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FOCUS ON BRAIN SCIENCES

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AT 31. HOW  
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Tiffany Scholl is a remarkable woman who nearly died from a stroke before childbirth and was restored to full health by an interdisciplinary team at Sunnybrook.

Photograph by Tim Fraser  
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**PUBLISHERS**  
Craig DuHamel  
Pamela Ross

**EDITOR-IN-CHIEF**  
Simon Beck

**ART DIRECTOR**  
Frank Perito

**FEATURE WRITERS**  
Jane Doucet, Augusta Dwyer,  
Pat Lynch, Celia Milne

**CONTRIBUTORS**  
Dan Birch, Laura Bristow,  
Natalie Chung-Sayers, Alexis Dobranowski,  
Allison Dunfield, Sybil Edmonds,  
Jennifer Foster, Sally Fur, Wendy Glauser,  
Monica Matys, Katherine Nazimek,  
Angela Pirisi, Tereza Radman,  
Nadia Norcia Radovini,  
Katie Rook, Marie Sanderson

**PHOTOGRAPHY**  
Tim Fraser, Doug Nicholson,  
Peter Power, Dale Roddick

**PRODUCTION MANAGER**  
Michelle MacKay

## GLOBE EDGE

**Teena Poirier**  
DIRECTOR, CLIENT ENGAGEMENT & GLOBE EDGE

**Charlene Rooke**  
EDITORIAL DIRECTOR, GLOBE EDGE

**Liz Massicotte**  
PROGRAM MANAGER, GLOBE EDGE

**Sally Pirri**  
DIRECTOR, PRODUCTION, THE GLOBE AND MAIL

**Isabelle Cabral**  
PRODUCTION CO-ORDINATOR, THE GLOBE AND MAIL

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**ALL CORRESPONDENCE**  
Sunnybrook  
2075 Bayview Avenue, Suite D100  
Toronto, Ontario M4N 3M5

questions@sunnybrook.ca  
www.sunnybrook.ca

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# WE ARE SUNNYBROOK

faces of  
our staff  
and our  
community

## WHEN KNOWLEDGE IS POWER

*Justin Lorentz is a genetic counsellor at the Odette Cancer Centre, the Male Oncology Research & Education Program lead and an avid blogger. His mission is to identify, educate and support women and men who are at an increased risk for cancer.*

**KN:** Do you believe in fortune tellers?

**Lorentz:** (Laughs) I do. I believe in psychics, fortune tellers and mediums. I've never been wooed by one, but, in theory, I believe.

*How do you predict who is at an increased risk for cancer?*

Rather than looking to the future, I look to the past – to a family history. We offer genetic testing to patients or families we suspect have hereditary cancer, looking mostly for the BRCA1 and BRCA2 genes. We all have two working copies of these genes, but if someone is born with a mutation in one copy, they'll be at higher risk of developing certain cancers.

*Last year, Angelina Jolie went public about undergoing a mastectomy after finding out she carried the BRCA1 gene mutation. BRCA1/2 are known as breast cancer genes. That's true. For women born with this gene mutation, the lifetime risk for breast and ovarian cancer jumps significantly. But many people aren't aware that men can also be affected by these gene mutations.*

Men can be carriers that pass on the mutation from one generation to the next, and they can be at an increased risk for breast and prostate cancer.

*Is the lack of public awareness about how BRCA affects men your motivation behind the Male Oncology Research & Education (MORE) program?*

Men with prostate cancer tend to die *with* prostate cancer, but men who have the gene mutation are more likely to die *of* their prostate cancer. It's significantly more aggressive; yet, we do the exact same screening for guys who

have the mutation as we do for the general population.

The MORE program is about answering big questions: Should men with the mutation be screened differently? Are there other genes that can help us predict risk? Why is prostate cancer so prevalent in guys of Caribbean ancestry? We want to figure out how men at an increased risk for prostate cancer can be better managed, so that they can get the best care possible. If we can predict cancer, we may be able to prevent it.

*You're giving people a glimpse into whether or not they are likely going*

the  
**GENETIC  
COUNSELLOR**

*to get cancer. Is ignorance bliss? Information is power: It's a tool people use to make the best decision for themselves. Men and women with these gene mutations have options – whether it's having breasts or ovaries removed or doing regular screening to nip cancer in the bud. If someone chooses to know whether they have a BRCA gene mutation, they can adapt treatment or sometimes their life plans. With hereditary cancer, it's never just about one patient; it's about a whole family.*

*Interview by Katherine Nazimek*



the  
RESIDENT

## YOU CAN CALL HER “DOCTOR”

*Dr. Tiffany Florindo is a new Family Medicine Resident graduate and winner of the Steve Kandell Award for clinical excellence in family medicine at Sunnybrook.*

**MM:** *Becoming a physician takes a long time, 10 years or more, depending on your area of specialty. How do you go the distance?*

**Dr. Florindo:** It definitely takes a lot of persistence and a good line of credit! You also need a huge support system and a “person” – the one who is going to kick your butt when you feel like throwing in the towel.

*So who is that “person” for you?*

I’m lucky because I have two: my mom and my sister.

*The field of medicine is not for the lighthearted. Does anything make you queasy?*

I really don’t like when joints and bones are not where they are supposed to be. Oh, and bodily fluids. Depending on the night, those can end up on your scrubs. White is not an optimal colour to invest in when purchasing work attire.

*How do people react to you as a young doctor?*

That depends on the patient. Some think it’s refreshing to have someone “younger” in charge of their care. That being said, I’ve also been called student, kid, girl ... anything but doctor. I find it best to smile through it. Eventually they realize that I’m not just there to ask silly questions and I actually know what I am talking about. It keeps me humble.

*You were recently elected by your peers to be chief medical resident. That’s a great honour!*

Yes, it definitely is. I’m confident in my abilities, but realize that I still have so much to learn.

*Confidence must have been just what the doctor ordered when you did a placement in Moose Factory, Ont., a small island in James Bay.*

When I first stepped off the plane and realized there was no cell phone service, I thought, “What have I gotten myself into?” But the group up there is completely amazing. I spent a few days further north in a community of only 200. When you’re the only one around, without much support, you learn a lot about yourself and your medical training kicks into high gear. It makes me realize I’m doing exactly what I was meant to do.

*Interview by Monica Matys*

## THERE IN TIMES OF TRAUMA

*Furmas Rahman is living proof that hard work and determination will help you succeed. While working as a patient service partner in Sunnybrook’s Emergency Department, he completed his full-time degree in nursing in April and aims to pursue trauma nursing.*

**LB:** *How did you become interested in nursing?*

**Rahman:** I started working at Sunnybrook in the Critical Care Unit as a patient service partner (PSP) in 2002. At that time, I just needed a job, but as I worked alongside the team I became very interested in all the different professions that support critically ill patients. Ultimately, I found that nursing was my true calling.

*What exactly does a PSP do in the Emergency Department (ED)?*

I support and assist the nurses with whatever they need. This could be walking or positioning a patient, stocking medical supplies, even supporting the team in the trauma room, if necessary. It really is a team effort in the ED, so anything I can do to fill in the gaps and make things run smoothly is what I’m there for.

*How did you manage your PSP job and go to school full time?*

It really was about finding a balance. I love Sunnybrook and the patients here, so the job was like a bonus. The work here also really reinforced what I was learning at school during the day. The ED has been a “real world” classroom. It also helped that my colleagues were very supportive of me.

*What is it about trauma nursing that interests you?*

Trauma patients have always affected me. I see a young person who has numerous injuries from a car crash, and I think, “That could be me or my family member.” It is very humbling to work with these patients, and it takes a lot for them to get back on their feet again. I want to help those people get back to doing the things they enjoy.

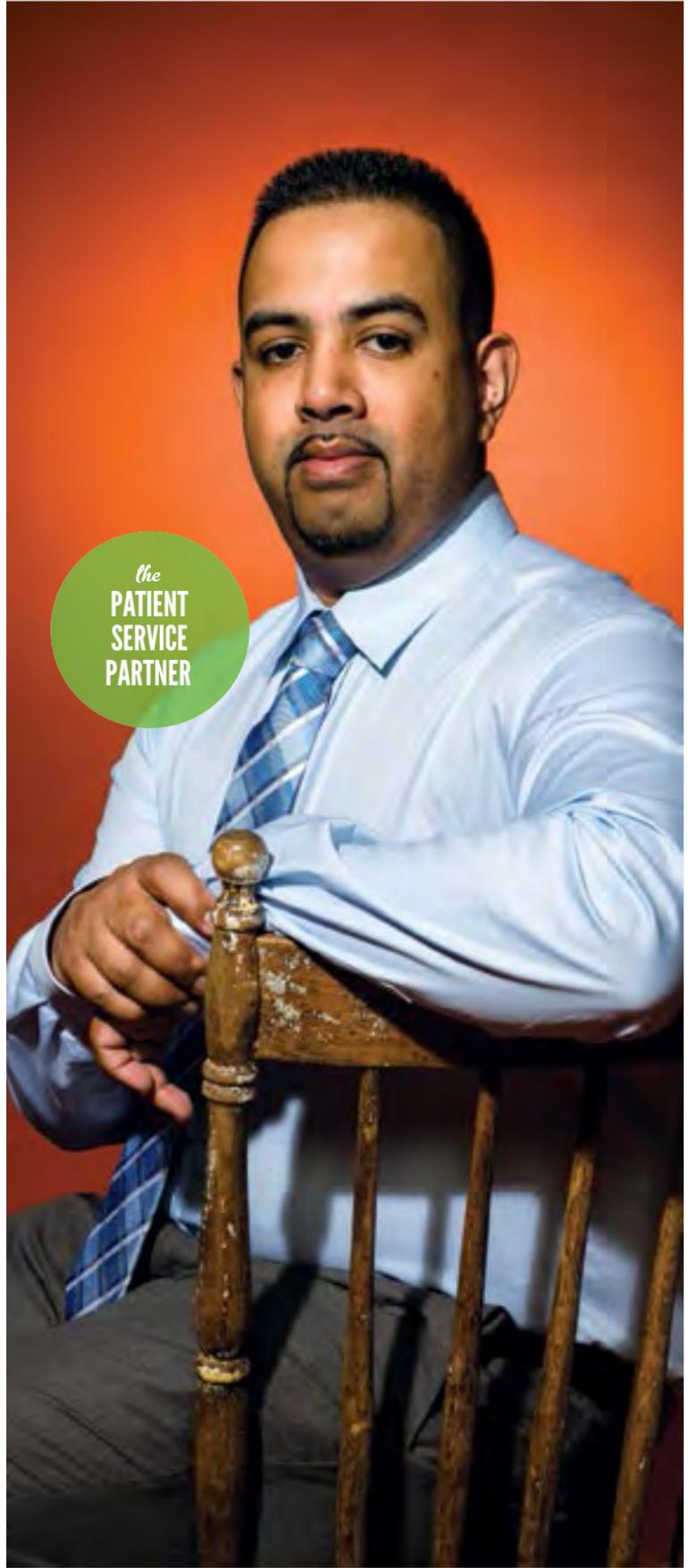
*Is it true what they say about full moons and the ED?*

Well, sometimes when I’m driving in for my night shift and I see a full moon I think, “Hmm ... this could be interesting.” But I really have to be prepared for the fact that any day could be a day without time to catch my breath. The ED is very unpredictable, so I have to go in assuming my shift will be non-stop.

*After all that hard work, how does it feel to have earned your degree?*

It’s such an incredible feeling to know that I accomplished this goal. I didn’t think I would be able to do this, but I did and I really have everyone at Sunnybrook to thank for that. My colleagues encouraged me to keep at it. They would say, “You can do it, Furmas!” They made it that much easier because they had my back through it all.

*Interview by Laura Bristow*



the  
PATIENT  
SERVICE  
PARTNER



the  
NURSE  
RESEARCHER

## FEELING HER PATIENTS' PAIN

*Yvonne Ramlall is a registered practical nurse (RPN) and nursing researcher at the Holland Orthopaedic & Arthritic Centre. She was recently awarded the 2014 Dr. Robert B. Salter Award from the Canadian Orthopaedic Nurses Association (CONA).*

**SF:** When did you know that you wanted to be a nurse? Can you describe when and what it was that led you into this profession?

**Ramlall:** Sadly, my dad passed away when I was eight years old. He was a porter at the general hospital in British Guyana, and I recall my mother telling me that my dad wanted me to be a nurse. He had planned to send me to London to live with his niece and attend nursing school.

When I came to Canada, I went to school and was employed for 25 years in a private medical laboratory, the last 15 years working as a hematology technologist. The owner

and president of the lab was diagnosed with a terminal illness, and there was no guarantee of my future there. My own mother had died six weeks earlier after suffering a stroke. Distraught, I took some time off and completed a floral design course. It was then that I decided to honour my mother and father's memory and go down a new path and become a nurse.

*As a member of the interprofessional care team on the acute surgical floor at the Holland Centre, what do you find most rewarding about your role as an RPN?*

Being able to continue my commitment to practise. I also love innovative research and sharing the knowledge gained to improve patient care and education for patients having major orthopaedic surgery. Being a leader and a mentor to students and new staff, as well as advancing the practice of nursing, is also rewarding.

