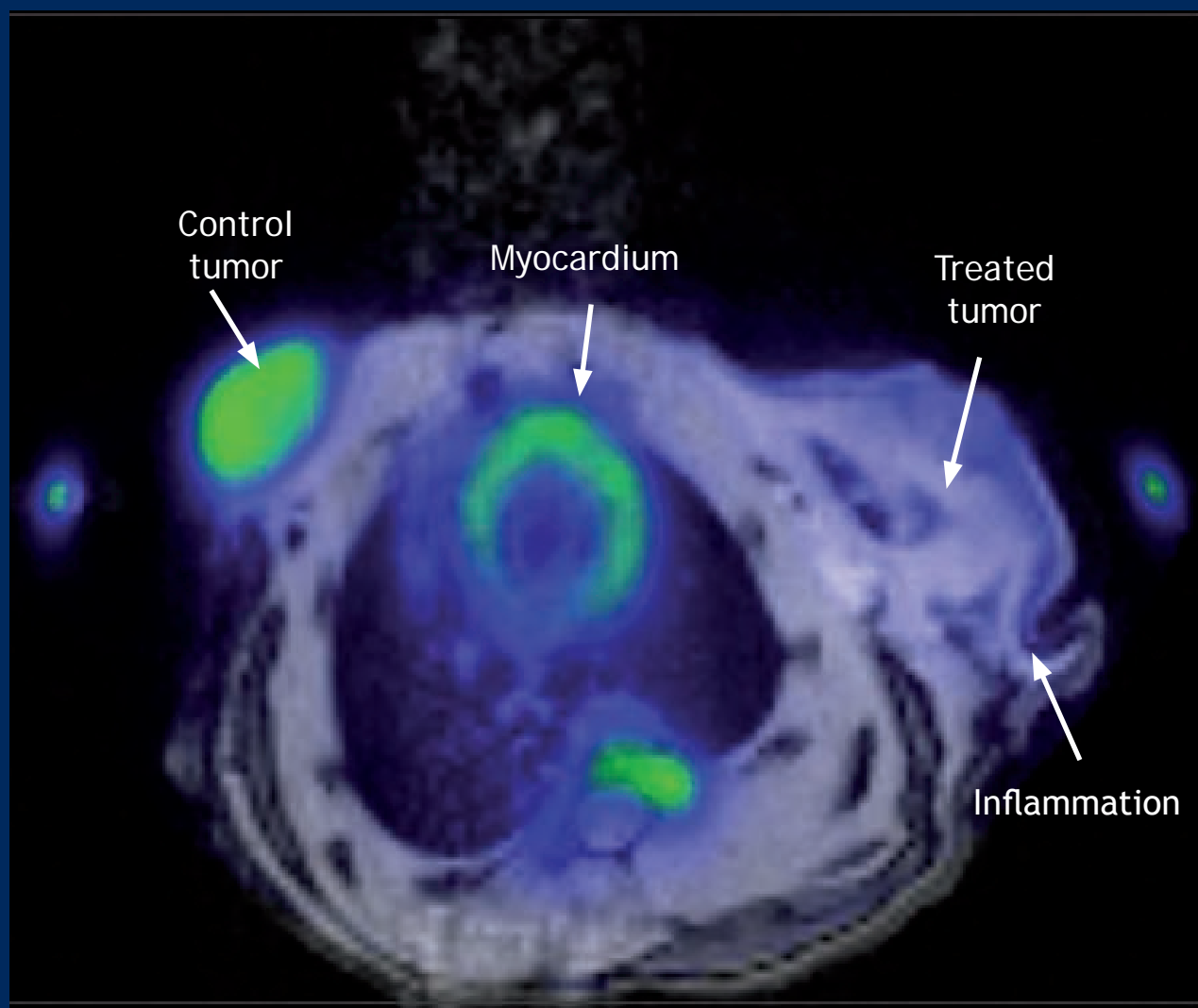


# CIHR/NSERC MEDICAL IMAGING WORKSHOP REPORT

October 6-7, 2009  
Vancouver, British Columbia



Co-registered PET/MRI images of a rat with control (left) and treated (right) tumors, also showing high  $^{18}\text{F}$ FDG uptake in the heart muscle.

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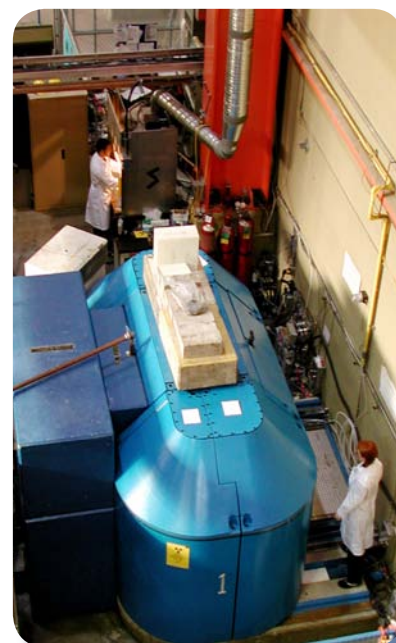
## EXECUTIVE SUMMARY

Medical imaging is a rapidly growing field that has become an integral part of modern health care. Canada has an active medical imaging research community that spans a wide range of scientific disciplines and boasts many successes, ranging from innovative technology advances to novel clinical applications. There are currently several unique Canadian strengths in the field of medical imaging, including:

- *The Canadian Light Source – one of the few synchrotrons in the world and a powerful tool for academic and industrial research.*
- *The Centre for Probe Development and Commercialization (CPDC) - the world's first facility focusing on all areas related to the development of molecular imaging probes.*
- *TRIUMF – one of the world's leading subatomic physics laboratories that brings together dedicated physicists and interdisciplinary talent, sophisticated technical resources, and commercial partners.*
- *Numerous individual imaging research networks and centres, located at universities, hospitals and research centres across the country.*

Medical imaging unites researchers from the physical and life sciences. As a result, cross fertilization and trans-disciplinary collaborations yield research outcomes that have applicability across many fields, industries and borders. The research domains that encompass biomedical imaging can be grouped as follows:

- *Technology and device (hardware and software) development.*
- *Probe development and biological characterization (including MR contrast agents, optical probes and radiotracers). This area of research includes the evolving field of imaging biomarkers and their potential contribution to the concept of personalized medicine.*
- *Multi-centre clinical trial capacity to specifically support biomedical imaging research. This area of clinical research supports the evaluation of new agents and imaging techniques in large patient populations as a means of identifying those that should proceed to the next phase of clinical trials or to clinical practice. It may also be used to integrate imaging biomarkers into drug development trials and clinical outcomes research.*
- *Health technology assessment. Health services and policy research to assess the societal benefit, cost efficacy and cost effectiveness of new and existing imaging modalities.*



An overhead view of TRIUMF's TR-13 cyclotron.  
Image courtesy of TRIUMF

As a field, medical imaging falls within the mandate of both the Natural Sciences and Engineering Research Council (NSERC) and the Canadian Institutes of Health Research (CIHR). Indeed, CIHR and NSERC already have a successful partnership - the Collaborative Health Research Program (CHRP) that promotes collaborations between researchers from the physical and life sciences. Recently the two funding agencies also collaborated on an accelerated response initiative to address the critical shortage of  $^{99m}\text{Tc}$  following the closure of the nuclear reactor at Chalk River. Building on these successful partnerships, CIHR and NSERC organized and co-hosted an invitational workshop on medical imaging on October 6th and 7th, 2009. The workshop provided an overview of Canadian imaging research strengths; international comparators with imaging activities in the UK and US; and an opportunity, through discussion, to identify strategies to jointly advance the Canadian medical imaging field.

Many recommendations emerged from the workshop, but a recurring theme was the sense that the national and international impact of Canadian research in biomedical imaging was less than the sum of its parts.



Unlike the US, which has several imaging networks and supporting infrastructures such as the American College of Radiologists Imaging Network (ACRIN) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), Canada has neither a national imaging strategy nor national broad-based networks. Instead, funding is dispersed in smaller aliquots to support focused and independent imaging programs. To date, there has been no mechanism created to coordinate Canadian imaging activities or to cultivate a network designed to leverage the strengths and prior investment in infrastructure. The absence of an Imaging Institute, or even a coordinating capacity within funding agencies, such as CIHR, is not conducive to the development of world-class discovery, translational and clinical biomedical imaging research in Canada.



An opportunity, therefore, exists to promote the coordination of research funding across the country in order to facilitate translational research capacity and foster opportunities for regional and national collaborations. Coordination could be achieved through the creation of either an Imaging, or Biomedical Technology Institute or a networking centre that would facilitate and coordinate research between multiple existing imaging sites. Technology development is moving towards combined imaging modalities and individual imaging technologies are applicable to a number of clinical disciplines. Large networks, linking existing centres would facilitate the translation of research outcomes, through pre-clinical studies and into clinical practice.



*LabPET™ Small Animal Scanner commercialized by AMI Inc. Image courtesy of Roger Lecomte*

In addition, the absence of a facilitated and coordinated mechanism for conducting clinical trials has limited the impact, clinical use and health services research opportunities for successful biomedical imaging research (whether based on devices, drugs or software developments). Only a fraction of imaging and biomarker research finds its way into clinical trials and even less into clinical practice. The range of potential uses of biological imaging is enormous, but the flow of knowledge from the technology inventions to pre-clinical investigations to clinical implementation is relatively weak in Canada. There are vast libraries of markers in universities and industry that have not yet been thoroughly investigated for clinical application. Canada has enormous talent in basic science and technology, but without strong and sustainable links to the clinical setting, medical advances are often not realized or are lost to other countries. One solution to this problem would be the development of a national imaging clinical trials network to organize, coordinate and review quality and regulatory requirements for Canadian imaging trials.

The network would support:

- *The introduction and validation of new imaging probes.*
- *The integration of imaging biomarker trials into cooperative group trials, drug development trials and clinical outcomes research.*
- *The development of an evidence base to support current or new imaging methodologies for specific clinical indications.*



*A patient prepares for a PET scan of the brain. Image courtesy of TRIUMF*

Biomedical imaging is by necessity a multidisciplinary field requiring large teams that include researchers from both the physical and life sciences to sustain and advance progress in the field. However the Canadian capacity to fund large teams is weak and new support mechanisms for large



multidisciplinary teams are required to facilitate the translation of discovery research (whether for devices or drugs) through animal studies and into early stage clinical trials. Such teams must include technology development researchers, PhD medical imaging researchers and clinical scientists and could potentially be supported through an expanded version of the existing CIHR/NSERC CHRP program. In addition, teams of



*A radiochemist prepares a radiotracer at TRIUMF.  
Image courtesy of TRIUMF*

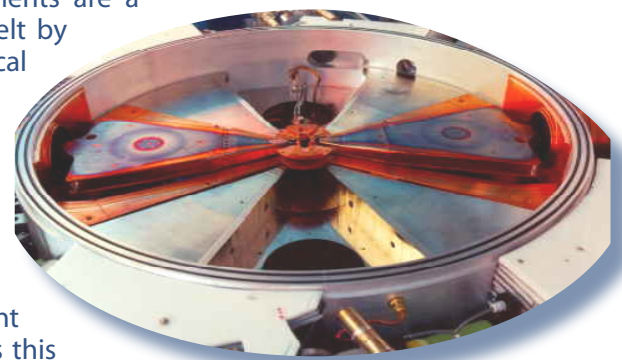
biomedical and clinical researchers would benefit from an environment, such as a hospital, that includes the necessary imaging equipment, physicians and the patient population. Specific mechanisms are needed to address the lack of physician/clinician researchers through training programs, core competencies within the Royal College of Physicians and Surgeons, appropriate financial supports and reversal of the current climate within academic settings that fails to provide adequate academic credit for clinical translation.

The absence of ongoing mechanisms and processes to facilitate commercialization of biomedical imaging research output places the Canadian community at a marked disadvantage when compared with colleagues and competitors in the European Union, the United States and Asia. While the Centres of Excellence for Commercialization and Research (CECR) program created the first program for commercializing molecular imaging probes – CPDC, its funding was for a five-year time frame. To fully realize the promise of existing strengths, Canadian researchers need: increased sustainable support for the commercial-

ization of molecular imaging probes and technologies, including investments in small high tech companies; improvement in Canada's capacity to manage all phases of intellectual property development; creation of private-public partnerships at a provincial level; and the support for specific programs that improve Canadian commercialization successes, like the CPDC, and that promote entrepreneurial know-how and ownership of discoveries.

A large infrastructure deficit is building in biomedical imaging research. Many of the most successful research groups were funded through early rounds of Canadian Foundation for Innovation (CFI) competitions. The equipment supported by these successful applications is now coming to the end of its useful life and no mechanism has been identified – provincially or federally – for upgrade and replacement. Defined strategic support envelopes are urgently needed for hardware, software and image processing, and for probe development. In addition, sustainable long-term funding is needed to support the operating costs of existing teams and centres, including support for highly qualified personnel.

The cost of medical care and technology has continued to rise over the last decades – the Organization for Economic Cooperation and Development (OECD) has reported that the major cost drivers of health care expenditures are the development and diffusion of medical technologies and new drugs. Few people, particularly politicians, believe that new technology investments are a cost saving measure. The main restraints in health care are felt by provincial governments, yet the majority of research and medical investigation funding comes from the federal government. As new technologies, treatments and tests move into the clinical environment it will be essential that their impact on the health care system is understood. Given the structure of the Canadian health care system, it is important to incorporate considerations of access to quality imaging services within the Canadian context. The initiation of strategic discussions around health services imaging research, health technology assessment and clinical and cost effectiveness studies would help address this issue.



*An interior view of the "dee" structures in a medical-isotope producing cyclotron  
Image courtesy of TRIUMF*

The issues and recommendations discussed during the workshop will be considered by CIHR and NSERC and shared with other agencies and organizations with an interest in advancing the Canadian medical imaging field.

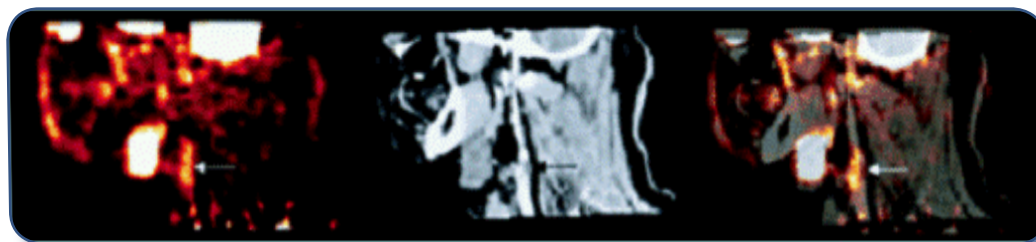


# CIHR/NSERC MEDICAL IMAGING WORKSHOP REPORT

## INTRODUCTION

On December 28, 1895, Professor Wilhelm Conrad Röntgen published “On a New Kind of Rays” in the Proceedings of the Physical Medical Society of Würzburg. His elucidation of the science underlying X-rays was rewarded by every major scientific prize of the era, including the first Nobel Prize. It was, however, the unintended culmination of a trail that began with scientists like Dr. William Gilbert (1540-1603), who invented the term ‘electron’, the engineer Michael Faraday (1791-1867) who invented the dynamo, and the mathematician James Clerk Maxwell (1831-1879) who described the characteristics of electromagnetic energy. Professor Röntgen discovered X-rays while experimenting with his latest technological acquisition, the Lenard tube, which had been invented by Phillipp Lenard (1862-1947) only a few years earlier.

Medical imaging has progressed far more rapidly and further than any of these distinguished scientists could have imagined. The electroencephalogram (1929), the electron microscope (1950’s), nuclear medicine (1950’s and 1960’s), CAT scans and MRI imaging systems (1970’s) are now considered core medical technologies. Molecular and functional imaging is one of the fastest growing fields in medicine. In addition to routine X-rays, the most common imaging techniques in current clinical practice are: computed tomography (CT),



PET

Contrast CT

Fusion

*Vulnerable Plaque in the Carotid Artery PET/CT Fusion with 18F-deoxyglucose  
Rudd et al, Circulation 2002;105:2708*

magnetic resonance imaging (MRI), ultrasound (US), and single photon emission computed tomography (SPECT). CT and MRI scanners, ultrasound units and gamma cameras are now an essential part of clinical practice. Positron emission tomography (PET) and magnetic resonance spectroscopy (MRS) are also increasingly used in the management of patients with heart disease, cancer and neurological disorders.

These technologies alone, or in combination, are increasingly used to probe biological function, identify early precursors of disease, guide surgical interventions and monitor treatment responses. During the last 40 years, medicine and technology have combined to create diagnostic tools capable of detecting pathology before irrevocable damage occurs. With the capacity of diagnostics to reach earlier in the course of disease, the medical paradigm has shifted from detection of disease to the detection of the possibility of disease. Within this decade, we’ve seen the introduction of therapeutic interventions that are tailored to an individual’s critical biomedical indicators. Researchers predict that therapeutic interventions will soon be tailored to match the specific signatures of disease.

## BRIDGING THE GAP BETWEEN THE PHYSICAL AND LIFE SCIENCES

Most of the radiological imaging techniques, such as CT and MRI, evolved as clinical tools to image anatomy. Nowadays, nuclear medicine (SPECT and PET), functional MRI and other developing modalities endeavor to image physiology and biological processes at the cellular and molecular level. Thus partnerships between basic scientists such as physicists, engineers, chemists, biologists, material scientists, informaticians, and physicians such as radiologists, pathologists and endoscopists (the 'traditional' imagers), and clinicians such as surgeons, ophthalmologists, neurologists and dermatologists are, literally, vital to progress in the field.



As a field that spans both the physical and life sciences, medical imaging connects the research domains of the Natural Sciences and Engineering Council (NSERC) and the Canadian Institutes of Health Research (CIHR). The two organizations already have an existing partnership – the Collaborative Health Research Program (CHRP) which was established to bring together physical and life science researchers to advance research that occurs at the boundary of the two disciplines. In addition, there are plans for a joint initiative between NSERC, CIHR and the National Research Council (NRC) on medical devices which will include an imaging (anatomical and molecular) component. Recently CIHR and NSERC jointly launched and co-funded a rapid response Request for Applications (RFA) to address the critical shortage of  $^{99m}\text{Tc}$  following the prolonged closure of the nuclear reactor at Chalk River. In October 2009, CIHR and NSERC again joined forces to organize an invitational workshop on Medical Imaging.



