Funded: Centre for Research in Image-Guided Therapeutics

A Centre is Born

By Stephanie Roberts

On a late summer's morning crisp with expectation, Dr. Colin Carrie, parliamentary secretary to the minister of industry, and Dr. Eliot Phillipson, president and CEO of the Canada Foundation for Innovation (CFI), announced an investment of $74.6 million to build and equip the Centre for Research in Image-Guided Therapeutics at Sunnybrook Health Sciences Centre. It is the single largest award ever made to the hospital.

"Sunnybrook Health Sciences Centre has been a pioneer and world-leader in the field of image-guided therapeutics research. The new facility will undoubtedly lead to the development and application of innovative imaging approaches to the diagnosis and management of cancer, heart disease, stroke, musculoskeletal and other disorders," said Phillipson.

The centre, which will be unique in Canada, will develop and test state-of-the-art medical imaging technologies, therapeutics and standards of practice, and translate them into the clinic. It will transform medical imaging by enhancing diagnosis and therapy for some of the most urgent problems in health care.

Carrie and Phillipson announced the federal funding, made through the CFI's Research Hospital Fund (RHF), on August 20, 2008, at an event to celebrate the four Toronto-area recipients. In addition to Sunnybrook, SickKids (which hosted the event), the Centre for Addiction and Mental Health, and the University Health Network received awards.

"I am personally proud of our researchers, through whose work Sunnybrook Research Institute has tripled in size over the last five years to become one of the largest research institutes in Canada," said Dr. Barry McLellan, president and CEO of Sunnybrook. "This grant will allow our research teams to take giant strides forward in improving the health of our patients and achieving our vision of inventing the future of health care."

"This is one of our most gratifying moments," said Dr. Michael Julius, vice-president of research at Sunnybrook. "We are thrilled with the CFI's recognition of the transformative potential of this research. Their investment is a tribute to our scientists and their teams."

Sunnybrook Research Institute (SRI) submitted a budget of $143 million to build and equip the centre. The CFI will fund up to 40% of a project's cost; it awarded the full amount to SRI, $57 million. The remaining $86 million was secured from other funding agencies, industry partners, SRI and Sunnybrook Foundation. On top of this, the CFI awarded $17.2 million to SRI toward the running of the centre, bringing its total investment to $74.6 million, and the total project cost to $160 million.

Dr. Eliot Phillipson, president and CEO of the Canada Foundation for Innovation, talks with Dr. Sandra Black, director of the neurosciences research program at SRI, at the Research Hospital Fund announcement held on August 20, 2008

Establishing this centre will add more than 100,000 square feet of research space to Sunnybrook. Dr. Kullervo Hynynen, director of the discipline of imaging at SRI, leads the centre, which amasses a team of 55 scientists and clinician-scientists spanning every discipline and four research programs (cancer, cardiac, musculoskeletal and neurosciences) at SRI.

"With this award, we can build a centre that will be the only one of its kind in the country and perhaps in the world," said Hynynen. "It will help us do the innovative research in medical imaging, with an emphasis on developing new therapeutics, for which Sunnybrook is known globally. It will also be very attractive to collaborators, industry partners and young trainees."

Many saw the RHF as a once-in-a-lifetime opportunity. The $500 million fund was created by the federal government in 2003 as part of its Accord on Health Care Renewal to answer the cry of help from hospitals for more research space. In the first competition, in 2004, $57 million was awarded. This, the 2007, competition was the final and fiercest one. There were two streams: one for clinical research and the "large-scale institutional endeavours" stream for huge, space-hungry projects. It was this latter stream, the one to which SRI and 27 other hospitals applied, that generated the most buzz. Unlike regular CFI programs, the focus was on space, not apparatus, although some equipment was admissible, capped at 30% of the project cost.

Also unlike regular CFI competitions, the RHF was open only to hospitals. This, rather than moderating the competitive heat because fewer institutions could apply, increased it acutely, as most of the major research hospitals in Canada submitted proposals, and for big dollars. The CFI's infrastructure budget was $427 million. Hospitals requested almost three times that: $1.1 billion. In the end, only eight proposals made it through.

While the need was all about space, the proposal's success was all about science.

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Making up the Centre for Research in Image-Guided Therapeutics are four institute-wide 'platform' facilities, each spanning a range of disciplines and research programs at Sunnybrook Research Institute. This unique structure was designed in this way to maximize interaction among scientists, and to speed discoveries seamlessly along the continuum of translational research.

