Better Way to Biopsy

Gabor Fichtinger's robot-assisted device offers a less-invasive way to detect and treat prostate disease.

By Dave Beaudouin

Using a simple robotic arm tipped with a needle, Gabor Fichtinger and his research team are hunting a killer that accounts for nearly 31,000 deaths a year in the United States. The disease is prostate cancer, the country's third leading cause of mortality among men.

Currently, early detection of this cancer involves a manual clinical procedure called a transrectal ultrasound (TRUS) guided needle biopsy. However, the male prostate gland, about the size of a walnut, has a delicate suspension system that can easily be damaged if a biopsy needle exerts too much squeezing or pushing, Fichtinger explains.

Despite its wide use, TRUS-guided biopsy has been shown to miss the presence of cancer in approximately 25 percent of cases. Given that approximately 65 million prostate biopsies are performed annually in the United States, revealing around 220,000 new cases a year, this 25 percent rate of failure is unacceptable to Fichtinger.

A Johns Hopkins University associate research professor, Fichtinger has joint appointments in the Whiting School of Engineering departments of Computer Science and Mechanical Engineering, and in Radiology at the School of Medicine. He also is the director of engineering at Hopkins' Engineering Research Center for Computer-Integrated Surgical Systems and Technologies (ERC CISST), where he leads a team researching computer-assisted systems for inserting thin delivery devices though the skin to target locations.

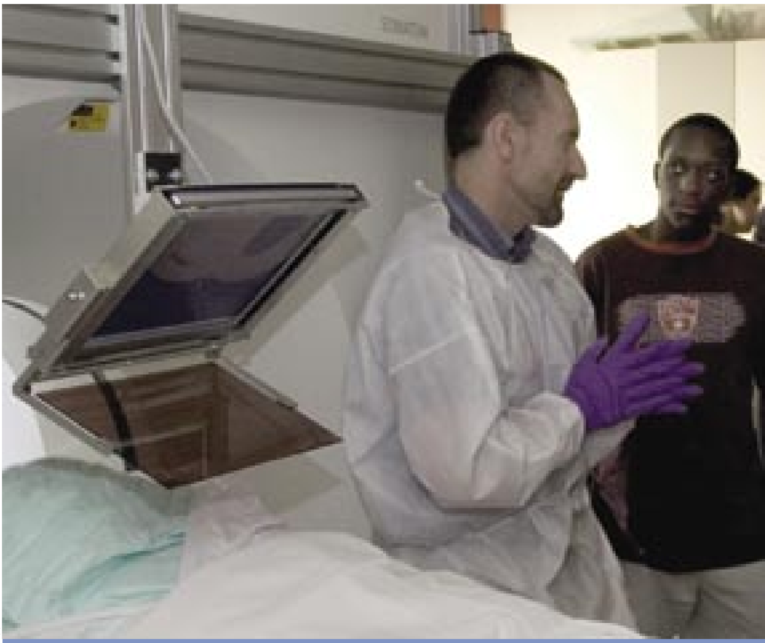
"Using TRUS, if we are dealing with a cancer that's the size of a sugar cube, there's no guarantee that we can see it," Fichtinger says. "And even if we can see it, the deformation and dislocation caused by using a handheld device gives us no assurance that we will hit the prostate accurately."

A Sharper Focus for Diagnosis

Fichtinger earned his PhD in computer science in his native Hungary, at the University of Budapest. Drawing from his early background in computer graphics and biomedical visualization systems, as well as his engineering expertise, Fichtinger began devising an alternative to TRUS after arriving at Hopkins. His goal was to have a sharper eye—and a steadier hand—to make prostate disease diagnosis and research more effective. Robotic assistance could provide more precise and predictable movement and needle placement. But Fichtinger also wanted the system to provide enhanced imaging to enable a higher rate of disease detection. To do so, he needed a robotic device that could operate inside of a conventional closed MRI scanner.