## GOALS AND OBJECTIVES OF THE WORKSHOP

The goal of the workshop was to obtain an overview of medical imaging in Canada and explore ways to strengthen the science and accelerate the uptake of new research outcomes and technology developments into clinical practice. Canadian and international researchers were invited as representatives for their respective fields, or models of program delivery, with expertise ranging from technology development to clinical trials and delivery of care (see Participant List, Appendix 1). The objectives of the workshop were:

- To identify important national and international trends in imaging research and provide international comparators and benchmarks;
- To identify future Canadian needs for imaging research, such as device and network development that would transform the field leading to improved patient outcomes across the disease spectrum;
- To develop strategies for identifying strategic priority areas in imaging research; and
- To explore mechanisms for promoting sustainable collaborations and integration between the life and physical sciences that would facilitate the translation of research findings to clinical practice.



The two day workshop included a series of presentations, followed by periods of open discussion and smaller breakout group discussions on focused topics (see Agenda, Appendix 2).

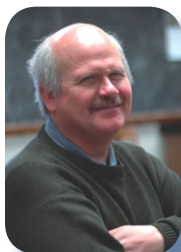
The speakers for each session (technology, pre-clinical, clinical/translational) provided a state of the art overview of the science in their individual areas of expertise, followed by broad, wide-ranging discussions among participants.



## SCIENTIFIC PRESENTATIONS AND DISCUSSIONS

### TECHNOLOGY DEVELOPMENT

### SYNCHROTRON BIOMEDICAL IMAGING



#### Presenter: Dean Chapman

The Canadian Light Source (CLS), Canada's national centre for synchrotron research, is located on the University of Saskatchewan campus in Saskatoon. The CLS is a powerful tool for academic and industrial research in areas such as environmental sciences, natural resources and energy, health and life sciences, and information and communications technology. Although principally used in basic fundamental biological research to provide an understanding of the basic biology of cells, tissues and organs, some of the methods are translatable into animal models and even clinical settings. For example, the cartilage in tissue is visible, permitting observation of the progression of diseases such as osteoarthritis. Synchrotrons offer unique modalities of contrast that allow the visualization of processes, impossible by other means. Synchrotrons can be used to model other imaging modalities, providing a tool to understand the technical aspects of these methods and producing benchmarks for the optimal combinations/settings. Virtually any monochromatic system can be modeled, including X-rays. The Saskatchewan facility is human 'capable' but doesn't currently have a specific human beam-line. The clinical utility of synchrotrons is limited because of the difficulties getting access to beam time; the large size of the machine; the need for safety systems for human use; and the large operating costs. However synchrotrons have been used in human research to answer questions requiring imaging resolution that is impossible to create using other technologies. For example, *in vivo*, it has been used for Absorption



Synchrotron facilities worldwide

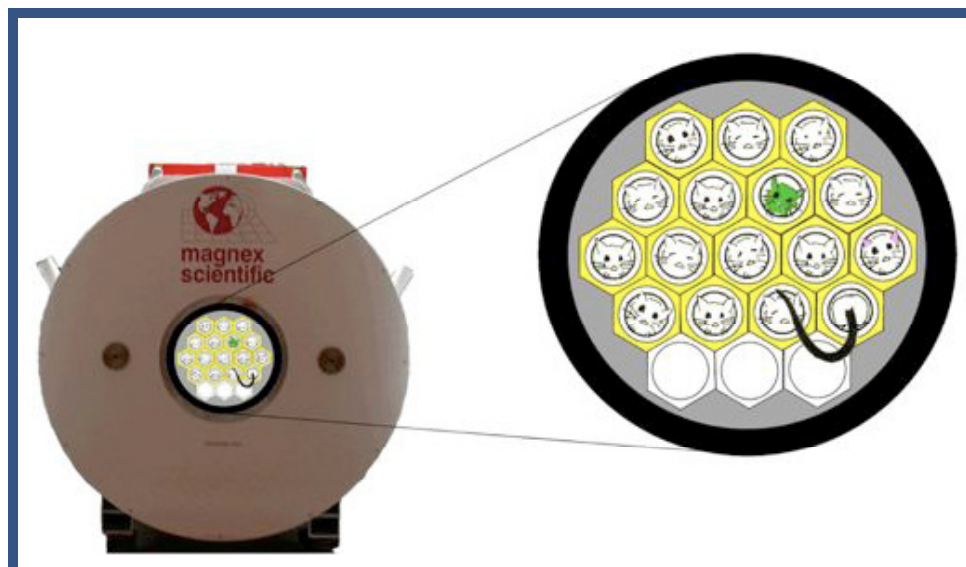
Imaging, K-edge Subtraction, Fluorescence Imaging, Phase Contrast Imaging, Analyzer Based Imaging, Diffraction Enhanced Imaging, and Multiple Image Radiography. In other parts of the world, synchrotrons are being used more frequently in clinical applications. For example, the synchrotron facility at Trieste is undertaking mammography and producing stunning images using the Konica system of phase contrast, which delineates the edges of tumors. Synchrotron-based research is now moving toward functional imaging of organs such as the cardiovascular system and lung, and gene imaging, and holds increasing promise as a clinically relevant imaging modality.

## **MAGNETIC RESONANCE IMAGING – TECHNOLOGY DEVELOPMENT**



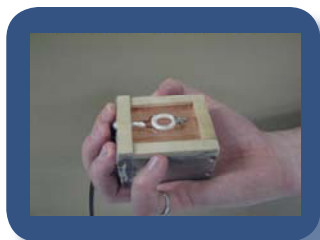
### **Presenter: Bruce Balcom**

MRI is used in the biomedical environment to image structure through the magnetic response of water molecules perturbed by static and radiofrequency magnetic fields. MRI is normally used to image soft tissues, but can also image hard tissues. Non-hydrogen (not water or fat) imaging is relatively common, for example, imaging sodium concentration and distribution in the brain. The technological trend in MRI is towards improved sensitivity and specificity. The use of higher field strength improves the quality of MRI images through better signal quality and improved signal to noise ratios, but the cost of increasing field strength is substantial. Research is also underway to improve coils, probes and magnet design. There is a great deal of interest in the development of combined modalities, because by undertaking simultaneous PET and MRI scans, both metabolic and structural information can be collected. The combination can work to identify important metabolic changes and localize them structurally with such scans, if followed by SPECT, offering unprecedented resolution. The challenge is to combine different imaging modalities in one device.



*High Throughput Mouse Phenotype Analysis  
Image courtesy of Dr. Mark Henkelman, University of Toronto*

Another exciting innovation is the development of a hand-held MRI device, which would represent a major advance in bedside diagnostics. However, there are numerous barriers to the adaptation of technological advances to the medical setting, in part because the pathway for involving clinicians in the evaluation of new



hand-held MRI  
Image courtesy of  
Bruce Balcolm

technologies is missing and researchers generally have neither time nor the skills to promote their work. This lack of collaboration between the researchers developing technologies and the clinical scientists needed to adopt the technology has slowed or prevented the uptake of many medical technologies. Canada does not seem to breed or attract people with entrepreneurial skills and know-how, although the apparent success of the Imaging Networks of Ontario Challenge Fund may indicate hope in this area. Regardless, the barriers to medical technology research in Canada are such that many of our highly technically skilled MRI students leave Canada for positions in the UK, Germany and the US where investment in medical technology development is more robust.

## TECHNOLOGY DEVELOPMENT: MOLECULAR IMAGING PROBES

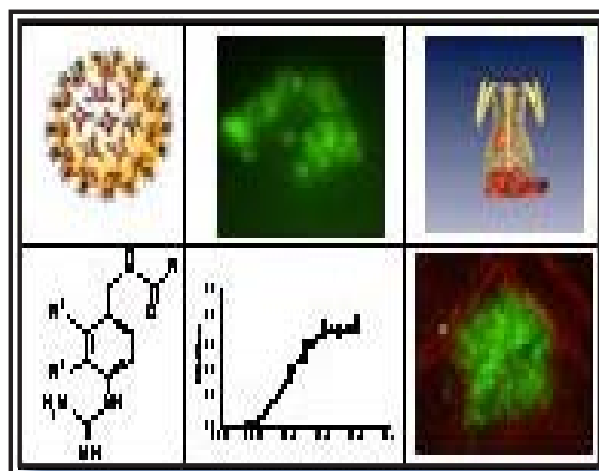


### Presenter: John Valliant

A probe is designed to be a biologically inert chemical compound that enables the non-invasive study of biological processes in the cells and organs of living organisms. There is wide application throughout medicine because probes can mark changes in biological processes (such as glucose uptake) as opposed to simply observing anatomical changes. Therefore, it is possible to detect changes in tumour (or other disease) biochemistry before you can detect changes in tumour size –an important factor for monitoring response to therapy. Molecular Breast Imaging (MBI), which is probe based, for example, can identify smaller cancers than standard mammography. Molecular imaging can also be used for margin evaluation and therefore guide biopsy and treatment and for evaluating the distribution, receptor occupancy properties and pharmacokinetics of new drug candidates. Emerging research in the use of multiple probes for complementary targets, or multi-modal probes that are detectable by more than one imaging modality, is underway and takes advantage of the fact that probes can be developed for virtually any imaging modality.

The probe discovery and development process requires that the researcher prove that the probe is linked to the correct target. It begins with basic biochemistry, e.g. the identification of a biomarker that is more

active in a disease state. Creating the actual probe requires new chemistry, engineering, and validation through chemical biology. Translation into medical science begins with animal studies and ends with clinical trials. At the beginning of the process, NSERC usually provides most of the funding, with CIHR and provincial health/research agencies supporting the early evaluative work, while the Network Centres of Excellence (NCE) has recently provided limited support for commercialization (through the above mentioned CECR program). There is no funding available, at present, for evaluating novel probes in large multi-centre trials.



Molecular Imaging Probes  
Image courtesy of John Valliant



## IMAGING TECHNOLOGY NEEDED FOR MEDICAL RESEARCH AND TRANSLATION IN ISCHEMIC HEART DISEASE



### Presenter: Frank Prato

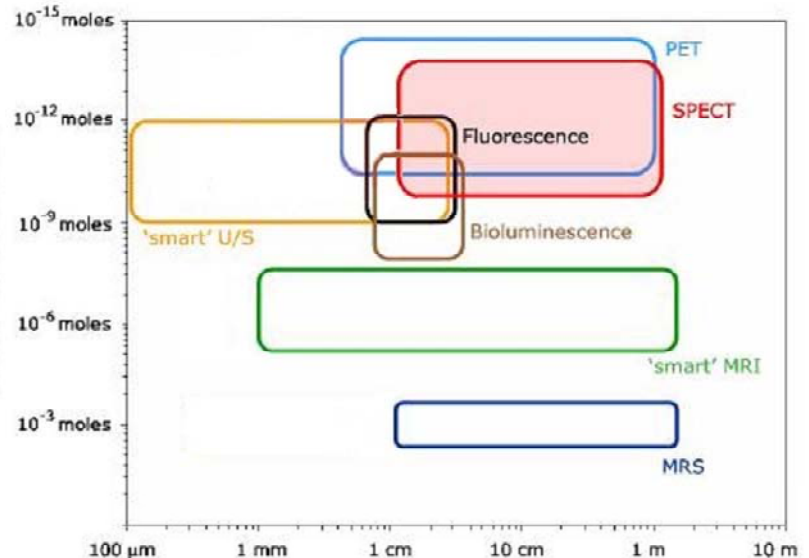
Death in Canada and the developed world from “heart attack” has decreased significantly in the last 25 years; an amazing three-fold decrease in men and more than two-fold in women. These advances can be attributed, at least in part, to advances in imaging – angiography, Nuclear Medicine, MRI and CT. Reductions in death from acute disease have resulted in an increase in those living with life-threatening congestive heart failure (HF). The Heart and Stroke Foundation of Canada reports that approximately 400,000 Canadians are living with HF and that 50% of these people will die within five years of diagnosis. Note that this is a general trend with more and more patients suffering from chronic disease such as cancer and diabetes. It is not enough to progress from acute disease to chronic disease. We also must find cures. The area of medical imaging represents the only non-invasive way to confirm/detect mechanistic cause at a whole body, organ, sub-organ and cellular level of disease in humans. What is needed for both mechanism discovery and personalized medicine is the detection of biomarkers which are specific for disease.

There are significant challenges as we strive to image biomarkers which have increasing specificity for disease:

- As the disease specificity of biomarkers increases, the trend is that their concentration, relative to background, decreases. Once this concentration drops below the picomolar level there is currently no way to non-invasively image them directly.
- For human imaging (and large animal imaging) there is, among the available imaging modalities, an approximate inverse relationship between spatial resolution and sensitivity. For example, nuclear medicine methods can detect a picomolar concentration (above background) of a biomarker if it is distributed over centimetres cubed of tissue while MRI can only detect a micromolar concentration but can do so in a millimetre cubed.
- Only for those biomarker probes developed for nuclear medicine imaging is there a track record of regulatory approval for introduction into humans.

Molecular and Hybrid Imaging provides novel strategies/opportunities to meet these challenges:

- The sensitivity of nuclear medicine can be improved through hybrid imaging by combining the anatomical and functional (MR, CT) with the functional/metabolic and molecular (PET, SPECT). Sensitivity of Nuclear Medicine probes can be optimized by reducing non-specific uptake, if anatomical context can be determined using another modality. We have shown that a contrast to noise criterion for detection can be lowered,



Matrix of large animal/human molecular imaging technologies - Adapted from Meikle et al PMB 2005, 50 R45-R61  
Image courtesy of Frank Prato



and further, that SPECT and PET reconstruction and equipment design can be improved, by using anatomical information.

- Hybrid platforms, especially PET/MR and SPECT/MR will allow multiple biomarkers to be simultaneously detected. Probe delivery (e.g. myocardial blood flow) can be quantified by MR and used in tracer kinetic modelling to improve biomarker detection by PET or SPECT.
- Hybrid platforms can be used to detect the presence of multiple biomarkers which by themselves have insufficient specificity but sufficient concentration for detection but provide improved disease specificity when detected simultaneously. For example, blood flow by MR and detection of myofibroblasts by SPECT or PET could be specific for local remodelling in heart failure.
- For hybrid PET/MR and SPECT/MR, a reporter probe can be developed for MR that produces a micromolar signal when biomarker concentrations are below 1 picomolar. Currently this cannot be used in humans, but clinical trials which involve the injection of non-human DNA into humans for diagnostic use in oncology have recently begun.

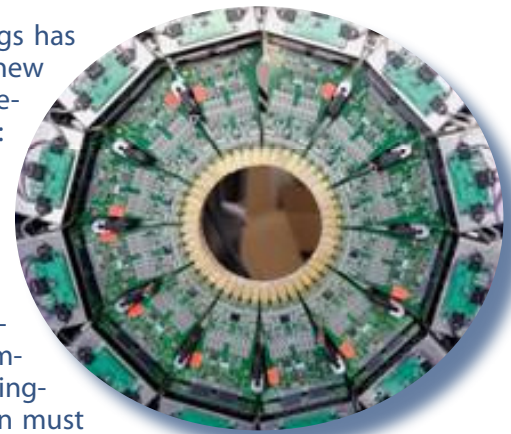


3T Siemens  
Image courtesy of Frank Prato

As the proven technology for advances in biomarker technology is PET and to a lesser extent SPECT and as development of a single probe for use in humans is an onerous task much of which has to be done for each independent centre, a network of medical cyclotron and radiochemistry facilities is needed to streamline this technology. This is not the case for other imaging technologies wherein new medical imaging methods can easily be transported from one site to another. In PET/SPECT imaging there is the added requirement to get approval for the injected material as well as implement the new equipment technologies. Only a well managed network of radiochemistry facilities will make Canada competitive in biomarker detection and deliver personalized medicine to the patient.

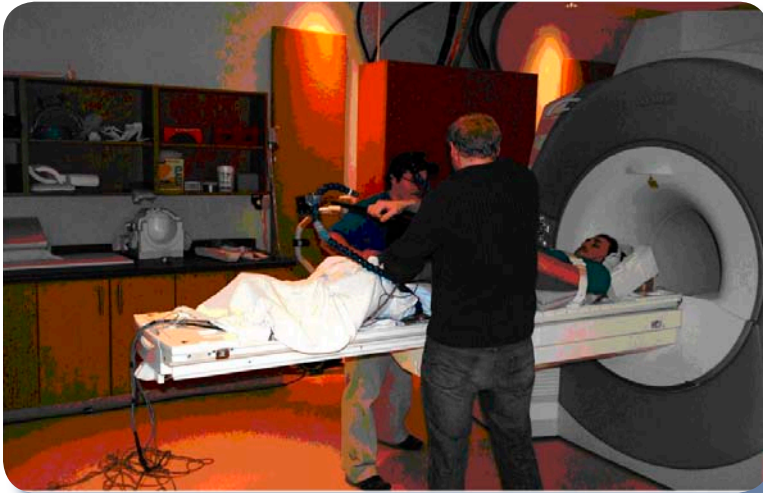
## **TECHNOLOGY DEVELOPMENT – OPEN DISCUSSIONS**

The development of software and its translation into clinical settings has been identified as a missing link. Without user-friendly software, new technology cannot be adopted to the clinical setting. Funding the development of information technology (IT) translation is problematic: funders do not accept that IT is part of the research and the software isn't of real commercial interest. In fact, the dollar value of many medical devices is not sufficient to attract funding from large companies, and many small companies don't have the financial resources to invest in research and clinical development. There is an important gap in the Canadian commercialization pathway and partnerships between CIHR and NSERC will likely be pivotal for advancing medical imaging in Canada. Universities vary considerably in their ability and willingness to support commercialization and successful commercialization must often be world wide – a difficult task for small start-up companies. One possible solution could be the creation of Canada Commercialization Chairs modeled after the Canada Research Chairs Program.



