Getting to the Heart of Cardiac Imaging

A research discovery leads to a new lifesaving diagnostic tool—and a new company.

By Dave Beaudouin

Cardiologists have a problem. When they look at conventional images of the heart, they can't see a true picture of the motion of the heart muscle. As a result, they cannot detect mechanical strain or deformation, one of the early warning signs of cardiovascular disease.

Jerry Prince believes he has a solution. The key to effective cardiac imaging lies in a closer examination of the "donut," according to Prince. He is the William B. Kouwenhoven Professor in the Whiting School of Engineering's Department of Electrical and Computer Engineering, a researcher at the Center for Imaging Science, and co-director of the Image Analysis and Communications Lab.

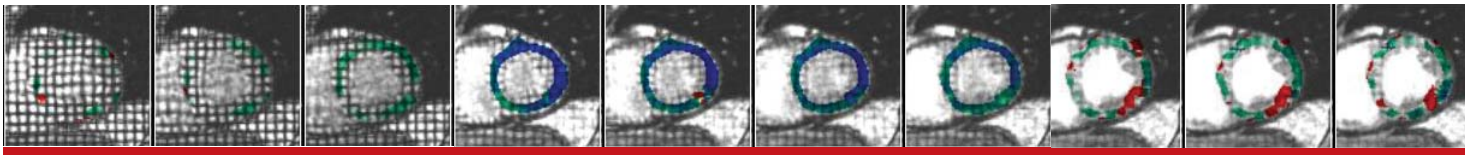
"Imagine a cross-section of the human heart as a donut," Prince explains. "The thickness of the donut is the muscle, with the hole being where the blood passes. When scanned by most traditional imaging techniques, this area between the two contours on the inside and the outside of the donut is going to be fairly constant in intensity—there's no resolution to show differentiation of the muscle fibers."

However, "tagged" magnetic resonance imaging (MRI), developed in the late 1980s, does make possible the capture of such critical detail. Prince says MRI tagging, in which a computer "marks" locations on the heart muscles and then tracks their movements, produces a clearer, more precise picture. "An MRI provides better resolution," he explains. "You can see details better. With MRI tagging, you can see what's going on within the walls of a heart muscle. It can image the way the muscle is working. There's no other technology that can do that now."

However, this advance in cardiac imaging has had its shortfalls, challenging Prince and his Hopkins colleagues to seek new solutions over the past decade. Simply put, the imaging process in its original configuration was much too slow, and therefore too costly, to be used for regular patient screening tests. "The diagnostic use of tagged MRI is problematic in that you can gather scanned data in a half-hour, but it then takes several hours to process these data," says Prince. As a result, physicians instead have relied on older imaging techniques like ultrasound for cardiac testing, even though potential problem spots might be missed. To make MRI tagging more useful—and more clinically feasible—a new method of processing the data was necessary. "It was always on my mind that we needed a better way," Prince recalls.

The Breakthrough Development: HARP MRI

In the late 1990s, Prince and his then-graduate student assistant, Nael F. Osman, found the answer. (Osman, who earned his PhD in 2000 at the Whiting School, is now an assistant professor in the Johns Hopkins School of Medicine's Radiology Department). The two scientists discovered that the motion of an MRI tagged heart generates an individual signal, which can be captured and decoded through the proprietary software they developed. The result produced high-resolution images like those created by conventional MRI tagging, but at a fraction of the original processing time. Prince and Osman presented a paper in 1999 that announced their new invention: harmonic phase (HARP) MRI. Their new imaging system combined proven MRI tagging technology with rapid processing software.



Part of a sequence of tagged MR images of a normal human heart. The images are analyzed with the Diagnosoft HARP tool and the regional strain of the heart is shown as color. Blue indicates normal contraction, green indicates low contractility, and white is no contraction.

"HARP MRI is just a very efficient processing method that can take the data you get from a scanner and produce maps of the motion or internal mechanical strain in the heart, which is really the characterization of local muscle deformation," says Prince. For the first time, there's now a way to provide the essential missing link to transform MRI tagging into a practical, cost-effective, and potentially lifesaving technology. As a result, notes Prince, "We think it will be a critical component of any cardiac MRI exam."

While a patient is still inside a magnetic resonance imaging scanner, by using HARP MRI, physicians will have an efficient means of determining whether a heart disorder or damage actually exists. If a problem is found, the immediate availability of images will help doctors decide whether the patient requires surgery or just a change in diet and exercise. In addition, the HARP MRI system can be used to check the effectiveness of new drugs designed to revive stunned heart muscles.