*How did you initially get involved in nursing research?*

I have always been passionate

about improving the pain experience of patients, following total joint replacement. In 2006, I applied for a fellowship through the Registered Practical Nurses Association of Ontario (RPNAO). My first study was based on the knowledge that was learned through the Joint Pain Management Collaborative, an initiative that spans across Sunnybrook. I wanted to find out if patients were meeting their goals after surgery. Were they getting enough pain medication? With early discharges, how were they managing at home? For me, these were relevant and very important questions.

*You have travelled throughout the world to present your research. Can you share a little of this?*

In 2012, I presented my second research study on the pain experience of patients whose primary language is not English, following primary total hip or knee replacement surgery. More than 200 people from close to 20 countries were represented at the conference in Qawra, Malta. I have also presented my research in Dublin; Bristol,

England; and Melbourne, Australia. It is a wonderful experience to exchange ideas and overcome challenges with orthopaedic nurses from around the world!

*Recently, you were awarded the Dr. Robert B. Salter Award from CONA. What happens next?*

To be honoured with this award and know that I have contributed to research, and to knowledge translation, has inspired me tremendously. Once you start doing research, it's hard to stop!

*What is it about research that makes you want to do more?*

By asking questions, we get answers. Sometimes those answers can tug at the heart. Not doing something about the negative outcomes will not improve the patient's experience. Then, by not challenging yourself to ask the difficult questions, one will not be able to influence the change that is needed.

*Interview by Sally Fur*

PHOTOGRAPHY BY DOUG NICHOLSON

## ALWAYS ASKING, "HOW CAN WE DO IT BETTER?"

*Those who meet William Tran are immediately struck by his positive energy and passion for patient care. He is a clinical radiation therapist at Sunnybrook's Odette Cancer Centre and a research project manager for a clinical study, led by Dr. Gregory Czarnota, into chemotherapy treatment monitoring using ultrasound for patients with locally advanced breast cancer.*

**NC-S:** What do you find most fulfilling about what you do?

**Tran:** I really enjoy supporting patients. Often they struggle with what the future holds, and it's nice to know that your efforts can potentially help them through that uncertainty. We hope that our research will reduce the "not knowing," and allow us to track treatment effectiveness earlier and to better tailor treatment for these patients.

What's also fulfilling is the interesting mix of research and clinical care with which I'm involved. I'm always asking questions: 'Why are things the way they are? How, or should, things be different? How can we do it better?' I guess you could say, uncertainty also allows us the opportunity to make changes. For example, to improve treatment approaches and perhaps do things differently – to explore new thinking.

*What does "new thinking" look like?*

The most recent thinking in cancer care is about treatment tailored specifically to the individual patient. We're also studying a newer frontier, using ultrasound imaging to monitor and characterize cancer cell death or the biochemical changes within cells, to better inform the course of treatment for each person.

*You mentioned that you're always asking questions. Where does that sense of curiosity come from?*

I guess it's about being open to different points of view. It's about not being complacent and to constantly explore ideas. Perhaps it's to challenge whether we should do things differently or to reaffirm that our approaches are effective the way they are.

Coming from a place rooted in new frontiers – having arrived to Canada as refugees, my family and I fled postwar Vietnam in 1980. Canada opened its arms. For that embrace, I am forever grateful and determined to always push for positive change – to give back and to make a difference.

*Interview by Natalie Chung-Sayers*



the  
RADIATION  
THERAPIST



the  
SOCIAL  
NETWORKERS



## RULERS OF ENGAGEMENT

*Brent Creelman, Senior Digital Media Strategist, and Sivan Keren Young, Manager, Digital Communications, have tweeted and Facebooked their way to making Sunnybrook the leading Canadian hospital in the social media stratosphere. Sunnybrook's use of social media to improve the patient experience is now recognized as a leading practice by Accreditation Canada.*

**MS:** When did you first become interested in social media?

**Creelman:** I was in Grade 7 when I created a website to talk about my favourite TV shows. I learned about web development and also the importance of storytelling. That

spurred me to study journalism at Carleton University.

**Young:** I developed my interest in the same grade. We've come a long way when you consider the high-reach impact of today's social media channels.

*Speaking of high reach, aren't you responsible for captivating a whole country by live-tweeting heart surgery?*

**Creelman:** It was incredible! In three days Sunnybrook gained 5,500 new Twitter followers. We had no idea the tweet would have such an impact. Teachers actually let their classes watch and ask questions, so it tied in really well with the hospital's focus on education.

*How did you sum up a complicated surgery in 140 character tweets?*

**Creelman:** You're definitely limited

by space with Twitter. You need to grab attention quickly. We also added photos and videos to make it really compelling.

*Sunnybrook's online voice is really conversational and friendly ...*

**Young:** We just started talking to people on Facebook and Twitter. One of our goals is to improve our patients' experience. It can be something as simple as answering a question about where to find a late-night coffee. This is really about engaging with our patients and families, and ensuring that we respond to their needs.

*You must have some stories?*

**Creelman:** We monitor all social media for references of the hospital. From time to time, Sunnybrook gets compared to *Grey's Anatomy*. Apparently we have a few Dr. McDreamys (laughs).

**Young:** There are also those simple day-to-day moments that are captured. On Halloween, we posted pictures on Facebook of a family's premature twins still in the hospital's Neonatal Intensive Care Unit, dressed up as a ladybug and a turtle. It elicited such an emotional reaction from our followers.

*Have there been any bumps along the way?*

**Young:** When Sunnybrook first started using social media, Facebook and Twitter were relatively new, and we were such early adopters. Sunnybrook took a leap of faith; we were willing to make mistakes and learn. And if we can make just one patient's day better, every day, then that's a good day.

*Interview by Marie Sanderson*

PHOTOGRAPH BY DOUG NICHOLSON



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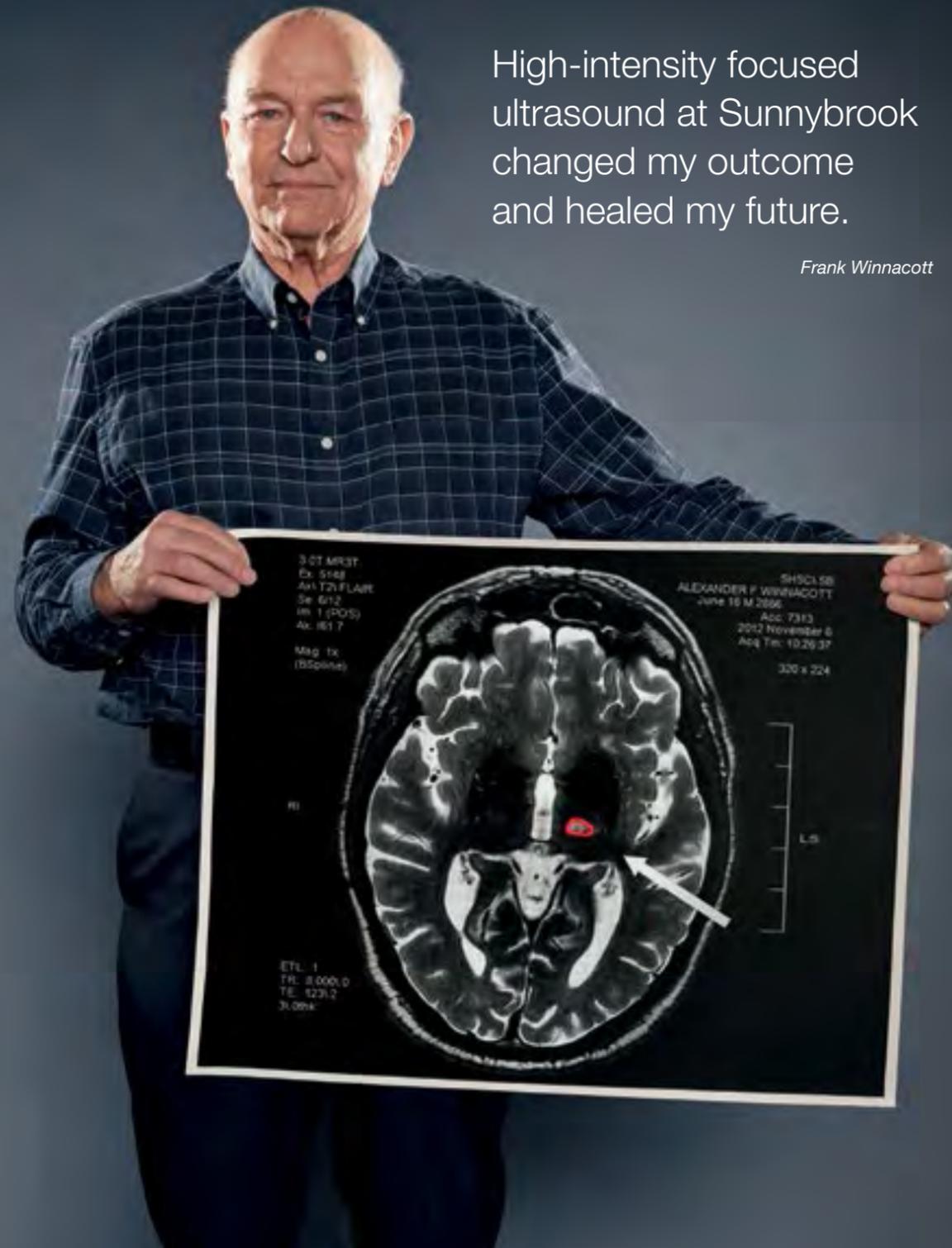
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### THE POWER OF TOUCH

Jessica Ganas shares a special moment with her moments-old daughter Juliana, who was born via a skin-to-skin Caesarean section earlier this year. This innovative way of delivering babies by C-section, emphasizing skin-to-skin contact and bonding between mother and baby, is being led in Canada by physicians at Sunnybrook.

Babies born by C-section are typically given to their mothers three-to-five minutes after birth, after being cleaned off and receiving routine care. In a skin-to-skin C-section, the baby is put directly on the mother's upper abdomen after the medical team pushes the baby underneath the drape separating the medical team from the mother's upper body. The baby then settles directly on the mother's bare chest.

"Skin-to-skin contact immediately after birth helps babies regulate their temperature and glucose levels. It promotes bonding, and babies often initiate breastfeeding on their own from that position as well," says Dr. Jon Barrett, left, seen here with Dr. Kirsten Niles and registered nurse Andrea Pryce.

— Sybil Edmonds

Photograph by Doug Nicholson



# DECODING THE FUTURE

A genomic revolution is coming, in which our DNA will be unlocked to reveal what health issues are programmed within us all, providing the keys to personalized treatments. Sunnybrook researchers are already at work charting the road map to this Holy Grail of medicine

By Pat Lynch

**Dr. Michael Julius is waxing poetic on the future of medicine, proffering a vision of health care 70 years hence.**

A doctor sits bedside with a patient, a tablet cradled on her lap. It contains the entire medical history of that individual from pathology to hospital visits, diet and lifestyle notations: every piece of imaging. Lab studies and regular checkups. Treatments. Side-effects and reactions to drugs. And, perhaps most significantly, nestled alongside this robust electronic medical record will be an overview of that patient at his most fundamental level: a roadmap of his DNA.

For the patient of the future, medicine will be fully customizable.

“The genomic revolution,” says Dr. Julius, the vice-president of research at Sunnybrook, “has essentially provided us with the telephone book of who each of us is at the nucleic acid level, our DNA. It’s key to what’s going to happen to us through life and actually dictates how we are going to respond to things and how we aren’t. And the next 50 years or so are going to be dedicated to the investigation of how these pieces of DNA get turned on and how they get turned off, in circumstances of health, as well as in circumstances of disease.”

He leans forward, tapping the table for emphasis.

“But [the medical community] is not yet capitalizing on this information that’s becoming ever more rapidly available to guide our creation of the care map for an individual patient.”

A collaboration between Sunnybrook and the Ontario Institute for Cancer Research (OICR), however, may help change that. Designed to bridge the gap between ongoing research and future clinical application, the two organizations have embarked on a project that promises to help speed up the delivery of personalized medicine, a movement focused on the application of new-found genomic research to patient diagnoses and therapies. But before any of that can happen, Dr. Julius says, the infrastructure has to be built to house all the necessary information to make effective clinical decisions.

“What we’re doing at Sunnybrook Research Institute,”

he says, “is we’re building this Ferrari, which is the IT architecture.”

Sam Marafioti, Sunnybrook’s chief information officer and vice-president of corporate strategy, is co-ordinating the construction of that Ferrari, which will help bridge the information silos that exist between clinical and research departments. It’s a project that’s technically been underway for years as patient data that had been housed on paper was transferred to computer via records like MyChart (a personal patient-accessible health record) and Sunny-care (patient e-health charts accessible by Sunnybrook clinicians). Now, with advances in technology, Marafioti is bringing together all of those parts (and then some) into one, integrated system.

“We’re now integrating all these substructure systems that have been built independently into what we call the EPR,” he says. “And we’re broadening the functionality of that to include the integration of information from regional systems. It’s a cumulative patient profile – that [includes] all of the family practice information on the same patient who’s being cared for by a primary care doctor. So we’re following the patient through a life cycle with all the information from different settings of care.”

The OICR brings genome sequencing expertise – and experience with the informatics hubs that make sense of such data – to the table. Recognized as a leader in gene sequencing and analysis, the OICR currently supports the research and clinical trials of 27 Ontario cancer centres and co-ordinates the International Cancer Genome Consortium, a research project that is sequencing 25,000 cancer genomes from 50 different types of cancer. Its partnership with Sunnybrook aims to create the framework that will allow precision medicine to move from concept to reality, combining longitudinal patient data with pathology, imaging, clinical studies and, eventually, genomic sequences. It’s a massive undertaking, and one that’s been started in a somewhat disconnected fashion in hospitals the world over. The key to moving it forward at an effective pace, however, is by partnering up.

