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MEDICAL AND PHARMACOLOGICAL ADVANCES

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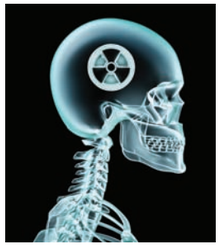
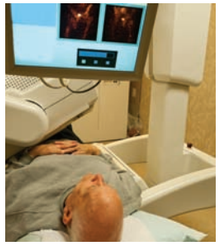
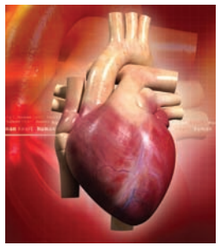
SUMMARY







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MEDICAL AND PHARMACOLOGICAL ADVANCES

François Lamoureux,
M.D., M. Sc.

PRESIDENT OF THE QUEBEC ASSOCIATION OF NUCLEAR MEDICINE SPECIALISTS

ANTIMATTER AT THE SERVICE OF NUCLEAR MEDICINE

We can now measure and visualize the metabolic activity of an organ in a human being and detect its functioning and integrity. This is positron emission tomography (PET) or, expressed another way, the functional imaging of cell metabolism.

Using PET, we can detect certain pathologies, such as cancer, which initially alter the normal physiology of cells.

In order to live, function and reproduce, the organism's normal cells need energy in the form of glucose (a sugar that can be metabolized by the organism.) This energy source is indispensable to all the living cells of the organism, and this sugar is found naturally in the blood. The more active a cell is, the more sugar it consumes.

A cancer cell that has lost all control over its unbridled multiplication must constantly consume large quantities of energy in the form of glucose (sugar).

In nuclear medicine, a glucose analog, deoxyglucose, is used as a decoy: it mimics glucose by entering cells but in a form that cannot be used as an energy source by the cancer cell.

To detect intracellular deoxyglucose, the molecule is radioactively labelled beforehand with a positron (antimatter) in the form of fluoride-18 (F-18).

As it accumulates in cancer cells, the positive electrons (e+) of F-18 come almost immediately in contact with the cell's negative electrons (e-). This produces a disappearance of the injected matter and antimatter, an annihilation reaction in which two photons are emitted at 180 degrees in the form of external radiation.

« The surgeon becomes a robotic manipulator whose movements are measured in millimetre precision. Robotic arms extend the surgeon's hand. Integrated cameras magnify vision by more than 15x. »

The cell becomes radioactive and the emitted rays are captured by an external PET camera. Powerful computers interfacing with the PET camera identify abnormal areas of radiation emission, a sign of the abnormal accumulation of F-18 FDG in the cancerous tissue.

The cancer tumour is detected and its activity is measured. Then a 3-D reconstruction is done, in multiple slices and dynamically. The result is an exploratory metabolic autopsy of the patient *in vivo* that is non-invasive.

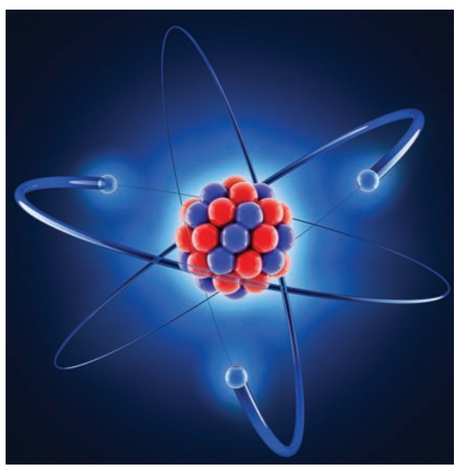
The external shape of the PET camera's detector resembles a tomodensitometer or magnetic resonance imaging device, but its function is completely different. The other two devices produce mainly anatomical images of the organs of the human body.

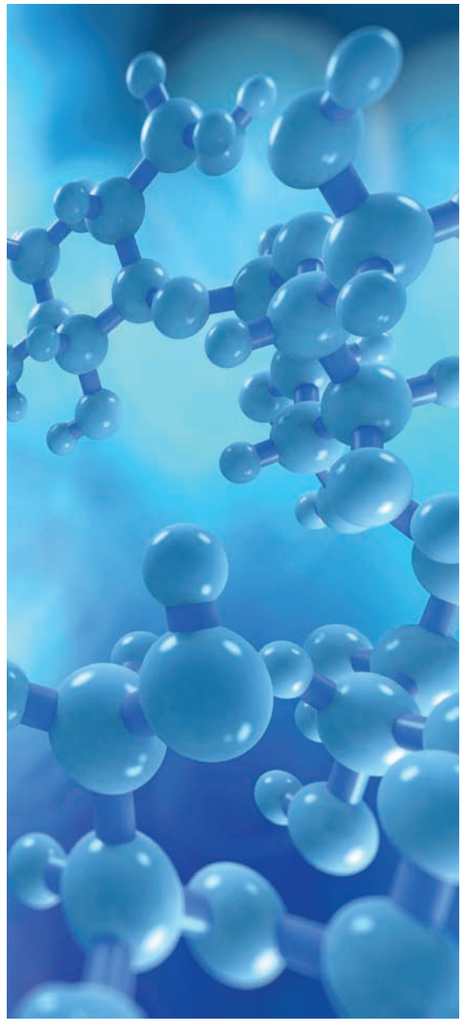
Moreover, today PET cameras are being teamed up with tomodensitometry detectors and, in the near future, will also be paired with magnetic resonance imaging devices in order to better localize the site of pathological processes.

With a simple intravenous injection of F-18 FDG that is painless and without identifiable side effects, we are pushing the diagnostic limits ever further and tracking down cancer cells in their very last cellular bastions.

While F-18 FDG is currently the most commonly used radioactive tracer, it is not the only one. Carbon-11, oxygen-15 and nitrogen-13, for example, can also be used to conduct neurological, cardiac or pulmonary exams.

In Quebec, PET technology is currently available in some nuclear medicine units. In mid-2008, thanks to new facilities in such places as Montréal, Quebec City, Chicoutimi, Gatineau, Rimouski and Trois-Rivières, this newly deployed technology enabled





patients in centres that were not equipped with these cameras to have access to PET scans within a reasonable timeframe.

There are no inter-hospital charges or costs for either hospitalized patients or outpatients. The cost of each PET scan performed in a hospital centre is individually, directly and completely covered by the Government of Quebec. PET scans are prioritized based on a patient's clinical condition, whatever and wherever that may be, and not on the patient's physical location or the physical location of the PET camera.

Considering that PET technology has been applied as a just and universal social measure for all patients in Quebec, this is a success story and an example to follow. ■

« With a simple intravenous injection of F-18 FDG that is painless and without identifiable side effects, we are pushing the diagnostic limits ever further and tracking down cancer cells in their very last cellular bastions. »

Dr Norman Laurin M.D., FRCP
PRESIDENT: CANADIAN ASSOCIATION OF NUCLEAR MEDICINE 2012-2014

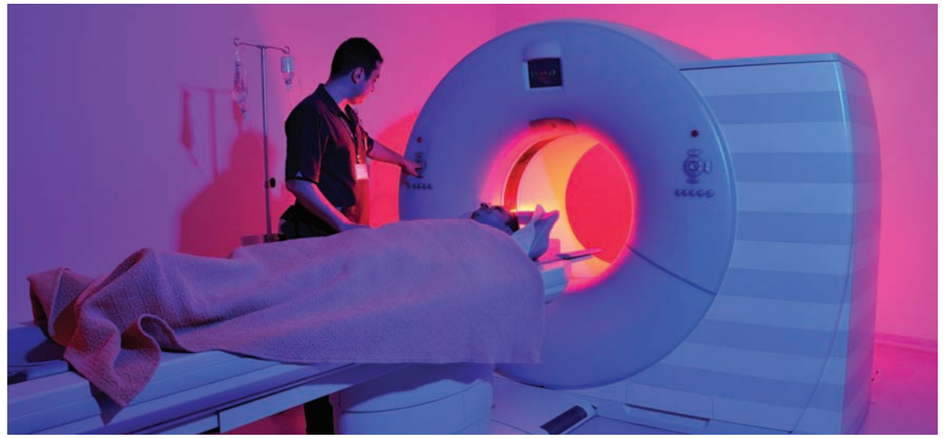
NUCLEAR MEDICINE, A DAY-TO-DAY MEDICAL SPECIALTY AND ITS CHALLENGES

Nuclear Medicine is the medical specialty involved in the diagnostic and therapeutic use of radioactive substances. We are one of the 29 medical specialties recognized by the Royal College of Physicians of Canada and we form an important part of both the imaging and therapy team in most Canadian hospitals. Nuclear Medicine's unique advantage resides in its ability to image and evaluate the various metabolic processes occurring in the human body, in a non-invasive and dynamic mode (as they happen in real time, often over several minutes and sometimes hours). This gives us an exceptional access to most physiologic and disease processes and opens the door to what we believe is the future of medicine: metabolic and personalized medicine. The rapid development of hybrid imaging devices (combining Nuclear Medicine conventional cameras and PET scanners with CT scanners) has brought the benefits of precise localisation and anatomic characterization to traditional Nuclear Medicine, making it much more powerful.

We nevertheless face serious challenges, very much like the rest of the medical community. With fewer funds available for health care, the development of imaging technology is continuously being questioned and we must strive to keep our just place in the medical team. The delay in the deployment of Positron Emission Tomography (PET Scans) in Ontario is a good example of it. The regulatory environment regarding the approval of radiopharmaceuticals in Canada (the products used in Nuclear Medicine procedures) must not unduly retard their adoption in our departments, so that Canadians are allowed world class access to newer imaging drugs. Finally, Canada must seriously consider the safety of its Molybdenum/Technecium supply (the main products used in Nuclear Medicine departments) as it prepares to close down its NRU reactor in Ontario (one of the world's most important sources of medical isotopes).

It is our profound belief that progress in radiopharmaceuticals and imaging technology will continue to ensure a bright future to our specialty. The quality of Nuclear Medicine in Canada is the envy of much of the rest of the world. Canadians do not like to brag about themselves generally, but in the case of Nuclear Medicine and the peaceful use of atomic energy, they should. After all, Canada was the first country in the world to recognize Nuclear Medicine as a medical specialty, and we were (and still are) world leaders in the production of medical isotopes and nuclear reactors for peaceful use.

CANADIAN NUCLEAR MEDICINE IN THE 21ST CENTURY



Dr Andrew Ross
President, Canadian Association of Nuclear Medicine

It was the best of times; it was the worst of times. This adage can well be applied to Canadian Nuclear Medicine practice in the early 21st century. New technology and the promise of exciting tracers to diagnose illness and therapies abound. Nuclear Medicine plays an integral role in investigation and treatment of patients. However, jeopardy in terms of regulations, healthcare economics and isotope supply work to temper the excitement. The challenge for those with knowledge of the potential is to be active and proactive to capture as much of the positive as possible.

