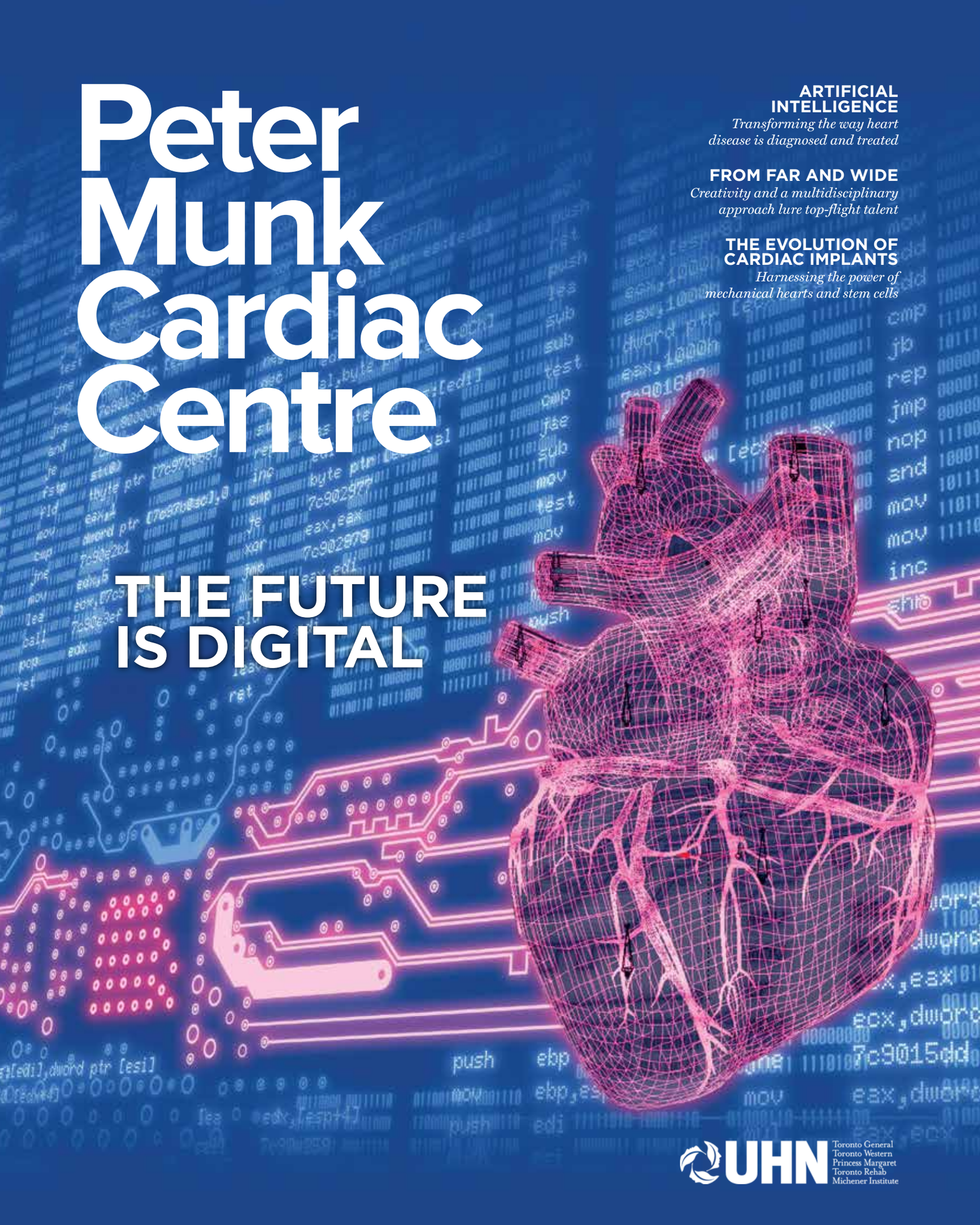
Peter Munk Cardiac Centre

THE FUTURE IS DIGITAL

ARTIFICIAL INTELLIGENCE
Transforming the way heart disease is diagnosed and treated

FROM FAR AND WIDE
Creativity and a multidisciplinary approach lure top-flight talent

THE EVOLUTION OF CARDIAC IMPLANTS
Harnessing the power of mechanical hearts and stem cells



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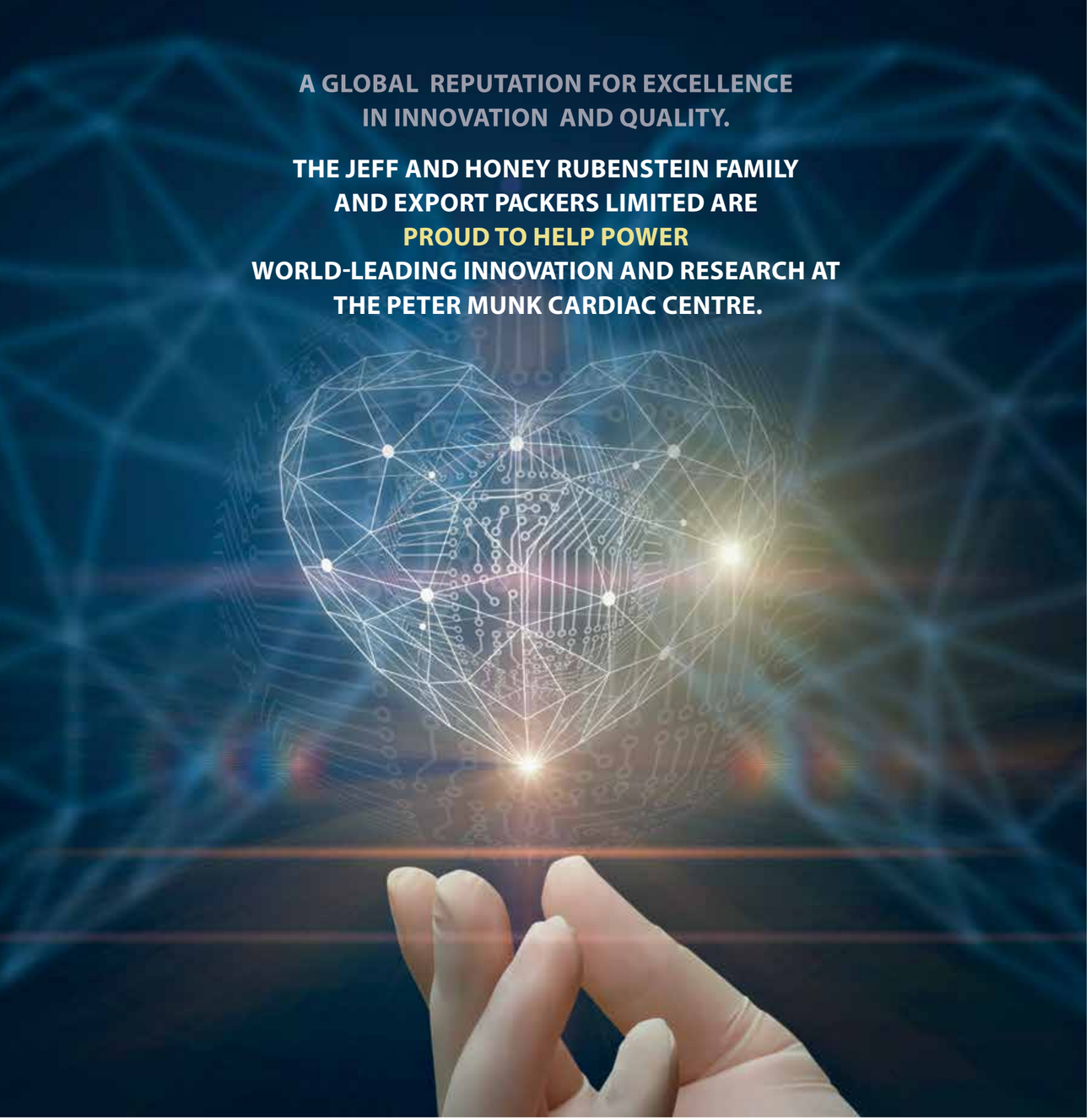

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EDGE

The Peter Munk Cardiac Centre

Innovation Committee

More than 40 projects have been launched so far and some of these projects, all funded by philanthropy, have significantly changed and influenced the way health care is delivered in Ontario and across Canada

by Shelley White

William Charnetski is a big believer in "celebrating our champions" here in Ontario. But touting our homegrown accomplishments is something we, as Canadians, don't always do well enough, says Ontario's chief health innovation strategist. ¶ "It feels like with anything other than hockey, we seem to require that people go elsewhere and establish themselves, [to] gain the inherent credibility that makes them more popular at home," he says.

The Peter Munk Cardiac Centre (PMCC) Innovation Committee was created by Dr. Barry Rubin, right, and Dr. Harry Rakowski. They were looking for a "unique and nimble process" to evaluate and launch innovative proposals to impact cardiac and vascular care. William Charnetski, opposite page, is Ontario's chief health innovation strategist. He says the PMCC committee is an exciting Ontario health-care story worth celebrating.

Talking up the province's health-care success stories has been a priority for Mr. Charnetski and his team since he took on the newly created position in Ontario's Ministry of Health and Long-Term Care in 2015. So when he attended a meeting of the Peter Munk Cardiac Centre (PMCC) Innovation Committee, Mr. Charnetski knew he was witnessing an exciting Ontario health-care story worth celebrating.

"I love the structure," says Mr. Charnetski of the dynamic committee that's been called the *Dragons' Den* of health care. "It's obviously [comprised of] smart, passionate, hard-working people. The notion that the hospital's doing it this way is important, and it's important for us to showcase the work that's being done."

Created in 2012 by Dr. Barry Rubin, Medical Director of the PMCC, and cardiologist Dr. Harry Rakowski, E.D. Wigle Chair in Hypertrophic Cardiomyopathy Research, the PMCC's Innovation Committee reinvented the wheel when it comes to funding health-care projects. Instead of small groups of doctors making funding decisions, the committee is made up of more than a dozen people of diverse backgrounds and skill sets, and several committee members come from outside of the medical field entirely. Surgeons, scientists and cardiologists mix with hospital administrators, entrepreneurs and business leaders on the committee, and everyone has an equal vote.

Submissions are accepted quarterly instead of annually, and over 1,000 employees at the PMCC can submit a proposal, from nurses to radiologists to anesthesiologists.

The PMCC's Innovation Committee is an exciting concept that could provide a model for other health-care organizations to follow, says Mr. Charnetski.

"To have it organized in the way that the committee is organized is potentially really powerful, when you're one of Canada's biggest hospitals," he says.

He applauds the fact that the PMCC's Innovation Committee combines the expertise of those in the health-care realm with those in the business world.

"I truly believe that the optimal solutions to the challenges that face the health-care system will come from the collaboration of the public sector and private sector," says Mr. Charnetski. "That's a critical success factor for me."

A 'UNIQUE AND NIMBLE PROCESS'

When Drs. Rakowski and Rubin came up with the idea for the PMCC's Innovation Committee, they were looking for a "unique and nimble process," says Dr. Rakowski.

"The idea was to get not just physicians, but [also] other people who were non-physicians – allied health-care professionals and business leaders – to really look at [ideas] and ask, 'Is this truly innovative?'" he says. "The key things are: Is it going to have [an] impact? Is that impact measurable? And is it cost-effective?"

While traditional granting bodies require pages and pages of detailed proposals, applicants to the PMCC's Innovation Committee must only answer 10 questions, plus commit to a cost-effectiveness study. And while most funding organizations are proud of the fact that they reject 85 per cent of proposals, says Dr. Rakowski, he and Dr. Rubin wanted to buck that trend.

Instead of simply turning away unsuccessful applicants, the committee provides constructive input and guidance, helping them improve their proposal and possibly submitting again a few months later.

"Our goal is to fund as many good ideas as we can," he says. "So we're going to help you improve your proposal, we're going to work with you. We're going to look at your research project and improve the design. We're going to look at your budget and streamline, so you can achieve the same thing but spend less money. We want you to succeed."

Marnie Weber has been a member of the PMCC's Innovation Committee since its inception. Ms. Weber is Executive Director, Strategic Developments, at University Health Network (UHN), and she says that it can be challenging to take an innovative idea from concept to changing practice.

"We're a big research engine in Canada, but that's insufficient to bring something into clinical practice," says Ms. Weber. "How do you actually get it spread across other organizations in Ontario? And how do we ensure that it becomes a core part of the health-care system?"

People who like to research and are driven to advance the practice of medicine are not necessarily entrepreneurially minded, says Ms. Weber. And that's why the mix of people on the PMCC's Innovation Committee is key to its success.

"The committee is formed both with very smart business people, but also people who are keeping an eye [as] to what's relevant to patients and what's relevant to society," she says. "[The medical professionals] on the committee are great educators, clinicians and researchers. And the laypeople bring the perspectives of the general public and what matters to patients or family caregivers, as well as their own business investment backgrounds. So you get this great dynamic of people trying to understand and see where this idea can go further."

The committee spends about $1-million per year, raised through philanthropy, says Dr. Rakowski. The amount given to each applicant varies, but they look at the funds as seed money, with the end goal of helping the recipients be self-sufficient.

The PMCC's Innovation Committee is funded in its entirety by generous philanthropic donors who put their put their trust in the panel to direct funding to projects with opportunities for greatest impact.

More than 40 projects have been funded by the PMCC's Innovation Committee so far, some of which have gone on to influence and even change practice in Ontario. One example is a blood conservation project pioneered by anesthesiologist Dr. Keyvan Karkouti (see story on page 46). An initial seed investment of $80,000 resulted in multinational, multicentred trials, additional funding and an additional generation of studies, says Dr. Rakowski.

"It is saving blood product consumption by about 40 per cent, which translates into fewer complications of blood product delivery and health-care cost savings," he says.

Another example is an "anti-oxidant cocktail" created by UHN interventional neuroradiologist Dr. Kieran Murphy that reduces the negative effects of X-rays on DNA (see story on page 48). Like Dr. Karkouti's project, that initial seed funding resulted in additional research studies, says Dr. Rakowski. Now, Dr. Murphy has produced a product with "commercial potential and tremendous health benefit for low cost."

The PMCC's Innovation Committee is a model that can be replicated elsewhere because it runs on philanthropy, says Ms. Weber. Interest has been coming in from government and other health-care institutions, as well as elsewhere in the UHN.

"Other programs within the UHN have said, 'If cardiac can do it, we should have something similar, too,'" she says.

CHANGES ON THE WAY

Though the core philosophy of the PMCC's Innovation Committee will continue as is, Dr. Rakowski says there are changes planned to improve its effectiveness and efficiency. The PMCC has recently acquired some unique pieces of equipment, he says, so they plan to incorporate specific categories of funding to help understand how this new technology can be best utilized.

For example, the PMCC acquired a PET-MRI scanner, which allows physicians to see a fused image of both an MRI (which looks at structure) and a PET (which looks at metabolic function). "There are certain diseases where that information may be vitally important to decision-making, so we're specifically funding some of those [projects]," he says.

The PMCC will also soon be getting a leading-edge piece of equipment in partnership with an Israeli company that produces holographic 3-D imaging. The machine can take any three-dimensional image set – from echocardiography or MRI, for example – and create a holographic image of the heart. The PMCC will be the first in the world to use the device for a cardiac application, says Dr. Rakowski, and so they are soliciting projects to help them discover its potential benefits.

Dr. Rakowski says the PMCC's Innovation Committee may expand its research in areas such as information technology, genomics and personalized (or precision) medicine, targeting treatments to individual patients. And the makeup of the committee will also be changing soon, with a venture capitalist joining this year.

Regardless of these moves forward, Dr. Rakowski says the committee will remain true to its original vision. It's important for the committee to retain its independence, he says: "Not being beholden to anybody or having institutional bias or favouritism to anybody." Dr. Rakowski notes that even committee co-founder Dr. Rubin is treated the same as everyone else – one his proposals was recently sent back to the drawing board.

"We have a vision, and we are committed to it," says Dr. Rakowski. "If you lose that intimacy or the nimbleness, then you simply become an administered bureaucracy. And [what helps to make] this committee unique are those qualities, which we obviously don't want to lose."

ARTIFICIAL INTELLIGENCE LAUNCHES A NEW ERA IN CARDIAC CARE

From diagnostics to therapeutics, artificial intelligence is set to change the way cardiovascular diseases are identified and treated

By Marjo Johne

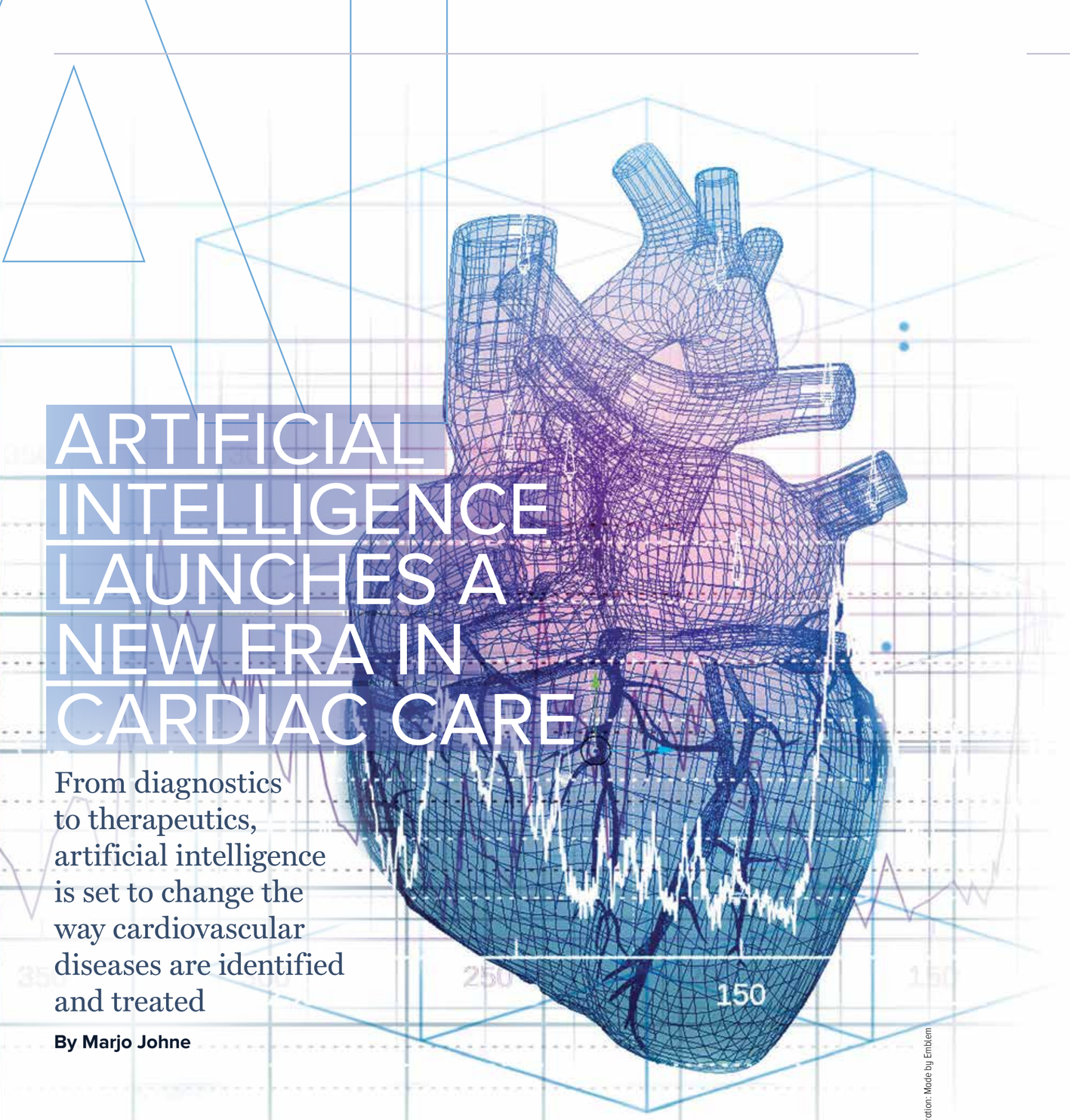


Illustration: Made by Emblem

A diagnosis of coronary artery disease usually comes after a series of procedures, including blood tests, exercise to reproduce symptoms, an electrocardiogram, a chest X-ray and, finally, cardiac catheterization, where a thin tube is inserted through the heart's blood vessels to check blood flow and function in various parts of the organ.

