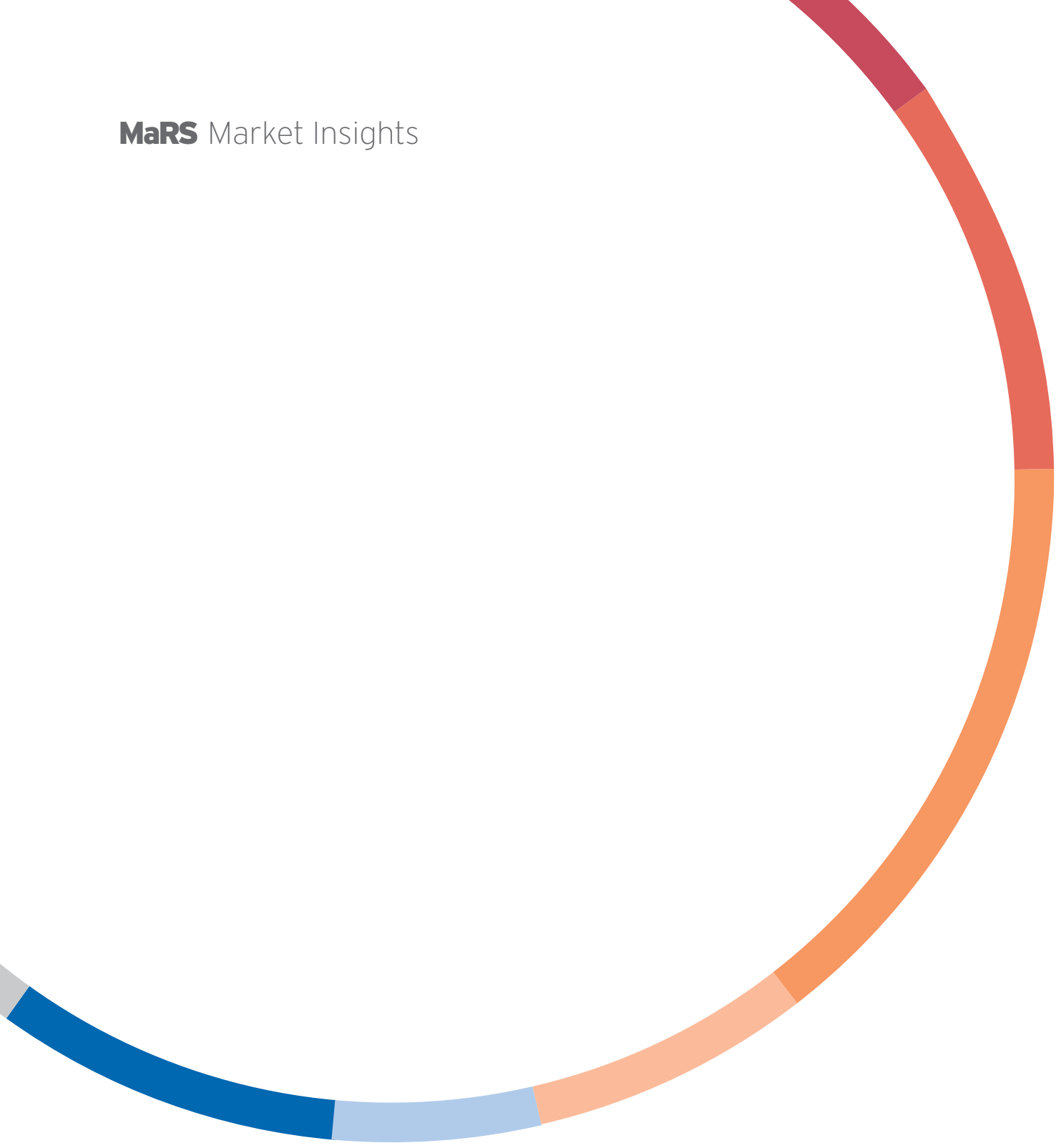
MaRS Market Insights



Life Sciences

A Bright Future for Diagnostic Imaging in Ontario

Acknowledgments

We would like to express our gratitude to the many executives, organizations, institutions and researchers who contributed to this paper. Particular thanks are due to John MacRitchie, John Fielding and Marc Nantel of the Ontario Centres of Excellence; Dr. Kullervo Hynynen and Dr. Gregory Czarnota of Sunnybrook Research Institute; Dr. Kieran Murphy at the University Health Network; Dr. Aaron Fenster of Robarts Research Institute; and Dr. John Valliant of McMaster University's Centre for Probe Development and Commercialization.

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Acronyms

CAD—Computer-Aided Detection

CAT/CT—Computed Axial Tomography

CTA—Computed Tomography Angiography

CAGR—Cumulative Annual Growth Rate

DICOM—Digital Imaging and Communications in Medicine

fMRI—Functional Magnetic Resonance Imaging

IHE—Integrating the Health-care Enterprise

MRI—Magnetic Resonance Imaging

MR—Magnetic Resonance

OEM—Original Equipment Manufacturer

PACS—Picture Archiving and Communication System

PHAST—Photoacoustic Scanning Tomography

PET—Positron Emission Tomography

RIS—Radiology Information System

SPECT—Single Photon Emission Computed Tomography

RF—Radio Frequency

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Introduction

Research programs at Ontario's hospitals and universities are turning out some of the world's brightest minds in biophysics, engineering and medicine. These successes make Ontario home to a host of innovative thought leaders in medical imaging. Anchored by world-class research institutes and funding for collaborative partnerships, the Ontario medical imaging community is a dynamic centre for imaging innovation in North America.

This paper focuses on diagnostic imaging and the Ontario-grown companies that are breaking new ground to bring cutting-edge imaging capabilities to the world.

Diagnostic imaging is a subset of medical imaging dealing with "the use of X-ray, ultrasound, radioactive isotopes and magnetic resonance to produce a visual display or representation of structural and functional information of the inside of the human body."[1] This report concentrates on diagnostic imaging modalities* and accompanying software tools. In particular, we look at:

- **ionizing radiation** (X-ray, computed axial tomography and nuclear imaging, including positron emission tomography and single-photon emission computerized tomography)
- **non-ionizing radiation** (including magnetic resonance imaging, ultrasound and infrared)
- **software packages** such as Radiology Information Systems (RIS), Picture Archiving Communication Software (PACS), computer-aided detection (CAD)/ image analysis tools and workflow optimization applications

Canadian clinicians and researchers have long been leaders in the field of diagnostic imaging. Physics professor John Cox of McGill University was one of the first to use the X-ray in a clinical setting. In 1881, the professor used a makeshift X-ray machine to locate a bullet in the leg of a man who had been shot. Using the radiograph as a guide, the man's doctor was able to extract the bullet and help convict the shooter.

Today, diagnostic imaging has many clinical applications. The technology is used to guide clinicians and researchers in the fields of cardiology, oncology and neurology, as well as musculoskeletal imaging, ophthalmology, dermatology and dentistry.

Drivers of growth in diagnostic imaging

The health-care environment

The combined effects of an aging population, the increasing incidence of chronic disease and the current economic downturn have caused public health-care costs to skyrocket in recent years. This trend is projected to continue.

The US

In the US, it is expected that 20% of the country's GDP will be spent on health care by 2017.[2] It is widely recognized that programs such as Medicare and Medicaid run the risk of facing bankruptcy in the coming decade. The management of health-care costs is therefore a matter of heated political debate south of the border.

Canada

In Canada, an increasing emphasis on reducing wait times is driving demand for improved imaging equipment and software. Canada's Wait Time Reduction program was implemented in 2004 by the federal government. As part of the 10-year, $41 billion federal Action Plan on Health, $4.5 billion was allocated to the Wait Times Reduction Fund, to be spent on wait time reduction initiatives between 2005 and 2010.[3] This spending has resulted in an increase in diagnostic imaging capacity and a marked reduction in average wait times for MRI and CT-based diagnostic imaging procedures.[4, 5]

Emerging markets

Improving regulatory efficiency in emerging markets is driving the development and adoption of more advanced imaging technologies. In early November 2009, China took an additional step toward streamlining medical device regulation in the world's most populous country. At a meeting of the US-China Joint Commission on Commerce and Trade in Hangzhou, China, announced that it will no longer require companies to register products in the country of export as a condition of registration in China. Instead it will accept product registration documents issued by any foreign country. Chinese regulators will also take a risk-based approach to clinical trials. For certain classes of medical devices, Chinese officials will take into account the results of trials conducted outside of China, rather than requiring that all trials take place domestically. The easing and streamlining of regulatory approvals in

* Imaging modality: Any of the various types of equipment or probes used to acquire images of the body, such as radiography, ultrasound and magnetic resonance imaging.

