



UNIVERSITY OF OTTAWA
HEART INSTITUTE
INSTITUT DE CARDIOLOGIE
DE L'UNIVERSITÉ D'OTTAWA

THE BEAT™

A COMPENDIUM OF INFORMATION ABOUT THE UNIVERSITY OF OTTAWA HEART INSTITUTE

HIGHLIGHTS

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(from Canadian Cardiovascular Congress, Toronto, pages 2–3)

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(from American Heart Association Scientific Sessions, New Orleans, pages 3–4)

"This recognition underscores the important work and contributions of Canada's research community, which is second to none."

– Dr. Robert Roberts,
President and CEO, UOHI
(from Heart Institute President Awarded Royal Society of Canada's Highest Medal of Honour, page 5)

The Heart Institute's trial results showed that using eptifibatid did not significantly improve patient outcomes. In fact, the study found that using the drug increased the risk of bleeding.

(from Heart Institute Trial Suggests Widely Used Drug Not Necessary, page 5)

The Heart Institute has the rare capability to develop and produce novel and extremely short-lived tracers onsite, providing a wider range of imaging options in both clinical and research applications.


(from Medical Tracers: Shining a Light from Inside, page 6)



UNRAVELLING THE MUMMY'S TALE: Hetep-Bastet is not a typical Heart Institute patient. For one thing, she is approximately 2,500 years old. For another, she's an Egyptian mummy! She visited the Institute in November for a CT scan as part of a collaborative research effort involving the Canadian Museum of Civilization, l'Université du Québec à Montréal, and the University of Western Ontario. The ongoing project uses non-invasive imaging to learn about life in ancient Egypt by studying the bodies and preservation methods of mummies. The Heart Institute has an appropriate high-resolution CT scanner and couldn't turn down such an interesting opportunity. Following her scan, the mummy returned to the Canadian Museum of Civilization to go on display in her restored coffin as part of "Tombs of Eternity: The Afterlife in Ancient Egypt." The exhibition will run until August 2009. The University of Ottawa Heart Institute: now taking referrals from archaeologists.

Conference Roundup: The Heart Institute at CCC and AHA

The Canadian Cardiovascular Congress (CCC) and the American Heart Association (AHA) Scientific Sessions are the largest cardiovascular conferences in Canada and the world, respectively. At the 2008 meetings held this fall, University of Ottawa Heart Institute staff presented a remarkable number of basic and clinical research studies, led workshops on clinical and research practice, and gave invited talks on their areas of expertise.

The extent of the Institute's involvement in these meetings reflects its growing stature and its respected position on the national and world stages, while the range of science presented underscores the dynamic research environment fostered at UOHI. The roundup on the next three pages offers a selection of highlights from the two conferences. 

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Canadian Cardiovascular Congress, Toronto

As the term “congress” implies, CCC is actually a collective meeting of the major professional societies in Canada related to cardiovascular medicine. Everyone from cardiologists and surgeons to nurses and allied health professionals are represented at the Congress, and no other institution was more visible this year than the University of Ottawa Heart Institute. With more than 100 oral and poster presentations, workshops, session chairs, and panel and debate slots, it was hard to find a meeting room where the Institute wasn't presenting, leading the discussion or being referred to by others.

Clinical Practice for Endocarditis and Aortic Stenosis

Cardiologist Dr. Kwan-Leung Chan moderated a particularly spirited workshop and debate about the 2007 American Heart Association Endocarditis Prophylaxis Guidelines. The new guidelines represent a major departure from previous recommendations for the prevention of endocarditis, or infection of the heart. They call for antibiotic use in fewer patients and in relation to a smaller number of invasive procedures. For example, they recommend a single dose of antibiotics before a dental or respiratory procedure, while eliminating a post-procedure dose.

The expert panel, which included Heart Institute cardiac surgeon Dr. Roy Masters, debated the validity of the new guidelines. Dr. Chan presented three case studies and called individually on Canadian Cardiovascular Society (CCS) physician members, representing cardiovascular care centres across the country, to offer their perspectives. Physicians generally agreed there is a need to follow individual clinical judgment for each case rather than relying solely on recommendations for guidance. They also emphasized the necessity of good dental care in their patients and the larger populace as a means of reducing the risk of endocarditis.