It can take weeks, even months, for each patient to go through these gold-standard procedures.

But this decades-old way of diagnosing coronary artery disease could soon be a thing of the past, thanks to artificial intelligence (AI) technology.

"With our technology, you just lay down, take off your shirt and, with a hand-held, battery-operated device, your doctor can take a three-minute recording that collects 10 million data points," explains Don Crawford, president and CEO of Analytics 4 Life Inc., a Toronto-based company focused on artificial intelligence-based medical devices. "This data is then sent to a cloud storage device, and from there our computers take that data and create a three-dimensional image of the heart, along with a detailed report," explains Mr. Crawford.

"By the time the patient has their shirt back on, the physician has already received the report on their computer. And based on this report, they can let their patients know whether or not they need to go to the cath[eterization] lab."

The Analytics 4 Life technology, currently being tested in a dozen hospitals in the United States, is at the leading edge of artificial intelligence in cardiac care – an emerging field of science that's set to change the way cardiovascular diseases are diagnosed and perhaps even treated.

At the University of Nottingham in England, researchers used machine learning – where AI algorithms trained themselves – in order to find patterns to predict which patients would have their first heart attack over the next 10 years. After scanning close to 300,000 patient records, the researchers found that the AI algorithms did significantly better in predicting heart attacks than assessments based on the commonly used American College of Cardiology/American Heart Association guidelines.

In India, a start-up called Cardiotrack recently rolled out a technology platform that uses a hand-held device, cloud storage and artificial intelligence to capture and analyze electrocardiogram signals for specific heart conditions.

"The possibilities with artificial intelligence are truly exciting," says Brian Golden, Sandra Rotman Chair in Health Sector Strategy at the University of Toronto (U of T) and the University Health Network (UHN) and vice-dean of professional programs at U of T's Rotman School of Management. "The ability to instantly recognize patterns and make sense of data from these patterns will improve diagnosis speed and quality, reduce wait times, improve health outcomes and reduce costs."

In Canada, the stage is set for AI to transform how heart disease is diagnosed, treated and managed. And the Peter Munk Cardiac Centre (PMCC) is right in the centre of this exciting transformation, powered by digital data, ubiquitous connectivity and intelligent machines.

Armed with a $100-million donation from the Peter and Melanie Munk Charitable Foundation, the centre has forged a partnership with U of T's Vector Institute for Artificial Intelligence, which was launched last March to advance deep learning research and develop world-leading AI talent.

"This is the first formal health-care partnership that the Vector Institute has engaged in, and we anticipate that what we do with the Vector [Institute] will be the model for what it does subsequently with cancer, neurosciences and other health disciplines," says Dr. Barry Rubin, Chair and Program Medical Director, Peter Munk Cardiac Centre

Together, the PMCC and the Vector Institute will build an AI team that includes a lead computer scientist, software engineers and PMCC clinicians. This team will work to identify heart problems that can be solved through AI and machine learning.

"We will use predictive models and decision support to tailor patients' care to their unique clinical and genomic traits," says Dr. Rubin. "We will use natural language processing to communicate with patients in real time, no matter what language they are speaking. Taken together, this will improve the efficiency of health-care delivery, outcomes and patient satisfaction."

What will AI-supported cardiac care look like to patients and health-care professionals? Dr. Rubin paints a sample scenario, where doctors can remotely monitor patients with conditions such as abnormal heart rhythms and then bring to the hospital those who are identified as at risk of death or serious heart damage, based on AI algorithms that can analyze billions of biological and research data points.

"You can use the AI approach to pinpoint which patients face potentially lethal events, and bring them to the hospital before that happens," says Dr. Rubin. "So you're managing patients outside the hospital and using the real value of AI to predict and prevent these lethal events."

The great wealth and quality of digital health and research data at the PMCC are critical to the success of the centre's AI goals, says Dr. Rubin. The PMCC recently flowed six of 47 disparate clinical and research databases into a vast "data lake," and it is now working to bring the remaining databases into the same central reservoir.

By integrating all this data – blood tests, clinical notes, X-rays, ultrasounds, CT and MRI scans, pathology slides and genetic information – in one location, clinicians and researchers can use AI to discover potential causes of heart disease. These discoveries, in turn, can lead to new cures.

"For example, if we have data on 10,000 patients with a narrow heart valve, and it turns out that 2,000 of these patients have a similar gene mutation, we could determine how that gene works and develop new therapies that would prevent the heart valve disease from ever developing in patients with that mutation," says Dr. Rubin.

Toronto is one of the two epicentres for thought leadership in AI – the other place is Silicon Valley in California – and boasts a robust ecosystem for AI- and digital-based health-care innovations, says Ying Tam, head of health at the venture services for MaRS Discovery District, a Toronto innovation hub that connects entrepreneurs, business experts, researchers, educators and social scientists.

He points to Ontario companies such as Cloud DX and Deep Genomics, which use AI and machine learning to diagnose disease and design more targeted therapies.

While AI champions continue to innovate in health care, it will likely take years before many of these new technologies are adopted in clinical practice, says Mr. Tam. Regulations that govern medical technology are complicated, says Mr. Tam, and could work against the very nature of artificial intelligence. For instance, when an organization such as the U.S. Food and Drug Administration approves a medical solution, it does so based on a specific information package. With AI, information continues to change as the underlying algorithms learn from existing and new data.

> *"What we do with the Vector [Institute] will be the model for what it does subsequently with cancer, neurosciences and other health disciplines."*
>
> **Dr. Barry Rubin,** Chair and Program Medical Director, PMCC

Nevertheless, AI solutions have already been proven in other areas in health care. Dr. David Jaffray, Senior Scientist at Princess Margaret Cancer Centre in Toronto, points to the use of algorithms at the hospital to automate the design of treatments for cancer patients.

"The technology is very attractive because it allows us to design the treatment sooner, treat patients sooner and even ensure that the treatment plans follow the appropriate protocols," he says.

This level of AI-enabled efficiency can, in the future, also help hospitals to optimize the use of their resources, while ensuring the best outcomes for patients, says Dr. Rubin.

"If we had complete data on all of our patients, we could use AI to predict which patients that had heart valve surgery would stay in hospital three days or 10 days after their operation," he says. "Using this AI-based approach, we will be able to better plan and better utilize our health-care resources."

Having cemented its partnership with the Vector Institute, the PMCC must now work to integrate AI into practice – an undertaking that requires a shift in mindset around patient care.

"We will need to train clinicians and students at the PMCC to work in environments where AI-based predictions will inform treatment decisions and the management of patients," says Dr. Rubin. "There's no question that AI and machine learning are the future."

Heart valve innovations:

Novel procedures and devices keep pumping in

Transcatheter Aortic Valve Implantation (TAVI) has changed the game in heart valve care and saved the lives of patients who were considered too high-risk for surgery. With TAVI now well-entrenched in clinical practice, cardiac doctors are looking out for the next big thing in heart valve repair and replacement

by Marjo Johne


Dr. Maral Ouzounian


Dr. Mark Osten


Dr. Tirone David


Dr. Robert James Cusimano


Dr. Eric Horlick

Game-changing. Life-saving. Grand slam. Phenomenal. These are just some of the words doctors and patients use to describe Transcatheter Aortic Valve Implantation (TAVI), which replaces a damaged heart valve with a replacement valve inserted through a small incision in the leg.

TAVI has been a godsend for patients considered too high-risk for open heart surgery. The results so far have been outstanding, with an estimated 20 per cent reduction in deaths a year after the procedure. Large randomized studies on high-risk and moderate-risk patients have also shown the benefits of a procedure that can put the patient back home the next day.

"TAVI completely revolutionized how we take care of patients with aortic valve disease," says Dr. Maral Ouzounian, cardiac surgeon at the Peter Munk Cardiac Centre (PMCC). "Before TAVI, patients who were frail or elderly would not be sent to a surgeon for assessment because of concerns they would not make it through surgery. TAVI has really changed that – we regularly perform TAVI on patients beyond the age of 90 [years] – and most often, they go home within a day or two of the procedure."

With TAVI now well-entrenched in clinical practice, doctors and scientists are eyeing the next wave of innovations in heart valve care.

A huge momentum in innovations

TAVI has created a huge momentum in heart valve innovations and has set the stage for future transcatheter valve technologies that are tackling the other three valves of the heart through less-invasive procedures. As a recognized leader in heart valve care, the PMCC has early access to many of these innovations – initially through clinical trials, and then more widely after regulatory approval. The PMCC is on the cutting edge of these advances and is one of a few centres in Canada routinely providing transcatheter valve repair or replacement for each of the four valves of the heart.

Experience and infrastructure key to accessing new technologies

"To access these innovations, you need a highly functional and experienced team with a strong reputation nationally and internationally," says Dr. Ouzounian. "We've been doing TAVI since 2006 and are recognized nationally as a centre able to tackle cases of great complexity. That's important to companies that are developing these new technologies. They want an experienced group, who work well together to achieve outstanding results with novel technology – there's just too much at stake. The expertise we bring to the table is critical to achieving great results for our patients."

Having a robust and sophisticated clinical infrastructure has also been critical in gaining early access to new innovations, says Dr. Mark Osten, a PMCC cardiologist and lead investigator into new structural heart disease devices.

He points to the PMCC's state-of-the-art operating rooms, which include two hybrid rooms – one that features a CT scanner and fluoroscopy machine and another that incorporates diagnostic imaging equipment – that support more complex procedures.

"The companies that make these new technologies recognize that we have the infrastructure, the support of our institution and an incredible breadth of experience in cardiac and structural heart disease," says Dr. Osten. "We do some of the highest-risk cases in the country."

So what new heart valve innovations are the PMCC doctors testing these days? The latest technologies offer the potential for major improvements in quality of life for patients who otherwise would be in profound heart failure or die. Novel technologies have been applied to each of the four valves of the heart, relieving leaking and stenotic (narrowed) valves and improving a patient's symptoms.

UP AND COMING: THE LATEST INNOVATIONS AND APPLICATIONS IN HEART VALVE CARE

MitraClip

Doctors at the PMCC use a device called the MitraClip to treat patients with severe mitral valve regurgitation, a disease characterized by a distorted left ventricle that stretches the mitral valve opening or by abnormalities of the valve itself that prevent the valve flaps from closing properly. This gap causes blood flowing into the left ventricle to leak backward into the lungs.

When a patient has severe mitral valve regurgitation, they may become breathless, and the heart becomes enlarged over time. Traditionally, this has required open heart surgery to repair or replace the valve. The PMCC has been an international leader in pioneering surgical techniques for this condition. In some cases, because of previous heart surgery, poor pump function or other medical problems, patients are just too sick or too weak to tolerate open heart surgery.

This is where the MitraClip comes in. Many patients who cannot tolerate open heart surgery may be helped by the clip.

The clip is implanted through a catheter based technique via a vein in the leg. The MitraClip is a V-shaped clamp with movable arms that can open and close to pinch leaking valve leaflets together, ensuring that they meet, reduce leaking and restore proper functioning of the valve. Tissue eventually grows over the clip to further support the clip. Patients can often be discharged home the next day.

The MitraClip can help patients with a severely leaking mitral valve who are not surgical candidates, says Dr. Tirone David, cardiovascular surgeon and the Melanie Munk Chair in Cardiovascular Surgery.

"We use the MitraClip for patients who are not operative and are symptomatic" he says. "We offer this procedure as palliation, and it does offer relief and improved quality of life for many of our non-operative patients. Surgery works better, but not everyone is suitable for heart surgery".

Tricuspid valve repair

In the right side of the heart, the tricuspid valve – which has three flaps, or leaflets, that open and close – regulates the flow of blood from the right upper chamber (right atrium) to the lower chamber (right ventricle). When the lower chamber is enlarged, the tricuspid valve stretches and pulls apart, and the flaps no longer meet in the centre, causing blood to regurgitate back into the upper chamber.

To repair this faulty valve, doctors at the PMCC are participating in a clinical trial testing a new therapy called the Forma System, which involves the placement of a balloon-like device into the centre of the valve. The foam-filled polymer balloon – also referred to as a "spacer" – is implanted through a vein in the upper chest using a catheter – a similar technique to implanting a pacemaker.

"Will it work? I think it will help to reduce the problem, but I'm not sure if it will completely fix it," says Dr. Robert James Cusimano, a cardiac surgeon, and clinical researcher at the PMCC, who holds the David and Stacey Cynamon Professorship in Cardiovascular Surgery Innovation and Education. "That's what we are looking to find out."

Often overlooked, the tricuspid valve is a complex structure that resembles three parachutes with strings attached to the heart. Tricuspid valve regurgitation usually doesn't trigger any symptoms until the condition becomes severe. At its worst, it can lead to heart failure, severe swelling of the legs and fluid in the belly, says Dr. Cusimano.

"It can become very dangerous when you don't fix the problem," he says. "The Forma System – which is still an investigational therapy and not available for use outside a trial setting – could be one way to do this."

Transcatheter mitral valve replacement

The success of TAVI has encouraged researchers to push for similar advances in minimally-invasive mitral valve replacement. A number of medical device manufacturers have developed transcatheter options for this procedure, says Dr. Ouzounian.

"We are still in the early days of mitral valve replacement compared to TAVI," she says. "In many ways, TAVI is easier because the aortic valve is anatomically more straightforward and has a whole lot of calcium in it to anchor the replacement valve."

A number of medical device manufacturers have developed their own version of transcatether mitral valve replacement. Dr. Ouzounian says she and the other cardiac specialists at the PMCC are evaluating one particular system that is part of a clinical trial.

"At this point, we don't know which transcatheter mitral valve replacement technology will be successful. They're all different, with their own set of advantages and risks," she says.

Regardless of which technology is used, transcatheter mitral valve replacement is considered a high-risk procedure, says Dr. Ouzounian. Because of this, doctors at the PMCC are considering patients according to a detailed experimental protocol, to select those best suited to the technology.

"We will be looking for specific patient traits, as well as specific mitral valve anatomy, including the amount of calcium in the valve leaflets, and whether the opening and the geometry of the valve and surrounding structures are optimal," she says. "Right now, there really isn't anyone in the world with enough experience in this type of procedure, and it is still experimental."

Percutaneous pulmonary valve implant

The PMCC recently started assessment of a second-generation device to fix pulmonic valve disease, often related to a congenital heart condition where blood may not flow properly from the heart to the lungs because the valve between the right ventricle and the pulmonary artery is defective.

Like TAVI, the new device – a collapsible cylinder with scalloped edges – is inserted into the dysfunctional valve through a catheter.

"Patients with pulmonic valve disease tend to develop problems when they're very young, so they often have operations as babies or children, and these procedures eventually fail in adulthood," says Dr. Osten. "We have had devices for a particular anatomic subset of these patients for almost a decade, and the long-term results have been very rewarding. The next generation of devices, which are now being evaluated in trials, will be able to address a much larger population of patients with this problem. The potential to replace the pulmonary valve, through a small vein in the leg, in most patients during their most productive years – is just around the corner."

Back to TAVI: From revolution to evolution

TAVI continues to evolve in its applications. Dr. Eric Horlick, a cardiologist at the PMCC, sees a future where TAVI is the go-to treatment for most, if not all, aortic valve patients. "Right now, there is more TAVI being done in the U.S. than conventional surgical aortic valve replacement."

He points to clinical trials now evaluating patients who are low-risk for surgery and treating them with TAVI. The PMCC is participating in these clinical trials, which are likely to change the way care is delivered to a very common form of valve disease.

"Operationally, the U.S. has seen greater adoption of TAVI for moderate-risk patients," says Dr. Horlick, who holds the Peter Munk Chair in Structural Heart Disease Intervention, which focuses on research into minimally-invasive approaches to managing inherited or acquired heart defects. "Right now, there's TAVI funding in Ontario only for high-risk patients. We hope this will change as more and more compelling positive data supporting TAVI becomes available. For the last several years, we have been performing TAVI without a general anesthetic, under minimal sedation and without any surgical incisions in the groin. The procedure typically takes less than an hour. Recovery from TAVI in 2017 has become much easier for the patient. They can be at home, recovering in 24 hours."

In search of the next big thing

What could be the next game-changer after TAVI? Dr. Paul Fedak, a researcher for the Heart and Stroke Foundation of Canada and a professor in the Department of Cardiac Sciences at the University of Calgary, says the next big breakthrough in valve care is likely to come from tissue engineering innovations.

"I think in the future, we will have replacement valves that are designed for each patient out of their own cells and tissues," he says. "These will be real game-changers because you'll be less prone to infection and won't need blood thinners, the valves will never break down and when they're used in a younger patient, they'll have the potential to grow as the patient grows, which is a huge deal."

In the meantime, the research and clinical teams at the PMCC continue to examine new and emerging technologies in heart valve care. Drs. Osten and Horlick recently travelled to Israel as part of a project to evaluate the usefulness of holographic imaging of the heart during a medical procedure.

The three-dimensional digital image, which floats in mid-air and can be touched, manipulated and even cut up to show the inner anatomy of the heart, is a novel technology with potential applications in education and, most significantly, as a tool in the operating room and catheterization lab.

"Cardiac imaging plays a major role in structural heart disease intervention. If a technology can help us have a greater understanding of the cardiac and vascular structures, this will ultimately translate into better decision-making and clinical outcomes for our patients. With holographic imaging, we will hopefully be able to define the anatomy with more precision and potentially use it to guide us live through these minimally-invasive procedures," says Dr. Osten. "That's something that's potentially a game-changer, and we are going to be the first and only hospital in the world to evaluate it. It will be exclusive to the PMCC."

International fellows come to learn the 'PMCC Way'

Hundreds of national and international physicians apply each year to train with Peter Munk Cardiac Centre specialists in a unique program

by Shelley White

Dr. Diego Delgado and Dr. Carolina Alba, cardiologists from Argentina, were two of the fellows from around the globe hoping to bring PMCC teaching back to their home institutions.

At the Peter Munk Cardiac Centre (PMCC), the world's best and brightest come together for a common cause: to save lives.

Walking through the halls of the PMCC, it's not uncommon to encounter groups of international fellows intently discussing a complex case with staff physicians. These fellows hail from all over the globe – Asia, South America, the U.S., Europe, Africa – bringing knowledge with them and then taking what they've learned back to their home countries.

Each year, hundreds of national and international physicians apply to obtain postcertification training with experienced specialists at the PMCC in areas such as: adult congenital heart disease, cardiovascular surgery, vascular surgery and heart failure and transplantation. While they learn, the fellows provide much-needed manpower to help PMCC staff with the day-to-day work of treating patients.

The PMCC's fellowship program attracts international physicians because of its excellent worldwide reputation, says Dr. Barry Rubin, Medical Director of the PMCC.

"We are a growing, expanding, international brand," he says.