“In the absence of Yo-Yo Ma conducting the health-care

system, saying, 'You have to do this,' and 'You have to do that,'" says Dr. Julius, "we've been working in a vacuum, with everybody starting to do everything on their own. And there's no way for us to accomplish our goal with each of us working separately. We all have to work together."

And that work has just begun, with a highly specific focus.

## START SMALL, GO BIG

Ductal carcinoma in situ (DCIS) is an early form of breast cancer that is particularly difficult for clinicians to decide how to treat. It's often argued that DCIS patients are treated too aggressively, undergoing chemotherapy or mastectomies that might not be entirely necessary. As an early cancer, DCIS is not life-threatening, but because it can progress into a lethal cancer, it's often treated aggressively upon diagnosis, an approach that, from the patient's point of view, can have drastic effects on quality of life. From an economic standpoint, health-care money is perhaps being wasted on treatments that provide little or no benefit to the patient in the long run.

Sunnybrook's breast cancer program has developed the largest cohort of DCIS patients in the world, offering the larger collaborative project – that of developing an informatics system capable of housing data that will lead to the evolution of precision medicine across the globe and across diseases – a place to start.

"Like I said, we're building a Ferrari," says Dr. Julius of the infrastructure being assembled for this project. "And I want to make sure that when we turn the key, that it is actually going to start and that gas will flow, so [for now] we're focused on a very contained project, ductal carcinoma in situ."

Because it's an early form of breast cancer, DCIS is im-

portant to focus on, says Dr. Martin Yaffe, a senior scientist at Sunnybrook Research Institute and the architect of an information system dubbed the "biomatrix," which will form the backbone of the hub that grows out of the project with the OICR.

"You don't die from DCIS," says Dr. Yaffe. "Some people would even argue that you don't need to find it – but it's clear that some DCIS progresses and becomes invasive cancer, so if you can stop the disease at the state of DCIS, you've basically prevented a lethal cancer, which is kind of the Holy Grail."

Over several years, the project will analyze more than 5,000 DCIS tumours, says Tom Hudson, the president and scientific director of OICR.

"It's a great pilot project to build an informatics system that's suitably big," he says, referring to the size of Sunnybrook's DCIS cohort. "And it's ambitious in terms of the science. We expect to generate some great knowledge with applications in the future, like how to treat early cancer."

The genetic information gleaned through DCIS tumour analysis will be partnered with clinical data to help build a platform offering practitioners a robust picture of a patient's health.

"We had a review of [Sunnybrook's DCIS] program a year ago from international scientists who came and looked at it and said, 'This is an extraordinary resource,' and endorsed the plan," adds Hudson. Assessing which genes are mutating and why – which is part and parcel of OICR's genomic sequencing work – will eventually lead to a better understanding of which therapies will be of use to patients and which will not.

"Current convention of how we treat cancer patients is based on large numbers of patients treated in various different ways without looking at their genome, across the globe,"



Dr. Michael Julius (left) and Sam Marafioti

says Dr. Julius. "We look statistically at what works best for the population as opposed to the individual. We'll eventually be able to identify which short circuit the tumour you have arose from. And that actually is going to dictate how, ultimately, we're going to treat that person's cancer, as opposed to [how we'd treat] cancer writ large."

But genome analysis involves big data, all of which has to live somewhere and be easy to access and analyze. "This project has become not just about DCIS, but also the development of an information management structure that's going to be able to track a lot of data, with new architecture and new databases for medicine," says Hudson.

It is, in essence, the foundation for precision medicine across the board.

## THE FUTURE COMES AT A COST

So how long will it take for Sunnybrook and OICR's project to yield results that reach the clinic?

Sunnybrook's Dr. Julius contends that results may filter down to the clinical level within two years. OICR's Hudson has his money on something closer to four. Marafioti, the CIO, is already looking beyond the DCIS project and predicts that the infrastructure being built now will next be used to track and study dementia. So the Sunnybrook/OICR project, which Marafioti expects to last 10 years and to cost upward of \$100-million to complete, will yield results that go beyond the initial field of study.

For his part, Dr. Julius estimates the current collaboration – funded by research grants secured by Sunnybrook Research Institute scientists – will take further investments in the neighbourhood of \$200-million over the next five to 10 years.

Regardless, says, Dr. Julius, "the right thing to do is to move this initiative forward. [Genomic analysis] is one of those tsunamis that will have to be adopted with the greatest of care, systemically. The best minds – ethical minds, privacy minds, scientific minds – need to be brought to bear on this issue. But not to capitalize on it would be backward. This is ever-forward thinking, which is, essentially, the essence of science." ■

PHOTOGRAPH BY DOUG NICHOLSON

## A YOUNG SCIENCE

The first map of the human DNA was completed by the Human Genome Project in 2003, but it was only, in essence, a rough draft. It located the genes on the chromosomes, but it wasn't until 2007 that the first individual genome was fully sequenced, a process that determines the exact order of the four chemical bases that comprise a DNA molecule. Variations or mutations in those sequences can help researchers pinpoint markers of disease, and that analysis is a large part of the

work that's been undertaken by the International Cancer Genomics Consortium. It's a massive undertaking, but is essential work if personalized medicine is ever to become commonplace.

"We're closing the net on a number of susceptibility genes," says Sunnybrook's vice-president of research, Dr. Michael Julius, "but it's going to take, I would argue, 50 to 100 years before we understand not only that we've got the names of everyone in the [genetic] telephone book, but also how the variations play against one another."

This is a science that's still in its relative infancy.

It will, however, have signifi-

cant implications in years to come as researchers, armed with increasingly better (and cheaper) technology, become familiar with a wider variety of gene mutations and are able to pass along their findings to aid in prevention, diagnosis and treatment.

The cost of gene sequencing, once prohibitive, has dropped greatly since 2007 with advances in technology, but the process remains essentially the same.

In the case of screening for cancers, the kind of work being done at the Ontario Institute for Cancer Research, the lab requires two things: a sample of the tumour to be sequenced

(with patient consent) and a blood sample, which allows researchers to compare the genes the patient has inherited from his or her parents to those in the tumour. The differences tell the story of the cancer mutation.

"Often we'll find 10,000 mutations," says Tom Hudson, president and scientific director of the Ontario Institute for Cancer Research, "but we have to find which of those are actually actionable – they provide information on drug response or prognosis – so it's not just sequencing, it's interpretation of the data that's extremely hard. This is still a new science."

– Pat Lynch

# WHOSE GENES ARE THEY, ANYWAY?

The promise of genomics is huge, but it's also an ethical minefield.

If a genome sequence alerts a patient to a predisposition to Alzheimer's, is that person now obliged to share such information with family members who stand a good chance of sharing that genetic fate? What if those family members have no desire to find out? Would a life insurance company issue a policy to a client whose sequence suggests a drastically shortened lifespan?

Could abuse of this burgeoning science lead to a dystopian future of made-to-order babies?

Ethical spectres have presented themselves since the earliest days of genomic study and have, for good reason, become part of what drives the privacy initiatives of informatics projects like the Sunnybrook Cancer Research Biomatrix, happening in conjunction with the Ontario Institute for Cancer Research.

As Sunnybrook senior scientist Dr. Martin Yaffe explains, because this project is research-based, all of the patient information currently being entered into its database is anonymous, though all of it has been acquired with patient consent. He says: "Once the data

are in the system and a researcher wants to do any analysis, everything is 'pseudo-identified.' So when you're working with research, you can't identify the individual. But you do know, say, that this person is 39 years old, male and has the general characteristics that are important in doing the research."

But since the goal is eventually to move this informatics system beyond the research phase to the practical application of personalized medicine – something that requires the use of patient identities – the team has to balance privacy with future goals.

"When we're talking about personal health information, we're talking about increasing regulatory hurdles," says Dr. Michael Julius, vice-president of research. "[That's] not inappropriate with respect to the maintenance of privacy, so the governance team on this project includes the chief information officer and the chief privacy officer; it includes scientific leadership, risk management and various governors of the board of Sunnybrook, because eventually we must have the appropriate policy framework in place to utilize this information." – Pat Lynch



Tiffany Scholl



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# *rethinking the brain*

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Sunnybrook's Brain Sciences Program brings together diverse experts to tackle some of society's most urgent illnesses: dementia, stroke and mood disorders

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By Celia Milne  
Photography by Tim Fraser

## Tiffany Scholl was just 31, and pregnant, when she had a massive, life-threatening stroke.

She had developed two complications of pregnancy: HELLP syndrome, which causes thinning of the blood, and eclampsia, which causes high blood pressure and convulsions.

Tiffany, a Toronto hairdresser, was rushed to Sunnybrook, where doctors went into high gear to save her life. She had suffered a brain hemorrhage deep within the left side of her brain. She had experienced an epileptic seizure. She was in a coma.

There were other medical problems: She developed significant swelling in her brain, so the neurosurgery team was on stand-by in case she needed emergency surgery. The blood vessels in her brain went into spasm with severe narrowing. One of the major arteries in her brain had partially torn and developed a blood clot, posing an immediate risk for another stroke.

While Tiffany lay unconscious, an obstetrical team delivered her baby by emergency C-section at just 29 weeks gestation. It was June 23, 2013. Her baby girl, Clementine, only survived until July 3. Dr. David Gladstone, a stroke neurologist at Sunnybrook, remembers how close Tiffany's husband, Mario, came to losing both his daughter and his wife. "It was very tense. We were hoping for a miracle," the doctor says.

Choosing her treatments posed a dilemma. "On the one hand, she needed blood thinners to prevent more clotting. But on the other hand she had bleeding in the brain that made any treatment more risky. It was a delicate balance," says Dr. Gladstone. Tiffany was in good hands, as Sunnybrook is one of Ontario's Regional Stroke Centres and has the expertise to tackle the province's most dire cases.

After several days in a coma, Tiffany woke up. Because of the stroke, she had lost her ability to comprehend, to remember and to speak. She was paralyzed in her right arm and right leg.

"People told me that I had had a baby and that it had died. I didn't understand. I started crying and fell asleep," says Tiffany. "It was better that I didn't understand."

Sunnybrook is also a leader in poststroke psychiatric symptoms. When Tiffany later became angry, agitated and delirious, the psychiatry team was called in to consult.

Tiffany stayed at Sunnybrook for two months and

steadily improved in every way, relearning to walk and talk. Another two months in a rehabilitation centre, and she was ready to go home.

Now, just over a year later, Tiffany is back at work and actively participating in both running and cycling fundraisers. "Someone who doesn't know me would never know I had a stroke," she says. She is very keen to try again to have a baby, and will be cared for in Sunnybrook's High-Risk Stroke and High-Risk Pregnancy clinics.

Her remarkable recovery is a testament to both the resilience of the human brain and Sunnybrook staff's expertise and teamwork across disciplines. "They were pretty awesome," says Tiffany. "They took good care of me."

Helping people recover their brain health is one of Sunnybrook's most urgent priorities. The reason is obvious: It's difficult to find a family, community or workplace completely untouched by either a disorder of the brain, such as stroke, dementia and trauma, or a disorder of the mind, such as depression, anxiety and addiction.

Within seven years, brain diseases will become the leading cause of death and disability in Canada. "We are dealing with the most compelling and devastating illnesses that are going to face us in the next 50 years," says Dr. Sandra Black, Sunnybrook's director of the Brain Sciences Research Program. The program is guided by the principle that only through cross-disciplinary collaboration will scientists find the necessary answers to guide them – psychiatrists working with neurologists working with neurosurgeons working with neuropharmacologists, family doctors and neuroimaging experts, as well as nursing and allied health teams.

To fortify these connections permanently, Sunnybrook is creating a new, state-of-the-art Brain Sciences Centre to house these experts under one roof. The new space will send a message to patients, whether in the youth psychiatry division – the largest in Ontario – or cognitive neurology or stroke recovery: "We care about you." A lead gift has made this dream possible and, with efforts under way to raise awareness, additional private donations will make it real.

Working collaboratively across disciplines has a tangible impact on patients in two important ways. One is that embracing



psychiatry inside brain sciences gives it the same status as any illness, reversing centuries of ill-treatment when "mental" patients were ostracized and isolated. "Fighting stigma is part of the reason mental illnesses are aligned with brain sciences. They are all brain sciences," says Dr. Black.

The other reason: Each disorder of the mind, brain and body teaches researchers and clinicians something about the others. Sunnybrook has unearthed some surprising new discoveries that wouldn't have been possible if psychiatry were still in its own silo. For instance, a significant number of stroke patients like Tiffany develop psychiatric illness after their stroke because of brain changes.

"How is mood affected by stroke? How is cognition affected by heart disease? How can dementia cause depression? Our whole team thinks along that line. You ask those questions because you are thinking of the brain," says Dr. Black.

**"How is mood affected by stroke? How is cognition affected by heart disease? How can dementia cause depression? Our whole team thinks along that line. You ask those questions because you are thinking of the brain."**

Dr. Sandra Black

## WHEN THE MIND HURTS THE BODY

Another fascinating example of the brain, mind and body interface is a psychiatric illness called conversion disorder. Sunnybrook psychiatrist Dr. Anthony Feinstein is a world-leading expert in this field.

