INNOVATION & RESEARCH IN SURGERY 2016
INNOVATION & RESEARCH:

BEYOND THE CUTTING EDGE
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Advances in surgery have typically occurred at times when new solutions are being sought for improvements in surgical care. In recent times, these advances have taken place through a distinct desire to make all surgical disciplines more minimally invasive, and all the while more effective with better patient outcomes and safety. It is for this reason that this innovation Prospectus is so timely for the Department of Surgery. Many of the Surgeon-Scientists and Surgeon-Investigators whose research programs are outlined within the pages of this document are true innovators, pushing the envelope towards new surgical discoveries. These discoveries have included novel drugs for improving stroke recovery, better implants for joint and spine degeneration, better ways of preparing organs for transplantation, among many other innovations. I am indeed proud that the Department of Surgery at the University of Toronto has made surgical innovation one of its hallmark pillars of its current strategic plan.

Most of the innovations to date have been borne out of the willingness and industry of the dedicated surgeons whom we chronicle in this document. But it is my great hope in the future that direct support from the Department of Surgery will be available to foster a community of surgical innovation which will lead in Canada, and for that matter, in the world.

I do hope that you will enjoy reading through the pages of this Prospectus. We have much to be proud of in the Department of Surgery with our demonstrated abilities to innovate and change paradigms for patients undergoing surgery.

Sincerely,

James T Rutka MD, PhD, FRCSC
RS McLaughlin Professor and Chair
Department of Surgery, University of Toronto
Orthopedic surgeon Rod Davey has been instrumental in establishing the Toronto Western Hospital’s international reputation for advanced techniques in joint reconstruction and minimally invasive surgery. He works with several international orthopedic companies as both a designer and developer, focusing on the femoral stem implants used in hip reconstructions.
Dr. James Drake is a neurosurgeon at the Hospital for Sick Children, as well as the Hospital Head of Neurosurgery. His lab focuses on bioengineering and its surgical application for diagnosis and treatment of hydrocephalus, as well as image-guided surgery.

**KidsArm**

In 2012, Dr. James Drake brought surgeons, engineers, and software designers together to develop the KidsArm, a semi-autonomous robot used for minimally invasive pediatric surgery. It is a tabletop surgical tool with hand controllers, allowing surgeons to navigate to the treatment region at a quicker rate and without disturbing delicate blood vessels.

**MRgFUS and Robot Technology**

Magnetic Resonance Imaging (MRI) uses 3D images to create real-time navigation for surgeons. It is also used to focus ultrasound waves to distant targets to create precise thermal coagulation of tissues. These virtual reality models are used for pre-operative planning, and for providing residents with a comprehensive educational experience. Image-guided robotics also aids in minimally invasive surgeries and contributes towards a decreased risk of infections, improved recovery times and overall patient care.

**The Centre for Image Guided Innovation and Therapeutic Interventions (CIGITI)**

CIGITI’s projects are directed towards pediatric robotics, simulation, and imaging. Collaborative projects have included: a stainless steel template for reconstructing the forehead of patients undergoing craniofacial surgery, a pediatric laparoscopic simulator to track surgeon movements, a laparoscopic ureteroplasty model, a simulator for ear and ophthalmological exams, a brain simulator for endoscopic procedures, and patient-specific models of complex congenital cardiac abnormalities. A number of these projects have been successfully commercialized.
Dr. Tony Finelli performed the first robotic prostatectomy at UHN and oversaw the implementation of the procedure within the division. Along with Dr. Bernardini (Gynecologic Oncology), he performed the first robotic pelvic exenteration and urinary diversion in Canada. Although he has applied the technology to other uro-oncologic procedures, the focus at UHN has been on safety and maintenance of standard that equals and often exceeds that achieved with conventional open surgery. Also, Dr. Finelli oversaw the safe implementation of robotic surgery and served as a mentor to other centers in Ontario.