Translational Research Facility


Dr. Juan Carlos Zúñiga-Pflücker and Dzana Dervovic

The translational research facility at Sunnybrook Research Institute (SRI) will have four labs enabling innovative research into and development of new biological agents, vaccines and devices for image-guided interventions.

The **laboratory for cellular and molecular regeneration and repair** will be dedicated to harnessing the regenerative potential of different types of stem cells, and developing methods for directing stem cell differentiation to repair cardiac and immune system dysfunction. Scientists will work to design new tissue regeneration strategies, and novel methods to visualize this process in vivo. It expands upon the Centre for Molecular and Cellular Response and Repair at SRI, part of the McLaughlin Centre for Molecular Medicine, and SRI's Advanced Regenerative Tissue Engineering Centre.

The **molecular targeting and therapeutics laboratory** will be a chemistry lab outfitted for the creation, purification and validation of novel imaging contrast agents and drug delivery systems. Work in this lab will speed the translation of new imaging agents, molecules and particles to phase 1 clinical trials. The aim is to develop innovative approaches to medicine in which the molecular signature of disease can be detected and imaged, thus enabling precise and targeted treatments.

The **molecular therapeutic good manufacturing practice (GMP) laboratory** will enable scientists to design and test cGMP-grade biologicals—cell-based drugs and agents produced under strict guidelines. In doing so, this lab will expedite the translation of preclinical findings to patients, particularly those with cancer, cardiac disease or immune dysfunction. A truly multidisciplinary facility, it will bring together scientists and clinicians who are committed to exploiting the exciting potential of cell-based therapies.

The **biomedical device development laboratory** will be Canada's first such lab. It will bring together into one facility all the device-making equipment SRI has, and add essential new components to the facility, including clean rooms and laser machining equipment. For the first time in one centre, researchers will be able to design, fabricate and test complex medical devices for clinical evaluation, primarily in cancer and cardiac disease, and, ultimately, for commercialization.

Principal researchers who will use this facility are **Drs. Charles Cunningham, Dan Dumont, Stuart Foster, Donald Plewes** and **Juan Carlos Zúñiga-Pflücker**. A score of other scientists and clinician-scientists at Sunnybrook will also benefit from it.

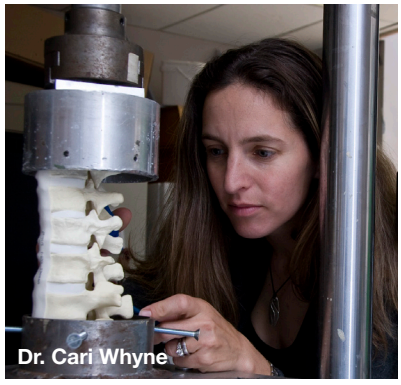
Preclinical Testing Facility

The preclinical testing facility at Sunnybrook Research Institute (SRI) will have a vivarium, a suite for image-guided surgery, and the multimodality small animal imaging centre (multi-MoSAIC). This facility, which will be unique in Canada, is vital to the Centre for Research in Image-Guided Therapeutics; it integrates all aspects of the centre's preclinical and clinical research, and will be indispensable in speeding the translation of results from bench to bedside.

The construction of a new **vivarium** primarily for large preclinical models is perhaps the most urgent need for SRI, as the current use of preclinical models for research is far lower than the capacities of researchers. A new vivarium, moreover, is essential to SRI's ability to attract new scientists and trainees who use preclinical models. The aim of all of these researchers is that which is at the heart of the centre, and indeed SRI: to develop and evaluate novel diagnostic, monitoring and therapeutic approaches to alleviate human disease and suffering.

The **image-guided surgery facility** will be a state-of-the-art operating suite used to develop and optimize minimally invasive procedures for musculoskeletal (MSK) and cardiovascular surgical applications, and noninvasive imaging methods for neurosciences and cancer applications. The rooms will house specialized equipment, including a C-arm (for fluoroscopic X-ray procedures), an O-arm (conebeam computed tomography) and a 3-D ultrasound imaging system. Few labs in the world are set up for computed-assisted surgical MSK applications or large preclinical models of cardiovascular disease. This facility will enable both and go further, by integrating the specialized imaging technology (like conebeam computed tomography and 3-D ultrasound) with work to optimize its translation into treatment for complex MSK conditions.

Multi-MoSAIC will bring together researchers in magnetic resonance, micro-computed tomography, micro-positron emission tomography and ultrasound into one facility where they can apply innovations in imaging research to pertinent biological questions. A main focus will be on cancer; for example, scientists will use molecularly targeted ultrasound-activated microbubbles to target blood vessels in tumours. This centre will house state-of-the-art infrastructure, including a 7T magnetic resonance imaging system.