"I think the HARP concept could revolutionize or dramatically change the way we do cardiac stress testing," says cardiologist Joao Lima, who has used the system. "With it, we can receive quantitative results in a matter of minutes," adds Lima, who is associate professor of Medicine at the Johns Hopkins School of Medicine. "It allows us to see the degree and extent of the heart problems. There's nothing else that can do that right now."

From Inventors to Entrepreneurs

Once word of their new and highly marketable invention spread, Prince and Osman thought commercialization offers would follow in short order. To their surprise, none materialized. "To some extent, we were a bit naïve," says Prince. "We expected MRI companies to become interested right away. But that wasn't happening, although there was a growing interest in the research community."

Faced with the daunting tasks of promoting awareness of their invention, pursuing the next level of research and testing for it, and maintaining the pace of their academic duties, the two inventors hit upon a novel strategy. They would create a company to market HARP MRI while providing licensed beta versions of it to a few select cardiac MRI research groups around the world for evaluation and feedback. To that end, Diagnosoft, Inc. was founded in June 2002.

"We realized that having a company might serve a couple of purposes," says Prince. "First of all, it would provide a mechanism to get this product out to the research community, and in that way offload some of the burdens from us. Also, it would provide a mechanism for creating a uniform product that we could track and issue revisions for over time. At the same time, we knew that there would be an eventual market out there for HARP MRI if the software were made available. So it seemed the right time to make our software available commercially as well as to qualified researchers."

New Partners, Next Steps

In less than two years, this initial strategy has paid off. According to Prince, "The top research community is looking at what we're doing now and wanting to be involved. We have quite a strong following that is working with us to help refine and critique the beta product." Prince expects his company's first product, HARP Diagnosoft, to be released in a commercial clinical version sometime over the next year.

In the interim, Diagnosoft itself has grown. Two more partners have joined Prince and Osman, and the company also includes a team of three software developers in Egypt. In addition, Diagnosoft has benefited from the University's ongoing support through the Whiting School's Office of Industrial Initiatives. According to Lani Hummel, the office's director, " The University is becoming increasingly supportive of faculty who start companies." Hummel's office operates as the front line of that support, providing guidance to a range of resources for fledgling companies—from start-up funding from venture capitalists and state organizations to business assistance and marketing development. "These services are valuable for anyone wanting to learn about the process of getting a product out of the University and into the commercial marketplace," she says.

In the case of Diagnosoft, Hummel notes, "I think that Jerry and Nael have done all the right things to get their company started, and they've done everything they need to do to take the company to the next level." Diagnosoft has an option agreement with the University that allows for start-up time to raise money while testing the prototype technology.

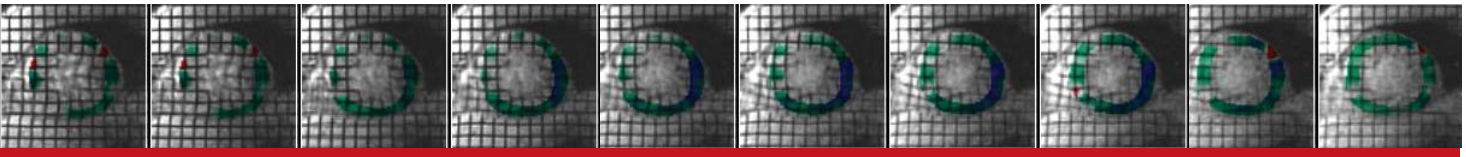
In return, Prince appreciates the University's role in getting his company off the ground. "I have to give Hopkins a lot of credit for going along with me," he says. "From the start, they stepped right up and wanted to help and be a partner in this activity. They have supported us throughout the patent process and continue to do their part."

Looking back at six years of whirlwind change in his professional life, Prince is somewhat amused by the turn of events but decidedly upbeat about his future. "I could have easily come to this point in my career and not have any invention that could be considered marketable," he admits. "But it was just too compelling not to do it. The entrepreneur thing is new to me, but I find it exciting and rewarding," he says with a smile. "Ours is a good story—a lot of strong work ethic and at the same time, a bit of luck."

Visit the Image Analysis and Communications Lab (IACL) at iacl.ece.jhu.edu/ and visit Diagnosoft, Inc. at www.diagnosoft.com .

Thanks to Phil Sneiderman for his contributions to this article.