The challenge of working with an MRI scanner was threefold, according to Fichtinger. First, such scanners do not allow access to the patient during imaging. That meant his device had to work within the extremely cramped space of the MRI's core, where conventional medical robots and mechanical linkages cannot. Second, due to the MRI's magnetic field, which is 300,000 times more intense than that of Earth, any ferromagnetic materials or electronic devices could heat up and become hazardous to the patient. And third, a real-time in-scanner guidance method was needed to operate the device. "Therefore, our primary objective was to develop a prostate biopsy system that coupled superior imaging quality with accurate delivery hardware, inside a conventional MRI scanner," says Fichtinger.

During a six-week summer program for pre-college students, Gabor Fichtinger teaches the techniques used in computer-integrated surgery. These students taking part in Johns Hopkins' Advanced Academic Programs are in the cadaver lab at the School of Medicine.



Will Kirk

"This is a robot that doesn't even work like a robot, but still does a procedure that nobody had been able to do before." —Gabor Fichtinger

Sophisticated Solution, Made Simple

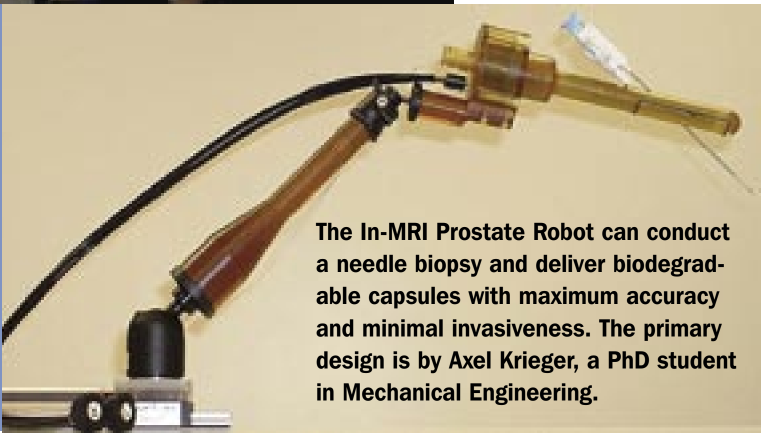
Just two years after its conception, the prototype was ready. The In-MRI Prostate Robot is elegant in its simplicity yet remarkably sophisticated in its design. “That’s the beauty of it,” Fichtinger says with a laugh. “This is a robot that doesn’t even work like a robot, but still does a procedure that nobody had been able to do before. Although a lot of thinking went into its development, it is as simple as it needs to be to do the job.”

Using actuation cables, the physician or technician controls the robot. Once its extendable arm is inserted rectally into the patient, the robot uses real-time MRI-based position sensors to calculate precisely the sequence of movements needed to bring its needle to an intended target point.

The robot’s general-purpose needle delivery system not only can do biopsies but can also deliver capsules. These capsules could place markers to help target subsequent therapies, or deliver a genetically engineered virus or a radiation therapy seed.

The MRI scanner can constantly collect high-fidelity images and sends them immediately to the robot’s treatment monitoring computer. The resulting 3D representation of the device is superimposed on the anatomic images. This enables the physician to monitor and adjust the motion of the device toward its target.

Beyond its diagnostic and therapeutic uses, the new robot offers a significant application as a research vehicle, Fichtinger says. “We now can do long-term follow-ups with patients to take measurements, or do biopsies to track any pathological changes. With an MRI, there are also endless possibilities for functional imaging,” he notes. “We can look at a number of indicators related to the prostate that we would have no way to see in ultrasound.”



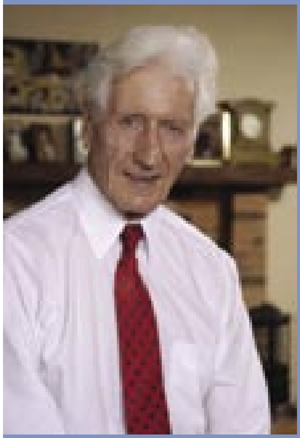
The In-MRI Prostate Robot can conduct a needle biopsy and deliver biodegradable capsules with maximum accuracy and minimal invasiveness. The primary design is by Axel Krieger, a PhD student in Mechanical Engineering.

