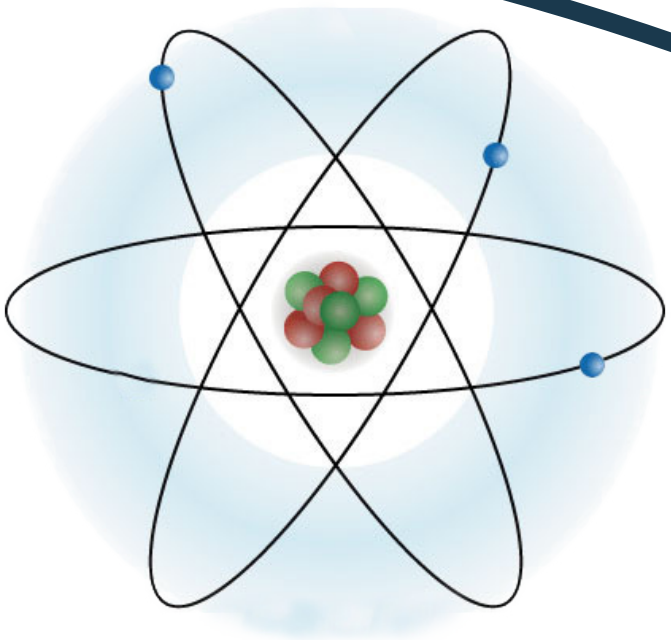


Alternative Radiopharmaceuticals for Medical Imaging

Overview and Outcomes

Canadian Institutes of Health Research
Instituts de recherche en santé du Canada
Canada

Alternative Radiopharmaceuticals for Medical Imaging

Background

Medical imaging is one of the fastest growing fields in medicine. The development of innovative new imaging modalities, contrast agents, molecular probes and radiopharmaceuticals has significantly improved our ability to study biological structure and function in health and disease, and continues to contribute to the evolution of medical care. Imaging technologies that require the use of radiopharmaceuticals such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) fall within the field of nuclear medicine, a small but essential sub-specialization within the field of medical imaging. It is estimated that about 1.5 million nuclear medicine procedures are performed annually in Canada. Over 80% of all nuclear medicine investigations involve radiopharmaceuticals labeled with Technetium-99m (^{99m}Tc). The ^{99m}Tc is produced from Molybdenum-99 using generators manufactured by just two companies in North America: Covidien and Lantheus. The world's current supply of ^{99m}Tc is remarkably fragile, relying on the continued operation of just a handful of aging nuclear reactors that produce the Molybdenum-99. About 20% of the world's supply of Molybdenum-99 is made in Canada at the National Research Universal (NRU) nuclear reactor at Chalk River. Although alternative, non-reactor technologies for producing molybdenum-99 and its medically-useful daughter ^{99m}Tc have been known for many years, this technology has never been commercially developed as there has always been a plentiful supply of nuclear reactors around the globe.

The Health Challenge

The emergency closure of the NRU in 2007 led to a significant disruption in the supply of Molybdenum-99 and the cancellation of large numbers of medical procedures due to the ensuing shortage of ^{99m}Tc. Although the shutdown was for a relatively brief period, the crisis highlighted the fragility of the Molybdenum-99 supply chain. The second closure of the NRU in 2009 resulted in a major interruption in supply, leading to a serious situation in the health care system due to challenges accessing Technetium-labeled radiopharmaceuticals. The continuing uncertainties in the supply of medical isotopes, especially ^{99m}Tc, caused both the clinical and biomedical research communities to look for alternative ways to produce the ^{99m}Tc needed for diagnosis and clinical care and also to explore the potential of alternative medical isotopes to replace ^{99m}Tc as the radiopharmaceutical label of choice in certain clinical procedures.

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

NSERC CRSNG

Cat. No. MR4-14/2012E (paper)
ISBN 978-1-100-21003-2
Cat. No. MR4-14/2012E (PDF)
ISBN 978-1-100-21004-9

Alternative Radiopharmaceuticals for Medical Imaging

The Research Response

In June 2009, CIHR took the lead in organizing a research response to the health crisis caused by the ^{99m}Tc shortage and, in consultation with the Health Canada Expert Advisory Group on Radiopharmaceuticals, a Request for Applications (RFA), "Operating grant: Alternative Radiopharmaceuticals for Medical Imaging", was launched jointly by CIHR and the Natural Sciences and Engineering Research Council (NSERC) with a combined investment of $6 million over two years. The initiative was supported by six CIHR Institutes:

- The Institute of Cancer Research
- The Institute of Circulatory and Respiratory Health
- The Institute of Infection and Immunity
- The Institute of Musculoskeletal Health and Arthritis
- The Institute of Neurosciences, Mental Health and Addition
- The Institute of Nutrition, Metabolism and Diabetes

The goal of the RFA was to provide the needed short-term impetus to speed the development of replacements for the PET and SPECT ^{99m}Tc–labeled, reactor-produced radiopharmaceuticals, especially those radiopharmaceuticals where no viable alternative existed in clinical applications.