Dr. Chan also led a well-attended workshop on aortic stenosis, the most common

heart valve disease. The session included a presentation comparing the diagnostic accuracy of Doppler echocardiogram with heart catheterization for the measure of pressure gradients. While a trip to the cath lab is the gold standard, the study showed that use of an energy-loss coefficient with non-invasive Doppler echo gives results very close to catheterization. The ASTRONOMER study, led by Dr. Chan, was also discussed. Results from this pan-Canadian trial to assess the effect

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of cholesterol-lowering statins on the progression of aortic stenosis are expected to be published in early 2009.

New Findings for PCI and STEMI

Dr. Michel Le May presented the results of the three-year ASSIST drug trial at a session on late-breaking research. In the trial that involved percutaneous coronary intervention (PCI), also known as coronary angioplasty, Dr. Le May found that eptifibatide, a popular anti-platelet drug, did not improve patient outcomes and increased the risk of bleeding. During another crowded session, Dr. Marino Labinaz compared the use of different drug therapies for STEMI patients transported to the Heart Institute for primary PCI. He also cited Dr. Le May's ASSIST trial, which was first reported in Washington, D.C., at the 2008 Transcatheter Cardiovascular Therapeutics Symposium. In a third

session, also filled to capacity, STEMI Co-ordinator Melissa Fong compared primary PCI results between women and men, showing that fewer women undergo the procedure, and when they do, the so-called door-to-balloon time is an average of 10 minutes longer when they arrive as STEMI patients. Part of the reason for the difference, she noted, was that women tend to delay in reporting health difficulties, and when they do, they are already seen as high-risk cases. The age

differential at onset of severe heart attack plays a role, since women tend to present symptoms when they are older, and this too increases their risk of mortality.

Making the Next One Your Last

Dr. Andrew Pipe gave several talks, including one to an enthusiastic audience on the importance of smoking cessation for the prevention of cardiovascular disease (CVD). Dr. Pipe emphasized that smoking is the number one modifiable health issue in Canada and that it is the only CVD risk factor that can be completely eliminated. He went on to outline the highly effective Ottawa model developed at the Heart Institute. The model involves proactively approaching Institute patients about smoking cessation, providing nicotine replacement therapy to reduce discomfort from withdrawal, and dosing nicotine replacement appropriately for individuals so that cravings

are eliminated. His take-home message was that smoking cessation must be part of any and all comprehensive cardiovascular care programs.

Gene Therapy

In a featured oral presentation, PhD student Allen Teng reported on new findings related to gene and cell therapy for the treatment of cardiovascular disease. The hope is to use gene therapy to generate the growth of new heart tissue to replace damaged tissue. Teng and his colleagues at the Heart Institute's Ruddy Canadian Cardiovascular Genetics Centre have identified a novel gene associated with highly vascularized tissue such as the heart. This gene, when paired with another, greatly increases production of the VEGF protein, which is involved in the growth of vascular blood vessels. Little is currently known about the newly identified gene and its related protein, but the presentation immediately sparked collaborative interest from researchers at other institutions.

Phone-Based Follow-Up

Keeping patients on course following discharge can be a challenge. Kathryn Eastwood, an RN with Cardiac Telehealth, presented interim findings on the Heart Institute's use of interactive voice response (IVR) with acute coronary syndrome patients. Acute coronary syndrome includes unstable angina and the NSTEMI and STEMI forms of myocardial infarction. Eastwood explained to the standing-room-only audience that IVR involves the use of a system that generates automated phone calls to patients at specified intervals post-discharge – in this case, at 1, 3, 6, 9 and 12 months. The patients are presented with a question tree that assesses and encourages their compliance with treatment guidelines. Based on patient responses, a nurse may intervene when appropriate. To date, patients indicate that they like the system, and the early data show it to be effective. The Heart Institute already employs IVR in relation to other conditions.



Cardiologist Dr. Kwan-Leung Chan, Cardiac Telehealth nurse Kathryn Eastwood, and doctoral student Allen Teng were among the Heart Institute presenters at the Canadian Cardiovascular Congress in Toronto.



Heart Institute posters at CCC were eye-catching and stood out among the sea of panels in the convention centre. Topics ranged from patient management and transformative learning to medication safety and defibrillator advisories.

The Importance of Cardiovascular Data Standards

Cardiologist Dr. Ross Davies led an important workshop on cardiovascular data standards. The panel included the current and incoming CCS presidents and the steering committee chair for the Canadian Heart Health Strategy. Without agreed-upon standards for the collection, storage and sharing of data, doctors can encounter difficulties in getting complete and accurate patient information. In addition, the use of competing formats or collection protocols can render data incompatible and useless for clinical research. Access to standardized data is an essential basis for improving the delivery of care. The workshop provided an overview of existing provincial data systems and concluded that there is good coordination across the country in the move from procedure-based systems to a delivery-of-care-based approach. This shift is intended to better reflect the “patient journey”

through the health care system. Accurately reflecting this journey will require the participation of all centres within a given region. The workshop concluded with a commitment from the president of CCS to keep the issue of data standards high on the agenda in order to encourage continued progress.