The deployment over the last decade of the advanced SPECT/CT and PET/CT imaging cameras, which accurately show changes in physiology caused by diseases linked with the anatomy has enhanced the relevance and importance of Nuclear Medicine, expanding its scope within diagnostic medicine. PET in particular has seen exponential growth. After a slow deployment (outside Québec), virtually all provinces now possess or have access to, and have recognized this important diagnostic tool. However, many jurisdictions place limitations to access.

The growth has almost entirely been fuelled by FDG, radioactive labeled sugar. Its power to diagnose and provide important information about cancer has revolutionized how this disease is investigated. It can also provide important information in certain patients with heart disease and brain disorders. There are many other promising tracers used elsewhere such as radioactive dopamine which has use in difficult to manage cancers and amyloid agents which can provide vital information to help manage some patients with dementia.

Radiolabelled therapeutic agents have seen some limited utilization in Canada, but this lags other countries. Much of this relates to regulatory issues and the relative small market Canada represents, which decreases the initiative of companies to pursue efforts for use here. Agents such as alpha emitters for bone metastasis and other agents in neuroendocrine cancer show great promise for treatment. Working together, we can hopefully obtain expanded access for Canadian patients to these important therapies.

A challenge to overcome is the regulatory burden placed on tracer approval. This will continue to be one of the most important issues to provide access. Other jurisdictions, notably Europe, are more advanced in this regard. It is paramount we continue to educate the regulators to recognize the unique status of radiopharmaceuticals. Currently, they fall under the full regulatory burden of drugs. This equates the minute doses of near physiologic molecules labelled with fast decaying tracers used in Nuclear Medicine to mass distributed therapeutic agents from large pharmaceutical companies. It is important to provide safe, well studied agents. However meeting the current regulations is not only challenging but highly expensive for these special agents.

The other major jeopardy for Nuclear Medicine is the "made in Canada" problem involving supply of our workhorse medical isotope, 99-Technetium. In 2016, closure of the Chalk River reactor, which is the only North American producer, will precipitate a highly jeopardized supply chain causing price escalation and potential shortages.

Nuclear Medicine has and continues to be a vital contributor to patient care. There is a dedicated team of professionals including doctors, technologists, radiopharmaceutical scientists and a supporting industry. There is a bright future with much opportunity to further enhance this vital work. It is important that all who understand or have been touched by it, work to help overcome the challenges to its continued success.

INTERVIEW WITH
DR ALP NOTGHI
PRESIDENT OF THE BRITISH NUCLEAR MEDICINE SOCIETY

1. British medicine has always been one of the most advanced in the world. What is the situation of nuclear medicine?

Nuclear medicine has always been one of the smallest specialities in medicine. However, in the UK, because of its multidisciplinary nature and close association with physics and radio-pharmacy, it has always attracted people with broader interests beyond just medicine, and usually scientifically-minded, often from all over the world. This has helped to maintain its niche in the forefront of advances in nuclear medicine worldwide.

2. Is nuclear medicine accessible all over United Kingdom?

There are over 200 hospitals with nuclear medicine services in the UK. Some are dedicated nuclear medicine departments which are involved in research and development, mostly in larger hospitals and also deliver the more specialised investigations and therapies, whilst other departments deliver only the more common NM procedures, making these accessible for most of the UK population.

3. How many centres have Positron Emission Technology (PET)? And how many future PET centres will there be in the next five years?

PET facilities are mostly associated with cancer care centres (cancer hobs for each region) or are research based (all together, 63 PET cameras in the UK). However, there is a need for expansion in the services and with the recognition of developments in non-cancer applications of PET, there are plans to expand this to more centres and make it routinely available for more hospitals, as local expertise and local one-to-one discussion of cases with referrers (MDT meetings) are recognised to be as important as the test itself.

4. How is training done for nuclear medicine specialists and technologists?

Nuclear medicine training is one of the Royal College of Physicians specialities. However, with integration of hybrid imaging for attenuation correction, localisation and now, diagnostic scanners, we have developed a program to include an initial 3 years training in radiology (culminating in fellowship of the Royal College of Radiologists), followed by 3 years nuclear medicine training (including a minimum of university diploma in nuclear medicine); still remaining a RCP speciality. Technologist training is a separate training scheme from radiographers. However, closer integration may be necessary as an increasing number of hybrid cameras have diagnostic CT.

5. Nuclear medicine is expanding worldwide. How do you share your expertise with colleagues of other countries, and especially in Canada?

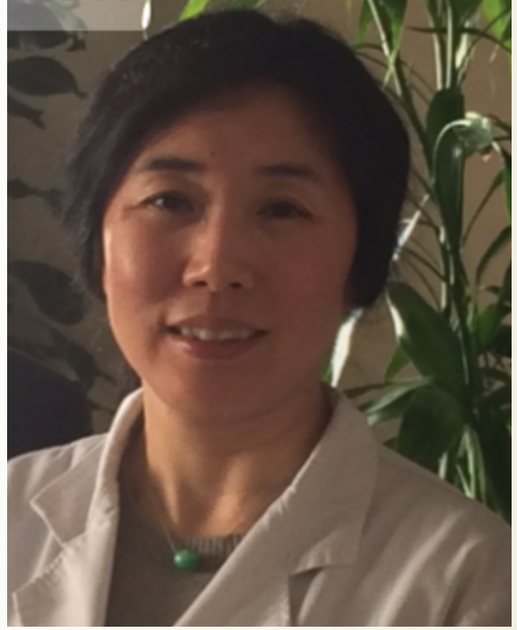
I see closer links between the British Nuclear Medicine Society with sister societies and organisations such as Canadian Association of Nuclear Medicine as a positive step which brings together the expertise developed which would have mutual benefit for the countries.

6. Where do you think nuclear medicine is going in the near future, and what should nuclear medicine specialists do next?

There are exciting developments with new tracers (in particular PET) and therapy which will expand the role of NM. New camera technology with increasing resolution and sensitivity has meant faster patient throughput, reduced radiation and better images, increasing the appeal of NM as a diagnostic modality. Better integration of hybrid technology (diagnostic CT and MRI) has meant we should rethink the patient pathways, reducing the number of patient visits and delays in diagnosis, giving more accurate diagnoses by combining the information from different modalities. There is a strong case for development of more SPECT agents as well as PET agents as the availability of SPECT is more universal, and in general costs of tests are lower.

7. Finally, what is your best wish for nuclear medicine?

To successfully integrate new developments into nuclear medicine whilst remaining a strong independent speciality and providing unique molecular and physio-pathological information, thus helping to understand and alter disease processes, therefore improving patient care. ■



INTERVIEW WITH
PROFESSOR WEI HE M.D. PH.D.
DIRECTOR OF NUCLEAR MEDICINE DEPARTMENT AND PET/CT CENTER FU DAN UNIVERSITY, AFFILIATED WITH SHANGHAI HUA DONG HOSPITAL

1. China is the most populated country in the world and amongst the most powerful countries in the world. Professor He, you are personally one of the most influential Chinese leaders in medicine. What is the situation of nuclear medicine in China?

We are at the early stages of deployment of nuclear medicine. Our central government recognizes the power of nuclear medicine and, consequently, is very supportive. As we need better diagnostic tools, we have the chance to rapidly get the state of the art equipment in a cost effective perspective. So all the existing and new nuclear medicine departments have, or will have, at least the most modern SPECT/CT and many departments also the PET/CT. Only a few university centers will get the PET-NMR technology, mostly for research purposes.

2. How many centers are there in China at the present time?

Approximately 1000 SPECT/CT units and 250 PET/CT units. More than 98% are independent nuclear medicine departments under the responsibility of nuclear medicine specialists.

3. How many new nuclear medicine centers do you think will open in the next three years?

I think approximately 400.

4. How is training done in China for doctors and technologists?

At the moment, only two universities offer a training program and our residents acquire additional expertise through other international nuclear medicine programs. There is a need to further develop this aspect in our training programs. For our technologists, there is not actually a formal training program. Most of the expertise is acquired locally. This also is a field that we need to look to develop partnerships with other countries, like Canada for example, where you have well recognized technologist schools in nuclear medicine.

5. Nuclear medicine is expanding rapidly worldwide. How do you keep in touch, share your expertise and develop new nuclear medicine applications with, for example, your Canadian colleagues?

Today, the world gets smaller. So we participate in many international meetings, we offer our young doctors the possibility of going abroad for additional fellowships and we believe in exchanges of visiting doctors. We also use the e-journals and e-training a lot. For example, in my department in Shanghai, we have the Hermes platform and through it we use the CLOUD to easily exchange and access training material, so we can adopt it for China. We have already close links with our Canadian colleagues and we are looking to increase it in the near future, either for our technologists or for our doctors and vice versa.

6. For many all over the world, Shanghai is the example of a city of the future. What is the situation of nuclear medicine in Shanghai?

Shanghai and Beijing are the two leading cities with good economic situations. We have very well educated staff and we have many channels to the world. Our young specialists travel the world and bring back the best for our nuclear medicine departments. Also, almost all of them master the English language.

7. Finally, Professor He, what is your greatest wish for China and Canada regarding nuclear medicine?

As China and Canada share the same vision of nuclear medicine, as in fact the molecular speciality of today, I long to share more our mutual expertise, our knowledge. So in our day to day work, our patients could benefit rapidly from the contribution of nuclear medicine and its molecular power to diagnose diseases earlier, and also offer them rapidly the most appropriate treatments that nuclear medicine brings also to the patient in many situations. Canada and China have so much in common that we could easily share what each of us has, the best in clinical guidelines, training programs and research. ■

THE USE OF PET IN NUCLEAR MEDICINE AND ITS SHAMEFUL LIMITATIONS OF ACCESS IN CANADA

Jean-Luc Urbain, M.D., Ph.D., CPE
Past President, Canadian Association of Nuclear Medicine

Jean-Noël Talbot, M.D., Ph.D.
Professor at Pierre and Marie Curie University (Paris),
Past President, Île-de-France Association of Nuclear Medicine

The very basis of Diagnostic Nuclear Medicine consists in its unique ability to trace, thanks to a very minute amount of radioactivity, the very same molecules that the human body processes to carry out all living tasks. This unique approach enables non-invasive imaging to evaluate the physiology and pathophysiology of our tissues and organs. The quintessence of the added value of nuclear medicine to medical diagnosing is nicely illustrated by Positron Emission Tomography (PET), the most recent modality in clinical non-invasive imaging.

Introduced in the late 50s, PET has, nowadays, evolved into a critical clinical diagnostic tool for the management of patients with cancer, inflammatory, cardiac or neurological diseases. Coupled with the anatomic definition of Computerized Tomography Scanners or Magnetic Resonance Imaging, PET/CT and PET/MRI are the ultimate clinical imaging instruments to detect, pinpoint, characterize, quantify, manage and follow the vast majority of diseases afflicting human beings at the molecular level.