"We have a clear mission to be the No. 1 heart centre in the world." Fellows also want to study with the PMCC's many "superstars" in the field, he adds, such as cardiac surgeon Dr. Tirone David, cardiologist Dr. Heather Ross and vascular surgeon Dr. Thomas Lindsay.

While at the PMCC, fellows learn the "PMCC Way," says Dr. Rubin. It's a philosophy that is the cornerstone of the institution and includes three pillars: a mandate to work in multidisciplinary teams, a commitment to using the best equipment in the world and an unremitting focus on innovation.

"Lots of people talk about this, but we actually walk the walk," he says.

Dr. Rubin says that one of the goals of the international fellowship program is to teach fellows the PMCC Way in the hopes that they will bring it back to their home institution in Tokyo or Buenos Aires or Bangalore.

"The real mark of success is: 'Did that person ascend to a leadership position and then start training other people locally, the way they were trained at the PMCC?'" says Dr. Rubin. "That's when you know you've really had an impact."

Meet four physicians who have had that impact since their time as international fellows at the PMCC:

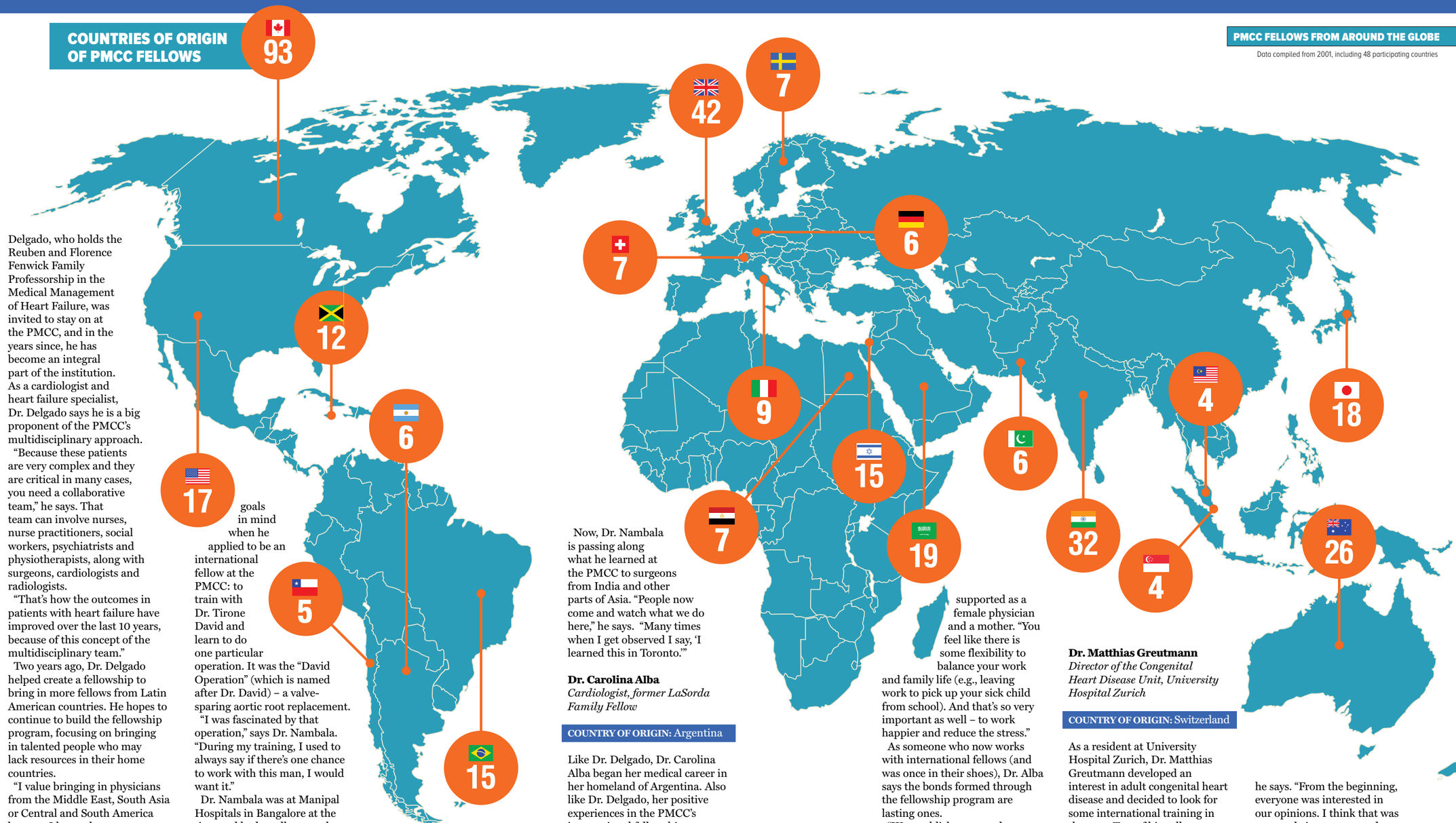
Dr. Diego Delgado
Cardiologist, Reuben and Florence Fenwick Family Professorship in the Medical Management of Heart Failure

COUNTRY OF ORIGIN: Argentina

Dr. Diego Delgado was a cardiologist in his native Argentina when he decided to further his training internationally. He says he was drawn to the PMCC because the transplant program was new, and he was looking for a challenge.

"I was already trained in advanced heart failure and transplant mechanical devices, so for me it was going to be more of a challenge to help build a program from scratch, versus going somewhere that was already established," he says.

After his fellowship, Dr.



PMCC FELLOWS FROM AROUND THE GLOBE	
Data compiled from 2001, including 48 participating countries	
COUNTRY	**TOTAL**
Ireland	7
Belgium	6
Finland	5
New Zealand	5
Spain	5
South Africa	4
Mexico	3
Netherlands	3
France	3
Philippines	2
Syria	2
Greece	2
Iceland	2
Sudan	2
China	2
West Indies	1
Slovenia	1
Poland	1
Hungary	1
Portugal	1
Czech Republic	1
Hong Kong	1
Norway	1
Lebanon	1
Russia	1
Korea	1
Thailand	1
Guyana	1
St. Lucia	1
Brunei	1
Austria	1
St. Kitts	1
Antigua	1
Trinidad & Tobago	1
Romania	1
Nigeria	1
Iran	1

Delgado, who holds the Reuben and Florence Fenwick Family Professorship in the Medical Management of Heart Failure, was invited to stay on at the PMCC, and in the years since, he has become an integral part of the institution. As a cardiologist and heart failure specialist, Dr. Delgado says he is a big proponent of the PMCC's multidisciplinary approach.

"Because these patients are very complex and they are critical in many cases, you need a collaborative team," he says. That team can involve nurses, nurse practitioners, social workers, psychiatrists and physiotherapists, along with surgeons, cardiologists and radiologists.

"That's how the outcomes in patients with heart failure have improved over the last 10 years, because of this concept of the multidisciplinary team."

Two years ago, Dr. Delgado helped create a fellowship to bring in more fellows from Latin American countries. He hopes to continue to build the fellowship program, focusing on bringing in talented people who may lack resources in their home countries.

"I value bringing in physicians from the Middle East, South Asia or Central and South America because I know that we can create a huge global impact by training these people and having them go back to their own country," he says. "I've seen it."

Dr. Sathyaki Nambala
Chief cardiac surgeon, Apollo Hospitals, Bangalore

COUNTRY OF ORIGIN: India

Dr. Sathyaki Nambala had two goals in mind when he applied to be an international fellow at the PMCC: to train with Dr. Tirone David and learn to do one particular operation. It was the "David Operation" (which is named after Dr. David) – a valve-sparing aortic root replacement.

"I was fascinated by that operation," says Dr. Nambala. "During my training, I used to always say if there's one chance to work with this man, I would want it."

Dr. Nambala was at Manipal Hospitals in Bangalore at the time and had a colleague who had trained with Dr. David. The colleague was going to an international conference in Barcelona, Spain, so Dr. Nambala gave him his CV in the hopes he could pass it on to Dr. David. Two months later, Dr. Nambala was on his way to Toronto to be an international fellow at the PMCC.

"I actually landed in December," he says. "I'd never seen snow in my life before."

During his time at the PMCC from 2006–07, Dr. Nambala had the chance to work with Dr. David and see the "David Operation" first-hand. "He's probably the best surgeon I've worked with in my life so far, and that experience is something I don't think I'll ever forget," he says.

Now, Dr. Nambala is passing along what he learned at the PMCC to surgeons from India and other parts of Asia. "People now come and watch what we do here," he says. "Many times when I get observed I say, 'I learned this in Toronto.'"

Dr. Carolina Alba
Cardiologist, former LaSorda Family Fellow

COUNTRY OF ORIGIN: Argentina

Like Dr. Delgado, Dr. Carolina Alba began her medical career in her homeland of Argentina. Also like Dr. Delgado, her positive experiences in the PMCC's international fellowship program convinced her to stay on after her fellowship was over.

"One important aspect of the fellowship program at the PMCC is that all are treated with respect," says Dr. Alba.

"Fellows and other team members – no matter what their position at the hospital – can give an opinion," she says. "Everybody is heard here."

Dr. Alba says she has also felt supported as a female physician and a mother. "You feel like there is some flexibility to balance your work and family life (e.g., leaving work to pick up your sick child from school). And that's so very important as well – to work happier and reduce the stress."

As someone who now works with international fellows (and was once in their shoes), Dr. Alba says the bonds formed through the fellowship program are lasting ones.

"We establish very good relationships with everybody who comes here, so everybody feels engaged," she says. "I am able to tell you that because I have been a fellow until recently, so I know very well the intimate feeling of all the fellows. And when they move back to their countries, we keep the connections, which turn into opportunities to collaborate with patient care and research."

Dr. Matthias Greutmann
Director of the Congenital Heart Disease Unit, University Hospital Zurich

COUNTRY OF ORIGIN: Switzerland

As a resident at University Hospital Zurich, Dr. Matthias Greutmann developed an interest in adult congenital heart disease and decided to look for some international training in the area. Two of his colleagues had been fellows at the PMCC, so he also applied.

"It was well-known that Toronto is the place to be for congenital heart disease," he says.

Dr. Greutmann was a fellow at the PMCC from 2008–10, and says he was struck by the "openness" and "spirit" at the hospital.

"I always felt extremely welcomed by the team there," he says. "From the beginning, everyone was interested in our opinions. I think that was extremely important, and that's what I brought back to Switzerland."

Connecting with other international fellows from around the world while at the PMCC has also been a boon, says Dr. Greutmann.

"If a patient comes to me and tells me, 'I am going to travel here or there,' I'll say, 'I know someone,' and I'll refer them," he says. "I am still connected all over the world."

And he is always pleased to see his former PMCC colleagues at international conferences, such as the recent World Congress of Pediatric Cardiology and Cardiac Surgery in Barcelona.

"The whole Toronto group met for a dinner, and it was very nice," he says. "It's like my Toronto family."

A steady stream of innovations point to the day when electronic pacemakers may be obsolete

Development and advancements on the heart-regulating apparatus over the past decade have been phenomenal

By **Chris Atchison**

DR. GORDON CHONG MAY HAVE DEDICATED HIS CAREER TO FIXING TEETH, but his golden years have included an unexpected education in cardiac care – specifically, his own.

A retired dentist, Dr. Chong has been the recipient of four pacemakers since being diagnosed with congestive heart failure in 2011. His pacemaker has since been fitted with a defibrillator to keep his heart functioning in the event of a major cardiac incident.

"It seems to be working well, but the condition I have is still deteriorating," says Dr. Chong. "I'm being assessed for a heart transplant or a mechanical device that will get me over the hump for a while."

Dr. Chong, a patient of the Peter Munk Cardiac Centre (PMCC), is one of more than 10,000 Canadians who receive electronic pacemakers each year and one of more than 120,000 Canadians currently living with the life-saving technology.

The tiny devices treat arrhythmias – abnormal heart rhythms – and help the heart beat at a steady, normal pace. Pacemakers average about a seven-year lifespan before their batteries need replacing.

Dr. Chong has a unique perspective on the evolution of the heart-regulating apparatus, thanks to his medical background.

"I spent two years [studying] at the Hospital for Sick Children when I graduated and have been following (pacemaker development) for the past few years…and in the last decade, the amount of knowledge and technology, and bringing together of biometrics and biology, has been phenomenal," the 73-year-old says.

Indeed, the devices have come a long way since the invention of an external, toaster-sized pacemaker in 1950 by Canadian engineer John Hopps, in conjunction with researchers from the University of Toronto.

Despite its many shortcomings – the device required an AC power source, creating obvious mobility challenges for patients – Hopps's pacemaker was regarded as a drastic improvement over previous rudimentary devices.

That was until a team in Minnesota developed a battery-powered, belt-worn pacemaker later that same decade.

Fully implantable devices

01

became available in the 1960s. Continued improvements have reduced the pacemaker's size, while improving battery life and overall effectiveness. The development of specialized models, such as biventricular pacemakers, has further improved patient survival rates and quality of life.

It's not only the direct technological advancements in pacemaker design that have researchers and clinicians excited, but also innovations in related treatments and diagnostic procedures that could one day make electronic pacemakers virtually obsolete.

One of the most common heart rhythm disorders is atrial fibrillation, which affects millions of people worldwide. The condition causes disabling symptoms of palpitations and an increased risk of heart failure, stroke and death. An important treatment option for patients who cannot be managed with medications is a heart procedure known as catheter ablation, where regions of the heart muscle causing atrial fibrillation are burned away. However, this procedure may not work well in many patients because the regions causing atrial fibrillation are not apparent with current technology.

This is where University Health Network's Thomas I. (Toby) Hull Centre of Excellence in Heart Rhythm Disease program aims to be innovative.

Consider the work of Dr. Vijay Chauhan, a cardiologist at the PMCC who is developing new technology to localize atrial fibrillation electrical drivers in order to improve catheter ablation for patients with atrial fibrillation.

Dr. Chauhan and his team have set out to find what he calls "the flashing beacon in the heart" that may sometimes trigger and sustain the condition.

To curb atrial fibrillation, doctors often begin with drug treatments, and if unsuccessful, they will then perform a catheter ablation around the pulmonary veins to normalize the patient's heart rhythm.

But catheter ablation has only a 50 per cent success rate, particularly in patients whose atrial fibrillation persists all the time, due largely to the fact that atrial fibrillation in these patients often stems from abnormal electrical areas in the heart outside the pulmonary veins that doctors can't see or treat.

"That brings in the notion of finding and ablating electrical drivers that can be outside pulmonary veins," Dr. Chauhan says.

But without an effective tool to do exactly that, Dr. Chauhan and his team developed a mapping technology which systematically analyzes the atrial fibrillation electrical signals from hundreds of regions in the heart. With a study currently underway, researchers should know in a year whether the new treatment does, indeed, improve catheter ablation success rates.

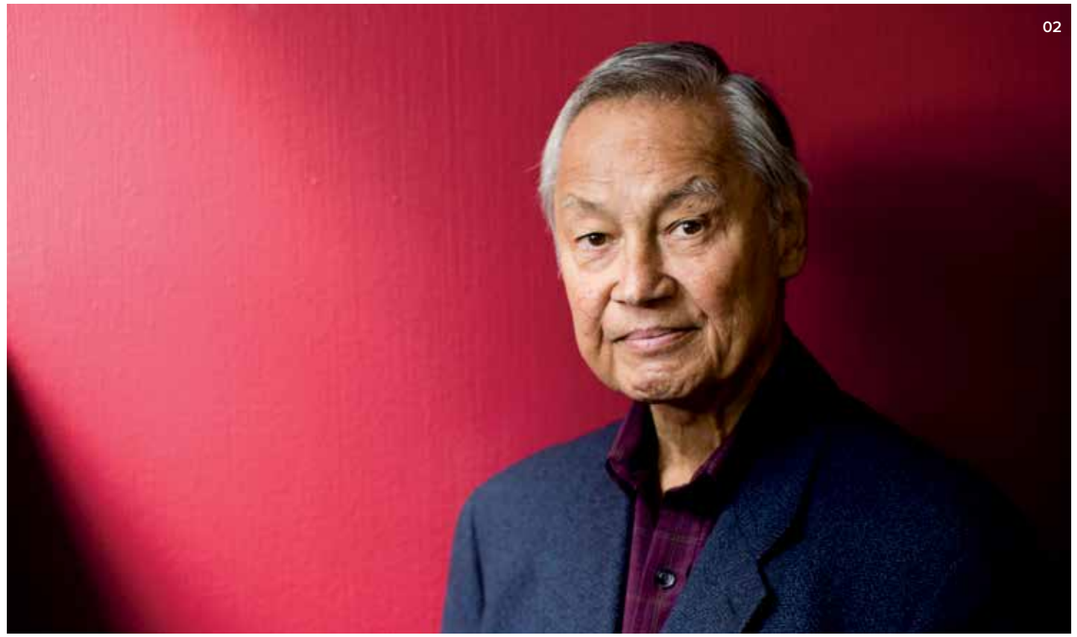
Other researchers, including Dr. Gordon Keller, Director of the University Health Network's McEwen Centre for Regenerative Medicine in Toronto, are using trailblazing biological innovations to improve heart health and potentially mitigate the use of pacemakers.

In 2016, Dr. Keller and his team announced that they had produced sinoatrial node pacemaker cells – which regulate the heart's rhythm with electrical impulses – from human pluripotent stem cells. The pacemaker cells were injected into rat hearts and assumed a biological pacemaker function, exactly as planned.

"The groundbreaking advancement could lead to the development of a biological pacemaker for humans that would offer immediate benefits over current electronic pacemaker devices, which have limited battery lives and are unable to adapt to changes in heart sizes in pediatric patients. The team's long-term goal is to produce the human heart cells that make up the organ's chambers, including the ventricles and atria. The goal is to use these ventricular cells to create new muscle in the hearts of patients who have experienced a heart attack. The whole idea of using cells we make in a lab to treat patients may be closer than we thought," Dr. Keller says.

01 Drs. Vijay Chauhan and Andrew Ha, cardiologists at the PMCC, and their team looking for "the flashing beacon in the heart" that may trigger atrial fibrillation.

02 Dr. Gordon Chong, a retired dentist and patient at the PMCC, has had multiple pacemakers since 2011.



Paving the way to truly mend a broken (donor) heart in the future

Anticipated breakthroughs by Peter Munk Cardiac Centre doctors and scientists could lead to more donor hearts, fewer rejections, advanced stem cell treatments and repairs to a patient's own heart

By **David Israelson**

THREE DECADES AFTER THE FIRST SUCCESSFUL HEART TRANSPLANT WAS ACHIEVED IN TORONTO, the medical mysteries keep unravelling, and the miracles keep multiplying.

"We have done more than 700 transplants, and I have been here long enough to have worked on 500," says Dr. Heather Ross, world-renowned cardiologist and Director of the Ted Rogers and Family Centre of Excellence in Heart Function and the Cardiac Transplant Program at the Peter Munk Cardiac Centre (PMCC), part of the University Health Network.

"It's still a remarkable achievement every time it happens," Dr. Ross says.

Thanks to new research and technology, it's getting more remarkable all the time. Doctors and scientists are on the verge of breakthroughs that promise to increase the success of heart transplants and which may vastly expand the number of patients who can receive the life-saving treatment.

The first successful heart transplant in Toronto took place on November 17, 1968, at St. Michael's Hospital, performed by Dr. Clare Baker on Charles Perrin Johnston, who lived until 1975. It took place after two earlier transplants in Toronto in which patients died within a week of surgery, as well as less than a year after the world's first heart-to-heart transplant was performed in South Africa by Dr. Christian Barnard.