China may pave the way for a more rapid trials process and earlier adoption in a major Asian market. This may provide early validation and needed revenues for imaging companies hoping to break into North America.

Ontario focus

Growth drivers in Ontario's diagnostic imaging sector

STRONG RESEARCH BASE AND LEADING RESEARCH INSTITUTES

Diagnostic imaging companies and researchers in Ontario specialize in developing imaging technologies in a number of areas. Foremost is the development of image analysis, processing, segmentation and CAD applications. Ontario also has a strong research and commercial base in performance improvement solutions for imaging hardware and software, as well as in developing the PACS II platform. Another area of interest for Ontario researchers and imaging start-ups is the use of optical technology to replace MRI. Ontario companies have a strong showing in MR technologies and there is a great deal of activity and interest in the image-guided surgery segment.

Underpinning Ontario's strong research output in medical imaging are a number of world-class research institutes, including Sunnybrook Research Institute, the University Health Network (UHN), the London hub—Lawson Health Research Institute, Robarts Research Institute and the University of Western Ontario (UWO), and the Ottawa Medical Physics Institute. The University of Toronto, Baycrest Research Centre and McMaster University also have strong research programs in medical imaging.

Sunnybrook Research Institute

At Sunnybrook, research is focused on ultrasound, MRI, digital mammography, X-ray and optical PET imaging.[6] Sunnybrook has established fruitful partnerships with GE Medical Systems, Philips, Kodak and Anrad. The institute has had several successful spin-outs including Sentinelle and VisualSonics Inc.

University Health Network

The UHN employs 500 medical imaging staff and with a multi-million dollar fleet of imaging equipment, runs the largest radiology training program in the world. The organization has relationships with the four major imaging OEMs, as well as with several leading therapeutic device manufacturers.

Lawson Health Research Institute

Lawson researchers partner with a host of leading corporate and governmental players to develop new imaging technologies. With 33 dedicated researchers, eight patents issued and three successful spin-outs, Lawson specializes in hybrid imaging and biomedical imaging. Lawson researchers hope to leverage the latest developments in nanotechnology, artificial intelligence and molecular biology to develop leading-edge mechanisms of disease identification and personalized medicine.

Baycrest Research Centre for Aging and the Brain

Baycrest brings together researchers at the Rotman Research Institute and the Kunin-Lunenfeld Applied Research Unit for patient-focused collaborations to develop new modes of diagnosis and treatment for neurological and age-related disease.

Robarts Research Institute

Robarts has a long history of innovation, invention, commercialization, and entrepreneurial success in medical imaging. Robarts' imaging group has licensed technology to eight different companies. Over the past seven years, Robarts' imaging group has been awarded 33 patents with another seven pending. Using X-ray, ultrasound, CT and MRI, Robarts' imaging group conducts research across nine broad themes, including cancer, cardiovascular imaging, respiratory imaging, brain and mind imaging, musculoskeletal imaging and other non-diagnostic imaging disciplines.

Examples of successful spin-outs from Robarts' imaging group include XLR Imaging, Enhanced Vision Systems (acquired by GE Healthcare) and Atamai.

University of Western Ontario

Through UWO's Medical Physics Program, researchers have an opportunity to specialize in intensity modulated arc therapy, field-cycled magnetic resonance imaging (MRI), non-invasive imaging and flow visualization ultrasound techniques. Members of UWO's Department of Medical Biophysics stand out as leaders in medical imaging, cellular biophysics and cancer radiotherapy,

while engineers in the Biomedical Systems Research Group have significantly advanced areas such as image-guided prostate therapy and neurosurgery. UWO has also established a Biomedical Engineering Graduate Program to train the next generation of world-class biomedical engineering experts.

University of Toronto

The Department of Medical Imaging at the University of Toronto is the largest in Canada.[7] The department employs 150 full-time faculty members based in six teaching hospitals.[8] The University of Toronto's Medical Imaging department specializes in abdominal imaging, breast imaging, cardiothoracic imaging, musculoskeletal imaging, neuroradiology, nuclear medicine, pediatric imaging, and vascular and interventional radiology.[9] The university offers Royal College accredited programs in radiology and nuclear medicine, with subspecialties in neuroradiology and pediatric radiology.[10] Affiliated with the University of Toronto, the Centre for Addiction and Mental Health (CAMH) is Canada's largest addiction and mental health teaching hospital. CAMH conducts imaging-assisted research in the areas of PET brain function mapping and neuroscience. The University of Toronto also runs distinguished programs in computer science, recently ranked eighth in the world by Shanghai Jiao Tong University's Academic Ranking of World Universities.[11]

McMaster University

Located at McMaster University, the Centre for Probe Development and Commercialization (CPDC) is an Ontario Ministry of Research and Innovation Centre of Excellence for Commercialization and Research. The CPDC is the world's first facility focused on the development of molecular imaging probes (chemical compounds that provide a non-invasive means to diagnose disease at its earliest stages).[12] The CPDC has experts in regulatory affairs and has established strong industry partnerships to accelerate commercialization of new technologies. The CPDC receives federal funding through the Networks of Centres of Excellence program and is also supported by national and international partners.

Queen's University

The Department of Physics at Queen's University is one of the leading physical research institutes in Canada. The Condensed Matter Physics & Optics research subgroup at Queen's is leveraging a growing strength in optics research and light-matter interactions in optical materials and nanostructures. They cover a range of research topics including quantum optics, nanophotonics, spintronics, organic LEDs, scanning probes, and ultrafast nonlinear optics. The Engineering and Applied Physics subgroup is conducting groundbreaking experimental research in the fields of photonics, quantum information technology, medical physics, non-destructive evaluation, materials physics, electronic device physics, and plasma physics. The department's efforts in medical imaging include investigations into high-frequency ultrasound, 3D real-time ultrasound, optical coherence tomography, low-energy computed tomography and cancer radiation dosimetry.

TALENT

As evidenced by the number of successful spin-outs emerging from Ontario's imaging research institutes, these centres are a catalyst for entrepreneurial ventures. Similarly, the local presence of Merge Healthcare, a provider of imaging software solutions, has generated a pool of talented imaging software specialists in Ontario.

COLLABORATION

According to interviews conducted with the UHN, researchers at Sunnybrook and UWO, and representatives of the Ontario Centres of Excellence (OCE), Ontario clinicians and researchers make a practice of partnering for extremely fruitful collaboration. This willingness to collaborate distinguishes the Ontario diagnostic imaging community from other imaging research locations.

Dr. Kullervo Hynynen, Senior Scientist at Sunnybrook Research Institute and seasoned entrepreneur, notes that the time-pressed and revenue-focused clinical culture in the US makes developing new products in Canada significantly more attractive. For Dr. Hynynen, it's a matter of reaching more patients with better care: "I have always worked with companies. I see that that's the only way to get the technology to all the hospitals. Why do the research if you are not willing to help make a product so that it benefits people?"

Dr. John Valliant, Scientific Director and CEO of the CPDC, points out that collaboration across research disciplines is also very strong in Ontario, particularly compared to the US.

Going forward, many agree that researchers at Ontario universities with strong computer science programs will have a growing opportunity to collaborate more closely with those in the medical field to develop high-powered medical image processing and analysis applications. Research programs in applied mathematics at the University of Waterloo have recently turned out the core technologies behind two new imaging software start-ups, Segasist and Client Outlook, highlighted later in this report.

