

Life Sciences
Minimally-Invasive Medical Technologies



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Acknowledgments

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Introduction

The health-care industry in Canada is in the midst of a period of dramatic change. Disease and demographic trends are converging to place hospitals and other institutions in the North American health-care system under tremendous strain. With skyrocketing national health-care costs due to the rapidly rising incidence of chronic disease and an aging population, cost-saving alternatives to traditional therapies are attracting attention. **The long-term cost-savings associated with the use of most minimally-invasive surgical devices and therapeutic treatments presents a strong economic case for the accelerated adoption of these technologies in North America and abroad.**¹ In addition, the movement toward minimally-invasive medicine has been gaining momentum in medical spheres over the past decade. There is an increasing body of evidence to indicate that in many cases, the use of minimally-invasive medical technologies is associated with superior clinical outcomes over traditional therapies. As a result of these developments, the market for minimally-invasive medical technologies is poised for significant growth.

Medical practitioners measure the invasiveness of a surgical procedure or therapeutic treatment as a function of incision size and collateral tissue damage, plus recovery time. Minimally-invasive medical technologies are surgical or therapeutic devices that reduce the physical impact of a medical procedure. In doing so, these devices reduce the length of required hospital stays, the likelihood of post-surgical or post-treatment complications, scarring, pain, and in some cases, the cost of the procedure itself, on a per-patient basis.²

The province of Ontario has committed to supporting investment in image-guided surgery and minimally-invasive medical technologies

that are in line with Ontario's Innovation Agenda, as announced in the spring of 2008. Recognizing that Ontario researchers and institutions have an opportunity for global leadership in minimally-invasive medical technology, the province has implemented an array of programs to support the work of scientists, researchers and industry in the establishment of a technology cluster in this field in Ontario. The objective of these programs is to create jobs and encourage growth in these sectors, but also to provide better services, improved outcomes and lower costs in the health-care sector overall.³

Minimally-invasive medical technologies draw on knowledge from a multitude of scientific and engineering disciplines. Robotics, mechatronics and materials science as well as imaging, software design, physics and medicine all play a role in today's minimally-invasive medical technology industry.

Ontario is home to an array of companies developing minimally-invasive medical devices, as well as a host of researchers and research institutions working to advance minimally-invasive medical science. Given the combination of academic expertise in medical imaging and bio-engineering, the concentration of world-class clinical research centres, and the availability of government funding and support for clinical research and technology development, Ontario is positioned to become a significant contributor to the market for minimally-invasive medical technologies.

This report addresses a range of minimally-invasive medical technologies, both surgical and therapeutic, on the forefront of innovation. The report also discusses clinical opportunities and adoption trends in the most promising therapeutic areas, namely cardiovascular surgery, cancer treatments and cancer-related surgeries.

Medtronic

Medtronic is a global leader in medical technology. With over 40,000 employees in 120 countries, and annual revenues of \$15.8 billion, Medtronic is a pioneer in the development of minimally-invasive medical technologies. The company specializes in a variety of medical disciplines, developing surgical tools and devices for cardiac rhythm disease management, neuromodulation, spinal and biologics issues, diabetes, cardiovascular disorders, and ENT.

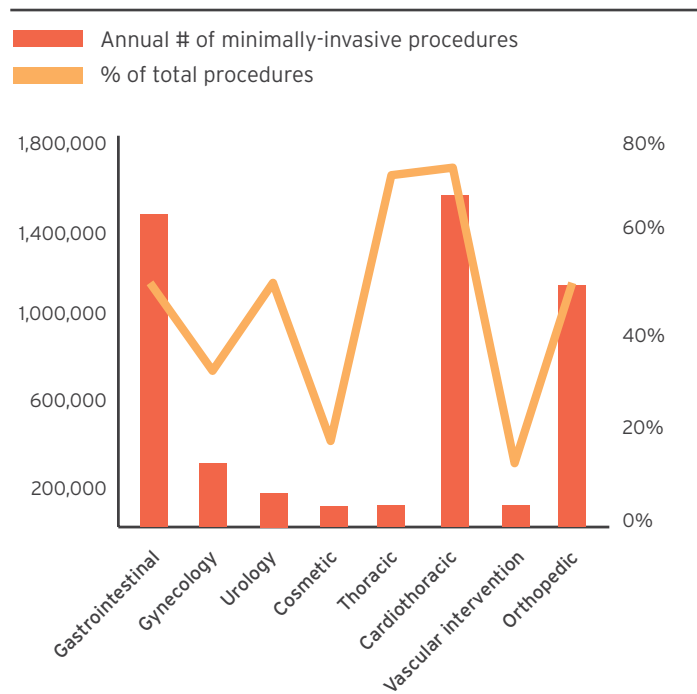
Medtronic of Canada was the first subsidiary of Medtronic to be established outside of the US. In 1974, they located their Canadian headquarters in Mississauga, and in September 2009 moved to Brampton. The company employs over 420 Canadians. Medtronic has regional offices in Vancouver and Montreal, with a facility in Montreal, Medtronic CryoCath, that specializes in the manufacture of atrial fibrillation ablation catheters.

Speaking about the increasing importance of minimally-invasive medicine, Neil Fraser, President of Medtronic of Canada, notes that **many of yesterday's major surgery areas are completing the transition toward the use of minimally-invasive techniques.**

According to Fraser, the move away from open surgery has also accelerated the adoption of advanced, surgical navigation and intraoperative imaging technologies to compensate for the lack of direct visualization.

With a multitude of procedures and an extremely large and growing addressable market, Fraser expects cardiac and vascular surgery to continue to account for a large portion of the demand for minimally-invasive medical devices and technologies. Strides are also being made toward advancing the use of these technologies for applications in cancer treatment, orthopedics and brain surgery.

Figure 1
Share of minimally-invasive surgeries worldwide.



Source BBC Research⁸

Industry overview

The less-invasive medical technologies market can be divided into seven major segments:

1. image-guided surgical systems and navigational devices
2. endosurgical equipment
3. electrosurgical devices
4. medical lasers
5. surgical robots
6. digital operating rooms
7. other surgical devices (including stents, catheters and guidewires)⁴

A handful of multinational health sciences companies dominate the North American market for minimally-invasive medical technologies; however, each market sub-segment has its own established leaders. The market for image-guided surgical systems and navigational devices is led by Medtronic and GE, while Boston Scientific and Johnson & Johnson control the coronary stent market, with a combined market share of 85%.⁵ Because the size of the minimally-invasive medical technologies market as a whole is so large, there are also a host of tier II and tier III companies competing alongside larger players. In Canada, Medtronic and GE compete with other established diagnostic imaging companies such as Philips and Siemens in the image-guided surgical systems market, as well as with start-ups such as Sentinelle Medical (a medical imaging company specializing in devices designed to detect very early-stage cancer tumours) and IMRIS (a developer of MR-integrated therapies for neurovascular, cardiovascular and neurosurgical applications).

An area of significant growth in recent years has been the North American market for medical robotics. Medical robotics aid in precision surgeries, image-guided biopsies and remote surgeries. Intuitive Medical, based in Sunnyvale, California, is the leading player, controlling 91% of the market. **Medical robotics is the fastest-growing segment in the robotics industry, and several companies with robotics divisions are contemplating full-scale market entry.** Two such companies include Sharp (electronics) and MDA (aerospace). At present, MDA is conducting two pilot projects in Canada for the development of medical robotic systems, NeuroArm and KidsArm. With a legacy of excellence in engineering and robotics and a host of robotic experts associated with the development of MacDonald, Dettwiler and Associates' Canadarm, Canadian companies have an opportunity for leadership in this segment.

Market share for minimally-invasive medical technologies

In 2007, minimally-invasive surgeries accounted for 15% of all surgical procedures performed in the US.⁶ This percentage varies significantly across surgical procedures by type. For the same period, 100% of all angioplasties, 85% of all gallbladder surgeries, and 75% of all lung biopsies were performed using minimally-invasive techniques, while only 15% of all heart valve replacement surgeries were performed using minimally-invasive techniques.⁷

While there are no published data available in Canada comparing the market share of minimally-invasive surgical procedures to traditional techniques, market penetration of minimally-invasive surgical technologies is likely lower than in the US. This is because budget-driven Canadian hospitals have traditionally been slower to adopt new medical technologies than their US counterparts.⁹ Figure 1 shows the comparison worldwide, by procedure, of the number of minimally-invasive procedures against total surgeries.

Market size and growth

In 2009, the global market for minimally-invasive medical technologies was estimated to be worth \$16.4 billion, growing at a forecasted rate of 11% to 2014.¹⁰ The US accounts for 60% of this market and Canada makes up approximately 1% to 2%.¹¹ Figure 2 shows the forecasted growth in the market for minimally-invasive medical technologies.