“The mind can turn off the body,” he says of the condition, in which psychological stress is revealed in physical ways. One of his most dramatic cases was a young man who came to Sunnybrook in a wheelchair. The man had lost all sensation in his legs and one of his arms. While symptoms certainly mimicked a stroke, Dr. Feinstein suspected conversion disorder. With the man's permission, Dr. Feinstein gave him a strong sedative to suppress anxiety and allow him to talk freely about things that had been repressed. The man explained that he had been sexually abused and never told anyone. Why would this cause numbness?

Dr. Feinstein, alongside colleagues from the University of Waterloo and the University of Toronto, recently completed a study to find out. They first needed to develop an instrument that would stimulate a paralyzed limb while the patient was inside a functional MRI machine.

They studied 10 subjects with conversion disorder, one of the largest samples reported to date. They applied stimulation to the paralyzed limb, and brain imaging showed an overactivation in the brain's limbic system, which controls emotion, behaviour, motivation and memory. At the same time, they observed suppression of the brain's sensory system. Sure enough, psychological pain shuts

down body functions. “Conversion disorder is the most florid manifestation of this interplay between emotion and physical symptoms. What you feel influences physical functioning. Freud would be vindicated if he saw this result,” says Dr. Feinstein. Their study was presented at the recent American Academy of Neurology annual meeting in Philadelphia.

The patient's treatment included talk therapy and medication. He is walking now, and able to catch a ball with the arm that was previously paralyzed. (We have changed some details to protect anonymity.) “The diagnosis, treatment and recovery of conversion disorder highlights why Sunnybrook's collaborative methods are beneficial,” says Dr. Feinstein. “To make this discovery, we needed imaging expertise, plus psychiatry, plus neurology, working together.”

## NEW FRONTIERS IN BRAIN SCIENCE

Two colleagues of Dr. Feinstein's are also exploring interesting frontiers at the interface between brain, mind and body. Psychiatrist Dr. Nathan Herrmann and neuropsychopharmacologist Dr. Krista Lanctôt are using sophisticated brain

imaging to find out whether lithium, a common psychiatric medication, can successfully help regenerate and grow brain areas after a stroke. The study is funded by the Heart & Stroke Foundation. If lithium is successful in increasing grey matter, it will be an example of a mind medication being used in a brain disorder. “Having medications that support brain recovery after a stroke is a major unmet need right now,” says Dr. Lanctôt.

Another study by Drs. Herrmann and Lanctôt will test why people with coronary artery disease (CAD) have a stronger risk of depression and cognitive decline. They believe one of the reasons is that certain byproducts of fat breakdown involved in the development of CAD, called ceramides, can harm brain cells. Ceramides are overproduced in response to inflammation, a key feature of CAD.

They are recruiting 129 CAD patients from a cardiac rehabilitation facility to test this theory. Results from this study, which is funded by the Canadian Institutes of Health Research, may be helpful in developing new treatments to prevent memory decline in patients with CAD.

“We believe there is definitely a relationship between the mind and the body. By finding out the links between disease states and what's going on in the brain, we hope to find new treatments,” says Dr. Herrmann.

Sunnybrook is answering the urgent call to learn more about this amazing three-pound organ, the brain. While not all patients do as well as Tiffany did, Sunnybrook's dedication to collaborative care and research across physical and psychological disciplines sets the stage for recoveries such as hers. “It is truly incredible that she survived and has been able to rehabilitate and recover so well – physically, cognitively and emotionally,” says Dr. Gladstone. “This is the type of excellent recovery that we wish all our patients with stroke and brain injury can achieve.”



Dr. Anthony Feinstein

## STUDYING RISK RESEARCH AIMS TO PUT AN EARLY BRAKE ON ALZHEIMER'S

By Jane Doucet

Groundbreaking new research into Alzheimer's disease is offering volunteers between the ages of 65 and 85 who have no apparent symptoms of the disease, but are at risk of developing it due to their family history or other factors, an opportunity for anti-amyloid treatment.

Four clinical study research sites in Canada are taking part in the National Institutes of Health-funded international A4 study (A4 stands for Anti-Amyloid Treatment in Asymptomatic Alzheimer's), including Sunnybrook, which aims to recruit 20 participants for the study.

“This is a revolutionary study because we're taking a step toward maybe being able to do something to identify and treat Alzheimer's very early, before the symptoms are apparent,” says Dr. Sandra Black, the study's principal investigator at Sunnybrook.

According to the Alzheimer Society Canada, an estimated 750,000 Canadians currently have Alzheimer's disease or a related dementia. The number of Canadians with Alzheimer's or dementia will more than double to 1.5 million within a generation. So there's an urgent need to learn as much as possible about this debilitating disease.

Today's medications only temporarily ease some symptoms, and scientists don't know exactly what causes Alzheimer's disease. The disease appears to develop when the combined effects of various risk factors and brain changes cross a certain threshold, overwhelm the brain's natural self-repair mechanisms and reduce its ability to maintain healthy nerve cells. Advancing age is one of the most significant risk factors (the average age of



Dr. Sandra Black

patients is 75); other risk factors include genetics, diabetes, head injury, clinical depression, stroke, high cholesterol, high blood pressure, obesity and sedentary lifestyle.

A4 study participants in Canada, the United States and Australia will have an amyloid PET brain scan, which could indicate a higher risk if positive. Then the “pioneer volunteers,” as Dr. Black refers to them, will be randomized to receive infusions every month for three years; they won't know until the study ends whether they received an experimental anti-amyloid antibody, called solanezumab, or a placebo.

Solanezumab is designed to help remove the toxic amyloid beta protein, which drives Alzheimer's, before it causes too much damage. “It's not a good thing to have amyloid uptake in the brain,” says Dr. Black. While the medication failed in previous studies to treat full-blown Alzheimer's, it appeared to help slow cognitive decline in the subset of patients at a milder stage of the disease.

“Alzheimer's may develop under the radar for decades,” says Dr. Black. “With the proper identification and treatment, we may be able to remove the toxic amyloid and delay mental decline.”

PHOTOGRAPH BY DOUG NICHOLSON

# *Exercise: fertilizer for the brain*



New research from Sunnybrook reveals physical activity's power to improve symptoms of bipolar disorder and OCD

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By Celia Milne  
Photography by Tim Fraser

Fay Ganz

**F**ay Ganz is 56 and has bipolar disorder. She feels fine today, happily balancing volunteer work in mental health care, renovations to her Toronto home and daily power walks with friends, but it has been a long and rocky road to wellness.

For the first 20 years of her illness, Fay weathered severe manic episodes followed by bouts of deep depression. Throughout her 20s and 30s, she says, the ups and downs of her illness “felt like riding a roller coaster at the Exhibition.” She accomplished a lot in that time – marrying the love of her life, Howard, finishing university, having three kids and becoming a nurse – but the unpredictable nature of her disorder exacted a terrible toll.

She endured a taxing journey, moving from doctor to doctor, from drug to drug, in and out of hospital, all the while without a clear diagnosis, baffling and scaring family and friends.

Manic behaviour in the early days meant going into hyperdrive: trying to be the best at everything. “Something snapped, and I had to prove myself. I didn’t sleep. Sleeping was weakness. I was going to be the best daughter, the best employee, the best friend, the best girlfriend. The more I experienced the ability to be the best, the more I pushed for more. Until I started becoming psychotic,” she says.

Later in her illness, Fay’s mania often led her away from her husband and children. Sometimes she saw things that weren’t there, resulting in erratic behaviour. “I would fall off the rails and my husband would have to go and get me,” she says. In between the times when Fay felt high, depressive episodes robbed her of joy. “I kept going because of the kids, but I had no quality of life.”

In 1999, Howard implored Fay to get the help she needed. She came to Sunnybrook and became a patient of Dr. Ari Zaretsky, chief of psychiatry, who is also vice-president of education. They developed a treatment plan that would ultimately stabilize her mood. The therapy had several pillars: a medication regime designed specifically for Fay, a commitment by both doctor and patient to cognitive behavioural therapy, regular mindfulness meditation by Fay and a fourth, quite surprising, component: exercise.

“I work with a trainer and I also power walk with

friends first thing in the morning,” says Fay. “It makes a big difference. It gives you a sense of accomplishment. You get out of the house and see things. You say hi to people; you get endorphins. I really feel good.”

Psychiatrists in Sunnybrook’s Brain Sciences Research Program treat mood and anxiety disorders from adolescence to old

age. Exercise, which is part of the new trend toward self-management, is an increasingly recognized treatment tool in illnesses such as depression, bipolar disorder and obsessive-compulsive disorder (OCD). “There is burgeoning literature on how it works and the deliberate use of exercise,” says Dr. Zaretsky.

Research reveals that exercise increases

production of a protein called brain-derived neurotrophic factor (BDNF), which encourages the growth of new neurons. BDNF increases brain plasticity and the resilience of brain cells to stress. Dr. Zaretsky calls it brain fertilizer.

“Exercise is now viewed in those with severe mental illness not just as recreation, but also as brain rehab. That’s relatively new,” he says.

Aerobic exercise and its effect on adolescents with bipolar disorder are being studied by Dr. Benjamin Goldstein, director of Sunnybrook’s Centre for Youth Bipolar Disorder, together with his colleague Dr. Brad MacIntosh in the Brain Sciences Research Program. In the study, adolescents with bipolar disorder completed a concentration task in a magnetic resonance imaging (MRI) scanner before and after 20 minutes of stationary cycling. Brain scans revealed they were able to complete the task with less brain effort after exercising. Importantly, obesity and blood vessel functioning impacted the effects of exercise, suggesting brain-body connections that can inform personalized treatment approaches. “In real life, if adolescents are able to better focus and maintain their attention, then exercise will have major benefits to their quality of life,” says Dr. Goldstein.

New research at Sunnybrook has also found that exercise is helpful as an add-on therapy in OCD. The World Health Organization lists OCD among the top 10 causes of medical morbidity worldwide. It affects 2.5 per cent of the population and can often be chronic and lifelong. Known treatments, such as medication and cognitive behavioural therapy, tend to only reduce symptoms by 25 per cent and 50 per cent, respectively. “So if someone is hand washing four hours a day and improves by 25 per cent, that person is still hand washing three hours a day,” says Dr. Peggy Richter, director of Sunnybrook’s Frederick W. Thompson Anxiety Disorders Centre. “Quality of life is not substantially restored.”

Dr. Richter and colleagues at the centre did a pilot study of exercise to see if OCD patients benefited. “It looks extremely promising,” she says. Exercise led to a decrease in obsessions, such as incessant worries about germs or bad things happening, and compulsions, such as checking and cleaning. Sunnybrook is now leading a multisite, national trial testing exercise in 400 to 500 patients with OCD.

“I think it’s extraordinarily exciting,” says Dr. Richter. “Here’s something we should be doing anyway. If you exercise, not only do you increase your cardiovascular health and feel better and lower your risk for type 2 diabetes, on top of that you may improve your mood, and we believe improve symptoms of OCD, too. And this treatment is completely safe and free of side-effects. How do you beat that?”

**“Exercise is now viewed in those with severe mental illness not just as recreation, but also as brain rehab. That’s relatively new.”**

Dr. Ari Zaretsky



Fay Ganz: “You say hi to people; you get endorphins. I really feel good.”

# Bubbles in the brain

Sunnybrook physicians are about to test a pioneering technique to get anti-cancer drugs through the blood-brain barrier **By Augusta Dwyer**

A significant obstacle to delivering chemotherapy to the brain is about to be breached at Sunnybrook. In what he called “one of the most exciting studies that we’ve done,” Dr. Todd Mainprize is going to be using something almost deceptively simple: microscopic bubbles of air, with the aid of ultrasound, to temporarily break through the body’s most effective protection system, the blood-brain barrier.

“In the brain, unlike most of the body, the lining of those very small blood vessels are sealed,” explains Dr. Mainprize, a neurosurgeon and the acting head of neurosurgery. Its purpose is to keep out toxins, “so very few chemicals can get into the brain,” he says, “that the brain doesn’t want, including drugs.”

Microbubbles have been around for a long time, originally designed to enhance the images doctors can see when doing conventional ultrasound scanning. These bubbles, usually three to five micrometers in diameter, increase the contrast between the blood and tissue, allowing for clearer pictures of what is going on deep inside the body.

When made up of useful chemicals instead of air, microbubbles have also become a potent new form of drug delivery, bursting apart inside organs when hit with ultrasound waves and releasing their contents, where needed.

What Dr. Mainprize is doing, however, is using the microbubble’s capacity for oscillation to tear apart the protein seals, or tight junctions, that attach the blood vessels of the capillaries together and allow chemotherapy drugs a way into the surrounding tissue.

Where that will prove extremely useful, he says, is in those regions right around a brain tumour, an approximately two-centimetre rim within which cancer cells are sparser – about one for every 10 brain cells, or less – yet still dangerous. While the tumour itself can be removed, “what we can’t get at,” says Dr. Mainprize, “are these cells, the ones where about 10 per cent are cancer cells. The blood-brain barrier is still intact, which means it’s a challenge to target chemotherapy there.”

As a result, the tumour can come back, and more often it does so within that immediate rim. “If we could treat that two-centimetre core more effectively,” he speculates, “we could, in theory, significantly improve survival from the current 14-month average. Because it would likely come back, now it would come back at a further distance, where the cancer cell ratio is more like one in 100. It would take longer for the tumour to grow back, for example. That’s our hope.”