Digital APD-based PET Scanner  
Image courtesy of Roger Lecomte

Probe development is a promising field of research, but new probes will not solve any problems unless approved for use in humans and a new agent for targeted molecular imaging in humans hasn't been approved in 15 years. Regulatory requirements are perceived as an increasing barrier and are widely regarded as an enormous burden, due to the numbers of phases and the accompanying paperwork. This complexity results in very high costs such that Phase 2 trials, which define how a probe is to be used in humans, are regarded as impossible to conduct in Canada. However the creation of the Centre for Probe Development and Commercialization (CPDC) may provide the opportunity to establish a national network - a "plug and play" imaging trials network - that can evaluate new technologies and probes, and exploit the use of imaging in drug development. Such a structure could support team development, through a granting program, to establish and sustain linkages between innovative basic probe science, medical devices and clinical translation. The network could also cultivate both knowledge and commercialization advantages and could include national training programs for basic scientists and fellows with an international exchange component. The current inability to undertake large clinical trials is an additional factor in our failure to get new probes into clinical practice. The existing clinical trials networks are driven by the service needs of pharmaceutical companies. There are few or no incentives for imagers to be involved. In addition, there are very few imaging trials scientists, so developing Canadian capacity in clinical research would have to be part of the endeavor.



*Image courtesy of Centre for Functional and Metabolic Mapping, Robarts Research Institute, UWO*

In the wake of two recent incidents (breast-cancer screening tests in Newfoundland; autopsy interpretations in Ontario), concern about the quality and consistency of diagnostic imaging services across the country is crucial. The combined administrative information gathered within a network would be an important tool to understand comparative values and effectiveness and to, in concert, facilitate access to the latest diagnostic technologies.

A Canadian Medical Cyclotron Network, with radio chemistry facilities would help streamline technology advances. Such a network would ideally be multi-modality with standard operating procedures across centres, enabling national filing for clinical trials approval. It would be essential to bring the technology developers and bioinformatics capacity into the network, along with clinical scientists. The formation of a national network would facilitate large trials, ending the current system of small ad hoc trials repeated across the country - as was the case for biomarkers of estrogen receptors. Canada has a modest number of imaging research facilities, partic-



*3T Siemens TRIO MRI  
Image courtesy of Paul Matthews*

ularly around medical isotopes, so a national network is possible and would help to leverage the knowledge that is developing across the country.

As new technologies, treatments and tests move into the clinical environment, it will be important that the impact on the health care system is understood by governments. While a cost savings argument cannot be easily made and claims that technology can save money in health care are sometimes greeted with great cynicism by politicians, there are several examples of success, such as the introduction of FDG patient tests in BC. Canadian governments should be interested in networks because they will provide a resource to develop and study how to optimize the use of technology throughout the health care system. The Canadian public should be interested because of their dependence upon the publicly funded health care service to provide them with high quality, dependable diagnostics and treatments.



*Medical Cyclotrons in Canada  
Image courtesy of Frank Prato*

## PRE-CLINICAL STUDIES

### PRECLINICAL PET TECHNOLOGY AND BIOMARKER DEVELOPMENT



**Presenter: Roger Lecomte**

PET imaging in animal models can be undertaken in controlled conditions, is non-invasive and can be repeated in the same animal. It is a powerful technological tool for research into molecular pathways because it is able to study molecular targets, receptors and drug binding sites, the relationship between genotype and phenotype, and gene expression and the assessment of gene therapy. A large number of PET radiotracers are being investigated for research applications, many of which have clinical diagnostic potential.

Micro-PET is a technology that serves as a bridge between preclinical studies in animals and clinical trials. It permits faster screening of investigational compounds, reduces the time to clinical use, and lowers costs because the investigators can make decisions about a compound's suitability earlier than otherwise. Additionally, studies can be conducted using small numbers of animals. The Université de Sherbrooke built its first animal PET scanner in 1995. The demand for its services grew steadily: in 2001, the Sherbrooke Molecular Imaging Centre was the second most active preclinical PET research centre in the world (after UCLA), by 2005, Sherbrooke had licensed its own LabPET Digital APD-based PET Scanner, and in 2008, Gamma Medica-Ideas (formerly Advanced Molecular Imaging (AMI) Inc.) introduced a multimodality platform (Triumph Flex™) offering PET, SPECT and CT in a single instrument that is now commercialized worldwide by GE Healthcare.



*Sherbrooke Animal PET Scanner  
Image courtesy of Roger Lecomte*





*PET scanning of a rat with a tumor being treated by photodynamic therapy.  
Image courtesy of Roger Lecomte*

However, developing technology takes as long as developing biomarkers. For example, it required 11 years to move from the idea to the first image, 13 years to produce a prototype scanner and 23 years before the release of a commercial product. Sherbrooke's success with LabPET would not have been possible without continuous long term funding. The size of the investment was not as important as its reliability because it kept the development team and key staff, including technologists and information technology specialists, together over the lifespan of the development.

In terms of the future, multimodality imaging such as combined PET/MRI and PET/CT offers the greatest potential for advances in diagnosis and patient management because physiology, biochemistry and anatomy can be studied simultaneously. The more specific the probes become, the greater the need for multi-modality platforms and many multimodal probes such as PET/MRI, PET/fluorescence and others remain as yet unexplored.

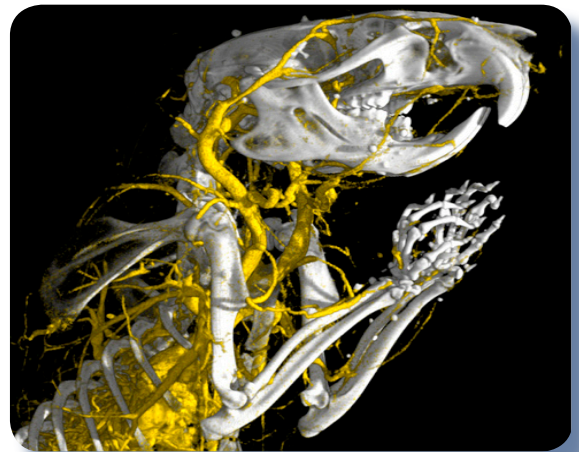
## **PRECLINICAL IMAGING: MICRO-CT AND MSK APPLICATIONS**



### **Presenter: David Holdsworth**

There is a strong group of micro-CT technology developers and users within Canada, with developers in London, Sherbrooke and Saskatoon. Micro-CT facilities are to be found in Montreal, Toronto, London, Hamilton, Guelph, Calgary and Vancouver. There is also a strong industrial base in Canada, including Enhanced Vision Systems (EVS, London), General Electric (London), and Gamma Medica-Ideas (London, Sherbrooke).

The potential for synergy with other modalities exists, and is under development at Advanced Molecular Imaging (AMI), Inc. (Sherbrooke) and Visualsonics (Toronto). Additionally, Canada has a track record of private-sector research collaborations, notably with the Ontario Research Fund Preclinical Imaging Network. Canada has a high level of technical performance with state-of-the-art equipment that is capable of spatial resolution from 10  $\mu\text{m}$  to 150  $\mu\text{m}$ , dynamic imaging of perfusion, gated imaging of respiratory and cardiac function, quantitative imaging of architecture and anatomy and rapid whole-body imaging of animals to determine phenotype and composition.



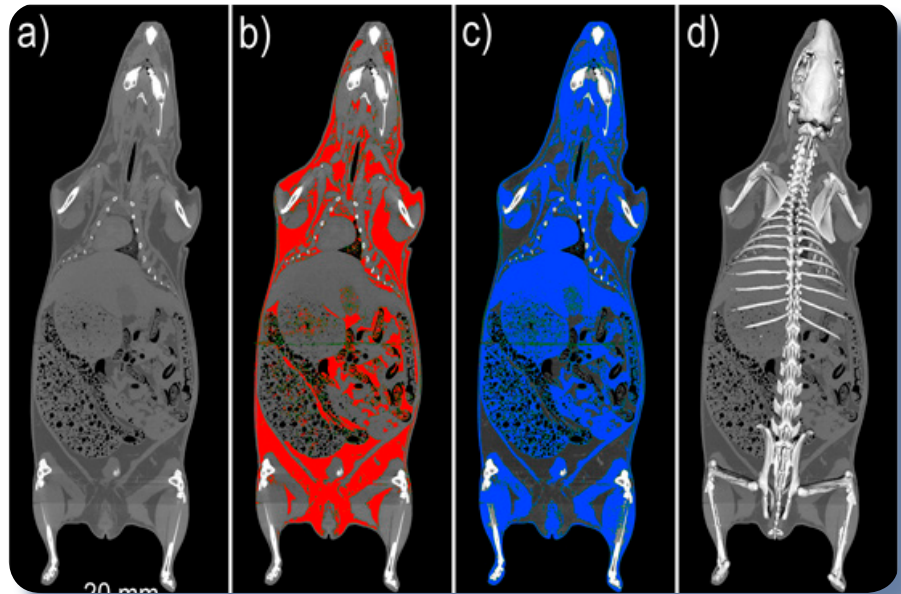
*Dual-energy micro-CT of bone and vasculature in a rat model, using Pb-based contrast  
Image courtesy of P. Granton*

However, micro-CT has had limited penetration with the broad research community. It is regarded as a niche application and is considered by some as an expensive alternative to histopathology. Additionally, the highest possible spatial resolution requires high dose exposures. Additional challenges are:

- *Limited coordination between development sites in Canada.*
- *Difficulty in validating new analytic micro-CT techniques because the standard against which they should compare is not clear. There is speculation that micro-CT is the standard!*
- *There have been significant improvements in detectors and computers, but the machines are not being built with upgrade paths. As a result, there is a substantial risk of rapid obsolescence of expensive infrastructure - according to some, within five years.*



There are important opportunities to be considered. Higher-throughput could improve cost-effectiveness and lead to wider adoption. Enhancements to both acquisition systems and post-processing algorithms would improve the throughput, as would the development of automated acquisition and remote access for *ex-vivo* specimens and the optimization of acquisition parameters to minimize scan time. For example, researchers in the area of bone healing in rats were able to reduce the cost of the assessments using micro-CT to \$30 per animal from the \$300 which was the cost of paying for veterinary pathology. Micro-CT can be used for the quantification of functions that are best studied in living animals, such as gated imaging of lung and cardiac function, studies of tissue metabolism and perfusion and kinematics of joint motion. There are opportunities to develop multispectral and multimodality imaging by multi-channel analysis, dual-energy CT, micro-CT / SPECT / MRI / PET combinations, associating function with anatomy through acquisition and post-processing algorithms to enhance automated segmentation of tissue groups, and through a combination of micro-CT imaging and conformal therapy delivered in animal models. The bulk of basic science is still accomplished with optical microscopy, luminometry and fluorimetry. Synergistic developments in cellular imaging and micro-imaging applications other than CT, SPECT, PET and MRI are routes by which optical microscopy and live-cell imaging can be combined.



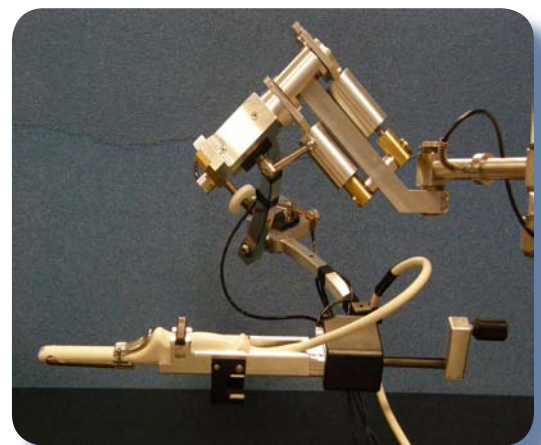
Whole-body micro-CT of guinea pig, showing adipose, lean, and mineralized tissue  
Image courtesy of T. Regnault

### PRE-CLINICAL: PATH FROM CONCEPT TO CLINICAL USE

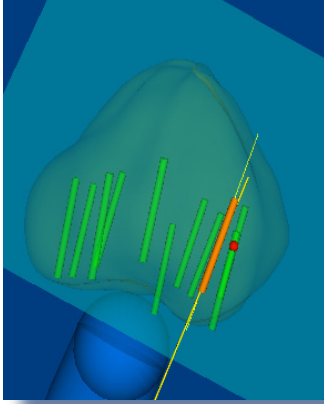


#### Presenter: Aaron Fenster

To become leaders in the field and fulfill the promise of our laboratory work, an investment in clinical translation is vital. Canada is particularly well placed in regards to image guided interventions and medical devices such as medical robotics. In fact, both the cost of clinical translation and the regulatory barrier for these are relatively low. More importantly, Canada has world leaders in research in these areas and a track record of clinical translation successes such as the CT scanning for stroke imaging. Canadian universities have academics with good track records for commercialization and imaging companies have been formed as a result of academic collaborations. An example of a Canadian success story comes from the development of image guided intervention for prostate cancer using a 3-dimensional ultrasound imaging technique for targeted needle biopsy. The device needed two years for FDA approval and commercialization, but only about



Mechanical Guidance System  
Image courtesy of Aaron Fenster



*Prostate with biopsy cores shown in bright green and the planned biopsy core in yellow  
Image courtesy of Aaron Fenster*

six weeks to get approval as a class 3A device in Canada for use in clinical trials. It is now undergoing clinical trials in both Canada and the US. Potentially, image guided procedures could be developed for prostate, brain and breast cancer; for cardiac diseases, and studies of the abdomen – both clinical and commercial success can be envisioned.

The single largest barrier to clinical translation of new technology is the lack of physician time to bring clinical trials forward. Their expertise is essential to move research into the clinic. They are the end users of technology and they understand where the clinical priorities lie. However, the barriers are high. While initiatives to train clinicians to be scientists could be very useful, it is recognized that they face immense challenges. Competition for their time in clinical settings, patient care, dependence upon fee-for-service, and unsupportive academic environments in regards to academic credit for clinical translation and clinical trials, lack of core competencies within the Royal College of Physicians and Surgeons of Canada and the lack of peer mentors all contribute to the difficulty to recruit and retain physician investigators

### **PRE-CLINICAL STUDIES – OPEN DISCUSSION**

The funding and know-how for the development of systems ready for clinical testing, e.g. capable of addressing problems like regulation, intellectual property and other issues is weak or absent in many academic settings. Prototype development expertise and the experience to accelerate the path to commercialization are weak in Canada. Although pre-clinical imaging is an important part of drug development, large pharmaceutical companies are reluctant to invest in this area, even though the least expensive part of pharmaceutical development is arguably during the preclinical phase.

Today's pharmaceutical industry is in crisis and rethinking its role in research and development. It is likely that pharmaceutical research will begin to focus on core molecule development and look for partners who will undertake the pre-clinical phases. Opportunities to work with pharmaceutical companies will arise by understanding their objectives and packaging proposals to address those objectives.



*Image courtesy of Frank Prato*

Currently, access to PET imaging is hampered by two principle barriers: the purchase price and maintenance cost of the infrastructure (cyclotron, radiochemistry, scanners) and access to highly qualified personnel. Creating a stable financial infrastructure requires high throughput fee-for-service, a secondary source of funding, or both (as in the case of the US NIH, which has centre grants that allow the sites to offer subsidized fee schedules). Subsidizing the services has increased the numbers of researchers who use the facilities and maximized access to the technology. Without the stable funding that the American centers enjoy, fee-for-service isn't a sustainable model for science in Canada. In fact, experience indicates that funding agencies are unwilling to pay even 50% of the true cost; to charge more will risk that funding request will be denied. Without a supporting partner, the facilities cannot be maintained and upgraded to ensure Good Manufacturing Practices (GMP) compliance, which substantially raises the costs of running a facility. It's a Catch-22

because without sufficient funds to sustain GMP, it is impossible to attract a commercial partner. Centers with sustaining funding are more attractive to investors – in fact, participants from Canadian facilities with sustaining funds have been approached by American investors.

The incentives to form interdisciplinary teams are lacking in Canada. Multi-disciplinary teams are necessary to link development to clinical translation. NSERC has strengths in supporting multi-disciplinary teams, but the Canadian capacity to fund teams is notably weak and CIHR no longer offers program and team grants. The loss of team grants in recent years has been a particular blow to sustainability, since the loss has affected all levels of highly qualified personnel from students to clinicians.

Despite these challenges, Canada has an opportunity to take a lead in the pre-clinical research area through the formation of a national network for small animal imaging comprised of the existing nodes that are engaged in developing and using micro-CT, micro-SPECT, micro-PET and micro-MRI. The development and sharing of standard operating procedures and the opportunity for collaboration would be valuable in and of itself.

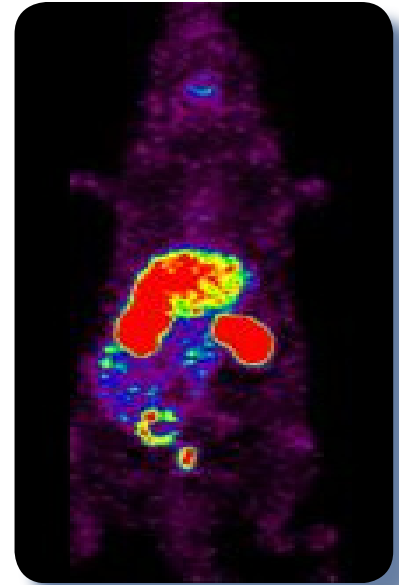


Image of a mouse injected with  $^{64}\text{Cu}$ -labelled Phthalocyanine (Courtesy J.E. van Lier & R. Lecomte, U. Sherbrooke)



## CLINICAL AND TRANSLATIONAL STUDIES

### PERSPECTIVES ON MRI IN CANADA



#### **Presenter: Ravi Menon**

Because water is ubiquitous in the body, MRI can be used to measure structure and ultrastructure, function, biochemistry, and physiology. As water molecules preferentially diffuse along myelin tracts, MRI is frequently used to study the brain and is capable of showing plaques in the brains of Alzheimers patients and demonstrating functional brain changes that precede behavioural deficits by perhaps as much as 20 years. MRI can also be used to produce quantitative maps of myelination in the brain, which is important in neurological diseases such as multiple sclerosis. The push to higher fields is driven by the need to increase speed and resolution and the desire to use other nuclei and novel contrast agents. A 7 Tesla (T) MRI can show many neurotransmitters and neural or glial markers. It can be used to measure metabolism and observe changes in rates in the brain. With  $\text{H}_2^{17}\text{O}$  MRI, it is possible to measure oxygen consumption in the brain. In Canada, MRI has been used to assess cerebral vascular reserve after stroke, or in dementia, without using contrast agents. It may be possible to use this method to map cardiac



function. In other countries, MRI has been used for pre-surgical planning in neurosurgery, with notably improved clinical outcomes. In Canada, it has not been possible because of a simple barrier: there is no billing code. One area for future research is the development of enhanced contrast agents and novel molecular probes.