PUBLIC FUNDING

The Ontario government is an active partner in the growth of the Ontario medical imaging cluster. Several organizations support academic research and industry–academic collaboration, including the Ontario Institute of Cancer Research, the OCE, which includes the CPDC and others, and the Ontario Ministry of Research and Innovation, which funds medical imaging researchers and associated start-ups. Htx.ca – The Health Technology Exchange, also funded by the ministry, supports small and medium enterprises partnering with public research institutions for clinical validation and other commercialization efforts.

Progressive policies on the part of academic funding agencies make Ontario home to a number of imaging consortia drawing together cross-disciplinary imaging expertise to leverage directed research opportunities and combined grant applications. The Behavioural Research and Imaging Network (BRAIN) is a neuroimaging consortium anchored by the Rotman Research Institute and Baycrest. The Ontario Consortium for Cardiac Imaging is an Ontario-wide effort to coordinate cardiac imaging research across all imaging modalities.

In essence, these networks were created to bridge gaps between basic imaging research and clinical imaging applications in defined medical areas (e.g., circulatory and respiratory sciences). Their main objective is to evaluate the benefits, harms and cost-effectiveness of existing and novel imaging technologies for use in various clinical applications.

Growth challenges

Looking ahead to the future growth of Ontario's diagnostic imaging cluster, domain experts and those at several of Ontario's successful imaging companies agree that certain challenges remain.

INDUSTRY ANCHORS

The lack of a global medical device original equipment manufacturer (OEM) in Ontario presents a challenge for local imaging equipment companies seeking to reach the world market. The establishment of an imaging research or manufacturing division by GE, Philips, Siemens or other major imaging equipment OEM in Ontario would create an easier path for sales and distribution partnerships. Although these partnerships do occur, without a company to do for medical imaging what RIM did to catalyze innovation and market activity in Ontario's mobile communications industry, Ontario's imaging equipment sector must grow in slow stages.

With regard to imaging software, Ontario benefits from the presence of Merge Healthcare (formerly Cedara), and AGFA Healthcare. These two companies act as anchors for the local medical imaging software segment and have resulted in several spin-off companies. They have also encouraged the growth of a highly skilled workforce in medical imaging and software development.

CLINICAL TRIALS AND REGULATION

Burdensome and costly clinical trials processes prevent Ontario companies from reaching the stage of development necessary to attract the interest of major OEMs. According to a senior executive at GE Healthcare, the onerous clinical trials process in Canada caused GE to shutter many of its local operations. "We used to do a lot of clinical trials in Canada. In the past years, because of government restrictions, we've done virtually none. In Canada, clinical trials have to happen almost after a product is launched. For medical imaging equipment, trials should ideally take place one or two years prior to launch. Because of Canada's regulatory restrictions, it is increasingly difficult to conduct early-stage trials and develop partnerships with local start-ups early on."

With the importance that imaging OEMs place on clinical results, Canada's clinical trial and regulatory processes hinder the development of early-stage imaging companies. According to a former executive at AGFA Healthcare, the regulatory environment is a key frustration when bringing new imaging technology to the Canadian market. "Even if it's been approved for clinical use in other markets, technology has to be re-approved by Health Canada. That's a process that can take many months, maybe even years. [...] Regulation may not stop a technology dead in its tracks but it can certainly limit the penetration and

growth. PET scanning has been in clinical use in other countries for nine years, but until this October regulatory bodies had not approved marker chemicals for use in the scans. Ontario was one of the last provinces to make PET imaging reimbursable."

Similarly, Dr. John Valliant, Scientific Director and CEO of the CPDC, feels that a broad clinical trials network is key to supporting imaging research produced in Ontario. "I think we need to develop a clinical trials network where physicians have an incentive to get involved. Clinical trials are at the heart of getting this stuff out to market." As an example of the potential power of a strong clinical trials network, Dr. Valliant points to the case of the Ontario Clinical Oncology PET Trials run by the Ontario Clinical Oncology Group. The broad-based trials are serving to evaluate the sensitivity of PET scanning to a number of different cancers in order to outline the role for PET cancer scanning in Ontario.

INCENTIVE MISALIGNMENT AND INADEQUATE IMAGING INFRASTRUCTURE

In the US, hospital income derives from insurance claims and is linked to patient diagnosis. Different diagnoses lead to different fixed-fee compensation rates by insurers. US hospitals must therefore manage resources carefully and limit unnecessary procedures, including diagnostic scans. On the other hand, US hospitals compete for patient flow and often use star doctors and leading-edge technologies to draw patients. In addition, treatment of diagnostic imaging procedures is very different outside hospitals in the US. Non-hospital doctors and clinics are compensated on a fee-for-service model and are therefore not financially motivated to limit patient procedures, resulting in a culture of "over testing." In this culture, patients often demand tests and scans they perceive to be of high value. In addition, doctors practising "defensive medicine" may order a battery of tests and scans that are medically unnecessary. And with the increasing complexity of new imaging technologies, doctors themselves may not fully understand which tests are relevant or appropriate.

Analysts estimate that up to one-third of all patient medical imaging in the US is wasted or unnecessary. Compared to Canada, US hospitals and clinics invest more heavily in medical imaging equipment, pay more per procedure, and in many cases may yield a better return on investment for medical imaging ventures. However, these advantages may be short-lived. Radiology applications represent a $100 billion cost to the US health-care system, and health insurers in the US are actively seeking ways to correct issues of overspending on imaging.
In Canada, hospitals receive funding from the government based on performance. Physicians, on the other hand, are reimbursed according to a pay-per-procedure plan. Aside from prestige, Canadian doctors generally receive no return on the time they invest to learn new technologies.[13] This creates a disincentive among Canadian practitioners to explore and make use of new innovations in medical imaging.

Compared to the US market, Ontario also lacks sufficient imaging infrastructure to test and use the technology developed by local companies and researchers. The US has seen a much greater investment in medical imaging clinics, and also makes use of more advanced imaging technologies. In particular, Ontario lags far behind in the clinical use of PET, and continues to lack widespread access to medical imaging.

REFERENCE INSTALLATIONS AND PROCUREMENT COORDINATION

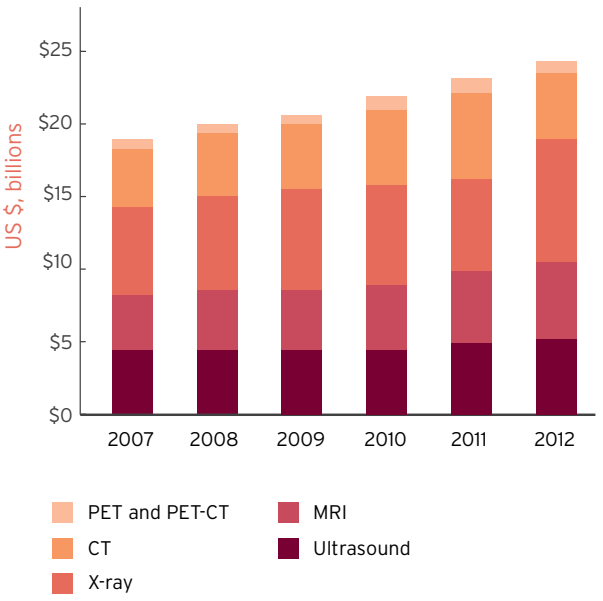
For diagnostic imaging start-ups hoping to distribute their technology through a major OEM, the ability to secure early sales is extremely important. Because of budgetary concerns and a lack of physician incentives, Canadian imaging start-ups face an uphill battle when attempting to sell to hospitals and clinics directly. This lack of reference installations is a major hindrance to Ontario companies seeking partnerships with major OEMs.

Because funding for medical equipment purchases comes from a single source, the Canadian government, an opportunity exists for coordinated procurement and streamlined supply chain management among hospitals and clinics. This would increase buy-side negotiating power and would lead to significant cost savings for both buyers and sellers. Unfortunately, due to the decentralized approach to hospital management in Ontario, these potential cost savings are not being realized.[14] Medical imaging equipment vendors must sell their products "door-to-door," while hospitals and clinics pay premium prices for their products. This situation may improve as organizations such as Local Health Integration Networks emerge to fill the gap.[15]

Market dynamics in diagnostic imaging

The global diagnostic imaging equipment market is estimated to be a US$20.6 billion industry, growing at an average rate of 4%, year-over-year. X-rays are the most common diagnostic imaging modality worldwide, while PET and PET-CT scanning are the least.