Dr. Finelli currently Co-chairs a committee at Health Quality Ontario on robotic surgery. The objective of this committee to evaluate and make recommendations on robotic surgery such that there is plan for responsible dissemination that diminishes harm, and is medically and fiscally responsible.
DR. HOWARD GINSBERG

St. Michael’s Hospital
Staff Surgeon, Division of Neurosurgery

Sunnybrook Hospital
Sunnybrook Biomechanics Laboratory

University of Toronto
Assistant Professor, Department of Surgery
Assistant Professor, Institute of Biomaterials and Biomedical Engineering
Dwayne Miller Laser Research Group

Ryerson University
Tavakoli Research Group, Department of Physics
Kolios Research Group, Department of Physics

Dr. Howard Ginsberg is a neurosurgeon at St. Michael’s Hospital, trained in both orthopedic and neurosurgical spinal surgery techniques. He has been instrumental in developing a new spinal fusion device, image-guided navigation techniques during spinal surgery, and surgical approaches for the thoracic spine. Dr. Ginsberg’s research focuses on the application of engineering towards neurosurgical procedures, with the goal of improving patient safety and outcomes.

Mobile C-arm Ziehm Vision FD Vario 3D

One of Dr. Howard Ginsberg’s most notable projects includes the introduction of German device Mobile C-arm Ziehm Vision FD Vario 3D to St. Michael’s Hospital. The intra-operative scanner works with navigational computers to offer surgeons accuracy within the range of half a millimeter, in terms of screw placement in the spine. It provides patients with a minimally invasive alternative, and lowers both patient and surgeon exposure to radiation from the x-rays generally used. The C-arm is a superior option for surgical accuracy and patient outcomes.

Laser Scalpels

Dr. Ginsberg is currently collaborating on an exciting project with the aim of developing a ‘smart laser scalpel’. The system uses a pico-second infrared laser (PIRL) to destroy tissues with virtually zero scar tissue formation. Using real-time mass spectrometry, the laser is able to identify the type and character of the tissues being cut.

Bioengineering Ventures

Dr. Ginsberg has consulted extensively with industry in North America and Europe on a variety of projects. These include: A new model of ventriculoperitoneal shunt that is able to remotely monitor and regular pressure while in the brain, novel spinal hardware devices, groundbreaking surgical navigation techniques using image-based guidance, an innovative method of monitoring brain parenchyma for strokes, ischemia, and hemorrhages in real time, creative strategies for annulus repair during lumbar disc surgery, and software for the simulation of spinal surgery and its application to teaching and pre-operative planning. In addition, Dr. Ginsberg has worked in the venture capital field and continues to advise early stage start-up technology companies seeking guidance.
The O.R. ‘Black Box’

Approximately 9,200 to 23,000 Canadians die annually from preventable adverse effects in hospitals. Drawing reference from the ‘black box’ used in aircraft investigations, Dr. Grantcharov designed a device for error analysis in the operation room. It records the video and audio of the surgical procedure, and generates an electronic record of the activity. His ultimate goal is to improve patient safety through upholding the highest standards in surgical protocols. In addition, the OR Black Box could change the culture of the OR by identifying both technical and non-technical issues such as communication and decision-making processes between the surgeons, nurses, and anesthesiologists. The equipment is currently being tested with minimally invasive procedures at St. Michael’s Hospital. The analysis team has already been able to detect the smallest errors, which encouraged the Hvidovre Hospital in Copenhagen to adopt it for their own testing. The Canadian Association of General Surgeons has expressed its support for Dr. Grantcharov’s innovative design and its potential to raise surgical standards, improve patient outcomes, and provide high-quality surgical education.
Radiofrequency Ablation Technology

Radiofrequency ablation (RFA) is a method for destroying cancerous tumours through radioactive power. Currently, the RFA devices use a long thin needle for treatment and are generally used for tumours smaller than three centimeters. A PhD student in Dr. Michael Sherar’s lab at the Ontario Cancer Institute discovered that a coil-shaped probe operated at a higher frequency was effective at treating larger volumes, which meant it could treat tumours larger than three centimeters. After undergoing pre-clinical evaluation and production refinement, Dr. Michael Jewett is currently conducting the Phase I clinical trial at UHN. The RF coil device is currently being tested in both liver and kidney cancer patients, with early promising results. Dr. Jewett and Dr. Sherar ultimately aim to license the technology with a medical device manufacturer, due to its clinical benefits. For instance, it is less likely to disrupt blood flow around the delicate tissues while simultaneously being able to treat larger affected volumes. The coil-shaped device will ultimately be able to treat many more affected patients and improve their health outcomes.

Dr. Michael Jewett is an accomplished urologist at the Princess Margaret Cancer Centre (UHN). His research focuses on cancers of the kidney, bladder, and testis, and the application of technology assessment and clinical informatics.