Rapid Development with the Right Team

Spurred by a grant from the National Institutes of Health, the now-patented In-MRI Prostate Robot moved from concept to human trials in a remarkably short period—just 24 months. Fichtinger credits this rapid development to one critical factor. “This project could not have been done without the collaboration of other specialists in a wide range of disciplines,” he says. Among the principal contributors he cites Louis L. Whitcomb, professor of Mechanical Engineering; Ergin Atalar, professor of Radiology and of Biomedical Engineering; Axel Krieger, a PhD candidate in Mechanical Engineering; and Robert C. Susil ’97, an MD/PhD student in Biomedical Engineering. “It’s definitely been a team accomplishment,” says Fichtinger.

To learn more about the ERC CISST, visit engineering.jhu.edu/~erc-cisst and to learn more about Gabor Fichtinger’s other projects, visit www.cisst.org/~gabor .

“It was really an amazing, precise procedure...”—Bob Siblo



Will Kirk

Bob Siblo never expected to encounter a robot. Then again, he never expected to have cancer. But when a screening test in 2004 showed that he had high levels of PSA (prostate specific antigen), indicating the likelihood of prostate cancer, Siblo began looking at treatment options. At the National Institutes of Health in Bethesda, Maryland, he decided to become a test subject for a novel procedure, one that employed MRI scanning and targeted radiation therapy using the Johns Hopkins In-MRI Prostate Robot.

“My entire treatment process only lasted from March to July,” recalls Siblo. “It was really an amazing, precise procedure that made me feel very comfortable. I never felt any discomfort or side effects.”

Since his treatment, Siblo, who lives in Annandale, Virginia, has nothing but good news to report. “In just one year, my PSA levels have gone from 9.1 down to 2.1,” he says. “So everything at this point seems to be fine.”

What Are the Chances...

...that a new composite building material will crumble? For Lori Graham-Brady, the answer involves building ways to define and test the risks in structural systems.

By Dave Beaudouin

We may look at a building and perceive solid slabs of concrete, but Lori Graham-Brady is seeing something else. She's weighing the possibility of it cracking and failing. Just how many of our modern buildings possess this element of risk? According to the associate professor in the Whiting School's Department of Civil Engineering, all of them do, though most thankfully in very small degrees.

"Everybody knows that risk is there when you build a building," says Graham-Brady, "no matter how remote that risk is. There is no structure where there's a 100 percent certainty of it never failing." However, a greater problem, she warns, is the current climate regarding risk assessment. "If you ask somebody what an acceptable level of risk is, the answer is invariably zero," she notes. "This is particularly true when a project is initiated by legislators who are very risk-adverse. This situation has been a real hindrance for civil engineers who want to measure risk more accurately in terms of the materials they use to build."

Probability as a Tool

Graham-Brady began her professional career as a nuclear engineering consultant analyzing pressure vessels in power plants. She then earned a civil engineering PhD at Princeton University (1996), taking her interest in structural engineering and mechanics into a new direction: probabilistic mechanics, a discipline employing the use of probability to model the behavior of building materials for their structural reliability. Using computer models, an engineer can project the viability of a certain structural material, such as a steel I-beam, to withstand such variables as weight over time.

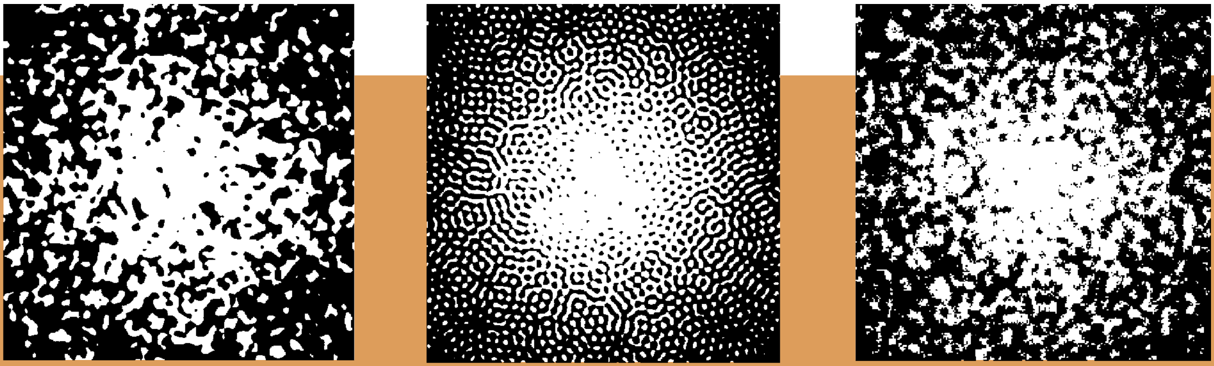
"Probability is a conceptual tool that tells us about how unknown and uncertain quantities can vary," according to Graham-Brady. "Knowing that there's uncertainty around our predictions, we assign a likelihood to different values around that prediction."