The objectives were:

» To advance research into alternative, non-reactor, means of producing clinically useful radionuclides of Technetium and to bring these methods to the clinic within the shortest time possible;

» To advance research into the development of alternate PET and SPECT radiopharmaceuticals that could replace those labeled with ^{99m}Tc in certain imaging procedures and for which the radiolabel can be produced by means other than a nuclear reactor; and

» To fast track the production and testing of candidate radiolabelled tracers resulting in clinical studies to validate the new entity during, or by the end of, the two-year granting period.

Due to the acute and potentially chronic shortage of ^{99m}Tc for essential medical procedures and the urgency of the unmet health needs, CIHR and NSERC introduced several innovative amendments to the regular funding process. Firstly, the regular CIHR RFA application timelines were significantly shortened to fast-track the disbursement of funds and the start of research; and secondly, the funding cap on individual grants was removed allowing applicants to request the funds needed to meet the RFA objectives without the restraint of an arbitrary funding cap. A total of 19 applications were received in response to this RFA of which seven were funded. The funds awarded to each project ranged from $430,000 to $1.3 million over two years, a clear endorsement of the decision to allow the researchers the freedom of requesting the appropriate funds required for individual projects.

Alternative Radiopharmaceuticals for Medical Imaging

Research Outcomes

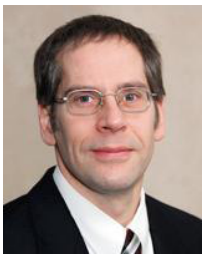
After just two years of funding the research, outcomes from the seven projects are impressive and promise viable alternatives to the nuclear reactor production of the medical isotopes necessary for routine clinical practice.

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
François Bénard 	Thomas J. Ruth Edouard Asselin Paul Schaffer Stefan Zeisler Frank Wuest Anna Celler Steve McQuarrie Eric Turcotte Brigitte Guérin Mike Kovacs	British Columbia Cancer Agency	Cyclotron-based production of technetium radioisotopes	$1,304,396

Research challenges: The goal for this team was to determine whether cyclotron produced ^{99m}Tc could be manufactured in an automated, efficient and cost effective manner to produce a radiopharmaceutical that would be safe for human use and equivalent to, or better than, the current generator-produced isotope.

Research results: The initial feasibility data from this large multi-disciplinary team of physicists, engineers, nuclear chemists, radiochemists and physicians from four different universities in four provinces enabled them to obtain an additional $16 million from the Non-Reactor Based Isotope Supply Contribution Program (NISP), launched, in 2010, by Natural Resources Canada (NRCan) as part of the federal "Isotope Supply Initiative". Using the combined funding, the team has demonstrated that sufficient quantities of high quality ^{99m}Tc can be produced using existing medical cyclotrons to enable mid-sized cities and even large metropolitan areas to meet their own demand. The team has developed practical systems with high production yields for all types of medical cyclotrons, including self-shielded cyclotrons where solid targets are notoriously hard to work with. Cyclotron production appears to be economically competitive, and cyclotron-produced ^{99m}Tc can reconstitute commercial technetium radiopharmaceutical kits without problems. The team achieved a global first with the production of technetium on a General Electric (GE) cyclotron. As almost half the existing cyclotrons in North America are GE machines these existing cyclotrons currently making isotopes for PET imaging can be easily adapted to make high quality ^{99m}Tc. The team now has a complete, practical system to produce ^{99m}Tc using existing medical cyclotrons that can be exported to other centres and this technology is now ready for clinical translation, and uptake into routine patient care where it will save hospitals time and money and reduce patient wait times for critical diagnostic tests.