Dr. Michael Jewett

University Health Network
Staff Surgeon,
Division of Urology, Princess Margaret Cancer Centre

University of Toronto
Professor, Department of Surgery
Postgraduate Teaching Award, Best Surgical Teacher
Past Chairman & Program Director, Division of Urology

Affiliations
Chair, Kidney Cancer Research Network of Canada
Farquharson Clinical Research Chair in Oncology
President-elect, Canadian Urology Association
Member, NCI Renal Task Force

Recognition
Distinguished Contributions Award, American Urological Association
Medal of the Society of Urological Oncology
Lifetime Contribution Award, Canadian Urological Association
Recipient of the Queen’s Jubilee Medal, 2012
Dr. Shaf Keshavjee is the Surgeon-in-Chief at the University Health Network, staff surgeon at the Toronto General Hospital, Senior Scientist and Director at the Latner Thoracic Research Laboratories, and Director of the Toronto Lung Transplant Program and Head of the Lung Transplant Program at the Hospital for Sick Children. His specific research interest is in lung injury related to transplantation. His current work involves the study of molecular diagnostics and gene therapeutic strategies to engineer better organs for lung transplantation.

Toronto Ex Vivo Lung Perfusion System

Dr. Keshavjee developed the Toronto Ex Vivo Lung Perfusion System, which allows donor lungs to be kept alive outside of the body. This technique allows the lungs to be assessed, treated and/or repaired prior to transplantation into a patient in need. Dr. Keshavjee’s developments have become standard to transplantation programs around the world, saving lives and improving clinical care. For example, UHN had an 30% increase in the number of lung transplants. He is also developing gene and stem cell therapy to improve the condition of potentially injured and/or inflamed lungs prior to their transplantation.

Dr. Keshavjee was made an Officer of the Order of Canada in 2014 for his remarkable healthcare achievement.
Mingyao Liu is the Head of the Respiratory and Critical Care Research Group at the Toronto General Research Institute, as well as a Senior Scientist of the Latner Thoracic Surgery Research Laboratories at the Toronto General Hospital. He is currently the Interim Director of Institute of Medical Science, which is the largest graduate unit in the Faculty of Medicine for graduate training in clinical departments. His research focuses on the cellular and molecular mechanisms of acute lung injury, especially in lung transplantation. He targets intracellular signal transduction pathways for drug discovery. He has developed nano-formulations for drug delivery.

**Nano-drug Delivery for Acute Lung Injury**

Over the past 2 decades, Dr. Mingyao Liu has been exploring the intracellular signal transduction pathways for acute inflammation. He targeted on Src protein tyrosine kinases and protein kinase C isozymes. He developed a novel nano-formulation using self-assembly peptide, together with amino acids to enhance solubility for hydrophobic chemical compounds. He demonstrated the safety and efficacy of this strategy and developed it as a general platform for drugs with different chemical structures.

Recently, his group developed a gold nano-particle peptide hybrid system to delivery rationally designed intracellular peptide drug for specific inhibition of protein-protein interaction. These approaches have great potential to be developed further for clinical applications.

In addition, his group collaborated with pharmaceutical companies to test drugs in pre-clinical studies, aiming for translating the therapeutics for clinical trials. A pipeline from cell culture, small animal model, large animal model and damaged human lung declined from lung transplantation programs has been developed to test new drugs and formula for potential clinical usage.
Subarachnoid hemorrhages (SAH) occur when there is bleeding into the space around the brain filled with cerebrospinal fluid. Approximately 90% of patients who experience spontaneous SAH will reach the hospital in time, but typically half will then suffer from permanent disabilities or do not survive. One of the most common complications after the SAH includes delayed cerebral ischemia (DCI), or ‘re-bleeding’, for which there are no safe or effective treatments.