In the Winner’s Circle

The Heart Institute was a major presence on the award front as well. Dr. Alex Kulik won the CCS Young Investigator Award for his presentation and manuscript on the impact of statin use. Dr. Kulik completed his training at the Institute and plans to return following fellowships in the United States. His award-winning paper is currently in press for publication. Cardiac surgery resident Vincent Chan won the Paul Cartier Cardiac Surgery Resident Award. Sponsored by the Canadian Society of Cardiac Surgeons, the award is the top national prize in its category. Dr. Chan’s win for his presentation on tricuspid valve repair

marked the third year in a row that the prize has gone to a Heart Institute resident.

Plenary Session Highlights

The Congress also offered excellent plenary talks from international experts. As part of her keynote address, American cardiologist Dr. Susan Bennett delivered a warning to medical professionals on gender bias in heart health. Women’s risk factors for major heart events such as heart attack and stroke increase with age, but their diagnosis and treatment lag behind those for men. Women have longer time to treatment compared with men, and treatment is an independent predictor of mortality. This is particularly true in acute myocardial infarction, said Dr. Bennett, Director of Women’s Heart Health at George Washington University Hospital. Further, many clinical trials, particularly in the United States, under-represent women, and not all drugs work the same in women because too little is known to exploit their advantages.

For the State-of-the-Art Lecture, Dr. Valentin Fuster provided his vision for the future of cardiovascular medicine. The Director of the Cardiovascular Center at Mount Sinai Medical Center and Scientific President of Spain’s national centre for cardiovascular research in Madrid advocated a move from treatment of disease to health promotion. He argued that treatment is costly and has provided only modest gains in patient longevity. With aging populations and high rates of obesity, Dr. Fuster told the audience, the economics of treatment over prevention are not sustainable. He also promoted the early encouragement of promising students to enter careers in scientific research.

Special thanks go to Dr. Rob Beanlands. As Chair of the CCS Scientific Program Committee, Dr. Beanlands assembled an excellent program covering clinical and basic research as well as clinical practice. Session audiences frequently exceeded room capacity, attesting to a job well done. ❧

American Heart Association Scientific Sessions, New Orleans

The American Heart Association (AHA) Scientific Sessions is the big league in the world of cardiovascular medicine conferences. Roughly 25,000 medical and research professionals attended the November meeting in New Orleans’ sprawling convention centre, and it’s likely that every major cardiovascular institute in the world was present in some form. The Heart Institute was well represented with more than 20 program items. Genetics and vascular biology were the major themes.

Ongoing Impact of a Major Discovery

In 2007, three genome-wide association studies identified the 9p21 genetic variant as an independent risk factor for coronary artery disease (CAD) and myocardial infarction (MI). The first and largest of these was published by a Heart Institute team led by Drs. Ruth McPherson and Robert Roberts. Seventy-five per cent of

the population has at least one copy of the risk variant. Dr. Sonny Dandona of the Heart Institute’s Ruddy Canadian Cardiovascular Genetics Centre presented findings showing that 35 per cent of angiography patients with one copy of the variant had CAD, while 46 per cent of those with two copies had CAD. This compared with 28 per cent in those with none. The study also showed that the number of risk variants present predicts the severity of disease.

Just how significant is the 9p21 discovery? A group from Emory University followed later in the same session with a presentation showing that presence of the 9p21 variant in smokers doubles their risk of CAD. In another session, a group from Johns Hopkins called 9p21 far and away the strongest locus in the genome for MI.

It became clear throughout the conference that the Heart Institute’s original 9p21 finding has had great influence on

the research community. In many sessions, the variant was the subject of presentations or was mentioned in discussions. In a joint AHA/European Society of Cardiology symposium on genetic studies, 9p21 was identified as a “hugely exciting

The Genetics of Atrial Fibrillation

Atrial fibrillation (AF) is the most common cardiac arrhythmia. In a session on the genetic determinants for AF,

The great significance of 9p21 is that the finding has been shown to hold true in independent populations in Canada, the United States and Denmark.

find” by Hugh Watkins of Oxford University, and Chris O’Donnell of the National Institutes of Health (NIH) stated that the great significance of 9p21 is that the finding has been shown to hold true in independent populations in Canada, the United States and Denmark.