In the next 30 years, the possibilities for innovation range from incremental improvements in technology and medication to *Star Trek*-like procedures that are so stunning they're barely imaginable.

Dr. Ross says the breakthroughs and discoveries that medical teams are working on now include:

- new medications that lower the risk of cellular rejection;
- the use of donor hearts that were previously considered too damaged to transplant, making transplants available to many more people;
- the possibility of stem cell treatment to repair damaged hearts; and
- taking a patient's own heart and putting it "on the hoist" – removing it temporarily for repairs and then reinstalling it, rather than replacing it with a donor's heart.

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> ***"We're probably taking only up to 35 per cent of the hearts from donors. The rest are turned down, sometimes because the donors are really old or have heart disease."***
>
> **Dr. Mitesh Badiwala,** Cardiac Surgeon

01 Dr. Mitesh Badiwala and his team are working on a host of new technologies, some which will be able to repair heart damage as fast as possible.

02 Dr. Heather Ross, Director of the Ted Rogers and Family Centre of Excellence in Heart Function, has worked on 500 of the more than 700 heart transplants done to date at the Toronto General Hospital and the PMCC.

"In the first 30 years, nothing has really changed in terms of the surgery itself – until recently," says Dr. Mitesh Badiwala, a cardiac surgeon at the PMCC.

"We'd take a donor's heart, flush it and package it in a cooler full of ice." Donors are always those who have been declared brain-dead, with no hope of recovery.

Brain death is declared when it is clearly irreversible, and it is a legally accepted concept of death in virtually every country in the world.

Still, even when a donor has been declared brain-dead, doctors can't use hearts that are damaged. So, many people who need transplants are placed on waiting lists.

"We're probably taking only up to 35 per cent of the hearts from donors. The rest are turned down, sometimes because the donors are really old or have heart disease," Dr. Badiwala explains.

At the same time, "there are hearts out there that we know have only temporary damage, and even though the donor is brain-dead, the heart has the potential to recover," he says.

Understandably, grieving families want a donor's heart to be used quickly to save someone, so Dr. Badiwala and his team are working on technology that can repair temporary heart damage as fast as possible.

"We're testing the machine in the lab now. We hope that later this year, we'll be able to use human hearts that have been discarded as too damaged for transplants and see how many we can bring back," Dr. Badiwala says.

"At some point, when we're confident that the hearts are working well, we'll be able to take them off the machine and use them for transplants."

Perhaps an even more exciting aspect of this research into correcting damage is that it may make it literally possible to fix a broken heart.

"It gives us an opportunity to potentially repair hearts, with new strategies that are being used in other labs," Dr. Badiwala says. New medications can be used experimentally without putting patients at risk, as leading-edge biotechnology such as gene or stem cell therapy are developed.

This goes beyond fixing the temporary damage that sometimes shows up in donors' hearts.

"We may be able to repair hearts that right now are not useable," Dr. Badiwala says.

The team is also about to begin clinical trials with DCD – or "donation after circulatory death" – hearts. Unlike hearts that come from donors who are brain-dead, DCD hearts have been considered unreliable for transplants because they stopped beating when the donor died.

Hospitals in Britain and Australia are now using DCD hearts.

"They've done this in those two centres nearly 50 times. My team and I visited the facility in Papworth, England (near Cambridge), and we were impressed. They were able to increase their volume of transplantation by more than 50 per cent," Dr. Badiwala says.

"We hope to decrease the incidence of patients who die while they're on waiting lists."

Donors' and families' wishes must be respected, including when it is appropriate to withdraw life support for a patient who will not recover. The legal definition of a circulatory death in Canada is when a person's heart has stopped beating for five minutes, Dr. Badiwala notes.

Which leads to a dream for the future. "We can dream of the device we're working on to repair hearts becoming a device not just to repair hearts for transplant, but [also] to repair your own heart," Dr. Badiwala says. "Take it out, put it on the machine and transplant it right back into you."

This is not as far-fetched as it sounds. He points out that patients on waiting lists already survive for short periods, even months sometimes, with mechanical heart devices. Maybe they can do so while their own hearts are on the hoist.

Yet as promising as the future may be, the present at the PMCC is pretty amazing, too, Dr. Ross says.

"I've been working in this area for 23 years, and every time we do a transplant it seems like the first time, in terms of miraculous and life-saving potential."

02

Banking on the future

A massive biospecimen and data repository at the Peter Munk Cardiac Centre holds the promise of more precise, personalized medicine

By **Marjo Johne**

THERE ARE OVER 163,000 OUTPATIENT VISITS TO THE PETER MUNK CARDIAC CENTRE (PMCC) each year, where cardiovascular diseases that range from arrhythmia to heart failure are treated. Over the last three years, a growing number of these patients have also become contributors to the centre's biobank – an ambitious research infrastructure project that's opening the way to a deeper understanding of cardiovascular disease and the treatments that work best for each patient.

"What we have at the PMCC is a unique opportunity to examine specimens from thousands of patients [in order] to look for biological markers and novel pathways of cardiovascular disease," explains Dr. Phyllis Billia, a scientist and Co-director of the Peter Munk Cardiac Centre Cardiovascular Biobank. "The goal ultimately is to use this information to discover potential new treatments for the various types of cardiovascular disease."

Housed in a secured facility at the PMCC, the biobank is a massive repository containing more than 25,000 blood and tissue samples – a significant increase from the roughly 2,000 samples collected two years ago. The recent acceleration of blood and tissue sample collection can be attributed to the efforts of the PMCC's Ted Rogers Centre for Heart Research site, where biobanking is an essential pillar to many of the research activities. To build the biobank, the PMCC asks patients who go through procedures that require the collection or removal of biological specimen – such as blood tests or surgery – for permission to store their tissue or blood.

These samples are then linked to patients' clinical data, including MRI and other imaging.

"This is one of the largest biobanks of its kind in Canada, representing a full gamut of cardiovascular diseases," says Dr. Billia, who notes that all samples and data are scrubbed of any details that could identify their source.

The PMCC Biobank, enabled through the efforts of the Ted Rogers Centre for Heart Research, holds out the promise of more precise, personalized medicine. With its large – and still-growing – collection of samples and data, the biobank gives scientists access to research material with much greater depth and breadth than what they would find in their own laboratory biobanks.

The value of biobanks to researchers is underlined by numerous success stories in various fields. In cancer research, the ability to screen banked tissue samples led to the discovery of an antibody – which was subsequently developed into a drug called Herceptin – that targets HER2-positive breast cancer cell receptors.

"The biobank is useful for those of us who do research on biological markers that we can measure from blood serum," says Dr. Michael Gollob, Chair of the Centre of Excellence in Molecular Medicine, a research program within the PMCC that's advancing personalized patient care by combining traditional clinical information with genetic, molecular, cellular and physiological data. "Having the blood or tissue samples from the biobank also enables us to extract DNA from those samples and conduct DNA-based research."

For patients, this translates into a future where therapies are fine-tuned to match each person's genetic makeup. Dr. Billia, for instance, is leading a study that uses blood from patients with hypertrophic cardiomyopathy – an inherited heart condition – to create laboratory models of the disease that are then used to test a range of treatments.

"This is a genetic condition with a 50 per cent chance of getting passed on to your children, and each child could potentially have different manifestations of the condition. One could have a long life expectancy, while another could just die suddenly from cardiac arrest," explains Dr. Billia. "By using a patient's blood sample to model the disease in the lab, we can test a library of drugs to see how the patient is likely to respond to each drug, allowing us to tailor treatment for each individual."

Dr. Gollob says the PMCC Biobank will also allow researchers to genetically model the different types of cardiovascular disease in various ways. For example: by identifying a specific DNA alteration of a particular heart cell leading to disease, scientists may be able to intervene on the pathway of the disease.

"From genetic discovery, we can then consider or innovate potential treatments targeting the disease-causing gene and its protein," says Dr. Gollob.

Dr. Richard Weisel, a cardiovascular surgeon at the PMCC and Co-director of the Biobank, says the biobank has already had an impact in cardiac surgery. As an example, he cites cases involving patients with dilated aortas, which would normally be removed and replaced once the affected blood vessels have grown to a radius of at least five centimetres.

"But some surgeons wondered if that's the right cut-off in deciding whether that blood vessel should be removed or not, mostly because we don't understand the mechanisms in which the dilation occurs," says Dr. Weisel, who is one of the scientists leading the PMCC Biobank. "So we took samples from the biobank and were able to look at patients who seem to have progression of the disease, versus those who did not."

This large-scale comparison gave doctors a better understanding of the disease and revealed certain genetic abnormalities associated with dilated aortas – new knowledge that has since led to new therapies for the condition, he says.

The PMCC Biobank continues to be a work in progress. A key goal, says Dr. Weisel, is to combine this project with other cardiovascular biobanks in Toronto and make the aggregate samples and data available to all researchers in the city.

"Our goal is to create a large consortium of cardiovascular researchers in the Greater Toronto Area who would have access to this incredible resource," he says. "We also hope to expand our capabilities to the extent where we'll have samples from all patients at the PMCC – something that's done as routine in some places in the United States and Europe."

> *"Our goal is to create a large consortium of cardiovascular researchers in the GTA who would have access to this incredible resource."*
>
> **Dr. Richard Weisel,**
> Cardiovascular Surgeon, PMCC, Senior Scientist, Toronto General Research Institute

01 Dr. Phyllis Billia, far left, Dr. Michael Gollob and Dr. Richard Weisel spearhead work at the Biobank, which stores more than 25,000 blood and tissue samples.

02 Dr. Billia says the goal of the Biobank is to discover new treatments for various types of cardiovascular disease.

Marva Lorde relied on a left ventricular assist device (LVAD) for two years before receiving a heart transplant.

Mechanical hearts are buying time for patients and groundbreaking research

Combined with stem cell technology, a patient's own heart can start pumping again

By **Bryan Borzykowski**

WHEN MARVA LORDE WENT TO BED ON THE NIGHT OF OCTOBER 25, 2007, nothing seemed out of the ordinary. The former bank employee had been enjoying a life of leisure after working for 34 years, and she was looking forward to going to her regular workout class in the morning. At some point during the night, though, a feeling of indigestion came over her, and soon after the clamminess and vomiting began.

Despite feeling ill, she drove herself to the hospital, where she learned she had experienced a massive heart attack and had to stay in the Coronary Intensive Care Unit for the next 10 days. "There was no pain, but on the inside damage was happening," she says. "I thought it was just a virus."

Over the next three years, the damage worsened to the point where, in 2010, her heart essentially stopped working on its own. Doctors had to implant a left ventricular assist device (LVAD) – a battery-powered mechanical heart that pumps blood through the body.

While Ms. Lorde had to plug it in every night, and she had to be mindful of the power cord sticking out of her chest, it helped improve her life. "I had to be careful, but I got around to do a lot of things, like my cooking and washing," she says. "I didn't feel sorry for myself."

Ms. Lorde received her mechanical heart (called a Duraheart) at the Peter Munk Cardiac Centre (PMCC), which, over the last 16 years, has developed a robust mechanical circulatory support program – it installed its 200th LVAD in late 2016.

In 2001, Dr. Vivek Rao, Division Head of Cardiovascular Surgery at PMCC and the Peter Munk Cardiac Centre Chair in Advanced Cardiac Therapeutics, launched the LVAD program in Toronto after working under Dr. Mehmet Oz at Columbia University, Department of Surgery, in New York, which has one of the world's largest mechanical heart programs.

Those first few years were challenging, as the program was exclusively funded by donors, which meant only about five to 10 devices a year were paid for. In 2012, though, the government began covering LVADs for use in patients on the heart transplant list, and the number of people receiving the device rose. Now, Dr. Rao and his team install about 30 annually.

MORE LVADS NEEDED

However, it's still not enough, says Dr. Rao. Most people with heart failure aren't candidates for heart transplants. They might have a history of cancer or lung problems that make them ineligible for a new transplant. LVADs, though, can help them live long and fulfilling lives. "Patients with heart failure who are not transplant candidates are given a death sentence," says Dr. Rao. "They have one or two years to live, and it's not a great life. But those who get these devices do live active lives. They're not restricted by heart failure anymore."

Now that funding has been extended to non-transplant patients, the number of LVADs installed should triple – from 30 to 90. That number could grow even more, as technology continues to improve. It may not be long before Dr. Rao is installing LVAD devices that charge without needing to be plugged in. "We'll get to the point where devices are completely implantable, and they charge like a watch battery," he says. "It won't impact life in any way, and you won't have to worry about your heart failing."

MAKING BAD HEARTS GOOD AGAIN

While the PMCC's mechanical heart program is mostly focused on implanting LVADs, it's also doing groundbreaking research around stem cell technology, says Dr. Terrence Yau, cardiovascular surgeon and Angelo & Lorenza DeGasperis Chair in Cardiovascular Surgery Research. He's currently trying to see if stem cells injected into the heart can help the patient's heart work on its own again.

Dr. Yau is taking patients with LVADs, putting stem cells into their heart and then turning down the LVADs to reduce their pumping function. Normally, if an LVAD is turned off or down, the patient's heart almost instantly fails. However, in the first phase of testing, Dr. Yau found that half of the patients who received stem cell injections could tolerate a reduction in the LVAD's power, compared to only 20 per cent of those patients who did not receive stem cells.

The second phase of the trials are now underway, which will see even more stem cells injected into LVAD patient hearts. The goal? To get people's hearts pumping again. "We want to be able to take the LVAD out and leave the patient with their own heart," says Dr. Yau. "There's nothing better than having your own well-functioning heart."

Ms. Lorde knows that better than most. In 2012, she received a heart transplant, which meant she no longer needed the LVAD. Now she can do everything she used to do, including going to exercise classes. "I've never felt better," says Ms. Lorde. "And that LVAD really helped me as I was waiting for a transplant."

The look and function of Left Ventricular Assist Devices (LVADs) have evolved over the years and are now being combined with other treatments, such as stem cell technology, to restore function to a patient's own heart:

2001
Heartmate I
(1,225 g)

2004
Novacore
(550 g)

2006
Heartmate II
(450 g)

2010
Duraheart
(540 g)

2010
Heartware
(160 g)

2014
Heartmate III
(200 g)

Imaging...with heart and innovation

A cutting-edge PET-MRI machine has enabled doctors to find new, less-invasive ways to improve the lives of patients and conduct new research

By **Kira Vermond**

Dr. Maral Ouzounian, opposite, Dr. Patrick Veit-Haibach, left above, and Dr. Michael Domanski are part of the team-based approach at the PMCC that works to maximize innovation using the PET-MRI machine.

ANYONE WHO HAS EVER SLID THROUGH THE TUNNEL OF A MAGNETIC RESONANCE IMAGING (**MRI**) machine likely remembers its raucous whirring and knocking, not to mention the squeeze of a snug 70-centimetre-wide bore.

But for some patients undergoing procedures at the Peter Munk Cardiac Centre (PMCC), the time spent in the life-saving imaging machine will result in something even more – Positron Emission Tomography (PET) images.

Back in April 2016, the centre acquired and installed one of only about 160 PET-MRI combination machines in the world, giving cardiology researchers access to the cutting-edge, hybrid technology. While MR uses strong magnetic fields to generate hyper-detailed images of the body's organs, a PET scan offers information about metabolic changes happening in organs or tissues. The images are generated simultaneously.

It's the best of both worlds, explains Dr. Patrick Veit-Haibach, Clinical Director of the PET-MRI, Joint Department of Medical Imaging (JDMI), and a German radiologist and nuclear medicine physician who came to Canada from Switzerland in April 2017.

"A PET-MRI should give you complementary information about the disease," he says. "At least for certain research questions, it's very important to have real-time simultaneous imaging, so you don't have a delay between one image and another."

Now, the machine is being used to conduct new research, determining everything from how heart and brain health are connected to pinpointing dangerous aortic aneurysms.

HEART AND BRAIN LINK

Take the work being done by Dr. Michael Domanski, Division Head, Cardiology. He's studying the link between aging arteries and neurological disorders such as Alzheimer's, which causes memory loss and cognitive decline.

As people age, their arteries stiffen, which exposes them to increased delivery of energy to the small blood vessels in the brain. "The brain gets more of a pounding," says Dr. Domanski. "So the question is: 'Can we link this pounding to Alzheimer's?'"

Dr. Domanski's team will be using a combination of PET-MRI and hemodynamics – measuring pressure and flow – to examine the effect of arterial stiffness on damage to the brain.

If his team can correlate pressures and flows with changes in the brain, they will have taken a step toward better understanding the link between blood vessel changes and loss of intellectual function.

"That's the grand scheme," he says.

AVOIDING THE WORST

Meanwhile, Dr. Maral Ouzounian, a cardiac surgeon who specializes in aortic disease at the PMCC, has a grand vision of her own. After moving to Toronto from Houston in 2014, she has performed many surgeries on patients with aneurysms or dissections in their aorta.

The aorta is the main artery that carries blood away from the heart to the rest of the body. If an aneurysm forms there – the artery wall weakens, so that it balloons out – it can quickly become a serious, life-threatening medical emergency if the aneurysm tears and bursts.

"If you tear your aorta at home, most of the time you don't even make it to the hospital; it's a fatal event," she cautions.

Most people don't even realize they're living with an aneurysm until it shows up on an unrelated echocardiogram or CT scan. Then the surgeon has a decision to make: operate to remove it or take a wait-and-see approach.

Some aneurysms are stable and are unlikely to rupture. But others are far more dangerous. The problem is, it's not easy to tell one from the other, so physicians depend on their size as a guide. In the part of the aorta that is close to the heart (root or ascending), aneurysms are repaired if they are larger than 5.5 centimetres.

Yet size can be misleading, says Dr. Ouzounian. Some will rupture or dissect when they're smaller, while others remain stable even as they hit the six-centimetre threshold.

But her new research could change when and how surgeons decide to operate. By using the hybrid PET-MRI machine, Dr. Ouzounian is looking at novel ways that imaging can help predict which patients have vulnerable aortas. Not only does it allow her team to examine inflammation of the aortic wall, which can't be completed with a CT scan or an ultrasound, but she can also look at the biomechanical properties of the wall. How stiff or compliant is it? How is the wall handling the pressure?

Once patients have their PET-MRI scan, they're wheeled to surgery, where Dr. Ouzounian removes the aorta and replaces it with graft material. The patient's aortic tissue is then taken to the lab, where it is examined under the microscope and tested for tensile strength. There, she can determine if the aortic wall was, in fact, weak and prone to rupture.

It's early days for Dr. Ouzounian's research, but she hopes the PET-MRI results will give surgeons a new, less-invasive diagnostic tool that will tell them which aortas are vulnerable.

"If we do find parameters that are predictive, we could tailor our therapies more to the specific individual," she says. "The PET-MRI gives us a much more in-depth look at somebody's aorta and allows more personalized decision making."

Considering the risk of death is only less than 1 per cent for elective surgery, it's no wonder Dr. Ouzounian is looking for ways to avoid risky emergency surgeries.

She's pleased she's been able to conduct her potentially life-saving research at the PMCC, where she works daily alongside vascular surgeons, interventional radiologists, cardiology partners and even geneticists.

"I really like the team-based nature of the work at [the] Peter Munk [Cardiac Centre] and the opportunity to do high-end surgery and research," she says. "My goal was to be an academic aortic surgeon – and this is the best place to do it." ▮

WHY USE A PET-MRI?