Over the past three decades, there has been a vast array of medical positron emitting isotope compounds that have been synthesized and tested for the imaging and quantification of cell receptors, metabolic and signaling pathways using PET.

In 2012, approximately 2.5 million PET procedures were performed in the US. The main application of PET has been and remains the tracing and quantification of glucose metabolism using 18F-FDG, a molecule of glucose labeled with a radioactive fluorine. 18F-FDG, PET/CT or PET/MRI has become the tool of choice for diagnosing, staging, prognosing, monitoring and following up patients with cancer, since the cancer lesions usually display an increased glucose metabolism. FDG PET is also useful for detecting, at the whole-body level, unknown infectious or inflammatory foci. In addition, three other oncology PET tracers have also been registered in France and in several EU Member States for imaging prostate or primary liver cancer (fluorocholine), neuroendocrine or brain tumours (FDOPA) or skeletal malignancies (fluoride). Furthermore, very active research programs to develop PET tracers of apoptosis, tumour angiogenesis and biomarkers for imaging breast cancer, prostate cancer, melanoma, colorectal cancer and renal cancer will expand diagnostic options and enable personalized targeted therapies.

While 18F-FDG PET represents about 90% of the clinical PET procedures, increasing by 10% per year, cardiac PET studies using rubidium now represent 10% of the PET studies. Over the past two decades, rubidium has indeed provided the cardiologists with a very

effective tool to diagnose complex cardiac diseases with increased confidence and to select the patients who will benefit most from revascularization. The development of PET cardiac tracers for the imaging of perfusion and the vulnerable plaque will further increase the functional value of PET by providing molecular information on acute coronary syndrome, cardiac heart failure and offering more effective preventive and treating approaches.

In the neurology field, a recent breakthrough has come for the FDA approval of Amyvid (Eli Lilly), Vizamyl (GE) and more recently, NeuraCeq (Piramal), the new PET biomarkers for early imaging of amyloid substance deposition leading to Alzheimer's disease.

Unfortunately, PET programs in the English part of Canada are still largely underdeveloped compared to the US, Europe and now Asia. Besides the Province of Quebec, where PET scintigraphy has flourished over the past decade, the implementation of clinical PET in the rest of Canada, particularly in Ontario, has been marred by severe restrictions by the provincial governments. While both Quebec and Ile de France (Paris region) performed about 50,000 PET procedures per year for a population of ca. 9 million, only 12,500 PET scans have benefited the 13 million Ontarians. Based on conservative estimates derived from cancer registries and the incidence and prevalence of the various types of cancers affecting Canadians, it is estimated that Canada should perform between 200,000 and 250,000 oncology PET studies per year.

We sincerely hope that the article published in this magazine by Éric Turcotte from Sherbrooke on the indications of PET will encourage the health care authorities across Canada to finally provide its citizens with 21st century PET access. ■

NUCLEAR MEDICINE TECHNOLOGY TODAY AND THE ROLE OF THE TECHNOLOGIST

The Canadian Association of Medical Radiation Technologists (CAMRT) is the national professional association and certifying body for 12,000 radiological, nuclear medicine and magnetic resonance imaging technologists and radiation therapists (MRTs). CAMRT offers a suite of programs and services that advance the profession and the health of Canadians, and is the authoritative voice on issues that affect its members. 1,350 of these are nuclear medicine technologists.

Nuclear medicine procedures involve the application of radiopharmaceuticals in the diagnosis and treatment of disease. Nuclear medicine has been described as "radiology done inside out" because it records radiation emitting from within the body rather than radiation that is generated by external sources like X-rays.

Nuclear medicine scans are conducted by a certified nuclear medicine technologist (MRT). To become a certified technologist, one must first complete an undergraduate education program that is accredited by the Canadian Medical Association. The MRT provides the essential link between the sophisticated technology and compassionate patient care. In the course of performing their work, their expertise is applied to administering radioactive chemical compounds, known as radiopharmaceuticals, and performing patient imaging procedures using sophisticated radiation-detecting instrumentation. They also carry out the computer processing and image enhancement before providing images, data analysis, and patient information to the physician for diagnostic interpretation.

During an imaging procedure, the technologist is responsible for patient care. Not only do they obtain pertinent history, describe the procedure and answer any questions but they also closely monitor the patient's physical condition during the course of the procedure.

CHALLENGES AND OPPORTUNITIES OF THE FUTURE

Over the past few decades there have been exciting new developments in the field of nuclear medicine. Positron emission tomography (PET) has gained broad adoption. It uses very short life isotopes that are produced in cyclotrons. PET imaging is very sensitive and allows the visualization of functional processes in the body. It is used mainly in clinical oncology and neuroimaging. PET scanners are now often combined with CTs (PET-CT) and MRIs (PET-MR) to produce high quality anatomic and metabolic information. In Canada, the adoption of PET imaging has been slowed by the limited number of cyclotrons and the high cost of the procedures.

Single-photon emission computed tomography (SPECT) on the other hand is highly dependent on reactor produced medical isotopes. 2 of the 9 reactors used in the supply chain are scheduled to stop production in 2016 (including the Canadian NRU at Atomic Energy Canada Limited, Chalk River, and the French OSIRIS reactors). Together, these reactors account for about 25% of the current worldwide annual production volume. Other major existing producing reactors, except for OPAL in Australia, are aging and scheduled to shut down by 2030. There are many projects under way around the world to create alternative sources of supply. The Canadian government, for example, has invested over $35 million in research and development of innovative new approaches that involve the use of cyclotron technology to produce technetium-99m, an isotope used for 80 per cent of nuclear medicine diagnostic procedures. However, at this time, it is uncertain as to whether these projects will be fully operational on time to ensure a steady and reliable supply when the reactors close.

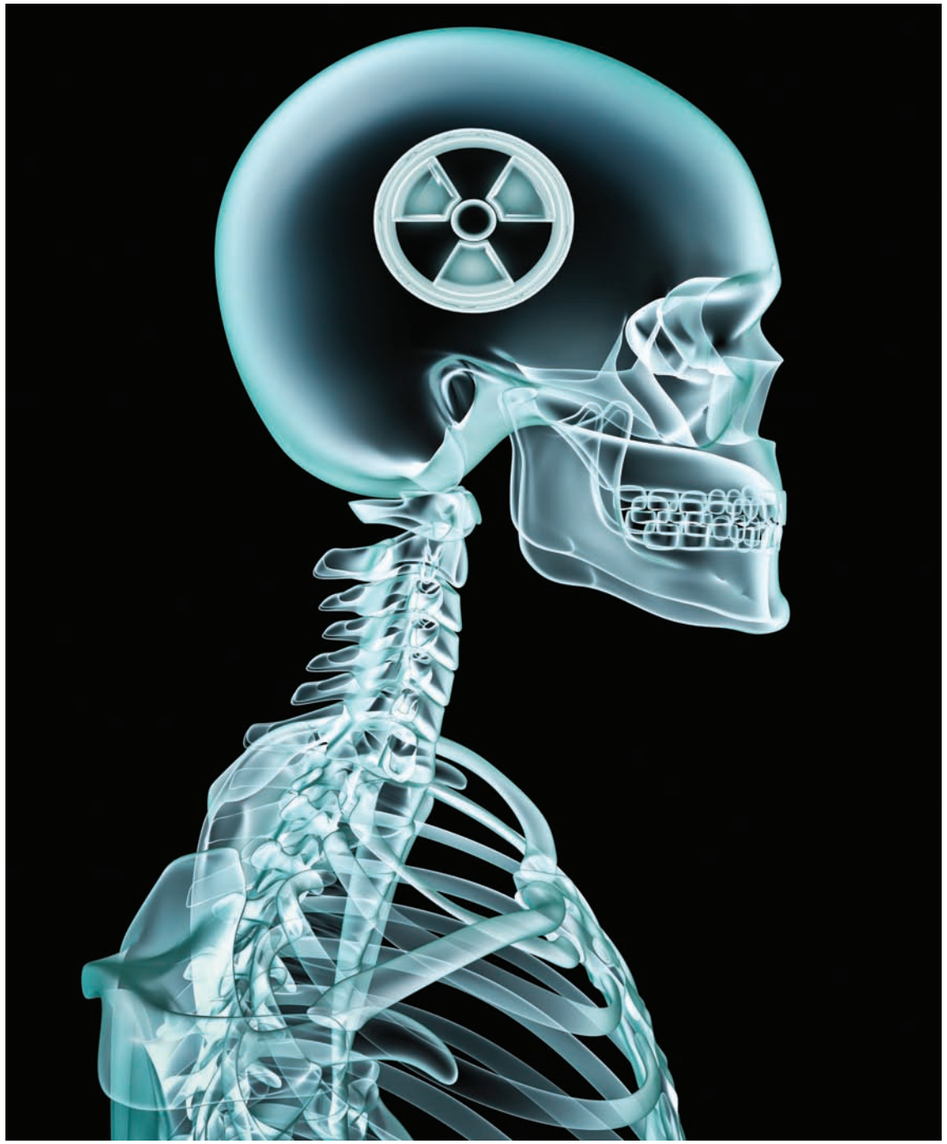
The CAMRT is monitoring the situation and coordinating ongoing investigation through dialogue and information sharing with CAMRT members, international colleagues and other national healthcare associations. Discussions are ongoing, with Health Canada, with provincial and territorial government representatives, and various industry players. The goal is to monitor the situation closely and stimulate the emergence of mitigation strategies that will ensure little or no disruption to Canadian patients who require a nuclear medicine scan. ■

François Couillard,
B. Eng, MBA, CMC,
CEO of the Canadian Association of Medical Radiation Technologists (CAMRT)

FRACTURES

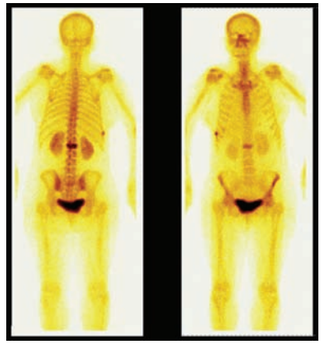
A DIFFERENT APPROACH: THE ROLE OF EARLY BONE SCANNING

Christopher O'Brien
MDCM; FRCPC
Medical Director, Nuclear Medicine
Brantford General Hospital



The three-phase bone scan is a very sensitive technique used in the detection of fractures of any cause. The sensitivity can be further increased through the use of SPECT and the specificity can be improved by adding the technique of SPECT/CT. The sensitivity ranges from 80% to 98% depending on when imaging is performed and whether SPECT is used, or 24 hour delayed imaging is obtained. Thus the sensitivity at 24 hours post event is 80%, 95% by 72 hours and 98% by one week.