Isabelle Thibodeau reported on her work in the Heart Institute’s Genetics of Cardiac Arrhythmias Research Laboratory. Gap junction channels are responsible for electrical conductivity in the body. They allow the electrical impulses in the

(continued on page 4)

(American Heart Association Scientific Sessions, continued)

heart to fire in a regular, co-ordinated fashion. These channels are made up of Connexin 40 proteins. Mutations associated with this protein can impair conductivity in the heart muscle and result in the irregular patterns that are the hallmark of AF. Thibodeau's research has uncovered two novel mutations of Connexin 40. One may point to a new mechanism for increased risk of AF related to calcium signalling.

The Vascular Biology Squad

The Vascular Biology Laboratory of Dr. Ed O'Brien was out in force at AHA with an impressive total of five oral and moderated poster presentations. Several

interest in the technique because it allows the surgeon to easily visually identify all major vessels, and a triple bypass can be completed in less than four hours. While the procedure is technically demanding, it can be performed with standard instruments. This helps lower barriers to adoption.

The Heart Institute's Dr. Joel Price presented findings on the impact of age in cases of patient/prosthesis mismatch (PPM) following aortic valve replacement. The study compared survival and functional status in patients under the age of 70 versus those over 70. PPM occurs when the replacement valve is too small for the recipient. Results showed that, in

events such as thalidomide use. Dr. Joseph Ross of Mount Sinai School of Medicine in New York discussed his report, published in the *Journal of the American Medical Association* in April, that detailed the pharmaceutical industry's practice of ghost-writing medical research studies that are then published in academic journals.

Picking up on the theme of genetics, the "Genetics and Genomics Decoded" session made some key points about what we can expect in the future. Until the field gets to the point of conducting functional genomic studies and genetic clinical trials, there will be only limited clinical application of genetic medicine. Unravelling the tangle of genetic complexity will require an under-



Several presentations continued the Vascular Biology Lab's groundbreaking work on the protective role of heat shock protein 27 (HSP27).

of these continued the Vascular Biology Lab's groundbreaking work on the protective role of heat shock protein 27 (HSP27). Dr. Yong-Xiang Chen reported that overexpression of HSP27 in mice resulted in reduced atherosclerotic lesion area in both males and females. This study also found reduced inflammatory response and fewer foam cells, the precursors to lesion formation. Another member of the lab, Paromita Deb-Rinker, found that differential gene expression is involved in HSP27 vessel protection by comparing areas of mouse aortas that are more and less prone to atherosclerosis. Kevin Sun presented on the protective effect of selectively activating estrogen receptor beta. Doing so reduced lesion size and inflammatory response. It is likely that HSP27 is involved in this process. Finally, Katey Rayner, recipient of the University of Ottawa 2008 Faculty of Medicine Excellence Award, reported findings that show estrogen mediates the release of HSP27 into the bloodstream and that macrophages are the source of the released protein. Each of these studies puts a piece of the HSP27 puzzle into place. The overall goal is to eventually develop a drug therapy based on the protein and its atheroprotective mechanisms. Following a different line of research, Dr. Xiaoli Ma reported that coating stents with the protein GKSI can enhance the repair of arteries, improving the effectiveness of drug-eluting stents.

Surgical Practice

Surgeon Joseph McGinn of Staten Island University Hospital presented on his collaboration with the Heart Institute's Dr. Marc Ruel in developing the new surgical technique of multi-vessel small thoracotomy coronary artery bypass grafting. This keyhole surgical procedure has been pioneered jointly, with 100 of the first 300 surgeries performed at the Heart Institute by Dr. Ruel. Results have been excellent, with patients reporting greatly reduced pain and significantly shorter recovery times. There is a great deal of

the under 70 age group, those with PPM had increased mortality and increased recurrence of congestive heart failure. In patients over 70, PPM had no significant effect on overall survival or functional status. Interestingly, a study coming out of Florida reported that coronary artery bypass grafts performed on octogenarians were nearly as successful as those performed on younger patients. These issues will become more and more prominent as the overall populace, and surgical patients in particular, increase in age.

Adult Congenital Heart Disease in Canada

At the last minute, Heart Institute specialist in adult congenital heart disease (ACHD) Dr. Luc Beauchesne was unable to attend the conference. Fortunately, a co-author was able to step in to present results of the survey Dr. Beauchesne led of ACHD clinics. There are now more adults than children with congenital heart disease in Canada. The study marked the first survey of all 15 clinics across the country, looking at four major factors: staffing, infrastructure, database capabilities, and wait times. Several findings were of interest. One third of Canadian pediatric cardiologists are affiliated with an ACHD clinic, compared with 3.6 per cent of adult cardiologists. In a perhaps related finding, wait times are currently more than double the acceptable targets. In all, approximately 22,000 patients are being actively followed, and less than one quarter of all ACHD patients are under care.