- It combines the spectacular structural imaging of an MRI with the ability to detect physiological changes in blood flow, viability and function.
- Images are taken simultaneously – quicker than using two separate imaging machines.
- A small amount of ionizing radiation is a real boon, particularly for pediatric patients who must be monitored their entire lives. •

Virtual care leaps forward

Advanced technology helps doctors empower patients' self-care

By **Daina Lawrence**

01

MORE THAN ONE MILLION CANADIANS CURRENTLY LIVE WITH HEART FAILURE, and 50,000 new cases are diagnosed each year. These numbers cost the Canadian health-care system more than $3-billion annually, according to the Heart Research Institute (Canada).

"We have an epidemic of heart disease, more specifically heart failure. And we can't keep doing big-box medicine," says Dr. Heather Ross, Director of the Ted Rogers and Family Centre of Excellence in Heart Function and a cardiologist at the Peter Munk Cardiac Centre (PMCC).

While medical advances in Canada are helping to treat those with heart disease, there are new systems that put the onus, as well as the power to drive an individual's health, back in the hands of the patient.

Innovations in heart failure research are spearheaded at the University Health Network (UHN) site of the Ted Rogers Centre for Heart Research, which is an integral program of the PMCC. Here, Dr. Ross and her team are using smartphone apps, digital platforms and even a Bluetooth-enabled monitor implanted into a patient's lungs to help manage symptoms and triggers of heart failure, educate patients and limit hospital trips.

Cardiovascular disease is one of this country's largest killers. Someone in Canada dies every seven minutes from a heart attack or stroke, according to the Heart and Stroke Foundation of Canada.

But this advanced technology helps health-care providers offer timely, optimal and efficient patient care with real-time patient data in the hopes of reducing the strain on Canada's health-care system.

"Virtual care has been a term that has been thrown around, but I think this is virtual care on steroids," says Dr. Ross. "What we have is a set of virtual tools to enhance self-care and to enlist patients in their own care, because patients are the largest work force in health care."

The main objective is to create an easy-to-use, patient self-care and treatment program that is both mobile and electronically based. Patients don't need to go to the clinic as often, and they can track symptoms and progress at the touch of a button, showing them how lifestyle choices can have an effect on heart health.

"If you think about obesity, diabetes, physical inactivity – all things that are risk factors for heart failure – if we can engage patients, we should be able to dramatically reduce the incidence or prevalence of heart disease, and therefore, heart failure," explains Dr. Ross.

And while some of the inner workings of these systems are staggeringly complex, the equipment the patients use at home is fairly simple.

Patients don't need to come into a clinic for a weigh-in. They can simply stand on a scale hooked up to an app on their smartphone, and the details are sent digitally to a team of health-care providers. At least this is the thinking behind Medly, a mobile application system designed at UHN that consists of a blood pressure cuff and scale that are digitally linked to a Bluetooth-enabled device.

Meredith Linghorne is a Nurse Practitioner-Adult at the PMCC, and she is on the receiving end of Medly's patient data.

"Medly allows us to see key clinical data, such as changes in weight and patient's symptoms, without having them come into the clinic," says Ms. Linghorne. She says that patients are asked to monitor their blood pressure, heart rate, weight and simple symptoms on a daily basis – something that would have been impossible before without daily trips to a clinic or a hospital.

"With this information, I know when they're getting into trouble. And this particular app is designed so they will get immediate feedback from us after taking their measurements, or the app tells them to contact us to discuss the problem."

02

03

01 Dr. Heather Ross notes that the epidemic of heart disease in Canada means new monitoring methods, such as CardioMEMS, must be developed.

02 Nurse Practioner Meredith Linghorne shows a patient how to use CardioMEMS, a mobile application system that allows real-time measurement of a patient's fluid status. The PMCC was the first health-care centre in Canada to implant a CardioMEMS device.

03 Medly, the mobile application system designed at UHN, consists of a blood pressure cuff and scale that are digitally linked to a Bluetooth-enabled device.

For the clinicians, this advanced technology marries the vital components of self-management and education in cardiac health care.

Dr. Jane MacIver, nursing professor in cardiovascular research for the Ted Rogers Centre for Heart Research, says it's about the teachable moments this type of technology provides. A large part of cardiac health is providing patients with information about how lifestyle choices affect one's heart health.

Her work is focused around CardioMEMS, a system designed in the U.S. and only used on two patients in Canada so far, as approval is pending. CardioMems is a heart monitor that is inserted into a person's lung artery and gives real-time blood pressure readings back to the clinician, allowing for more immediate lifestyle or medication adjustments.

For instance, if a person has been neglecting a healthy diet and reaching for sodium-rich snacks, CardioMEMS will pick up on the effects. "For the patient, it allows them to see how the changes they make in their life can affect their reading," says Dr. MacIver.

"It's more impactful than saying, 'Don't take any more than 1,500 milligrams of salt. It doesn't mean anything to them, but they can see [a salty] buffet is bad because it causes weight gain."

As part of Dr. MacIver's research, her team will measure the out-of-pocket expenses associated with the CardioMEMS device. It's true there is no direct cost to the patient for the device itself, but Dr. MacIver explains there can be extra costs such as increasing the bandwidth on an individual's Internet to accommodate the device and its Bluetooth readings. There will also be home visits to CardioMEMS patients to study ease of use.

"I think it's one thing if the technology makes sense to a clinician, but if we find out it is really ineffective for the patient, then are they really going to use it," says Dr. MacIver. "It's taking it one step further and saying, 'Yes, we have this technology, but let's look at how it's actually picked up in the real world.'"

Solving the complex puzzle of aortic disease

A team approach allows doctors to offer solutions, and quality care, to patients like Nazmoon Griffith

By **Judy Gerstel**

NAZMOON GRIFFITH POINTS TO HER CHEST AND ABDOMEN TO ILLUSTRATE THE SURGERIES at the Peter Munk Cardiac Centre (PMCC) that repaired her aorta, the main artery that carries blood throughout the body.

Perched on the seat of her walker in her Toronto, Ont., studio apartment, she traces lines vertically and diagonally across the front of her body.

"They cut here," she says, as if unzipping a zipper, "and here. And here."

Mrs. Griffith adds: "Then again here. And here."

The 73-year-old native of Guyana, who came to Canada in 1968, says she doesn't remember much these days. And she wasn't concerned about the details of the procedures, the months of days and nights in the Cardiovascular Intensive Care Unit (CVICU), the blood transfusions, the postop stroke, dialysis and time on the ventilator.

Her 31-year-old great-niece, Melissa Rahaman, a member of the Canadian military, talked with the doctors and explained the procedures and risks to her.

"My aunt doesn't have the most education," says Ms. Rahaman. "She didn't really understand what was wrong with her. I had to keep track of everything. I did a lot of my own research."

She also found the surgical team leader, Dr. Thomas Lindsay, Division Head of Vascular Surgery and the R. Fraser Elliot

Chair in Vascular Surgery, to be "super approachable. I didn't feel nervous about asking him questions. He was very reassuring, and he was really involved, checking on her every day."

Dr. Lindsay, in turn, appreciated Ms. Rahaman.

"Sometimes the patient is blissfully unaware," he says. "Her niece was invaluable. When problems arose, we made sure to talk to the niece, as well."

Even the fact that the case was one of the first of its kind in Canada and involved a large, highly skilled and creative team meeting and planning six months in advance of the first operation was of no great relevance to Mrs. Griffith.

What does impress her, though, is how she was cared for.

"They treated me so well," she recalls. "Everybody knows me, almost like family."

She's also impressed with the result.

"I thank God I'm alive," she says. "People who know me say, 'You're looking good.'"

Mrs. Griffith's aorta was so enlarged and damaged from top to bottom that it required total reconstruction.

"They fabricated a whole new aorta for her," explains Ms. Rahaman, summing up the complex and innovative treatment that saved her great-aunt's life.

While Ms. Rahaman is impressed with the surgical achievement, she is in complete awe of the care and attention devoted to her great-aunt by the staff at the PMCC.

"They all looked out for my aunt," she says. "I was worried that she was going to slip through the cracks. She's one of my favourite people. She brought my father with her to Canada when he was 17," recalls Ms. Rahaman.

"At [the] Peter Munk [Cardiac Centre], they treated her like she meant something, not like some low-income, old lady from Scarborough. She pulled through because of the care she received. She was treated like she was deserving of this."

In addition to the conventional degenerative aneurysms – the bulging that can result in ruptures – Mrs. Griffith had a rare chronic dissection: a separation inside the aorta that left two channels instead of one through which blood flowed, with the weaker one transporting the blood.

When aortic dissection occurs on an emergency basis, as a sudden tear followed by a rupture, death usually follows within hours or days. Acute aortic dissection was the cause of death for actors John Ritter and Alan Thicke.

With extensive aneurysms and chronic dissection, Mrs. Griffith required complex and innovative surgery to save her life.

"Only a handful of these operations are done to treat chronic dissection," explains Dr. Kong Teng (KT) Tan, Division Head, Interventional Radiology.

"She was the first case in Canada. Stents are not currently designed for this, so we had to think outside the box. Everything had to be perfectly planned from step one."

He adds, "You think about it a lot. It makes a big difference where you cut. You get one shot to get it right. You get it wrong, it's almost impossible to fix. Errors in the procedure cannot be resolved. In my mind, I went through a thousand steps for this. It was like planning a chess game, planning steps ahead."

Mrs. Griffith may not have been aware of all the risks – the greater risk of doing nothing versus the risk of surgery, or she may not remember the conversation about risk with her great-niece. She does recall going to see her family doctor a few years ago and being referred to the PMCC.

"She came to hospital in reasonable shape, but she had a very extensive problem with her aorta," recalls Dr. Maral Ouzounian, a cardiac and an aortic surgeon.

"Most people who have an aneurysm have it in one section of the aorta, either close to the heart or in the arch or in the abdomen," she says.

"The aorta leaves the heart, curves around as the aortic arch, then travels down through the chest and abdomen," explains Dr. Ouzounian.

"Her aorta was very large and [the enlargement] went all the way from very close to her heart, through the arch and down the thorax (chest) and abdomen to her legs."

She adds: "She's a small, petite woman, but she was all aorta inside."

02

A normal aorta is less than three centimetres. Mrs. Griffith's was more than six centimetres.

Two different aortic surgical teams used two different approaches and techniques, with the first team, led by Dr. Ouzounian, leaving a set-up inside Mrs. Griffith for the second repair.

The surgical teams operated in stages, like relay race teams, albeit with time for the patient to recuperate in between.

"Many hospitals use one technique – either open surgery or endovascular [inserting a grafted stent through the artery]," explains Dr. Ouzounian.

"At our place, we've built a team where every single person who comes in with a complex aortic problem is the subject of team review meetings: 'Should this patient have open or endo, or a combination of both?'" she says.

"Because we offer the whole spectrum of approaches, we can tailor for each patient what we think is best."

Dr. Ouzounian's team used an open surgical technique to build a new aortic arch for Mrs. Griffith. The colourful name of the procedure is more Disney than scientific: frozen elephant trunk.

Dr. Ouzounian cut through Mrs. Griffith's sternum and set about replacing her entire aortic arch with a customized synthetic tube

01 Dr. Kong Teng Tan, Dr. Thomas Lindsay and Dr. Maral Ouzounian are part of the surgical team that selects and performs individualized procedures for patients with aortic problems.

02 Nazmoon Griffith was impressed with both the results of her treatment and the level of personal care she received at the PMCC for a disease that caused the deaths of well-known actors Alan Thicke and John Ritter.

> *"The only way to fix an enlarged aortic artery a few decades ago was to do a major open repair. But a way was invented to do it through inside the blood vessel, under X-ray control with a custom-made, flexible synthetic tube that can go around corners."*
>
> **Dr. Thomas Lindsay,** Division Head of Vascular Surgery

with an open branch "hanging in the breeze," she says. That's the "elephant trunk" to which the second surgical team would attach another tube, to replace the thoracic and abdominal aorta.

For the complex open chest procedure, "you need the heart lung machine, because the arch involves all the blood vessels to the brain, the upper body and the arms, so you need to turn off or reduce the blood flow to the brain for a certain amount of time," clarifies Dr. Ouzounian.

"If I just turned the blood flow to the brain off at normal body temperature, I'd only have three or four minutes [to install the tube], but by dropping the body temperature to 20 degrees and providing blood flow to the brain, we have up to 30 to 40 minutes."

And while the patient is cool, so is the surgeon.

"I don't get fussed too much," she says. "Obviously, some moments are stressful. The clock is ticking, and there's minimal blood flow to the brain. It's not the time to talk about dinner plans. We're very focused."

The entire operation takes about five or six hours, and Dr. Ouzounian says she now does about 15 total arch replacements a year.

"We've had other patients since Mrs. Griffith who have needed total arch elephant trunk and distal aortic repair, but it is unusual to replace someone's entire aorta from the top to all the way down to the legs."

While Mrs. Griffith was recovering from the arch replacement, Dr. Lindsay, Dr. Tan and their team were preparing for the second stage surgery, the endovascular aortic artery repair (EVAR), a relatively recent procedure.

"The only way to fix an enlarged aortic artery a few decades ago was to do a major open repair," explains Dr. Lindsay.

"But a way was invented to do it through inside the blood vessel, under X-ray control, with a custom-made, flexible synthetic tube that can go around corners."

A copy of Mrs. Griffith's CT scan was sent to the manufacturer of the device, and a plan for construction of the made-to-measure Dacron mesh and metal tube was sent back to Dr. Lindsay and Dr. Tan.

"If we agree with the plan we sign it, and six to eight weeks later we receive the device, which we put in through the patient's arteries in a high-tech operating room with radiology equipment," says Dr. Lindsay.

Shortly after Mrs. Griffith's new custom-made graft arrived by courier in a long cardboard tube, Dr. Lindsay, guided by Dr. Tan and his imaging equipment, attached it to the elephant trunk that was left hanging by Dr. Ouzounian and began the delicate work of reattaching blood vessels." "Everything's about catheters and wires," explains Dr. Tan. "The majority of the procedure requires fine catheter skills."

Postoperatively, Mrs. Griffith experienced partial paralysis, requiring a leak to be created in order to improve blood flow to her spinal arteries. Several weeks later this leak was sealed without any paralysis, completing the aneurysm repair.

"We had to do some fancy rescue work," recalls Dr. Lindsay.

In the end, he says, "we have essentially replaced this woman's aorta, from near her heart all the way down to below her belly button, where it divides into the legs.

"We did it with one major open operation and the rest through the groin. What is the innovation? That is the innovation," he says.

"We're constantly in a state of innovating, figuring out how to do it better. And I work with colleagues who think the same way. That's what's so enjoyable about working at the PMCC."

Dr. Lindsay explains: "The field is evolving, and we're coming up with creative solutions to get these patients safely through everything they need. If you have all the tools at hand, you can offer a personalized approach to fixing the problem."

He says that "the postop care from intensivists and ICU nurses is also critical. "These patients need very specialized nursing; they need spinal drains."

As well, says Cindy Dickson, Registered Nurse, "vascular patients tend to heal slower than people who don't have vascular disease."

Ms. Rahaman recalls that her great-aunt's postop condition was precarious. "She had a stroke and had to be on dialysis, and at one point was not doing well with her legs. Things could have gone either way."

That she survived "is pretty much due to the dedication of the surgeons, the ICU staff and the nurses in [wards] 4A and 4B," says Ms. Rahaman.

"All the nurses recognized her, [since] she's been there so many times," says Ms. Rahaman. "Even the nurses off her case came by to say, 'Hi.' And many times they told me they saw her in very bad shape. She was really, really sick. I would ask questions, and those nurses were extremely knowledgeable. They really know what they're doing."

She concludes: "The fact that she is living her life and continuing to be healthy is pretty good."

Mrs. Griffith has her own summing up of the PMCC team that saved her life.

She points to her head and says, "There are very smart doctors there."

DID YOU KNOW...

- Aortic disease is often hereditary. If someone has a thoracic aneurysm – a bulging of the aorta in the chest area (thorax) – there's a 20 per cent chance that it is due to genetic factors and that other members of the family also have or are at risk of developing a similar aneurysm, explains Dr. Maral Ouzounian, a cardiac and aortic surgeon. Young patients with a thoracic aneurysm or those with a family history may be offered genetic testing. All first-degree relatives of patients with thoracic aneurysms should be checked for a similar aneurysm with imaging to identify aortic problems before rupture or dissection occurs. Other factors that may cause damage to the walls of the aorta include aging, hypertension and tobacco use.
- Ruptured aortic aneurysms and dissections are estimated to cause almost 3,000 deaths annually in Canada.
- People with aortic aneurysms rarely have symptoms. The bulging of the aorta and other arteries are typically found during screening or imaging for other health issues, such as those identified by ultrasound or CT scans done to investigate other diseases. Rarely, depending on the size and the location, aneurysms may cause pain in the upper body; shortness of breath, wheezing or chronic coughing; and difficulty swallowing or the coughing up of blood. Dissections are tears that occur in the aorta and generally cause severe chest or back pain and require emergency evaluation and treatment.

01

Growing into adulthood when you are born with heart disease

Specialized medical teams at the Peter Munk Cardiac Centre lead the way globally in the treatment and care of adults born with a heart defect

By **Daina Lawrence**

FIFTY YEARS AGO, BABIES BORN WITH COMPLEX CONGENITAL HEART DEFECTS had a less than 5 per cent rate of survival to adulthood, as surgical strategies that would eventually treat many of these patients were still in their infancy or not available.

Today, more than 90 per cent of these babies make it into adulthood, creating a whole new patient demographic where there are currently more adult patients living with congenital heart disease than children – and medicine must now do its best to keep up.

The rapidly growing field of adult congenital heart disease (ACHD) deals with patients who had one or more structural abnormalities of the heart present at birth. Thanks to advances in diagnosis and treatment, these people survive to adulthood despite their birth defect, but need continued follow-up and care throughout their adult lives.

"In the last few decades, this specialty [ACHD], has really taken off," explains Dr. Rachel Wald, a cardiologist with the Toronto Congenital Cardiac Centre for Adults (TCCCA) at the Peter Munk Cardiac Centre (PMCC). "Initially, these children simply didn't survive, and that's just not the case anymore. Now this expanding patient population requires a specialized team of physicians and nurses to look after them."

To treat the rapidly growing number of ACHD patients in Canada, the TCCCA and the PMCC were at the forefront of the creation of a multidisciplinary team of specialized cardiologists and congenital heart surgeons who work to marry the pediatric and adult cardiac worlds. The clinic is one of the oldest and largest of its kind in the world, with more than 9,500 active patients.

"Within ACHD, the ties to the pediatric world are exceptionally strong because congenital heart disease was once strictly a pediatric condition," explains Dr. Wald, originally a pediatric cardiologist who further sub-specialized in the care of adults with congenital heart disease.

Treating congenital heart defects in adults often requires an understanding of the unique complexities of each patient, as many have more than one medical issue. "We believe the best way to balance out this team is to have a diverse array of physicians with complementary vantage points," adds Dr. Wald.

When an ACHD patient comes to the centre for surgical or advanced medical treatment, members of the team gather to discuss the best approach for that individual. There is a limited amount of medical evidence to guide therapies, as these patients are often among the first of their kind to survive into adult life.

Unlike other areas of medicine, where there are many people with a certain disease who can be studied to help inform future medical decisions, with ACHD there aren't huge numbers of patients who have reached adulthood.

For instance, a surgical technique to help treat babies born with hypoplastic left heart syndrome – which occurs when the heart's left side isn't able to effectively pump blood, forcing the right side of the heart to pump blood to the entire body – wasn't available until the 1990s. Before then, this birth defect was fatal.