To place these figures in context, the market for molecular diagnostics is expected to grow at a cumulative annual growth rate of 14% through 2015, while the biopharmaceutical market is expected to grow 6.7% per year through to 2015.^{12, 13}

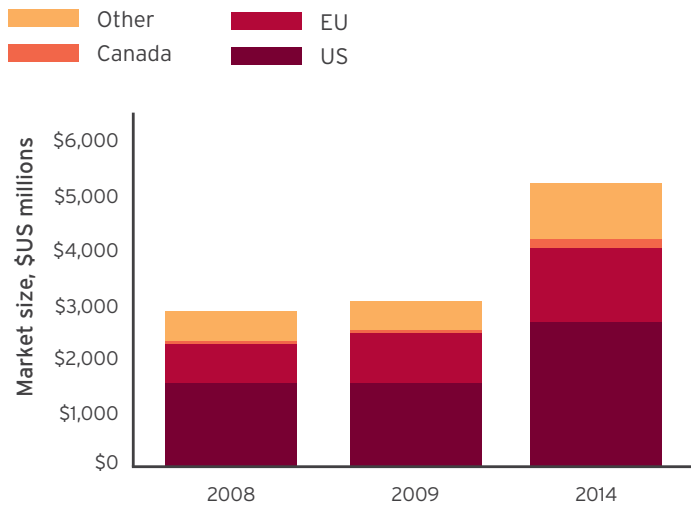
Worldwide, cardiothoracic surgeries account for over 70% of the demand in the minimally-invasive medical technologies market.

This is expected to remain an important market as the population ages and the incidence of cardiac disease continues to rise. In the US, minimally-invasive medical technology sales are greatest for endosurgical equipment. In contrast, **the area of greatest growth in minimally-invasive medical technologies is in medical robotics, with an average expected growth rate of 41% to 2015.**

Figure 3 shows breakdown by device type of the market share of minimally-invasive medical technologies.

Figure 2

Forecast growth in the market for minimally-invasive medical technologies.



Source BBC Research¹⁴

Geographically, the US and Japan are expected to see the highest overall increase in demand for minimally-invasive technologies, with growth rates of 7.8% and 8.1% (compound annual growth rate) respectively over the coming four years.¹⁵

Commercialization challenges

At present, developers of new minimally-invasive medical technologies face an uphill battle in order to bring their products to market. Adoption barriers for minimally-invasive medical technologies include their high initial cost, characteristically long hospital sales cycles, hospital inertia, overall and historically declining reimbursement rates in the US, and a complex and lengthy regulatory process for market approval.

While these make for fairly unattractive market entry conditions, the situation is expected to improve over the longer term, as the economic case for minimally-invasive technology improves.

High cost of new technology adoption

The implementation of a new clinical pathway, as treatment moves from an invasive to a minimally-invasive procedure, consumes considerable resources. The adoption of new minimally-invasive medical technologies by hospitals and health centres is hampered by cost concerns as well as by anxieties over liability and safety issues. New minimally-invasive medical technologies typically involve complex and highly specialized equipment. These devices also tend to be extremely expensive compared to the standard surgical equipment, and require that staff receive extensive training before the devices can be used.

The cost of acquiring and installing a “minimally-invasive surgery” (MIS) operating room can be anywhere from \$200,000 to \$300,000,

not including surgical and imaging equipment.¹⁷ In addition to this initial investment are the ongoing operating costs to fund the new technology, and a significant training curve for hospital personnel.¹⁸

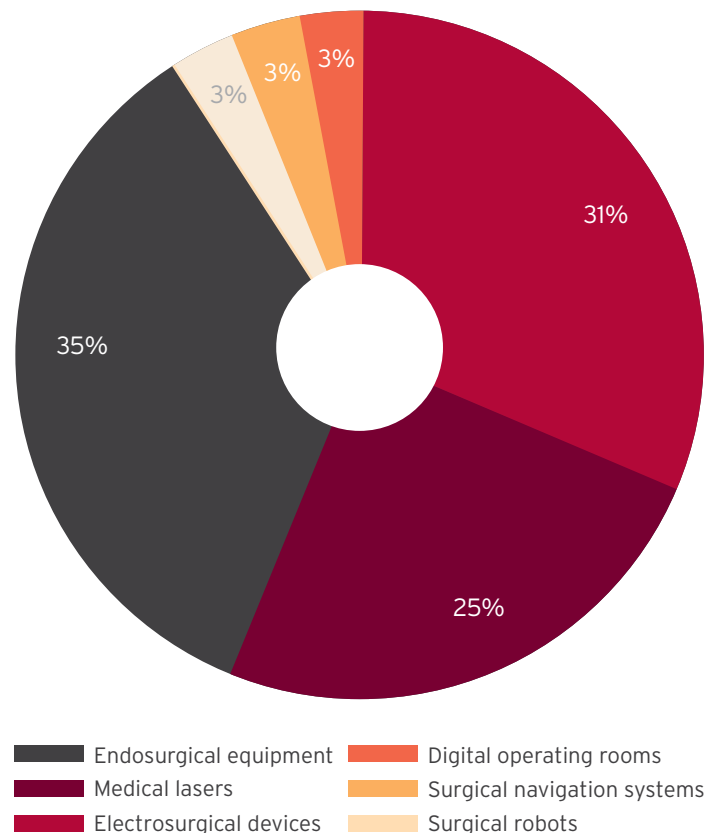
Intraoperative imaging devices used in complex, image-guided procedures (such as IMRI machines) require hospitals to invest US\$2 million to \$3 million up front. These machines also require a substantial training commitment by key hospital staff who would otherwise be conducting revenue-generating medical procedures. Additionally, the balancing effect of cost-savings to the hospital based on shorter hospital stays, lower rates of complication and lower re-admission rates associated with minimally-invasive methods is lost due to a lack of incentive alignment between hospitals, physicians and health-care payers. **New minimally-invasive medical technologies therefore require a substantial volume of evidence-based case studies (both in terms of clinical outcomes and hospital-cost reductions) in order to induce hospitals to make an investment.** For start-ups with new technologies, this can be a significant barrier to commercialization.

Hospital inertia, long sales cycles and lack of a standard sales procedure

Sales cycles for new medical technologies in hospitals (even when the products are relatively inexpensive) are extremely long and costly. In

Figure 3

Market share of minimally-invasive medical technologies by device type.



Source BBC Research¹⁶

the pharmaceutical industry, the role of the sales force is generally limited to promoting new drugs to physicians. For a new medical device, a company's sales representatives must develop a deep understanding of the product and be able to demonstrate to physicians how they work and how they outperform existing technologies. The sales representatives must also provide technical support to the surgeon and the entire operating team throughout the training cycle, while simultaneously working to convince hospital administrators of the cost savings realizable with the use of the new device. To further complicate matters, acute-care hospitals are complex organizations with highly involved decision-making processes. In the past, decisions relating to the acquisition of new equipment or to the implementation of a new procedure were largely the purview of individual surgeons and practitioners. In today's cash-strapped hospitals, the majority of technology investment decisions require consent from hospital administrators as well as approval on reimbursement from health-insurance payers. Additionally, **as surgical procedures grow increasingly complex, multidisciplinary surgical teams have replaced individual specialists as the end-users of new technologies.** This expands the scope of new technology marketing efforts, which must generate a consensus among an array of different specialists in order to obtain buy-in at the surgical level. This increasingly convoluted approval process engenders substantial delays for purchasing decisions on new medical technology.

Finally, very few regionally standardized processes exist for conducting hospital sales. Alberta has recently adopted a centralized purchasing approach for all medical technologies and British Columbia is developing a similar initiative. However, for the remainder of Canada and the US, the purchasing of medical technology is highly fragmented. For each sale, individual hospitals conduct their own assessment of existing techniques compared with the results of adopting the new medical technology. Even if the adoption of a different surgical procedure associated with the use of a new, minimally-invasive technology proves to offer substantial advantages, it is highly unlikely that all hospitals in a given region would adopt the technology unanimously.

Poor reimbursement standards for new medical technologies

In the US, the largest market for minimally-invasive medical technologies, hospital reimbursement for medical procedures works as follows: government and health insurance companies are responsible for reimbursing hospitals and surgeons for almost all surgical procedures that are non-experimental and non-cosmetic.¹⁹ Reimbursement rates are fixed, depending on the procedure performed, the insurance plan, and other factors.²⁰ These fixed amounts do not take into account the actual cost incurred by the hospital or surgeon, and these amounts are also not related to the specific device used in the procedure.²¹ This makes it extremely

Claron Technology

Claron specializes in computer vision and volumetric data visualization applications. One of the core technologies developed by Claron is the ability to recognize anatomical regions in CT, MRI and ultrasound scans. The process involves automatically registering a volumetric scan with pre-annotated volumetric data from an example patient, rather like an atlas. Claron's technology then copies locations, regions and labels from the "atlas" to the contents of new scan. This, together with many other analysis and visualization algorithms, has been packaged into a modular development and delivery medical-imaging software platform, named Withinsight. Claron licenses the Withinsight platform to other companies, allowing them to create a wide range of applications using medical imaging data. Claron has also developed the MicronTracker, a vision-based position-tracking device for image-guided surgery. This technology has applications in neurosurgery, as well as for ear, nose and throat surgery.

