IMAGES OF

SUNNYBROOK RESEARCH INSTITUTE SPIN-OFF SENTINELLE DOES DOUBLE-DUTY WITH AN MRI BED THAT IMPROVES WOMEN'S COMFORT WHILE MAKING MORE EFFICIENT USE OF TECHNOLOGY

EXCELLENCE

The image Cameron Piron pulls up on his laptop computer is as disturbing as it is beautiful. It is a mammogram of a woman's breast, its cloudy appearance obscuring a deadly secret: a tumour nestles inside the white swirls. Piron, who is president of Sentinelle Medical, a Toronto company spun off from Sunnybrook Research Institute (SRI) to produce breast magnetic resonance imaging (MRI) devices, along with supporting electronics and software, knows it's there because he knows it's there—not because the blotch of disease is visible to the naked eye. Which is just the point.

Alongside this shot is an MRI of the same breast. In this one, the cancer is unmistakable: a glowing white pool at an intersection of a dozen spidery tributaries.

Sentinelle celebrates the superiority of the latter over the former, particularly for a segment of the breast cancer population. And the celebration is made material with Sentinelle's development of a breast MRI biopsy system that extends a conventional MRI scanner's application to places previously unimagined. Sentinelle's innovation is one of the first medical devices developed at Sunnybrook that has secured United States Food and Drug Administration (FDA) approval.

DR. DON PLEWES

Mammography has long been the standard for breast cancer detection. But it is failing women who carry the BRCA1 or BRCA2 gene. The breast tissue of these women, at risk for contracting cancer at a much earlier age, is quite different from that of postmenopausal women. It tends to exhibit an abundance of cycling fibroglandular tissue, a characteristic that complicates a mammogram's ability to pick up subtle differences for their similar appearance to tumours.

MRI is a three-dimensional technology that uses the nuclear properties of hydrogen protons in body tissues—which offer rich signatures—and the dramatic contrasts among them to highlight breast tumours. It has the advantage of not using ionizing radiation, which has a proven—if extremely small—carcinogenic risk. And MRI bypasses the fibroglandular issue thanks to the intravenous injection of a contrast agent that ultimately sequesters in tumours as a result of tumour angiogenesis, a biological process whereby cancer cells recruit and create new blood vessels to support their need for tumour growth. These blood vessels are different from normal blood vessels in that their permeability to this contrast agent is somewhat higher.

Research is ongoing, but the emerging conclusion is that MRI is the best bet for early detection of breast cancer in this population—about 84% versus 36% for mammography and 33% for ultrasound, based on findings from a large Sunnybrook study headed by Dr. Ellen Warner at the Toronto Sunnybrook Regional Cancer Centre. It is, says Dr. Don Plewes, a senior scientist at SRI, co-principal investigator of the study and founding member of Sentinelle, "just a spectacularly ingenious and fantastic imaging method." That MRI—traditionally used mostly for neurological applications—is now acknowledged as an optimal breast-cancer detection tool makes perfect sense to him.

Soon after Sentinelle launched, exploding onto an MRI scene dominated by big players like GE, Philips and Siemens, its founders became aware of an inherent challenge to their field. Breast MRI is limited in its ability to facilitate the next logical step after breast cancer has been detected: intervention.

In the conventional unfolding of events, a patient undergoes an imaging procedure and, if evidence of a suspicious mass is discovered, the next

DR. DON PLEWES AND CAMERON PIRON

step is to draw a tissue sample for histopathology. But for those scenarios in which only MRI can detect the tumour, this unfolding can be problematic. Undertaking a biopsy under the influence of a powerful magnet in the tight confines of an MR unit is often unrealistic, and only in an ultrasound setting can a technician draw a tissue sample and feel reliably ensured, thanks to the visual touchstone, that the tip of the needle is in the tumour, and that it's capable of slicing out a sample for microscopic analysis.

What if, Plewes conjectured, you could take MR images of a patient, wheel her out of the magnet room and into another room, still in the bed, coordinate the 3-D MRI images with an ultrasound probe and extract the tissue—even though the radiologist may not see the tumour?

In 1992, Plewes handed the project of developing technology that could handle MRI-guided biopsies to Piron, then a medical biophysics graduate student at the University of Toronto, where Plewes is a professor. It was June 2004 before the pair cast their eyes across the technology they'd produced and decided that it, in conjunction with the experience they'd amassed in its creation, might provide the basis for the formation of a commercial enterprise.

"We were presenting this technology at conferences," says Piron, "and we had world-class researchers and clinicians saying, 'When can we get one of these tables?' It occurred to us that there might be an opportunity, or even an obligation, to take this to the next stage."

The modular design of Sentinelle's stretcher allows better access to the breast than does the typical MRI bed, which, says Piron, "has terrible ergonomics with only a small window to get at the breast." If a patient's tumour is medial—in the middle of her breast—radiologists using Sentinelle's bed can biopsy from the middle, meaning they needn't cross as much tissue as if they had approached it laterally, which they would have to do with a conventional system.

But the most remarkable thing about the bed is that it adapts the old standard such that it can accommodate not only an MRI session but a biopsy, as well. A patient in it—lying prone, her breasts pendant and snug against the coils in the sophisticated boxes designed to house them—needn't change her position for MR and ultrasound imaging.

It is, says Plewes, a more efficient use of all the imaging modalities. "Now you're using ultrasound and MRI for what they're both best suited: ultrasound for real-time guidance and MRI for initially detecting the tumours and then quickly releasing the magnet for the next patient. By fusing these imaging modalities, you get the best of both worlds and maximize the utilization of expensive MRI resources."

Just the same, the scientists don't demur from an admission that going commercial was a leap that came with hurdles. It was all tied into a mentality shift, says Piron, from being "perfectionists in R&D" to negotiating a new range of tasks previously outside their purview.

The future for Sentinelle, says Piron, is all about improving accessibility to MRI for cancer detection and management. Indications for MRI have opened up like a hand in the time since Sentinelle first nudged into the picture, and the company has plans to go beyond breast cancer.

"We talk up the notion at Sunnybrook of bench-to-bedside research," says Plewes, currently on sabbatical from U of T at UBC. "That's true, but in order for things to reach the bedside in a general way, it really needs to be bench to bedside to commercialization. Unless some other entity can acquire the technology you've used to get from bench to bedside, it's useless. We tend not to talk much about that third piece, but it's actually critical for the first two to be meaningful." LP

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