Highlights from Other Sessions

Other interesting sessions were numerous. The topic of bias in clinical trials is a hot one that was addressed in "What Is the Emperor Wearing? Unbiased Evidence from Clinical Trials." Swiss cardiologist Dr. Thomas Luscher drew on the story of the emperor's new clothes to point out the illusion of safety in drug testing and approval in the aftermath of catastrophic

standing of other modes of inheritance, such as mitochondria and mRNA, and of epigenetics. As things stand, the capacity for data generation far exceeds interpretive and analytic capabilities, but to fully understand functional pathways, we will need to integrate other "-omic" approaches such as proteomics and transcriptomics.

The plenary session "Personalized Genomics: Ready for Prime Time?" brought together a number of leading thinkers. Francis Collins of NIH gave a nice overview of where we are and what lies ahead. Thanks to rapidly advancing technology, we are at a point where all genes are essentially candidate genes for genome-wide association studies. Over 400 alleles have been validated, but for most the associated risk is small. Individuals can have their personal genomes screened, but the results are of little practical use. There is a great deal to be done to move genomics to the clinical care setting. Kelly Ormond from Stanford University spoke on the application of genetic testing to clinical practice. Family history is an independent risk factor, with around 40 per cent of patients having moderate to high risk of cardiovascular disease. The results of genetic tests are not necessarily clear-cut, and the demand for genetic counsellors will increase greatly as more and more patients seek help in understanding their results. Addressing ethical and societal issues was Hank Greely, also from Stanford. Our idea of genetics has been skewed, he said, because researchers identified the clear-cut, Mendelian traits early on. Now we are dealing with small-effect variants that may only be salient in interaction with multiple other genes or unknown environmental factors. Soon, all patients will have their full genomes in hand, but we aren't even close to having the systems in place to help physicians make sense of the information or help them effectively convey the significance to their patients. Maybe by next year the outlook will be less daunting. 🌸



Dr. Luc Beauchesne, scientist Paromita Deb-Rinker, and Dr. Xiaoli Ma all authored Heart Institute studies presented at the American Heart Association Scientific Sessions in New Orleans.

Heart Institute President Awarded Royal Society of Canada's Highest Medal of Honour

The Royal Society of Canada (RSC) represents Canada's highest level of learning and research in all areas of scholarship. On November 15, the RSC honoured Dr. Robert Roberts, President and CEO of the University of Ottawa Heart Institute, for his outstanding achievements and pioneering work in cardiovascular science. Dr. Roberts was awarded the prestigious McLaughlin Medal, widely recognized as one of the country's most significant tributes for excellence in medical research.

"The research undertaken by Dr. Roberts has led to new screening techniques for heart disease. His work has also led to the identification of genes that are responsible for, or influence, the

development of cardiovascular disorders," said Dr. Yvan Guindon, President of the RSC. "His work has forged new avenues of investigation through molecular cardiology. At the same time, he has cultivated world-class researchers at the Heart Institute and elsewhere, demonstrating a commitment both to his research and to his students."

An internationally renowned scientist, physician and educator, Dr. Roberts has conducted landmark research in molecular cardiology that has opened new frontiers in cardiovascular medicine, with a focus on causes and more personalized treatments of inherited heart diseases. His current research uses molecular genetics to unravel the DNA puzzle in heart failure

(cardiomyopathy) and irregular heartbeat (atrial fibrillation). These are two of the many areas in which the Heart Institute is investigating factors that influence the development of inheritable heart diseases.

Dr. Roberts was appointed President and CEO of the Heart Institute in 2004. His research accomplishments here include the founding of the Ruddy Canadian Cardiovascular Genetics Centre, Canada's only genetics research centre focused exclusively on heart disease, and one of only a handful of such facilities worldwide.

"I am extremely honoured to be recognized in this way by the country's senior national body of scientists and scholars," said Dr. Roberts. "This recognition underscores the important work and contributions of Canada's research community, which is second to none."

A native of Grole, Newfoundland, Dr. Roberts finished his studies at Dalhousie University and the University of Toronto before leaving for the University of California, San Diego to conduct research in cardiac metabolism. He then became Director of Cardiac care at Barnes-Jewish Hospital at Washington University in St. Louis, Missouri. He returned to Canada to join the Heart Institute after serving as Chief of cardiology at Baylor College of Medicine in Texas, where he retains his title as professor of medicine.

