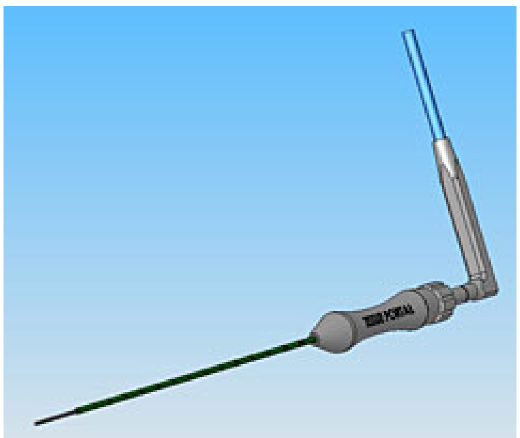
Medical Xpress

New medical technique punches holes in cells, could treat tumors

February 12 2007



An electrode used for irreversible electroporation, which could soon be used to treat tumors in humans. (Image courtesy of Oncobionic Inc.)

A large animal study has shown that certain microsecond electrical pulses can punch nanoscale holes in the membranes of target cells without harming tissue scaffolding, including that in the blood vessels - a potential breakthrough in minimally invasive surgical treatments of tumors.

The study on pigs, the first large animal trial for the irreversible electroporation (IRE) technique, is described in the February issue of the journal Technology in Cancer Research and Treatment. IRE was developed at the University of California, Berkeley, which holds a number of patents on the technology.

"I've been working in this area of minimally invasive surgery for 30 years now," said Boris Rubinsky, UC Berkeley professor of bioengineering and mechanical engineering and lead author of the paper. "I truly think that this will be viewed as one of the most important advances in the treatment of tumors in years. I am very excited about the potential of this technique. It may have tremendous applications in many areas of medicine and surgery."

Rubinsky co-authored the paper with Dr. Gary Onik, director of surgical imaging at Florida Hospital Celebration Health. They founded Oncobionic two years ago to commercialize IRE. Oncobionic is in the process of being sold to AngioDynamics, a New York-based manufacturer of medical devices for minimally invasive surgery.

Rubinsky is currently on a leave of absence from UC Berkeley to help bring this technology to market. During his leave, he is heading the Center for Biomedical Engineering in the Service of Humanity and Society at Hebrew University of Jerusalem in Israel.

It was first reported in the early 1970s that the application to cells of very fast electrical pulses - in the microsecond and millisecond range - creates an electrical field that causes nanoscale pores to open in the cell membrane. But research since then has mainly focused on reversible electroporation, which uses voltages low enough to temporarily increase the cell membrane's permeability. The holes in the cell membrane created by reversible electroporation close up shortly after treatment, allowing the cell to survive.

"This concept of reversible electroporation really caught on in modern biotechnology, especially over the last decade," said Rubinsky. "It is used primarily to help get genes and drugs into cells. The field of irreversible electroporation was pretty much forgotten."

The researchers' work on irreversible electroporation is an outgrowth of studies done on a "bionic chip" that Rubinsky and his UC Berkeley students were developing. The bionic chip merged living cell tissue with electronic circuitry. In the course of understanding whether electroporation was successful, the researchers discovered a range of electrical current that would cause permanent damage to cell membranes without generating heat and thermal damage.

Irreversible electroporation uses electrical pulses that are slightly longer and stronger than reversible electroporation. With IRE, the holes in the cell membrane do not reseal, causing the cell to lose its ability to maintain homeostasis and die.

The researchers say that IRE overcomes the limitations of current minimally invasive surgical techniques that use extreme heat, such as hyperthermia or radiofrequency, or extreme cold, such as cryosurgery, to destroy cells.

They point out that temperature damage to cells also causes structural damage to proteins and the surrounding connective tissue. For liver cancer, the bile duct is at risk for damage. For prostate cancer, the urethra and surrounding nerve tissue is often affected.

Electroporation, on the other hand, acts just on the cell membrane, leaving collagen fibers and other vascular tissue structures intact. The researchers said that leaving the tissue's "scaffolding" in place allows healthy cells to regrow far more quickly than if everything in the region was destroyed.

In the new study, the researchers set out to demonstrate that the IRE technique could produce reliable and predictable results in a large animal model. They performed the IRE surgical technique on 14 healthy female pigs under general anesthesia, using the same procedures as if the patients were human.

They used ultrasound imaging to guide the 18 gauge stainless steel electrodes to target areas in the pigs' livers. The researchers applied 2,500 volts in eight 100-microsecond pulses spaced 100 microseconds apart to create lesions in the livers. They found that the lesions were immediately apparent as dark spots on the ultrasound images, giving real-time feedback during the procedure. The livers were then examined 24 hours, three days, seven days and 14 days after surgery.

"All of the vessels, down to the microvasculature, remain intact with IRE treatment, so the healing process is amazing," said Onik, who performed the surgery for the study. "Where it might take a year for a cryosurgery lesion to resolve, IRE lesions resolved in two weeks. That has major implications in terms of monitoring what you're doing and knowing that the cancer has been killed."

Another chronic drawback of heat or cryo treatments for cancer is the difficulty in treating cells that are immediately adjacent to the blood vessels. Because blood maintains a relatively stable temperature, it actually transfers heat or cold away from a treatment area in an attempt to return the region to a normal temperature range. That means some cancerous cells might actually survive treatment.

"That counts for a lot of failures when treating liver cancers," said Onik. "With IRE, you can destroy cancerous cells right next to the blood vessels. It's a more complete treatment. In my clinical experience, this is about as good as it gets. We've been using other techniques for a long time. This provides significant improvements over other treatments."

Onik does sound a note of caution, however. "While we are obviously very excited about this advance in tumor ablation, we are in the early stages of our learning curve," he said. "Experience developing cryosurgical ablation has taught us that we undoubtedly have much more to learn, and there is always the potential for unexpected results."

Although the tissue in this study was healthy, the researchers found in a prior cell culture study that IRE effectively kills human liver cancer tissue.

The IRE technology was cleared for human use by the U.S. Food and Drug Administration in November 2006. Onik is scheduled to begin human clinical trials for IRE this summer.

Source: UC Berkeley