In 2009 Claron introduced ClaroNav, a platform for surgical navigation that combines its MicronTracker product with Withinsight visualization technology. Several minimally invasive surgical navigation solutions have been developed on the ClaroNav platform since its release. For example BrainsGate (www.brainsgate.com) has used the ClaroNav technology to implement the navigation system that is a key component of their stroke treatment solution. BrainsGate technology is based on the principle of on neuro-stimulation and promises to deliver a treatment option for ischemic stroke patients when there are no pharmacological alternatives. The electromagnetic stimulation is delivered with a device that needs to be placed in the sphen-

palatine ganglion (SPG) with an accuracy of a few millimeters. The system, including the navigation solution provided by Claron, is currently in the final phase of a large international clinical trial and has already been used for several hundred procedures. Other minimally invasive solutions based on the ClaroNav platform are currently under development, including an intra-operative neuro navigation solution, a trans-magnetic stimulation guidance system for the treatment of pharmacological resistant depression and a solution for the placement of dental implants.

As part of the company's future technology development plans, Claron is working to create an oncology solution in collaboration with Dr. Curtis Caldwell, a leading scientist at Sunnybrook Health Sciences Centre.

From a team of two in 2005, Claron has grown to include 23 employees and several contractors, some of whom work remotely from other parts of the world. The company was listed in the 2009 and 2010 annual PROFIT 100 ranking of Canada's Fastest-Growing Companies, published by PROFIT magazine. A MaRS Incubator client, Claron has been profitable from its first year in business, and did not seek out any external financing. The company's mantra of "start simple" has served Claron well by enabling the team to bring reliable, high-performing new products to market rapidly, while maintaining avenues for further customization and refinement. The company looks forward to continuing to advance the frontiers for computer-vision technology in medicine.

difficult for health-care providers to recover the cost of expensive equipment, such as minimally-invasive medical technologies, especially when a cheaper and well-understood procedure is already in place.²² Added to this is the overall downward trend in reimbursement rates in the US.²³ **Medical reimbursements in the US are falling across the board, while technology costs have continued to rise.**²⁴ For example, between 1991 and 2004, the cost of orthopedic implant devices in US rose 132%, while the associated reimbursement rate increased by only 16%.²⁵

With US hospitals entering a period of crisis resulting from rising demand and falling reimbursement rates, commercializing minimally-invasive medical technologies that require a high initial investment on the part of hospitals presents a significant challenge.

In Canada, obtaining reimbursement for newly approved minimally-invasive medical technologies is similarly challenging. According to Neil Fraser, President of Medtronic of Canada, hospital budgets rarely receive a readjustment to account for the adoption of new technologies. Similarly, provincially-administered physician reimbursement schedules are slow to adjust to the availability of new medical technologies.

A final problem to consider is the economics of minimally-invasive technologies for the surgeons themselves. In a study published by Texas' Anderson Cancer Center, it was found in one case to be vastly

more remunerative for a surgical practice to continue conducting comparatively invasive surgeries rather than opting for equally effective but less invasive surgical interventions.²⁶

In the study, it was shown that typically surgeons in the US “were paid nearly 40% less for sentinel node mapping and lymph node dissection than for radical mastectomies for early-stage breast cancer. As an example, a surgeon who performed 100 radical mastectomies in one year would earn \$107,503, whereas a surgeon performing 100 segmental mastectomies with sentinel lymph node dissection would earn \$64,344—a disparity of \$43,159.” On the other hand, the results also showed that “patients who had segmental mastectomy and sentinel lymph node dissection returned to work after an average of three days, compared to 19 days for patients who underwent segmental mastectomy and axillary dissection, or 26 days for patients who had radical mastectomy. They also had fewer overnight hospital stays (14% vs. 96% and 98%, respectively), and fewer days on post-operative medication (one day vs. nine and 10 days).”

Commercialization opportunities

Market dynamics in both Canada and the US have produced an increasing demand for procedures and technologies able to cut costs of hospitalization and reduce the morbidity and mortality rates associated with medical procedures. Despite the commercialization challenges discussed above, adoption and diffusion rates for minimally-invasive medical technologies are set

Sentinelle Medical

The early 2000s were an exciting time for Cameron Piron, who was doing graduate work in medical biophysics at Sunnybrook Research Institute. The human genome had recently been decoded and the genes known as BRCA 1 and 2 had been discovered to be associated with staggeringly high risk of lifetime cancer development in women. At the same time, no strategy or medical technology was in place to manage patients who tested positive for high cancer risk and who would benefit enormously from early tumour detection. Explains Piron, “*The problem was that there was really no solution for how to manage those patients. X-ray mammography had a very poor ability to detect small tumours in these women. Ultrasound was very poor, and nuclear imaging as well.*” Piron and his team decided to focus on magnetic resonance imaging (MRI) technology in order to develop a solution for the early detection of small cancer lesions. Piron had already developed the key components for a new, highly sensitive MRI modality, including adjustable MR coils that could be moved to fit women more closely, and magnetic pulse sequencing technology to optimize image acquisition. From here, Piron and his team developed software-driven image analysis tools and worked with a partner to perfect needle navigation for highly accurate biopsies. Ultimately, Piron hoped to create a specialized platform that could be seamlessly integrated into existing MRI units to enhance the successful detection, biopsy and diagnosis of very early-stage breast cancer. “*We cycled through many different iterations of different versions of the medical technology, with each one getting great clinical feedback and slowly improving to*

the point where we had developed a very advanced system. It was a stretcher that attached to an MRI magnet and which included coils and peripheral software that helped in the early diagnosis and then the ability to biopsy these tumours.”

Sentinelle's success in breast MRI derives from a three-pronged value proposition that can easily be adapted for the successful detection and biopsy of other cancers. Because MRI does not use radiation, it can be used safely for yearly screenings with high-risk patients. Offering much-improved efficiency and accuracy, radiologists can screen patients more rapidly and with better results than by using traditional techniques. Also, MRI provides a unique solution to the detection and biopsy of very small tumours. Sentinelle is currently working to create similar advances in the treatment of prostate cancer, and is examining other cancers as well.

Breaking new ground in the medical-imaging industry and bringing vastly improved detection tools to the market, Sentinelle's life-saving technologies present a giant leap forward for patients and clinicians in the fight against cancer.

In August of 2010, Sentinelle Medical was acquired by Hologic Inc. of Bedford, Massachusetts. Hologic is a provider of premium diagnostics, medical imaging systems and surgical products dedicated to serving the health-care needs of women. Management at Hologic look forward to working with the team at Sentinelle to continue developing leading-edge breast and body MRI applications.

Dr. Aaron Fenster

Dr. Aaron Fenster, Director and scientist at the Imaging Research Laboratories of the Robarts Research Institute, works to advance the role of image-guidance in surgical applications. A key driver behind his research efforts in minimally-invasive medicine is the use of lower-cost imaging techniques to enhance the accuracy and reduce the physical impact of certain surgeries while keeping procedure costs low. Prostate and breast biopsies as well as cardiovascular interventions number among the most common surgical procedures around the world. It is estimated that over one million biopsies are performed in the US every year for breast cancer alone.⁴⁴ With an increasing volume of these surgeries each year, hospitals are looking for ways to reduce costs while maintaining the quality and diagnostic sensitivity of these operations. Dr. Fenster is currently developing real-time image-guided surgical solutions that employ lower-cost 3D and 4D ultrasound imaging. Recent innovations involve the development of 3D ultrasound-guided biopsy and cancer therapy tools. These can be used in tandem with pre-procedural MR images to precisely locate and target problem tissues.

to increase significantly as a result of several converging trends. These include a gradual transition in most health-care systems toward the use of technologies that reduce the cost per procedure and increase capacity, a move to replace the current pay-per-service reimbursement paradigm with a pay-per-outcome system, and the increasing influence of patient demand and preferences in technology adoption. These trends, along with rapid advances in the development of medical technology, are expected to drive the market for minimally-invasive medical technologies.

Cost and efficacy assessments

An increasing body of evidence suggests that the use of minimally-invasive medical technologies results in superior clinical outcomes for the treatment of certain diseases, such as prostate cancer.²⁷

This has caught the attention of governments and regulatory bodies both north and south of the border.

In Canada, the federal and provincial bodies for health technology assessment (HTA) lead efforts on medical technology evaluation and standardization. At the federal level, health technology assessment is coordinated by the Canadian Agency for Drugs and Technologies in Health (CADTH). CADTH plays an important role in Canada's 13 provincial and territorial public insurance plans, but focuses mainly on cost-benefit analyses for projects deemed to be of national interest. Assessment of medical devices takes place mainly at the provincial level. The Ontario Health Technology Advisory Committee (OHTAC) is credited as being one of the most effective HTA groups in Canada, with a reputation for excellence in evaluating new technologies and assisting hospitals in promoting evidence-based medicine. Unfortunately, differences between provincial HTA operations limit their effectiveness in promoting the adoption of best practices nation-wide.²⁸ As the progress and findings of the CADTH and the provincial HTA bodies unfold, hospitals can expect to

see a gradual increase in the number of minimally-invasive medical technologies promoted in Canada.