The reason that the sensitivity is lower with early imaging is that the osteoblasts must become activated and it is osteoblastic activity that is assessed with the bone scan. The higher sensitivity is usually achieved by 48 hours after the event. Up to 72 hours post event may be required for the severely osteopenic patient.



A bone scan can be tailored to assess a specific site only (e.g. the hand or foot) or a more regional assessment (e.g. the pelvis and lower extremities). At times a whole bone assessment may be required, especially in cases of more severe trauma. By tailoring the study, one can assess both the area of discomfort and also have the ability to assess for referred pain from occult fractures elsewhere.

It is important to realize that there is no increase in radiation exposure as one takes more images, as the radiation exposure comes from the injection. The addition of SPECT does not add any more radiation either as this is a simple 3-dimensional reconstruction technique. SPECT/CT, however, does add a very small amount of extra exposure linked to the CT, but a low dose technique is used to keep this exposure to a minimum.

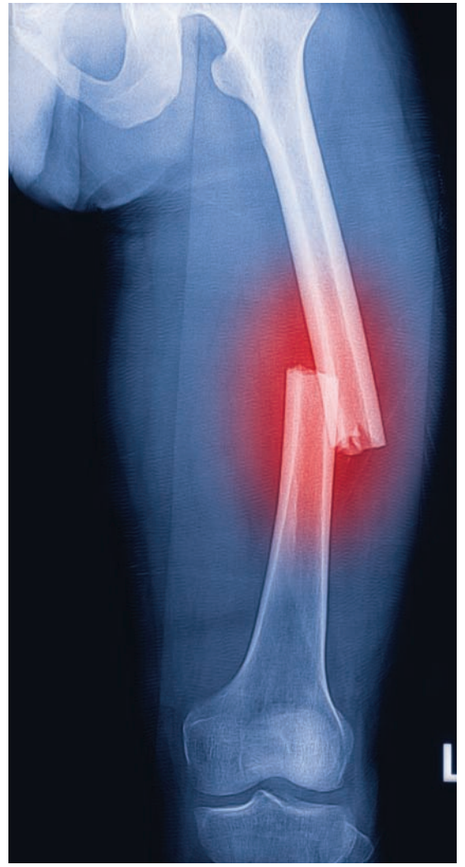
PATIENT MANAGEMENT ISSUES

When a patient presents complaining of bone pain, it is important to obtain a history to assess for possible post-traumatic causes, perhaps insufficiency causes, or perhaps neoplastic causes. After the history and if clinical indication exists, then the first imaging is usually plain film X-ray of the area of discomfort. If X-rays are obtained very shortly after the event, the sensitivity is low: 10 to 15% (especially with stress fractures and in those individuals with low bone density), and it may take up to two weeks or more before changes become more apparent with plain film X-ray. Thus there is the need for a follow-up X-ray if clinical symptoms persist.

However, even with this we see many patients presenting to Nuclear Medicine to obtain a bone scan to assess the possibility of fracture, even one month after the event because X-rays are still normal or inconclusive, and because of this the patient may not have received optimal clinical care.

To maximize patient care, one could consider a bone scan as the next imaging technique if initial X-rays are normal and clinical symptoms remain. Thus, one could consider performing a bone scan much earlier in the work-up of the patient due to its very high sensitivity which rivals MRI (sensitivity of 85 to 95%).

If referring physicians begin to request bone scanning earlier after initially negative X-rays in order to optimize patient management, then it will be necessary for the Nuclear Medicine department to establish a rapid response process to fast track patients with suspected fractures. If the waiting time is 2 to 3 weeks, this does not do the patient any good. In addition, the Canadian Medical Association Wait Time Alliance has suggested that urgent cases (which include fractures) should obtain a bone scan within one week of the request and preferably within around 48 hours of the request, in ideal situations.

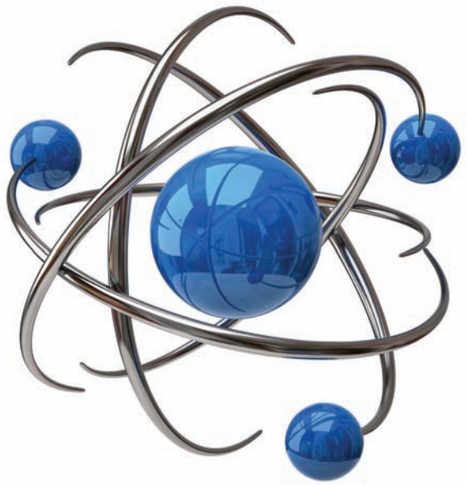


I believe that by following this approach, the diagnosis of fractures will be made quicker, patients can then be referred for appropriate management sooner, and the patient will be able to return to routine activities of daily life and will also have better pain control.

In conclusion, the routine bone scan is a safe and highly sensitive technique (98% at one week) and with the addition of SPECT/CT, it now has high specificity as well. It should be considered as the next imaging technique if X-rays are normal and clinical symptoms persist one week after the initial X-rays. In addition, the Nuclear Medicine departments will have to set up a process to fast track these requests in order to optimize patient care. ■

STATUS OF NUCLEAR MEDICINE IN ONTARIO

Christopher O'Brien
NDCM FRCPC
President, OANM



Dear colleagues,

On behalf of the Ontario Association of Nuclear Medicine (OANM), I wish to thank you for the opportunity to bring you this update. There are many challenges faced by Nuclear Medicine in Ontario that are not found in Quebec. There are also benefits that aid patient access to Nuclear medicine procedures, so all is not gloom!

CHALLENGES

1. Physician Qualifications

In Ontario, Royal College Certification in a specific speciality is not required in order to practice that speciality. Although there are around 150 physicians practicing Nuclear medicine in Ontario, only approximately 60 of these are actually certified as Nuclear Medicine Specialists by the Royal College. Many of these are dual certified either in Nuclear Medicine/Internal Medicine or Nuclear Medicine/Radiology. The OANM believes that this brings strength to the speciality. However, we are concerned that many physicians only have a few months exposure to Nuclear Medicine during residency training in Radiology, but yet they are allowed to practice full Nuclear Medicine if granted privileges by their hospitals. This is possible as neither the College of Physicians and Surgeons of Ontario (CPSO) nor the Ministry of Health require speciality certification. The level that these physicians are functioning at is unknown. In Quebec, Certification in Nuclear Medicine is a requirement.

2. Positron Emission Tomography

It was only in October 2009 that the Government of Ontario allowed PET to become an insured procedure through OHIP. The indications for PET remain the most restrictive in Canada: these can be found through the following link: www.petscansontario.ca.

Initially, there was funding for only 2400 patients for the entire province of Ontario (10 PET centers) compared to the 24,000 for Quebec. It is anticipated that within the next year, funding will increase to 7000 patients, still well below the Quebec numbers and well below the numbers seen across Canada, though the situation for Ontario patients is improving through co-operative efforts between the Government and the Nuclear Medicine community.

3. Funding for Procedures

Quebec follows a global fee structure for operational funding for Nuclear Medicine services, whereas Ontario follows a fee for service model, both for Operational (Technical fee: T Fee) and Professional remuneration. In other words, the money follows the patient. This has allowed the waiting lists for Nuclear Medicine procedures to be very small, studies usually done within a week or two for non-urgent cases. In Ontario, we usually do 8000 bone scans and around 12,000 heart scans per month. Almost all of our hospital departments have SPECT/CT units, although none of our non-hospital clinics (Independent Health Facilities: IHFs) have any. This is due to difficulty in obtaining authorization to have a CT in non-hospital locations and lack of funding for the CT component of SPECT/CT procedures: Attenuation correction and Image Localization. These CTs are non-diagnostic. There is no private system in Ontario.

4. Medical Isotope Shortage

As in Quebec, the availability of medical isotopes has been a challenge. Even with the present shortage, we have been able continue to offer all services to all of our patients when needed. This has been accomplished through the efforts of the industry to source other suppliers of isotopes, technologists and clerical staff in juggling schedules and coming in on weekends, and to the physicians for taking a leadership role. This has come, however, at a significant increase in costs which have yet to be reimbursed by either the federal or provincial governments, calling into question the sustainability of some of our departments, and subsequent patient access to required Nuclear Medicine procedures.

Though both provinces face a different set of challenges, the future does look bright for the speciality: new equipment and isotopes are becoming available which will allow a more detailed assessment of patients at lower radiation exposures, as well as the increased access to PET and new PET isotopes. This will allow the unique information obtained through Nuclear Medicine procedures to continue to help you manage your patients. ■

POSITRON EMISSION TOMOGRAPHY (PET)

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Clinical Research Head of the Molecular Imaging Center (CIMS)
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Positron Emission Tomography (PET) is a cutting edge, non-invasive, diagnostic imaging technique which allows the measurement of biochemical processes or the expression of cellular receptors by the use of positron-emitting radioactive tracers. The imaging tracers most often contain atoms naturally found in organic molecules, but in the form of radioactive analogues of Oxygen (^{15}O), Nitrogen (^{13}N), Carbon (^{11}C) or Fluorine (^{18}F) atoms.

Developed during the 70s to study the normal and pathological brain function, in the 90s, PET became an important clinical tool for oncological imaging following the demonstration of its usefulness in the detection of several cancer types.

Initially confined to research centers, PET has spread rapidly since 1998 to the vast majority of important oncologic centers in industrialized countries. Since 2001, PET has been paired to axial computed tomography (CT) (Figure 1) in order to better locate lesions by relation to the anatomical structures. It also facilitates the interpretation of results by improving the specificity and, furthermore, combined PET/CT data allows the planning of radiation therapy treatment. PET/CT images also have a considerable advantage for planning the surgical approach, since an accurate anatomical localization may be established. It is also possible to merge any PET study to any three-dimensional imaging including MRI and SPECT tomography, even if they have been obtained on different devices or at different times (Figure 2).

Gradually, the price of PET/CT devices has dropped by half and now can be purchased for 1.2M$. The scanner allows the accomplishment of a full study from the neck to the pelvis in less than 25 minutes, thus improving considerably the productivity of PET and helping to reduce the cost of each exam (throughput of 15-20 exams per scanner per 8 hours). Since 2005, PET/CT technology deployed quickly in the public and the private health systems across Canada. However, in 2014, access to PET is very different from east to west provinces and Canada is still behind many developed countries. Quebec is by far the province providing the best access to this technology. Quebec is also the first province which has deployed the latest generation of PET/CT devices to regional hospitals away from academic and research centers.