The arrangements discussed in this article have been reviewed in accordance with Johns Hopkins' conflict of interest policies. Nothing in this article constitutes or implies an endorsement by The Johns Hopkins University of Diagnosoft, Inc., its products, or services.



Part of a sequence of HARP tagged MR images of a patient's heart, showing the lack of blue coloring (normal contraction).

Snapshot: Diagnosoft's Two Co-founders

Jerry L. Prince: (left) Chief scientist and chairman of the board for Diagnosoft, Inc. In 1989 Prince joined the Whiting School's faculty. He is the William B. Kouwenhoven Professor in the Department of Electrical and Computer Engineering and holds joint appointments in the departments of Radiology (School of Medicine), Biomedical Engineering, and Applied Mathematics and Statistics. He also is a researcher at the Whiting School's Center for Imaging Science and co-director of the Image Analysis and Communications Lab. Prince received a 1993 National Science Foundation Presidential Faculty Fellows Award and was Maryland's 1997 Outstanding Young Engineer. Together with Nael F. Osman '00 PhD, he has filed three patents related to MR image analysis.

Nael F. Osman '00 PhD: (right) Chief technical officer for Diagnosoft. While earning his doctorate at the Whiting School, he co-invented the HARP technique for rapid analysis of tagged MR images with Jerry L. Prince, his research advisor. Osman is now an assistant professor in the Radiology Department of the Johns Hopkins School of Medicine and a talented software systems architect. Prior to studying at Hopkins, Osman helped to develop a voicemail system now being marketed in Egypt.

IBM and Hopkins: An Innovative Approach in Bioinformatics

By Eileen Murphy and Janet Schumann

Computing power that used to fill a room can now fit in the palm of a hand. But not all of today's computational challenges can be met by equipment that can fit in a hand, or even on a desktop. Those involving vast amounts of complex information require leading-edge supercomputers with extraordinary processing capabilities.

Thanks to the IBM Corporation's recent gifts, the Center for Cardiovascular Bioinformatics and Modeling (CCBM) at the Whitaker Biomedical Engineering Institute now has the powerful computers it needs to create multi-scale computational models. These models, ranging from the genome and proteome to single cells and the whole heart, are expected to lead to important breakthroughs in the understanding of cardiovascular disease and to the prevention, diagnosis, and treatment of heart problems and other human disease.

Whiting School researchers and their colleagues at the Johns Hopkins School of Medicine will be using the powerful information systems being built to understand how genes and proteins interact to influence heart disease, and to target treatment solutions.

In June 2003, IBM recognized the center's work by naming Johns Hopkins University one of two charter members of IBM's Life Sciences Institutes of Innovation Program (the other is the University of Indiana).

IBM also awarded the CCBM a Shared University Research (SUR) Award for its ongoing work in mathematical and computational life sciences and informatics. CCBM's director is Raimond L. Winslow, who in 1998 created a virtual heart that could simulate cardiac arrest—very useful in researching lifesaving drugs. A professor of Biomedical Engineering, Winslow also has joint appointments including those in the Whiting School's departments of Computer Science and of Electrical and Computer Engineering.

The SUR grant will fund equipment and graduate fellowships in Winslow's programs at the Whitaker Institute.

IBM's awards bring to the CCBM massive computing capability and research opportunities. Over the next three years, the company's support for CCBM will total $1.2 million, primarily in graduate fellowship support, student aid, and equipment. Cumulatively, IBM has contributed more than $4.7 million to the Johns Hopkins University. Provost Steven Knapp described the Institutes of Innovation Award as representing "a collaboration between a world-class organization and a world-class university that share a dedication to harnessing innovation in the interest of meeting real human needs."

Dr. Carol Kovac, general manager of IBM Life Sciences said, "When we first talked about innovation institutes, we decided that we would build on longstanding collaborations. This institute is founded on a real intellectual and scientific collaboration between JHU and IBM." She spoke at the ceremony held in November 2003 at the Whiting School's Clark Hall to present the Institutes of Innovation award.

Dr. Carol Kovac (second from left), general manager of IBM Life Sciences, presented an IBM Life Sciences Institutes of Innovation award to Johns Hopkins University at a ceremony in Clark Hall in November 2003. Hopkins participants were (from left) Raimond L. Winslow, director of the Center for Cardiovascular Bioinformatics and Modeling; Steven Knapp, provost and senior vice president for academic affairs; Andrew S. Douglas, interim dean of the Whiting School; and Murray B. Sachs, director of the Whitaker Biomedical Engineering Institute.