On a parallel path, Ontario's Community Care Access Centres (primarily aimed at providing care to patients in their homes) have recently initiated a pilot project for implementing outcome-based tendering for certain services offered. The plan is called the Integrated Client Care (ICC) model, and it aims to contain anticipated increases in health spending in the home-care market by creating incentives for adopting cost-saving innovations.²⁹ If successful, this initiative is expected to be translated to Ontario's hospitals as well, and may pave the way for wider use of minimally-invasive medical technologies.³⁰

In the US, the government recently allocated over \$1 billion to conduct comparative effectiveness studies across competing medical technologies and methods. This initiative will identify and promote the use of safer and more effective medical technologies, and will encourage standardization across the health-care system, leading to greater uniformity in US patient-care overall. This could be a boon for new, minimally-invasive medical technologies and treatment methods that outperform traditional procedures.³¹

Additionally, recent US health-care reforms, as well as the trend toward integrated care in Ontario, favour specialized hospitals. If realized, this trend may increase demand for more advanced medical technologies, including minimally-invasive medical devices.

Increasing patient demand for minimally-invasive procedures

Patients are increasingly aware that minimally-invasive medical methods are associated with shorter hospital stays, less pain, less scarring, faster recovery times, fewer complications and better health outcomes. As patient-empowerment continues, it will drive demand for minimally-invasive treatment methods.³²

According to a recent report by Frost & Sullivan Vital Signs, patient satisfaction is becoming an increasingly important competitive differentiator among health-care providers in the US.³³ A move toward greater public transparency into patient outcomes and patient satisfaction rates across US hospitals is part of what is driving this trend.³⁴

Patient satisfaction is also becoming an important issue in Canada. In the most recent Throne Speech and the 2010 Ontario Budget, there were clear indications that the Canadian government intends to address quality issues across the health-care system "through a path of constant reform."³⁵ This may mean the introduction of quality-based health-care legislation calling for increased accountability among health-care providers and a review of the *Public Hospitals Act*.³⁶ A recently tabled bill, "Excellent Care for All" (introduced by Ontario Health Minister, Deb Matthews) proposes to link Ontario hospital CEO compensation to performance indicators, chief among which would be patient satisfaction and patient outcomes.³⁷

Hospital revenue models in transition

A dramatic shift in the revenue model for US hospitals is currently underway, and its effects are rippling through the North American

health-care industry as a whole. US hospitals are transitioning away from a pay-for-service model and toward one that compensates on the basis of patient outcomes.³⁸ Whereas the current model rewards hospitals as a function of the sheer number (and type) of procedures performed, in future, hospitals will receive revenue as a proportion of cases (in specific disease groupings) treated *successfully*.³⁹ This creates an avenue of opportunity for minimally-invasive medical technologies that deliver statistically superior patient outcomes compared to relatively more invasive therapies and surgical procedures.

Alterations to the hospital procedure-based pay system

US hospital pay is undergoing a further change. In the past, treatments delivered within particular disease groupings were funded differently based on whether a procedure was delivered on an in-patient or out-patient basis. The current trend is to provide equal hospital compensation for particular disease groupings regardless of whether they result in a hospital stay or not.⁴⁰ Medical technologies that are able to increase patient throughput and decrease the length of hospital stays are expected to thrive in this environment.

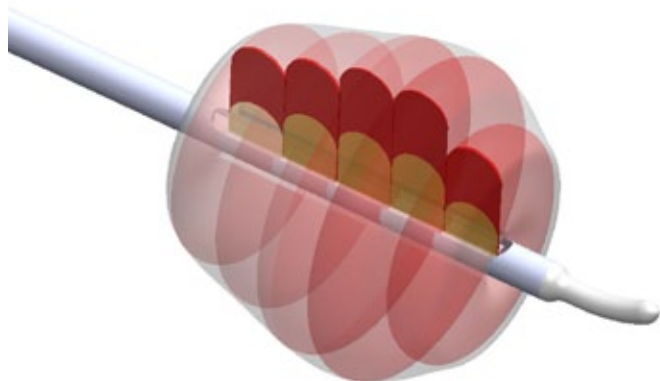
In addition, with the recent economic crisis, the declining financial health of many hospitals has meant a reduction in capital expenditures and an increase in competition among hospitals for patients. To satisfy patients who are demanding shorter hospital stays and more rapid recovery times, as well as insurance payers who are agitating for lower reimbursement rates, hospitals are accelerating their adoption of new technologies that increase their capacity utilization and profitability.⁴¹

Scientific and technological advances

The technological advancement of medical devices themselves is driving the market for minimally-invasive technologies as new

Figure 4

Profound Medical's energy wand emits thermal ultrasound in two different wavelengths (red & yellow) to treat the irregular shapes, and changes in radii, unique to each man's prostate.



Source Image courtesy of Profound Medical Inc.

technological capabilities open the door for novel and vastly improved surgical and treatment methodologies.⁴² Examples of market-driving technologies include real-time imaging applications made available with increases in computing power, improvements in equipment portability, nano- and biomaterials, and robotics.

Increases in computing power enable high-precision, image-guided surgery

Increasing computing power and greater data storage capabilities have led to advancements in medical imaging, image registration and image processing. This in turn has allowed for great strides forward in surgical navigation systems. The majority of current surgical navigation systems combine diagnostic data obtained pre-operatively with intraoperative imagery from multiple modalities to assist surgeons to plan and execute complex procedures with greater accuracy. The evolution of surgical navigation systems is one of the main drivers associated with the adoption of image-guided, minimally-invasive surgical tools and methods.

Surgical navigation systems have numerous advantages:

- They reduce operating costs due to shorter procedures and limited blood loss.
- They enable the execution of more complex surgeries.
- They reduce the risk of failed operations and the need to re-operate.
- They increase the productivity of the surgical team.

As mentioned earlier, the market for surgical navigational tools is extremely active, with image-guided equipment manufacturers competing head-to-head with software developers for market share. Ontario's Sentinelle Medical and Claron Technology each develop specialized tools for use in surgical navigation systems.

Improved equipment portability and image quality in lower-cost imaging modalities

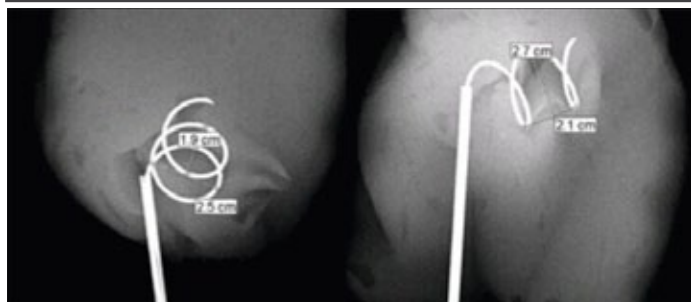
Recent developments in ultrasound imaging, including 3D/4D imaging, elastography, and customized probe design, have led to an increasing use of ultrasound imaging modalities in the operating room.⁴³ Ultrasound is used more and more in image-guided surgical systems, and 3D/4D capabilities have created an opening for the use of ultrasound in conjunction with pre-operative MRI or CT images, improving the accuracy of procedures while lowering their cost and the cost of the surgical system overall.

Advances in nanotechnology and biomaterials

Advances in nanotechnology have allowed for the development of new and more targeted delivery methods for molecular imaging probes. Using viral vectors, liposome, and other nano-delivery technologies, clinicians will soon be able to administer lower doses of radioactive isotopes while increasing the resolution of certain imaging applications, allowing for the identification and therapeutic radiation of much smaller tumours in cancer therapy.

New molecular imaging probes allow for very precise planning of radiation therapies by limiting radiation exposure to very small, targeted areas. Imaging probes, such as those produced by the Centre for Probe Development and Commercialization in Hamilton, Ontario, are facilitating the development of safer, more efficient

Figure 5 Coil RFA



Source OICR/UHN press release: Coil-RFA—Novel Radio-Frequency Ablation Technology for Treatment of Solid Tumours

therapeutic procedures. Their contribution to this emerging field was recently recognized through a partnership with GE Health care to develop new molecular imaging tools.⁴⁵

Nanotechnology-based delivery methods for MRI and CT contrast agents also promise to improve visualizations for image-guided cardiac procedures, offering more information to the surgeon during the operation. As an example, contrast-enhanced MR imaging significantly improves endoleak detection during and after the endovascular repair of abdominal aortic aneurisms.⁴⁶

Additionally, developments in biomaterials have led to the use of advanced substances in the construction of implantable devices. For example, materials used in the construction of stents and their coatings now work to reduce the rate of stent restenosis, or the repeat narrowing of coronary arteries, post-procedure.⁴⁷

Advances in electrosurgical tools

The number of surgical applications involving the use of lasers is growing and currently includes interstitial laser coagulation, photo-selective vaporization, various tumour ablation procedures, laser-assisted angioplasty, and many other techniques.⁴⁸ Recent advances in laser technology are allowing for the use of more powerful and more portable medical lasers in place of typically more-invasive medical devices.