Six patients will be recruited for a Phase One,

proof-of-principle and safety trial. Each one of them will put on a helmet containing cool water and about a thousand ultrasound transducers and then lie within a regular magnetic resonance imaging (MRI) machine. Microbubbles will be injected through a vein in the patient’s wrist and begin their journey throughout the body. Once the microbubbles reach the targeted area in the brain they will receive low-frequency ultrasound pulses through the skull, causing them to oscillate in size, opening those protein connections and disrupting the blood-brain barrier. The patient will then receive chemotherapy which can now penetrate the tumour-affected brain through the opened blood-brain barrier. The patient will then undergo surgery.

Studies have shown that immediately after the application of ultrasound to the microbubbles, those tight junctions disappear. They begin forming again after about six hours, and in 24 hours, they are all back. “The body just grows them back,” says Dr. Mainprize.

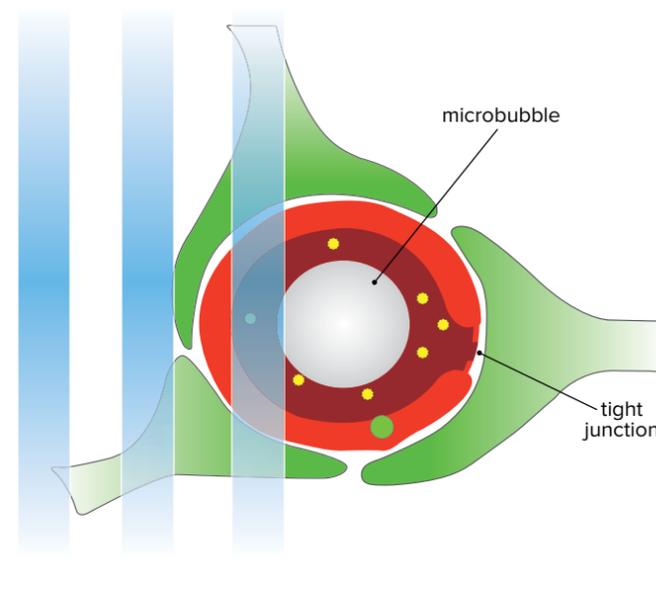
The technique was originally discovered by Dr. Kullervo Hynynen, director of physical sciences at Sunnybrook. He not only discovered that it was possi-



Dr. Todd Mainprize

ble to get ultrasound through bone, something previously thought impossible, but also that it could force microbubbles to disrupt the blood-brain barrier.

The microbubble method is one Dr. Mainprize hopes might improve on previous attempts to enhance chemotherapy delivery to brain cancer patients. These have included the laying of drug-soaked wafers onto the cavity left by surgical removal



Low-frequency ultrasound pulses (represented by blue bars) disrupt the microbubbles, causing them to oscillate in size and open the tight junctions of select areas of the blood-brain barrier. This allows targeted delivery of drug treatment.

of the tumour. The wafers slowly dissolve and permeate the brain, but, according to Dr. Mainprize, “have not been that effective.”

Convection-enhanced delivery, meanwhile, is designed to “circumvent the circulation altogether,” he says, “putting a kind of ‘catheter’ into the brain and just slowly and carefully pushing fluid into the brain tissue area.”

Another method, osmotic disruption, involves a sugar alcohol called mannitol. It achieves the opposite effect of a microbubble, temporarily shrinking the cells and simultaneously stretching open the tight junctions. But like intra-arterial chemotherapy that lets high doses of drugs into brain arteries through tiny “catheters”, it is not very selective, disrupting the entire blood-brain barrier.

“What we can do, with microbubbles and ultrasound,” says Dr. Mainprize, “is open up the blood-brain barrier by a millimetre in a particular area, or we can open up much wider areas. We can pick where we want to do it.”

There have been enormous advances over the past decade in figuring out the pathology of glioblastoma, the most common and aggressive form of malignant brain tumour, such as “which pathways are disrupted, how they are disrupted and how that affects the growth of the cell,” says Dr. Mainprize. “And we now have a variety of molecular inhibitors and potential therapeutic targets, but they haven’t translated into a very good clinical response. Part of that may be that we just can’t deliver them to the area where we want to deliver them.”

“If we could open up the blood-brain barrier and deliver chemotherapy at the same time patients are getting an MRI scan, which people with brain cancer get every two or three months, we may impact survival for these patients.”

## THE NEXT FRONTIERS

According to Dr. Mainprize, once his Phase One clinical trials have shown that blood-brain barrier disruption with microbubbles is safe and effective, “the amount of potential applications to be examined is endless.” Here are a few examples:

**ALZHEIMER’S:** The accumulation of peptide plaques and tangles of tau protein that characterize the brains of people with this disease are what interfere with their

brain functions. Newly identified antibody and modified-antibody treatments have shown positive results in preventing and even clearing away the buildup. “They have these antibodies that seem to work well preclinically,” says Dr. Mainprize, “but they are large in size and are not able to penetrate the blood-brain barrier effectively.” Opening the barrier to permit the entrance of antibodies, therefore, could help alleviate many of the symptoms of the disease.

**DEPRESSION:** With some psychiatric patients, their condition has

proven to be resistant to medical treatment, which is known as medication refractory depression. “We know from previous studies,” says Dr. Mainprize, “that there are certain areas of the brain that seem to be less responsive in something that is called cingulate gyrus area 25,” a region that, studies show, is overactive in depression. “Maybe, if we open the blood-brain barrier and get antidepressants in, the patient may start to respond.”

**BREAST CANCER:** Sometimes breast cancer cells can break away and travel through the

patient’s lymph or blood system into the brain. They are different from the cancer cells of a brain tumour, but just as hard to get at because of the blood-brain barrier. While there are lots of “excellent breast cancer chemotherapy drugs out there,” says Dr. Mainprize, “there is suboptimal penetration. If we could open up the blood-brain barrier we could deliver those drugs to tumour cells, and perhaps avoid surgery on a patient with breast cancer that has spread to the brain. That,” he adds, “would be perfect for a second study.”

# Unmasked: a silent cause of strokes

By Jane Doucet

**B**edros Kashkarian is happy to be alive, and he credits Sunnybrook neurologist Dr. David Gladstone and his potentially life-saving stroke research for keeping him that way.

One Saturday in February, Bedros was serving a customer at his retail store in North York, Ont., when he suddenly had trouble speaking coherently. While the episode only lasted about a minute and nothing like it had ever happened before, it concerned the 67-year-old enough to see his family doctor that Monday, who referred him to Sunnybrook. Dr. Gladstone saw Bedros the following day at Sunnybrook's recently expanded Rapid TIA Clinic within the hospital's Regional Stroke Centre.

The clinic, specializing in stroke prevention, gets patients fast-track access to state-of-the-art diagnostic tests of the brain, heart and the blood vessels. Bedros was diagnosed with a "transient ischemic attack" (TIA) or mini-stroke, which is often a forerunner of a larger stroke. But all his tests came back normal. Dr. Gladstone, who has been researching such strokes of unknown cause for years, is principal investigator of the world's largest randomized clinical trial of advanced heart monitoring in stroke patients. The \$1.7-million Canadian Stroke Network-funded EMBRACE trial recently completed. The findings revealed that one in six people with an unexplained stroke TIA has silent atrial fibrillation, a potentially dangerous irregular heart rhythm that can lead to more strokes if left untreated. The findings of the major 16-centre Canadian study were published in the prestigious *New England Journal of Medicine* in June.

One of the big challenges in stroke medicine is that one in every four strokes is "cryptogenic," meaning its cause can't be pinpointed. The EMBRACE trial studied 572 patients aged 55 and older who had experienced a recent stroke or mini-stroke of unknown origin and in whom standard heart monitoring had failed to detect atrial fibrillation. Participants were randomized into two groups: The



"This is practice-changing research," says Dr. David Gladstone (right), with patient Bedros Kashkarian.

first received an additional 24 hours of standard monitoring, and the second received a new strategy of continuous monitoring for 30 days at home using a high-tech chest electrode belt that automatically detects episodes of atrial fibrillation.

In the trial, the prolonged heart monitoring strategy picked up a new diagnosis of atrial fibrillation in 16 per cent of patients, compared to a mere 3 per cent of those who only received standard monitoring. The enhanced detection of atrial fibrillation led to significantly more patients being prescribed stronger anti-clotting medications to better prevent recurrent strokes. The trial, led by Sunnybrook and co-ordinated at the Li Ka Shing Knowledge Institute of St. Michael's Hospital, is an example of successful research collaboration across the University of Toronto.

Prevention of strokes due to atrial fibrillation is a "global public health issue," according to the study. Atrial fibrillation is a risk factor for stroke because it can promote the formation of blood clots in the heart that can travel to the brain. It's important to detect because it can be effectively treated with certain anti-clotting medications, which drastically reduce the risk of more strokes.

With the EMBRACE trial findings in hand, Dr. Gladstone sent Bedros home with one of the new high-tech heart monitors, which he wore 24-7 for two weeks and revealed that he had a 12-hour-long episode of atrial fibrillation. Based on this result, Dr. Gladstone was able to prescribe stronger anti-

clotting medication that he'll take daily for the rest of his life to prevent further strokes.

"This is practice-changing research," says Dr. Gladstone. Based on the results of the trial, we've literally changed our Sunnybrook stroke clinic protocols overnight to provide enhanced patient care." "These research findings represent a major clue in solving the mystery of cryptogenic strokes. We have found a highly effective strategy for improving the detection of atrial fibrillation in stroke patients that we hope will translate into many more recurrent strokes prevented."

Next steps will include testing the value of the new high-tech heart monitoring for atrial-fibrillation screening in the healthy general elderly population aiming to prevent strokes from happening in the first place. Dr. Gladstone is launching the new study called SCREEN-AF this fall, which will be conducted as part of the Canadian Institutes of Health Research-funded Canadian Stroke Prevention Intervention Network in partnership with the Population Health Research Institute at McMaster University in Hamilton.

Sunnybrook's stroke specialists are leading the way in stroke research that has immediate applications for improving patient care globally. Based on his recent experience, Bedros has become one of Dr. Gladstone's biggest advocates. "Today I feel great," he says. "I'm here because of the important work Dr. Gladstone's team is doing and because he didn't give up trying to find out what caused my stroke." 

PHOTOGRAPH BY DOUG NICHOLSON

A MitraClip heart procedure at Sunnybrook changed my outcome and healed my future.

Steve Segal



The MitraClip procedure uses small incisions and guide wires, repairing previously unreparable heart valves, giving people like Steve a new life.

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Change the outcome.  
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Patient Matthew Carvalho receives an adjustment from Winfried Heim, manager of prosthetics and pedorthics.

## Constructing hope

The team at SCIL who create an array of prostheses aim to give patients new life after the trauma of physical loss

BY ALLISON DUNFIELD

Matthew Carvalho sits in an examining room in the Sunnybrook Centre for Independent Living (SCIL) and takes off both his legs. He's here at the centre, tucked away in a sunny, treed corner of Sunnybrook's campus, for a fitting for a new socket for his left leg.

Matthew, who was born without three of his limbs (he has his own left arm), has used a variety of prostheses over the years and has had countless fittings for new parts. "I feel like the alignment is definitely off on this one," he says to Winfried Heim, manager of prosthetics and pedorthics, after one of the legs has been adjusted. "Okay, let's take it off again,"

says Heim, jokingly adding, "Tell me if I'm tickling you."

"This is the life of an amputee," says Matthew, of Mississauga, Ont. "Trial and error."

But he says the last two years, during which time he's been a Sunnybrook patient, have been the best. The experts at SCIL have allowed him to be a collaborative partner in his ongoing prosthetic treatment, experimenting with different materials and lighter prostheses. It could also be his close relationship with Heim, whose easygoing and gentle manner with his patients, along with his willingness to try new things, is one of the reasons

patients here thrive. "It's all Winfried – everything has changed. My legs are a lot more comfortable ... my way of life has been a lot better for sure," says Matthew.

Heim and the 25-member team of prosthetists, technicians and other experts at SCIL helped more than 7,000 patients last year through the prostheses, pedorthics, podiatry and rehabilitation programs.

The group is known for assisting people, including complex trauma patients, regain their independence and mobility by fitting them with customized prostheses and providing them with individualized rehab and treatment.

SCIL serves individuals who lose limbs in a variety of ways, from diabetes and cancer to congenital disorders and trauma. Heim says that one of the most important things the team at SCIL must do when meeting each new patient is to appreciate that amputees are "terrified" when they first arrive, and that the team's role is as much psychological as medical. "It is a big trauma. People really do not want to lose a body part. It becomes part

of our duties to help them overcome that – to make them believe there is life after that."

Prostheses are made in the on-site lab by a team of technicians and prosthetists. "Creating a custom prosthesis is a marriage of art and science", says Iona MacRitchie, Managing Director of SCIL and the Working Condition Program. "There is the artistic part of trying to achieve the right fit and look; and then there is the science of it in properly distributing the weight and forces, calculating correct alignment and helping make the prosthesis a functional part of the person."

The first step to create a new limb is to make a socket, which is the part that the stump, or residuum, sits inside and attaches to the artificial body part. The prosthetist takes detailed measurements of the residuum and then creates a cast of it – similar to that for a broken limb. When that cast dries, plaster is poured into it to make a form of the limb. The form is then carefully smoothed down and filed until it becomes an exact replica of the residuum.

