

Silencing a killer

Last year 28,000 American men died from prostate cancer. Three engineering professors hope to reduce that number by developing new methods to diagnose, contain and treat the deadly disease.

By O.K. Carter



Chances are you know somebody with prostate cancer. A friend, family member or co-worker. If you haven't been touched personally, you've heard these names: Colin Powell, Norman Schwarzkopf, Arnold Palmer, Nelson Mandela,

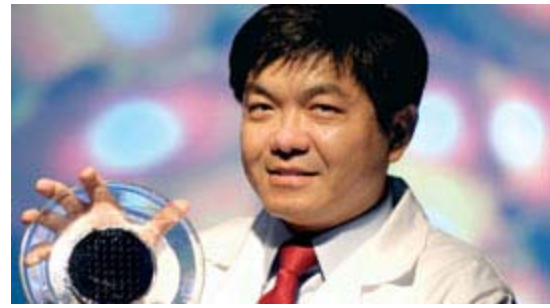
Joe Torre, Rudolph Giuliani, Robert De Niro. All are prostate cancer survivors. Others like Frank Zappa, Telly Savalas, Bill Bixby, Linus Pauling and Don Ameche weren't as fortunate.

UT Arlington researchers would relish changing a critical mortality statistic, the one that ranks prostate cancer as the second leading cause of malignancy-related deaths in American men. With collective grants totaling more than \$1 million, [electrical engineering](#) Professor J.C. Chiao and [bioengineering](#) professors Hanli Liu and Kytai Nguyen are developing tools to better combat the illness.

Having recently lost a beloved uncle to prostate cancer, Dr. J.C. Chiao is more determined than ever to perfect his device that predicts if prostate cancer cells will migrate to places like the bones or lungs, often resulting in death.

For Dr. Chiao, the work is more than academic. He recently lost a beloved uncle to the disease.

“When that happened, the research became a much more personal calling,” he says. “When I speak to any group on my prostate cancer research, I remind them that this is not an abstract problem. One of every six men in the audience at that moment is likely to eventually develop prostate cancer.”



Chiao and Dr. Nguyen received a three-year grant from the National Cancer Institute at the National Institutes of Health to identify and quantify the chemical factors promoting prostate cancer cell migration from the primary tumor to a secondary site. Chiao is developing the actual device while Nguyen focuses on the chemical factors.

Nguyen secured a three-year award from the Department of Defense to develop polymer magnetic nanoparticles for the targeted and controlled release of drugs to only the prostate cancer cells.

Dr. Liu has a \$518,000 grant from the Department of Defense’s Prostate Research Program to continue the development of an optical detection system that will enable physicians to find the most suspicious lesions, determine their severity and identify the small cancers unlikely to cause harm.

Put in a more sequential way, Liu’s research focuses on developing a precise diagnostic imaging device to determine if prostate cancer exists and, if so, to what degree. Chiao and Nguyen are exploring the propensity of prostate cancer cells to spread to other organs and what chemicals within the body contribute to this.

In addition, Nguyen’s research aims to treat prostate cancer with a targeted nanoparticle chemotherapy that will concentrate treatment in the affected area, increasing the efficiency of treatment while reducing side effects.

“I’m convinced that what not too long ago sounded like science fiction—nanoparticle medicine—is going to make major inroads in medical treatment.”

Optical detection

Current early-detection tests have shortcomings, so physicians often depend on biopsies to find cancerous tissue, Liu says. “Basically the process depends on taking as many as 20 small tissue snips from the lemon-sized prostate in what amounts to a hit or miss procedure.”

Technology has not yet replaced these needle biopsies. But Liu's hybrid optical procedure aims to dramatically improve the test's accuracy.

Her method utilizes the optical qualities of reflected light. When the prostate gland is illuminated, normal and cancerous tissue absorb or fluoresce colors differently, letting doctors know in real time whether to remove a piece of tissue at that location.

Improved accuracy and less discomfort are potential benefits of Dr. Hanli Liu's optical method to detect prostate cancer. Clinical testing of her procedure could begin in three to five years.



In short, many of those painful snips won't be necessary. The premise is that accuracy will improve and patients will endure less discomfort.

"The goal is to allow physicians to find the more suspicious lesions that may have cancer, correctly estimate the severity of the cancer and identify tiny, low-grade cancers that are not likely to cause problems," Liu says. "The problem now with the randomness of the needle biopsies is that patients are over-treated, not a good thing, and some are under-treated, with potentially fatal consequences."

Liu has researched the effectiveness of visible and near-infrared light to detect tumors for several years and recently enlisted the support of industrial engineering Assistant Professor Seoung Kim, who will use his expertise to statistically identify cancer tissues from normal prostate glands.

"My collaborators and I believe we are developing a much more accurate way to do biopsies," says Liu, who estimates that clinical testing of this optical detection method could begin in three to five years.

Dr. Kytai Nguyen's research uses magnetic nanoparticles to control the release of drugs only to prostate cancer cells. Doctors can guide the particles to affected areas with a highly precise magnetic belt.



