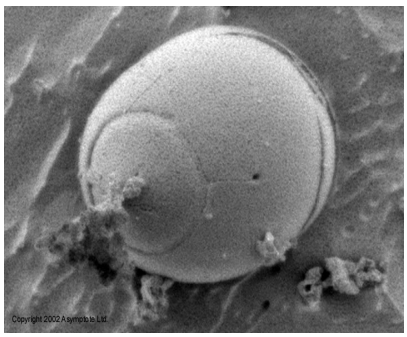
To turn these particles into heaters, they are subjected to an oscillating electromagnetic field, where the field's direction changes cyclically. Application of the magnetic field generates a directional force on each magnetic particle. When the magnetic field oscillates at high frequency--switching directions thousands to millions of times per second--the direction of the force changes according, so that the average force in zero.

Creating these rotating forces requires energy, which is taken from the oscillating magnetic field. Some of this energy may cause the nanoparticles to rotate or vibrate. However, the cyc nature of the magnetic field essentially "freezes" the nanoparticles in place, preventing their net movement in space. The remaining amount of applied energy is converted into heat, causing the nanoparticles and their surrounding biological material to warm up.

Hitting The Target

The study of cancer treatment with nanoparticles in an oscillating magnetic field began in the 1950s. Unfortunately, most studies were conducted with inadequate animal models, inexact thermometry, and poor magnetic field parameters, so that any clinical implications were far from practical. More than three decades later, it was found that distributed clusters of magne iron oxide nanoparticles exhibit an extraordinary heat rate, causing rapid temperature elevat at a relatively low concentration. This discovery began the modern era of thermal cancer treatment using magnetic fields.

In the late 1970s, researchers suggested that special coatings on the magnetic nanoparticles would cause them to selectively penetrate into cancer cells. This concept would allow intravenc delivery of the nanoparticles into the body, followed by natural aggregation of the cancer tumor with nanoparticles. Recent developments biochemistry make this novel approach feasible. For example, molecules based on certain antibodies can be prepared to attach to magneti particles on one end and to a protein or residue the target cell surface on the other. Research ar development efforts are still required in order to make this technology feasible. Once selective coating is available, electromagnetic heating will



Freeze fracture electron microscopy of a suspension of human erythrocytes frozen with glycerol (10% v/v) as cryoprotectant. Click here for an enlarged image.

offer the unique advantage of selectively heating only the cancer tumor.

Engineers In The Clinic

Several researchers are putting all the pieces of this technology together to develop a single method. Sara Majetich in the Department of Physics at Carnegie Mellon University has developed a few nanoparticle types that appear be perfect candidates for thermal treatment of cancer tumors. At the Department of Mechanica Engineering at Carnegie Mellon, I have develope a device and technique to control the temperatu and thermal dosage during the thermal treatmer of tumors. Dr. Majetich and I are currently workir in collaboration with John Patzer and Roberto Lopez from the Department of Surgery and Chemical Engineering at the University of Pittsburgh to develop an animal model to study this exciting new technology.

The contribution of engineering to the development of this clinical application is not limited to technology development, but also encompasses research methods. At the research level, th engineering concept is very different from the clinical one. A typical clinical research plan ca be considered a diagnostic process, based on a large number of experiments that are analyzed with statistical tools. On the other hand, a typical engineering research plan is a prediction process, based on mathematical modeling of physical phenomena.

In our study, we perform thermal analysis to predict the temperature distribution and thermal dose distribution in the magnetic heating process. This kind of prediction is an essential tool our experimental design, and eventually, will become a clinical planning tool.

Sponsored by the U.S. Department of Energy.

For more information about nanotechnology, visit EurekAlert!'s Nanotechnology *In-Context Module*.