Dr. Cari Whyne

Principal investigators who will use this facility are **Drs. Michael Bronskill, Greg Stanisz, Bojana Stefanovic, Brad Strauss** and **Cari Whyne**. Many more scientists and clinician-scientists from across Sunnybrook will also benefit from it.

The Centre will add more than 100,000 square feet of research space to Sunnybrook, primarily on two new floors atop the main (M) wing.

Clinical Research Facility

The clinical research facility at Sunnybrook Research Institute (SRI) will create three new centres: the neurointervention centre, the minimally invasive electrophysiology and vascular procedures centre, and the magnetic resonance imaging (MRI)-guided focused ultrasound surgery centre. It will also create shared clinical research working space.

The **neurointervention centre** will use image-guided technology to develop new and better ways to treat stroke and dementia, and to enhance recovery from stroke. It will house equipment for electrophysiological monitoring and biofeedback, and for quantification of movement, gait and balance. Researchers will use trans-skull MRI-guided focused ultrasound with clot-busting agents to achieve faster and more effective stroke treatment. They will also test the usefulness of this technology to deliver drugs to the brain to treat tumours there. There are only two devices with this capability in the world, each of which operates at a different frequency. Researchers at SRI will build the world's first focused ultrasound device that incorporates both frequencies.


Dr. Kullervo Hynynen (right) and Sam Pichardo

The **minimally invasive electrophysiology (EP) and vascular procedures centre** will build on Sunnybrook's Imaging Research Centre for Cardiac Intervention (IRCCI), a unique facility that assembles an array of imaging methods into a single suite designed for patient studies so that results can be translated quickly into the clinic. The new centre will extend the capacity of the IRCCI, enabling more patients to be studied, and new and different studies to be done. Scientists will develop and test image-guided cardiovascular therapies for electrophysiology, heart tissue regeneration and revascularization, and minimally invasive vascular and cardiac surgery.

The **MRI-guided focused ultrasound surgery centre** will be unique in Canada. It will crystallize SRI's position as a leader in the development, assessment and clinical translation of MRI-guided focused ultrasound surgery devices. Clinical and basic researchers will work with engineers and industrial partners to develop and test focused ultrasound devices to treat uterine fibroids and other benign tumours in preclinical models and then in patient trials. They will also develop versions of the technology for potential use in the treatment and palliation of cancer. The facility will have a dedicated 3T magnet and a clinical focused ultrasound surgery device.

Principal researchers who will use this facility are **Drs. Sandra Black, Peter Burns, Greg Czarnota, Alexander Dick** and **Kullervo Hynynen**. A score of other scientists and clinician-scientists from across SRI will also use it.

Treatment Planning, Analysis and Evaluation Facility

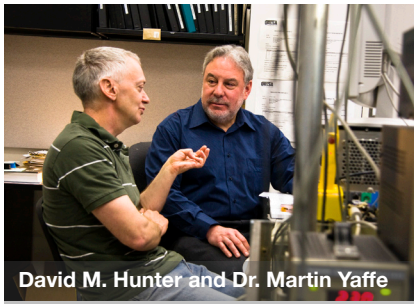
The treatment planning, analysis and evaluation facility at Sunnybrook Research Institute (SRI) will combine a state-of-the-art image-processing lab with a facility for whole-mount 3-D histopathology and immunohistochemistry to provide exceptional capabilities in validating and optimizing new techniques that SRI scientists are developing for imaging in cancer, and cardiovascular and neurological conditions.

The **image-processing laboratory** will gather into one space all SRI scientists and engineers working on image-processing techniques to form a critical mass of talent. Researchers will perform advanced analysis and visualization of the huge amount of image data produced for diagnosis and treatment planning to be able to make effective use of these data. The lab will improve cross-fertilization between different application areas and modalities, and eliminate duplication of commonly used software components. It will also offer software training to researchers at Sunnybrook to help them improve their understanding and application of image analysis techniques, and thus move study results into the clinic faster. Rooms will house high-end graphics workstations, and there will be a 3-D viewing room equipped with a stereo projection facility.