Prosthetist Jody Riggs, who presides over an area filled with plaster forms of all sorts of stumps and looks more like an artists' workshop than something you'd find in a hospital, says it takes a lot of experience to make a proper socket that minimizes discomfort for the patient while being worn. If it's even a little off, it could cause sores and injury. "A lot of it is by the feel."

To get the amputee started, typically a "test" piece or "clear check socket" is made using the plaster form, usually out of a see-through plastic. This allows the prosthetist to attach the leg or arm and check the fit

before the definitive socket is made. The reason is that patients' stumps often change shape and size as fluids and swelling go down following amputations, says Riggs. Once satisfied with the clear socket, technicians use the form to make the permanent, laminated socket by pulling a PVA (water-soluble plastic) sheet and layers of sockinets and carbon tape or fibre over the form and then topping it with liquid resin that hardens into a shell. After it hardens, the completed socket can then be attached to another plastic shell containing the mechanics of the leg.

Technician Paul Russell says the job has "a bit of an artistic feel and flow," as some need their sockets to be very strong and others want them to be light. "You're trying to walk the line between something that's strong enough and something that is not too heavy."

Leg and arm parts can be merely cosmetic (made at SCIL), myoelectric or robotic. Some of the more complex limbs are made off-site. But the most important part is the custom socket, Heim emphasizes. "It is the fitting on the person that is the most important part. If you cannot wear it, you cannot use it."

It's also why patients often develop a strong, lifelong bond with their prosthetist. The more the experts get to know the amputees, the better they are able to create sockets that work for their lifestyle. Getting the artificial limb for the first time can be a life-changing experience for amputees.

Judith Reid, a 57-year-old diabetic from Toronto, had her below-the-knee amputation in September 2013 after complications from gangrene. Like many patients who come through SCIL, after her wounds healed she was

Right: A prosthetic device for an above-elbow amputation. Below: Matthew's prosthetic legs include carbon frame sockets and hydraulic controlled multi-axial knee joints.



sent to Sunnybrook's St. John's Rehab to learn how to use her prosthesis. After some preprosthetic training to strengthen her body and to learn how to

balance, Judith was given her new leg and was shocked that "it felt quite natural" and she was able to take some steps immediately. She attributes her success to the staff, who "struck the right balance between giving me encouragement and telling me [that based on] what I did yesterday, maybe I could do a little more tomorrow."

Rehab is done very methodically, says physiotherapist Betty Cheung, to ensure the patient is successful in being able to use a prosthesis. Patients receive both physio and occupational therapy during an intensive in-patient stay that typically lasts two to four weeks.

What many people don't know is how difficult it is to use prostheses. Cheung says those with above-the-knee amputations can expend 50 per cent more energy walking than able-bodied people. Patients begin walking using parallel bars, then graduate to walkers, crutches and canes. The best moments come when they meet their goal of being able to go home.

Another patient, Kevin Godsell, had an above-the-knee amputation in January after he cut himself and it led to an infection in his foot, which moved up his leg. The 35-year-old from Scarborough, Ont., says even though when he first put on his prosthesis he found it "horrendous, bulky and unnatural," he kept at it with the encouragement of staff. Within a week he was walking and encouraging other patients with his progress. And he's looking forward to his new goal – to run five kilometres with Cheung next year.

He has nothing but praise for the Sunnybrook staff in helping him get his life back. "The experience was amazing – it blew me away. I didn't think I would be able to walk ... It was like they had goals for me that I couldn't even see," he says. "They are really good at what they do." ❧



PHOTOGRAPHY BY DALE RODDICK



Surgeon Dr. Albert Yee

metastases, which is being led by Sunnybrook's Dr. Albert Yee, a spine surgeon and associate scientist at Sunnybrook Research Institute.

Fred learned in late 2013 that his PSA count was again out of control, suggesting that his prostate cancer was on the move. He had been on medication to control his PSA levels ever since being treated with radiation for the cancer in 2003.

Fred's prostate cancer had spread to his spine, a common target for prostate metastases. As Fred notes, the cancer was eating away a portion of his lower spine – the left side of his L4 vertebra, to be precise. Fred's medical oncologist at Sunnybrook, Dr. Scott Berry, mentioned Dr. Yee's experimental trial, which pairs PDT with a minimally invasive surgical procedure for stabilizing spinal structures.

Here's how it works: After a photosensitizing drug is given to the patient intravenously, Dr. Yee accesses the trouble spot in the spine through a small incision. He inserts a tiny laser, shining light of a specific wavelength matched to the drug at the spinal tumour for five to 15 minutes, depending on the dosage required.

The photosensitizers in the tumour absorb the light and produce a form of oxygen that destroys nearby cancer cells. Dr. Yee then goes about repairing the tumour-damaged spinal bone by injecting orthopaedic cement to enhance bone stability.

Fred says he wasn't apprehensive about taking part in the trailblazing trial, adding that the aim of the combination treatment made great sense from a layman's perspective: Do everything possible to kill the tumour before shoring up the spine.

Dr. Yee emphasizes that incorporating PDT into the treatment of spinal metastases won't eliminate the need for a multipronged approach. Radiation, chemotherapy and pain medication will all continue to have roles in enabling patients to have the highest possible quality of life. Fred, for instance, received spinal radiation weeks before the procedure.

Tumours that invade and fracture the spine can cause great pain and can ultimately lead to paralysis. "Some patients can't even walk because their back pain is so bad," says Dr. Yee, noting that stabili-



Fred Simons was one of the first patients in the groundbreaking trial.

zation can immediately and dramatically curb the pain. Fred was fortunate not to be experiencing such pain, though he did find that he could move his legs much more freely and with less discomfort after his surgery.

#### SURFACE MATTERS

The use of PDT for skin cancer isn't as novel as it is for spinal metastases, but it remains a niche treatment in Ontario. Sunnybrook became just the second hospital in Ontario – and currently the only one in Toronto – to offer skin cancer PDT when it launched the service in May.

The program at Sunnybrook's Odette Cancer Centre – currently treating a limited number of patients – is using PDT for skin conditions that can turn into cancer, such as actinic keratosis, and for some skin cancers themselves, including Bowen's disease and superficial basal cell carcinoma.

The treatment uses a photosensitizing cream that is spread directly onto the lesion. Within about three hours, the skin is sensitized and ready to be targeted by red light. The light is applied for about seven minutes, and the whole process is then repeated during a second session one week later.

Toronto resident and marketing professional Jill Carey, 60, was the first to receive skin PDT at Sunnybrook. The actinic keratosis – often called sunspots – that covered Jill's cheeks and forehead was the target of the therapy. A redhead with fair skin, Jill laments the casual approach she and many of her generation had about sun protection when she was young. "When we were growing up, they didn't have sunscreen. Everybody used oil," she says. "I spent entire summers at pools."

In the past, Jill has had skin lesions treated with other methods, including surgery and cryotherapy, which uses an extremely cold substance to freeze the lesion. PDT has been shown to be as effective, while providing a superior cosmetic result, she says.

"It's a targeted therapy. It doesn't harm surrounding, healthy tissue because the photosensitizer selectively accumulates in precancerous and cancerous cells," says Steve Babic, PhD, a medical physicist at the Odette Cancer Centre. Dr. Babic is part of the multidisciplinary team that brought the skin PDT service into being. Emily Sinclair, an advanced practice radiation therapist, Dr. Toni Barnes, a radiation oncologist and head of the skin cancer care team, and others are important members of the group.

"The entire staff was great, and the whole experience was very positive," Jill says.

Fred also speaks highly of the care he received from Dr. Yee and his team. "One of the most impressive things about this whole procedure was the degree of co-operation taking place between the various disciplines. It really was quite remarkable," he says, adding that "everyone was enormously supportive and helpful."

So what does the future hold for PDT at Sunnybrook? "My colleagues and I have our eyes set on larger clinical trials that could one day pave the way for PDT-stabilization to be offered across the country," Dr. Yee says.

Meanwhile, Sinclair and the skin team want to continue to grow their program. "Now that we've established this service, we hope to optimize it through our research and be able to treat more patients," she says. ☘

## LIGHT BENEFITS

A relatively new procedure in Canada that was approved for use in the 1990s, photodynamic therapy (PDT) is probably best known for its treatment of skin conditions, including skin cancer. Researchers around the globe are studying its possible application to a wide range of cancers, from bladder to brain to prostate.

For appropriate patients, the therapy has several benefits, such as:

- No long-term side-effects and excellent cosmetic results
- Can treat large areas of skin with multiple lesions
- Can be repeated many times at the same site, if necessary, and does not preclude other interventions, such as surgery or radiation

But PDT also has its limits. Because it can only work on sites accessible to light, PDT is primarily used to treat conditions on or just under the skin or on the lining of internal organs or cavities. As well, patients must take precautions during and after treatment because the photosensitizing agent will make them sensitive to light for a defined period.

– Dan Birch

## The right wavelength

Sunnybrook has become the first hospital in the world to harness the power of light to treat spinal metastases

BY DAN BIRCH

When most people think of light, they don't think of it as a tool to help destroy cancer cells.

In the case of skin cancer, the idea of using light is particularly counterintuitive: Isn't it ultraviolet light that causes skin cancer?

All light, however, is not created equal. While UV light exposure increases risk for skin cancer, certain types of light can work in combination with special drugs and oxygen to kill cancer cells, while leaving normal, healthy cells unscathed.

Sunnybrook is now harnessing the power of light to treat spinal metastases (cancers that have spread to the spine) and skin cancer with a treatment called photodynamic therapy or PDT. Sunnybrook recently became the first in the world to apply PDT to spinal metastases in patients, and the hospital is just one of two in Ontario using PDT for skin cancer.

Fred Simons, an 80-year-old Toronto resident and grandfather of four, is one of 30 patients taking part in the world's first clinical research trial of PDT for spinal



Dr. Markku Nousiainen (left), director of the orthopaedic residency program, with Dr. Sebastian Tomescu.

## Ready, willing – and able

A pioneering program for orthopaedic residents measured by skills, not time

BY ALEXIS DOBRANOWSKI

Would you let a pilot fly a jumbo jet without first checking her technical skills? Probably not.

For that matter, what about allowing an orthopaedic surgeon to perform a knee replacement after he completes just a written exam? Not for much longer.

The Competency Based Curriculum in the Division of Orthopaedics Residency training program at the University of Toronto (U of T) is the only program in Canada that's designed similar to an airline pilot's training. It ensures residents are competent on simulators before treating patients, evaluates them on necessary skills as they go and ensures that they meet all objectives of training at the end of their curriculum. The program was designed five years ago by a team of

Sunnybrook and University of Toronto surgeons and implemented as a pilot with a grant from the Ontario Ministry of Health and Long-Term Care. It's been gaining worldwide attention from medical educators.

"Typical residency training is time-based or 'tea-steeped,'" says Dr. Markku Nousiainen, an orthopaedic surgeon at Sunnybrook and director of the orthopaedic residency program. "If you do five years of training and then pass an exam, you are deemed to be capable of practising independently."

That came as a shock to Dr. Sebastian Tomescu. "In medical school, I was surprised to learn that your exam is just in an oral and written format. No one is checking to ensure that you are a skilled

surgeon. I thought there'd be a technical exam at the end."

When Dr. Tomescu was accepted into U of T's orthopaedic residency program, he learned of a pilot program that would be quite different than traditional training. "It would be competency-based. I could spend as little or as long on rotations and skills as I wanted or needed, then be assessed," he says. "And at the end of it, I would know that I was competent in the necessary skills."

He agreed to be part of the pilot. First up: a surgical skills "boot camp" in the simulation lab.

"The boot camp brings everyone up to speed," Dr. Tomescu says of the month-long course he now instructs. "It teaches all the little things that are important: how to properly put on gloves, gown and mask, and how to correctly scrub in."

Then there are the basic orthopaedic skills: anatomy, how to treat simple fractures, how to cut bone and drill holes. The residents become familiar with the instruments and the proper techniques for using them, all in the comfort of the simulation lab. After boot camp, they

begin their rotations in the hospital. Dr. Nousiainen recalls the first time he was asked to suture on a patient. It didn't go quite as he hoped.

"I had the wrong size of gloves; I didn't even know what size of gloves to use. The blood stopped flowing to my fingers. And I was so afraid of the staff person getting angry at me that I did a terrible job," he says. "You are too worried about the environment you are in. You are trying to impress, so your hands get shaky. If you practise in a low-stress environment first, you can say to yourself, 'Although I'm in a different environment and people are watching, I know I can do this skill.'"

Dr. Tomescu recalls the first time that he was asked to perform in the operating room (OR) after boot camp.

"I felt I was capable of doing a lot more than what the surgeon was asking me to do. The senior resident was asked to put the screws in, and I thought, 'I know how to insert those, too!'" he says. "I actually felt good – I felt like I could already do a lot. I was both comfortable and confident."

Dr. Nousiainen says after boot camp, the first-year residents have the skill level of upper-year trainees.

"When it comes to their first time in the operating room, they are already ready to go," he says. "To learn those skills in the OR wastes time. When it comes time to assist during a real operation on a live patient, they've already mastered those skills and they can work on becoming more efficient and effective."

Another major difference in the competency-based training program is the constant feedback and evaluation – written tests, verbal exams and evaluations in the skills lab and operating room.

"We also have '360 exams,' where multiple health-care professionals are asked to

provide feedback on our performance – the physiotherapists, cast technicians, nurses," Dr. Tomescu says. "There are also assessments of our interactions with the patient and family both before and after their surgery: 'How did you prepare the patient? Did you explain the risks and benefits? Did you answer the patient's questions?'"