Alternative Radiopharmaceuticals for Medical Imaging

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
Robert deKemp 	Robert Beanlands George Wells Philippe Pibarot Eric Turcotte Karen Gulenchyn Gerald Wisenberg J-C. Tardiff F. Harel D. Coyle	University of Ottawa Heart Institute	Rubidium-82 PET: Alternative Radiopharmaceutial for Myocardial Imaging (RB-ARMI)	$1,121,700

Research challenges: Cardiovascular disease remains the leading cause of death in Canada and about fifty percent of all the ^{99m}Tc used in nuclear medicine is used for the diagnosis of coronary artery disease. The challenge for this team was to determine whether another isotope that is not generated by nuclear reactors, such as rubidium-82 (^{82}Rb), could be used to replace the ^{99m}Tc currently used in routine clinical practice.

Research results: This multidisciplinary team, that spans eight research and clinical imaging institutions in Ontario, Quebec, and Alberta, has shown that rubidium Positron Emission Tomography (PET) is an accurate, cost-effective alternative to ^{99m}Tc SPECT that could be easily used in multiple Canadian centres for the diagnosis and management of coronary artery disease. Increased use of rubidium has the potential to reduce the demand for ^{99m}Tc by 10-40%, and improve the standard of care for many Canadians at risk of heart disease. The team has already completed quality assurance and standardization of 'low-dose' rubidium PET myocardial perfusion imaging at seven of the participating centres. The team has also compared non-invasive rubidium PET against the gold-standard of invasive coronary angiography and the initial results indicate ~90% accuracy using rubidium PET myocardial perfusion imaging for the detection of obstructive coronary artery disease at a substantially reduced cost, compared to earlier methodologies. Rubidium-82, used with advanced PET imaging, appears to have significantly higher accuracy and five to ten times lower radiation dose than the conventional technetium or thallium SPECT alternatives. Clinical trials are now in progress to compare the prognostic value of rubidium PET against conventional technologies. Two US patents have been awarded, and the technology is licensed to their partner DRAXimage Inc. An important milestone was reached in September 2011, when the rubidium-82 generator commercial product, Ruby-Fill™ (Jubilant DRAXimage Inc., Kirkland, QC) received 'Notice of Compliance' approval from Health Canada. This product is expected to become commercially available in Canada later this year, and in the US and Europe the following year.

Alternative Radiopharmaceuticals for Medical Imaging

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
Urs Hafeli 	François Bénard	University of British Columbia	Replacement of ^{99m}Tc-Macroaggregated Albumin with Biodegradable ^{68}Ga-Labelled Microspheres for Lung Perfusion Imaging	$428,594
	Don Brooks François Bénard		Substitution of ^{99m}Tc-labelled Red Blood Cells with a ^{68}Ga-Labelled Polyglycerol for Cardiac Blood Pool Imaging	$445,437

Research Challenges: Dr. Urs Hafeli received funding for two separate projects focused on finding a replacement for the ^{99m}Tc used as the current agent of choice in: i) lung perfusion imaging for the diagnosis of lung disease (macroaggregated albumin labeled with ^{99m}Tc); and ii) heart imaging to evaluate ventricular heart function (^{99m}Tc – tagged red blood cells).

Research results: Experimental results in the lung perfusion study are promising and a number of hurdles have been overcome in the manufacture of the synthetic biodegradable microspheres to be labeled with the PET isotope Gallium-68 (^{68}Ga), a non-reactor produced isotope that will replace the SPECT ^{99m}Tc labeled albumin particles that are the current standard. A new microfluidics chip technology recently developed by this group will soon enable toxicity tests and early clinical trials with the new product. If successful, this new technology will replace the need for ^{99m}Tc in this medical procedure and will have the added benefit of avoiding the contamination risk of using the blood product albumin. Further, the uniform size of the manufactured microspheres will prevent some of the potentially toxic effects caused by microaggregated albumin in patients with severe pulmonary disease.

In the heart imaging study, ^{68}Ga coupled to a biocompatible polyglycerol polymer (^{68}Ga–HPG) will be used to replace ^{99m}Tc-labelled red blood cells. This new PET radiopharmaceutical is easier and faster to prepare and use than the current radiopharmaceutical; it doesn't require blood handling; and does not interact adversely with chemotherapeutic drugs. ^{68}Ga–HPG behaves in vivo as predicted and has been shown, in animal models, to be completely non-toxic. In addition the new reagent is active at a third of the radiation dose of the ^{99m}Tc currently used. The product has already passed Health Canada-required toxicology and safety tests in animals and will soon be tested in first phase 0 human trials. The successful implementation of this technology will reduce the complexity of blood pool imaging for clinicians, as the currently used three procedures will be replaced by one, and will provide a safe, efficient alternative that will significantly reduce patient waiting times and potential adverse drug interactions.