High-intensity ultrasound is one of the most promising technologies at play in the market for minimally-invasive ablation procedures. The development of high-intensity ultrasound technologies was made possible by the miniaturization of high-energy ultrasound transducers, which enable the delivery of high-energy ultrasound radiation in close proximity to tumours and problem tissues. Clinical applications for this technology include prostate tumour ablation and ablation procedures for atrial fibrillation.

The best-known high-intensity ultrasound devices are High-Intensity Focused Ultrasound (HIFU). HIFU is primarily used in prostate ablation. This technology, developed by Inserm (French Institute of Medical Research) and EDAP TMS in the early 1990s uses a focused ultrasound beam administered through the transrectal wall by a robotic arm. The devices developed by Inserm are currently approved for prostate ablation in the EU and Canada, and are under FDA review in the US.

A slightly different technology was developed by Profound Medical (profiled later in this report). Profound Medical employs an MRI-guided, high-energy ultrasound beam with a number of very small transducers aligned on a probe introduced through the urethra (see Figure 4). This approach differs from HIFU technology since the Profound Medical device does not make use of a focused ultrasound beam.

Another ablative electrosurgical therapy that has recently emerged as a potential alternative to classical invasive procedures is Radio Frequency Ablation (RFA). RFA is a minimally-invasive procedure performed by interventional radiologists. Image-guided, percutaneous RFA induces thermal injury to offending tissues through electromagnetic energy deposition.⁴⁹ It is now considered a feasible treatment option for patients with primary hepatocellular cancer or limited liver metastases. RFA is also seen as a promising technology for the treatment of breast cancer.⁵⁰

In Ontario, Dr. Michael Sherar of the University Health Network is working to develop a coil-based RFA technology (see Figure 5) funded by the Ontario Institute for Cancer Research. This technology is being designed for the minimally-invasive treatment of un-resectable tumours in kidney-, lung-, pancreas- and breast-cancer patients.

Coil-RFA produces a superior thermal profile in tissue, enabling uniform ablation of tumours up to 6 cm in size in one treatment, and provides a minimally-invasive alternative to traditional treatments.

Advances in robotics

Even though surgical robots have been around for the past 20 years, medical robotics remains an emerging field. Only with the recent launch of the DaVinci robotic arm, developed by Intuitive Surgical, has the necessary level of precision and dexterity in medical robotics been achieved to make medical robotics safe and competitive with human-handled instruments. While safety and dexterity are

Attodyne

Attodyne is an early-stage company developing high-performance “picosecond” lasers. Attodyne’s laser technology, developed by professors Dwayne Miller, Michael Cowan, Darren Kraemer and Kresimir Franjic at the University of Toronto, brings ultrafast laser capabilities to precision cutting without mechanical or thermal damage to surrounding tissues. Attodyne’s commercially viable picosecond-pulsed lasers are compact, practical and easy to use, and they have a low-cost design.

In surgery, Attodyne’s lasers have been shown in pre-clinical animal studies to cut with increased precision and to reduce scarring and accelerate healing when compared to conventional lasers as well as to scalpels and other mechanical tools.

Attodyne launched its first line of laser products in early 2010, and is currently selling lasers for research purposes and industrial applications.

Titan Medical

Titan Medical is a Toronto-based company focused on the development and commercialization of robotic surgical technologies. Titan Medical's flagship product is the Amadeus Robotic Surgical System. The Amadeus system incorporates multi-articulating arms, enhanced vision systems, haptic feedback technologies, and advanced communications functionality for unparalleled dexterity, sensitivity, precision, and ability to conduct surgery remotely. The Amadeus surgical platform is in the process of obtaining US regulatory approval from the FDA, with clinical trials planned at UC Davis in 2012. Titan Medical enjoys development partnerships with some of the world's leading robotic engineering and design firms, including CAE and Kuka, as well as with the Canadian telecommunications giant, Bell Canada. Titan Medical is a public company and trades on the TSX Venture Exchange.

clearly important issues in medical robotics, recent advancements in user-interface design and mobility have resulted in a watershed opportunity for robotics in the operating room. Newer robotic surgical systems allow surgeons to perform highly complex surgeries while minimizing blood loss. At present, only 10% of all surgeries are performed using medical robotics. Companies such as Toronto-based Titan Medical, along with the British Columbia research centre, NeuroArm, and Toronto's Hospital for Sick Children, are attempting to accelerate the adoption of robotic surgical systems.

Advances in robotics also provide an important driver for progress in minimally-invasive, image-guided therapies. Dr. Gabor Fichtinger, a professor at Queen's University's School of Computing, is currently working to develop a transrectal, MRI-guided robotic prostate biopsy system, which will allow real-time MRI-guided prostate biopsy using a standard MRI machine. This approach combines the advantages of high-resolution MRI imaging capability with the precision achievable through the use of robotics. The novel use of robotics to perform biopsies inside an MRI unit opens the door for broader and better uses of MRI systems.

In addition to advances in precision and dexterity, improvements in haptic feedback capabilities in surgical robotics are expected to create new opportunities for medical robotics, including applications for remote surgery and surgical training.⁵¹

Clinical opportunities for minimally-invasive medical technologies

Historically, the most successful applications of minimally-invasive medical technologies have been angioplasty and laparoscopic cholecystectomy. By making these treatments more accessible, these procedures led the early market for minimally-invasive devices. Beginning in 1970 and through the early 1980s, the overwhelming success of these technologies, spurred a broader trend toward the practice of minimally-invasive medicine.

In recent years, advances in medical device engineering have created

new clinical opportunities for minimally-invasive medical technologies and made some existing opportunities more attractive, both from an outcome-based and cost-effectiveness perspective.

Today, minimally-invasive medical technologies have a broad range of clinical applications, with cardiothoracic and orthopedic surgery comprising the largest markets overall.⁵²

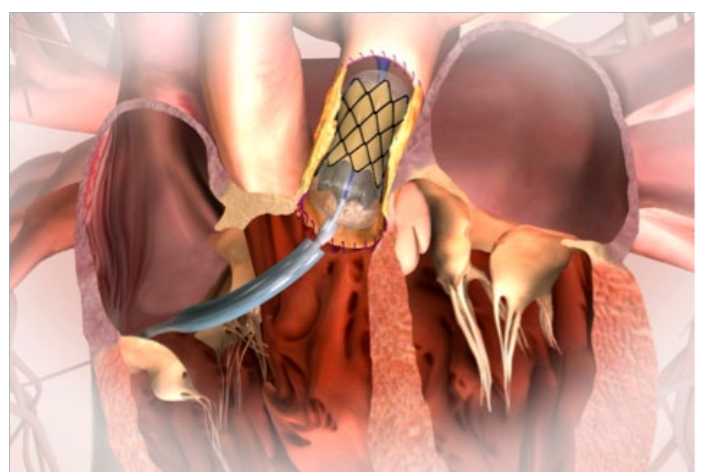
Cardiac applications

The most common minimally-invasive procedures for cardiac surgeries are angioplasty and other catheterization techniques. In the US, there were over 1.4 million catheterization procedures in 2009, by far the largest segment of all cardiac operations.⁵³

In Canada, the number of cardiac revascularization procedures, including angioplasty (with and without vascular stenting) and bypass surgeries, was 52,000 between 2007 and 2008. Adjusted for population growth and aging, this represents a 7% drop from the previous year.⁵⁴ The decrease is attributed to an increasing emphasis on preventative measures and the adoption of minimally-invasive techniques, including the use of drug-eluting stents for cardiac revascularization, as well as a shift away from relatively invasive coronary bypass surgeries toward angioplasty-based interventions.⁵⁵

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder.⁵⁶ Chronic AF is a precursor to a number of pervasive cardiovascular complications, including stroke. Approximately 15% of all strokes are the result of atrial fibrillation, which in severe cases can also cause heart failure. Both the medical community and medical-device manufacturers have begun to focus greater attention on the AF market in recent years.⁵⁷ Exemplifying this trend, Medtronic has recently acquired two AF ablation technology companies, Cryocath Technologies of Quebec, and Ablation Frontiers, based in California.⁵⁸

Figure 6 The insertion and deployment of a transcatheter valve placed via a small incision in the groin (as opposed to a full sternotomy).



