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INNOVATOR OF THE YEAR

Innovation that Resonates

In his quest to advance the early detection of breast cancer, Cameron Piron, the 2008 *R&D Magazine* Innovator of the Year, is staying at the forefront of a renaissance in magnetic resonance imaging.

More than 60,000 medical and science professionals from 100 countries attended the Radiological Society of North America's (RSNA's) annual meeting at McCormick Place in Chicago last month. The world's largest event for radiological sciences and technology—including x-ray imaging, computed tomography, and magnetic resonance (MR), among others—this show represents a fusion of advanced physics, mathematical theory, and high-speed computing for medical advancement.

In attendance was Cameron Piron , president and CEO of Sentinelle Medical Inc., Toronto, Ontario, who was there representing both his company and its marquee technology, the Vanguard G-Series system, a specifically designed detachable imaging table to provide comfort, speed, and flexiblity for breast cancer screening.

It was Piron's second time in Chicago in little over a month. He was previously at *R&D Magazine's* R&D 100 Awards event at Navy Pier to accept his 2008 Innovator of the Year Award.

"RSNA's annual meeting is a massive show this year," he said prior to the event, which helps highlight the importance of MR technology to medical imaging. Used to produce high-quality images of the inside of the human body, MR imaging (MRI) reads radio frequencies emitted when protons align and re-align under changing magnetic fields provided by large coils.

With refinements over time, MRI has advanced beyond its roots in tomography to become a volume imaging technique. Better still, and in part because of Piron's work, it has also become a dynamic technique able to deliver temporal data as well. However, for years the technology was tied to large expensive machines which were uncomfortable and generally best used for MR's original medical purpose: head and spinal studies.

Piron, who entered the medical field with a background in systems engineering at a pivotal point in the understanding of how cancerous tumors behave, set a goal for himself to build a system that would finally bring fast, useful imaging to women at risk for breast cancer. Along the way, the research behind his product spawned four academic papers (two of which won international awards), 15 invited talks (two winning awards), 22 abstracts, and the core intellectual property (IP) for Sentinelle Medical. To date, Piron has developed or co-developed two patents (granted) as well as 10 provisional patents and 19 that are filed.

Bringing MRI to the fight against breast cancer

Born on Prince Edward Island, Piron moved to the city at a young age. In Toronto, his father worked for medical device supply companies in what become known as a sort of medical alley. The city had developed world-class medical institutions and in particular the Univ. of Toronto and the Univ. of Western Ontario, London, became well-known for their strong service and technology. There were also medically oriented research centers, such as Sunnybrook Research Institute, Toronto, and Robart's Research Institute, London, Ont.

Piron started out in systems design engineering at the Univ. of Waterloo, Ont., then joined the medical biophysics program at the Univ. of Toronto. He soon learned he was one of many students advancing from

systems engineering, which was blend of mechanical and electrical engineering with a heavy dose of physics and math, to medical biophysics.

The medical biophysics program, meanwhile, was combination of medicine, genetics, and immunology, but Piron quickly joined the imaging technology group, separate from the main campus. Though still fully affiliated with the Univ. of Toronto, it is well removed from downtown near one of the largest teaching hospitals in Canada, Sunnybrook Medical Center.

"The idea was to get an imaging research group immersed in the hospital environment," he says. It integrates MRI, ultrasound, and x-ray technologies on one floor, allowing students to work together and overlap with each other on projects. Here, Piron began his career in cancer imaging.

Of the nearly 200,000 American women who find out they have breast cancer each year, as many as 10% have a hereditary form of a genetic mutation—the BRCA1 and BRCA2 genes—that greatly increases their risk of cancer, according to the National Cancer Institute. This is particularly true, historically, for breast and ovarian cancer. Worse, carriers of these genes have fibrous tissue in the breast that complicates mammography's ability to detect subtle differences between tumors.

Sentinelle's Vanguard G-Series system unites detection and treatment. Magnetic resonance imaging and ultrasound can be done from the same comfortable platform. Photo: Sentinelle Medical Inc.

Recognizing the need to develop quick and efficient screening methods to catch cancer development early, especially in women with these mutations, medical researchers needed a better way to both detect cancer and translate that detection into treatment. Conventional surveillance with mammography and clinical breast examinations is often unable to detect potential risks, especially in younger women whose higher breast density compromises the low sensitivity of mammography.

"Early detection is the best way of managing cancer," says Piron. Several studies, he says, point to the importance of a physician finding the cancer before it reaches "stage 0"; that is, before it reaches about a centimeter in size. "If you were to resect that tumor, you would have a five to 15 year survival rate in the patient, which is almost the same as if the patient didn't have cancer at all. That's pretty astounding," says Piron. "Basically it means if we can see it and guide treatment to that tumor, it's as close to a cure as you can imagine."

That reality is becoming more widely known, says Piron, and right now imaging technology is the mainstay of efforts to maximize early detection. But early in his career, the tools for finding such small tumors did not exist. Magnet coils, designed for signal-to-noise ratio of antennas, were not appropriate for the sort of imaging Piron intended; breast tumors start small and double in size in a very short time frame. Also, the coils at the time, he says, did not have any real access for doing intervention work, such as it was.