The SUR award will provide CCBM with technology that can simulate complex and highly detailed models of heart cells, tissues, and organs, and seek variations in gene expression during disease states. Researchers expect to gain insights that could lead to new, more effective drugs for treating heart-related illnesses and to novel approaches for the understanding, cause, diagnosis, and treatment of other human diseases. IBM funds about 50 SUR awards a year, collaborating with institutions worldwide. In the process, it facilitates valuable connections among top researchers in academia and industry.

Murray B. Sachs, Massey Professor and director of the Whitaker Biomedical Engineering Institute, notes that the infusion of resources through the Institutes of Innovation designation will advance programs that "point the way to closer collaborations between the schools of Medicine and Engineering, which will place Hopkins among the leading institutions in computational biology, a crucial component of modern biomedical research."

Adds Winslow, "The future holds tremendous opportunity. There is a great deal of interest throughout the Whiting School in computational technologies. IBM is going to be a treasured partner in moving forward."

For more information on the Center for Cardiovascular Bioinformatics and Modeling, visit www.ccbm.jhu.edu . For more on IBM's efforts in the life sciences, visit www.ibm.com/lifesciences .

The Robb Challenge

Whiting School National Advisory Council member Dr. Walter L. Robb challenges donors to join him in funding graduate fellowships for engineering's future leaders.

Dr. Walter L. Robb has issued a challenge to Whiting School of Engineering alumni, leaders, and friends to join him in supporting graduate students at the School. Robb's gift of $500,000 will match contributions of $50,000 or more designated for the establishment of Engineering fellowships.

People are surprised to learn that Walt Robb is not a Hopkins alumnus, as he is a well-known figure on both the medical and University campuses. He freely shares his wisdom and leadership, including as a member of the Whiting School's National Advisory Council. Since the mid-1980s, his service has included membership on the Advisory Board of the Whitaker Biomedical Engineering Institute and on the Presidential Counse–lors (an advisory group to William R. Brody, president of the Johns Hopkins University).

Robb and his wife, Anne, who live in Schenectady, New York, have not forgotten to support their own alma maters, but as they have learned more about the very special qualities of Johns Hopkins, they wanted to play a part in the expanding programs and progress of the Whiting School. Robb says, "All over the country, I see Johns Hopkins University graduates who have contributed to our technical understanding and through that, to our quality of life."

"All over the country, I see Johns Hopkins University graduates who have contributed to our technical understanding and through that, to our quality of life." —Dr. Walter L. Robb

The Robb Challenge will help ensure that tomorrow's leaders have access to the best graduate programs and mentoring by the Whiting School's nationally acclaimed faculty.

Robb and the Whiting School are especially interested in encouraging donors who have not previously made gift commitments at the level of $50,000. Although corporate matching gifts are welcomed and encouraged, they will not count toward a donor's $50,000 qualifying amount. To qualify for the Robb Challenge, pledges will be matched on a first-come, first-served basis and need to be paid within five years.

Now a management consultant and president of Vantage Management, Inc., until December 1992 Robb was General Electric Company's senior vice president for corporate research and development. He directed the GE Research and Development Center, one of the world's largest and most diversified industrial laboratories, and served on the company's Corporate Executive Council. For 13 years, Robb headed GE Medical Systems. In September 1993, he received the National Medal of Technology from President Bill Clinton for his leadership in the CT and MR imaging industry.

At age 65, Robb retired from GE, and began a second career. For the past 10 years, he has served on the boards of more than 10 start-up companies; six have gone public or been acquired. As a strong supporter of New York's "Tech Valley," he is a frequent angel investor. The founders of these new companies soon learn that he doesn't just invest and patiently wait. During his many visits, he wants to be challenged for his ideas, not just his investment. Presently, he serves on the boards of two public companies, Celgene and Mechanical Technology, Inc.

A member of several community and alumni boards, Robb co-chairs the effort to upgrade a historic theater in Schenectady. Just for fun and to keep the team in the area, he purchased the Albany River Rats, an American League Hockey team. As the farm team of the New Jersey Devils, the River Rats proved to be a real source of excitement on his sports agenda. He also enjoys skiing and playing tennis. To celebrate his 70th birthday, he and his three sons climbed Mt. Kilimanjaro, the highest peak in Africa.

For more information on the Robb Challenge, contact Associate Dean Michael Moyer at (410) 516-8723 or moyer@jhu.edu .