Her research team has three goals: develop a portable, on-site, low-cost optical spectroscopic means to guide needle biopsies; create a definitive system for using spectroscopy and fluorescence to identify cancer lesions; and establish a classification system for identifying prostate cancers based on optical spectroscopic signals.

Beating the spread

Chiao and Nguyen work with clinicians and researchers at UT Southwestern Medical Center, including physicians Ganesh Raj, J.T. Hsieh, Victor Lin and Chin-Rang Yang. They want to develop a simplistic and affordable device that will predict if prostate cancer cells will migrate to places like the bones or lungs and then metastasize, often resulting in death.

In his office Chiao flips a small, not-quite-square tab of what looks to be clear plastic. What he has is a potentially life-saving microfluidic device. He preaches simplicity, and this diagnostic tool is certainly that.

“We’re trying to come up with a catchy name for it,” he says with a laugh. “The formal name is microfluidic platform for cancer cell study. It is like an ant farm because through the transparent plastic you can observe in real time how prostate cancer cells move, deform, divide and grow.”

Close scrutiny of the piece of transparent polymer reveals tiny tunnels that are actually microfluidic channels connecting reservoirs. The sizes of the channels, similar to the cancer cell sizes, are in tens of micrometers.

Prostate cancer cells are in one reservoir, and organic chemical attractants as identified by Nguyen are in other reservoirs, all connected by the microfluidic channels.

The hypothesis: Cancer cells may be attracted to certain chemicals manufactured by the body. If so, they will migrate through the microfluidic channels to those chemical attractants that with the spread of prostate cancer are most commonly found in bones or lungs. In some cases the cancer cells ignore the chemicals, migrating not at all or very slowly toward them. In other cases the cells go to great lengths to migrate.

The research seems to confirm what cancer specialists have suspected: Cancer is a personal disease. Different prostate cancers have varying tendencies to migrate, and the bodily chemicals that serve as attractants for cell migration in some people might not do so in others.

“Can we break the cycle so that cancer cells don’t want to go to a second organ to grow?” Chiao asks. “We have to understand which chemicals attract them to move.”

Metastasis is a complex organic process, and Chiao and Nguyen stop short of saying that the microfluidic platform can predict with certainty whether it will occur, even if it’s obvious that cancer cells are migrating.

“But we are 100 percent sure that our device can be used to measure how cancer cells migrate,” Chiao says. “That will bring us more information about the risk potential for

metastasis. Prostate cancer by itself can be managed with high survival rates, so the big issue is to stop spread or metastasis.”

The tiny platform device has clearly indicated cancer cell migration in some patients who suffer from metastasis, but cost is a critical consideration.

“Right now it costs us about \$30 to manufacture each device in our UTA laboratory,” Chiao says. “But with mass production, it’s likely that each platform can be built for as little as a dime and certainly for less than a dollar.”

The duo visualize that eventually the platforms will make it easy to diagnose cancer cell migration tendencies, identify the various chemical attractants involved and develop highly personalized chemotherapy treatments that are effective and less painful.

“And not just for prostate cancer,” Nguyen adds. “This process has far wider application potentials, for example for breast cancers and lung cancers.”

Targeted cancer fighters

Cancer researchers know that restricting chemotherapy agents only to the areas affected improves the efficiency of the treatment and reduces discomfort. Figuring out how to do that has proved difficult, but Nguyen’s research shows promise.

Her approach uses polymer magnetic nanoparticles for the controlled release of drugs to only the cancer cells. Imagine a microscopic particle that contains not only a cancer-fighting drug but a protein-based peptide that is welcomed and incorporated by cancer cells—but not by healthy cells in other areas.

In addition, because the nanoparticles are magnetic, doctors can guide them to affected areas with a highly precise external magnetic belt.

“Too, because the particles are magnetic, the buildup in the affected area can easily be measured by a scan,” Nguyen says. “When the buildup is sufficient, we can vibrate the particles with magnetic currents, causing a heat buildup within them, which then causes the nanoparticle to collapse.”

As they collapse, the particles release their cancer-fighting drugs, the process essentially ending when the magnetic excitation ceases. The remnants of the nanoparticles themselves will eventually be eliminated through natural cleansing processes.

How small are the nanoparticles? Nguyen says it would take thousands of them to form a cluster the size of a grain of sand.

She is collaborating with Drs. Weina Cui and J.T. Hsieh of UT Southwestern. Preliminary studies by former Ph.D. student Maham Rahimi helped secure the grant.

Though this focus is on prostate cancer, Nguyen believes the targeted nanoparticle approach will have other medical applications, ranging from treatment of breast cancer to problems related to plaque in the circulatory system.

“I can’t say we’re on a new frontier here, but we do have new tools to make some old ideas work that simply weren’t available a few years ago,” she says. “I’m convinced that what not too long ago sounded like science fiction—nanoparticle medicine—is going to make major inroads in medical treatment.”

In the not-too-distant future, the prostate cancer research of Liu, Chiao and Nguyen on better detection, more efficient chemotherapies and targeted applications could make the disease more manageable.

And reduce the mortality roll call.

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