"This was really the fundamental problem that people hit. People were able to see tumors that they were only able to see with MRI, yet they weren't able to see them with any other imaging modality," says Piron. This meant techniques for performing biopsies of breast tumors were underdeveloped.

It's a continual problem in radiology, he continues.

"The ability to see new disease is always coming up and what has to lag afterwards is a way to perform interventions on those new tumors."

The MR magnet was first developed along a long, horizontal bore for neurological imaging. Only fairly recently has its use been adapted for oncological purposes, such as breast, colon, prostate, and even liver cancer screening for early stage detection. For breast cancer in particular, MRIs are frustratingly inconvenient. Having a patient lie down in a long narrow tube is not the ideal way to image a soft tissue like the breast. Nor is it good for biopsies or other treatments.

From 1997 to 2000, Piron participated in an ambitious study that screened 180 women aged 25 to 60 who were at a high risk for breast cancer. Conducted at Sunnybrook & Women's College Health Sciences Center, Toronto, Ontario, the study screened women using both MRI and ultrasound in addition to the traditional methods of screening. The results proved the value of the comparatively advanced methods, but it was MRI that was the most highly vindicated, finding 11 of the 15 cancers discovered the study. In comparison, seven were found by ultrasound, seven by mammography, and just two by clinical breast examination methods. The team concluded that MRI

significantly improved cancer detection rates and improved accuracy and specificity with subsequent screenings.

Piron shared in a Lynne Cohen Foundation Prize with the 13 others after the research was presented at a New York Univ. symposium in April, 2004. In part because he was the technical engineering lead on this study (the others were surgeons and oncologists), he was in an ideal position to investigate the possibility of developing a system that used both ultrasound and MR technology.

In fact, Piron had already been working on a new system for breast imaging for many years, acting on some ideas from Sunnybrook senior scientist Don Plewes, who felt a solution should be found for an easy way to conduct both MRI and ultrasound on a patient.

"A Hybrid Breast Biopsy System Combining Ultrasound and MRI," published IEEE Transactions in Medical Imaging in 2003, was the first description of the system design and initial accuracy results for the new biopsy system, which successfully integrated both MR and ultrasound imaging modalities. A comparison of core biopsies using MR vs MR/ultrasound showed a marked improvement in detection, nearly 25%, suggesting a hybrid system would reduce the need for repeat MRI scans.

Meanwhile, the Sunnybrook study led to another larger study that showed an 84% detection rate of cancer using MRI, as opposed to just 36% for mammo-graphy and 33% for ultrasound.

A critical mass had been reached, and medical insurance companies were recognizing its value. These studies led to Blue Cross covering costs for MRI screening for high risk patients, a move that helped spur further R&D.

"We were very early in the game in use of MRI for breast or any cancer in screening and detection," says Piron, so the development of antennas, software, and needle guidance systems, which have become widespread for functionalized MRI, was uncharted territory. His work at Sunnybrook put him is direct contact with clinicians, who responded to prototypes with certain demands. In time, Piron's team was forced think outside the MRI "tunnel".

"As we moved forward we realized there were some very fundamental constraints on the magnet configuration at the time," says Piron. They removed the MRI table from the magnet and redesigned the front end of magnet. They then revamped the table to be used with the magnet. From there, they found new ways to apply antennas that would improve the signal-to-noise ratio of the system. At the same time, Piron had familiarized himself with the analytics component of MR technology, drawing on his exposure to signal processing and Fourier domain mathematics to develop what would become the Aegis BRIGHT software platform.

"Because MR basically relies on contrast agents to detect tumors—and it's a dynamic system—we are able to get 3-D information at over time. We have a 4-D data set," says Piron. It's important, he says, to interpret that data through color coding and other techniques so that the radiologist is not drowning in data. It allows the radiologist to look at the data in an efficient manner and interact with it through reformatting 3-D data to get a better idea based on the contrast and morphology of the tumor.

The founding of a company

Prior to founding Sentinelle, Piron concurrently worked as VP of R&D for two small medical device companies, Samarit Medical and Pinel Medical, where he was involved in product development, manufacturing process definition, sales, service, and marketing functions.

Sentinelle Medical's MRI products are blend of ergonomics and high-technology. Photo: Michael Wybenga

But his work on what would become the Vanguard was so promising, in 2004 he and several collaborators entered the private sector. Spun off from Sunnybrook, Sentinelle Medical Inc. established itself as a manufacturer of breast MRI coils and software. With co-founders, Gal Sela and Chris Luginbuhl—as well as Plewes—Piron initially led a very small team, but it quickly grew as progress was made with the company's Variable Coil Geometry, which allows imaging coils to be customized for each breast of every patient. The theory behind a variable magnet is that it would substantially improve signal-to-noise ratio, one of the crucial needs for detecting small tumors. Piron's background in engineering and mathematics greatly aided in this development.