In applying probability to structural engineering, a question might arise, for example, how likely is it that a certain type of steel is 10 percent weaker than the average? How can an engineer be certain if this is true? "The grade of steel that I'm using may have an assigned strength, but in reality that's just an average value," Graham-Brady explains. "If there's some possibility of a flaw due to fabrication or human errors, that value could vary significantly. Probability theory simply is a way of assigning likelihoods to building weaker or building stronger."

Civil engineers have long known that certain building materials, like metals, are more stable and thus more predictable. Other materials, concrete in particular, possess what Graham-Brady calls "significant random aspects." Concrete has a wide range of variables contributing to its composition, from its mix of different aggregates (gravel materials) to the length of its curing time. As a result, she says, "The response in traditional engineering is to make the concrete-based structure a certain amount stronger than it has to be—or to assume an extra degree of loading, so we're sure to cover any loads that we didn't predict."

Modeling Microstructural Stress

While such rules of thumb can apply with conventional materials, new composite building materials can prove challenging to use, even if they offer such obvious benefits as ease of use or lower cost. "Engineers are uncertain about them, because they haven't built with them the way they've built with concrete," says Graham-Brady. "They don't know how variable these materials are, and then how to design structures using them."



These images modeling graded materials were created by Lori Graham-Brady's PhD students, who are using translation processes to computationally simulate microstructures in order to study their properties.

“There is no structure where there’s a 100 percent certainty of it never failing.”

—Lori Graham-Brady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The Day the Rows of Rivets Upzipped On April 28, 1988, at 24,000 feet above Earth, a large section of the upper fuselage of an aging 737 operated by Aloha Airlines peeled away in mid-flight. This classic example of fatigue cracking, notes Lori Graham-Brady, associate professor of Civil Engineering in the Whiting School, clearly showed the potential threat of small cracks that are difficult to detect in visual inspection. “This is a good example of how small-scale uncertainties (in this case flaws) can lead to large-scale catastrophic failure,” she says.

While the pilot somehow landed the plane safely, a flight attendant lost her life as a result of the explosive decompression. Noted *Air Safety Week* (November 12, 2001), “That industry-changing accident set in motion a comprehensive effort of inspections and, where necessary, repairs, to assure the structural integrity of pressurized fuselages.”

Graham-Brady’s current research focuses on providing a means to better understand the uncertainties of these newer random composite materials. Using computer models, her lab team is studying their microstructural properties by applying a load and then analyzing the resulting pattern of local stresses.

Through such modeling, Graham-Brady eventually hopes to develop a software application that is useful in answering structural reliability questions in the design of more complex structural systems—from bridges to automobiles. “We want to create a product that solves real engineering problems involved with structural behavior,” she says, as well as “any issue where they’re concerned about strength and the integrity of the materials used in enforcing that strength.”

While the current constraints of computer processing make such modeling difficult, Graham-Brady is confident that she will achieve her goal—and the value it provides. “Basically what I’m working on is risk management—assessing the risk of materials that may behave more poorly than expected, thus causing a negative impact within a structural system,” she says. “The insurance industry, for one, is very interested in this kind of issue from an underwriting standpoint. The outcome of this research will help define the probabilities that can cause structural systems to fail. We want to take that understanding of risk and do something good with it.”

To learn more about Lori Graham-Brady’s teaching and research, visit www.ce.jhu.edu/lori.


In June, Graham-Brady traveled to Rome to accept the Junior Research Prize from the International Association for Structural Safety and Reliability. The award recognized her outstanding work in micromechanical materials modeling.