Figure 1 Forecast global medical imaging market value by modality



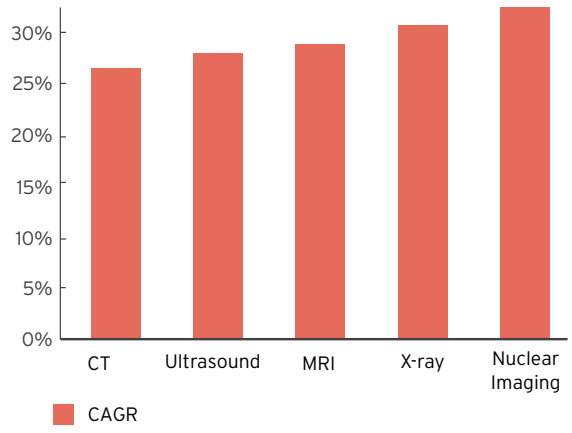
Source: Kalorama Information, 2009

In Canada, revenues from the sale of diagnostic imaging equipment reached $185 million in 2008. This represents less than 1% of the global market and less than 2% of the US market.

With a 26% cumulative annual growth rate, CT equipment is expected to be the fastest growing segment for Canadian imaging modalities by revenue over the coming six years.[16]

According to a recent report by research and consulting

Figure 2 2008 to 2015 Forecast revenue growth at diagnostic imaging equipment companies in Canada



Source: GlobalData, 2009

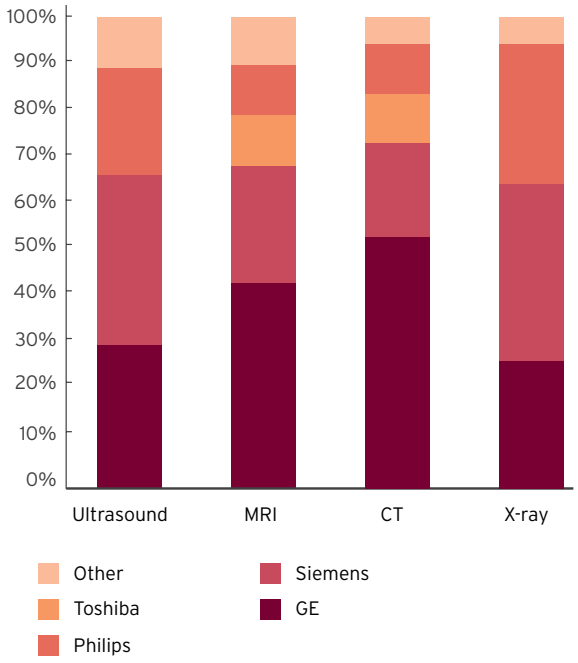
firm Frost & Sullivan, growth in diagnostic imaging software is set to outpace growth in hardware and equipment. The market for diagnostic imaging software is divided between picture archiving and communication software (PACS—the operating system behind most diagnostic imaging equipment) and image analytics. The worldwide PACS market generated approximately US$2.8 billion in revenues in 2008, and is expected to grow at a CAGR of 9% to 2015.[17] Companies in the US control approximately 50% of the total PACS market, while Canadian firms hold an estimated 3.5%.[18]

Image analytics is an emerging market with an expected CAGR of 14.3% to 2015.[19] Image analytics refers to software tools designed to extract and render meaningful information from high-data medical images. This represents an area of significant opportunity for Ontario companies drawing on local imaging research and academic programs in applied mathematics. The main functionalities falling under the category of image analytics include image processing, image reconstruction, image segmentation, CAD, 3D/4D image generation and quality control tools.[20]

Industry Overview

The market for diagnostic imaging equipment and devices is relatively mature. Most orders are for new machines to replace aging installed systems. The market is controlled by four global conglomerates with a combined market share of 80% in diagnostic imaging: GE Healthcare, Siemens, Philips and Toshiba. The following table highlights US market share distribution by imaging modality:

Figure 3 US market share distribution by modality



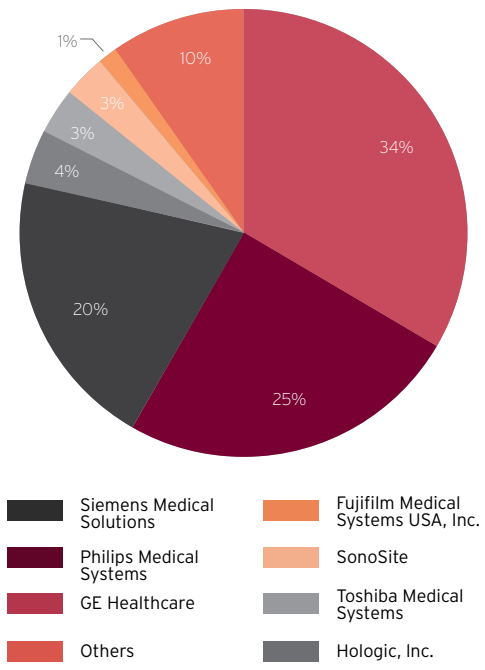
Source: BCC Research, 2007; Frost & Sullivan, 2007

In Canada, GE Healthcare is the largest diagnostic imaging player, with 34% of the market, followed by Philips and Siemens.

In diagnostic imaging software, the same large players control the market. GE Healthcare, Siemens and Philips dominate both the RIS/PACS market and the advanced visualization market.[21] Toshiba is attempting to gain momentum in the PACS/image analytics market through partnerships with companies such as Vital Images and TerraRecon.[22] Advanced visualization remains highly fragmented, with a large number of small players competing in niche markets.

For both medical imaging equipment and software companies, the generally accepted route to market is through a distribution partnership with one of the major OEMs. These partners offer procurement relationships with major hospital and clinic organizations, as well as a global sales force. The challenge for start-ups is to develop a product with sufficient market potential to be a valuable addition to the OEM's portfolio. The changing nature of start-up-OEM relationships in medical imaging is discussed in greater depth in later sections of this report.

Figure 4 Canadian market distribution by imaging modality



Source: GlobalData, 2009

Trends and opportunities in diagnostic imaging

Fusion/multimodality

An important trend in diagnostic imaging is an increasing interest in fusion and multimodality imaging. For specialties such as cardiology and oncology, the merging of imaging modalities such as PET/CT, SPECT/CT and MRI/PET creates an opportunity to run the full gamut of imaging scans from the same unit, at the same time.[23] It also allows for the merging of information from complementary imaging modalities for a more complete set of diagnostic information.[24] In addition, multimodality and fusion imaging increases the comfort level of patients since it does not require repositioning, and also speeds the overall imaging process.[25]

Portable imaging equipment

As the market for diagnostic imaging equipment matures, new opportunities are emerging for imaging modalities that can be used by mobile doctors or health-care workers in the field. Portable units give doctors access to diagnostic imaging when they need it, with less queuing and faster image availability. Providing access to imaging functions in the field gives medical personnel the ability to rapidly identify time-critical medical issues, and increases the accuracy of patient triage. Specialized portable models also provide needed imaging modalities at a much lower price point compared to expensive, multimodality installed systems.[26] The trend toward greater portability is particularly evident in the ultrasound market.

Low-cost options take precedence over diagnostic sensitivity

The diagnostic imaging market is facing increasing competition from refurbished equipment manufacturers and low-cost equipment manufacturers in developing markets. Rising price-consciousness throughout the health-care system has created an opportunity for refurbished equipment to replace new systems [27]. Low-cost imaging equipment from China is also putting downward pressure on prices.[28] A growing system-wide reversion to low-cost, low-end equipment is limiting access to superior imaging platforms at the expense of diagnostic sensitivity and patient welfare.[29]

Partnerships versus acquisitions

According to industry experts, the early 2000s saw numerous acquisitions in the diagnostic imaging space by dominant players. The pace of strategic acquisitions has slowed in recent years due to the overall weakness of the North American venture capital industry and the resulting failure of diagnostic imaging companies to reach commercial viability. The situation is slightly better for companies in Europe where venture capital investment in the space has consistently exceeded other regions since 2004.[30]

The new strategy among large corporate players in diagnostic imaging is to leverage licensing agreements and work collaboratively with technology suppliers rather than to acquire these companies outright. One senior executive notes, "around the turn of the century, [imaging OEM] companies were in heavy acquisition mode in medical imaging. That has gone down over the last years and there is a greater focus on establishing collaborations, licensing agreements and partnerships. I think a lot of it stems from the probability of poor success with acquisitions."