At Sunnybrook, he had been used to working with three or four people at the most, but as many as 30 people at once were soon employed on the development of what would become the Vanguard platform. Typically, the MRI scene was saturated by big players, the likes of Siemens, Philips, and GE. Sentinelle sood out; it was one of the first companies to develop its own MRI platform, says Piron, so much of the work was pioneering.

"We literally built multiple prototypes of the system every month of the course of a year," says Piron. The team evaluated access, patient comfort, and clinician's comfort and finished with a product much different than in the early stages. The final iteration allowed better access, more room for the patient, and allowed space for multi-modality products, which are the next stage of products for Sentinelle.

Flexibility continues to be a key product characteristic—often the company must optimize its solution for the magnets that are out there in service. This means that its proprietary receiver-array antenna must be tailored to 1.5 T or 3 T systems. These antennas collect the signal created by the magnetic field, sending it to the computer. The antenna plugs into the magnet, and data acquisition is performed off of the magnet system.

Antenna use is becoming popular in MR technology now, says Piron, because the sensitivity is good and it allows biopsies to be performed at the same place.

"Initially the intention was not to take this to multiple sites. It was just a solution to a research project at Sunnybrook. As we started presenting it and writing papers on it and having people coming to see it, it became very clear this was becoming a solution that many people needed and many people requested," says Piron.

Now, the company is driving its coil technology and its stretcher technology for safe patient transport as well as its Aegis BRIGHT software. Piron sees a tremendous potential for improvements for coil technology for the increase of signal-to-noise ratio. He anticipates an increase in the ability to use the rich variety of information acquired during MR.

Clinicians are beginning to pick up on that tool as MR increases in use and are now using it to determine whether the right chemotherapy is being applied to the patient pre-surgery. This ability has shown significant improvements in clinical outcome, says Piron, and as a result, he views MR largely as a therapy tool.

"MR is relatively primitive compared to other imaging techniques. There's still a lot of room for improvement," he says.

Success leads to new directions

Sentinelle's growth mirrors that of MR innovation in general. At the RSNA show, Sentinelle was just one of dozens of companies pursuing new approaches to medical imaging using MR technology, but it also remains one of the fastest-growing and innovative small companies. At that show, Sentinelle announced they would be entering into a distribution agreement with Toshiba America Medical Systems Inc. for the Vanguard T-Series coil. Under the agreement, Toshiba will offer the 1.5 T, eight-channel tabletop breast coils for Toshiba's own systems, the Vantage Atlas and Vantage Titan. According to Bob Giegerich, director of the MR business unit at Toshiba, the Sentinelle variable coil geometry coils increased the single-to-noise ratio when they were used in Toshiba's MR system. With these coils, exams using the Toshiba systems can also be performed feet first, reducing patient anxiety and claustrophobia.

Clearly, the deal is advantageous for Sentinelle, which will be able to expand the accessibility of its successful system which is already used in more than 100 hospitals and facilities throughout North America. These include the H. Lee Moffitt Cancer Center and Research Institute at the Univ. of South Florida, Scripps Memorial Hospital, Sunnybrook Health Sciences Centre, and most recently Mountain Medical Imaging Center in Salt Lake City, Utah.

Piron has also recently expanded the board of directors at Sentinelle, which already includes health professionals at major hospitals and executives involved in several radiology-related companies. The company itself is expanding, too. Now leading 75 employees, Piron says they are now doubling in size every six months. His work is being recognized on a larger scale as well; earlier this year, Piron earned a "Best Young Innovator" Award from Ontario's Ministry of Research and Innovation.

"I think it was a series of steps. It was a direction that really brought me challenge and pleasure," says Piron, who credits his previous exposure to the medical device field while working for his father's medical devices company. Ludwig Piron helps develop and market medical devices products with Pinel Medical in Waterloo, Ontario.

"On one end [we're] doing research on MRI, which is very high-tech, whereas he had very low technology but equally pragmatic solutions that were helping people in a hospital. I was able to see the two sides of the medical technology industry and see the importance in both," says Piron.

According to Danielle Whittemore, who wrote a profile about Piron for the "Imprint Online" newspaper, he still has strong ties to Sunnybrook. Many employees at Sentinelle are from the school. The atmosphere at Sentinelle is one of collaboration, where everyone from Piron to the newest employee pitches in new ideas or solutions to problems.

The enjoyment of bringing medical solutions to lots of people is, he says, as equally motivating as the challenge of developing the technology itself. He hopes his work will help significantly reduce the burdens on the health care system. Costs go up exponentially the later a cancerous tumor is detected.

"I think everyone has a story of someone who has been affected by cancer, so there's a motivation there, too," he says.

—Paul B. Livingstone

RESOURCES

- **Sentinelle Medical Inc.**, Toronto, Ontario, 866-735-3744, www.sentinellemedical.com
- **Sunnybrook Research Institute**, Toronto, Ontario, 416-480-6100, www.sunnybrook.ca/research