His early research focused on quantifying and diagnosing coronary artery disease. He created a screening method to help identify patients susceptible to cardiac arrest and heart attack. This assay remained the standard for the diagnosis of myocardial infarction throughout the world for more than three decades. Subsequently, he focused on the application of recombinant DNA techniques to cardiac growth and the molecular genetics of heart failure. These efforts would eventually result in his

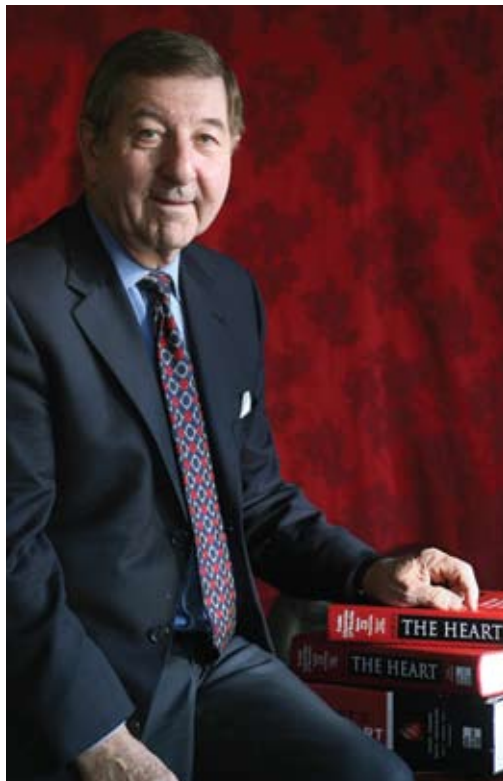
recognition as of one of the founders of molecular cardiology.

He co-authored and edited the first textbook on molecular cardiology in 1993 and has since authored numerous textbook sections on the topic. He has over 700 publications, and since 1989 has been associate editor of *Hurst's The Heart* – recognized as the "bible" of cardiovascular information. In 2002, he was designated a Most Highly Cited Researcher.

Dr. Roberts is the recipient of numerous prestigious awards. These include the Distinguished Scientist Award from the American College of Cardiology (1998), the Award of Meritorious Achievement from the American Heart Association (2001) and Master of the American College of Cardiology (2007). In 2005, he was awarded the Robert Beamish Leadership Award.

As a world leader in cardiovascular medicine, Dr. Roberts has a clear vision for the future. "In the past 25 years, the model for heart disease has largely moved from acute treatment to one of chronic disease management," he said. "Today, we have the blueprint of the human genome, and our understanding of genetic risk factors is advancing rapidly. Our next challenge will be to fully map an individual's cardiovascular risk profile and implement a personalized prevention strategy. In this way, it is entirely reasonable to expect that we can eliminate heart disease in the coming decades."

The McLaughlin Medal celebrates important research of sustained excellence in the medical sciences. Two Heart Institute scientists have previously won the award: Adolfo J. de Bold in 1988 and Yves Marcel in 1997. The presentation of this honour to Dr. Roberts reflects the continuing history of research excellence at the Institute. 🌟



"It is entirely reasonable to expect that we can eliminate heart disease in the coming decades."

– Dr. Robert Roberts,
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Dr. Robert Roberts is the recipient of the Royal Society of Canada's McLaughlin Medal for his outstanding achievements in cardiovascular science.

Heart Institute Trial Suggests Widely Used Drug Not Necessary

A popular antiplatelet drug administered intravenously during the treatment of severe heart attacks does not improve outcomes for patients undergoing an angioplasty. The drug – known generically as eptifibatide (pronounced ep-ti-fy-bah-tide) – also increases the risk of bleeding. The results follow a groundbreaking clinical trial conducted at the University of Ottawa Heart Institute that sought to determine the efficacy of a drug that is widely used, particularly in the United States.

The three-year trial, called ASSIST, was designed to test the safety and efficacy of eptifibatide in serious heart attack patients who underwent an emergency angioplasty – known as primary PCI, for percutaneous coronary intervention – to open blood and oxygen flow to the heart. The study involved a total of 400 patients diagnosed with ST-Segment Elevation Myocardial Infarction (STEMI), with 201 undergoing primary PCI using eptifibatide and 199 without the drug. The Heart Institute's trial results showed that using eptifibatide did not significantly improve patient outcomes. In fact, the study found that using the drug increased the risk of bleeding.