Alternative Radiopharmaceuticals for Medical Imaging

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
Terrence Ruddy 	Corinne Bensimon Pasan Fernando Lihui Wei R. Glenn Wells	University of Ottawa	Iodine-123 Radiolabeled Rotenone for Myocardial SPECT Perfusion Imaging	$1,053,521

Research Challenges: For patients with suspected or known coronary artery disease, myocardial perfusion imaging using ^{99m}Tc has proven to be a cost effective procedure and in fact more than half of all the ^{99m}Tc used in nuclear medicine is used for this procedure. The challenge is whether the ^{99m}Tc labeled radiopharmaceuticals used in current practice can be replaced. Instead, can radiotracers for myocardial perfusion imaging be labeled with an alternative isotope - iodine-123 (^{123}I), an isotope that does not require nuclear reactors for production?

Research results: In a little more than two years, this team has successfully moved from concept to patent application and will begin a phase 1 clinical trial in May 2012. A new SPECT perfusion radiotracer – an iodinated (^{123}I) rotenone derivative, CMICE-13, has been developed and has been validated in animal models, and demonstrated to be superior to standard perfusion tracers using ^{99m}Tc compounds. The manufacturing process for the new tracer is reliable, relatively simple, and shows good yield, purity and stability. Animal toxicology studies have been successfully completed as preparation for the phase 1 clinical trial. The team has successfully produced a SPECT ^{123}I myocardial perfusion imaging radiopharmaceutical (patent application filed) with high myocardial uptake proportional to blood flow, no requirement for a nuclear reactor, potential for reliable production, and routine availability across Canada.

Alternative Radiopharmaceuticals for Medical Imaging

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
John Valliant 	Gregory Pond Karen Gulenchyn Anne Goodbody Travis Besanger Karin Stephenson	McMaster University	The formulation and clinical testing of I-123 Iodohippuran as an alternative to ^{99m}Tc MAG3 for assessment of renal function in patients with kidney disease	$477,826

Research Challenges: Technetium 99m (^{99m}Tc) mercaptoacetyltriglycine (MAG3) has been in routine clinical use in renal scintigraphy since 1986 and produces good imaging-based diagnostic information on renal structure and function. The challenge is to develop an alternative renal imaging agent – ^{123}I-*o*-iodohippurate (^{123}I–OIH) as a safe and effective alternative to ^{99m}Tc MAG3 for patients with suspected kidney disease.

Research Results: The team has successfully developed a kit formulation for preparing the new imaging agent for clinical use. The manufacturing process is well-controlled and yields a kit that is reproducible, stable and with an interim shelf life of six months at 25^{0}C. A liquid kit comprised of two vials has been developed and will be used to produce the new radiopharmaceutical, ^{123}I–OIH. To date, ^{123}I–OIH produced with the kit shows good radiochemical purity, low variability and a shelf life of 24 hours at 15-30^{0}C. A clinical trials protocol has already been conditionally approved by Health Canada and regulatory and ethics approvals are being sought to evaluate the new product in human subjects. A clinical trials application is currently being prepared and approval is anticipated in the Spring of 2012.

Alternative Radiopharmaceuticals for Medical Imaging

Nominated Principal Investigator (NPI)	Co-Principal Investigators	Host Institution of NPI	Project Title	Funding over two years
Pamela L Zabel 	Muriel Brackstone Irina Rachinsky Rob Stodilka	London Health Sciences Centre Res. Inc. (Ont.)	Seventy-to-Ninety % Reduction of ^{99m}Tc Required for Breast Cancer Lymphoscintigraphy	$541,339

Research Challenges: In breast cancer, tumour spread to the sentinel lymph node (the node that first receives lymphatic flow from a primary tumour) is a powerful and predictive prognostic factor. A radioactive tracer that is efficiently trapped in the first one or two sentinel nodes allows for less invasive surgery and fewer complications for patients when compared to dissecting multiple nodes. Current practice requires the use of a 99mTc sulphur colloid. However use of this product requires a filtration step that wastes 70-90% of the radioactivity. In times of 99mTc shortage, this is a major disadvantage. The challenge is to find a 99mTc labeled tracer that does not require filtration in order to make the best use of the available 99mTc.