Source Image courtesy of Medtronic of Canada

In Ontario, Colibri Technologies, a spin-off from Sunnybrook Health Science Centre, develops next-generation intracardiac echocardiograph catheters for image-guided ablation to treat atrial fibrillation. At the moment, these procedures have a 4% to 6% complication rate and only a 50% to 75% success rate, largely due to inadequate image guidance. Colibri's technology enables high-quality, 3D intracardiac imaging at a dramatically lower price point than any other intracardiac echocardiography (ICE) catheters currently available.

Other minimally-invasive cardiothoracic procedures, including heart valve replacement surgeries, still suffer from low adoption rates in North America. Less than 15% of all heart valve replacements are performed in the US using minimally-invasive technologies, in spite of recent technological advancements in this area.⁵⁹ However, as intraoperative real-time imaging capabilities improve, it is expected to drive broader adoption of minimally-invasive techniques for cardiac surgeries.

Figure 6 shows the insertion and deployment of a transcatheter valve placed via a small incision in the groin (as opposed to a full sternotomy).

Orthopedic applications

Minimally-invasive techniques are also widely used in orthopedic surgery. Arthroscopic surgery is the most common minimally-invasive procedure performed in the US, with over 900,000 surgeries conducted in 2007. Arthroscopic surgeries and arthroplasties have benefited greatly from advancements in computer-guided instruments and surgical robotics. Given the persistently long wait times for hip- and knee-replacement surgeries, opportunities remain

in the field of orthopedic surgery for broader use of minimally-invasive technologies.

Cancer applications

Image-guided, localized radiation therapy and minimally-invasive tumour biopsy procedures are both growing areas in the cancer-related clinical application of minimally-invasive medical technologies. In addition, an area that has profited from recent advances in robotics and computer-guided instruments is urological surgery, where image-guided prostate biopsy and prostatectomy are the most common procedures. At present, an estimated 45% of all prostate biopsy and prostatectomy procedures in the US are performed using minimally-invasive techniques. Industry observers expect that this percentage will continue to increase steadily in the years to come. New image-guided, computer-assisted prostate ablation techniques greatly improve post-surgical outcomes for patients by reducing incidences of impotence and incontinence. These technologies also enhance early tumour detection in the prostate for this aggressive cancer, and provide a more precise and effective means of treating this disease with minimal side effects. These advantages are driving the market for minimally-invasive prostate ablation tools. Profound Medical, based in Toronto, is an innovator in this market.

Centre for Image-Guided Innovation & Therapeutic Intervention (CIGITI)

The CIGITI is a research centre housed at Toronto's Hospital for Sick Children (Sick Kids). The Centre develops image-guided surgical tools and robotics designed specifically for pediatric applications. Today, most designers of medical devices focus on adults, since they account for over 90% of the market. These adult-targeted tools are later redesigned for use on children. Unfortunately, in most cases, scaling medical devices down to child-friendly sizes is not practicable. The tools tend to lose their precision and become less robust.⁶⁸

Dr. Peter Kim and his team at the CIGITI are attempting to design tools that work better in both small and large bodies. By initially focusing on small, tightly constrained environments, the tools developed at CIGITI scale naturally to the larger adult patient. The work at CIGITI revolves around three themes: "smart" surgical tools, integrated real-time imaging and virtual surgical simulation.

The development team is creating KidsArm, a MR-compatible surgical system for pediatric and adult patients. KidsArm integrates image guidance with minimally-invasive surgical tools. This work is being developed in partnership with MDA, Philips and L3 Communications.

The next phase of research and development at CIGITI will focus on the use of disruptive technologies in surgical applications, including dexterous, integrated minimally-invasive surgical tools to increase surgical efficiency. This work includes dexterous endoscopes for fetal intervention and non-invasive high-intensity focused ultrasound for tumour treatments. Private sector partners for these efforts include MDA and Philips.

The final phase of the work is to focus on nanomedicine, developing innovations that leverage the benefits of micro- and nanotechnology for *in situ* imaging and therapeutics. Work is currently underway to investigate technologies using non-Newtonian fluid and nanogel, nanoblades, micro-optical mirror and ultrasound transducers, and nanodroplets and nanobubbles.⁶⁹

In addition to developing advanced medical devices and therapeutics, CIGITI also creates educational materials for doctors and surgeons, including realistic virtual organs and virtual reality-based simulations for surgical training.

Ontario focus

Growth drivers: Strong research base

Robarts Research Institute

With world-class research scientists and over \$10 million worth of imaging and engineering equipment for medical research, Robarts Research Institute's Imaging Research Laboratories (IRL) are a significant driver of innovation in medical imaging.⁶⁰ Robarts has benefited from a local base of expertise in diagnostic imaging, strong engineering competency from the University of Waterloo, and a track record of successful spin-outs including Enhanced Visual Systems (acquired by GE in 2002) and XLR Imaging.

Led by Dr. Terry Peters, the image-guided surgery and therapy program has benefited from significant financial support in the form of grants and other public funding. Dr. Peters and his team recently announced the receipt of a \$6.4 million grant to fund a joint project between Robarts and the Canadian Surgical Technologies & Advanced Robotics program (CSTAR). The project is aimed at developing image-guided, minimally invasive intervention and simulation technologies.⁶¹ The CSTAR program leverages core competencies in research, validation and education to support the development and clinical implementation of emerging medical device technologies. The program is designed to facilitate the efficient translation of new technologies and device knowledge into clinical practice.⁶²

STTARR Innovation Centre

Located in the MaRS Discovery District, the STTARR Innovation Centre is a collaborative effort between Princess Margaret Hospital's Radiation Medicine Program and the University Health Network. STTARR stands for Spatio-Temporal Targeting and Amplification of Radiation Response.⁶³ The STTARR Program provides a platform for cutting-edge multidisciplinary radiotherapy research. STTARR integrates cellular, pre-clinical, computational and human research to maximize the development of effective cancer treatment strategies, including radiation therapy. A key focus at STTARR is to understand how tumours and normal tissue respond to radiation. By leveraging the strong cancer research environment at the UHN, STTARR promotes national and international collaboration in the development of advanced therapeutic approaches to cancer treatment. The Animal Imaging and Precision Radiation Facility, known as CORE II at STTARR, is involved in the development of more effective and less invasive radiation therapies. Work is done at CORE II to identify biological targets of the molecular pathways that influence tumour progression and a patient's response to radiation therapy, linking these targets to the implementation of innovative radiation treatment strategies.⁶⁴

Centre for Research in Image-Guided Therapeutics

In 2008, Sunnybrook Health Sciences Centre was awarded \$75 million in public funding to build and operate the Centre for Research in Image-Guided Therapeutics.⁶⁵ The Centre was founded to develop innovative imaging approaches for the diagnosis and management of cancer, heart disease, stroke, musculoskeletal disorders, and other medical conditions. While scheduled for completion in 2011, projects already underway include the development of an inverted HIFU device guided by MRI to enable doctors to operate without

breaking the skin, and the development of a method to apply focused ultrasound to the brain, guided by MRI, to temporarily disrupt the blood-brain barrier and permit the delivery of drugs, genes and antibodies to the brain.

Centre for Image-Guided Innovation & Therapeutic Intervention (CIGITI)

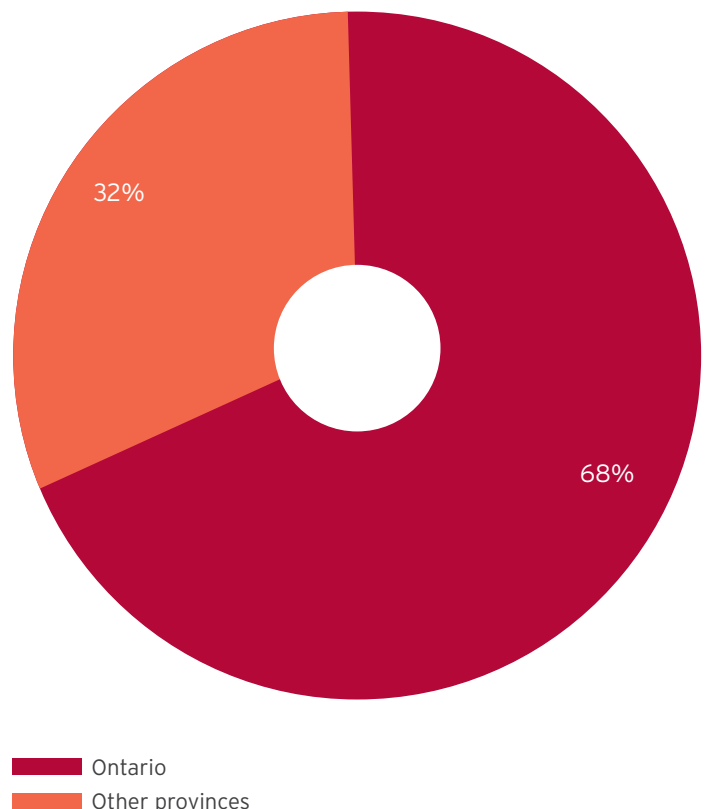
Based in Toronto, the CIGITI brings together surgeons, engineers and software developers from universities and the private sector to develop innovative technologies applicable to robotic and minimally-invasive surgery. CIGITI is divided into three research themes: imaging, robotics and simulation. The Centre has been awarded over \$20 million in public funding for projects with its industrial collaborators, Philips, MDA and L-3 Communications.⁶⁶ The Centre is set to continue work to develop the KidsArm robotic surgical system, the first robotic surgical arm designed for pediatric surgery. KidsArm will be capable of working in small and delicate spaces, under supervised image guidance, offering enhanced dexterity and precision and resulting in time-savings both in surgery and treatment.⁶⁷

The Perk Lab—Laboratory for Percutaneous Surgery

Located at Queen's University, the Perk Lab focuses on developing enabling technologies for image-guided percutaneous and intra-

Figure 7

Proportion of active clinical trials for minimally-invasive medical technologies in Ontario.