"We believe there is no supporting evidence to be incorporating this drug therapy for the treatment of acute STEMI patients," said Dr. Michel Le May, Director, Coronary Care Unit Research Group. "In fact, there is increased risk associated with its use. As a result, we expect this study will reshape our current clinical practice of medicine in managing the treatment and care of heart attack patients."

Dr. Le May presented the findings of the ASSIST trial first in Washington, D.C., at the 2008 Transcatheter Cardiovascular Therapeutics (TCT) Symposium, where interventional cardiologists from around the world gather to discuss innovative techniques and therapies in cardiovascular medicine. The results were also made public at the Canadian Cardiovascular Congress in Toronto.

This class of antiplatelet drugs has become routinely used in angioplasty, particularly in the United States, said Dr. Le May. The study suggests that eptifibatide is not necessary. Further, an oral dose of antiplatelet drug is generally prescribed. 🌟



Dr. Michel Le May led the ASSIST trial assessing the efficacy of the commonly used antiplatelet drug eptifibatide.

Medical Tracers: Shining a Light from Inside

The University of Ottawa Heart Institute already has the only comprehensive nuclear imaging facilities in Canada dedicated to cardiovascular medicine. Now the Institute is extending its medical tracer development and production resources on two fronts. It is expanding in-house facilities and production capacity, and it is pursuing an innovative collaboration with MDS Nordion, the world's largest producer of medical isotopes.

Home to Canada's National Cardiac PET Centre, the Heart Institute has a comprehensive suite of nuclear imaging capabilities. Technologies for patient diagnosis and clinical research include positron emission tomography (PET) and single photon emission computed tomography (SPECT). MicroPET and microSPECT scanners, for small animal imaging, mirror clinical capabilities and support research into new and improved imaging techniques, new therapeutic approaches, and basic physiological and molecular mechanisms. The use of identical non-invasive procedures for imaging human and animal cardiac function is a significant advantage in translating research findings to the clinical setting.

As important as these high-resolution scanners are, they would show us nothing without radiological tracers to light the way. By emitting small amounts of radiation as they move through the body, tracers make it possible to visualize specific disease and treatment processes. The Heart Institute has the rare capability to develop and produce novel and extremely short-lived tracers onsite, providing a wider range of imaging options in both clinical and research applications. Dr. Rob Beanlands, Director of the National Cardiac PET Centre, sees this capability as critical to advancing the field. "The future of nuclear imaging is the development of new tracers," he said.

A medical tracer is a radioactive isotope that is paired with a biologically active molecule that can be used to image specific physiological or disease processes, or to help guide therapy. Nuclear imaging is also referred to as molecular imaging because the visualization occurs at the cellular and molecular level. Because tracer molecules are designed to interact with specific types of cells and tissues, different molecules can illuminate different processes.

In cardiology, the most common diagnostic parameters are metabolism and the flow of blood to heart tissue, known as perfusion. The workhorse for perfusion

imaging is the PET tracer rubidium-82. For metabolism, it is fluorodeoxyglucose (FDG). When metabolism is imaged, a patient is injected with FDG and a PET scan is performed to see where the FDG travels and how quickly it is absorbed. Because FDG mimics glucose, the heart metabolizes the radioactive molecule in a similar way. The scan shows the rate at which the heart muscle absorbs FDG from the bloodstream, and the concentration of the molecule in the heart provides a measure of blood flow to the tissue. In this way, the physician can assess the viability of the myocardium.

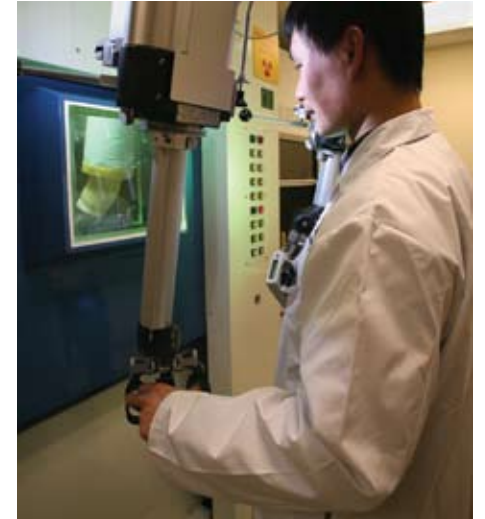
The ability that SPECT and PET have to image functional processes is what differentiates them from magnetic resonance imaging (MRI) and computed tomography (CT), which provide detailed structural information about a patient's anatomy.