The technological capacity of MRI has been constantly increasing and Canada has consistently adopted new technology, albeit somewhat later than others. Until recently, this has been an advantage because the early adopters spent most of their time learning how to make the machines work. However, in the last 10-15 years Canada has begun to fall off the curve, taking more than five years to acquire new technologies. Canada has fallen behind in

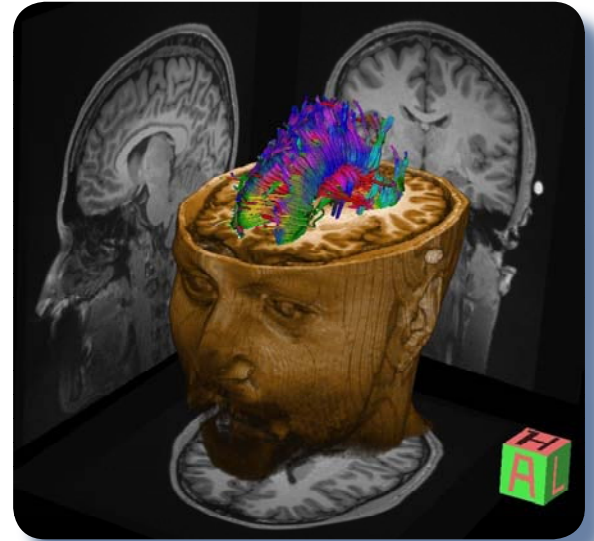
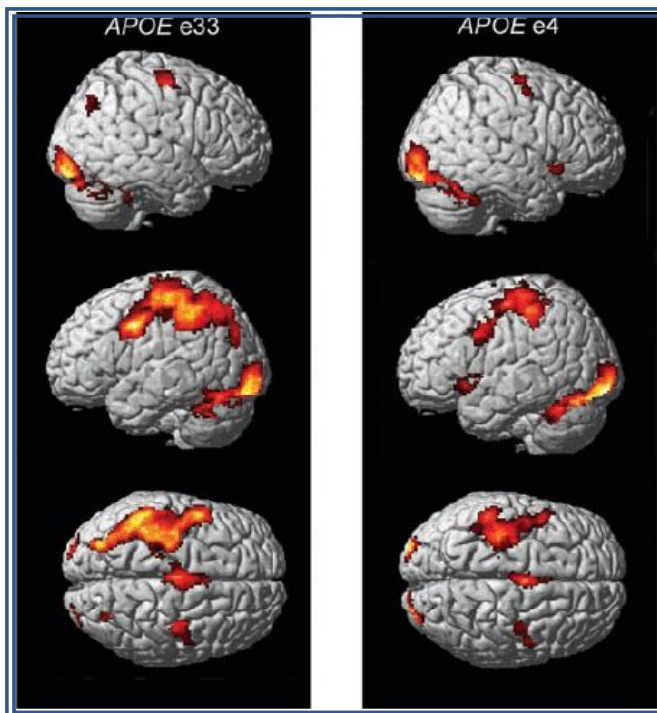


Image courtesy of Ravi Menon



Courtesy Lars Nyberg, Karolinska

other important, structural ways: Health Canada guidelines haven't changed since 1987 and, in fact, Health Canada has permitted Canadians to follow FDA regulations, which were updated in 2003.

Two of the 15 most cited MRI scientists of the past two decades are Canadian and Canada is the data hub for many international MRI trials. Canada has 1% of the magnets and 5% of the scientific output in MRI research with 93% of all imaging papers in Nature and Science in the past 15 years involving MRI technology. The latest large magnets are exorbitantly expensive to run (the newest 9T facility in France will cost almost \$10M per annum), so the key, in Canada, to maintaining competitiveness and productivity in the face of magnetic field escalation may be core infrastructure funding.

## **BENCH TO BEDSIDE**

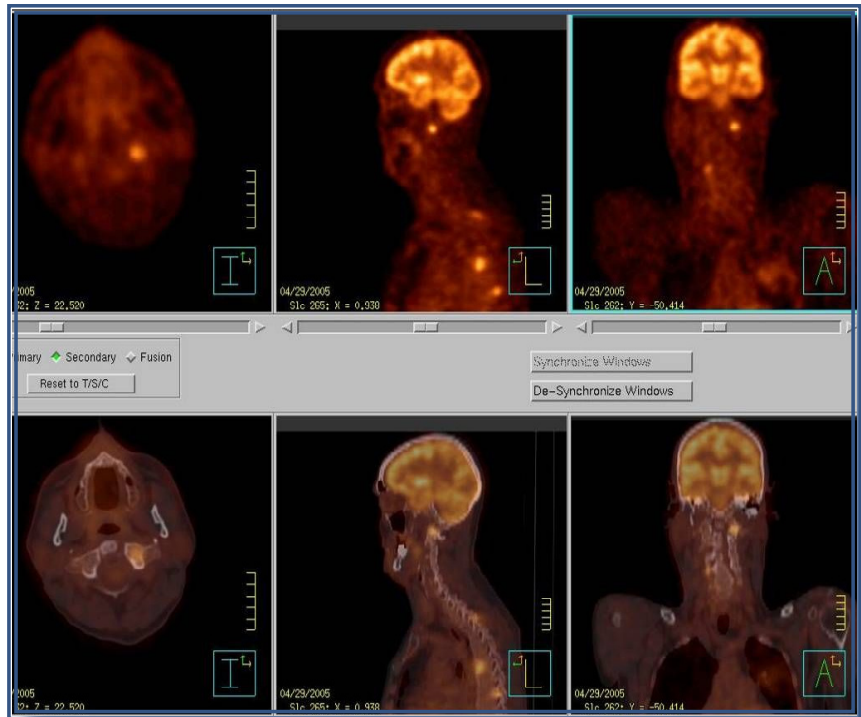


### **Presenter: François Bénard**

Hybrid imaging devices, new contrast agents and radiolabelled probes are at the leading edge of imaging research in the clinical setting. There are a number of important clinical problems that must be solved in oncology. For example, the determination of the hypoxic volume within a tumor boundary is difficult to assess when trying to define the target for radiation therapy. It is also possible to miss small nodes when defining the target volume, so accurate staging is important. Consider also cancers, such as prostate and possibly some breast cancer, with highly variable growth rates. Some of these tumors may be indolent and may



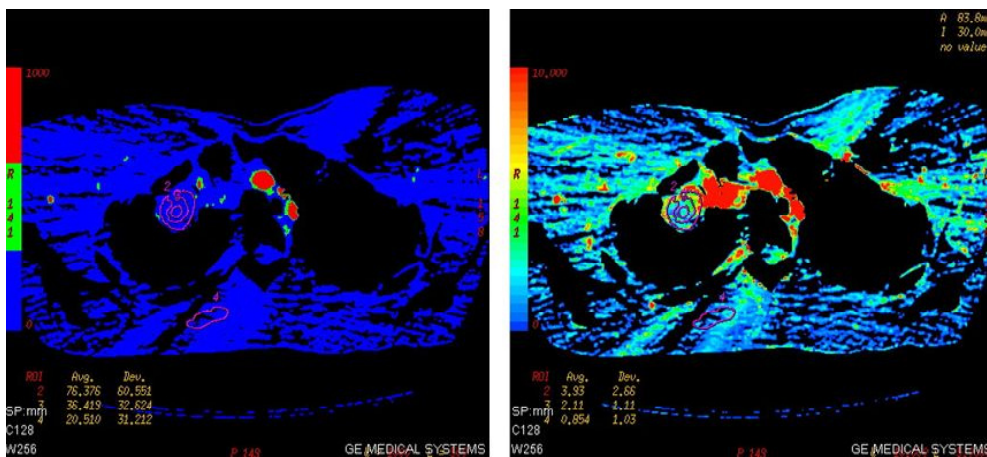
never cause problems, especially in the elderly population. It is important to differentiate between those that must be treated and those that should be monitored. Imaging tools, such as PET imaging of cellular proliferation or glucose metabolism, could provide some answers. When cancers are treated systemically, the population-based response rate to some treatments may be as low as 20%, but predicting whose tumor will respond and whose won't evades us in many cases. Another facet of this problem is the assessment of response to novel targeted therapy, which may cause a reduction in tumor growth rate but cause limited shrinkage. Gleevec® is an example of a successful treatment that does not initially cause a change in tumour size, although it does shut down tumour metabolism. In these cases, assessing response to treatment (e.g. PET measurement of glucose metabolism) is essential.



*Cancer Imaging with PET/CT  
Image courtesy of François Bénard*

Oncologists now recognize that tumor cells are heterogeneous and in order to understand how each sub-population is responding, several probes may be needed to evaluate a therapy. Clearly, functional and molecular imaging may come to play an important role in measuring cancer response to therapy. This is currently not a precise science – the response of tumors is based on assessment of the dimension of a tumor, but PET and other functional imaging techniques such as dynamic contrast-enhanced MRI can detect response earlier than morphological methods. Treatment predictors are also needed as there is huge heterogeneity across tumor sites and even within single tumors. For example, the level of variability for estrogen receptors expression across tumors in the same patient may be as high as 30%. If imaging or non-imaging biomarkers were available for every treatment to stratify patient populations into those most likely to respond and those in whom a response is improbable, then patients could be spared unnecessary side-effects from ineffective

treatments. This would revolutionize cancer management and open the door for targeted/personalized therapies. Herceptin is one example of a drug that was successfully introduced because it had an immunohistochemistry biomarker to identify the responder patient population. There may well be other drugs that have been discarded because a biomarker did



*blood flow imaging with dynamic contrast-enhanced CT  
Image courtesy of François Bénard*

not exist that could identify the responder patient sub-sets. Although a drug company initially may not be enthusiastic to realize that 70% of a patient population will not respond to a given drug, it is likely that if the sub-population with a very high response rate could be identified, the drug will have very important clinical utility.

## **MOLECULAR IMAGING RESEARCH IN ONCOLOGY**



### **Presenter: Karen Gulenchyn**

One example of imaging clinical trials that illustrates the challenges and provides some lessons learned is the work that has been done on the integration of PET into the health care system of Ontario. In the early 2000's, elements of the medical community were recommending that PET be used clinically. Because of the general poor quality of translational studies in imaging, Health Technology Assessment experts were skeptical that there was sufficient evidence to support the introduction of FDG PET imaging. Following a literature review of the use of FDG PET imaging in oncology, cardiology and neurology, it was determined that the existing evidence was considered insufficient by the Ontario Ministry of Health to justify the clinical introduction of expensive PET technology. The call for proposals was issued in June 2002 and six trials were developed, three of which were randomized controlled trials (RCT). The trials took much longer to complete than initially anticipated for a variety of reasons, including the lack of experience of many of the researchers conducting the trials and the need to accrue a large number of patients. Despite these challenges however, three of the five original trials have been completed, two with positive results. One of these two was closed early because the efficacy of PET was demonstrated and in both cases these indications were approved for clinical use. The experience demonstrated the need for improved informatics tools and a quality assurance program to ensure consistency in the parameters of the scanners used.

The trials were difficult to do because a great deal of education and training was required, and consensus had to be developed across multiple disciplines. The development of protocols was hampered by the lack of trained imaging investigators and the challenge of getting the imaging community to accept randomization. Finally, training imaging technologists in the principles of Good Clinical Practice (GCP), including consent procedures was required. Key success factors for future networks would include:

- *Having a clear definition of the question. Is it about an individual patient outcome or a health system outcome?*
- *Having a clear focus: Identify and validate the best probe for each target produced with GMP.*
- *Identifying the best imaging modality.*
- *Ensuring that project groups are multidisciplinary e.g. chemists, oncologists, pathologists, clinical trials personnel and others.*
- *Focusing on multi-site trials where possible to ensure the efficient use of probes and imaging technology.*
- *Demonstrating the excellence in the clinical trial methodology, through robust data management systems and through quality assurance processes.*

Potential PET imaging approaches for future trials might include response assessment with glucose utilization and metabolism, DNA proliferation and apoptosis; and patient therapy stratification with hypoxia imaging. Other examples would include permeability imaging using MRI/MRS and flow measurement associated with drug delivery, using ultrasound.

Canada has certain strengths that could be better exploited. Our publicly funded health care system, specialized centers for delivery of cancer care, access to a large population of patients who tend to be treated by specialists and based on common protocols lay the groundwork for networked clinical trials. There are al-

ready some good clinical trials networks, such as Ontario Clinical Oncology Group, Ontario Institute of Cancer Research, and the Western Canadian Network. An option to reduce the cost of trials is to consider how to make multiple applications based on the intervention's function instead of by disease. The recent clinical trial network for sodium fluoride is a good example of how we can work together.

## CLINICAL AND TRANSLATIONAL RESEARCH: CARDIOVASCULAR SYSTEMS



### Presenter: Rob Beanlands

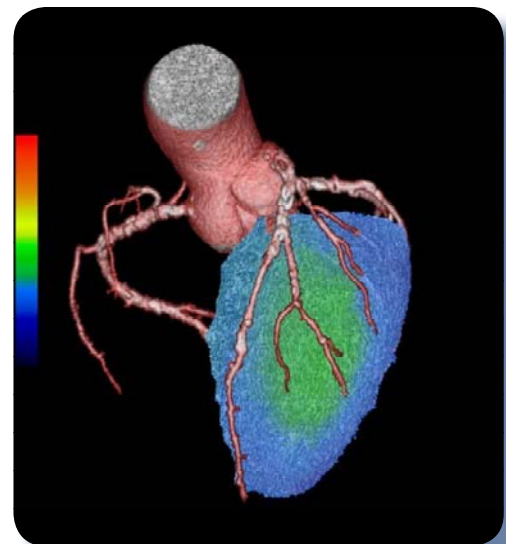
Atherosclerosis and other acquired diseases affecting the cardiovascular system generally begin asymptotically at a young age and progress in a gradual step-wise manner until reaching a critical point when symptoms and/or serious events may occur - often suddenly. An important goal is to prevent or delay ischemic events, heart failure, and sudden death at the earliest stage possible. For the treating physician, there are still many unanswered questions such as: How can we identify patients most susceptible to heart failure (pre-heart failure?) Does early plaque definition make a difference? Can micro-vascular disease be a target for therapy and what therapies? How can biomarkers help to detect and monitor disease, and to direct therapy? There is also confusion about which tests are best and will give the fewest false positives and false negatives and about how to diagnose and treat patients with advanced or multi-system disease. Currently, there are no techniques to directly visualize coronary microcirculation in humans *in vivo*, no good animal models for atherosclerosis and only unsatisfactory models for heart failure. The challenge is to find alternative means to create clinical utility and translate disease knowledge to clinical use.

Imaging is an important tool but too often there are concerns about the accuracy of the tests, the availability of the best technology, and concern about the best use of new probes. In addition there are regulatory and cost considerations. These concerns are offset by the potential utility of coronary CT angiography, high resolution MRI, the quantitative functional capability of PET and the promise of combined modalities such as SPECT and PET/CT and MRI/PET. Combined with emerging biomarkers, these technologies offer the means to specifically direct therapy in ways considered impossible a short time ago. The recent development of a new perfusion agent is set to revolutionize cardiac imaging and change the way cameras are made. Many of these new technologies can be used for imaging in a variety of clinical situations. There are many commonalities between cancer and cardiovascular imaging requirements, except that in oncology the aim is to kill the cells and in cardiology it is to fix them.

Provincial networks and teams exist such as the Imaging Network of Ontario whose collaborative research is funded by the Ontario Research Fund. There are already two large national imaging networks or teams in cardiovascular imaging that are being developed. "IMAGE Heart Failure" is a large team grant with nodes across Canada and in Finland. Different cities are responsible for



*Pre-clinical Siemens Inveon PET/CT  
Image courtesy of Paul Matthews*



*Courtesy of Rob deKemp et al  
J Nucl Card 2007*

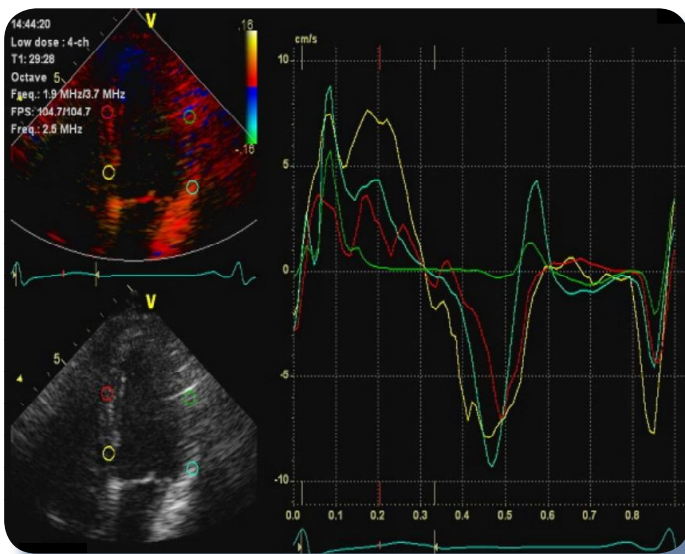


different core modalities – e.g. MRI in Calgary and London, PET in Ottawa, SPECT in Toronto and Ottawa. As clinical practice sometimes makes it difficult to randomize in one city, cohort design matching will be combined in a unique manner with randomization strategies and used to compare results. There are three levels of projects within the network from animal models to patient platforms. The overall objectives are:

- *To determine the impact of imaging strategies on relevant clinical outcomes and decision making in patients with heart failure;*
- *To establish standardization, quality assurance measures and central databases to achieve reliable outcome driven research; and*
- *To apply this as a platform for evaluation of new and emerging biomarkers in heart failure*

The Canadian Atherosclerosis Imaging Network “Hearts and Minds” (CAIN) (PI: JCTardif) is funded by a Network grant from CIHR and more recently by CFI to support an integrated communication network. This project arose out of a workshop funded by the

CIHR Institute of Circulatory and Respiratory Health. It is a pan-Canadian multidisciplinary collaboration with over 20 participating sites, with core imaging laboratories throughout the country. Research topics include 3D ultrasound for looking at carotid plaques and PET/CT and MRI to investigate the natural history of plaques and intravascular ultrasound to understand coronary atherosclerosis through direct imaging in large patient populations.