As with the studies performed in conventional nuclear medicine (bone or thyroid scan, myocardial perfusion, etc.), PET/CT is performed after the intravenous injection of a radioactive substance called radiotracer. Over the past few years, several radiotracers have been developed for the detection of cancer and the most important is the fluorine-18 Fluorodeoxyglucose (^{18}F-FDG). The fluorine-18, with a half-life of 110 minutes, is the isotope of choice for

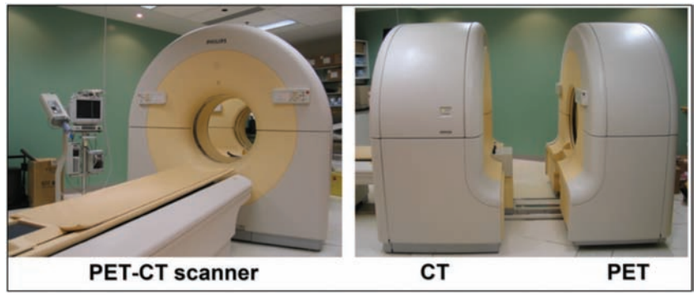

Figure 1 :
PET/CT scanner allowing to sequentially obtain an axial tomography (CT) and a positron emission tomography (PET) during a same medical visit.

cancer imaging. This isotope can easily be distributed to multiple institutions and its long half-life allows it to accumulate at levels that are sufficient for imaging with adequate contrast for tumor detection. The molecule of ^{18}F-FDG is an analogue of glucose obtained by substituting a hydroxyl (-OH) group of a glucose molecule by a radioactive fluorine atom with a nucleus that contains more protons than neutrons. This atypical ratio of protons/neutrons makes the atom unstable and the latter must expel a positive charge in the form of a positron to regain its stability. The PET devices are conceived to detect radioactive emissions induced by these positrons, and to precisely locate this emission inside the body. At the cellular level, the ^{18}F-FDG uses the same transmembrane carriers as glucose, and its passage is transporter – and insulin – dependent. After its entry into the cell, the ^{18}F-FDG is phosphorylated by the hexokinase, but it rapidly stops advancing into the glycolysis cascade. It thus becomes sequestered in the cell where it accumulates. The ^{18}F-FDG permits to obtain cellular information relative to the cell viability and metabolism based on the metabolic rate of the cellular glucose.

The excretion of ^{18}F-FDG is mainly through the urinary tract, regardless of if the patient is diabetic or not,

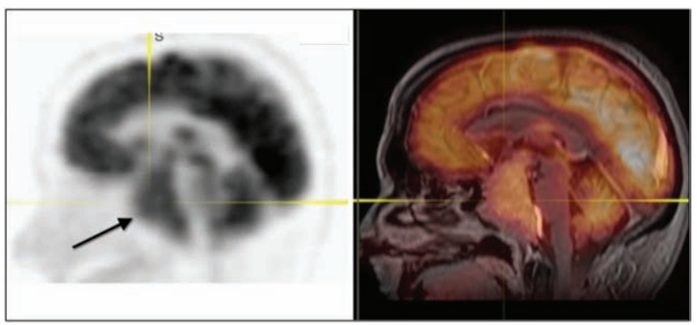

Figure 2 :
Current software which enables the merging of PET not only with the CT, but with all 3D imaging modalities, including MRI. PET-MRI fusion allows better localization and characterization of the neoplastic cerebral lesions (the arrow shows a voluminous pituitary prolactinoma).

because the ^{18}F-FDG molecule is not completely reabsorbed by the renal tubules, unlike glucose. There is also a certain proportion, very variable from one individual to another, which is excreted by the intestines. Figure 3 (left) shows a normal biodistribution of ^{18}F-FDG compared to the image on the right which illustrates the important consumption of ^{18}F-FDG by striated muscle due to a non-respected fasting/glucose-free procedure. Figure 3 (right) is considered non-diagnostic. Consequently, the exam must be repeated at a later date.

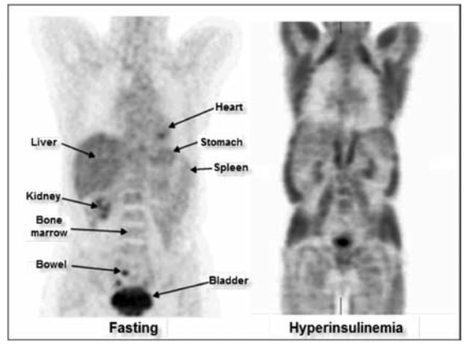

Figure 3 :
PET studies performed in two different patients. The image on the left illustrates a normal biodistribution of FDG in a patient having observed the fasting procedure. The image on the right has been obtained in a patient with dextrose solute (diffuse muscle uptake induced by hyperinsulinemia).

The ^{18}F-FDG PET is aimed at four main fields of clinical application: oncology, cardiology (Figure 4), neurology (Figure 5) and infection/inflammation (Figure 6). Overall, in a general hospital, more than 95 per cent of the examinations currently carried out are for oncologic indications. The rationale behind the use of ^{18}F-FDG PET in oncology is based on the increased use of glucose by the neoplastic cells, a phenomenon closely linked to the neoplastic transformation. A rapidly growing neoplasia is also ischemic in its center, hence favoring the metabolic pathway of lactic acid, which greatly increases the demand for glucose. A non-negligible proportion of the uptake also comes from the inflammatory cells surrounding the tumor. It should be noted, however, that these phenomena vary significantly depending on the type of neoplasia.

Although PET is excellent to detect neoplastic lesions, it has limitations. Some cancers have slower growth and do not substantially increase their ^{18}F-FDG accumulation and may remain undetectable (false negative). The activated neutrophils and macrophages can consume a lot of glucose and the highly inflammatory lesions can also incorporate this radiotracer (false positive). In particular, active granulomatous inflammation (tuberculosis, sarcoidosis) as well as abscesses

can cause false positive results (Figure 7). Conversely, some well-differentiated cancers, such as prostate cancer, high mucinous content tumours, well differentiated neuroendocrine tumors, and certain lobular breast cancers may have a low uptake. Others, such as the hepatocarcinoma, possess phosphorylases, which allow cells to quickly eliminate the ^{18}F-FDG. A list of clinical indications for oncology PET with ^{18}F-FDG is detailed in Tables 1 and 2. Taken together, lung cancer (Figure 8) and lymphoma indications represent about 50% of the available imaging time on a PET scanner.

PET should be an accessible exam to be considered by a specialist as well as the family physician. However, for a better management of the resource, it is important to recognize the strengths and weaknesses of the technique in order to ensure that the examination can answer the clinical and therapeutic dilemma. The following guiding points are to be considered if a PET/CT exam is to be requested:

Does the patient need to be fasting? Is fasting mandatory for all patients? What about diabetic patients?

Patients arriving for their exam must obey the fasting procedure (sugar-free) for at least 6 hours prior to the exam. Diabetic patients can take their oral hypoglycemic agents and their slow onset insulin dose in the morning of the examination day. However, special attention should be paid to metformin because this medication is responsible for a very intense bowel uptake (Figure 9). Thus, metformin should be stopped at least two days prior to PET if an intestinal lesion is suspected.

All sources of glucose (including lozenges, mints, gums, glucose in solution) must be strictly avoided so as to maintain circulating insulin at the basal level. If there is any doubt about the patient's glucose intake in the last six hours, the study should be deferred in order to observe fasting procedure for at least six hours (Figure 3). It is also required that the capillary blood glucose level at the time of injection is less than 10 mmol/L. If the result is higher than 10 mmol/L, one to two doses of rapid i.v. insulin can be injected in order to normalize the blood glucose level. An additional waiting period of 60 minutes is necessary to allow the exogenous insulin to be metabolized. The exam will be postponed to a later date if it is not possible to normalize the blood glucose level. It is therefore important to ensure that the diabetes is well controlled and that the glucose level is normalized (or almost) and stable before requesting an ^{18}F-FDG study.

Is there a reasonable doubt of neoplasia in respect to the clinical and para-clinical evaluation?

The prescription of an oncology PET study should ideally be limited to patients with proven or strongly

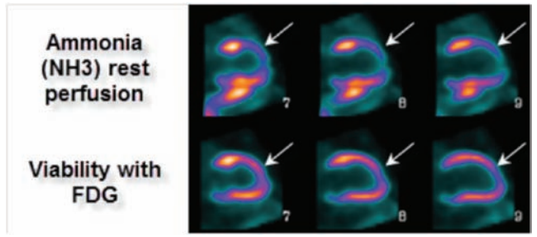

Figure 4 :
This PET exam uses ammonium to assess myocardial perfusion at rest and FDG for viability. This exam is more sensitive than Thallium for the demonstration of severely ischemic regions at rest or hibernating myocardium in order to orient the therapeutic approach (to increase the ejection fraction and decrease morbidity). The example illustrates severe hypoperfusion at rest (rest ischemia) in the region of the descending anterior, completely viable on the FDG study. The study therefore suggests that this wall will resume a normal kinetic after revascularisation that will result in gain of ejection fraction.

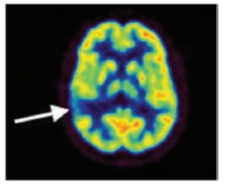

Figure 5 :
Brain FDG PET in search of inter-ictal epilepsy foyers. Right temporal hypometabolism testifies to an epileptic foyer (arrow).

Table 1:

- Characterization of a mass: benign versus malignant
- Evaluation of the extension of the disease (staging and restaging)
- Orientation toward the most accessible biopsy site
- Detection of occult primary tumor site in patients with metastatic disease
- Detection of residual disease after chemotherapy/ radiotherapy or surgery
- Radiotherapy planning (delineation of gross-tumor-volume)
- Differentiation between relapse and post-surgical/ post-radiotherapy changes
- Biochemical evidence of relapse (elevated markers) without clinical signs or radiological evidences
- Follow-up or surveillance when conventional studies are equivocal or suspicious

suspected neoplasia. A clear clinical question should be included in the request form for the exam. It is the responsibility of the requesting physician to be as clear as possible.

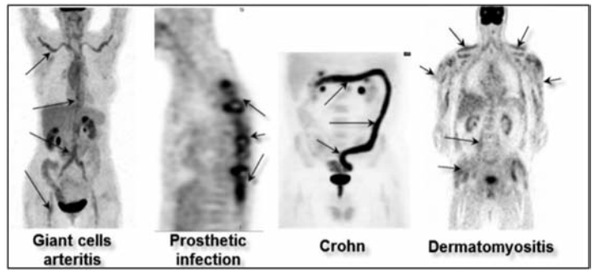

Figure 6 :
PET FDG is not only useful in oncology. It can be used for the diagnosis and monitoring of giant cell arteritis, the search for infectious foyers (ex: infection of orthopaedic materials), the diagnosis of myositis/dermatomyositis and even in the assessment of inflammatory intestinal diseases.

