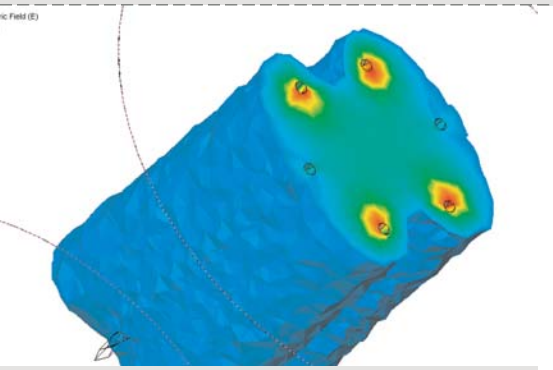
Genetronics

COSMOSEMS HELPS REFINE PROMISING CANCER TREATMENT



Helping to determine and optimize the electrical field strength throughout the volume of space around the electrodes.

➜ Genetronics, a San Diego-based drug delivery company, specializes in developing technology and hardware that has the potential to allow physicians to more efficiently and cost-effectively deliver life-saving drugs or beneficial genes to patients with catastrophic illnesses, including cancer. The company is the technology leader in electroporation therapy (EPT), the application of very brief, carefully controlled, pulsed electric fields, to human cells. This process causes pores to open in the cell membrane (permeabilizes them), and allows pharmaceuticals or genes, injected in the area prior to the application of the electric pulse, to gain access to the cell's interior. The cell pores close up a short time later, trapping the chemotherapeutic agents inside the cancer cell, so they can destroy the cell.

The Challenge

Chemotherapy can be a very effective treatment for many types of cancers. However, the cell membrane that surrounds each cancer cell makes it difficult for some chemotherapeutic agents to penetrate inside and cause cell death. In addition, physicians infuse these agents throughout the body in high concentrations. Unfortunately, this system-wide application often has serious side effects, killing healthy as well as cancerous cells, while also causing nausea, hair loss, weakness and other symptoms.

For years, cancer researchers have been trying to find a way to target chemotherapeutic agents more precisely, to deliver the agents to only that part of the body affected by a cancer. This could make it possible to deliver the chemotherapy more effectively, and reduce, or even eliminate side effects.

Solution

One way to reduce the doses required to kill cancer cells is to make the cells in a tumor more permeable, that is, make it easier for the chemotherapeutic agents to penetrate the cell membrane, and enter the cell. COSMOSEMS and SolidWorks are playing a vital role in testing certain features of Genetronics's MedPulser®, a device that applies an electric pulse technology to cancer cells, making them more permeable to chemotherapeutic agents.

The Details

In a study sponsored by Genetronics, and performed by Dr. William Panje at Rush-Presbyterian-St. Luke's Medical Center in Chicago, ten patients with head and neck cancer were treated with EPT and a chemotherapeutic agent. All ten patients experienced tumor shrinkage, with five of the ten experiencing complete tumor reduction, and another three of the ten experiencing tumor reduction of 50% or more. Thus far, the results of clinical trials using EPT to treat refractory (resistant to cure) head and neck cancers have shown higher response rates than standard treatments. EPT has the potential to be used in the treatment of many other accessible solid tumor cancers for which current treatment modalities cause significant morbidity, disfigurement or are not effective.

One of the key parts of testing and refining EPT is determining the appropriate electrical pulse and electrical field for different types of cells. COSMOSEMS and SolidWorks play a vital role in evaluating the electrical fields used with Genetronics's electroporation devices, helping to determine and optimize the electrical field strength throughout the volume of space around the electrodes.

Determining the Appropriate Electrical Field

The MedPulser® is essential to successful EPT. One of the most important issues in applying EPT effectively is determining the correct electrical pulse and electrical field strength necessary to increase the permeability of a particular type of cell. For example, the strength of the electrical field required to open the pores of plant or bacterial cells is greater than the strength of the field required to open up mammalian cells.