Source clinicaltrials.gov⁷⁷

cavity procedures.⁷⁰ Current work includes the development of an MRI-based robot able to detect and treat prostate cancer.⁷¹

Thunder Bay Regional Research Institute (TBRI)

Founded in 2008, the primary research focus of the TBRI is cancer research. Scientists and clinicians work with industry and academic partners to develop tools to bring molecular imaging and advanced diagnostic technologies to the patient. Research centres around three core themes: image-guided interventions, advanced detection devices and biomarker exploration.⁷²

Public research funding

Ten thousand scientists, clinical investigators and other researchers in Ontario conduct \$850 million of medical research each year across 25 research and academic hospitals.⁷³ Ontario is the largest hub of biomedical activity in Canada and the fourth-largest in North America.⁷⁴ Ontario's Ministry of Research and Innovation provides much of the public research funding in the province, through programs administered by organizations such as the Ontario Institute of Cancer Research and the Health Technology Exchange. Federally, public funding is available through the Canadian Institutes of Health Research, The National Research Council's Industrial Research Assistance Program, and Canada Foundation for Innovation.

Ontario Research Fund (ORF)

The Ontario Research Fund is part of the provincial government's plan to promote scientific excellence by supporting research that can be developed into innovative goods and services that will boost Ontario's economy. Through a commitment of \$730 million over four years, the province is providing leading Ontario researchers with support to undertake cutting-edge research.⁷⁵ Funding from the ORF is conditional upon equal participation of both private-sector partners and the research institutions themselves. As part of the ORF Research Excellence stream, two important projects related to the development of minimally-invasive medical technologies have received funding. One is a project led by Dr. David Jaffray to develop a way to adapt cancer radiation treatment to the individual. Private-sector partners involved in this project include Eigen, Elekta AB and RaySearch Laboratories. The other is a grant provided to the Thunder Bay Regional Research Institute to support work to develop molecular imaging tools for cancer patients. Private-sector partners for this initiative include Philips Health care, ANRAD Corporation and Sentinelle Medical Inc. By involving partners from the private sector in these research projects, the ORF is creating a ready avenue for developing world-class medical research into commercially viable products and services.

MaRS Innovation

In a unique partnership supported by the Government of Canada through the Networks of Centres of Excellence, BioDiscovery Toronto, and the MaRS Discovery District, MaRS Innovation is focused on advancing the commercialization of research by leveraging industry relationships, licensing and company-creation expertise.⁷⁶ MaRS Innovation is the result of a collaborative effort among 14 academic and research institutions to centralize the administration of support services aimed at commercializing intellectual property generated from scientific research.

Ontario Institute for Cancer Research (OICR)

The OICR is dedicated to research in the prevention, early detection, diagnosis and treatment of cancer. The Institute is an independent not-for-profit corporation funded by the Government of Ontario through the Ministry of Research and Innovation. The OICR facilitates research, provides funding opportunities, commercialization support and other incentives for the discovery and development of life-saving cancer therapies. The Institute supports the work of more than 50 internationally-recognized principal investigators in their research efforts. One of these researchers is Dr. Kullervo Hynynen, working out of Sunnybrook Health Sciences Centre. Dr. Hynynen is currently involved with the development of a low-cost, portable ultrasound-guided, focused ultrasound surgery system for tumour treatment. The system has significant cost advantages over comparable MRI-guided technology, while also allowing for reduced treatment time and superior exposure control, reducing the risk of over- or under-treating tumours. This is just one example of an array of research and technology development projects being conducted with the support of the OICR.

Health Technology Exchange (HTX)

HTX supports emerging and established Ontario-based companies as they develop, produce and commercialize innovative and market-leading medical and assistive technologies, including medical devices, diagnostic and imaging applications, and other technologies. HTX provides both funding and support services to early-stage medical technology companies. Funding programs focus on product development, clinical validation, technology assessment and procurement, and market development activities. Support services include assistance with regulatory issues, clinical evaluations, introductions to funding agencies and private investment sources, industry linkages, market intelligence, and the development of marketing and distribution channels. Many of Ontario's minimally-invasive medical technology start-ups work closely with HTX to develop and commercialize their innovations.

Favourable clinical trial environment for new medical technologies

With world-class clinical investigators and clinical trial facilities in Ontario, medical-device companies are able to access top-calibre clinical-research resources in the province. A large number of minimally-invasive medical device companies currently conduct clinical trials in Ontario. Figure 7 illustrates the extent of clinical-trials activity in the province.

According to clinicaltrials.gov data, over 68% of the 74 clinical trials for minimally-invasive devices initiated in Canada in 2009 were located in Ontario. In addition, Ontario was the preferred location for 8 of the 12 industry-sponsored MIS clinical trials initiated in 2009 in Canada.

Tax incentives

Canada's tax incentives for research and development activities are among the most generous in the G7 countries. Ontario companies may take advantage of the federal Scientific Research and Experimental Development (SR&ED) refundable tax credit, as well as an additional Ontario tax credit layered onto the same program. This amounts to a refund worth over 41% of eligible R&D expenditures in

Ontario. For pre-clinical research, companies that have a permanent establishment in Ontario are eligible for the Ontario Business Research Institute Tax Credit. This refundable tax credit is equivalent to up to 20% of eligible pre-clinical research expenditures.

Ontario's favourable tax environment has created opportunities for the growth of a vibrant pharmaceutical and biotechnology industry in Ontario. Ontario is home to approximately 50% of Canada's pharmaceutical and biotech companies, and approximately 60% of Canada's medical-device companies. All told, over 800 life-sciences companies in Ontario employ an estimated 40,000 people and generate more than \$10.7 billion in annual revenue.⁷⁸

Legislative commitment to health-care innovation in Canada

In 2004, Canada held a First Minister's Meeting on the Future of Health Care. This meeting resulted in the adoption of a ten-year plan emphasizing investment in health-system innovation through science, technology and research.⁷⁹ As a consequence, the demand for minimally-invasive diagnostic and patient monitoring equipment has risen substantially over the past four years. This trend is expected to continue through 2010.

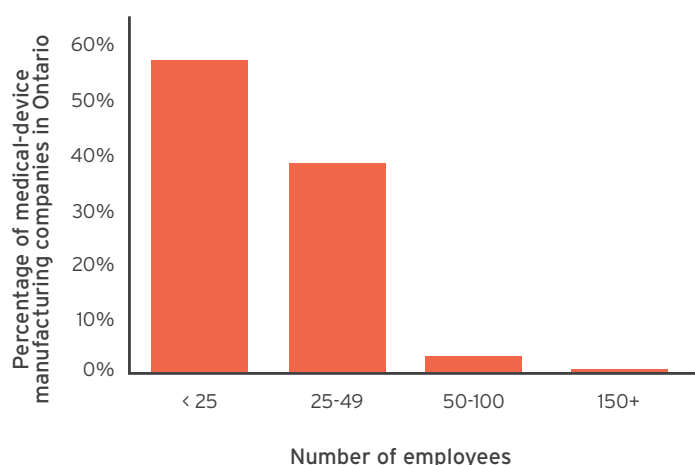
Growth challenges

Lack of established players in Ontario

While the legislative, regulatory and tax environments in Ontario make the province a fertile ground for commercializing minimally-invasive medical technologies, challenges remain. One of the chief difficulties in bringing new minimally-invasive medical technologies to market in Ontario is the lack of a substantial medical-device manufacturing and development capacity. Device development and manufacturing facilities are generally small in size, with the majority of firms (57%) employing fewer than 25 staff.⁸⁰ Figure 8 illustrates the percentage of Ontario medical device manufacturing companies by the number of their employees.

Figure 8

Percentage of Ontario medical-device manufacturing companies by employment.