The Royal College of Physicians and Surgeons of Canada has mandated that medical education programs become competency-based in the near future, Dr. Nousiainen says. A move to competency-based training is a move in the right direction for patients and the health-care system, he says.

"If we can produce physicians who are competent in all aspects of becoming a good doctor – technically skilled and also adept at managing health-care resources, good communicators and collaborators, I think we will have more efficient physicians joining the workforce," he says. "They won't waste money on tests, they will know the literature, they will know the best practices and they'll be better communicators with the health-care team. So competency-based training programs that incorporate these should lead to better, more well-rounded doctors."

Dr. Tomescu finished the residency program in four years, rather than the usual five. "There was more focused attention on ensuring we were learning and moving along," he says. "And if there was a problem or a challenge, there was remediation right away, and time was allocated to that task, so we could perfect it."

He passed his Royal College exams and is preparing to start a fellowship at Sunnybrook to further his specialty skills.

"I'm ready," he says. ■

## SHARING THE KNOWLEDGE

The Competency-Based Orthopaedic Residency Program at University of Toronto remains the first and only medical residency program in Canada based on trainees demonstrating professional competence on technical and other tasks related to their specialty, rather than on time spent on hospital rotations.

But other residency programs will soon be following suit, including some beginning this fall. Dr. Markku Nousiainen, orthopaedic surgeon and program director for the orthopaedic residency program, hopes to help other educators and program directors design effective competency-based programs. He participates in an international committee focused on competency-based education.

"We are world leaders in this area," he says. "There many other people who have written the original articles about doing it. But nobody has ever done what we've done here in Toronto and put a program in place. We are the only program that has five-plus years of experience."

Dr. Nousiainen and his colleagues have now hosted two workshops in Toronto for educators from around the world who are looking to design competency-based residency programs. He says, "The participants want to know 'How do we take the lessons learned at your centre and make this work in our centre?' We are leading the way."

"Our perspective on sharing our experience is this: Why reinvent the wheel? We are happy to share what we've designed and learned in our experience so that others can adapt it and make it work for their programs."

– Alexis Dobranowski

**14**  
Orthopaedic residents in competency-based pilot program at University of Toronto

**10**  
Toronto hospitals involved

**5**  
Years spent in a regular stream orthopaedic surgery residency training program

**4-5**  
Average years spent in competency-based residency (depending on how soon the trainees and their supervisors think that they are competent to move on)

**21**  
Modules to complete during competency-based residency

**200+**  
Hours spent in simulation lab

## Helping soothe a painful journey

*Sunnybrook ensured a serious burn patient got the right care at every stage – from acute care to rehab and back to the community*

BY KATIE ROOK

Kerry Comiskey recounts the events of September 1, 2013, in an even tone, rationing out detail after detail, of the hours before a cauldron of boiling water spilled over the lower half of his body.

There was a game with neighbouring cottagers, the beloved family dog always nearby, a slow walk up a steep flight of stairs to the corn roast, an unlucky stumble and then panic. His wife, Teresa, recalls catching a glimpse of a half-naked man running into the forest, her mind imagining it was a “wild man,” rather than her husband of 37 years.

They both reach easily for plot points: someone cooling Kerry with water from a garden hose, the 911 call, the improbability of nurse, Pam Gullo, being among the crowd of Labour Day partygoers. Speaking about it nine months later, there are silences that seem weighted by whatever bafflement and gratitude follow from surviving an accident that leaves skin from almost 50 per cent of your body sloughing off.

“I remember the pain was so excruciating,” Kerry says. “I didn’t say much. “My eyes kept going back. I am thinking, ‘I am not going to make it. I didn’t think I was going to go this way.’”

Kerry is one of hundreds of people treated each year at Sunnybrook’s Ross Tilley Burn Centre. Like many others, he arrived by helicopter as soon as doctors in cottage country determined that the critical state of their 61-year-old patient would be better managed at a world-class institution. Though an IV was implanted on Kerry’s hip, pulsing heavy drugs through his system, he was lucid enough for the dining room table-sized slab of stainless steel to make an impression. “That’s where they hose you down,” Kerry explains.

Kerry’s 4 a.m. admittance marked the

beginning of a months-long recovery process that would reshape his understanding of suffering, compassion, team work and gratitude. “What impressed me about the burn unit was how everyone worked as a team,” he says. “It’s a family. When you leave, you feel a loss. I cried.”

Social worker Anne Hayward is among the team of experts who made up Kerry’s care team. Every case is unique and can draw on a range of resources, including burn surgeons, nurses, physiotherapists, occupational therapists, social workers, dietitians, pharmacists, speech language pathologists and psychiatrists. Hayward set about supporting Kerry, according to the needs he made known.

“Kerry’s number one concern was making sure his family was okay,” she says. “Kerry is a normal guy, with a normal family, who had an accident,” says Hayward. “The challenge was to get [him] back to a new-normal life.”

The solution was an approach that championed ongoing communication. Hayward’s support of the Comiskey family was pivotal, Kerry says. “I’ll never forget her. I progressively got stronger through compassion, care and encouragement.”

One of Teresa and Kerry’s three grown children was particularly fearful of seeing her father in pain. Hayward was there for their first visit.

“I wanted her to see: ‘He’s still your dad,’” Hayward says.

Equally important was the care teams’ reference to and confidence in Kerry’s eventual recovery. They spoke about him returning to visit his care team after he was discharged. “When you see someone vulnerable, in their gown, we know that they will be better – they’ll one day be back in their street clothes – but, they don’t know that,” she says.

After about five weeks as an in-patient at Sunnybrook, Kerry was well enough to be discharged, but still required significant support. “I knew I was getting better when there was less blood on the bed,” he says, recalling how he was first able to gauge his progress.

Kerry was moved to St. John’s Rehab, an associate facility of Sunnybrook, where a team of health professionals helped him improve what functionality he was beginning to regain. Staff at St. John’s Rehab help patients relearn skills so basic they are seamless to most people: doing up buttons, bathing, preparing meals. They helped Kerry manage his scars, improve his range of motion and provided psychological support, as necessary. Just as it had been at the Burn Centre, an interdisciplinary approach to patients is taken.

Though she did not work directly with Kerry, occupational therapist

<b>250</b>	the maximum number of patients admitted to Sunnybrook’s Ross Tilley Burn Centre each year
<b>10</b>	beds in the Intensive Care Unit (ICU)
<b>4</b>	additional beds in the acute burn section of the ICU
<b>6</b>	dedicated inpatient burn rehab beds
<b>40</b>	admissions to inpatient burn rehab last fiscal year
<b>7,084</b>	outpatient rehab visits from burn survivors last fiscal year

Kerry Comiskey at home with his wife, Teresa.



The medical teams at Sunnybrook "gave my life back," says Kerry Comiskey.

Shahzia Adatia says the central goals of each custom-designed care team designated to individual patients and their families are consistent. "There are a lot of variables with how someone is going to cope with their injury," Adatia says. "There are a lot of people involved. We have all the science; the patient guides the treatment." All therapies are dedicated to managing scars, maintaining range of motion and strength, and addressing psychological needs, she says.

Early in his recovery, Kerry was so resolute about his comeback that he considered choice irrelevant. "I have a will to live. I have a lot to live for: Teresa, my family, watching my kids grow up and settle, my friends. I wouldn't give up."

Less than a year after the accident, many of Kerry's trips to Sunnybrook are voluntary. During a recent scheduled visit, a dermatologist took a biopsy to test for

a malignancy. While the procedure was by some standards routine, performing a surgical technique on a swath of fragile skin that has been grafted and is healing daunts even an indomitable-spirited outpatient. "It really tests you. It tests your relationships. I live every day now with a greater sense of gratitude," says Kerry. "I am realizing how special it is when you have great relationships."

Between regular checkups, Kerry says he likes to visit with the medical teams that saved his life. "I have a huge sense of being grateful for what they've done for me and my family. I'll never be able to thank them enough: Dr. Marc Jeschke [director, Ross Tilley Burn Centre] and the teams at the burn centre and St. John's Rehab gave me my life back," he says. "Anyone who faces a situation, they're in good hands at Sunnybrook." 🍷

**46**  
average age of burn rehab patients

**75 & 25**  
percentage of male and female burn rehab patients, respectively

**12**  
the minimum number of disciplines that make up patient-care teams. These include: burn surgeons, nurses, physiotherapists, occupational therapists, social workers, dietitians, pharmacists, speech language pathologists, psychiatrists, plus any other physician consultants and support workers from the blood laboratory and blood bank

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**All inclusive from Toronto:** Deluxe veranda suite category H (356 sq ft) at **US\$ 13,687 pp** based on double

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**26 DAY "WONDERS OF THE INDIAN OCEAN & MYANMAR/CAMBODIA" Apr 09 - May 05/15 "Singapore/Dubai"**

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## Under the microscope

When pathologists examine tissue to look for signs of cancer, it's an extraordinary meeting of art and science

BY WENDY GLAUSER

After 29-year-old Shawn Spooner had his first seizure, he was referred for an MRI, which revealed a mass on his brain stem. In March of 2012, Shawn underwent surgery at Sunnybrook to have the tumour removed, a process that took eight hours. "I tried to stay positive, but there's always that part of your mind that thinks the worst," recalls the project

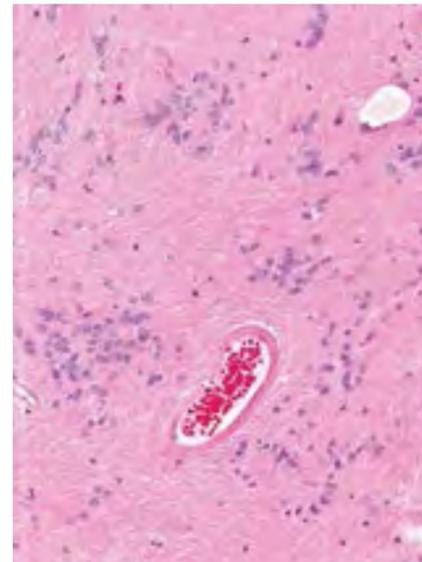
manager in the telecom industry. Doctors discovered there was another, smaller tumour, as well, but its location made it more difficult to remove, and doctors wanted to know more.

That's where Dr. Julia Keith of Sunnybrook's department of Anatomic Pathology, comes in. One of 40 neuropathologists in Canada, she analyzes tissue

samples – like those taken from Shawn's brain – to determine if someone has cancer and what type of cancer it is. There are, after all, hundreds of possibilities. Before she can do this, however, the tissue specimen must be transformed into a tiny piece of "art" affixed between glass.

How does this transformation happen? As soon as a piece of tissue is taken out, it's placed in a plastic container in a protective solution. Next, the label with the patient's information is checked and re-checked and a unique barcode is assigned to each specimen. "Minimizing errors is something that pathology departments take very seriously," explains Dr. Keith. Large samples of the specimen need to be cut by a pathology assistant, and each piece is put in a plastic tray or cassette

Left: Neuropathologist Dr. Julia Keith.  
Below: Photomicrograph of Shawn Spooner's brain tumour – known as a subependymoma – showing relatively low cellularity and a non-malignant appearance.



that's smaller than a matchbox, and is labelled with the patient's barcode.

Once in the trays, various solutions are added to the samples to dehydrate and harden them. Machines that use microwave technology can speed up this process. "We can now get a breast biopsy and in the same day do the processing; whereas, it used to have it sit in solution overnight," explains Dr. Corwyn Rowsell, deputy chief of Anatomic Pathology at Sunnybrook.

Next, a medical lab technologist adds hot paraffin wax to each cassette and places these blocks on trays of ice to allow the wax to harden. Each block is then fed into special machines and another technologist skillfully makes four-micrometre thick slices from the block. The slices are then carefully floated within a water bath, then deftly affixed onto a glass slide.

Some of the slides are then fed through a routine staining machine, while others are left as blank canvases. The reactive compounds in the routine stain (Hematoxylin and Eosin) turn the nucleus of each cell blue, while other structures, like the cell wall and proteins, stain pink. To the naked eye, the stained slide looks like purple fingerprints or ink blots.

Some samples need special stains, however, to identify unique structures, such as the bacteria causing an infection. These stains are prepared by a lab technologist,

and are based on Standard Operating Procedures formulas and applied with eyedroppers to the slides. One type of stain is made with real saffron; others have names like "Movat's Pentachrome" and "Gram stain."

Once a slide is stained, it's ready for Dr. Keith to examine under a microscope. In some cases, her trained eye can identify a cancer based on how the cells look, how numerous and spaced the cells are and how many cells are captured in the act of dividing. Says Dr. Keith, "You have to have a good eye and extensive training to interpret the things you see on the slide."

When Dr. Keith needs more details on what she's seeing, she'll order the plain tissue samples to be stained with other compounds – called immunohistochemical stains – to help identify cell and tumour types. Many cancers can spread (metastasize) to the brain or spine, from other sites in the body. "The first step is identifying metastatic disease, but then I want to know: 'Where did this cancer come from?'" explains Dr. Keith. For example, if a "TTF1 stain" stains the nuclei of the tumour cells brown against a blue background, Dr. Keith knows she's seeing a metastatic tumour to the brain, from the lung. Aside from immunohistochemical stains, Dr. Keith might also order genetic tests on a brain tumour (see sidebar).