*Image courtesy of Kwan-Leung Chan, University of Ottawa Heart Institute*

These networks and teams will enable better understanding of disease and therapies in heart failure and atherosclerosis. While they will also serve as platforms for evaluation of emerging techniques and biomarkers, much more is needed. With the vast array of developing methods and biomarkers means to accelerate their translation and determine potential clinical use are desperately needed.

## **CLINICAL AND TRANSLATIONAL STUDIES – OPEN DISCUSSIONS**

One of the major barriers to progress in the translational research area is the difficulty in moving potential biologic markers and radiotracers into clinical trials and use in the clinic. Unlike the US, UK and other countries, there is limited private and entrepreneurial investment in Canada for the development of new radiotracers and contrast agents. Multinationals are not investing in Canada because Canada is a small market. The cost of developing a manufacturing facility adherent to GMP is very high and undertaking toxicity testing in order to establish clinical feasibility costs over \$100,000 per compound for small trials, yet there are few incentives to attract this level of investment in Canada. Also, the cost of toxicity testing becomes prohibitive when seen as a proportion of the potential for profit. In Canada there is a gap between basic science, which is required to be completely novel, and clinical research which is criticized for failing to be innovative. This is a fundamental problem because the incentives for moving the science into the patient are absent in Canada at all levels of academia from the funding agencies to the universities.

Well-designed trials are costly and complex; those based on small sample sizes will generate results that cannot be generalized and that cannot be used to make sound decisions. Canada needs to make an organized effort to design better imaging clinical trials, which include normative backgrounds and standard



operating procedures. In the case of networks, clinical trials applications (CTA) could be disseminated across the network. The lead institution, or network “champion” could be funded to provide training for the specific trials and to help with the regulatory component (e.g. a Health Canada liaison to support submissions). It is well known that many tracers have multiple uses and applications. By working in a concerted fashion, it would be possible to design clinical trials to investigate the multiple applications of the tracer simultaneously. This should improve the speed of regulatory approval, as well as reduce the cost to both the developer and the federal government. It might also be possible to ‘pool’ for intellectual property submissions, e.g. applications for hypoxic models in cardiology, neurology, and cancer simultaneously rather than in separate IP applications. The efficiencies from a provincial government/institutional perspective are also important: more uniform adaptation of technology, compression of the numbers of modalities, and efficiencies in purchasing.



Another possibility might be joint bilateral agreements with Europe and the US, for agents with a low risk profile. Where use is approved in countries with similar high standards, we should have an expedited approval process. Perhaps a centralized resource for toxicity testing could be created and new labeling technologies developed that use smaller quantities of the precursor to keep costs lower and promote more expedient evaluation.

The cost of medical care and technology has continued to rise over the last decades. Few people, particularly politicians, believe that new technology investments are a cost saving measure. Nonetheless, Canadians are being sent to the US for treatment, monitoring and diagnostics because of the lack of availability of imaging and biomarker services in Canada. Some provinces are responding by purchasing services from private providers, as in Alberta and Quebec, apparently as a cost saving measure. Thus, it would appear that there is economic incentive for technology investment in Canada. Considerable savings could be realized by the appropriate management of treatment and diagnostic imaging. However, Canadian researchers have not succeeded in demonstrating that imaging technologies are cost effective and improve patient outcomes, either to the patients, public at large, or politicians. Without support from the average Canadian, it is difficult for politicians to prioritize funding for research. In the US, PET funding was not the result of a scientific process – it was a political process driven by a committed public.



Provincial governments would like to see a demonstrated clinical benefit, yet it may be impractical to wait for mortality data. Before the natural history of a disease is well understood, it can be difficult to know which proximal endpoints are appropriate. The regulatory process requires a level of certainty, but medicine and medical advances are iterative and dynamic. As provincial funders are reluctant to undertake research on comparative effectiveness, it is important for the medical community to design and build studies that can help governments get the information they need to demonstrate benefit for patients, taxpayers, industry, and the

economy. From the federal regulatory perspective, a valid surrogate or intermediate marker for biomarkers is acceptable, even without clear demonstration of clinical benefit.

## THE INTERNATIONAL PERSPECTIVE

### IMAGING FOR TRANSLATIONAL NEUROSCIENCES DRUG DEVELOPMENT

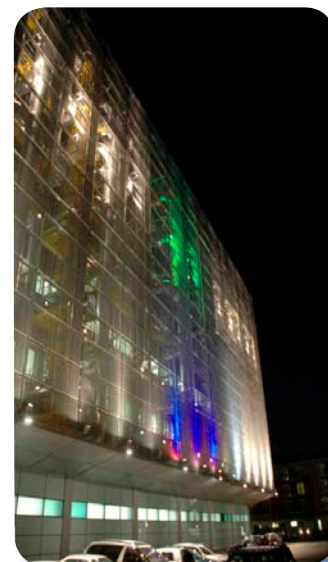


#### **Presenter: Paul Matthews**

The pharmaceutical industry is at a crossroads: between 2012 and 2014, drugs accounting for approximately 40% of large pharma earnings will come off patent. Replenishing the pipeline to maintain market value has been increasingly challenging. Current approaches to developing new pharmaceutical products is difficult, time consuming and costly: on average it takes 15-20 years to move a molecule into human testing, costs in excess of US \$1 billion and only about one in ten molecules that are tested in humans will make it to the market. Development pathways are also less certain for the major chronic diseases that form a major part of the unmet medical need. Pre-clinical models are typically poorly predictive. Pharmaceutical companies are highly motivated to find ways of making development decisions more confidently, quickly and at a lower cost. Imaging biomarkers could facilitate meeting all three goals, and remain useful after marketing where they can be used for differentiation, evaluation extension of indications and aspects of safety monitoring. Large costs can be avoided if imaging biomarkers are used to determine why one molecule might be better than another in earlier phase trials. Applications of imaging for experimental medicine studies can allow decisions to be made using human disease models and reducing reliance on pre-clinical studies.

The GSK Clinical Imaging Centre (CIC) at Imperial College is a facility operating at the academic-industry interface, as a partnership between the University of London's Imperial College, the Hammersmith Hospital and GlaxoSmithKline (GSK). As a pharma-based centre for imaging-based experimental medicine, the CIC is unique in the industry; as a centre dedicated to using advanced human imaging specifically to meet the needs of pharmaceutical medicine, it is unique in the world. This successful three partner initiative is based on a win-win-win scenario: construction of the building was undertaken through the three partners - Imperial College was pleased to share the costs because they were able to occupy one half of the building for less than a third of the cost projected for their original construction. In return, Imperial put in place structures that would support the collaborative agreement and an overarching grid to maximize the value for GSK by ensuring that overheads remain appropriate to the facilities used for each study. Additionally, Imperial reorganized their research services office to provide a single point of reference, which decreased the time required for the approval of research funds and their distribution. The CIC overarching goals are to support drug development, develop new imaging methods and support innovative training programs.

The CIC includes a full range of advanced tools for human imaging research, dedicated research radiochemistry and radiopharmaceutical manufacturing facilities, with a full GMP facility. The CIC is the largest UK clinical research imaging centre, with approximately 4,000 m<sup>2</sup> of clinical, laboratory and office space. They have a 3T MRI, two PET/CT, two cyclotrons, radio-chemistry and biology laboratories (supported by microPET). In addition, they have a dedicated specialist IT environment. The staff consist of over 70 FTE including radiochemists, biologists, physicians, clinical scientists, physicists, nurses, radiographers, data analysts and operations staff. In addition, staff is seconded from GSK units for their specific expertise to work alongside academic collaborators, fellows and trainees. Clinical and specialist imaging training are important components of CIC, fostering innovation and recruitment of excellence - a critical factor for sustainability. CIC has many training programs



*GSK Clinical Imaging Centre,  
Hammersmith Hospital, London  
Image courtesy of Paul Matthews*

(some of which are funded by outside sources such as the Wellcome Trust, the Medical Research Council and the European Commission), including doctoral training centres designed to expose clinicians to research.

The CIC's early focus has been on drug development in neurosciences and oncology, using molecules that are already at least in Phase 1 trials. The considerable expense of advanced, PET makes the business model for molecular imaging difficult to formulate for diagnostics development. However, in the context of decision-making for pharma, for which major drug development costs can be minimized or avoided by the activities, it may be a sustainable part of the business. PET can differentiate molecules clinically, provide a basis for selection of dose, evaluate distribution of therapeutic molecules into target tissues or sites of potential toxicity, and define measures of pharmacodynamics, all of which contribute to moving a molecule out of the pre-clinical development phase more rapidly. New combination modalities such as PET/fMRI promise even greater potential for these goals in the future.

Imaging can change the way clinical trials are done and redefine disease concepts. In combination with biomarkers, it is possible to move away from large population studies and, for example, confirm a potential for activity with biodistribution studies including as few as six to ten subjects. Imaging additionally can stratify populations by pathology or response to optimize the likelihood of drug response. Imaging thus is not simply a tool - it is a disruptive technology.

In the longer term, imaging could link diagnostics and therapeutics to enhance clinical value for high cost drugs, using biology (rather than adverse events) to drive dose selection and timing.

Canada already has important activities in this area. One example is a partnership between CIC and one of the workshop participants, Sylvain Houle, at Canada's Centre for Addiction and Mental Health (CAMH). The partnership has resulted in the development of the first agent, PHNO, to show specificity and selectivity as a novel dopamine (D3) antagonist *in vivo*. From PET studies, the dose originally selected for clinical application was shown to be sub-optimal. Further imaging studies showed that a higher dose achieved improved receptor occupancy and could move forward for clinical development.

Partnerships such as this illustrate the benefits of academic/industry collaboration leading to innovation. Such partnerships will be essential for exploiting the enormous libraries of molecules that are present in industry. For sustainable collaboration however, it is important to understand how to reward people for working collaboratively so that contributors are recognized in addition to the leaders. Also more imaginative career support is required for people who want to step out of existing structures that encourage intelligent 'discipline hopping.'

There are many benefits for industry of working with the academic community, for example, for access to new probes and the improved development of new techniques such as PET cameras and synthetic chemistry hardware. Three key issues for successful industry/academic collaboration are: understanding of mutual expectations, work in

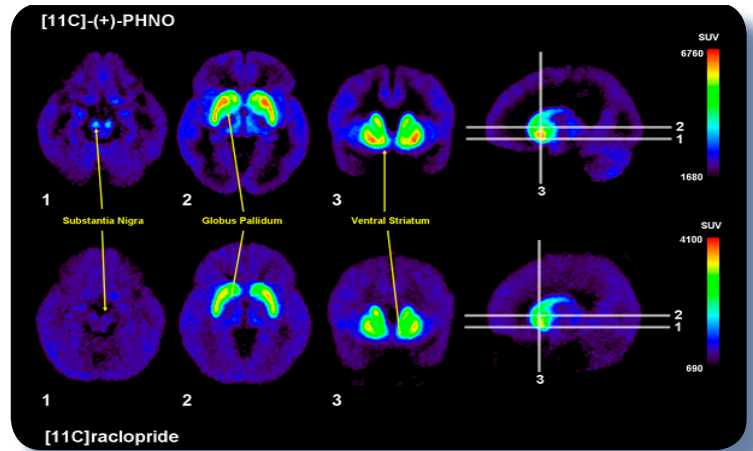


Siemens Eclipse Cyclotron  
Image courtesy of Paul Matthews



partnership, transparency of objectives and activities, and effective mechanisms for planning together.

The CIC is operating on the basis of a relatively new concept which is being closely watched by other companies. GSK carried the cost of the imaging centre. It is an expensive enterprise, but the CIC is already showing value: they are totally focused on the GSK mission and there are no delays in start-up, they have the experts and the “right questions being asked by the right experiment at the right time”. The CIC also appears as an exemplar for UK government policies for science and technology as a perspective, they wanted to foster a high tech environment championing public-private partnership in healthcare and pharma, major sectors for the UK economy.



Academic-industry discovery science: development of novel applications of the radiotracer PHNO  
Image courtesy of Paul Matthews

## FROM ICMIC TO ACRIN: FROM BASIC ONCOLOGIC IMAGING TRIALS IN THE US NATIONAL CANCER INSTITUTE FRAMEWORK



### Presenter: Barbara Croft

The goal of the *In vivo* Cellular and Molecular Imaging Centers (ICMIC) is to facilitate integration between the basic (molecular and cellular) and imaging sciences through the application of molecularly based imaging techniques that can non-invasively and quantitatively study cancer. The ICMIC program was created following the recommendations of an Imaging Sciences Working Group task group in 1998. The first three ICMIC were funded in 2000 for \$6M to support: research projects, core funding, developmental projects, and career development. As of 2010, eleven ICMIC have been funded and although the funding grew in the first six years, it has since been relatively flat. To date, the existing ICMIC have produced over 755 scientific articles, ten associated clinical studies, two patents and 21 patent applications and have undertaken 107 developmental projects. Their investigators include about 20 disciplinary groups within both the basic sciences and clinical sciences. This year marked a comprehensive evaluation, conducted by an independent agency, which was uniformly positive and may provide guidance for similar evaluations of network programs here in Canada. Observations that may be of particular interest to Canada are as follows:

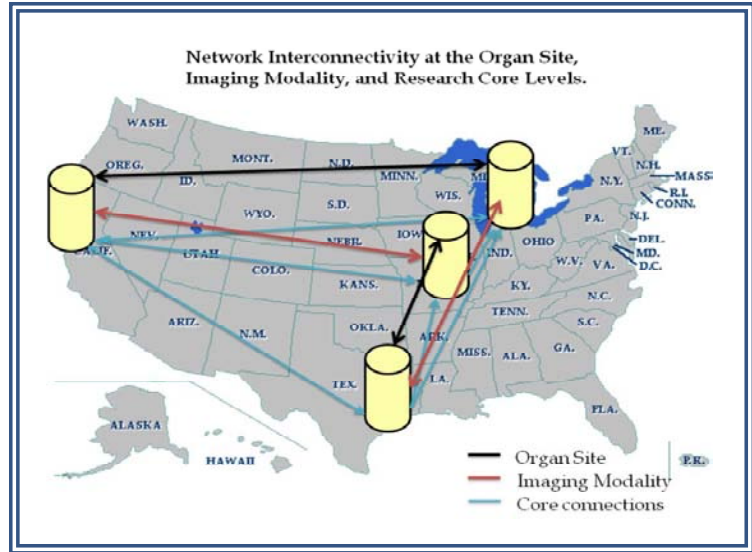
- *Very large sites did not tend to have external partners, possibly because they were self contained for their own work.*
- *Sites in small, less well developed institutions may not have enough potential collaborators to maximize their potential.*
- *The majority of the ICMIC sites also received funding for small animal imaging resources*

The ICMIC program has been very successful in bringing together many different disciplines from the physical and life sciences domains, with an emphasis on system wide integration. The outcome has been the development of innovative preclinical tools for drug development and new clinical imaging tools for both pre-clinical and clinical development. The ICMIC is just one example of the numerous cancer imaging programs supported by NCI, although it represents one of NCI's major investments. Details can be found at: <http://imaging.cancer.gov/researchfunding> Although NCI provides more funds for imaging than other NIH



Institutes, there are other NIH programs with an imaging component including the NIMH, NIDA, NIAAA: National Cooperative Drug Discovery and Development Groups (NCDDDG) for the Treatment of Mental Disorders, Drug or Alcohol Addiction (U01/U19), and Innovation in Molecular Imaging Probes (R01) (NIBIB, NIA, NIAMS, NICHD, NIDDK, NIMH, NINDS) (PAR-09-016).

The American College of Radiology Imaging Network (ACRIN - <http://www.acrin.org>) has had funding for cancer imaging research for the past 11 years (three rounds of funding). Each clinical trial site is funded according to protocol rather than “membership”. Participation is open to radiologists from academia, community hospitals and freestanding medical clinics; other cooperative groups; representatives from industry; and health insurance payers. There are sites in 32 states and the District of Columbia, and four other countries including Canada, which has five sites (one in Nova Scotia, one in Quebec and three in Ontario).



Participation in ACRIN offers the following benefits:

- Leadership
- Administration
- Data management
- Professional and regulatory support staff
- Biostatistics Center at Brown University

ACRIN manages the National Oncologic PET Registry which works to ensure access to Medicare reimbursement for certain PET scans. Fundamental changes in the use of PET took place when ACR was able to lobby for Medicaid reimbursement for PET scans.

There are several opportunities for collaboration with NCI and other agencies, including collaboration through the Network for Translational Research (NTR). The NTR goal is to accelerate the translational research of *in vivo* multimodal imaging and/or spectroscopic platforms from the laboratory and pre-clinical level to the clinical level, e.g. to develop, optimize, and validate imaging technology platforms and methods so that they can enter single or multi-site clinical trials and eventually be incorporated into clinical practice. Its work is accomplished through multi-disciplinary, multi-institutional research teams that are organized into a network. Currently four centres are funded across the US, which share five cores (standards and compliance, IT, chemistry probes and guided therapeutics, instrumentation and industrial relations, pathology and clinical studies).

Additional centres have been invited to become associate members including the Cancer Research UK (CRUK) cancer imaging centres. Canadian centres are encouraged to explore this opportunity.



Additionally, there are academic industry partnerships in early cancer detection, diagnosis and therapeutic response, including imaging as a biomarker. More information can be found at: <http://imaging.cancer.gov> which has a schematic describing how the NIH is linking the different initiatives and optimizing the current generation of imaging platforms for clinical trials.

Imaging may be the breakthrough to detect biomarkers at very early stages of neoplasia. After the Korean War, a study of autopsy results found that young men who had died in the war already had atherosclerotic plaques, a paradigm altering finding. One of the original uses of CT was to support autopsy and the Swiss use CT for this purpose. Perhaps there is an obligation to investigate “what people die with and not only what they die of.”