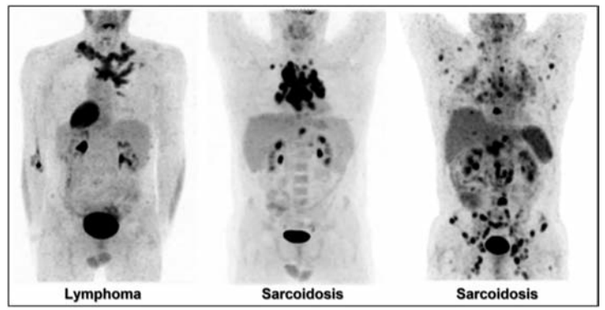

Figure 7 :
Active chronic inflammatory granulomatosis conditions, like sarcoidosis, can resemble a lymphoma (center), or even a plurimetastatic disease (right). Some criteria, including the symmetric hilum distribution, the disproportion between the size of lymph nodes and their activity, the presence of lymph nodes and splenic calcifications, are elements in favor of a granulomatous disease. In cases where presentation is more atypical (image on the right), only a biopsy can differentiate between the two entities.

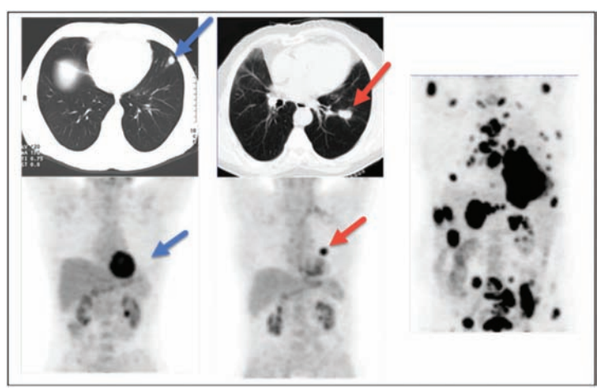

Figure 8 :
Evaluation of an undetermined lung nodule. Left Images (CT and PET): Lung nodule to the lingula presenting no significant metabolic activity, compatible with a benign/inflammatory nodule (blue arrows). Center Images (CT and PET): Lung Nodule near the left hilum presenting very significant metabolic activity that is compatible with primary pulmonary malignancy (red arrows). Right Image (PET alone): Plurimetastatic disease (bone, lymph nodes, adrenal glands) from the left lung.

What is the location of the neoplasia?

The degree of metabolism of a tumor must be put in relationship with the basal metabolism of the organ in which the tumor is sought (Figures 2 and 3). In some cases, this can cause interpretation problems and can limit the sensitivity of the examination. The bladder comes in at the first place of hypermetabolic organs due to the physiological urinary excretion. Fortunately, it is easy to significantly decrease the physiological activity in urinary bladder by diluting its activity through the i.v. administration of furosemide. This protocol allows therefore to image high grade bladder cancer and to make the assessment of its extension (Figure 10). In contrast, since this is not a procedure carried out on all patients, it is important to specify in the request for examination if there is a suspicion of bladder neoplasia, lesion to the outer wall (implant of a gynecological neoplasia) or at the edge of the bladder (metastatic lymph node). The brain comes in second place of hypermetabolic organs. Unlike the bladder, there is no easy method to decrease brain activity other than by sedation. It is therefore difficult to locate brain metastases in this physiologically very active organ. MRI remains the imaging of choice in the assessment of neoplastic cerebral lesions, but PET is the imaging of choice for monitoring post radiotherapy response.

What is the size of the lesion under evaluation?

The sensitivity and resolution of PET equipment is increasing from year to year. In the optimal conditions, the technology currently available can detect lesions in the vicinity of 4.5 mm. Unfortunately, these perfect conditions are almost impossible to obtain in the human body, and a reasonable estimate of the camera resolution would be at about 6 mm. If the anomaly to be imaged is sought in a mobile organ, the sensitivity decreases as a function of the amplitude of the movement. It is therefore difficult to identify a nodule of 6 mm located at the base of the lung or an infra-centimeter hepatic metastasis juxtaposed to the diaphragmatic dome. To overcome this limit, imaging techniques synchronized with the respiratory rate are now available (respiratory gating).

What is the histological type of the initial tumor and its grade in a context of staging, restaging or when evaluating treatment response?

The higher or more undifferentiated histological the grade is, the more it will accumulate ^{18}F-FDG. Because of their low glucose metabolism, some histological types do not uptake any or will accumulate very little of ^{18}F-FDG so that the role of PET with FDG is limited for these types of tumors: well differentiated prostate cancer, some hypernephroma, small lymphocytic lymphoma (chronic lymphoid leukemia), marginal zone lymphoma, lymphoplasmocytary lymphoma (Waldenstrom), leukemia, well differentiated hepatocellular carcinoma, minimally invasive lung carcinoma (bronchiolo-alveolar), any tumors with high mucin component, low grade neuroendocrine tumor, low grade sarcomas (particularly liposarcoma), teratoma, and some well differentiated breast cancer (particularly the lobular carcinoma).

How much time should we wait between a PET study and the last surgery, radiotherapy or chemotherapy?

Especially for the evaluation of a local recurrence or that of a treatment response, it is recommended to wait four weeks between the PET study and surgery or chemotherapy, or to wait three months after the last radiation treatment, since the local residual inflammation could cause false positive results. If performed too soon post-treatment, the evaluation may be associated, depending on the case, to a higher rate of false positives or false negatives. It is also important to mention that if the patient is under hormonal therapy, this medication can also affect PET results, same as chemotherapy.

Table 2:

Brain :
- Relapse versus radionecrosis of high-grade gliomas post-radiotherapy
- Primary brain tumor versus metastasis: primary site search

Head and neck :
- Search for a primary site explaining metastatic cervical adenopathy
- Initial staging in suspected advanced stage
- Residual disease assessment post-treatment

Thyroid :
- Thyroid cancer when thyroglobulin level is elevated and radioiodine scan is negative
- Staging and restaging of poorly differentiated thyroid cancer, Hurthle carcinomas, or medullary thyroid carcinomas

Lungs :
- Classification of an undetermined lung nodule
- Pre-operative staging assessment
- Radiotherapy planning in case of significant lung atelectasis
- Relapse versus scar tissue formation post-surgery or post-radiation
- Lower sensitivity for the bronchiolar-alveolar adenocarcinomas

Breast :
- Initial staging and follow-up of locally advanced or metastatic cancer when conventional imaging studies are equivocal or suspicious
- More accurate in triple negative cancers or HER-2 overexpression
- Less sensitive if lobular or well differentiated (hormonosensitive breast cancer)

Oesophagus :
- Initial staging to assess respectability
- Restaging after an induction chemotherapy and/or radiation
- Response to treatment
- Radiotherapy planning

Stomach :
- Useless in the detection of a primary
- Only useful in metastatic assessment

Liver :
- Differentiate between benign or malignant lesions when conventional studies are equivocal or suspicious
- Search for liver metastases
- Cholangiocarcinoma (other than tubular or mucinous)
- Less useful for the well differentiated hepatocellular carcinoma

Pancreas :
- Pre-operative metastatic assessment
- Less useful in the characterization of a mass

Colorectal :
- Local Recurrence versus scar tissue
- Unexplained markers elevation (CEA) in post-therapy context
- Pre-surgical evaluation of a single liver lesion
- Pre-operative adenopathy assessment and search for metastases
- Treatment response
- Less sensitive in the presence of significant mucinous component

Melanoma :
- Search for metastases (Breslow > 1.5 mm), Stages II and III
- Restaging in patients with recurrent disease following therapy
- Less useful in Stage I, because the metastatic risk is < 5 %

- Hodgkin and non-Hodgkin lymphoma :
- Routine pre-treatment staging
- Measure treatment response, chemotherapy and radiotherapy
- Evaluation of relapse
- Restaging before bone marrow graft
- Guide biopsy to the most accessible site

Gynaecologic (cervix) :
- Preoperative staging assessment
- Detection of residual disease after treatment
- Restaging at relapse
- Could be of interest for radiotherapy planning

Testicular :
- Search for metastases
- Chemotherapy / Radiotherapy response evaluation
- Teratoma content may cause false positive and false negative studies
- Residual mass assessment/surveillance

Bladder (with iv Lasix, voided bladder) :
- Preoperative staging
- Search for metastases in the context of relapse
- Treatment response evaluation

Prostate :
- Should not be used if well differentiated histology and Gleason < 8
- Staging if histologically undifferentiated

Sarcoma :
- More sensitive in high grade sarcomas
- Low grade tumors are frequently false negative

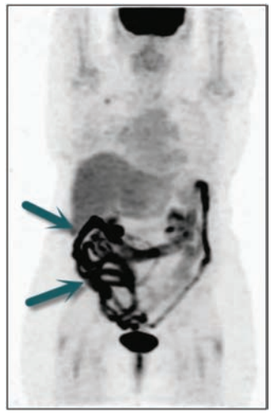

Figure 9 :
FDG PET performed while taking metformin. Metformin modulates a highly intense FDG accumulation in the bowel (blue arrows) which makes it impossible to detect bowel lesions. Metformin should be stopped at least two days before FDG PET.

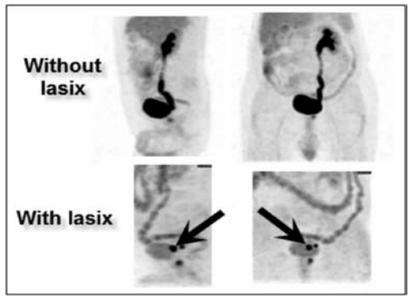

Figure 10 :
In the physiologically hypermetabolic organs, some maneuvers may be attempted in order to decrease the basal metabolism and to allow visualization of the tumor. Bladder cancer is the typical example of how the use of a diuretic helps the bladder to drain quickly so that the tumor can be easily set apart (black arrows).

Is there an infection near the site under evaluation? Is the patient known for a non-neoplastic disease that naturally uptakes ^{18}F-FDG?

FDG PET does not provide a way to differentiate between a neoplastic lesion and an active infectious or inflammatory process (Figure 6), since the two latter will avidly capture the ^{18}F-FDG. It is therefore difficult, for example, to differentiate active tuberculosis foyer from a primary pulmonary malignancy or an abdominal abscess of a colonic neoplasia from a lymphoma. Some benign pathologies, like sarcoidosis, active Wegener, tuberculosis, uterine fibroid, thyroiditis, stomach ulcers, acute or chronic cholecystitis and many others may capture FDG. Without biopsy of the lymph node, it is often difficult to differentiate by PET a sarcoidosis from a metastasis or a lymphoma (Figure 7), a uterine fibroid tumor from a sarcoma or yet, the histiocytosis from a multifocal bone metastasis.