In 1989 the FDA approved oral doses of nimodopine for its prevention, but it was only marginally effective because of the severe side effects. Dr. R. Loch Macdonald and his team developed NimoGel EG-1962 consisting of nimodopine and calcium channel blockers, encapsulated in a biodegradable polymer mixed with hyaluronic-based buffers. This unique formula allows for a single delivery directly into the space around the brain and a 21-day suspension of the nimodopine. EG-1962 has been highly successful in its pre-clinical and clinical trials and Edge Therapeutics is currently enrolling patients into Phase 1 and 2 multicenter clinical trials in the United States and Canada.
As a transplantation and surgical oncology surgeon at the Toronto General Hospital, University Health Network, Dr. McGilvray is internationally recognized as a pioneer in complex surgery of the liver and pancreas. His laboratory work is focused on the liver; he has spent many years asking how inflammation and infection damage the liver, and on how we can manipulate the liver to prevent, treat, or reverse this damage. He is also deeply invested in education, and three years ago co-founded the Toronto Atlas of Liver and Pancreas Surgery. This web-based Atlas marries state-of-the-art animation with real-time surgical footage. It is now a globally-used tool, accessed by surgeons interested in liver and pancreas surgical oncology and transplantation. Most recently, he started a patient education component to the Atlas, with the goal of creating a reliable resource that can be used by patients around the world.

“Reprogramming” the Liver

The field of nanomedicine has exploded in the last ten years, but its translation to clinical practice has been hampered by one large problem: the liver.

Nanoparticles are engineered, inorganic structures that range from 1-100nm in size. They have unique physical properties and can be made to destroy cancer cells or change the function of immune cells. However, the huge majority of nanoparticles injected into the bloodstream are sequestered in the liver, often far from the diseased tissue that they are intended to target. Where they go within the liver, and how and whether they change liver cell function, is very poorly understood.

Dr. McGilvray is now applying the knowledge and techniques developed by his work in liver damage to understanding how nanoparticles interact with the liver. With this understanding we can develop means of bypassing the liver – and thus increasing the ability of nanoparticles to target distant diseased tissues – and of targeting the liver specifically.

In the latter instance, Dr. McGilvray’s laboratory is working on using nanoparticles to “reprogram” livers to improve their function post transplantation. This work has already garnered support from the CIHR, donors supporting PMH, and transplantation-specific grants.
A Non-Traumatic Binder for Temporary Abdominal Wall Closures

Dr. Rezende-Neto’s innovative approach to post-operative care for open-abdominal surgical procedures requires neither stitches nor anesthesia in its application. A binder is placed on each side of the abdominal walls next to the incision sites, and applied with a calculated force that will gradually facilitate the muscle closure without irritating the skin or connective tissues.

Successful clinical trials at St. Michael’s have demonstrated that Dr. Rezende-Neto’s product eliminates the need for repeat trips to the operating room to facilitate wound closure, while allowing for potential site re-opening at the bedside if need be. His device can be used in conjunction with other wound vacuum therapies, and completely protects the skin from injuries. This revolutionary product will decrease both surgical costs and patient risks, particularly in comparison to conventionally used techniques.

Dr. Joao Rezende-Neto is a staff surgeon at St. Michael’s Hospital, specializing in trauma and acute care. He is a surgeon-investigator with the Li Ka Shing Knowledge Institute, as well as a member of the Institute for Biomedical Engineering and Science Technology with Ryerson University and St. Michael’s. His clinical research focuses on hydrogen resuscitation after injury, and has filed 3 patents for his technological developments in abdominal wall closures.
Smartphone Technology in Post-Operative Care

Dr. John Semple collaborated with Quality of Care Health Inc. to develop a mobile app for post-operative care, piloted at Women’s College Hospital from 2011-2012. Patients are able to send Dr. Semple photos of the incision sites and ask questions, allowing for immediate reassurance or answers—or to identify issues earlier. The app can be used on a smartphone or tablet, and allows him to confidentially assess patients after surgery without the need for a hospital visit. This type of interaction could potentially lower health care costs by decreasing the frequency of unnecessary hospital readmission, since concerns can now be addressed in real-time and from one’s own home. Patients have consistently provided high satisfaction ratings of his app, supporting recent literature evaluations of the acceptance of using mobile technology for medical conditions. Dr. Semple plans on marketing and distributing the QoC Health Inc. technology to other healthcare organizations in Toronto and across North America.
Neurosurgeon Michael Tymianski is currently the Head of the Division of Neurosurgery at the Toronto Western Hospital, as well as a Senior Scientist and Director of the Neuroprotection Laboratory at the Toronto Western Hospital Research Institute. He holds a Tier 1 Canada Research Chair in Translational Stroke Research and focuses his research on the development of therapeutic strategies for acute and chronic neural injuries.

**NoNO Inc.**

In 2003, Dr. Michael Tymianski founded NoNO Inc., a privately held biotechnology company dedicated to the research and development necessary for translating academic discoveries into human clinical trials. NoNO currently has 45 US and national phase patents pending, 7 patents issues, and 3 additional allowed. The company is actively seeking partnerships for product development and commercialization of its therapeutic programs.