## BREAKOUT SESSIONS

The afternoon of the second day was devoted to group discussions and the consideration of two scenarios for potentially moving imaging research forward in Canada. In the first scenario, participants were asked to consider what would be feasible, given a modest amount of funding that might be achievable through partnership (CIHR, NSERC and others), using existing funds, e.g. \$3-5 million per year for five years. They were asked to identify the most strategic use of these funds to ensure an acceptable return on investment and a significant impact on imaging research in Canada. In the second scenario, participants were asked to engage in “blue sky thinking”, and make recommendations as to what could be done that would be truly transformative in the imaging field if there were few, or no, financial constraints. Given Canada’s existing strengths, what single factor or infrastructure might enable our research community to take an international lead in the field of medical imaging?

## RECOMMENDATIONS FROM BREAKOUT SESSIONS

### **SCENARIO 1 - EXISTING FUNDS**

The following recommendations were presented and discussed:

#### **Centre for Clinical Evaluation of Imaging Technology**



The goal would be to conduct integrated clinical trials across the country, using standard imaging protocols. There would be several hospitals coordinating trials; the Centre would be coordinating site for the participating hospitals. The Centre’s specialized expertise and role in the development of clinical trials for imaging technologies and biomarkers would establish the standards particular to this type of clinical trial. The different sites would offer their particular expertise to the network. Multiple sites would be funded for specific clinical trials, but the creation of the Centre would create the networked environment necessary to facilitate collaboration between the physical and life sciences research communities and bridge the gap between the bench and the bedside. A coordinating Centre would solve the problem faced by individual centers that often don’t have the critical mass to do large, well-funded clinical trials. The funding would support data management and analysis, scientists and facilitation for networking and concerted action.

The Centre’s functions would include:

- *Developing protocols, and organizing and facilitating clinical trials, including obtaining ethics approval;*
- *Developing standard operating procedures for imaging techniques;*
- *Providing support for protocol development and biostatistics;*

- *Undertaking data collection, storage, processing and analysis across the various sites that are doing the trials;*
- *Supporting the patient sites, network and champions at the various sites; and*
- *Performing economic evaluations.*

## Clinical Translation Fund



This proposal recommended a fund of approximately \$5M per year to support focused initiatives of approximately \$500K per project for any activity that would move an existing technology into a clinical application and that could not be done through the regular open grants competition. This would include non-intuitive activities such as the development of validated preclinical disease animal models or new tools and technologies for basic biology, as long as there was a clinically relevant end-point. Examples of eligible projects might include bringing a new scanner to clinical testing, or clinical trials of existing biomarkers to determine efficacy. The requests for application (RFA) and grants would be

launched as two competitions throughout the year in order to allow opportunities for refining proposals and re-application. Proposals would have to produce a clinical outcome within five years. A dedicated training program in imaging for graduate students, postdoctoral fellows and physicians would be a core activity.

## Pipeline to Clinical Application



The goal of this proposal would be to drive the translation of basic and preclinical imaging research to clinical application through the formation of a network based on existing centres. An RFA would request proposals from any stage along the pipeline from the laboratory to clinical application with the objective of being in clinical trials within five years. A proposal could be an animal model or biomarker development as long as there is a clear pathway to implementation in the clinical setting. It would not be expected that any single project could move along the entire pipeline within the five-year timeframe. To encourage translation, there would be no cap imposed on the amount of money that could be requested, within the limits of the total funding envelope.

This would enable research teams to “think big” and request the funding needed to bring a project to completion, without imposed financial constraints.

Projects would have to be multidisciplinary with a strong emphasis on the inclusion of both technology development experts and clinician scientists. The existing CIHR/NSERC Collaborative Health Research Program (CHRP) already brings together the physical and life sciences but there is no requirement to engage clinical scientists. It was felt that this would be an essential requirement for a team wishing to advance to clinical testing. Recruitment and training of physician scientists, preferably during their MD/PhD training, would be required and a budget line to support this objective would be recommended. As well as the pipeline-to-patients approach, the proposal is unique in other ways. It would structurally encourage basic science researchers and clinicians to collaborate. Systematic development of measurement using quantitative data would be a core activity, recognizing the criticism of current imaging protocols as being very difficult to validate. Validation, particularly in the context of multiple sites undertaking measurement in many patients, is difficult but essential. It would drive the creation of entirely new quantitative parameters that, in turn, would drive advanced complex models of systems. A knowledge translation implementation

plan would be an important component of this program to ensure commercialization, where appropriate, and to facilitate the uptake of new methods and procedures into Canadian clinical practice.

## **SCENARIO 2 - FINANCIAL INVESTMENT OF NEW FUNDS (“BLUE SKY THINKING”)**

### **National Centres of Excellence in Imaging**



This proposal recommended the support of one or more enriched national imaging centres that would provide a national resource for the whole country. The structure could be modeled on existing centres such as TRIUMF, the nanotechnology program in Alberta and the NRC’s core centres. Internationally, the model would be similar to the recently funded UK imaging centres or the US ACRIN networks. A key criterion would be stable core and infrastructure funding for the centres. Each centre would already be an internationally recognized centre of expertise, either for a disease, a technology or both. Centres could be either single or multi-disease focused, but it is expected that most would be multi-modality. It is conceivable that one of the centres could be

the hub of an imaging clinical trials network, similar to the NCIC Clinical Trials Group. An alternative proposal would be to create an Institute of Biomedical Imaging or Imaging Sciences. To broaden the scope an Institute of Biomedical Technology was suggested.

### **Canadian Imaging Clinical Trials Network**



Increasing cost and burden of imaging in health care delivery requires a program national in scope and a national framework to ensure that we are using the technology in an appropriate and cost effective way. The network is differentiated from other clinical trial networks because of its focus on imaging and biomarkers. The goal of a Canadian Imaging Network would be the delivery of safe and cost effective imaging and biomarker-based health services that make an impact on patient outcomes. The program could be modeled on the US ACRIN concept: it would provide strong management and protected time for researchers, especially clinicians. As well, the network would develop an interface with

laboratories that are working on emerging pre-clinical science such as metabolomics. It would facilitate participating centers to build on their strengths. Technology assessment would be an important component of the network. Training and dedicated funded training programs at each of these centers would be essential. Functions of the network would include:

- *Technology maintenance, coordination of introduction of new technology – technology developed at one site could be disseminated at multiple sites;*
- *Production of standardized protocols and Standard Operating Procedures;*
- *Web-based trials databases that could handle imaging databases (anonymous raw data);*
- *Improved good clinical practice;*
- *The opportunity to focus on personalized medicine;*
- *The opportunity to engage with health services and policy researchers and provincial governments.*



Both public and private support would be needed to finance the network – potentially at a level of \$1 million per year initially, increasing to \$5 million per year for the next stage.

## Translational Grants for Medical Imaging



In this proposal, “transformational” funds would be provided to imaging sites that have already demonstrated success in order to move a new idea to a clinical environment. The funds would be released through a competitive process at about \$1M per annum for five years per centre, renewable after five years. Approximately 10 grants would be offered and it is anticipated that the funds would be awarded to the centres, rather than specific groups. The funds would be distributed through a competitive RFA that would pay for faculty, release time for physicians and support staff (notably for PET and MRI centers).

## CLOSING COMMENTS

Several themes arose repeatedly during the workshop. These included:

- *The need for sustainable funding for multidisciplinary research teams in medical imaging;*
- *The need for an evaluation of current and emerging imaging technologies;*
- *the requirement for multidisciplinary approaches that include both technology development experts and clinician scientists; and*
- *The need for research and clinical trials networks that capitalize on existing Canadian strengths to expedite the translation of new discoveries and advances into clinical benefits for patients.*

Of paramount concern, were the challenges facing translational research in Canada and the need to overcome existing barriers to more rapidly move new discoveries into the clinic to improve patient care and outcomes. This needs to be done in a Canadian context that is cognizant of the cultural and economic factors guiding health care delivery. This workshop report will form the basis for further discussions between CIHR, NSERC and other interested parties, with the goal of developing strategies for advancing medical imaging in Canada.









## Appendix 1 - Participants




Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Douglas N. Abrams</b> Director</p>	<p>Edmonton Radiopharmaceutical Centre 11560 University Avenue, Edmonton, AB T6G 1Z2</p> <p>Tel: 780 432-8970 E-mail : <a href="mailto:dougabra@cancerboard.ab.ca">dougabra@cancerboard.ab.ca</a></p>	<p>Our research is related to the radiosynthesis and development of radiopharmaceuticals for therapeutic and diagnostic use in Nuclear Medicine. Current work includes analogs of aromatase inhibitors, sentinel node tracers and melanoma and neuroendocrine tumour therapy.</p>
	<p><b>Bruce Balcom</b> Professor, Director of MRI Research Center</p>	<p>University of New Brunswick P O Box 4400, IUC Building, Room 231, Fredericton, NB, E3B 5A3</p> <p>Tel: 506 458-7938 E-mail: <a href="mailto:bjb@unb.ca">bjb@unb.ca</a></p>	<p>Magnetic resonance and Magnetic Resonance Imaging Measurement Methods. Instrumentation, hardware, data processing.</p>
	<p><b>Rob Beanlands</b> Chief, Cardiac Imaging</p>	<p>University of Ottawa Heart Institute 40 Ruskin Street, Room 1220, Ottawa, ON, K1Y 4W7</p> <p>Tel: 613 761-5296 E-mail: <a href="mailto:rbeanlands@ottawaheart.ca">rbeanlands@ottawaheart.ca</a></p>	<p>Dr. Rob Beanlands is a Career Investigator (HSFO) and international leader in cardiovascular nuclear imaging. His research investigates metabolic and cellular function in cardiovascular disease and responses to therapy. He is Chief of Cardiac Imaging and founding Director of the National Cardiac PET Centre, a state-of-the-art facility funded in part by two CFI grants and the only PET facility in Canada dedicated to cardiovascular disease. He is extensively published and offers experience in leading large, multicentre imaging trials, including PARR-2 and leads the provincially-funded cardiac PET registry (CADRE). He holds multiple peer reviewed grants with CIHR and HSFO, developing strong collaborative relationships within the University of Ottawa Heart Institute, with partner institutions across Canada and internationally. He is the Ottawa site co-PI for the Canadian Atherosclerosis Imaging Network, and Director of the Molecular Function and Imaging providing a multidisciplinary, translational research training program, encompassing basic sciences, regenerative therapies, imaging physics/engineering, cardiology, chemistry, and clinical research to over 30 graduate, post-graduate and clinical trainees. He leads the CIHR Team Grant, IMAGE-HF. He is also the former president of CNCS. He is the current SPC Chair of CCS, the Associate Editor for JNC and Governor and Board member for ACC, SNM Cardiovascular Councils.</p>
	<p><b>François Bénard</b> Professor</p> <p><b>Expert Working Group Member</b></p>	<p>University of British Columbia 675 West 10th Avenue, Vancouver, BC, V5Z 1L3</p> <p>Tel: 604 675-8206 E-mail: <a href="mailto:fbenard@bccrc.ca">fbenard@bccrc.ca</a></p>	<p>Detection of cancer by positron emission tomography; monitoring cancer response to treatment; development of new radiopharmaceuticals for cancer imaging.</p>

Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Steven Burrell</b> Research Director, Radiology</p>	<p>QE II Health Sciences Centre and Dalhousie University QE II HSC, Dept of Diagnostic Imaging, 1796 Summer St., Halifax, NS, B3H 3A7</p> <p>Tel: 902 473 6161 E-mail: <a href="mailto:sburrell@dal.ca">sburrell@dal.ca</a></p>	<p>My primary areas of research are in nuclear medicine, including: a) Oncology, including PET b) Cardiac nuclear medicine c) Brain perfusion and molecular imaging d) Small animal imaging.</p>
	<p><b>Anna Celler</b> Senior Medical Physicist/Associate Professor</p>	<p>Department of Radiology, VCHA/UBC Medical Imaging Research Group, VGH Research Pavilion, 828 West 10th Avenue, Vancouver, BC, V5Z 1L8</p> <p>Tel: 604 875-5252 E-Mail: <a href="mailto:aceller@physics.ubc.ca">aceller@physics.ubc.ca</a></p>	<p>Nuclear medicine, SPECT and PET, quantitative imaging with attenuation, scatter, resolution recovery and partial volume corrections, functional dynamic studies, image reconstruction, internal radiation therapy, internal dosimetry, tumour diagnosis and staging, myocardial perfusion imaging, quantitation of perfusion defect, dual-isotope imaging, methods for multidimensional data visualization and analysis, image fusion and registration, organ and tumour segmentation methods, electronic collimation and Compton camera, mathematics of inverse problems and optimization techniques.</p>
	<p><b>Dean Chapman</b> CRC - X-Ray Imaging, Professor of Anatomy and Cell Biology</p>	<p>Canadian Light Source University of Saskatchewan 501-121 Research Drive Saskatoon, SK S7N 1K2</p> <p>Tel: 306 966-4111 E-Mail: <a href="mailto:dean.chapman@usask.ca">dean.chapman@usask.ca</a></p>	<p>Synchrotron based biomedical imaging research: much of this work relates to imaging animal models of human disease using synchrotron specific methods such as diffraction enhanced, phase contrast and K-edge subtraction imaging. Imaging modality research: this research is directed to developing new methods of x-ray imaging with emphasis on application to biomedical problems. One example is a dedicated K-edge subtraction and fluorescence subtraction system for application to visualizing gene expression in small animals. Translational imaging research: some research emphasizes the translation of imaging modalities developed at the synchrotron to laboratory and eventually clinical imaging. One method presently being developed for laboratory and clinical applications is diffraction enhanced imaging.</p>
	<p><b>Guy Cloutier</b> Professor of Radiology and Bioengineering</p>	<p>University of Montreal LBUM-CRCHUM, 2099 Alexandre de Sève, room Y- 1619, Montreal, QC, H2L 2W5</p> <p>Tel: 514 890-8000 ext. 24703 E-mail: <a href="mailto:guy.cloutier@umontreal.ca">guy.cloutier@umontreal.ca</a></p>	<p>The Laboratory of Biorheology and Medical Ultrasonics (LBUM) pursues research in medical imaging and blood rheology. Our research programs intend to improve the diagnostic and follow-up of hyper-erythrocyte aggregation, a pathological state promoting the hyper-viscosity of blood and thrombotic side effects, arterial atherosclerosis, vascular aneurysms and deep vein thrombosis with new ultrasound imaging methods. The LBUM is also developing new methods to characterize the biomechanical properties of the vascular wall and their viscoelasticity of breast cancer lesions with ultrasound elastography. These research projects are realized in collaboration with clinical scientists, radiologists and cardiologists, fundamental scientists specialized in cardiovascular pathologies, biomedical engineers and medical physicists.</p>








Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Barbara Croft</b> Program Director</p>	<p>Cancer Imaging Program National Cancer Institute 6130 Executive Boulevard, Suite 6000, Bethesda, Maryland, 20892-7412</p> <p>Tel: 301 496-9531 E-mail: <a href="mailto:bc129b@nih.gov">bc129b@nih.gov</a></p>	<p>Barbara Y. Croft, Ph.D., is Program Director in the Cancer Imaging Program, Division of Cancer Treatment and Diagnosis, of the National Cancer Institute. She received her B.S. in Chemistry from Swarthmore College, and M. S. and Ph.D. from the Johns Hopkins University. Dr. Croft spent 29 years on the faculty of the Department of Radiology at the University of Virginia School of Medicine before joining the NCI 11 years ago. Her research is in the area of radiopharmaceuticals and nuclear medicine physics. She has been associated with the whole spectrum of oncologic medical imaging grants at the NCI, especially the Small Animal Imaging Resource Program, the Lung Image Database Consortium and the Imaging Database Resources Initiative funded through the Foundation for the NIH.</p> <p>The mission of the US National Cancer Institute's Cancer Imaging Program is to promote cancer imaging research in the service of oncology diagnosis and treatment. We do this by funding grants and contracts in basic and clinical research.</p>
	<p><b>Aaron Fenster</b> Director</p>	<p>Robarts Research Institute - University of Western Ontario 100 Perth Drive, London, ON, N6A 5K8</p> <p>Tel: 519 931-5708 E-mail: <a href="mailto:afenster@imaging.robarts.ca">afenster@imaging.robarts.ca</a></p>	<p>Fenster's group has focused on the development of 3D ultrasound imaging with diagnostic and surgical/therapeutic cancer applications in humans as well as mouse research models. His team developed 3D ultrasound imaging systems for: carotid atherosclerosis imaging and quantification, 3D ultrasound guided prostate cryosurgery and brachytherapy, 3D ultrasound guided prostate and breast biopsy for early diagnosis of cancer and 3D ultrasound imaging of mouse tumours and their vasculature</p>
	<p><b>Philip L. Gardner</b> President and CEO</p>	<p>Advanced Applied Physics Solutions 4004 Westbrook Mall, Vancouver BC, V6T 2A3</p> <p>Tel: 604-222-7436 E-mail: <a href="mailto:gardner@triumf.ca">gardner@triumf.ca</a></p>	<p>Isotope production and detector development</p>
	<p><b>Karen Gulenchyn</b> Chief, Nuclear Medicine</p>	<p>Hamilton Health Sciences and St. Joseph's Healthcare Hamilton HSC 1P-15, 1200 Main Street W., Hamilton, ON, L8N 3Z5</p> <p>Tel: 905 521-2100 ext. 75667 E-mail: <a href="mailto:gulenkar@hhsc.ca">gulenkar@hhsc.ca</a></p>	<p>Dr. Gulenchyn's primary research efforts in the past 5 years have been in the application of 18F-Fluorodeoxyglucose (FDG) PET imaging to clinical problems in oncology as part of the Ontario FDG PET evaluation process. She was the principle physician responsible for the design of the imaging protocols and led the Quality Assurance Subcommittee in concert with the principle physicist lead. Most recently the Hamilton group has begun to develop a program to assess the application of breast molecular imaging in women at high risk of developing breast cancer.</p>






Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>David W. Holdsworth</b> Professor, Dept. of Surgery</p>	<p>University of Western Ontario 100 Perth Drive, London, ON, N6A 5K8</p> <p>Tel: 519 931-5777 ext. 24154 E-mail: <a href="mailto:david.holdsworth@imaging.roba.uts.ca">david.holdsworth@imaging.roba.uts.ca</a></p>	<p>Dr. David Holdsworth is a Scientist in the Imaging group at the Robarts Research Institute. His research program involves the development and use of CT, MRI, and ultrasound techniques to investigate cerebrovascular disease and musculoskeletal disease. With respect to vascular disease, Dr. Holdsworth has previously been supported as a Career Investigator with the Heart and Stroke Foundation of Ontario, with funding to investigate the use of advanced Doppler ultrasound techniques to characterize diseased blood vessels leading to the brain. He is also supported by the CIHR to develop new x-ray based techniques to diagnose and treat diseased blood vessels within the brain, applicable to both endovascular and surgical therapy.</p> <p>In 2007 Dr. Holdsworth became the Dr. Sandy Kirkley Chair in Musculoskeletal Research and has shifted the focus of his research to musculoskeletal disease. Dr. Holdsworth and his team have developed new methods for musculoskeletal disease diagnosis and treatment for both basic pre-clinical and clinical applications. Dr. Holdsworth has developed new micro-CT techniques that have been applied to a variety of animal models including rabbits, rats and mice. With collaborators Naudie and Dunning, he has been funded by CIHR to develop new techniques to image the interface between bones and metal implants, and to improve current techniques for radiostereometric analysis following joint replacement.</p>
	<p><b>Sylvain Houle</b> Director, PET Centre</p>	<p>Centre for Addiction and Mental Health and University of Toronto 250 College Street, Toronto, ON, M5T 1R8</p> <p>Tel: 416 979-4651 E-mail: <a href="mailto:sylvain.houle@utoronto.ca">sylvain.houle@utoronto.ca</a></p>	<p>Application of Positron Emission Tomography and Magnetic Resonance Imaging to Mental Health and Addiction research. The research aims at understanding underlying mechanisms involved in those disorders as well as studying pharmacological treatment including early drug development. A major focus of the work is on the development of new PET tracers for research.</p>


Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Paul C. Johns</b> Professor of Physics</p>	<p>Carleton University 1125 Colonel by Drive, Ottawa, ON, K1S 5B6</p> <p>Tel: (613) 520-2600 ext. 4317 E-mail: <a href="mailto:johns@physics.carleton.ca">johns@physics.carleton.ca</a></p>	<p>Dr. Johns' research is in the physics of medical x-ray imaging and is currently supported by NSERC. Current work focuses on methods of using elastic (coherent) x-ray scattering to obtain diagnostic information in radiology. This encompasses precision measurement of the low-angle scattering properties of tissues and phantom materials, strategies for collimation design, and analysis and modeling of x-ray scatter imaging. Preliminary use of high-intensity x rays at the Canadian Light source BMIT facility for coherent-scatter imaging was made during commissioning of the facility this past winter and further work is planned. Dr. Johns also has an interest in the development of new detector technologies for digital radiography, in dual-energy radiography, and reconstruction techniques for computed tomography which minimize energy and scatter artefacts.</p>
	<p><b>Karim S. Karim</b> Associate Professor</p>	<p>University of Waterloo Dept of Elec. &amp; Comp. Eng, Waterloo, ON, N2L 3G1</p> <p>Tel: 519 888 4567 ext. 38336 E-mail: <a href="mailto:kkarim@uwaterloo.ca">kkarim@uwaterloo.ca</a></p>	<p>Solid state large area digital flat panel X-ray and gamma-ray detectors (amorphous silicon pixel amplifiers for digital fluoroscopy, amorphous silicon single photon counting detectors for full-body CT; high speed avalanche Frisch selenium detectors for SPECT and PET; solid state-Frisch grid detector for mammography tomosynthesis; multi-layer detector and Ross filters for dual energy CT and digital subtraction mammography)</p>
	<p><b>Agnes V. Klein</b> Director, Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics</p>	<p>Biologics and Genetic Therapies Directorate 200 Tunney's Pasture Driveway, Ottawa, ON, K1A 0K9</p> <p>Tel: 613 954-5706 E-mail: <a href="mailto:agnes_v_klein@hc-sc.gc.ca">agnes_v_klein@hc-sc.gc.ca</a></p>	<p>I am the Director of the Centre that evaluates and authorizes clinical trials and the review prior to marketing of radiopharmaceuticals, the topic of this workshop.</p>



Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Michael Kolios</b> Associate Professor / Canada Research Chair</p>	<p>Ryerson University Department of Physics, 350 Victoria Street, Toronto, Ontario, M5B 2K3</p> <p>Tel: 416 979-5000 ext. 07065 E-mail: <a href="mailto:mkolios@ryerson.ca">mkolios@ryerson.ca</a></p>	<p>Dr. Michael C. Kolios is an Associate Professor in the Department of Physics at Ryerson University, adjunct professor at the Department of Medical Biophysics at the University of Toronto and Canada Research Chair (tier II) in Biomedical Applications of Ultrasound. His work focuses on the biomedical use of ultrasound in diagnosis and therapy. He directs the advanced biomedical ultrasound imaging and spectroscopy laboratory at Ryerson University which houses state-of-the-art ultrasound imaging tools at frequencies ranging from 1 to 1000MHz. His work on tissue characterization using the frequency dependence of the backscatter has opened new avenues for ultrasound diagnosis. His primary research areas are ultrasound imaging and tissue characterization, high frequency ultrasound clinical and pre-clinical imaging, acoustic microscopy, optoacoustic imaging and optical coherence tomography. He also has an active interest in blood flow measurements using these techniques. Recently, his laboratory has expanded into the field of molecular imaging using ultrasound and optoacoustic techniques.</p>
	<p><b>Roger Lecomte</b> Scientific Head, Sherbrooke Molecular Imaging Centre</p>	<p>Université de Sherbrooke 3001, 12th Ave N. #1864, Sherbrooke, QC, J1H 5N4</p> <p>Tel: 819 820-6868 ext. 14608 E-mail: <a href="mailto:Roger.Lecomte@USherbrooke.ca">Roger.Lecomte@USherbrooke.ca</a></p>	<p>Professor of Nuclear Medicine and Radiobiology at Université de Sherbrooke and Scientific Chief of the Sherbrooke Molecular Imaging Center. Pioneering work in preclinical PET molecular imaging. Design, construction and exploitation of first avalanche photodiode (APD)-based PET scanner with which several premiere were achieved in small animals (rats and mice) imaging. Setup of the first preclinical PET imaging facility in Canada. Co-founder of Advanced Molecular Imaging (AMI) Inc., now Gamma Medica-Ideas Inc., to commercialize LabPET™ scanners, only APD-based fully digital PET scanner technology on the market. Current work on the integration of PET, SPECT, CT, MRI and optical imaging for multimodality imaging in preclinical applications. Biological applications in tracer development (11C-acetoacetate, 18FES/MFES, 64Cu-labeled peptides...), cardiology (perfusion, metabolism and function), oncology (photodynamic therapy (PDT), hormono/chemotherapy), neurology (epilepsy, aging), metabolism (diabetes, sepsis), tissue engineering (imaging of 3D tissue culture in situ). Biomedical engineering developments of instrumentation and ancillary devices for molecular imaging (e.g., microvolumetric blood counter, microfluidic blood sampler/analyzer).</p>





Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Ting-Yim Lee</b> Scientist</p>	<p>Lawson Health Research Institute 268 Grosvenor St., London, ON, N6A 4V2</p> <p>Tel: 519 685-8300 ext. 24131 E-mail: <a href="mailto:tlee@imaging.robarts.ca">tlee@imaging.robarts.ca</a></p>	<p>I have developed functional imaging methods with dynamic contrast enhanced CT scanning for the quantitative assessment of tissue blood flow, blood volume and capillary permeability surface area product. The measurements have been validated in the brain and the heart and tumors of the brain, liver and skeletal muscle against the gold standard measurements with microspheres. The developed methods can be easily implemented on clinical CT scanners using routine contrast agents and study procedures. As such, the methods have been applied to study acute stroke patients, ischemic heart disease patients, and cancer patients. In acute stroke, the method is able to separate ischemic but viable tissue from infarction as well as predict the likelihood of hemorrhagic transformation. Both features are critical in the decision of thrombolytic treatment. In ischemic heart disease, the method can detect hemodynamically significant coronary stenosis and thereby help to select patients who would benefit from revascularization. In cancer, the method can be used to study the development of angiogenesis in tumors and their response to anti-angiogenesis treatment with, for example, tyrosine kinase inhibitors of VEGF signaling.</p>
	<p><b>Lorenzo Leonardi</b> Medical Device Sector Coordinator</p>	<p>National Research Council of Canada 100 Sussex Dr., Ottawa, ON K1A 0R6</p> <p>Tel: 613 998-9469 E-mail: <a href="mailto:larry.leonardi@nrc-crm.gc.ca">larry.leonardi@nrc-crm.gc.ca</a></p>	<p>NRC has identified Canada's medical devices industry as one of the key sectors in which its expertise, multi-disciplinary competencies and infrastructure can make significant scientific and technological contributions to help industry respond to the considerable global medical device market expansion that is expected in the coming years. The NRC has identified Diagnostic Medical Imaging as a segment which NRC's scientific expertise and engineering know-how can make a significant impact. As Coordinator my role involves proposing, developing and coordinating cross-Institute activities in support of the medical device key sector strategy. In addition, develop and support external partner relationships that involve multiple Institutes and organisations.</p>
	<p><b>Howard Leong-Poi</b> Assistant Professor of Medicine</p>	<p>St. Michael's Hospital, University of Toronto 7-052 Bond Wing, St. Michael's Hospital, 30 Bond Street, Toronto, ON, M5B 1W8</p> <p>Tel: 416 864-5201 E-mail: <a href="mailto:Leong-poiH@smh.toronto.on.ca">Leong-poiH@smh.toronto.on.ca</a></p>	<p>My research program focuses on diagnostic and therapeutic applications for ultrasound using targeted microbubbles, including perfusion imaging and the molecular imaging of angiogenesis and stem cell engraftment; and gene and cell-based therapies for ischemic cardiovascular diseases and anti-angiogenic therapies for cancer treatment</p>

Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Martin Lepage</b>            Professeur agrégé            Canada Research Chair            in Magnetic Resonance            Imaging</p>	<p>Université de Sherbrooke            CIMS, Université de            Sherbrooke, 3001 12th Avenue            N., Sherbrooke, QC, J1H 5N4            Tel: 819 346-1110 ext. 11867            E-mail:  <a href="mailto:Martin.Lepage@USherbrooke.ca">Martin.Lepage@USherbrooke.ca</a></p>	<p>My primary research areas are the development of novel contrast agents for magnetic resonance imaging (MRI) and the improvements of pharmacokinetic modeling of dynamic contrast-enhanced MRI. The ultimate goal is to improve cancer detection, characterization and monitor treatment response.</p>
	<p><b>Nigel S. Lockyer</b>            Director</p>	<p>TRIUMF            4004 Wesbrook Mall,            Vancouver BC, V6T 2A3            Tel: 604 222 7353            E-mail: <a href="mailto:director@triumf.ca">director@triumf.ca</a></p>	<p>My primary area of interest is the development of PET detectors.</p>
	<p><b>Alex MacKay</b>            Professor  <b>Expert Working Group            Member</b></p>	<p>University of British Columbia            Department of Physics and            Astronomy, University of British            Columbia, 6224 Agricultural Rd,            Vancouver, BC, V6T 1Z1            Tel: 604 822-7890            E-mail: <a href="mailto:mackay@physics.ubc.ca">mackay@physics.ubc.ca</a></p>	<p>My research program involves the development and application of magnetic resonance imaging and spectroscopy techniques to the study of pathological processes in humans. We have worked with a variety of different medical conditions including multiple sclerosis, schizophrenia, and phenylketonurea. Our largest research project involves using magnetic resonance to measure myelin content in vivo.</p>
	<p><b>William Mackillop</b>            Professor            ICR Institute Advisor            Board Chair</p>	<p>Queen's Cancer Institute            Queen's University            Kingston, ON K7L 3N6            Tel: 613 533-6895            E-mail:  <a href="mailto:william.mackillop@krcc.on.ca">william.mackillop@krcc.on.ca</a></p>	<p>Cancer diagnosis, staging and prognosis.</p>
	<p><b>Kennedy Mang'era</b>            Director/Assistant            Professor</p>	<p>Health Sciences            Centre/University of Manitoba            RM GC219, 820 Sherbrook St.,            Winnipeg, Manitoba R3A 1R9            Tel: 204 787-3388            E-mail:  <a href="mailto:mangerak@cc.umanitoba.ca">mangerak@cc.umanitoba.ca</a></p>	<p>Radiolabeling of conventional anticancer agents with 99m-technetium and enhanced delivery of these agents into tumor sites by pre-conjugation with polymers; collaborator in exploration of alternative production for molybdenum-99 from enriched molybdenum-100 using accelerators.</p>


Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Paul M. Matthews</b>  Vice-President for Imaging, GSK and Head, GSK Clinical Imaging Centre and Prof of Clinical Neurosciences, Imperial College</p>	<p>Imperial College London and GSK Clinical Imaging Centre Hammersmith Hospital, DuCane Road, London WC12 0NN UK</p> <p>E-mail:  <a href="mailto:paul.m.matthews@gsk.com">paul.m.matthews@gsk.com</a></p>	<p>Paul M. Matthews, MD, DPhil, FRCP, OBE is Vice-President for Imaging, GlaxoSmithKline and Head, GSK Clinical Imaging Centre, Hammersmith Hospital, Professor of Clinical Neurosciences, Department of Clinical Neurosciences, Imperial College, London and Adjunct Professor of Neurology and Neurosurgery, McGill University. For over 25 years he has contributed to biomedical imaging research applying magnetic resonance and most recently is exploring integration of PET molecular imaging and fMRI for pharmacodynamic measures.</p> <p>The CIC is to become the internationally leading multidisciplinary center for molecular PET and MRI imaging for experimental human pharmacology in new drug development. The CIC was established to provide an in-house facility for advanced human imaging studies to provide a platform to help drive a transformation to new and better paradigms for drug development. The equipment and infrastructure allow application of state-of-the-art methods. Scientific staff with internationally-recognised expertise in PET and MRI have been recruited. CIC IT infrastructure offers the only compliant image acquisition-to-archiving environment available anywhere at present. It represents novel partnership between academia (Imperial College, London) and the world's second largest pharmaceutical company.</p>
	<p><b>Alexander J. B. McEwan</b>  Professor and Chair, Dept of Oncology, Faculty of Medicine and Special Advisor to the Minister of Health</p> <p>Expert Working Group Member</p>	<p>University of Alberta  Department of Oncologic Imaging, Cross Cancer Institute, 11560 University Avenue, Edmonton, AB, T6G 1Z2</p> <p>Tel: 780 432-8524  E-mail:  <a href="mailto:sandymce@cancerboard.ab.ca">sandymce@cancerboard.ab.ca</a></p>	<ul style="list-style-type: none"> <li>-Molecular imaging and imaging biomarkers</li> <li>- clinical translation</li> <li>- imaging trials</li> <li>- radioisotope therapy</li> </ul>
	<p><b>Ravi Menon</b>  Canada Research Chair and Deputy Director</p>	<p>Robarts Research Institute  PO Box 5015, 100 Perth Dr., London, ON N6A 5K8</p> <p>Tel: 519 663-5777 ext. 24148  E-mail:  <a href="mailto:rmenon@imaging.robarts.ca">rmenon@imaging.robarts.ca</a></p>	<p>My research is in the application of ultra-high field magnetic resonance imaging (MRI) in the area of basic and clinical neurosciences. We develop novel hardware and software solutions to allow MRI to be used to determine the structure and function of the brain in a variety of subjects from mice, to non-human primates to humans.</p>



Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Michel Meunier</b> Professor</p>	<p>École Polytechnique de Montréal Dept of Engineering Physics Montreal, Quebec H3C 3A7</p> <p>Tel: (514) 340-4711 ext. 4971 E-mail: <a href="mailto:michel.meunier@polymtl.ca">michel.meunier@polymtl.ca</a></p>	<p>I have a Canada Research Chair Tier I in Laser micro/nano-engineering of materials. The main mission of the Chair is to develop and model new laser processing of materials and laser-matter interactions for the applications in biomedical. Fabrication of new nanoparticles, nanoplasmonic structures, optical and plasmonics biosensors are being developed within the Chair. The infrastructure of the laboratory includes various femtosecond and nanosecond lasers, many bioplasmonic sensors and several optical characterization systems. Here are some examples of research projects and interests related to medical imaging:</p> <ul style="list-style-type: none"> <li>- Fabrication of new non-contaminated and functionalized plasmonic nanoparticles by laser processing for the application in biomedical, including imaging and cancer treatment (Photodynamic therapy). For instance, with our new process, we have developed new plasmonic alloys for potential use in multicolour imaging.</li> <li>- Development of highly sensitive plasmonics biosensors using phase sensitive detection and its applications in cell imaging.</li> <li>- Development of femtosecond laser nanosurgery of cells for performing gene transfection.</li> </ul>
	<p><b>Thierry Muanza</b> Assistant Professor</p>	<p>Segal Cancer Centre - Jewish General Hospital 3755 Cote des Neiges, room G-002, Montreal, QC H3T 1E2</p> <p>Tel: 514 340 8288 E-mail: <a href="mailto:thierry.muanza@mcgill.ca">thierry.muanza@mcgill.ca</a></p>	<ul style="list-style-type: none"> <li>- Combined modality therapy: Targeted molecules and ionizing radiation</li> <li>- Biomarkers</li> <li>- CNS oncology</li> </ul>
	<p><b>Frank Prato</b> Imaging Program Leader and Assistant Scientific Director</p>	<p>Lawson Health Research Institute 268 Grosvenor St., London, ON, N6A 4V2</p> <p>Tel: 519 646-6100 ext. 64140 E-mail: <a href="mailto:prato@lawsonimaging.ca">prato@lawsonimaging.ca</a></p>	<p>Frank S. Prato receives his MSc from U of T in Nuclear Physics and a PhD from U of T in Medical Biophysics. Since 1972 he has worked in the area of Nuclear Medicine imaging and since 1982 in the area of Magnetic Resonance Imaging. He is one of the few Canadian medical imaging physicists who has helped peer review funding in both these areas of imaging. As well, Dr. Prato has an active program in non-ionizing radiation protection and has helped set Canadian safety standards for MRI exposure and RF exposure. While president of the Canadian College of Physicists in Medicine he was one of the founders of the Canadian Organization of Medical Physicists. Current research in bio-medical imaging include PET/CT, SPECT/CT, PET/MR, EEG/MRI and photo-acoustic. Primary applications are to cardiovascular disease with some of the imaging methods being developed having application also to human neurological disorders and pre-clinical studies in oncology.</p>