So what did the slides of the tumour specimen removed from Shawn's brain reveal? From the routinely stained slides, Dr. Keith could tell right away the tumour wasn't usual. Most brain tumours have cells that are chaotically arranged and fast-growing. But in Shawn's case, the blue-stained nuclei of the cells were the same shape and size, and none of the cells were caught in the act of dividing. These traits, and the way the cells were clustered together with some spaces in the background, led Dr. Keith to a subependymoma. "Fortunately, it is one of the most benign brain tumours," she explains.

At Sunnybrook's Odette Cancer Centre, pathologists participate in multidisciplinary cancer conferences. These are regularly scheduled meetings bringing together cancer care professionals from different disciplines – to include pathology, radiology, surgical, radiation and medical oncology, nursing and pharmacy

– who discuss and share expertise on the complexities of a treatment plan for a patient, to ensure a co-ordinated approach.

Shawn isn't expected to need chemo or radiation for the remaining tumour. Instead, he goes for an MRI every six months to ensure the tumour hasn't grown.

Watching the tumour samples be cut, processed, embedded in wax and stained, it's easy to forget that each of these tiny samples tells a story. Fortunately, we're increasingly wresting control of these stories, which is why Dr. Keith is also involved in research and meets regularly with neuropathologists across the country and around the world. "The more we learn, the more we can personalize treatment," she says. "Pathology is changing extremely rapidly." 

## RECOGNIZING THE SYMPTOMS

"Genetic studies are featuring more and more in the diagnosis and how we predict how a patient will respond to a certain therapy," says Dr. Julia Keith, who increasingly sends tumour samples to specialized labs for genetic testing. "As pathologists, we need to stay up-to-date in terms of what types of testing are clinically useful and available, and sometimes we need to help propel the development of a certain test."

The shift toward including genetics to help classify tumours means a steep learning curve, which is why it's a key advantage that each pathologist at Sunnybrook has specialized expertise, focusing on diseases affecting a particular organ system. "The breast tumours are interpreted by the breast pathologist, the gynecological cancers are interpreted by the gynepathologist and so on," says Dr. Keith. Likewise, she focuses on diseases affecting the nervous system. "The diseases of the brain are unique. You need a dedicated expert to interpret brain tumours."

PHOTOGRAPH BY DOUG NICHOLSON



Breast cancer survivor Rayanne Dubkov and some of her firefighting colleagues who have raised money for the Louise Temerty Breast Cancer Centre.

## Fighting to extinguish breast cancer

*Women who battle blazes have a higher-than-average risk of the disease – which is why their colleagues are raising money to help beat it*

BY ANGELA PIRISI

When Rayanne Dubkov, 45, a Toronto firefighter and captain, was diagnosed with breast cancer a couple of years ago, she could point to no family history of the disease. “I’m the first in my family to have breast cancer – lucky me,” she jokes. Having spent her whole working life in the fire service, including 12 years in her hometown of Manchester, England, and the last 13 years in Toronto, she suspects the cancer was job-related.

Breast cancer, along with several other types of cancer, is an occupational hazard for firefighters. The risk is higher among firefighters compared to the general population, something the Ontario govern-

ment recently recognized by announcing new provincial legislation that will extend health-care benefits for firefighters with various cancers, a list that now includes breast cancer. And the number of cases may rise as more women are steadily joining what has historically been a male-dominated profession.

The elevated risk was one reason why the Toronto Professional Fire Fighters’ Association (TPFFA) donated \$100,000 to the Louise Temerty Breast Cancer Centre at Sunnybrook.

The firefighters’ commitment to fight breast cancer began with a North American-wide resolution by fire depart-

ments, predominantly staffed by men, to do something to show their support for curing a disease mainly suffered by their female colleagues. It was decided at a convention that all fire departments would engage in selling pink T-shirts to raise funds.

So since 2011, Toronto firefighters have been selling the pink T-shirts every September in support of breast cancer. And each October, during Breast Cancer Awareness Month, the Toronto firefighters are allowed to wear the pink T-shirt for one of their shifts. It’s been easy to rally support, says Frank Ramagnano, secretary-treasurer for the TPFFA, because so many firefighters have a friend, mother or sister who has gone through breast cancer. “The service has mainly sold the shirts to firefighters, who are buying them and giving them to friends and family members. “What we usually suggest to firefighters is that they buy it, wear it for a shift and then give it to a cancer survivor,” says Frank.

He says that helping Sunnybrook was a

natural choice. “It had partly to do with a long-standing relationship that our organization has had with Sunnybrook.” The TPFFA had already been supporting Sunnybrook’s Ross Tilley Burn Centre and regional skin bank. “We also wanted to keep the money local, since fire departments across North America are already raising money for breast cancer. So when we heard that Sunnybrook was going to open up a state-of-the-art [breast] cancer centre, we wanted to assist with that,” he says.

“It’s only through the firefighters’ donations and the community’s support that we’ve been able to create this centre, which allows all the different professionals who treat women’s breast issues to come together and work together. And it’s given us the space and the facility to create a number of integrated programs,” says Dr. Eileen Rakovitch, medical director of the Louise Temerty Breast Cancer Centre.

The centre embraces an integrated breast cancer care model, which essen-

tially offers patients one-stop shopping when it comes to diagnosis, treatment and follow-up care. The idea is to wrap care around patients’ needs to make the process as comfortable, quick and as stress-free as possible. “Our vision has been to ask ourselves: ‘What can we offer that women can’t get in the community, and how can we fill in the care gap?’” says Dr. Rakovitch.

For example, the Marion C. Soloway Breast Rapid Diagnostic Unit allows women to undergo assessment, which may include an ultrasound and biopsy, then receive results and discuss them with a surgeon all within a 24-hour period. PYNK is a breast cancer program within the centre that’s entirely focused on young women and issues that are unique to them, such as early menopause, fertility and preservation of eggs.

Meanwhile, the Immediate Breast Reconstruction Program offers eligible patients the convenience of seeing a surgeon and plastic surgeon in the same visit, so they can decide the best treat-

ment and discuss how to optimize the aesthetic results.

“The firefighters’ gift has tremendous impact,” says Dr. Rakovitch. “It buys certain pieces [of equipment] that we need, some supplies and dedicated nurses who can train other nurses. We have many different needs and uses for donations on all scales.”

Frank hints that they may soon set a new fundraising goal to reach. “And the pink T-shirt tradition will likely continue. I think it will become a firefighter tradition – the fire service likes tradition.”

Besides the commitment and generosity their breast cancer campaign shows, it also speaks to their tenacity. As Frank suggests, helping to battle breast cancer through this fundraising campaign isn’t unlike fighting a blaze: “Sometimes it takes a while to get a situation back to normal, but we never give up until we achieve what we set out to do.”

PHOTOGRAPH BY PETER POWER

# RESEARCH & INNOVATION

*the latest in leading-edge developments at Sunnybrook*

## FEED YOUR NEURONS

When it comes to exercise, there's no such thing as too little. Even short durations of exercise can change blood flow long after the workout is over. And fitness levels correlate with the level of blood flow to motor learning and memory parts of the brain.

Dr. Brad MacIntosh likens the phenomena to watering a garden. "When you exercise, you turn on your sprinkler. The sprinkler is like the brain's blood flow. Different patches of your garden benefit more from the water, and the more you water, the more it helps your garden," says Dr. MacIntosh, Sunnybrook research scientist. Of course, the garden, in this case, is a much more complicated neurovascular system that involves the blood supply to cells in grey matter and white

matter connective tissues.

Dr. MacIntosh's recent research focuses on patients participating in an exercise-based cardiac rehabilitation program, showing that fitness flushes the brain's grey matter with blood. The study was the first of its kind to use magnetic resonance imaging (MRI) to show there are brain regions that benefit from maintaining a healthy aerobic fitness level in patients with heart conditions.

What's the ultimate prescription for what type and how much exercise? Turns out it's a complex answer, going back to the garden metaphor, it depends on many factors, like the type of plants. One thing is certain, though, says Dr. MacIntosh: "If you're exercising, even just a little, your neurons are going to thank you."

## PROMISING TREATMENTS FROM THE KITCHEN

Sunnybrook research is aiming to bolster evidence that two common kitchen spices are beneficial to health.

Curcumin, a plant compound that gives turmeric its yellow colour, is being studied as an add-on therapy for bipolar disorder. Sunnybrook's division of youth psychiatry is enrolling adolescents in a study of curcumin to see if, along with regular medication, it helps control depressive symptoms.

"In treating bipolar disorder, we tend to layer on mood-stabilizing medications when one alone is not adequate, but there can be side-effects," says Dr. Benjamin Goldstein, lead investigator and director of the Centre for Youth Bipolar Disorder at Sunnybrook. "Curcumin is natural and generally very well tolerated, so it might produce benefits with fewer side-effects."

Curcumin is a staple of Ayurvedic medicine in India, and a large body of evidence in the West has confirmed its anti-bacterial, anti-oxidant, anti-viral and anti-inflammatory properties.

Another ancient therapy gaining modern relevance is the active ingredient in chili peppers, capsaicin, known for its anti-inflammatory and anti-cancer properties. Researchers in Sunnybrook's prostate cancer research group began to study it after noticing that one of their patients, who had been adding "hot sauce" to his diet, had a delay in progression of prostate specific antigen (PSA), an indicator of prostate cancer. Sure enough, they found several beneficial effects in laboratory mice: capsaicin was able to prevent prostate cancer from growing, prevent prostate tumour cells from metastasizing and render tumour cells more sensitive to radiation treatment.

Now, they are about to start human clinical trials to find out whether capsaicin is useful as a presurgery treatment to shrink tumours, and whether it helps prevent progression of prostate cancer in certain patients.

## BACK IN THE GAME

Hockey's brain-rattling hits have sparked national conversations about concussions. But concussions can also come from the mishaps of daily living and leave lingering symptoms like headaches, mood or anxiety disorders and fatigue.

Resting the brain is the first priority, but when symptoms last months, emerging research, pulled together in new treatment guidelines co-authored by Sunnybrook's Dr. Scott McCullagh, shows that resting for too long can be detrimental. People lose their physical fitness and they can become isolated and depressed.

The new guidelines will help primary health-care providers better manage postconcussion

symptoms. Still, there is little objective evidence health-care providers can use to pinpoint when the brain has healed enough to get back in the game.

"Current health-care scans usually appear normal in these patients. But, after a concussion, the ability for brain blood vessels to respond to physiological challenges is reduced," says Dr. Leodante da Costa, Sunnybrook neurosurgeon and winner of GE and National Football League's Head Health Challenge for brain injury research. "If you repeat an injury, the damage will accumulate and it will be worse than the first."

Dr. da Costa is working on an imaging method to identify patients and athletes at risk for secondary injury after a concussion. Using advanced magnetic resonance imaging (MRI), he aims to measure the response of blood vessels to better diagnose, monitor response to treatment and guide decision-making after a mild head injury.

## TRACK IT, TREAT IT

Millions of Canadians are living with mood disorders such as depression and bipolar disorder. To determine whether their treatment is working, patients are often asked to keep a journal to track important indicators like sleep, mood and appetite. But many don't comply because the task is difficult to remember and can be onerous.

Now Sunnybrook researchers are studying a novel approach to track and treat mood disorders. The Physician Access to Telemetry from Handheld / Mood Disorders study prompts patients with a one-minute daily survey on their mobile devices. In just a few taps and drags, patients can input how they are doing. That information is then sent back to the patient's doctor, creating a graph that paints a visual snapshot of each patient's progress.

"The hope is better quality information will lead to better results for patients with recurrent mood disorders, including fewer hospitalizations," says Dr. David Kreindler, principal investigator of the study and head of the Division of Youth Psychiatry. Dr. Anthony Levitt, co-investigator of the study and chief of the Brain Sciences Program, says, "If I asked you to describe the weather over the past month, that would be very hard to do. But when you use a graph or picture, it becomes easy. We think the same principle will apply to someone's mood. For example, if we can see a patient's mood improved or declined at the same time they started a certain medication, that will help us provide the best possible course of treatment."

The study, of patients aged 14 years and older with a diagnosed mood disorder, will continue over the next few months. If effective, it is hoped to make it a standard of care at Sunnybrook and beyond. •



The vintage Harvard plane during the 2013 Remembrance Day flyover in the skies above Sunnybrook.

Photographer Doug Nicholson takes a seat in the Second World War aircraft.

## From Doug's perspective

Our staff photographer has been a veteran chronicler of life and times at Sunnybrook

BY DAN BIRCH

Before Sunnybrook photographer Doug Nicholson took his seat in a Second World War-vintage aircraft last November, he had to do something he had never done for any other flight: put on a parachute. Being in the two-seat Harvard plane as it flew over Sunnybrook's Remembrance Day ceremony is one of the highlights in Nicholson's 25-year career at

Sunnybrook. He has been chronicling daily life at the hospital for the last 14 years, and before that was performing specialized diagnostic photography in ophthalmology.

For Nicholson, the highlights are numerous. He recalls the gratitude and selflessness of a young man from Mozambique who received a prosthetic leg here in 2003. He is awed

by Sunnybrook's growth and evolution into a centre of global stature. And most recently, he felt fortunate to be part of history as he and his colleagues live tweeted a heart bypass surgery last February. "When a TV crew shows up and starts filming us, as opposed to the doctors, you know that something special is happening," Nicholson says. 📸



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Be a hero to our heroes.

Commemorate Remembrance Day this year, by supporting Canada's heroic veterans at Sunnybrook.

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