Corporate ventures for OEM

In order to compensate for the lack of business funding available for imaging technology companies from traditional venture capital sources, most major imaging OEM's have established corporate venture funds. These include Siemens Venture Capital—Healthcare, and Philips Healthcare Incubator. GE recently joined the ranks with the October 2009 launch of the GE Healthymagination Fund. The US$250 million corporate venture fund is aimed at investing in innovative diagnostic, IT and life sciences technologies aligned with strategic objectives at GE Healthcare.[31]

Cost savings through software

New business models are emerging in diagnostic imaging software that allow users to structure costs based on a per-use or per-storage basis.[32] Developers are also offering pay-as-you-grow medical data archiving services.[33] Right-sizing imaging software packages allows hospitals and clinics to align imaging costs directly with patient flow so that they never risk paying for unused processing or storage capacity. Wireless communication technology is also reducing the cost of processing imaging data since it enables point-of-care image processing, thus increasing efficiency and reducing wait times.[34]

VisualSonics Inc.

Ontario-based VisualSonics Inc. is considered a world leader in in-vivo micro-imaging systems for non-invasive, pre-clinical research. The company's enabling technologies allow researchers at pharmaceutical and biotechnology companies, hospitals and universities to conduct research into cardiovascular disease, cancer and developmental biology, including genetic research, phenotypic study and drug development.[38] Key products for VisualSonics include the Vevo high-frequency ultrasound system and NeuroPak, a tool allowing researchers real-time access to tissue deep in the brain of a conscious animal.

VisualSonics, backed by venture investors VenGrowth, Hargan Global Ventures and others, is working to establish itself as a diversified health-care business and is seeking to move into the development of imaging technologies for human applications.

Diffusion Wave Diagnostic Technologies, Inc.

Diffusion Wave Diagnostic Technologies, Inc., an early-stage Ontario start-up, is approaching the problem of breast imaging from a different angle. The company is investigating the use of photoacoustic scanning tomography (PHAST) in breast imaging. Management at Diffusion Wave Diagnostic Technologies, hopes to arrive at a more cost-effective imaging solution that combines the image depth of ultrasound with the superior resolution of laser tissue optics as a more accessible solution for early-stage breast tumour detection.

Clinical applications

Doctors and radiologists employ an array of imaging modalities and techniques to diagnose illness. From pre-clinical research all the way to the detection of Alzheimer's disease, medical imaging equipment is continually evolving to identify disease earlier and with greater accuracy. Software tools are also essential to streamline imaging workflow and to help doctors analyze images.

Pre-clinical research

Diagnostic imaging modalities are used in pre-clinical research for drug development. Imaging has been identified by the FDA's Critical Path Initiative as a key technology for assessing, accelerating the development and guiding the use of new therapeutic options.[35] According to a report published by Frost & Sullivan, pharmaceutical companies could save up to US$38 million in development costs by making more extensive use of imaging techniques.[36] As an example, researchers at Boehringer Ingelheim, a European pharmaceutical company, are using high-content cellular imaging to support compound prioritization and decision making for a current drug discovery project.[37]

New developments, especially in the area of molecular imaging, are driving much of the current innovation in drug development. There are also important research applications for structural imaging in animal studies. Micro-imaging leader VisualSonics is active in this market.

Oncology

With over 7.6 million cancer deaths occurring annually and an estimated 12 million new cases diagnosed every year, oncology-targeted imaging techniques are an area of significant focus.

In oncology, X-ray and CT scans are the most widely used means of detecting lung cancer at its initial (and most treatable) stages. For breast cancer, mammography can identify tumours one to three years before a lump can be palpitated. Early diagnosis through mammography is thought to be a factor in the dramatic improvement in the 15-year survival rate during the 1990s among breast cancer patients in the US and Europe.[39] A 2007 report by BCC Research concluded that early detection of breast cancer reduces the risk of death in women aged 50 to 69 by 30%.[40] For women in their 40s, early detection can

reduce the risk of death by 17%.[41] Despite these findings, a task force recently organized by US Preventive Services has concluded that women at average risk of breast cancer in their 40s do not benefit from mammograms and should wait until age 50 before receiving annual checks. These recommendations contravene the protocols put forward by the American Cancer Society suggesting that all women get annual mammograms beginning at 40.[42] It is uncertain whether these new recommendations will have an effect on demand for mammography equipment.

Breast imaging modalities are one of the main areas of imaging research in Ontario. One company developing advanced breast imaging solutions is Sentinelle Medical Inc. The company, profiled in the Ontario Showcase section of this report, is developing a modular add-on to common MRI installations. The unit helps to provide better resolution and improved patient comfort without the capital outlay required for a dedicated system. Diffusion Wave Diagnostic Technologies, Inc., another Ontario start-up, is also developing imaging solutions for the detection of breast cancer.

Neurology

Brain imaging is seen as the most important application for many modern imaging modalities. MRI, CT, PET/SPECT and combinations of these have contributed to enormous advances in the diagnosis of numerous neurological disorders. Advances in structural imaging using MRI and CT, and in functional imaging using fMRI and PET, are recognized as the most promising imaging technologies to aid in the detection of Alzheimer's disease.[43] Researchers believe that innovations in MR/PET will result in the development of new standards for assessing the pathologies and progression of neurological disorders, including Alzheimer's disease, Parkinson's disease, epilepsy, depression and schizophrenia.[44]

XLR Imaging Inc., also profiled in the Ontario Showcase section of this report, is developing a dual MR RF coil using MR spectroscopy to provide enhanced sensitivity and superior resolution in MR imaging. XLR's systems are designed to maximize patient comfort while offering advanced neuroimaging capabilities.

Cardiology

In cardiology, Doppler ultrasonography is used to assess blood flow through tissues and organs to identify clots and plaques.[45] In the heart itself, ultrasound is used

Medipattern

Medical statistics can be downright frightening. According to Medipattern founder Jeff Collins, when analyzing breast ultrasounds, average radiologists identify cancer lesions correctly only 10% to 20% of the time. Among top radiologists, this improves to 50% to 60%. For the best in the field, accuracy levels can be higher than 99.9%. Medipattern's pattern recognition technology is designed to leverage the lesion identification abilities of the most talented experts to help more practitioners arrive at the right diagnosis more often.

Using more than 14,000 pathology-proven patient inputs, Medipattern's software fuses clinical methodology with interpretation, drawing from clinical expertise provided by leading medical advisors to create knowledge-based image analysis tools. The company's software suite, Cadenza™, was the first solution approved by the FDA for computer-assisted detection in breast ultrasound. The technology is currently being used in hospitals and imaging centres in New York and China. The company, which trades on the Toronto Venture Exchange, is now working to bring the industry's first breast MRI morphological analysis technology to market. Medipattern has also partnered with GE Healthcare to develop an ultrasound-based vascular imaging quantification tool, Vascular iQ.

Segasist Technologies

Segasist Technologies, an early-stage Ontario start-up, spun out of the University of Waterloo with support from the OCE, is developing an innovative image segmentation application. The company's software learns to segment medical images from manual image contouring operations carried out by its user. Using a suite of proprietary algorithms, the software helps to automate these tedious processes. Learning from user input, the tool grows more accurate over time. The company targets niche cancer disciplines, including prostate and brain cancer.

Client Outlook

Client Outlook has succeeded in overcoming a principal technical challenge in the integration of medical imaging data with health records applications and web-based image viewing. DICOM, the traditional imaging format employed by most imaging data capture applications, is inherently incompatible with web browsers.