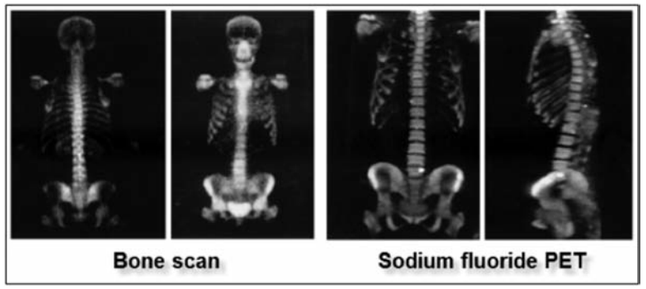

Figure 11 :
The future of the PET lays within the development of new radiotracers enabling sensitivity increase of already existing exams and/or newer indications. The development of sodium fluoride PET (NaF PET) as a replacement for the conventional bone scan is an example. This study is carried out 30 to 45 minutes after the injection of the radiotracer and the acquisition of the images only lasts for 35 minutes (compared to a waiting time of 4 hours and 40 minutes imaging, on average, for a regular bone scan). With NaF PET, which is more sensitive and faster, it is possible to locate metastases as small as 5 mm.

In other words, FDG may accumulate in places with active inflammation, be it acute, chronic, infectious or granulomatous. The distribution of the radiotracer and the appearance of lesions can sometimes allow the nuclear medicine specialist to distinguish between an infection, an inflammatory process or a neoplastic lesion, but it is important to remember that these conditions represent the most frequent cause of false-positive results.

FDG PET is now the oncology standard for several types of cancers. This very powerful diagnostic tool is only in its early stages in Canada and will be called upon even more in the coming years. Even if FDG is an excellent radiotracer for tumors and metastases localization, some cancers cannot be easily assessed with this radiotracer. Consequently, there is a need for new clinical tracers to increase the diagnostic accuracy of PET for cancers where FDG is less efficient. Sodium fluoride is one of the new tracers in clinic which allow earlier detection of the bone metastases (Figure 11). ^{18}F-MFES, an oestrogen derivative under clinical trial in BC and Quebec, is one of the most promising tracers for the detection and staging of hormonosensitive breast cancer (Figure 12).

Since there are multiple factors to consider in a FDG PET study, it is crucial to provide maximal clinical information to the nuclear medicine specialist who will be interpreting the imaging results (pathology reports, summary of surgical procedures, radiology results, blood biochemistry) in order to give a more precise answer to the clinical question. And, for more complex cases, a discussion with the nuclear medicine specialist may be relevant before prescribing the exam. ■

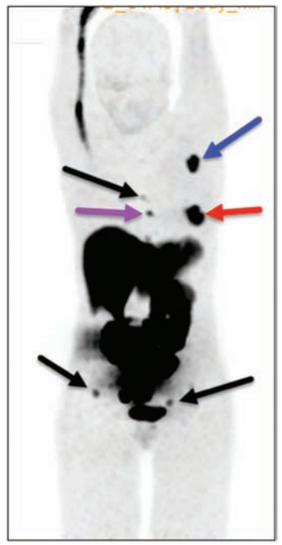

Figure 12 :
PET performed with ^{18}F-MFES, an oestrogen derivative highly sensitive to detect hormonosensitive breast cancer and metastasis. Clinical trials, funded by the Canadian Breast Cancer Foundation, are underway in Quebec and in the initial phase in BC. Red arrow: Primary breast cancer. Blue arrow: axillary metastasis. Purple arrow: internal mammary metastatic lymph node. Black arrows: Bone metastasis.

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NUCLEAR MEDICINE
IN THE DIAGNOSIS OF HEART DISEASE

Nuclear Medicine plays a vital role in the diagnosis of the patient with heart disease on a daily basis in hospitals and clinics across this country. In addition to aiding diagnosis, it frequently guides or directs therapy as well as monitors the success of those therapies in cardiac patients. We will look at its role in routine clinical practice and how it is best utilized given some common clinical settings.

Let's familiarize ourselves with the most common techniques used in Cardiac Nuclear Medicine today.

MYOCARDIAL PERFUSION IMAGING

By far, the most frequent tool used in Cardiac Nuclear Medicine departments is the Myocardial Perfusion Imaging study (MPI). This technique was previously more commonly referred to as a stress Thallium study. It has been re-named because the radiotracer used previously, Thallium-201, has been replaced for the most part by Technetium-99m-MIBI (**M**ethoxy**I**so**B**utyl**I**sonitrile) or Tc99m-Myoview (Tetrofosmin). These latter two agents allow better images of the heart using the current Single Photon Emission Computed Tomography or SPECT cameras in use today.

MPI involves injecting these tracers intravenously which localize within the heart muscle in direct relation to a patient's cardiac blood supply. The tracer distribution reflects this blood supply at the time of injection providing a "snapshot" of what has occurred up to three hours earlier when imaged under the camera later. Thus, a patient who is stressed on a treadmill or who is injected while having a spontaneous episode of chest pain can be imaged later when stable and the images can be compared to a study done while the patient is at rest or pain-free.

Also, in addition to looking at heart perfusion, we can look at wall motion and wall thickening with these agents using a technique called "gated SPECT." From this, we can estimate the heart's Ejection Fraction or EF, which is a valuable measurement tool of the heart's pumping ability.

Stress MPI is performed in two steps. The first step involves an injection of Tc99m-MIBI or Myoview at rest. Imaging under the camera is typically performed an hour later. Later the same day or on a separate day, the patient is exercised on a treadmill or, in patients unable to walk on a treadmill, given a drug that gives the same information as exercise.

Dipyridamole (or in the USA Adenosine) is used as the stressing drug in most patients who cannot adequately exercise, but also in patients who have a Left Bundle Branch block on ECG or patients who cannot or have not stopped their beta-blocker medication. It is contraindicated in uncontrolled asthmatics. Dobutamine is an alternative stressing drug for those patients.

At peak stress they are injected with the Tc99m-MIBI or Myoview and imaging repeated. The computer generated images of the blood supply to the heart are compared, slice by slice (Figure 1). These are inspected visually by the nuclear medicine physician, but are also compared to a sex-matched normal database. Perfusion defects present at rest generally indicate previous myocardial infarction (although artifacts and chronically ischemic tissue can also appear this way) (Figure2).

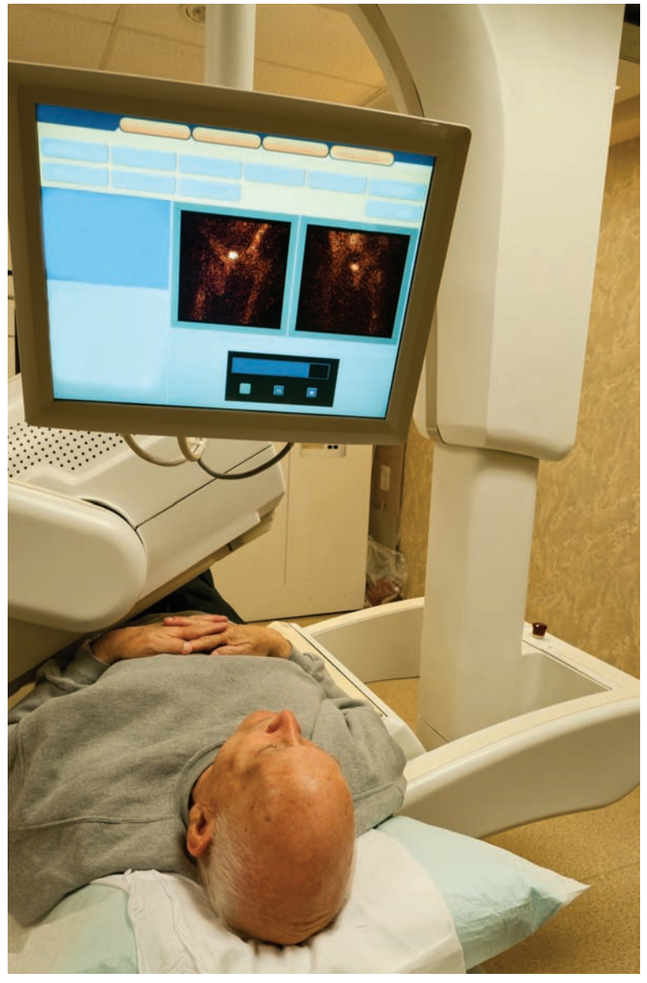
Reversible defects, that is, defects occurring during the exercise or stress study only, which show normal blood supply at rest, represent ischemic areas of heart tissue which are at risk for a myocardial infarction or heart attack (Figure 3).

The investigation of patients at risk for ischemic heart disease requires assessing the pre-test likelihood of disease in a particular patient. This is because MPI is best used for patients at an intermediate risk of having the disease.

MPI is generally a second tier study done in patients who have undergone a previous treadmill study in whom a diagnosis of ischemic heart disease cannot be made or in whom the volume of at risk myocardium needs to be determined. It is, however, also of great use in patients with resting ECG changes in whom a standard treadmill study will be non-diagnostic. As mentioned, pharmacologic stress MPI studies are a first tier study in patients who are unable to exercise, in patients unable to achieve a heart rate of 85% of their age-predicted maximum heart rate, but also in LBBB patients, because of a specific false-positive finding that occurs when these patients undergo a treadmill MPI.

Also, Persantine (or dipyridamole) MPI is particularly useful in the early days following a heart attack, when it can be safely used to study a patient as an alternative to exercise.

Increasingly, Stress MPI nuclear studies are being used as an initial investigation in women at interme-



diate risk for heart disease and diabetic patients, as we recognize the difficulty in diagnosing cardiac disease in these patients. Often, heart disease is silent and the standard treadmill study alone misses disease in these and other higher risk patient populations.

Stress MPI is used to direct which vessel is the likely "culprit" vessel in patients with two or more known diseased coronary arteries. Furthermore, once a patient has been treated either with bypass surgery, angioplasty or stent or with medical therapy, MPI is used to monitor response to therapy.

Pre-operative risk assessment of patients at risk for a cardiac "event" during or following surgery, particularly vascular surgery, is another common and vital role for this technique. The categorization of patients into low versus intermediate versus high risk frequently allows for identifying and treating a patient's heart disease before they have what may otherwise be a fatal surgical complication.

In some centers, injection of patients who present to the ER with chest pain with MIBI or Myoview can be a valuable tool when the ECG and enzyme markers are non-diagnostic. The presence of a normal examination can allow for early discharge and a low-risk categorization.

By far the most common use of this technique is in chest pain assessment. More and more in this country the MPI allows appropriate risk stratification and serves frequently as a gate-keeper to diagnostic cardiac catheterization. This non-invasive tool allows the most strategic and cost-effective use of this more limited resource.

Utilizing the technology of CT scanning, combined with Nuclear Medicine SPECT gamma cameras, SPECT-CT systems are now in place in most major centers. Using a low-dose CT of the heart done in conjunction with the gated SPECT MPI study reduces the number of artifacts in women and obese patients secondary to breast tissue and soft tissue "attenuation" artifacts respectively. The normal loss of information in these patient's studies is corrected by data from the CT study. The radiation dose received by the patient from these studies is low and still well within the diagnostic range.