The **3-D histology/immunohistology facility** will provide a strong capability in histopathology/immunohistochemistry that is tailored to the needs of researchers at SRI. Histopathology is required in research as the source of "truth data" in preclinical investigations, for validation of the information that is extracted from novel in vivo medical imaging techniques that SRI scientists are developing, and for assessing the effects of therapeutic intervention. The lab will address the demand from external researchers for techniques in 3-D whole-mount histopathology developed by Sunnybrook scientists, who are pioneers in the field, and allow SRI teams to develop new capabilities.

The work in this unique facility on image registration and analysis techniques will enable SRI scientists to fuse anatomic and functional information from new and developmental in vivo imaging systems with biological data from surgically resected tissue as presented in large-area 3-D histopathological datasets. This will allow researchers to gain insight into the molecular nature of disease processes; guide the development of new, targeted therapies; and provide validation for translation into clinical use.

Primary researchers who will use this facility are **Drs. Bob Kerbel, Anne Martel, Arun Seth, Graham Wright** and **Martin Yaffe**. Many other scientists and clinician-scientists from across Sunnybrook will also use it.


David M. Hunter and Dr. Martin Yaffe

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The Centre for Research in Image-Guided Therapeutics was conceived as a set of four interlocking "platforms," each involving a core of five scientists and over a dozen other researchers and clinician-scientists (see centre spread for overviews). Central to each platform and the proposal itself was an encapsulating focus on image-guided therapeutics: developing and using basic science methods and imaging technology to transform diagnosis and treatment across a range of medical conditions. This platform-based structure was unorthodox, driven as it was by methods and technologies and not by disease focus.

It was also risky. The CFI was used to evaluating proposals built around disease or organ foci. In beginning to develop the proposal, however, it became clear that this would be an artificial approach for SRI. What made sense—especially when evaluated with an eye to maximizing functionality, reducing redundancy and leveraging resources across the research institute—were facilities that could be shared by many to do research wide-ranging in its eventual clinical impact, under the framing "meta-theme" of image-guided therapeutics. Accepting that it was risky, the group proceeded to assemble the proposal.

It took nine months and a multitude of meetings to build. Research administration played midwife and led its development. Sunnybrook's facilities planning department helped construct the space elements. It was a long and sweaty summer, with all eyes trained on September 11, 2007, submission date.

After submission, review. A proposal had been born, but not yet a centre. Evaluation, always stringent, became even more so when, taking applicants by surprise, CFI added another level to the review after all proposals were in. It introduced a step between the usual expert committee and international assessment committee stages. In announcing this change, it noted that the third level was needed to balance ". . . the expert review of individual project themes with an assessment of the overall quality of the projects."

Speculation had it that this last-minute modification was induced in part by the difference of SRI's proposal, and perhaps others like it. A proposal organized around function-driven platforms sharing infrastructure rather than around disease areas couldn't be evaluated as a whole by, say, an expert in cancer or genomics. A different kind of expert, one skilled in evaluating facilities and complex programs, was necessary.

With this change communicated, review began. In the first stage, the proposal was disassembled into its constituent platforms; expert reviewers assessed the science within each platform in isolation, rating it for its innovativeness, appropriateness, ability to attract and retain the best researchers, and the like. In the next stage, the added step, a different body of reviewers drawn from all over the world received a stitched-up proposal, which they looked at as a whole, judging its potential to transform health care and build capacity, how well the platforms hung together, and the likelihood that construction would begin within 18 months of award, a CFI-set criterion. During this stage, the reviewers met with members of the SRI team to quiz them on the proposal, seeking clarification where it felt such was needed.

In the third and final stage, a panel of "blue-ribbon" international reviewers considered the reports from the first two sets of experts, and then went further. They analyzed how the proposed centre would advance the hospital's strategic research plan, and scrutinized the critical criterion of evidence of support from partners (that is, not the CFI). They also pitted competing proposals against each other. From all this, they determined which they thought represented the most effective investments in research infrastructure, recommendations that were communicated to the Board of the CFI, nine months after the proposal's submission.

On June 17, 2008, the Board reviewed the recommendations and made the final pronouncement, communicated to SRI via e-mail the next evening. The waiting was over. The news, joyous. Born was the Centre for Research in Image-Guided Therapeutics. When asked what he thought was the most important factor in the CFI's decision to invest in SRI, Hynynen said, "The quality of the research we do. It is excellent. We are changing how health care is done."

Dr. Peter Burns, senior imaging scientist; Dr. Eliot Phillipson, Canada Foundation for Innovation president and CEO; Dr. Sandra Black, director, neurosciences research program; and Dr. Anne Martel, imaging scientist, at the Research Hospital Fund announcement on August 20, 2008