DICOM images are generally greyscale and may contain up to 65,535 levels of grey. Standard web browsers on popular operating systems, coupled with consumer-grade monitors and video cards, are only capable of displaying 256 levels of grey. This leaves a tremendous gap in critical visual diagnostic information. Client Outlook has developed technology to receive, store, manage, display and share full-fidelity DICOM images in commonly configured web browsers without the need to install software. Integrated web-conferencing and annotation capabilities allow health-care professionals to collaborate, teach and consult from remote locations. Providing clinicians with web-based access to diagnostic imaging creates an opportunity for more efficient care, greater collaboration and faster patient turnaround times. Web-based access also reduces time spent searching for physical images.

The company is currently managing several pilot installations and is in negotiations with strategic partners for broad distribution.

to detect congenital abnormalities and problems with valve function.[46] X-rays are used for real-time cardiac imaging and image-guided catheterization, especially in developing countries. However, X-ray technology is rapidly losing ground to CT.[47] Coronary computed tomography angiography (CTA) is gaining momentum in cardiovascular diagnostics and is soon expected to become a viable alternative to catheter angiograms. CTA yields detailed images of blood vessels and blood flow non-invasively. It also has the advantage of being a more cost-effective and efficient procedure.[48] Myocardial perfusion imaging (MPI) is a form of functional cardiac imaging used to diagnose ischemic heart disease. MPI has been demonstrated to have an overall accuracy of approximately 83% and is comparable to other non-invasive tests for ischemic heart disease, including stress echocardiography.[49] Due to the amount of information available through the use of multi-modal imaging (e.g., PET/CT, SPECT/CT, MRI/PET, MRI/ultrasound), these technologies are also gaining ground in cardiology.

Globally, cardiovascular disease is the leading cause of death, and is expected to remain so. According to an epidemiology report by a leading market research firm, 30% of all deaths worldwide are attributable to cardiovascular problems.[50] With the increasing prevalence of cardiovascular disease, diagnostic imaging technologies that focus on the heart are expected to continue to evolve rapidly.

Software applications

Computer-assisted detection (CAD) and image analysis applications have increased in popularity due to advances in 3D imaging. This has driven growth in the adoption of tomographic imaging technologies, MRI and multimodal technologies. The use of advanced imaging software increases patient throughput by improving the efficiency of imaging equipment while also increasing diagnostic accuracy.[51] Several Ontario companies, including Medipattern, Claron Technology Inc. and Segasist Technologies, are active players in the image segmentation and CAD markets for various therapeutic applications.

An important factor driving the adoption of new imaging applications is the proliferation of imaging software operating platforms. Companies such as Merge (formerly Cedara) and AGFA are working to develop the next generation of PACS systems. These will enable better

application integration and remote access to imaging data with the use of thin-client and software-as-a-service technologies. Unfortunately, hospitals with large investments in legacy PACS platforms will delay the adoption of newer PACS systems. Imaging application companies such as Client Outlook and Clear Canvas are working to address these issues.

Client Outlook has developed a browser-based solution, eUnity, which allows clinicians to access DICOM (Digital Imaging and Communications in Medicine) images over the Internet. Clear Canvas has created an open source alternative to PACS systems for use in academic settings. This new system provides researchers with more flexibility and can be adapted to meet specific workflow needs.

Scientific and technological advances driving growth in diagnostic imaging

Diagnostic imaging hardware

Technological developments driving growth and innovation in diagnostic imaging hardware include advances in miniaturization technologies and increasing computing power, as well as expanded imaging capabilities from fusion and multimodality systems.

Miniaturization/computing power

Advancements in miniaturization technologies and increases in processing power and storage capacity are reducing the size of imaging devices. Ultrasound transducer probes are expected to grow smaller, decreasing the footprint of the overall unit.[52] Increasing computing power allows for increasingly complex imaging techniques, resulting in a continual increase in image resolution, which can be correlated with increased sensitivity and specificity of diagnosis.[53]

Fusion/multimodality

Inherent limitations prevent users from obtaining comprehensive image data through the use of single imaging modalities. Fusing functional and structural image modalities enhances the diagnostic information available from a single scan. Fusion imaging is expected to dominate the tomographic imaging industry in the future, particularly for 3D applications.[54] The use of fusion imaging in several clinical settings has been a major driver in the emergence of hybrid systems, such as PET/CT, SPECT/CT, MRI/SPECT, and MRI/PET.[55] Commercial PET/CT and SPECT/CT scanners are available today and have proven clinically useful, especially in tumour imaging and diagnosis.[56]

Diagnostic imaging software

The accelerated growth in diagnostic imaging software is likely driven by the use of more advanced tools to improve patient throughput, data acquisition speed and image fidelity in expensive-to-replace, legacy imaging equipment.

3D/4D imaging

Cardiologists are driving the adoption of volumetric imaging technologies to aid with cardiac and cardiovascular diagnostic functions.[57] Surgeons also make use of 3D imaging for surgical planning.[58] As the technology matures, more user groups will likely turn to 3D and 4D.[59] In order to extend access to volumetric imaging beyond radiologists, hospitals and clinics are turning to enterprise client-server and thin-client solutions.[60]

Computer-aided detection

Advances in CAD technologies are leading to improved image data translation between imaging modalities.[61] As fusion and cross-modality imaging increase in popularity, CAD software is expected to play an increasingly important role in the imaging market.

Workflow automation

The automation of imaging functions and the increasing ability of software platforms to process large quantities of data in short time periods is reducing the number of manual steps involved in imaging.[62] Innovation in workflow automation frees scarce practitioner time and optimizes the use of expensive equipment, driving demand in resource-strained health-care systems.

Enabling technologies

Enabling technologies helping to accelerate growth in the medical imaging software space include enhanced digitization capabilities, client-server communications technology and increasing applications interoperability.

Digitization

As the trend continues toward wholly digitized health, non-digital imaging modalities (e.g., X-ray, X-ray image intensifiers and fluoroscopic images) will need to make the transition.[63] Accordingly, demand for technologies enabling digital image recording among the remaining non-digital imaging methods is expected to grow.

Client-server technology

Expensive, hardware-based imaging workstations are giving way to lower-cost, commercially available computers able to connect to high-powered image servers remotely.[64] Using this computing architecture, central servers are able to distribute advanced visualization functionality to a large number of users, including PACS workstations, thus relieving bottlenecks in clinical workflow.[65] Thin-client-server configurations with PACS integration are expected to play an important role as the adoption of 3D imaging spreads, enabling the application of new business models in medical imaging (e.g., software-as-a-service and cloud-computing).[66]

Interoperability and standardization

Although there is still much progress to be made, improvements in network interoperability, the use of standard protocols (e.g., DICOM and IHE—Integrated Healthcare Enterprise), advanced data management capabilities and enterprise-wide resource planning have caused a significant increase in organizational efficiency at hospitals and clinics. As a result, the management of imaging functions is becoming more affordable, opening the market for new hardware purchases.[67]

Commercialization challenges in diagnostic imaging

Legal and regulatory constraints

US HEALTH-CARE REFORM

According to a recent report published by RBC Capital Markets, certain measures proposed in the US health-care reform bill can be expected to put additional price pressure on domestic medical device manufacturers, including makers of imaging equipment. If implemented, these measures may also open the market for global manufacturers of less costly equipment. Many of the proposed initiatives promote increased investment in IT solutions as opposed to imaging equipment, except in the case of equipment for research purposes.[68] One significant change would be the levy of a 2.5% excise tax on the wholesale price of devices sold in the US after January of 2013.[69] Another significant change would be the establishment of a national medical device registry, including Class III and Class II devices that are considered "life-supporting or life-sustaining".[70]

REIMBURSEMENT

A main hindrance in the commercialization of new diagnostic imaging technologies is the lack of adequate reimbursement policies for diagnostic imaging procedures in the North American market.[71] Reimbursement rates are particularly poor for newer imaging modalities and are a leading cause for the concentration of the imaging market among the four large OEMs.[72]

REGISTRATION

For most countries, registering for the sale of diagnostic imaging equipment and software is a lengthy, expensive and complex process.*