SPECT and PET use chemically different radioisotopes that emit radiation in different ways. In general, SPECT tracers decay more slowly and can remain active for days. The term for the period it takes a radioactive substance to radiate half of its energy is half-life. SPECT tracers tend to

Thanks to a grant from the Canadian Foundation for Innovation, he is overseeing a significant expansion of the Institute's facilities. The capacity of the cyclotron, a particle accelerator that produces the PET radioisotopes, will be doubled, lab space will be expanded, and three new workstations called hot cells will be added. Hot cells are heavily shielded enclosures for working with radioactive materials. New staff and trainees will also be brought in to work in the lab.

Tracer development at the Heart Institute is heavily collaborative. DaSilva works closely with imaging specialists, cardiologists and research staff to identify new parameters and ways to image them. There is no shortage of research topics. One area of interest is the development of new ways to bind with and label organic molecules. Others involve entirely new approaches. The ability to image the fate of stem cells in the body is of great interest, as is the use of nanoparticles to bind multiple molecules and increase signal strength.

The Heart Institute has the capability to image small animals using tracers and scanning technology identical to




Research associate Daniel Duan demonstrates the remote manipulator arms that are used with the "hot cell" in the Institute's new MDS Nordion-funded radiation lab. The hot cell is a heavily shielded workspace for safely handling radioactive materials.

two organizations together in a common physical location. Nordion has extensive experience with radiochemistry and radiopharmaceuticals, particularly in SPECT imaging.

"The Heart Institute is clearly in the vanguard of research into new applications of existing tracers, and they are bursting with ideas for developing new tracers," said Peter Covitz, PhD, MDS Nordion Senior Vice President for Innovation. "Combining the thought leadership of the Heart Institute with the execution capabilities and technical know-how of Nordion will allow us to move the field forward more quickly than either organization working on its own."

The new lab will focus on early-stage characterization of tracers. The Nordion scientists will evaluate new molecules and families of candidate chemical compounds. The new facility has all of the safety and containment handling equipment found in a commercial facility and can support all of the work necessary to take a new tracer to the point of transition to a manufacturing process. This will narrow the gap from early-stage discovery work to later-stage commercialization, assuming a new tracer progresses to that point.

The collaboration will also provide significant opportunities for education, training and information sharing. The Institute has submitted a grant proposal to support a series of eight to 10 symposia on imaging topics over the next two years. The new lab is also expected to attract more students to the program, providing additional manpower and training the radiochemists of tomorrow. 

"The future of nuclear imaging is the development of new tracers."

– Dr. Rob Beanlands, Director, National Cardiac PET Centre

have longer half-lives than PET tracers. Many PET tracers, including FDG, have very short half-lives and must be used within hours of production. These differences can be advantageous. SPECT tracers allow for imaging a process multiple times over a period of hours or days. PET tracers allow for imaging multiple parameters in quick succession since they clear quickly from the patient's system.

Because the chemistry of PET and SPECT tracers is very different, their development and production require different sets of expertise. Jean DaSilva, PhD, is the Head of Radiochemistry at the Heart Institute and a leader in his field. As a specialist in PET tracers, he draws on his multidisciplinary training in chemistry, radiation science and pharmacology. DaSilva manages the production of tracers for use in clinical imaging and conducts research into the development of new tracers. Academic radiochemists are a rare breed, and he sees the training of students as an important part of his work.

those used with humans. This means that a biological process is seen in exactly the same way in a mouse or a person. So, the variability is greatly reduced and translation simplified when moving from animal studies to clinical applications.

An example DaSilva offers is work being done in relation to diabetes. "People with diabetes have high rates of heart disease. We have a Heart and Stroke Foundation grant to study the signalling pathways that lead to heart disease in diabetic mice," he explained. "We have the ability to study signalling as well as glucose and fatty acids, all of which are altered in diabetes, in both humans and animal models."

The collaboration with MDS Nordion has been important in supporting translational research. As part of their agreement, Nordion supplied the Heart Institute with a very high resolution microSPECT scanner. Nordion has also opened a \$2.2 million lab at the Institute. This lab will bring the strengths of the



Inside the hot cell, remote arms allow scientists to manipulate heavy objects as well as fragile test tubes. It takes a good deal of practice and hand-eye co-ordination to prepare a sample from behind two inches of shielding.



Where tracers come from: The Heart Institute's cyclotron produces short-lived radioactive isotopes by aiming a stream of accelerated protons at a target substance. The target is the ring on the left with the blue flower-like pattern. A second target will be installed in the coming months to double the cyclotron's production capacity.