**PSD-95 Inhibitor Program**

Discovered by Dr. Tymianski and his laboratory in 2012, Na-1 is NoNO’s leading compound, used for the treatment of strokes and traumatic brain injuries. Phase 1 clinical trials were successfully completed without significant side effects and Phase 2 clinical trials are currently in the concluding phases. With strokes annually affecting over 700,000 North Americans, the future implications for Na-1 are boundless. Upcoming trials will focus on its effectiveness for vascular dementia, Alzheimer’s, and epilepsy.

**TRPM7 Inhibitor Program**

NoNO’s second focus is centered on Transient Receptor Channel TRPM7, which plays a key role in cell damage. The laboratory has identified compounds that inhibit its function, which has in turn increased the resilience of mammalian cells to damage in the cases of retinal, neuronal, myocardial, liver, and renal ischemia.
As a cardiac surgeon at the Toronto General Hospital and Peter Munk Cardiac Centre, Dr. Yau’s clinical interests include advanced heart failure, heart transplantation, ventricular assist devices, complex coronary artery surgery and valvular surgery. His laboratory work focuses on cardiac stem cell transplantation, cardiac protection during heart surgery, and novel technologies.

**Cardiac Stem Cell Transplantation**

Bone marrow is acquired the morning of the patient’s bypass surgery from the iliac crest and is then brought to the organ regeneration laboratory where research technicians use a clinical-grade magnetic separating device called the CliniMACS to isolate the appropriate stem cells. During this procedure, the patient rests until the afternoon’s operation. The isolation’s end result is several million stem cells that have been rigorously tested to ensure that they pass Health Canada-approved release criteria. The cells are brought to the operating room where Dr. Yau performs a coronary artery bypass graft (CABG). After the CABG is completed, he injects the stem cells into the heart’s damaged areas. Dr. Terry Yau’s cell processing system is highly innovative because it is carried out entirely in one day and one site in a dedicated cell facility. There has been extensive interest in the program and trial support from the stem cell research community within North America, other institutions, the lay press and public, and donors supporting PMCC and UHN.
Dr. Kazuhiro Yasufuku is a staff thoracic surgeon at the Toronto General Hospital whose work includes development of new technology for early diagnosis and ultra-minimally invasive thoracic surgery. He is the Director of the Interventional Thoracic Surgery Program and the clinical lead of Thoracic Surgery within the Guided Therapeutics Program at UHN, as well as leading the Thoracic Robotic Surgery. He is a Scientist at the Latner Thoracic Surgery Research Laboratory, Toronto General Research Institute and UHN.

**Image-guided Therapeutics**

Image-guided therapeutics in surgical oncology is currently receiving a lot of attention. Dr. Kazuhiro Yasufuku’s lab has been working on the development of minimally invasive image-guided therapeutics for lung cancer. In order to achieve this, he uses several kinds of nanoparticles. Nanoparticles accumulate in malignant tumor tissue via enhanced permeability and retention (EPR) effect after intravenous injection. This property can be applied to lung cancer therapeutics with a combination of imaging modalities. Nanoparticles are excited using near-infrared (NIR) light and emit light within a NIR window. This drove him to develop a fluorescence bronchoscope to visualize the fluorescence of nanoparticles in the tumor tissue, which will contribute to successful bronchoscopic detection of early-stage lung cancer. Moreover, the nanoparticles are known to have a photothermal effect that can convert light into heat at target sites. Nanoparticle-enhanced photothermal therapy is an emerging technique which in future can be used for lung cancer treatment in patients who are not fit for surgery. Indocyanine green (ICG) is a clinically-approved small molecular weight dye which emits NIR fluorescence when excited using a NIR light. NIR imaging with ICG is being applied to lung cancer surgery. Dr. Yasufuku’s lab has developed novel techniques for precise lung tumor localization as well as sentinel lymph node mapping (Figure 1) using a NIR thoracoscope. With a recent trend toward minimally invasive surgery, these techniques will be required and can be translated into human clinical trials. Dr. Yasufuku is also involved in creating the GTx (Guided Therapeutics) OR within Toronto General Hospital. This OR is used for translational research to evaluate safety, accuracy, and efficacy in new imaging modalities and real-time tracking and navigation technologies in a clinical setting.