Source Canadian Medical Device Industry Profile⁸¹

Less than 1% of all Ontario medical-device companies employ more than 150 people.⁸² In addition, none of the world's largest medical-device companies have a significant manufacturing presence in Ontario.⁸³

Fragmented reimbursement system and unclear technology assessment procedures

Another challenge to the successful commercialization of minimally-invasive medical technologies in Ontario is the complex reimbursement scheme for patient health-care expenditures. In Canada, medical coverage decisions for differing medical technologies are made at the provincial level. As a result, coverage standards differ significantly from province to province, making the Canadian market less attractive for new medical technology commercialization.⁸⁴

In Ontario, there are no established rules for submitting a particular medical technology for consideration to become a reimbursable patient health-care expense. The decision process for creating a reimbursement category for new medical technologies lacks transparency.⁸⁵

A complex regulatory system

The Canadian regulatory environment for the commercialization of medical devices is a hybrid of both the US and European models. While the system leverages the best elements of each model to ensure the safety of the medical-device market in Canada, this also has the consequence of making the regulatory process more difficult to navigate and less transparent.⁸⁶

In the US, the FDA currently makes use of a two-tiered approval system for minimally-invasive medical technologies. First, companies must undergo a pre-market notification process involving either a 510(k) submission for lower-risk devices (class I and class II), or a pre-market approval process for higher-risk (class III) devices (such as implantable devices and novel surgical tools). The majority of minimally-invasive medical devices require pre-market approval. This tends to be costly, lengthy and complex. Still, the US is and will remain the most attractive market for medical devices due to its size and its clear, transparent product market approval process.^{87, 88} Also, since the FDA's approval process is engaged in assessing new medical technologies from an early stage of development, it reduces the uncertainty of whether a device will be approved later on, and it increases the chances of approval in other markets as well.

In the European Union (EU), medical device approvals are conducted by the Notified Bodies (NB), which are third-party, private entities accredited by a member State to assess product compliance with certain established standards. The NB reviews technical files and performs periodic compliance inspections. Once the NB designates that a medical device conforms to the EU Medical Device Directive, the manufacturer can then label the product with the *Conformité Européenne* (CE) mark. This system has resulted in a rapid approval process; however, it places greater emphasis on device safety than on efficacy.⁸⁹

The Canadian regulatory process for medical device approvals takes a risk-based approach when assessing new medical technologies.⁹⁰

While Canada's approvals system offers superior risk-control over the US system and places greater emphasis on efficacy reviews for high-risk devices than does the EU, the submission requirements of Health Canada has made the Canadian market less attractive for new entrants. Our conversation with key players in this market suggests that this has led to a reduction in the number of new and more effective medical technologies available in Canada. Health Canada's Medical Device Special Access Programme was implemented as a partial solution to the problem. The Programme provides access in emergency cases to medical devices that have not yet been approved for sale in Canada or when conventional therapies have failed or are unsuitable. Unfortunately this has placed an additional administrative burden on a regulatory system that is already under considerable strain.^{91, 92}

Health-care funding constraints

Two decades ago, 32 cents out of every dollar of Ontario government program spending went to health-care expenditures in the province. In 2010, this figure is expected to reach 46 cents per dollar of program spending. Representatives at Ontario Finance speculate that by 2022, when the oldest members of the baby-boom cohort reach the age of 75, the costs associated with health care could reach 70% of program spending.⁹³ While support for hospitals, physicians and drug purchases (65%) represents the bulk of this spending, a substantial portion (16%) flows to capital purchases such as the acquisition of new medical technologies.⁹⁴

A recently approved Ontario budget is attempting to rein in health-care spending. The budget endorsed an increase of only 1.5% in base funding for hospitals, a rate of increase that is below current inflation. With constrained base funding, Ontario's hospitals will be forced to rationalize their investments in new medical technologies, focusing on cost control and operational improvements. For capital-intensive medical technologies that require spending approval

from hospital CEOs, this presents a significant hurdle to winning customers. According to Neil Fraser, President of Medtronic of Canada, *"hospitals do not adjust or get adjustments in their budgets for new technology very often."* Companies offering expensive, image-guided technologies will face a particular challenge in selling to hospital customers. Companies with minimally-invasive medical technologies who wish to break into this budget-constrained market must prove that their solution is cost-effective on a per-patient basis in order to obtain reimbursement approval. These companies must also persuade hospital buyers that their technologies will have sufficient longevity to recoup the hospital's original investment.

Comparatively small executive talent pool

A final difficulty in commercializing minimally-invasive medical technologies developed in Ontario is a relative dearth of experienced executives. In the US, minimally-invasive medical device start-ups are generally led by former senior executives recruited from industry-leading medical device manufacturers. Ontario does not have a similar pool of experienced executive talent from which to draw.

Company profiles

While challenges remain on the path to commercializing minimally-invasive medical technologies, this is a market poised for significant growth. Driving factors include technological progress, legislative and popular support, expanding clinical opportunities, and an increasing body of evidence that attests to long-term cost reductions and superior clinical outcomes associated with the use of these technologies. Ontario companies are uniquely positioned to take advantage of these opportunities and are supported by a strong provincial research base, aggressive funding programs and tax incentives, and a legislative commitment to foster medical technology leadership in the province and beyond.

Profound Medical

Profound Medical is a medical-device start-up spun out of Sunnybrook's world-class Imaging Research Group. Founded in June of 2008, the company has developed a novel, minimally-invasive medical device for the targeted treatment of prostate cancer. Profound Medical's innovation is an interventional, MRI-guided, trans-urethral thermal ultrasound ablation device that targets and eliminates prostate-cancer tumours with unmatched precision and without the need for invasive surgery.

Prostate cancer is the most common cancer among men, with approximately 25,000 new cases diagnosed in Canada each year. While surgery and radiation are viable treatment alternatives, these techniques are often associated with impotence or incontinence as well as damage to surrounding nerves and tissues.

"There is a huge emotional and psychological price to pay for the inability to treat prostate cancer successfully without side effects," says Paul Chipperton, CEO of Profound Medical.

Pre-clinical data show convincingly that Profound Medical's technology can achieve greater accuracy, precision and treatment speed than approved alternatives already on the market. If development and testing in human clinical trials mirrors that of the pre-clinical, there is the potential to dramatically decrease the risk of devastating side effects. In Chipperton's words, *"we have a long way to go, but there is the potential to change the face of prostate-cancer treatment."*

Chipperton and his team have met with representatives of the US Food and Drug Administration for approval of their plans to run their first

set of clinical trials. The company's products need to obtain regulatory approval in the US and a number of other jurisdictions, but the expected thirty-minute, non-invasive procedure could be available in as little as two years for some markets, available to patients diagnosed with medium- to low-risk prostate cancers—a group that represents approximately 84% of all those diagnosed with prostate cancer.

In May of 2010, Profound Medical participated in a trade mission to promote technology co-operation between Canada and Israel. As a result of this trip, Profound Medical announced that they have penned a technology and commercial development deal with Israel-based micro-motor manufacturer, Nanomotion. Nanomotion was selected as the company's lead supplier for a number of key parts for the production of Profound Medical's devices in time for the company's upcoming clinical trials.

Profound Medical also made headlines when the company was awarded the \$200,000 Premier's Catalyst Award for the Ontario start-up company with the best innovation. The award recognizes innovative Ontario companies whose technologies are likely to have a positive impact on society as well as the economy by creating jobs and addressing key issues that affect Canadians.

For everyone affected by prostate cancer in North America, Profound Medical's breakthrough technology is a long-awaited leap forward in the battle against this debilitating disease.

Colibri Technologies

Colibri Technologies is a medical-device start-up company seeking to develop image-guidance tools for several minimally-invasive cardiovascular procedures, such as atrial fibrillation ablation, percutaneous valve replacement, chronic total occlusions, and several other growing and emerging applications. Colibri's innovative ultrasound and optical imaging guiding catheters are directed toward making a number of minimally-invasive procedures safer, faster, easier and less expensive. Furthermore, Colibri's catheters will reduce the amount of x-ray radiation to which patients, physicians and other health-care members are exposed while potentially improving procedural and long-term success rates.

The company was founded by Dr. Brian Courtney and several other physicians and researchers at Sunnybrook Health Sciences Centre. The founding team comprises four physicians and a large number of well-respected researchers in imaging sciences. The company has a strong intellectual property portfolio, an experienced board of directors and a growing team of employees that are passionate about the company's mission to have a positive impact on patient care.

Colibri's technology enables high-quality, 3D intracardiac imaging at a dramatically lower price point than the 2D ICE catheters currently used by the majority of physicians. Dr. Courtney expects that the new catheters will go into production in 2012. He is currently seeking investment to drive product development and clinical trials. Colibri's next-generation intracardiac echocardiograph catheters (ICE) enable image-guided ablation for the treatment of atrial fibrillation. At the moment, these procedures have a 4% to 6% complication rate and only a 50% to 75% success rate, partly due to inadequate image guidance. Over the longer term, Dr. Courtney envisions a host of future applications using his catheter-based imaging innovation as a platform technology.

Colibri is in the process of perfecting its ICE technology for clinical use. Following a successful technology development phase, the team will build a direct sales force, leveraging relationships built during the product development process.

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