"Now we're seeing our first wave of adults surviving in their 20s, and we don't really know what's going to happen when this cohort survives another 10 years [and more], into their 30s, 40s and 50s," explains Dr. Wald. "You're trying to come up with an educated guess of which complications might happen, and how these can be prevented, however management is very much an evolving process, as our patients teach us what we need to be aware of."

The specialties of the team members make the treatment at the centre truly unique.

Not only are there the congenital heart surgeons and ACHD cardiologists who are experts in ACHD, but the team also consists of cardiac interventionalists (specialists trained in catheter-based treatment), electrophysiologists with expertise in heart rhythm problems, cardiac imaging specialists and several others with congenital heart disease expertise to help provide the most balanced patient care.

"Each colleague contributes his or her expertise to find the best treatment option for the individual patient," says Dr. Erwin Oechslin, an ACHD cardiologist, Director of the Adult Congenital Heart Disease program at the PMCC and Bitove Family Professor in ACHD. "Frequently, all of them are involved in the treatment of an ACHD patient."

Together, the ACHD team is recognized for its long-term outcome studies, care of pregnant women with heart disease, attention to psychological aspects and end-of-life questions in congenital heart disease patients and state-of-the-art adult congenital heart surgery and congenital catheter-based interventions. The introduction of a dedicated heart failure clinic for ACHD patients led by Dr. Lucy Roche, cardiologist, is one of the latest innovations at the PMCC. "The hearts of congenital heart patients are structurally abnormal from the very beginning, and their heart muscle is deemed to fail," says Dr. Oechslin.

It takes all of these experts working together to chart out the treatment and management for these patients, as the work is ongoing. The comprehensive approach and provision of patient-centred care, consolidation rather than dilution of experiences and a highly dedicated, multidisciplinary team make the TCCCA at the PMCC a provincial, national and international reference and resource centre. The wealth of expertise has also made TCCCA a hub for trainees in ACHD education with global impact.

"These patients are born with an abnormal heart from the very beginning, and after the surgeons remodel the heart, you end up with a very complex anatomy," says Dr. Oechslin. "What's important to remember is that these patients are not fixed, they're not cured," he adds. "They'll never be cured, only repaired. Most patients with a scar in their chest need lifelong specialized care."

And although their hearts have been repaired, Dr. Oechslin explains that adults with congenital heart disease are at increased risk for stenosed or leaky valves, significant arrhythmias, heart failure and early death, so it's vital to follow them to prevent a catastrophic outcome.

These patients are "survivors of modern medicine," according to Dr. Oechslin, as it was modern medicine that created this cohort of patients. And he says it's now the duty of the medical community to care for these patients into adulthood.

"There have been great advances in pediatric medicine in the last 50 years, and now we have a new generation of patients," he explains. "So we as physicians and as a society have an ethical responsibility to deal with the consequences of Western medicine. I predict a further growth of ACHD patients in numbers and complexity in the next 10 to 15 years. Leaders in health care need to find answers to the rapidly increasing disconnect between available resources and patient demand."

To provide the highest level of personalized care, the collaboration between these multidisciplinary specialists doesn't stop with the heart. Many ACHD patients have multiple health issues involving other organs and occurring simultaneously, and they require the care of dedicated specialists outside of cardiology.

"Many patients have psychosocial issues, liver problems or pulmonary arterial hypertension, which is high blood pressure in the lungs, so we collaborate with the specialists in these areas, as well," explains Dr. Oechslin.

The treatment and care for ACHD patients is about navigating uncharted waters, so it requires ideas from a multitude of experts to develop dynamic treatment options and map out guidelines for future generations.

For Dr. Oechslin, "it's this team approach and a pool of experts with passion, empathy and dedication who can find and provide the best care for these patients."

01 Dr. Erwin Oechslin and Dr. Rachel Wald are members of the PMCC team providing comprehensive treatment and care for adults with ACHD.

> *"What's important to remember is that these patients are not fixed, they're not cured. They'll never be cured, only repaired. Most patients with a scar in their chest need lifelong specialized care."*
>
> **Dr. Erwin Oechslin,** Director, Adult Congenital Heart Disease program, the Peter Munk Cardiac Centre

Pathologists' puzzle: mystery of the silver-coated heart valve

Dr. Jagdish Butany and the Peter Munk Cardiac Centre's determined team of detectives work to ensure the safety of novel cardiovascular devices

By **David Israelson**

THE MECHANICAL HEART VALVE THAT DR. JAGDISH BUTANY HOLDS IN HIS HAND looks surprisingly unassuming, about the size of a dime. Yet as director of cardiovascular pathology at the Peter Munk Cardiac Centre (PMCC), this particular valve took him on a mission around the world.

The mission was to solve a mystery – what was causing this manufacturer's new model of heart valve to be connected to infections in heart patients, resulting in their bodies rejecting the device and in some cases death.

The mystery started unfolding some 20 years ago, Dr. Butany explains.

"Normally, about 2 per cent of prosthetic heart valves that are implanted do get infected. You make something by hand or with machinery, and somewhere along the line, if the sterilization is not adequate, you can get bugs coming in," he says.

In the late 1990s, one of the manufacturers brought out a new model. It was offered to leading heart institutes at no extra cost because it included only a small improvement – a coating of silver along its edge that was intended to prevent infection.

Trouble is, more patients than usual actually had infections after receiving this device. Instead of the normal percentage of patients whose valves had to be replaced, within months the numbers kept going up.

"When we had eight [infections], I said, 'This is too much.' Unfortunately, prosthetic heart valves behave differently in different people," Dr. Butany says.

While Dr. Butany knew the problem needed attention, he didn't think dealing with this valve would become the cornerstone of his life's work.

There was a great deal at stake, though, not only for some of the over 55,000 people who have heart valves implanted every year, but also for the hospitals that need to make sure the devices work and the companies that invest tens and even hundreds of millions of dollars in developing valves.

Costing at least $4,000 each in Canada, synthetic heart valve looks deceptively simple. It's an outer ring with a disc or a membrane that opens and closes to let in blood and prevent it from flowing back.

As a pathologist, Dr. Butany looks at tissues, biopsies, lab results and even autopsies to determine what went wrong.

He works closely in evaluating and reviewing new devices with cardiovascular surgeons Dr. Tirone David, Melanie Munk Chair in Cardiovascular Surgery, and Dr. Christopher Feindel, Antonio & Helga DeGasperis Chair in Clinical Trials and Outcomes Research at University Health Network (UHN) and across the city.

Many people believe that doctors are highly influenced by drug and health-care companies, but "those days are gone," Dr. Feindel says.

The PMCC is particularly careful about which devices make the grade, Dr. Feindel adds.

"From time to time a new device will come on the market, and we'll start to see one-off or anecdotal situations where it isn't working quite right. Over time we might see a pattern," he says.

Dr. Feindel also sits on a Health Canada committee that reviews heart-related medical devices.

"We meet several times per year, and I sit on the advisory board. We get presentations on various devices that are coming on the market and then we talk about whether we see any pitfalls or have concerns," he says.

"We're not supportive of one company or another. We switch around, and sometimes the companies get upset. We have no problem being critical when it's necessary," he explains.

"On that committee we also have talked about follow-up, where something has already been approved, and we find down the road there are problems. Health Canada has made it very clear that they rely on clinicians [like those at the PMCC] to identify problems."

Pathology is at one end of the testing process that all medical devices must undergo, in many cases following the procedures of the U.S. Food and Drug Administration. (Health Canada tends to adopt the same standards.)

At the other end, before devices even reach the market, they are tested rigorously. Dr. Feindel says he can think of only a handful of situations in 30 years where devices didn't work properly.

But even one that slips through is too many, and problems still can come up, Dr. David says.

"In the worst cases, unfortunately, death is where the problem happens," he says. Even patients who survive a malfunctioning device must undergo removal and replacement heart surgery, and that's when Dr. Butany does his sleuthing.

"This particular valve was a real detective story. I spoke with Dr. Butany and told him something was just not right," Dr. Feindel says.

Dr. Butany took it from there, suspecting that the silver coating was the problem. It had been added by the manufacturer based on the same principle that has doctors apply silver nitrate drops to the eyes of newborn babies – to ward off infection.

His pathology research led him to suspect that rather than protecting against infection, the silver coating on the valves was toxic to cells in the heart muscle.

"I started talking to the manufacturer and continued [investigating]," Dr. Butany says. At one point, he presented them with the unusually high numbers of patients who had to have the silver-coated valve removed.

"They said that I'm biased," Dr. Butany says. The manufacturer had a lot at stake: in addition to the cost of research and development, by 2000 the company had sold 36,000 of these devices worldwide.

Not content to let this accusation sit, Dr. Butany prepared research papers and travelled around the world to deliver them, including a key presentation in Britain, making the case to reconsider the silver-coated valve. The team at the UHN in Toronto stopped using them, but Dr. Butany was determined to trigger a global review.

Late in 1999, the United Kingdom's Medical Device Agency heeded Dr. Butany's findings, issuing a warning against the valve. Australia and New Zealand followed suit.

"One day, about three years after I had my first concerns regarding the valve, I got a call from the manufacturer saying that the device was about to be withdrawn. They made the public announcement half an hour later, that morning," Dr. Butany says.

The process for reviewing devices is always itself being reviewed and fine-tuned, Dr. Feindel says.

"It's a fine line between allowing people to use new devices and being cautious," he explains.

For the future, "I think there are probably ways you could tighten the follow-up. There have been subtle changes in new trans-catheter valves [implanted into aortic valves], for example," Dr. Feindel says.

"We've learned a lot over the last few years, so if there's an issue with one, we need to know if it's a one-off situation, or are there more cases like it?"

01 Discovering the problem with this mechanical heart valve is part of the PMCC's dedication to rigorous testing protocols.

02 From left: Drs. Tirone David, Jagdish Butany and Christopher Feindel strive to fine-tune the process for reviewing new devices.

A special 'recipe' where PIE will get you TEE

Unique user-friendly modules developed by the Peter Munk Cardiac Centre provide state-of-the art medical education, enabling students worldwide to learn about and develop skills in complex procedures without real patients

By **Chris Atchison**

MOST OF US ASSUME THAT WHEN A MEDICAL STUDENT COMPLETES A DEGREE IN ONE AREA OF SPECIALIZATION such as anesthesiology, that student is ready to work medical magic in a clinical setting. That's somewhat true, but with an important caveat.

Like any professionals doing complex work, doctors need time and practice to perfect their craft. But when it comes to mastering key technical skills in medicine, getting practice time can be complicated.

Simply finding patients on whom to perfect diagnostic testing skills requires a mixture of the right timing and the right cases.

"If you are working on a day when it's all coronary bypass surgeries, and there's no valve pathology, then you don't gain any experience imaging and analyzing abnormal valves," explains Dr. Wendy Tsang, a researcher, cardiologist and staff physician in the Echocardiography Lab of the Peter Munk Cardiac Centre (PMCC).

The challenge is even greater when it comes to practising procedures such as transesophageal echocardiography (TEE), where a tiny probe is fed down a patient's esophagus in order to gain a clear and unobstructed view of the heart.

An indispensable tool, TEE is relatively challenging to master, making practice time crucial for the anesthesiologists tasked with conducting the procedure.

"You can't practise on people because sticking the probe down someone's throat isn't pleasant," says Dr. Gordon Tait, Assistant Professor of Anesthesia and Manager of Perioperative Interactive Education (PIE) at Toronto General Hospital.

"In cardiology, it's also not done commonly because you have to be heavily sedated, so the great majority of TEE is done in the operating room on patients about to have cardiac surgery."

About a decade ago, Dr. Tait took it upon himself to overcome that challenge.

His idea was simple: What if anesthesiologists had a virtual platform for practising TEE, rather than working on live patients? So the PIE team in collaboration with Toronto General Hospital anesthesiologist Dr. Annette Vegas, Professor of Anesthesia, set out to create a virtual TEE website that would allow people to learn how to perform the procedure without patient involvement.

"My personal motivation for creating PIE was to provide a state-of-the-art, interactive medical education, free for anyone," Dr. Tait explains. "All over the world, people are using these modules as part of their training. PIE doesn't run courses, but we create resources for other people who do."

The user-friendly modules offer instructional videos and a 3-D model of the heart that users can drag and turn to view various angles and cross-sections of the organ, simulating real-world TEE. Various other modules allow students to learn about topics such as heart valve assessment, obstetric anesthesia and heart failure, while also using virtual tools to examine other areas of the body such as the liver and the spine.

The TEE Standard Views module is available in nine different languages, including English, and is used daily by over 1,500 people in 200 countries.

"The one thing I like about [the PIE website] is that it's very democratic," Dr. Tait adds. "Every country in the world, no matter how well off they are, has access to the Internet. They have the same access in India or African countries or South America as [they do] at Yale University or Johns Hopkins University in the United States.

"It levels the playing field for medical education."

Because the platform is currently built in Flash Player – the soon-to-be-obsolete multimedia software for viewing rich media on the Web – Dr. Tait is attempting to fundraise in order to upgrade the platform to HTML 5, the next generation software for playing online audio and video.

> *"The one thing I like most about [the PIE website] is that it's very democratic. Every country in the world, no matter how well off they are, has access to the Internet...it levels the playing field for medical education."*
>
> **Dr. Gordon Tait,** Manager, Perioperative Interactive Education, Toronto General Hospital

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01 The work of Drs. Gordon Tait, Annette Vegass, Dr. Massimiliano Meineri and Wendy Tsang involving PIE fills a major gap in helping doctors and students learn new technologies and techniques.

Dr. Tsang – who was a contributor to 3-D TEE imaging sections with anesthesiologist Dr. Massimiliano Meineri, Associate Professor of Anesthesia – points out that the website helps standardize TEE instruction and student experiences. And that includes showing students of all skill levels the process in major detail, down to buttons being pushed and adjustments being made to the virtual TEE equipment in order to simulate a real-world experience.

Previously, she says, anesthesiologists or cardiologists learning TEE, or any diagnostic procedure, would be limited to the knowledge and experience of the doctor providing the instruction. The PIE website removes potential variance in the education process.

"To find the time to learn new technologies or techniques is difficult, especially once physicians have finished their training," she says. "Trainees in smaller centres and individuals practising in the community may not be able to go or have access to a centre willing to offer them the time to learn and practise. There was a major gap that needed to be filled."

From Dr. Tsang's perspective, upgrading the technology is essential at a time when even the most complex medical instruction is migrating into the digital realm. She points to the plethora of detailed YouTube videos demonstrating echocardiography that are free to the public as just one example.

"This is a step forward from someone thinking they have an interesting video and uploading it to YouTube," she says of the PIE website. "This has a more structured educational component.

"It also demonstrates how you can reach out to people who can't come [to your hospital or university] for training. It's free for anyone and has quality behind it. You can't necessarily guarantee that when you go online."

Recruiting and retaining the best and the brightest

Multidisciplinary research and creative thinking aid the Peter Munk Cardiac Centre in its relentless search for top talent

By **Mary Gooderham**

01

THE PETER MUNK CARDIAC CENTRE (PMCC) HAS BECOME A POWERFUL CENTRE FOR INNOVATIVE MEDICAL RESEARCH that attracts scientists from all over the world. "The multidisciplinary environment allows cross-fertilization of ideas by stimulating interaction across various medical specialties and scientific disciplines. This feature of our environment is attractive to bright, creative people," says Dr. Michael Domanski, Cardiology Division Director at University Health Network (UHN) and Mount Sinai Hospital.

Dr. Domanski, a specialist in advanced heart failure and transplant cardiology, made the move from the Icahn School of Medicine at Mount Sinai Hospital in New York to the PMCC "because it looked like a chance to make a difference in terms of research and also in patient care and teaching," he says. "The commitment of the organization to innovation is expressed by its leadership."

Dr. Patrick Lawler, a cardiologist who joined the PMCC's emerging cardiovascular clinical trials group in April, was attracted from his position at Brigham and Women's Hospital and Boston Children's Hospital, as well as Harvard Medical School in Boston, because the centre encouraged creative thinking and encouraged taking scientific risks.

"It seemed like there was a spirit of wanting to do different things and trying different approaches to a disease that we've been treating for some time," he says, noting that a good deal of research "has plateaued" in cardiovascular disease. "It's time for a fresh look and a fresh perspective, and I thought that the people here were the ones who might be able to do that."

Dr. Lawler, a Boston native who attended medical school and completed his residency at McGill University in Montreal, was impressed with the diverse group of people at the PMCC who have expertise in clinical trials, including epidemiologists, biostatisticians, regulatory scientists and administrators.

"Lots of aspects of science are a team sport, but having the right team is really essential to doing these large clinical trials and translational studies," he says, adding that international recruitment is part of an overall trend to "break down the borders" in medicine.

"One of the richnesses of the medical community here is the diversity of backgrounds that people bring from across the world," Dr. Lawler says. "It's important to continue that."

Dr. Barry Rubin, Medical Director of the PMCC, says that recruiting is among the stated goals of the Peter and Melanie Munk Charitable Foundation's third donation to the PMCC in 2011, along with retaining the best and the brightest.

"We've been unbelievably successful at doing that," he says, noting that key elements of the strategy have included establishing five new chairs and four centres of excellence. "Our vision is to be the best heart centre in the world, and you can't be that without having the best people."

Dr. Rubin says the new recruits in turn are attracted by the PMCC's vision, its multidisciplinary approach, its cohesive program and a "constant and unremitting focus on innovation." He calls the substantial number of recruits from the U.S. "the reverse of the brain drain," made possible with substantial funds from donors to the PMCC, including the Munks.

He says, for example, that Dr. Lawler "is truly at the cutting edge," and "every major heart centre" tried to hire him. "For somebody with his pedigree to look out over the landscape and choose the PMCC tells you about the draw that we have. He could have gone anywhere."

Another new recruit, Dr. Patrick Veit-Haibach, a radiologist and nuclear medicine physician, came to the PMCC's Joint Department of Medical Imaging in April from the University of Zurich. As director of Positron Emission Tomography/Magnetic Resonance imaging (PET-MRI), his clinical research focus is combining molecular imaging strategies, such as allowing physicians to assess the profusion, function and viability of blood flow at the same time. "You can follow the physiological pathway of diseases," he says.

Dr. Veit-Haibach is excited to be at the PMCC, given its "large patient population with all sorts of cardiovascular indications," as well as its enthusiasm for using molecular imaging in all sorts of trials.

"It makes it interesting," he says, noting that he's pleased to get a good deal of academic time at the PMCC, which has a strong focus on translating basic science to clinical science. "There's something to build up here, so we can understand disease, where it comes from and how to intervene successfully to bring relief to patients."

Interdisciplinary exchange is "very much encouraged" in his field, Dr. Veit-Haibach says, and the PMCC inspires teamwork. "Everybody's really collaborative and open to new ideas; that's not always the case in places where I've been," he says. "It can be more political."

The fact that the new recruits at the PMCC have associations with institutions outside of Canada will benefit research there, says Dr. Veit-Haibach, who expects to connect with research fellows at the University of Zurich.

Dr. Domanski says that multidisciplinary research is "implicit" and "critical to any endeavour" in the field of cardiology. "There are few things that you can do without any appeal to colleagues in other areas, from biostatistics to cardiac surgery to clinical epidemiology."

The people at the PMCC are particularly important, he says, including the philanthropists who make it happen.

"Those who finance this operation do more for medicine than most physicians ever do," he remarks. "Those people can buy a yacht and dock it in Monaco; instead, they're making a difference in their community and internationally."

Adds Dr. Domanski: "I would like the PMCC to be a hotbed of intellectual ferment and progress in research that improves public health. That's what we're all here for – to turn back the tsunami of heart disease."

The new faces at the PMCC will bring "dramatic change in the way that we manage patients with heart disease," Dr. Rubin predicts. "For all the investments that are made and all the science, the single most important thing here is the people we recruit – no question."