The electrical pulse, and electrical field strength required to open the cell pores are generated by the pulse generator of the MedPulser® System and applied through the needle electrodes of the Electrode Applicator developed by Genetronics. As Genetronics's Mechanical Engineer Chris Andre explains, it is possible to create electrical fields of different strengths, measured in Volts/centimeter, by applying varying voltages and different electrode geometries. Electrode geometries refer to the way the electrodes are shaped and arranged. For example, they might be in a coaxial configuration, parallel configuration, or pin configuration. The MedPulser® Electrode Applicator contains six needles arranged in a hexagon. Andre uses the electrostatic module of COSMOSEMS to model the electrical fields. Depending on the application, the strength of an electrical field might vary from 500 to 15,000 Volts/centimeter.

SolidWorks

➜ Helps optimize existing devices and create new instruments for researchers at Genetronics to use.

➜ Gave the ability to change an electrode geometry and analyze an electrical field within a half hour instead of days.

Electroporation and Cells

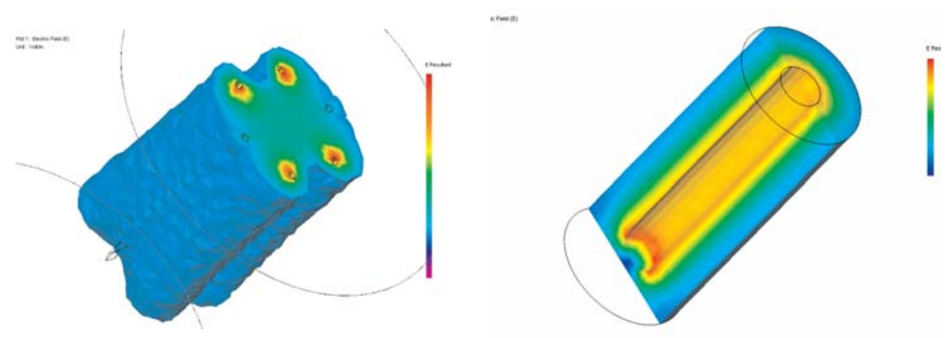
There are two parts to electroporation therapy. First, cells are injected with a chemotherapeutic agent. Then, Genetronics's MedPulser® System is used to apply an electrical pulse to the cells. The electrical field that is created opens up the cells' pores. The chemotherapeutic agent then can flow in through the aqueous (water) channels created by the electroporation process. The aqueous pathways permit many more oncolytic (cancer fighting) molecules of the chemotherapeutic agent to be transported into the cell. As a result, EPT can achieve significantly increased tumor destruction, compared to system wide application of chemotherapy. A short time after the electric pulse is applied, the cells' pores automatically close up again, trapping the chemotherapeutic agent inside the cells.

"When we pulse the MedPulser® Electrode Applicator," says Andre, "we never fire all six needles at once. Only four of the needles are active during a pulse. Two of the needles are at a higher potential, two are at a lower potential. The current flows when we have the voltage difference between these needles. We examine the electrical field created between the four needles, at a specific point in space, using the probe on the COSMOSEMS software. Of course, electrical field is not the only parameter relevant to electroporation. Pulse length, number of pulses, and other factors also affect the results. The analysis we obtain with COSMOSEMS helps to determine the electrical field strength through the volume of space in which we are performing the electroporation."

According to Andre, COSMOSEMS is also used in the development of other instruments in the Genetronics BTX product line. This product line includes different types of electrodes used by biotech researchers for whatever electroporation-related research they are involved in. "The idea is to use COSMOSEMS to help optimize existing devices and create new instruments for researchers to use," says Andre. "Researchers are performing electroporation on a range of cell types. These include mammalian cells, bacterial cells, and plant cells. By using COSMOSEMS with SolidWorks, we can help researchers get the optimal products they require for their electroporation experiments."

Andre and Sean Webb, another Genetronics Mechanical Engineer, are very enthusiastic about COSMOSEMS and SolidWorks. Andre says, "One of the nice things about COSMOSEMS is how well it works with SolidWorks. We can easily manipulate the electrode geometries in SolidWorks, and then analyze the resulting electrical fields using COSMOSEMS."

COSMOSEMS and SolidWorks have significantly sped up Genetronics product development. "The time savings are so dramatic they are, in a sense, unquantifiable," says Andre. "Using EMS, we can change an electrode geometry and analyze an electrical field within a half hour. If we had to do these three dimensional calculations for the more complicated electrode geometries by hand, it would take days."



Electric Field Strength Contour Plot of a 6 Needle Electrode Array

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