The US

In the US, radiation-emitting devices (e.g., X-ray, CT, PET and SPECT) must comply with safety standards and procedures legislated under the *Radiation Control for Health and Safety Act*.[73] In addition, companies must comply with requirements under the *Food, Drug, and Cosmetic Act*, including a pre-market notification submission (510(k) application) or pre-market approval (PMA) submission detailing the potential risk of the equipment or software.[74] Imaging equipment manufacturers and related software developers must also follow strict quality assurance guidelines.[75]

The EU

Imaging equipment is even more heavily regulated in the European Union than in the US. The EU's Medical Device Directives (MDDs) impose regulations on both basic imaging modalities and custom imaging equipment.[76] MDDs deal with equipment safety, electromagnetic compliance requirements, radiation exposure directives for physicians

* For a detailed comparison of the registration processes in Canada, the US, the EU and Japan, download Intertek's "Quick Guide for Medical Device Manufacturers" here: www.intertek-sc.com/pdfs/medical_markets

and radiologists, and patient data protection guidelines.[77] Adding an additional level of complexity, the MDD standards vary between the member states. Furthermore, imaging devices sold in the EU must comply with the region's Waste from Electrical and Electronic Equipment protocols.[78]

Canada

In most cases, the registration process for the sale of medical imaging equipment in Canada is even more challenging than selling into either the US or the EU. Companies hoping to sell into the Canadian market must obtain a marketing licence prior to distributing their product, whereas sellers in the US market must only complete a pre-market notification.[79] In addition, Canadian manufacturers require ISO 13485 certification before they can begin device production.[80] A possible result of the difficult-to-navigate regulatory system in Canada is that major medical imaging and other medical device companies may elect to commercialize their products in other markets, thus depriving Canadians of the opportunity to receive health care on the leading edge.

INTELLECTUAL PROPERTY PROTECTION FOR IMAGING SOFTWARE

Patents to protect software processes are difficult to defend, particularly when competing with multinational OEMs. While patenting offers some protection, the necessity for disclosure also exposes the underlying technology to the market. Trade secrets are an alternative to patenting, but make OEM partnerships more difficult since the protected application must be integrated into a broader software platform and supported while avoiding disclosures. Leveraging a strong intellectual property protection strategy is an important factor in attracting capital, and the difficulty of doing so in the market for imaging software may be inhibiting growth.

Channel constraints

OEM RELATIONSHIPS

For diagnostic imaging equipment and related software, commercialization pathways are extremely limited. Hospitals are highly risk averse and rarely agree to purchase equipment or software from start-up companies or other vendors without a prior relationship. As a result, most start-ups market their products through one of the large OEMs: GE, Siemens, Philips or Toshiba. Importantly, the relationships between imaging start-ups and OEMs are distinctly different from those in other life-sciences industry segments. While large pharmaceutical and biotechnology firms take an active interest in acquiring or co-developing new technologies, medical imaging OEMs generally only have an interest in products that are already commercially available and have established sales. For imaging start-ups, it is essential to establish a record of direct sales before approaching an OEM for a distribution partnership. According to a senior health-care executive at one OEM, "Unless it's a very key technology area that we find we are behind the curve on, we typically would like to see companies that have been through clinical trials and have established scientific results about the improvement of what their offering brings to the market. Ideally we would like to see companies that have established the start of a revenue chain. We tend to go in later with a more established company, even at the risk of paying a higher price in order to ensure that the technology is sound."

BUDGETARY CONCERNS

The current economic downturn has had a drastic effect on health-care spending, as governments and insurers cut budget allocations and decrease reimbursements.[81] As a result, hospitals are becoming increasingly cautious about capital spending, redirecting funds toward efficiency-enhancing programs instead. An April 2009 survey of members of the American Hospital Association found that 90% of hospitals had made cutbacks, with nearly 50% of them reducing staff and 80% cutting administrative expenses within the past year.[82] According to several other sources, capital expenditures were expected to drop anywhere between 20% and 50% in 2009, as hospitals delay replacing old equipment and halt new purchasing. This implies that sales of new imaging equipment to hospitals and major health centres will continue to be a challenge as purse strings tighten. A further threat to North American imaging equipment manufacturers is the rapid influx of lower-cost systems from Asia, which successfully take advantage of the increased price sensitivity of North American health-care institutions. In view of the drastic spending reductions at hospitals and clinics in recent times, one industry expert sees an accumulation of pent-up demand for imaging equipment and software. As conditions improve, he expects that demand in the medical imaging market will receive a needed boost.

Equity funding constraints

In addition to the budget constraints outlined above, the current economic climate has also had a negative impact on the quantity of capital available to start-up and early-stage diagnostic imaging companies. As a case in point, the number of investments in early-stage imaging companies in North America dropped from 11 deals in 2007–2008, to only five over the past 12 months.[83] Without sufficient funding, early-stage diagnostic imaging technology companies will be unable to reach the commercial scale necessary to attract the interest of OEM distribution partners.

Technology constraints

INTERCONNECTIVITY AND STANDARDIZATION

According to Jeff Collins, founder and CEO of Medipattern, the ongoing lack of interconnectivity and standardization across imaging modalities and software applications continues to hinder the medical imaging market. Most hospitals operate on several PACS systems and employ imaging equipment from numerous manufacturers, each with proprietary image visualization and communication platforms.[84] This forces radiologists and medical specialists to develop the skills necessary to operate each system, and creates an inherent reluctance to acquire new technology.[85] It also inhibits the sharing of medical imaging information among medical centres, a function that could result in enormous cost savings for hospitals and clinics.[86]

DIAGNOSTIC CONFIDENCE

Medical specialists and radiologists exercise extreme caution in their approach to using new imaging technologies. Added to the general reluctance among hospitals to purchase new imaging equipment, this creates an even greater hurdle for medical imaging entrepreneurs seeking to enter the market.

Dr. Kieran Murphy, Vice Chair and Deputy Chief of Medical Imaging at the UHN (and a highly successful five-time entrepreneur), offers the following advice to new medical imaging entrepreneurs struggling to break into the market: "Form relationships with world-class clinicians who can champion new technology in the medical world. Overcoming new technology resistance at the level of the clinician can create demand from within the medical organization."

ACCESSIBILITY

Another roadblock delaying the commercialization of imaging technologies is the ongoing inability of doctors and clinicians to access medical image data remotely. Hospital IT managers continue to search for effective and cost-efficient ways to make medical information available to non-local specialists. Once DICOM images and associated patient records become widely available to doctors through laptops and smartphones, demand for innovative imaging modalities and applications is expected to accelerate.

Ontario showcase

Sentinelle Medical Inc.

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 a 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 a 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 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 attaches to an MRI magnet, which includes coils and peripheral software, that helped in the early diagnosis and then the ability to biopsy these tumours."

By the time Sentinelle had developed a market-ready product, the company was in need of external funding. Rather than seeking capital from large corporate players or the traditional venture capital market, Sentinelle received its financial backing largely from luminary radiologists who understood firsthand the power and potential of Sentinelle's technology and were willing to champion its adoption in the market. Today, Sentinelle's breast MRI technology is available through each of the major MRI magnet manufacturers, including GE, Siemens and Toshiba. On Sentinelle's relationship with these major industry players, Piron explains, "They provide the magnets that our devices work on. They distribute our products and our products make their magnets work better and more efficiently for their customers. It's a non-exclusive distribution agreement between our sales team and their sales teams. It allows us to get much better coverage and our sales team is still relatively small (we have about 10 people), but it's growing pretty aggressively."

Sentinelle's success in breast MRI is based on a three-pronged value proposition that can easily be adapted to the successful detection and biopsy of other cancers. Because MRI does not use radiation, it can be used safely for yearly screenings in high-risk patients. With much-improved efficiency and accuracy, radiologists can screen patients more rapidly and with better results than through traditional techniques. In addition, MRI provides a unique solution to the detection and biopsy of very small tumours. Sentinelle is currently working to create a similar solution dealing with prostate cancer, and is branching out into other cancers as well.