Picture	Name	Contact Information	Research Interests Provided by the Participants
	<b>John A. Rowlands</b> Founding Scientific Director	Thunder Bay Regional Research Institute 980 Oliver Road, Thunder Bay, ON, P7B 6V4  Tel: 416-480-5708 E-mail: <a href="mailto:rowlandj@tbh.net">rowlandj@tbh.net</a>	Development of novel detector technology for x-ray, SPECT, PET and optical imaging. Development of combination imaging technologies, PET/MRI, x-ray/MRI, etc.
	<b>Thomas J. Ruth</b> Senior Research Scientist/Senior Scientist  <b>Expert Working Group Member</b>	TRIUMF/BC Cancer Agency 4004 Wesbrook Mall, Vancouver BC, V6T 2A3  Tel: 604 222-7526 E-mail: <a href="mailto:truth@triumf.ca">truth@triumf.ca</a>	My expertise centers on the use of accelerators for producing radionuclides and the development of automated chemistry systems for their isolation and incorporation into a form for performing measurements primarily using imaging as the technique. As PET Director for the UBC/TRIUMF Program from 1989-2008 I helped develop complex protocols using multiple radiotracers to address fundamental questions in neurology, principally related to Parkinson's disease. More recently I have begun to assist in the development of a research program cancer biology using PET at the BC Cancer Agency. I have served on numerous National and International panels related to the production and use of radionuclides including the IAEA, US Department of Energy and the National Academy of Sciences ( <i>Advancing Nuclear Medicine through Innovation: 2006-07</i> and <i>Production of Medical Isotopes with Highly Enriched Uranium: 2007-2009</i> ). I have served on several <i>ad hoc</i> working groups for Health Canada dealing with the use and regulation of positron emitting radiopharmaceuticals (PERs) in research. I am a member of the Canadian Association of Radiopharmaceutical Scientists, the Canadian Society of Nuclear Medicine, the Society of Nuclear Medicine, the American Chemical Society and the Society of Radiopharmaceutical Scientists (Treasurer, 2005-09). I have published more than 250 per reviewed papers and book chapters.
	<b>Vesna Sossi</b> Professor/PET Director	University of British Columbia 6224 Agricultural Rd., Vancouver, B.C., V6T 1Z1  Tel: 604 822 7710 E-mail: <a href="mailto:vesna@phas.ubc.ca">vesna@phas.ubc.ca</a>	PET imaging in humans and rodents with special emphasis on the dopaminergic system as related to Parkinson's disease. High resolution PET data quantification, modelling and interpretation.
	<b>Jean-Paul Soucy</b> PET Unit Director	Montreal Neurological Institute 3801 University St., Montreal, QC H3A 2B4  Tel: 514 398-8515 E-mail: <a href="mailto:jean-paul.soucy@mcgill.ca">jean-paul.soucy@mcgill.ca</a>	Image analysis in SPECT neurological studies; regional cerebral blood flow quantification with SPECT; cholinergic systems imaging with PET ligands of the acetylcholine vesicular transporter

Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Gilles Soulez</b> Director of the Research Imaging Platform</p>	<p>CHUM, University of Montreal, Dpt of Radiology, CHUM-Notre Dame, 1560 Sherbrooke east, Montreal, QC, H2L 4M1</p> <p>Tel: 514 890-8250 E-mail: <a href="mailto:gilles.soulez.chum@ssss.gouv.qc.ca">gilles.soulez.chum@ssss.gouv.qc.ca</a></p>	<p>Vascular imaging and interventional radiology. Modelization of aortic aneurysm using CT angiography. Image fusion to improve guidance during aneurysm endovascular repair. Prevention of endoleak following endovascular repair of aortic aneurysm by stent-graft optimization. Detection of vulnerable plaque using ultrasound elastography.</p>
	<p><b>Michael G. Sowa</b> Senior Research Officer</p>	<p>National Research Council of Canada 435 Ellice Ave, Winnipeg, MB, R3B 1Y6</p> <p>Tel: 204 984-5193 E-mail: <a href="mailto:Michael.Sowa@nrc-cnrc.gc.ca">Michael.Sowa@nrc-cnrc.gc.ca</a></p>	<p>Optical imaging, optical coherence tomography, nonlinear optical imaging, diffuse near infrared imaging, fluorescence imaging.</p>
	<p><b>Elizabeth Theriault</b> Assistant Scientific Director</p>	<p>CIHR Institute of Neurosciences, Mental Health and Addiction Canadian Institutes of Health Research Strangeway Building, University of British Columbia, 430-5950 University Blvd., Vancouver, BC V6T 1Z3</p> <p>Tel: 604 827-4744 E-mail: <a href="mailto:etheria@shaw.ca">etheria@shaw.ca</a></p>	<p>The Institute of Neurosciences, Mental Health and Addiction (INMHA) supports research on the functioning and disorders of the brain, the spinal cord, the sensory and motor systems, and the mind. The burden of disease in terms of the social, economic and health care costs associated with these disorders and related illnesses are staggering and there are indications that the number of people affected either directly or indirectly will continue to increase in the years to come.</p>
	<p><b>John Valliant</b> Associate Professor, Chemistry and CEO and Scientific Director</p> <p><b>Expert Working Group Member</b></p>	<p>McMaster University and Centre for Probe Development and Commercialization 1280 Main St. West, BSB-B231, Hamilton, ON, L8S 4K1</p> <p>Tel: 905 525-9140 ext. 21212 E-mail: <a href="mailto:valliant@mcmaster.ca">valliant@mcmaster.ca</a></p>	<p>Development of novel molecular imaging probes, probe discovery platforms and new approaches for radiolabeling molecules. The scope of our research program includes PET, SPECT and optical probe development for oncology, basic chemistry, preclinical studies and translation. Particular focus is on agents that can be used to assess metastatic potential of tumours.</p>

Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Brian C. Wilson</b></p> <p>Division Head/Professor</p> <p>Expert Working Group Member</p>	<p>Ontario Cancer Institute/University of Toronto 610 University Ave, Toronto, ON, M5G 2M9</p> <p>Tel: 416 946-2952 E-mail: <a href="mailto:wilson@uhnres.utoronto.ca">wilson@uhnres.utoronto.ca</a></p>	<p>My primary area is in optical imaging, for both pre-clinical research and clinical applications. This includes basic optical biophysics, instrument development, in vitro and in vivo studies, and clinical trials. Two main clinical applications are represented: I. multi-modal endoscopy for early cancer detection, with a focus on the gastrointestinal tract (esophagus, colon), and II. optical image guidance for cancer surgery, with a current focus on brain, prostate and head &amp; neck tumors. The techniques under development include fluorescence imaging (using both endogenous tissue fluorescence and molecularly-targeted agents), CARS imaging (coherent anti-Stokes Raman spectroscopy) and other non-linear light-tissue interactions, Doppler optical coherence tomography, and the use of optically-active nanoparticles as targeting agents and/or 'reporters'. For the work in glioma, we are integrating optical imaging with MRI, while in the prostate work it is being combined with robotic interventions (surgical and focal energy-based) The pre-clinical applications include both cell/tissue micro-imaging and in vivo small-animal imaging. The former includes multi-modal large-area confocal MACROscopy, and development of optical probes for specific molecular/genetic/metabolomic studies. The latter includes fluorescence tomography, intravital microscopies and DOCT, and bioluminescence imaging. Combination technologies are under development, for example, combining bioluminescence and CT.</p>



Picture	Name	Contact Information	Research Interests Provided by the Participants
	<p><b>Frank Wuest</b> Associate Professor and The Dianne and Irving Kipnes Chair in Radiopharmaceutical Sciences</p>	<p>Department of Oncology University of Alberta 11560 University Avenue Edmonton AB T6G 1Z2  Tel: 780 989-8150 E-mail: <a href="mailto:wuest@ualberta.ca">wuest@ualberta.ca</a></p>	<p>My research interest is embedded in the interdisciplinary field of radiopharmaceutical sciences, with special focus on radionuclide molecular imaging and therapy of tumors. My research program is aimed at the evaluation and translation of the diagnostic and therapeutic potential of novel molecular targets involved in the development and progression of cancer by means of radiopharmaceuticals for a better understanding and controlling of cancer to enhance patient care. My research activities are mainly directed to the design, synthesis and radiopharmacological characterization of novel radiopharmaceuticals by means of multimodality imaging techniques combining functional molecular imaging (PET and SPECT) with anatomical mapping (CT and MRI). This includes basic discovery research in the field of radiopharmaceutical chemistry, and pre-clinical translational cancer research for the discovery and functional characterization of tumor-specific proteins and other parameters of tumor micro-environment in vitro and in vivo. My special interest is application of small animal PET for translational cancer research in combination with other imaging methodologies like small animal MRI. The obtained biological data are used for the elucidation of structure-activity relationships and the detailed assessment of the potential clinical value of novel radiopharmaceuticals.</p>
	<p><b>Martin Yaffe</b> Senior Scientist</p>	<p>Sunnybrook Health Sciences Centre Rm S6-57, 2075 Bayview Ave, Toronto, ON, M4N 3M5  Tel: 416 480-5715 E-mail: <a href="mailto:martin.yaffe@sunnybrook.ca">martin.yaffe@sunnybrook.ca</a></p>	<p>My work focused around the development and evaluation of new methods for earlier and more accurate detection of cancer as well as techniques for the quantification of cancer risk and the monitoring of response to therapy. I have put considerable effort into the development of digital mammography and am now working on advanced 3 dimensional applications (tomosynthesis) and imaging of angiogenesis. Recently I started a research program in quantitative pathology where imaging techniques are used to improve sampling and make better quantitative use of information from tissue for diagnosis of disease and to serve as a "gold standard" for validation of new imaging techniques. Much of my work is directed toward breast cancer, but in my new role as director (with Dr. Aaron Fenster) of a large research program on cancer imaging through the Ontario Institute for Cancer Research, I am expanding my interests toward molecular and functional imaging for all types of cancer.</p>

## Meeting Organizers

Picture	Name	Contact Information
	<p><b>Kimberly Banks Hart</b> Associate, Institute Strategic Initiatives</p>	<p>CIHR Institute of Cancer Research Tel: 613 954-1965 E-mail: <a href="mailto:kimberly.hart@cihr-irsc.gc.ca">kimberly.hart@cihr-irsc.gc.ca</a></p>
	<p><b>Pierre Bilodeau</b> Director, Bio Industries Division</p>	<p>NSERC 350 Albert St., Ottawa, ON, K1A 1H5 Tel: 613 947-9452 E-mail: <a href="mailto:pierre.bilodeau@nserc-crsng.gc.ca">pierre.bilodeau@nserc-crsng.gc.ca</a></p>
	<p><b>Doris Braslins</b> Program Manager, Bio Industries Division, Research Partnerships Program</p>	<p>NSERC 350 Albert St., Ottawa, ON, K1A 1H5 Tel: 613 996-7229 E-mail: <a href="mailto:doris.braslins@nserc-crsng.gc.ca">doris.braslins@nserc-crsng.gc.ca</a></p>
	<p><b>Judith Bray</b> Assistant Director</p>	<p>CIHR Institute of Cancer Research Tel: 613 954-7223 E-mail: <a href="mailto:judith.bray@cihr-irsc.gc.ca">judith.bray@cihr-irsc.gc.ca</a></p>
	<p><b>Diane Christin</b> Institute Project Officer</p>	<p>CIHR Institute of Cancer Research Tel: 613 941-0997 E-mail: <a href="mailto:diane.christin@cihr-irsc.gc.ca">diane.christin@cihr-irsc.gc.ca</a></p>
	<p><b>David Hartell</b> Associate, Institute Strategic Initiatives</p>	<p>CIHR Institute of Cancer Research Tel: 613 941-4329 E-mail: <a href="mailto:david.hartell@cihr-irsc.gc.ca">david.hartell@cihr-irsc.gc.ca</a></p>
	<p><b>Morag Park</b> Scientific Director, CIHR Institute of Cancer Research</p>	<p>CIHR Institute of Cancer Research Tel: 514-398-2895 E-mail: <a href="mailto:mpark.ic-icr@mcgill.ca">mpark.ic-icr@mcgill.ca</a></p>
	<p><b>Maura Ricketts</b> Director, Office for Public Health</p>	<p>Canadian Medical Association Tel: 613 731-8610 x 2279 E-mail: <a href="mailto:Maura.Ricketts@cma.ca">Maura.Ricketts@cma.ca</a></p>

# Appendix 2 - Agenda



INSTITUTE OF CANCER RESEARCH/INSTITUT DU CANCER

## AGENDA

**Meeting:** CIHR/NSERC Medical Imaging Workshop  
**Date:** October 6<sup>th</sup> and 7<sup>th</sup>, 2009  
**Location:** Westin Bayshore Resort Hotel and Marina, Vancouver  
**Room :** Oak Room

### Workshop Objectives:

- To obtain a “snapshot” of the current state of Canadian imaging science and it’s alignment with the international scene;
- To explore sustainable mechanisms to integrate the physical and life sciences communities in the imaging field; and
- To generate a series of recommendations and strategies on how best to support translational research that will expedite the adoption of new technologies and procedures into clinical practice

**Facilitator:** Judy Bray

**Expert Working Group Members:** François Bénard, Alex MacKay, Sandy McEwan, Tom Ruth, John Valliant, Brian Wilson

### Monday, October 5, 2009

#### Bus leaves hotel at 6.00 p.m.

Time	Description	Lead
19:00 – 21:00	<b>TRIUMF Tour and Reception.</b> A bus will be provided to transport people to the TRIUMF site and back to the hotel following the tour. The bus will leave the hotel at 6.00 p.m. Please meet in the hotel lobby at 5.50 p.m.	Nigel Lockyer

### Tuesday, October 6, 2009

Time	Description	Moderator
08:00	<i>Breakfast in Oak Room – second floor of conference centre</i>	
08:40	<b>Welcome and Introduction</b>	Morag Park and Pierre Bilodeau
08:55	<b>Setting the Scene: Workshop Overview and Objectives</b>	Sandy McEwan
09:10	<b>Technology Development</b> <b>Speakers:</b> Dean Chapman, Bruce Balcom <i>Speakers: 15 minutes each, followed by 5 minutes each for</i>	Tom Ruth

	<i>questions for clarification – followed by 30 minutes of open discussion and the identification of key messages</i>	
10:20	<i>Health Break – Oak room</i>	
10:50	<b>Technology Development (continued)</b> <b>Speakers:</b> John Valliant, Frank Prato <i>Speakers: 15 minutes each, followed by 5 minutes each for questions for clarification – followed by 30 minutes of open discussion and the identification of key messages</i>	Tom Ruth
12:00	<i>Lunch – Marine Room – Ground floor of hotel</i>	
13:00	<b>Pre-clinical</b> <b>Speakers:</b> Roger Lecomte, David Holdsworth, Aaron Fenster <i>Speakers: 15 minutes each, followed by 5 minutes each for questions for clarification – followed by 30 minutes of open discussion and the identification of key messages</i>	Brian Wilson
14:30	<i>Health Break – Oak Room</i>	
15:00	<b>Translational imaging for neurosciences drug development: a paradigm for public-private partnerships</b> <b>Speaker:</b> Paul M. Matthews, MD, DPhil, FRCP, OBE - Vice-President for Imaging, GlaxoSmithKline and Head, GSK Clinical Imaging Centre, Hammersmith Hospital, Professor of Clinical Neurosciences, Department of Clinical Neurosciences, Imperial College, London and Adjunct Professor of Neurology and Neurosurgery, McGill University <i>40 minute presentation followed by 20 minute question and discussion period</i>	François Bénard
16:00	<b>From ICMIC to ACRIN: From Basic Oncologic Imaging Research to Patient Imaging Trials in the US National Cancer Institute Framework</b> <b>Speaker:</b> Barbara Y. Croft, Ph.D. - Program Director, Cancer Imaging Program, Division of Cancer Treatment and Diagnosis; National Cancer Institute, National Institutes of Health, USA <i>40 minute presentation followed by 20 minute question and discussion period</i>	François Bénard
17:00	<b>NRC/NSERC/CIHR Collaboration on Medical Devices</b>	Pierre Bilodeau/ Larry Leonardi
17:15	<b>Summary and identification of key messages, opportunities for partnership and potential themes for breakout discussions</b>	Sandy McEwan
17:45	<i>Reception in Marine Room – ground floor of hotel</i>	<i>All</i>
19:00	<i>Dinner – Le Gavroche Restaurant, 1616 Alberni Street</i>	



### Wednesday, October 7, 2009

Time	Description	Lead
08:15	<i>Breakfast in Oak Room</i>	
09:00	<b>Outline for the Day</b>	Judy Bray
09:10	<b><i>Clinical and Translational</i></b> <b>Speakers:</b> Ravi Menon, François Bénard <i>Speakers: 15 minutes each, followed by 5 minutes each for questions for clarification, followed by 30 minutes of open discussion and identification of key messages</i>	Alex MacKay
10:20	<i>Health Break</i>	
10:50	<b><i>Clinical and Translational (continued)</i></b> <b>Speakers:</b> Robert Beanlands, Karen Gulenchyn <i>Speakers: 15 minutes each, followed by 5 minutes each of questions for clarification, followed by 30 minutes of open discussion and identification of key messages</i>	Alex MacKay
12:00	<b>Summary of key messages from the presentations and discussions</b> – selection of 3-5 topics for the breakout session	Expert Working Group members
12:30	<i>Lunch in Marine Room – re-location to breakout rooms</i>	
13:30	<b>Break out Session – the objective is to generate recommendations and strategies for advancing the field of medical imaging in Canada.</b> Breakout themes will be selected by the working group members based on the preceding discussions and key messages. Participants will be able to self-select the group of most interest.	
14:45	<i>Health Break</i>	
15:00	<b>Report back from breakout sessions and open discussion</b> During this session, recommendations will be collated into a cohesive strategy for advancing medical imaging in Canada, from technology development to clinical applications.	Expert Working Group members
16:00	<b>The path forward and concluding remarks</b>	Morag Park/ Pierre Bilodeau
16:15	<b>Steering Committee Meeting – Marine Room</b>	