Research results: This team has developed and patented a 99mTc cysteine rhenium colloid (CRC) which is optimally sized for lymph node detection without filtration – conserving radioactivity and avoiding unnecessary waste of a precious commodity. In a review of data from 1205 breat cancer patients it was shown that the 99mTc CRC was equally efficient in identifying sentinel lymph nodes, showing superior trapping in primary nodes and less leakage past the first draining nodes. GMP contract manufacturing of the product has been performed and clinical trials submissions have been approved by Health Canada for 1000 patients for 4 different diagnostic tests. A commercial partner is now being sought to further refine the GMP manufacture and to collaborate on clinical trials to bring this promising agent to routine clinical use.

Clinical translation:
The Medical Imaging Trial Network of Canada (MITNEC)

As part of the 2010 federal "Isotope Supply Initiative", CIHR received $10 million over two years to establish a medical imaging clinical trials network that would have an initial focus on assessing the clinical utility of the new technetium products and alternative radiotracers being produced in projects like the ones described above. Following the launch of a Request for Applications in July 2010 and successful peer review by an international panel of experts, the Medical Imaging Trials Network of Canada (MITNEC) received funding in early 2011. In the short term, MITNEC will facilitate the coordination of imaging clinical trials and enable the clinical evaluation of new or improved imaging radiotracers and their uptake into routine patient care. The long term objective is to establish a national, sustainable, imaging clinical trials network that will provide a clinical platform for imaging research in Canada.

Now that MITNEC is fully functioning, it will be an invaluable resource for the teams funded under the Alternative Radiopharmaceuticals for Medical Imaging initiative. MITNEC will facilitate the multi-centre clinical trials that will lead to approval of the new radiopharmaceutical products by Health Canada and their subsequent uptake into clinical practice. Already the Sherbrooke and Vancouver sites, involved in the project led by François Bénard, are coordinating trials of their cyclotron-produced products though MITNEC. The Alberta group from the team hopes to do the same following their pilot trial of 30 patients scheduled to receive whole-body 99mTc scintigraphy as part of thyroid cancer evaluation, using their ABEC resin purification method of 99mTc. Similarly, for the project led by Robert deKemp, the team is working with MITNEC to allow clinical follow-up of all 6000 PET and SPECT patients at 6-months and 2-years after the rubidium PET scan, to compare the prognostic value of Rb-82 PET against conventional 99mTc and thallium SPECT myocardial perfusion imaging.

Economic Outcomes: Commercialization Opportunities

The Canadian government has announced that the nuclear reactors at Chalk River, our current source of the Molybdenum-99 used to produce clinical grade 99mTc will be closed in 2016. The concept of eliminating highly enriched uranium (HEU) from the production process for medical radionuclides has been accepted now by most governments around the world. The reactor industry globally, including Lantheus and Coviden, whose North American subsidiaries currently produce the Molybdenum-99 generators for 99mTc production in Canada, have been validating replacing the HEU currently used for Molybdenum-99 production with low enriched uranium (LEU). Thanks, in part, to the combined efforts of the US FDA, Health Canada and our Canadian research community, full regulatory approval has been achieved with Health Canada and FDA for using LEU-produced Molybdenum-99 in North American generators. Global collaboration of Molybdenum-99 production has increased. It is anticipated that the international Molybdenum-99 supply matrix will look much different in the future, especially in light of the emergence of new technologies.

The possibility of being able to produce sufficient clinical grade 99mTc to supply the needs of Canadian hospitals and institutions using new cyclotrons, and existing ones that can be adapted for this purpose, has the potential to transform the isotope production industry in Canada. This work began with the funding provided in the CIHR/NSERC the Alternative Radiopharmaceuticals for Medical Imaging initiative and will continue with additional support from NRCan, through NISP. It is anticipated that locally-produced 99mTc will prove to be both safer and more cost effective in the long term than the upkeep of aging nuclear reactors or the construction of new ones. In addition, local Canadian companies involved in these pilot studies, such as Advanced Cyclotron Systems Inc. in Vancouver will derive economic benefit from building a network of new TR24 cyclotrons throughout Canada with the possibility of expanding to a potential global market. This new Canadian technology holds great promise for future economic growth and diversification.

Although it is early days, the development of the many new products, radiopharmaceuticals and manufacturing methods described here has already generated patent activity, with a number of patents filed. For example, the rubidium generator designed by the deKemp team will soon become commercially available in Canada and may find a place in the global market. The same team has also recently filed a US patent application for "Radiolabeled Rotenone derivatives and their use in SPECT Imaging". Further, their new method of rubidium PET myocardial perfusion imaging performs as well as methods using current 2D-PET imaging but can be done at a substantially reduced cost. Similarly, the recently patented 99mTc cysteine rhenium colloid developed by the Zabel group will make a significant contribution to the conservation of available supplies of 99mTc. A commercial partner is now being sought to take this product to market.