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01 Dr. Patrick Veit-Haibach is a radiologist and nuclear medicine physician who came from the University of Zurich. He says the interdisciplinary approach at the PMCC inspires teamwork and innovation.

02 Dr. Michael Domanski is a specialist in advanced heart failure and transplant cardiology. The PMCC's multidisciplinary setting inspired his move from New York City.

03 Dr. Patrick Lawler, who was attracted to the PMCC because it encouraged creative thinking, believes having the right team is key to doing large clinical trials and translational studies.

The right test, at the right time

As the appetite grows for medical testing, a palatable app is feeding physicians timely information

By **Shannon Moneo**

Cardiologist Dr. Sacha Bhatia and his team led the Echo Wisely trial, which examined ways to reduce the number of unnecessary echocadiograms being performed. The initiative was funded by the PMCC Innovation Committee.

INNOVATION CAN BE LIFE-SAVING, but if new and more productive ideas never make it beyond the lab or test stage, it becomes innovation inaction. Within the fast-evolving world of medicine, as new technologies, drugs and procedures are unveiled each day, having solid proof that a new innovation works as promised usually leads to greater adoption. The Peter Munk Cardiac Centre (PMCC) is putting such innovations into action, recently finishing a nine-hospital study where an online application was used to guide physicians in the appropriate use of echocardiography.

When Dr. Barry Rubin was asked in 2013 by the Government of Ontario to examine the appropriate use of imaging tests, such as echocardiography and magnetic resonance imaging, he wanted no outside interference and the freedom to produce an honest report. The stakes were rather high because Canada spends more than $2.2-billion annually on such diagnostic imaging. Just a 10 per cent decrease in unnecessary testing would save $220-million each year. What Dr. Rubin, the PMCC's Medical Director, and his Expert Panel on Appropriate Utilization of Diagnostic and Imaging Studies found is that 10 per cent to 30 per cent of imaging tests are done for inappropriate reasons.

"When you focus on electrocardiography, it's a $140-million enterprise in Ontario, annually. If one-quarter of those tests were not carried out, it would produce savings of $35-million each year," says Dr. Rubin, a vascular surgeon and also a Professor of Surgery at the University of Toronto. "The goal is to control costs by ensuring tests are done only for the right reasons, in a safe environment, by individuals who are trained to carry out and interpret the tests."

So the problem then becomes: "What are the right reasons?" Enter Dr. Sacha Bhatia, a cardiologist at Women's College Hospital and at University Health Network. "One thing we know is that some people get care they probably don't need," he says. The danger then becomes that patients will get false positive results or benign conditions will be flagged, leading to more, often unnecessary, care in a setting where health-care resources are stretched. "The basic premise becomes: 'How do we make sure the patient gets the tests they need?'" Dr. Bhatia asks.

> *"One thing we know is that some people get care they probably don't need...the basic premise becomes: 'How do we make sure the patient gets the tests they need?'"*
>
> **Dr. Sacha Bhatia,** Cardiologist, Women's College Hospital and University Health Network

Echocardiography uses ultrasound to create images of the heart in order to examine its blood supply, determine how large the heart is, how well it contracts and how the valves function. The test, using an ultrasound probe and electrodes attached to the skin, is done when people are concerned about, for example, heart disease, dizziness, irregular heartbeat or shortness of breath. It costs approximately $100 for the physician to read the test results, plus another $100 for the actual test, Dr. Bhatia notes.

While a research fellow in cardiology at Massachusetts General Hospital and a research fellow at Harvard University from 2011–13, Dr. Bhatia learned of an "appropriate use criteria" guideline that he combined with a pocket card that described the criteria in the context of common clinical scenarios and twice-monthly e-mail feedback on the appropriateness of test orders. When used by a study group, there was a 26 per cent reduction in echocardiography orders. In 2013, Dr. Bhatia was awarded the Arthur E. Weyman Young Investigator's Award by the American Society of Echocardiography and the Young Investigator Award from the American College of Cardiology for his work.

"We used very simple educational material, looked at their order patterns and examined the appropriateness," he says. Physicians were provided with clear guidelines and recommendations, based on key indicators. But more importantly, the e-mail feedback informed the physicians how their peers were doing and which physicians were ordering fewer tests. "Doctors often don't get feedback on how they're doing," Dr. Bhatia notes. That information became significant because the doctors became more aware of how their patients were later doing and how much treatment cost.

In 2013, a University of Toronto study found that between 2001 and 2009, the rate of echocardiography increased by 5.5 per cent over the eight years, a rate that was adjusted for the rising number of older citizens and accelerating rates of disease. Dr. Bhatia attributes the rather high growth rate to patients' requests for tests and how physicians practise, meaning they don't refrain from ordering tests.

After returning to Canada, Dr. Bhatia began a similar 18-month study in 2014 at nine hospitals in Toronto, Kingston and Boston, involving almost 180 clinicians who were broken into two groups.

One group had no contact with Dr. Bhatia and his team. The second group got a YouTube video outlining the appropriate use of echocardiography and was given access to an online appropriate use criteria application for their phone. Research co-ordinators would record how often and why they ordered echocardiograms, and the data would be delivered to Dr. Bhatia. His team would input the information, and each month the physicians would receive an e-mail telling them whether the ordered test was appropriate or why it wasn't necessary. As the trial proceeded, there was a 25 per cent drop in the number of unnecessary echocardiograms.

"There were no incentives. We just gave them data in a very thoughtful way," Dr. Bhatia says. "By giving doctors information, we significantly changed their behaviour. It's about showing doctors how they practise in a way that's easy to digest, changing their practice for the better and improving their performance."

Or as Dr. Rubin says, "It's one thing to put together a recipe and another thing to follow it." He adds that Dr. Bhatia is putting into practice the recommendations from his 2013 report. "He's a superstar," Dr. Rubin says. "His work and the recommendations my expert panel made align. The problem had been that there were guidelines out there, but no mechanism to put them into action. He used technology to deliver a solution in a very effective way." The upshot is that doctors will order fewer tests, saving money, increasing access and reducing wait times for patients who require a heart ultrasound.

Dr. Bhatia, who also earned an Innovation in Quality Award last year, would like to apply the process to other tests. "It doesn't have to be limited to echocardiograms. It could be used for stress tests, CTs, MRIs, even for the prescription of drugs."

And as in the earlier U.S. study, Canadian physicians appreciate the rare feedback. "I think there's a real appetite to give doctors their performance data and how they can improve," Dr. Bhatia says. "No one wants to be mediocre."

(The results of the Echo Wisely study were published in the Journal of the American College of Cardiology *on August 21, 2017, a high-impact medical journal.)*

01

A breakthrough in lowering systolic blood pressure

A new e-counselling program is proving that with the right self-help support and education, people can make healthier lifestyle choices and – hopefully – live longer

By **Bryan Borzykowski**

EVERYONE KNOWS THAT A HEALTHY DIET AND REGULAR EXERCISE CAN LEAD TO A LONGER LIFE, but for most people, it's nearly impossible to break bad lifestyle habits. In 2010, Dr. Robert Nolan, Director of the Cardiac eHealth and Behavioural Cardiology Research Unit at Peter Munk Cardiac Centre (PMCC), set out to change that by helping patients connect heart-healthy lifestyle change to their personal goals for living well.

Over the last seven years, Dr. Nolan has been devising ways to help patients with hypertension create meaningful and long-lasting lifestyle changes. In the past, people would have consultations with a specialist and then be left to fend for themselves. Some might change their behaviours for a short period, but most would revert to old habits.

"They'd get educational sessions that would last a few weeks, but giving people information was not sufficient to help them feel ready and confident to sustain lifestyle change," says Dr. Nolan. "Without support to develop skills for putting a change plan into action, it was hard to shift old habits beyond a few weeks."

For patients with hypertension, short-term changes aren't good enough. If high blood pressure is not treated with a better diet, more physical activity, smoke-free living and taking medications as prescribed, then it could lead to a stroke or a heart attack. The best way to beat the problem is through meaningful change, he says.

While many hospitals and private centres have tried to help people kick bad habits through internet-based programs, most of these haven't been designed to provide the type of support patients receive in face-to-face counselling, says Dr. Nolan. Many Web-focused counselling programs are either interactive or automated – not both.

With the interactive programs, someone might instant message with a counsellor and discuss their issues, but when the conversation ends, the patient is left without support about what to do next. With the automated education, someone might input personal information on a website and get articles and data tailored to them, but when the reading ends, there's no clear idea on how to apply the information to their personal situation.

"Our programs often fail to provide guidance as someone interacts with a program within a single log-on session, or as we log on time after time," says Dr. Nolan. "We had to create a balance of the two."

Dr. Nolan developed REACH (Reducing risk with E-based support for Adherence to lifestyle Change in Hypertension), a comprehensive e-counselling program to help people make permanent changes to their lifestyle or "self-care behaviours". Their team included numerous experts, such as dietitians, psychologists, doctors, fitness experts, pharmacists and scientists, to create self-help videos that covered every aspect of a person's lifestyle.

Key questions that patients might have about lifestyle change were answered in this program. Not sure how to read nutrition facts on labels? Then take a video tour of a grocery store with a dietitian who shows people how items are categorized, what labels mean, how to navigate nutritional guidelines and more. Need an exercise regime? Watch a fitness expert give step-by-step instructions on how to set up a plan.

Virpi Kononen, a Toronto-based IT worker, swears by the program. In 2015, she was suffering from high blood pressure and a ringing in her ears. She was told that if she didn't eat better and get more exercise then she'd have to start taking pills. "And I didn't want to do that," she says.

The program was designed as a series of counselling sessions that take place once a week for the first four months, then once every two weeks for the next four months and then once a month for the last four months. The goal was to break old habits by the end of the year.

For Ms. Kononen these regular sessions were key. Reminders – through instructional videos, e-mails and other forms of communication – on how to eat better and exercise more allowed her to slowly change her habits. No one made her feel badly when she stumbled, which made her want to improve even more.

"You can't change everything overnight, but this program gave me control and empowered me," she says. "They gave me a series of small things to change that, over time, made a huge difference."

Starting in 2012, the program was in the testing stage for four years via a controlled trial, where some people received regular counselling and others followed Dr. Nolan's program. He wanted to see if people's blood pressure dropped and cholesterol levels improved. That would indicate that lifestyle changes had been made.

The results were fascinating, says Dr. Nolan. Systolic blood pressure, which measures the pressure in one's arteries during heart contractions, was lower by 10 millimetres of mercury, as compared to six for the control group. Another kind of blood pressure, pulse pressure, was also significantly reduced in the e-counselling group.

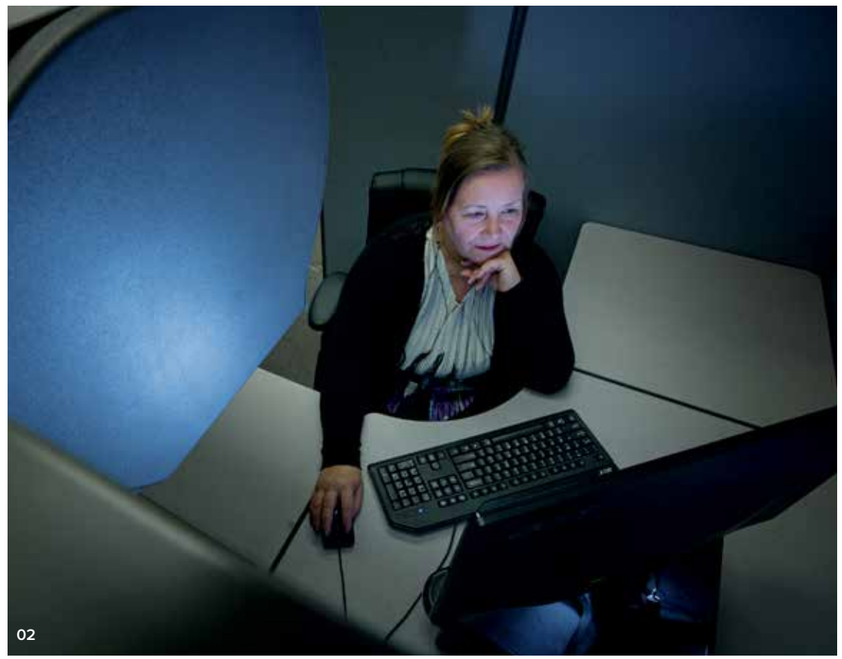
Patients' Framingham Risk Score, which measures the risk of experiencing cardiovascular disease (such as heart attack or stroke), was also down by about 2 per cent, while people in the e-counselling program increased their activity by walking about 1,200 steps per day more than the control group.

"We saw significant differences," he says. "We wanted to increase the degree to which people adhered to self-care behaviours [in order] to manage hypertension, and that's exactly what they did."

Ms. Kononen saw big changes, too. After a year, her blood pressure went back to normal, the ringing stopped, she's walking an average of 7,000 steps a day – 2,000 more than she did during the trial – and she says she's heathier than she has been in years.

For Dr. Nolan, the next step is to enroll all patients with hypertension into the program, but he also wants his program to be used nationally.

"Our goal is to look for partners who want to work with us, who can offer this on a population-wide basis," he says. "We want to continue making sure that we can demonstrate the effectiveness of this for not just reducing risk factors for heart disease, but also that we can help improve everyone's quality of life."



02

01 Dr. Robert Nolan, second from the left, and his team at the PMCC work to find ways for patients to deal with hypertension by creating important and long-lasting lifestyle changes.

02 For Toronto IT worker Virpi Kononen, regular sessions were the key to success in managing her high blood pressure.

To give or not to give

Rather than making it common practice, an innovative procedure can determine if a patient really needs a blood transfusion

By **Shannon Moneo**

DR. VIVEK RAO COULD ONLY TALK BRIEFLY. The Division Head of Cardiovascular Surgery, and the Peter Munk Cardiac Centre Chair in Advanced Cardiac Therapeutics, had just completed a heart transplant, but the 52-year-old patient was bleeding, and Dr. Rao had to return to the patient.

Beyond the complexity of operating on the body's life-giving organ, cardiac surgery poses the danger of difficult-to-manage or persistent bleeding. In the case of Dr. Rao's patient, a novel technique that addresses blood transfusions was successfully used. Employing what's called a point-of-care algorithm, Dr. Rao and his team determined that the man's platelets – the cells needed to help blood clot – were dysfunctional and so they were replaced.

"The point-of-care testing enabled the team to administer only the required platelets and not a wide range of blood products that would ultimately be unnecessary," Dr. Rao says. As well, Dr. Rao discovered a source of bleeding, which was also controlled. "The patient did well subsequently," he says.

Point-of-care tests are designed to be used at or near the spot where the patient is located, don't require permanent and dedicated space and are performed outside of clinical laboratories. An algorithm is a set of rules to be applied to calculations or problem solving.

At the Peter Munk Cardiac Centre (PMCC), the algorithm addresses blood loss after surgery and allows faster results for targeted therapy, says Dr. Keyvan Karkouti, Site Chief of Anesthesiology at Toronto General Hospital.

"The algorithm allows us, early at the bedside, to identify why patients are bleeding, and once that's identified, to find therapies to target abnormalities we identified," says Dr. Karkouti, who is keenly aware of the algorithm's value.

Between October 2014 and May 2015, a randomized controlled trial of the point-of-care–based transfusion algorithm was tested at 12 Canadian hospitals. None of the sites previously used point-of-care testing for bleeding management during cardiac surgery. During the seven months, the algorithm was used for 7,402 patients having coronary bypass surgery. Overall, the point-of-care algorithm reduced red blood cell transfusions, platelet transfusions and major bleeding following cardiac surgery.

For Dr. Michael Farkouh, the "out-of-box" thinking that led to this valuable algorithm is truly innovation in action. "It's a novel, very cost-effective way of improving outcomes," says the Chair of the Peter Munk Centre of Excellence in Multinational Clinical Trials.

With a limited blood supply and a push to conserve such resources throughout the health-care system, Dr. Farkouh, a cardiologist, foresees broad appeal for the algorithm. "We have the ability to tailor transfusions in patients," he says.

The algorithm works by determining if platelets, red blood cells or plasma are needed via a flow chart. After a blood sample is rewarmed, questions are asked, such as: "What are the clotting defects?" or "How much blood loss has occurred, based on the weight of sponges used to absorb patient blood?" The questions drill down to appropriate treatment, be it no blood products, the use of platelets, plasma or cryoprecipitate, a frozen blood product prepared from plasma.

When heart surgery is performed, heavy bleeding can occur. The more blood that is lost during surgery, the worse the outcome for the patient. Conditions that lead to excessive bleeding during surgery include complex heart surgeries, such as transplants, that result in longer times on the heart-lung machine; complicated, emergency heart surgery; and patients who were taking blood-thinner medications, Dr. Karkouti says.

Use of the heart-lung machine plays a significant role in degrading the patient's blood. During open heart surgery, the heart has to be stopped, so the patient is hooked to the heart-lung machine, which becomes responsible for delivering oxygenated blood to the body. Blood flows out of the heart's right atrium, through the machine and then the now-oxygenated blood flows back into an aorta. But as the blood courses through the machine, the circuitry diminishes the blood's clotting factors, which is one reason why patients need more platelets. As well, synthetic grafts, hypothermia and surgical trauma can affect blood's clotting ability and may lead to the need for transfusions.

Another operating room dilemma is how long a physician waits before treating the bleeding, Dr. Karkouti says. Watching and waiting to see if the bleeding slows is one approach.

Typically, surgeons first use Method A to stop bleeding, based on what they see, Dr. Rao says. If Method A doesn't work, Method B is implemented, then Method C, using the process of elimination, not an algorithm. The bleeding could be caused by a torn suture line, or the patient may have dysfunctional platelets.

The beauty of the algorithm is that it points surgeons in the right direction.

"So far, I've been impressed with the point-of-care algorithm to treat bleeding disorders," Dr. Rao says. "We can now target the actual problem, rather than using a shotgun approach. We're treating a problem – the bleeding – not the symptom."

One minor drawback has been the five or 10 minutes required to receive the point-of-care test results. "We're an impatient bunch," Dr. Rao says of his fellow cardiac surgeons. "They've told me, 'You want me to wait?'" The test also costs between $50 and $100 per patient, more than standard lab tests, primarily due to costs of chemical compounds, Dr. Karkouti says.

Over the last two years, the algorithm has been used for about 3,000 cardiac surgeries at Toronto General Hospital, Dr. Rao says. While the costs add up, there can actually be savings because fewer blood products, such as red blood cells, platelets and plasma, are used during transfusions, Dr. Karkouti says.

Even though Canadian hospitals do not pay for the blood products they use, there is a cost. In Ontario, the provincial government pays Canadian Blood Services.

Blood is an expensive, limited resource and carries serious risks. Each unit costs roughly $650 to $1,550 to deliver from the donor to the patient. Forecasts also predict that the demand may outstrip supply in the near future. As well, transfusions can lead to life-threatening complications, such as infections, acute hemolytic reactions, acute lung injury and volume overload. Moreover, a proportional relation between blood transfusion and mortality has been noted. "The algorithm does lead to better outcomes because we can implement interventions that reduce transfusions," says Dr. Rao, who believes U.S. hospitals will be interested, given that they pay for the blood they use.

But it's early days. "With the management of bleeding patients, there are still lots of questions," Dr. Karkouti says. "The algorithm has improved our care, but there are issues still to resolve of how to best manage patients. There's still a fair amount we don't know about why people bleed. The algorithm has taken us a fair ways, but we still don't know all the answers."