Part of Sentinelle's uniqueness as a company comes from the fact that it is so extensively vertically integrated, and that so much of the manufacturing and R&D takes place in North America. According to Piron, "we do production of our product here in downtown Toronto. Our manufacturing is basically in Canada and the US with a very strong North American presence. It was really important to keep it here because we are doing a lot of innovative things with the technology and it's important to keep an eye on quality. [...] It's really multidisciplinary from an engineering perspective, which allows us to take on entire projects and make sure they're completed seamlessly. [...] So we've managed to be really, totally vertically integrated which is kind of unique in this industry."

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

XLR Imaging Inc.

XLR Imaging Inc. is a spin-off company that originated from a collaboration between MRI scientists, engineers and the Robarts Research Institute of UWO in London, Ontario. XLR emerged as a developer of patient-friendly dual-tuned radio frequency (RF) coils for use in MRI units. RF coils transmit and detect RF energy, which interacts with protons in water molecules within the human body. This interaction provides detailed, high-quality images of soft tissue (muscle, brain, organs, etc.) typical of MRI exams. By incorporating spectroscopy and adding imaging capabilities to existing design platforms, XLR was able to fulfill an urgent need in the market for enhanced diagnostic imaging and improved spectroscopy sensitivity on systems already installed at most hospitals and imaging centres. While developing their product, the company focused on delivering high-performance imaging and spectroscopy combined with superior patient ergonomics. The result was a product with a user interface technology optimized for use in a clinical setting but also highly suited for scientific and medical research applications.

In terms of strategy, the team at XLR elected to defer offering traditional clinical products and instead identify and develop products to solve niche market issues that larger firms would be reluctant to compete on. "A larger player does not have the flexibility to provide highly customized products for such a niche market. They look to smaller companies to develop that kind of equipment. XLR has been approached in the past by OEMs, such as Siemens, Varian and Bruker, to develop solutions for their research customers, based on XLR's research product focus and research results published with collaborating customers."

According to Enzo Barberi, CTO and Director of Engineering of XLR, the greatest hurdle for an imaging equipment company is to commercialize the first product. "Bringing the first product to a market with large barriers to entry is the hardest part, but once you achieve success with one product, the momentum can build. Subsequent product development and market entry is less challenging once partnerships have been established and your company has proven itself. OEM relationships are key."

For Barberi, XLR's success has hinged on the company's ability to collaborate successfully with imaging centres for access to both imaging technology and the clinicians who use it, building demand. As a highly technical class of products, imaging hardware "begins with scientists and engineers, but requires that they work closely with clinicians to truly fulfill the market need."

Another key success factor for future growth identified by Barberi is an active emphasis on sales and marketing. "Moving from the research product market, where sales tend to come by word of mouth between scientists in the field, to the clinical market will require increased efforts on sales and marketing. XLR will focus appropriately on technology development, in addition to sales and marketing, to raise awareness among OEMs as well as potential customers for our new, and exciting, products."

XLR plans to continue to focus on extending its relationships with leading original equipment manufacturers in MRI. The company also looks forward to launching a new suite of imaging products and will potentially seek out formal venture capital funding to fuel further product development efforts.

Claron Technology Inc.

Doron Dekel and Claudio Gatti worked together at I.S.G. Technologies (now Merge Healthcare) and later in a start-up specializing in 3D ultrasound technology. The start-up was eventually sold, and the pair went on to found Claron Technology Inc. in 2001. Claron specializes in computer vision and volumetric data visualization for health care. One of the core technologies developed by Claron is a solution able to recognize anatomical regions in CT, MRI and ultrasound scans. This involves automatically registering a volumetric scan with pre-annotated volumetric data from an example patient, rather like an atlas. Claron's solution then copies locations, regions and labels from the "atlas" to the contents to 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 Withinsight 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 ear, nose and throat surgery. In addition to licensing its technology, the company provides custom development services and has a strong expertise in developing thin-client computing solutions that allow central medical image storage and computation servers to be accessed through a network.

From a team of two in 2005, Claron has grown to include 15 employees and several contractors, some of whom work remotely from other parts of the world. The company was listed in the 2009 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 has no dedicated sales or marketing staff, and all of its full-time employees have a strong hands-on technological background.

Claron began by performing custom contract engineering for medical device manufacturers, while developing the MicronTracker using the profits from its contracts. The company then expanded to other lines of businesses as opportunities for growth presented themselves. As one example, Claron developed a series of reusable software processing modules as internal tools to increase the efficiency of contract execution. These tools were then packaged with Withinsight as an OEM technology platform. Claron plans to continue to focus on the radiology and surgical markets. As part of the company's future technology development plans, Claron is also working to create a radiation therapy planning solution in collaboration with Dr. Curtis Caldwell, a leading scientist at Sunnybrook Health Sciences Centre. Claron recently introduced ClaroNav, a new platform for surgical navigation that combines its MicronTracker product with Withinsight visualization technology. Claron's longer-term strategic plan includes exploring the digital pathology market for virtual microscopy.

The company's mantra of "start simple" has served Claron well by enabling the team to bring reliable, high-performing new products to market very rapidly, while maintaining avenues for further customization and refinement.

For other aspiring life-sciences imaging entrepreneurs, Claudio Gatti, co-CEO at Claron, underlines the importance of great people, which in his opinion are what underpins any successful technology company. For Gatti, "people are key." Gatti also emphasizes the importance of maintaining an ongoing dialogue with potential customers while developing new products: "Development should not occur in isolation in a lab." This early and ongoing customer dialogue cements relationships with potential buyers and ensures rapid commercialization once the development phase is complete. In addition, Gatti recommends avoiding the tendency among scientists and engineers to be "paralyzed by analysis." Gatti sees agility and flexibility as an advantage in a market dominated by larger players. "Claron runs its business conservatively but takes risks on the technology. The problems we tackle are big and complex and there is always a chance of failure. Customers come to us because we have unique expertise, solid IP and a long track record of successfully completing challenging projects." Taking technology risks has worked well for Claron, given its consistent profitability. The company looks forward to continuing to advance the frontiers for computer vision technology in medicine.

Colibri Technologies

After graduating in 1997 from the University of Waterloo in computer engineering, Dr. Brian Courtney worked at a Toronto-based medical instruments company before returning to school for a Masters degree in electrical engineering. His research supervisors at Stanford University were cardiologists with strong backgrounds in engineering and medical device start-ups. They inspired Dr. Courtney to enter medical school at age 25. Now a final-year cardiology resident at the University of Toronto, Dr. Courtney is also a third-time entrepreneur. He co-founded Kerberos Proximal Solutions, a maker of devices to prevent the embolization of clots and plaque dislodged during angioplasty and stent placement procedures. Kerberos sold to FoxHollow Technologies for $32 million in 2006. Dr. Courtney went on to run Catharos Medical Solutions, a developer of devices to prevent kidney damage during catheterizations for patients with borderline kidney function. His latest venture, Colibri Technologies, is a spin-off from Sunnybrook Health Sciences Centre. Colibri develops next-generation intracardiac echocardiograph catheters (ICE) 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, partly due to inadequate image guidance.

Colibri's technology enables high-quality, 3D intracardiac imaging at a dramatically lower price point than any other ICE catheters currently available. Dr. Courtney expects that the new catheters will go into production in 30 to 42 months. He is currently seeking an investment to drive product development and clinical trials. Over the longer term, Dr. Courtney hopes to modify Colibri's catheter design for use in procedures for the treatment of chronic total occlusions, valvular disease, placement of left atrial appendage occlusion devices, and several other corrective cardiac procedures. Dr. Courtney envisions a host of future applications for 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. Many sales relationships are already in place since the company used feedback from early talks with potential customers willing to help inform product development efforts. Colibri also prefers to avoid a dependent relationship with one of the industry's major distributors in order to remain flexible. According to Dr. Courtney, "It provides us an opportunity to get a lot of important feedback from our customers in a direct manner, which is not as readily available if we go through a partnership or distributorship. This strategy also reduces our dependency on forming that partnership or distributorship, although we would obviously be open to entertaining such an arrangement with a highly motivated group."

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Organizations

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Centre for Addiction and Mental Health (www.camh.net)
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