The Centre for Probe Development and Commercialization (CPDC), which is lead by John Valliant at McMaster, provides the expertise needed to de-risk and commercialize new imaging probes and associated technologies. The CPDC, which was funded through the Networks Centres of Excellence (NCE) Centres of Excellence for Commercialization and Research (CECR) program, is currently leading the quality and regulatory aspects of the MITNEC program while also acting as one of the research sites in the NISP program. As the discoveries supported by CIHR advance, the CPDC is a unique Canadian program that has a specific mandate to commercialize new intellectual property and to export Canadian technologies to the global market.

Summary

As one of the world's major producers of Molybdenum-99, the precursor of the 99mTc used for the vast majority of nuclear medicine investigations, Canada has a vested interest in ensuring an adequate and reliable supply of the radiopharmaceuticals that have become an integral part of clinical practice and patient care. When faced with a critical isotope shortage, the Government of Canada took a number of steps to address the issue. CIHR and NSERC were the first to respond with the launch of the Alternative Radiopharmaceuticals for Medical Imaging initiative, described here. This was followed by a broader government two-year strategy, the Federal Isotope Supply Initiative, which included $30 million to Natural Resources Canada (NRCan) for the Non-Reactor Based Isotope Supply Contribution Program (NISP), designed to support the development of new accelerator technologies for 99mTc production; and $10M for CIHR to establish a national medical imaging clinical trials network that would be positioned to coordinate the multi-centre, multi-disciplinary clinical trials required to bring the new radiopharmaceuticals to the clinic. These programs also

leverage the $22M investment in the CPDC. In addition, Health Canada committed to reviewing regulatory requests for approvals of alternate isotopes and new reactor-based sources of 99mTc on an expedited basis to provide health care providers with options. In an effort to help mitigate short-term supply disruptions, Health Canada developed a regulatory toolkit to help the health care community access alternative isotopes and alternative imaging modalities.

Overall, this coordinated approach has enabled the initial feasibility studies supported by the CIHR/NSERC investment to advance at a faster pace. For example, the NISP funding enabled the research team led by François Bénard to expand their efforts to scale-up technetium production, particularly in Vancouver where the original team expanded following the full time assignment of several additional scientists. NISP funding supported cyclotron upgrades, and the design and construction of fully automated irradiation, extraction and production systems for the Vancouver site. In just two years, this research has produced new solutions for future 99mTc shortages and innovative methods for completely circumventing the need for reactor-produced 99mTc. The ability to produce clinical grade 99mTc isotope with the cyclotrons already existing in hospitals and institutes across the country, instead of nuclear reactors, is a major milestone for diagnostic imaging internationally.

In terms of finding alternatives for the 99mTc currently used in traditional imaging studies, the objective of five of the funded projects, tremendous advances had been made in a very short time frame. Viable alternatives to 99mTc are now available for the diagnosis of coronary artery disease and ventricular heart function, the evaluation of myocardial function, the diagnosis of lung disease, and the monitoring of renal structure and function. In addition, an improved method for preparing a 99mTc labeled radiotracer for assessing lymph node involvement in breast cancer has been developed that does not require the filtration step responsible for a huge loss of radioactivity. This new method will make optimum use of the available 99mTc, especially in times of isotope shortage.

The full research outcomes from the CIHR/NSERC Alternative Radiopharmaceuticals for Medical Imaging initiative will be known following the submission of the final reports from the teams in the Fall of 2013, but already the results are impressive, including many scientific presentations, peer–reviewed publications and patents. Several key factors, in addition to the support from the Federal Isotope Supply Initiative, were instrumental in facilitating the research progress made by these teams. First, the partnership between CIHR and NSERC, supported by six of CIHR's Institutes, brought together researchers from different fields and medical disciplines into large multi-disciplinary teams. This process was facilitated by the fact that teams could request the funds required for their ambitious projects unrestricted by a funding cap. Second, the accelerated RFA process enabled research to begin rapidly providing early feasibility data in time to apply for the subsequent NISP funding. Third, the rapid turnaround by CIHR in establishing MITNEC has provided a network capable of coordinating the essential multi-centre clinical trials to bring the new products to market and into widespread clinical use. Last, but not least, Canada has a cadre of exceptional researchers engaged in imaging research and many of these clinicians and scientists came together in the projects supported by this initiative.