Which leaves the hospital door open for further innovation in action.

01

01 Dr. Keyvan Karkouti, left, Dr. Stuart McCluskey and Cielo Bingley, a Perioperative Blood Conservation Co-ordinator, work together to find ways to ensure that with a limited blood supply, opportunities are found to conserve wherever possible.

DROPS OF BLOOD DATA

900,000: Average number of units of blood collected each year in Canada, outside of Quebec.

5: Average number of litres of blood in a person's body.

450 millilitres: Amount of blood that goes into a single donation. Often referred to as a "pint," a blood donation is 450 mL, not the actual 570 mL in a pint.

42 days: Maximum shelf life for red blood cells collected through blood donations. Most blood is sent to hospitals within a week. Platelets have a five-day shelf life. Plasma can be frozen, having a longer shelf life.

Every 60 seconds: How often, on average, someone in Canada receives blood or a blood product.

52%: Proportion of Canadians who say they or a family member have needed blood or blood products for medical treatment.

1 in 10: Number of people admitted to hospital who receive blood.

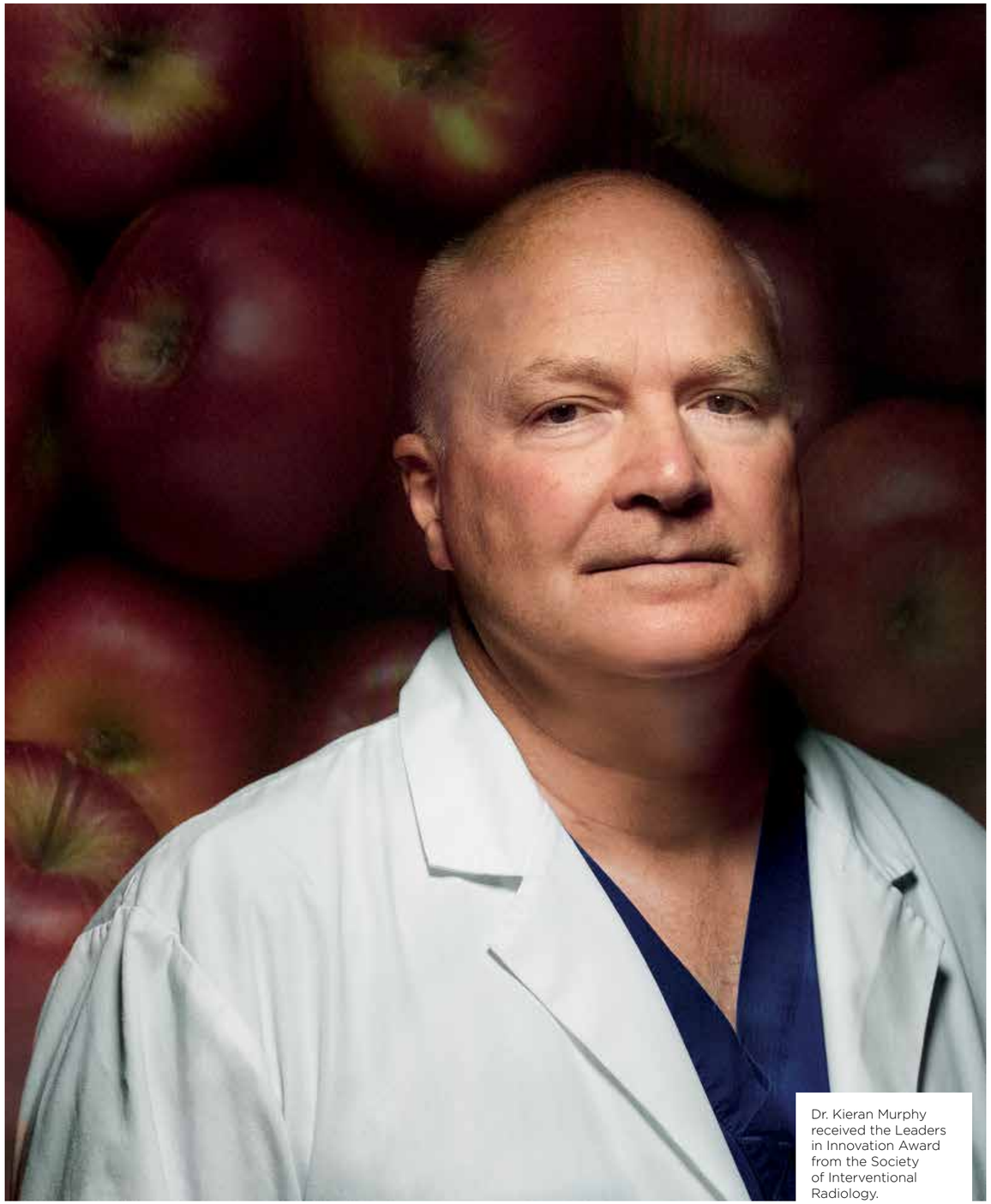
Heart transplant: Requires 40 units of blood, 30 units of platelets, 25 units of plasma and 20 units of cryoprecipitate.

2: Units of blood needed for hip replacement surgery.

6: Units of blood needed for heart surgery.

20: Units of blood needed for a burn patient.

50: Units of blood needed for a vehicle-crash patient.



Dr. Kieran Murphy received the Leaders in Innovation Award from the Society of Interventional Radiology.

A radiologist stirs up a vitamin cocktail to protect against radiation exposure

A chat with his mother-in-law and a walk with his dog gave this neuroradiologist the idea to use anti-oxidants to help lessen the dangerous after-effects from life-saving radiation

By **Mary Gooderham**

SURGERY PERFORMED UNDER X-RAY GUIDANCE HAS TRANSFORMED MODERN MEDICINE, allowing for minimally-invasive operations (from neurosurgery to gastroenterology procedures), reduced pain and shorter recovery periods for patients. It also means lower costs to the health-care system. But X-rays also subject patients, and especially doctors, nurses and technologists, to ionizing radiation, causing molecular changes in the body's DNA that have been linked to elevated risks for cataracts and cancerous tumours.

"It's scary; we are exposed to vast amounts of radiation over a career," says Dr. Kieran Murphy, an interventional neuroradiologist at Toronto Western Hospital who uses imaging-guided technology to fix fractures, perform biopsies and kill tumours in the spine, for example.

Medical professionals such as Dr. Murphy can take precautions, including wearing lead shields and lead-lined glasses, and they sport badges that monitor their radiation dosage. But it's impossible to avoid some exposure, he says. "It's a risk we bear because of our vocational committment to patient care."

Disturbed by reports of injuries among his colleagues, Dr. Murphy found the answer to the problem in a chat he had with his mother-in-law seven years ago, as she prepared for breast cancer treatment. She showed him a list of things she'd been instructed not to take before radiation therapy because they could reduce its effectiveness.

"They were all anti-oxidants," recalls Dr. Murphy, who, after viewing the list, then went on a walk with his dog Cora and met a fellow dog-owner who made anti-oxidants. They fell into conversation and were soon working together, making anti-oxidants that could be taken in advance of radiation exposure, in order to lessen DNA damage.

The result was an anti-oxidant cocktail developed in collaboration with researchers at Dalhousie University that includes quercetin, extracted from apple skins. The cocktail, which Dr. Murphy calls Coramed in honour of his dog's role in the discovery, is currently in clinical trials. After extensive research, the first clinical study was carried out using 10 patients undergoing diagnostic radiation and was funded by donors who supported the Peter Munk Cardiac Centre (PMCC) Innovation Committee.

"Without that, we wouldn't be at this stage; it was a very, very important step for us," says Dr. Murphy, noting that the trial showed the premedication treatment to be beneficial in reducing DNA breaks in the blood of patients exposed to diagnostic radiation.

The research is being closely watched by clinicians such as Dr. Lindsay Machan, an interventional radiologist at Vancouver Hospital who has experienced occupational radiation-induced cataracts and lost the sight in one eye as a result of cataract surgery. He says that the anti-oxidant premedication is an "exciting advance" in the effort to reduce the impact of radiation in imaging-guided surgery. "The data are impressive and encouraging."

Dr. Machan says that minimally-invasive procedures are "exploding" in fields such as cardiology, orthopaedics, vascular surgery and pain medicine. "The numbers are just increasing every year." Patients face little risk from their temporary radiation exposure and "enormous benefits," indeed a growing number of procedures can only be done by imaging-guided techniques, including delivering chemotherapy agents to parts of the liver.

Meanwhile, medical professionals performing procedures such as fluoroscopy and CT scans are exposed to continual low doses of radiation, yet don't see the danger, he comments. "No one has invented the perfect protection as yet – that's for sure."

The International Commission on Radiological Protection has suggested new exposure limits that are one-seventh of the previous average annual level. But Dr. Machan notes there is "tremendous individual variation in how people respond to radiation, and the idea of a threshold is somewhat arbitrary." His goals are to reduce the amount of radiation given off by imaging devices, improve radiation shielding and introduce innovative protective measures, such as Dr. Murphy's premedication treatment.

"It's one more step," he says. "There's no doubt in my mind that it will become a product."

The next study of Coramed will involve testing it on interventional radiologists, cardiologists and other medical professionals who work in a field of radiation, says Dr. Murphy. He expects one of the largest markets for the product to be airline crews, who are exposed to high levels of solar radiation from flying at high altitudes, especially on polar routes.

His research has been recognized by the Society of Interventional Radiology, which gave him its Leaders in Innovation Award in 2015. Murphy has also filed 64 patents on new medical devices and started six companies. He's grateful to be able to devote two days each week to research, and to be part of a "vibrant, intellectually active and questioning" community at the PMCC.

"We're not just here to do a job, but to change how the job is done," says Dr. Murphy, who hopes the premedication anti-oxidant will be on the market within about a year.

> ***"Without [donors support for the PMCC Innovation Committee] we wouldn't be at this stage; it was a very, very important step for us."***
>
> **Dr. Kieran Murphy,**
> Interventional Neuroradiologist, Toronto Western Hospital

The ability to run multinational trials is part of the expertise and experience that cardiologists Dr. Patrick Lawler (left), Dr. Michael Farkouh and Dr. Jacob Udell bring to the PMCC's cardiac clinical work and research.

Finding global solutions to cardiovascular disease

The Peter Munk Centre of Excellence in Multinational Clinical Trials is uniquely positioned to study the world

By **Kira Vermond**

CORONARY HEART DISEASE. It doesn't care if you're Canadian, American or living in India, Kenya or Spain. Political boundaries mean nothing to a condition that kills an estimated 3.8 million men and 3.4 million women globally each year.

So why shouldn't cardiac clinical trials and research also break geographic barriers?

That's part of the thinking behind the Peter Munk Centre of Excellence in Multinational Clinical Trials, launched in 2011 and one of seven Centres of Excellence established by the Peter Munk Cardiac Centre (PMCC) to transform the way patients with cardiovascular disease are treated around the world.

"We bring innovation and what we call the 'one-stop shop,'" says Dr. Michael Farkouh, the Peter Munk Cardiac Centre Chair in Multinational Clinical Trials, who came back to Canada in 2010 after working in the United States for 20 years, including 10 years directing the Mount Sinai Cardiovascular Clinical Trials Unit in New York City.

"When we develop new drugs and new devices, we have the ability that most centres in the world do not have to go from the early concept in innovation all the way to the large clinical trial," he says.

That's partly due to Dr. Farkouh's own experience running large multinational trials. While phase one and phase two trials typically involve smaller numbers of people chosen with very specific medical parameters in mind, multinational trials examine outcomes in thousands or even hundreds of thousands of people worldwide.

Take the FREEDOM Trial, co-led by Mount Sinai Hospital in New York and the Peter Munk Chair in Multinational Clinical Trials. It showed that when diabetic patients with multivessel coronary artery disease have bypass surgery, they live longer and are less likely to experience complications than those who undergo angioplasty.

The Tailored Antiplatelet Initiation to Lessen Outcomes Due to Decreased Clopidogrel Response After Percutaneous Coronary Intervention (TAILOR-PCI) study is another large trial the PMCC is currently co-leading with the Mayo Clinic. It's meant to determine whether patients with stents should receive the drug Plavix or another prescription.

Thirty per cent of people are actually unable to metabolize Plavix. They have a genetic variation in a liver enzyme that prevents it. Ultimately, the drug is next to useless for them.

But what if you could tell – through rapid genotyping – who is a good candidate for that standard medication and who should receive an alternate medication that's more effective for them?

The TAILOR-PCI study team uses genotyping technology – a quick cheek swab – in some of the 6,000 patients enrolled in the trial to see if genetic testing before prescribing medication after angioplasty leads to better patient outcomes. So far, the team has signed up more than 4,000 patients in Canada, the U.S. and South Korea.

"It's about trying to show that individualizing care is the way to go," says Dr. Farkouh. It's also the first and largest trial of individualized medicine that the U.S. National Institutes of Health (NIH) has sponsored, he explains.

The beauty of multinational trials is not merely the vast scope, but also how the data is actually collected and analyzed, says Dr. Patrick Lawler, a cardiologist, Boston native and new recruit to the centre who is a leading expert in preventing atherosclerosis cardiovascular disease.

Dr. Lawler says he was drawn to the PMCC because the centre's focus is unique: a strong interest in developing pragmatic clinical trials that intersect with real-world evidence by pulling data from actual clinical cases.

In a pragmatic clinical trial, a study could look at how blood in blood banks is used. Are patients being given the newest blood or the stock that has been shelved the longest? (Think milk growing nearer to its expiration date.) Then, when you follow these patients through their electronic health records afterward, what are the outcomes?

"These kinds of pragmatic trials are trying to make use of the fact that our health-care system is increasingly digital, electronic and connected," says Dr. Lawler. "In theory, this should be a more efficient system. The trials should cost a lot less money and they should be faster."

And as the TAILOR-PCI trial shows, the centre also specializes in precision medicine that focuses on making medicine more individualized for patients.

So why leave his full-steam-ahead career in Boston to come to the PMCC in Toronto?

"You know, I think what I was excited about was the spirit of innovation and creativity here. There's an environment that encourages scientific risk-taking," he says.

Dr. Jacob Udell, a cardiologist with expertise in women's health, diabetes and novel ways to protect patients from heart disease, arrived in Toronto from Boston in 2012, also at Dr. Farkouh's urging. Dr. Udell says he, too, was impressed with the Centre of Excellence when he saw an opportunity to join an emerging group ready to use big data in Canada and beyond.

"I want to leverage the power of our health information system in Canada and the U.S. to try to build a better wheel," he says.

One major study he has in the works looks at whether giving people with weak immune systems a more concentrated dose of flu vaccine will give them cardio protection. The outcome could be the difference between life and death for those with kidney disease, diabetes, cardiovascular disease and those with obesity who are underprotected by the regular shot.

The teams participating in the study have already completed one flu season. The results will be recorded in 2020.

Teamwork and collaboration are obviously paramount if large multinational clinical trials are to succeed. And Dr. Udell says the centre is working with nurses, nurse co-ordinators, lead administrators and senior leadership at the PMCC and Toronto General Hospital, as well as teams across the country and beyond.

"This couldn't have happened without everyone coming to the table," he says. "It's going to take work and rolling up our sleeves, but we're on the precipice of doing something pretty cool that will open the floodgates for many trials to come."

THE PETER MUNK CENTRE OF EXCELLENCE IN MULTINATIONAL CLINICAL TRIALS

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$28.8M
IN RESEARCH FUNDING

+163,000
OUTPATIENT VISITS

+10,000
CARDIAC & VASCULAR PROCEDURES

2,400
PATIENTS IN CARDIAC REHABILITATION

160
CLINICAL FELLOWS & RESIDENTS FROM AROUND THE WORLD

67
FUNDED PRINCIPAL INVESTIGATORS

35
HEART TRANSPLANTS

34
MECHANICAL HEART PUMPS

*Based on 2016 data

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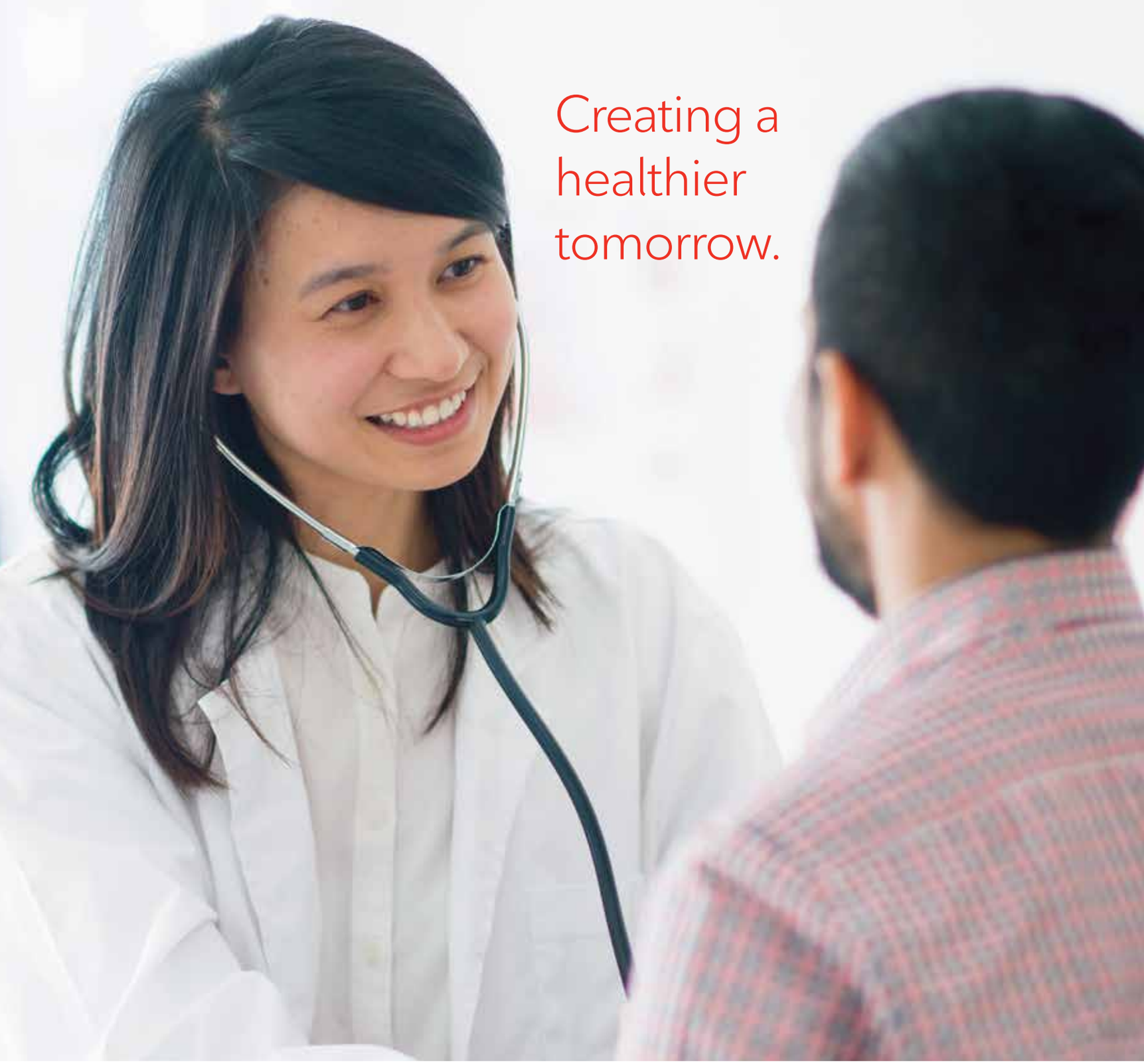

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