Ancillary information such as coronary artery calcification and even unsuspected lung and breast cancers have frequently been incidental discoveries during these procedures.

MULTI-GATED CARDIAC STUDY OR MUGA

The Multi-Gated cardiac study or MUGA is the other most common tool used daily in Nuclear Medicine departments. It is sometimes referred to as an Equilibrium RadioNuclide Angiogram (ERNA or RNA) or Gated Blood Pool Study. This study involves labelling a small sample of the patient's red blood cells with the radioisotope Technetium (Tc99m) and then re-injecting them intravenously. The labelled red cells remain for the most part in the blood pool and dynamic images of the heart are obtainable.

The "gating" relates to the recording of the data relative to a particular segment of the cardiac cycle when timed to the patients ECG complexes. A composite moving image of the heart is built up over a period of anywhere from two to ten minutes. The images can be acquired with the SPECT technique as well, resulting in both 2D and 3D images. They are then visually assessed for wall motion abnormalities. While typically done as a resting study, Stress MUGA examinations can also be performed.

Echocardiography is used more commonly to assess the heart non-invasively because of its ability to assess both wall motion and structure as well as valve assessment without exposing the patient to radiation. The MUGA study is still important today, however, for its ability to more accurately quantitate the Left Ventricular Ejection Fraction (LVEF), an important measure of cardiac function.

MUGA studies utilize a more accurate and reproducible "count based" method for determination of the LVEF rather than a geometric formula. Its value as a monitoring tool such as in patients at risk for chemotherapy-induced cardiotoxicity or for optimal selection of patients for techniques such as Implantable Cardiac Defibrillators makes it still in wide use today.

Stress MUGA studies are also still performed by labs utilizing the response of a patient's LVEF while exercising as a tool to help decide on the timing of valve replacement.

First pass cardiac techniques can be used in conjunction with the MUGA study to assess for intracardiac shunts and to obtain quantitative information about the Right Ventricle. This technique of obtaining very rapid images and radioactivity counts as the injected tracer passes through the heart on its first pass isolates the different chambers and allows for RVEF determination as well.

MYOCARDIAL VIABILITY STUDIES

In patients where large rest defects are seen on a MPI study and heart failure is present, the possibility exists that the defects represent areas of chronically ischemic and hibernating myocardium, rather than dead or infarcted tissue. This is important because by bypassing these patients, they can regain cardiac function. PET or Positron Emission Tomography is the most accurate tool for assessing for hibernating myocardium. Its availability remains limited, however, and in many centers Thallium-201 viability imaging can make the diagnosis albeit with reduced sensitivity.

Patients are injected at rest and a SPECT cardiac study is performed after 30 minutes. A repeat study is then performed at four hours after the initial injection. The studies are combined and computer analyzed. Areas of thallium redistribution represent viable but hibernating myocardium. A negative study does not exclude potentially salvageable tissue, however, and the patient may still benefit from PET imaging.

SUMMARY AND FUTURE DIRECTIONS

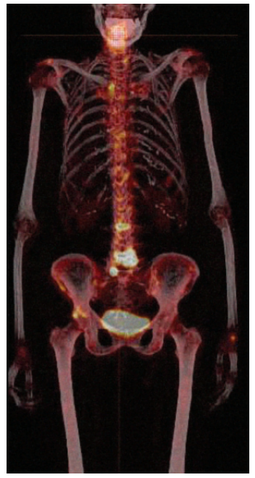
We have discussed the most common Cardiac Nuclear Medicine procedures used in clinical practice today. Less frequently utilized studies such as imaging of Cardiac Denervation using MIBG (MetalodoBenzylGuanidine), imaging of Apoptosis, Atherosclerotic imaging and other exciting and evolving Molecular Imaging techniques promise a "new and clear" future for Cardiac Nuclear Medicine. ■

HERMES

HERMES MEDICAL SOLUTIONS

EXPERIENCE

HERMES Medical Solutions is proud to take part in this year's special nuclear medicine edition alongside its fellow industry partners and family of 28,000 users.



With 39 years of experience as a medical imaging software leader, HERMES is dedicated to meet and exceed the clinical, developmental, educational and research needs of its users. Providing state-of-the-art software, HERMES offers innovative and cost effective healthcare solutions while maintaining the highest medical imaging quality standards, playing a key role in the patient continuum of care.

A Unique Platform: The Canadian Experience

Historically, nuclear medicine has benefited from excellent software but, rarely on a single platform. One computer is generally used to display a certain type of exam, another to archive the data and, another is used for specific or dedicated applications.

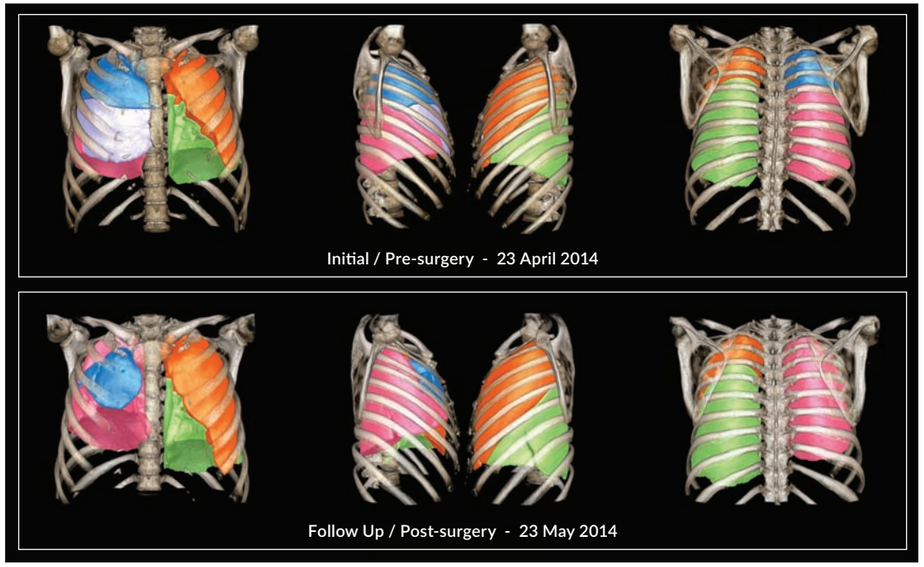
The lack of integration and the non-uniformity of components, continues to cause serious workflow obstacles for professionals working in imaging departments.

With crucial input from Canadian customers and nuclear medicine pioneers, the Montreal-based HERMES R&D team has developed Hybrid Viewer PDR™: A unique and user-friendly software for Processing, Display and Reporting (PDR). This all-in-one tool allows the display of all medical imaging modalities (including angiography and ultrasound), image fusion (SPECT-PET-CT-MR) including analysis of this data, processing of conventional nuclear medicine and, the ability to generate medical reports. This technology is used across Canada and present in about 80% of NM Departments in the Province of Quebec.

The raw and processed data is then stored in a metadata VNA in DICOM, native format, MS-Word™, MS-Excel™, .wav audio files, Adobe PDF™, etc. fully integrating with existing equipment in today's departments under a single master worklist.

A Quantification revolution

From the early days of nuclear medicine, quantification has been a key aspect; self-defining the practice and at the same time distinguishing from other imaging modalities. The arrival of Positron Emission Tomography (PET and its SUV scale) certainly contributed to advances in the field, but the essence of nuclear medicine still remains the Single Photon Emission Computed Tomography (SPECT) environment for a vast majority of Canadian medical centers. The new breed of cameras coupled with CT components and optimized with advanced reconstruction tools started paving the way for the day when a-SUV scale, similar to the one used in PET, would help us quantify images obtained from SPECT-CT scanners. Despite the increasing availability of PET, the number of specific tracers used with this technique is still suboptimal. Absolute SPECT-CT quantification (SUV) is now available and opens the door to a plethora of possibilities with dozens of proven tracers already in use.



Accuracy with Quantification tools

Previously used for teaching purposes or display modelling, 3D applications now enable automatic lesions detection or the ability to establish more accurate diagnostics in comparison with still largely used 2D tools.

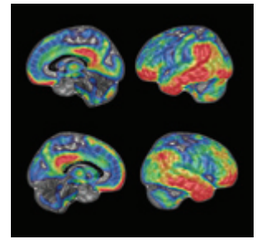
These amazing results can be obtained with the help of advanced segmentation methods especially useful with quantitative pulmonary studies. The Hybrid Viewer™ 3D module proceeds with an automatic co-registration of the SPECT-CT (and separate diagnostic CT if needed), an automatic L/R Lung and airways segmentation, a quick inter-lobar fissure definition, a fissure definition quality control, a lobar ventilation and perfusion quantification and an automatic report generation. Knowing that accurate results can drastically change the optimal surgical approach, comparative studies have been conducted between current 2D techniques (planar anterior image or real anterior reprojection divided in 6 segments) and 3D segmentation techniques. Preliminary results have shown differences ranging between -10% to +48% in the assessment of accurate volume calculation in ml.

Similar tools for automatic hepatic and kidney segmentation are now available and will help promoting for a closer collaboration between quantitative imaging and surgical departments.

QUANTIFICATION

Improved prognostic

HERMES is extremely proud to participate in high-level research to support healthcare professionals in the detection and treatment follow-up of diseases such as epilepsy, brain tumors, schizophrenia, Parkinson's and most recently Alzheimer's. New amyloid tracers, which are making their debut on the market, will facilitate HERMES efforts in assisting physicians worldwide in university facilities as well as in community hospitals, by providing them with normal templates for a precise and reliable quantification of the patient illness state. HERMES BRASS™ (Brain Registration & Analysis Software Suite) has appeared in more than 350 scientific publications and presentations around the world and has been validated with over 2 million patients.



TEAM WORK

HERMES employs a solid team of 21 members, dedicated to quantitative molecular imaging in Canada.

WORDLWIDE

Company offices are located in Sweden, Canada, the United Kingdom and the United States.

René Rebeaud
Managing Director

Benoit Galarneau
Research and Development Director

HERMES SUV-SPECT™

The HERMES SUV-SPECT™ revolutionizes quantitative imaging by exploiting the use of SPECT's full potential in regions where a large portion of the population still does not have access to PET and/or associated reimbursements. HERMES SUV-SPECT™ software algorithms enable a conversion of the recorded counts per voxel into activity per unit volume with SUV calculations, providing essential and accurate quantitative results.

François Hébert
Sales Director

Caroline Rochette
Senior Project Manager

HERMES VNM™

HERMES VNM™ includes HERMES VNA (Vendor-Neutral Archive) combined with the power of a complete clinical medical imaging platform, tailor-made for multi-vendor sites/multi-facilities integration. HERMES provides cost effective solutions worldwide from enterprise-wide architecture & infrastructure to storage, reading, analysis and processing services on its systems or via HERMES cloud, TeleHERMES™.

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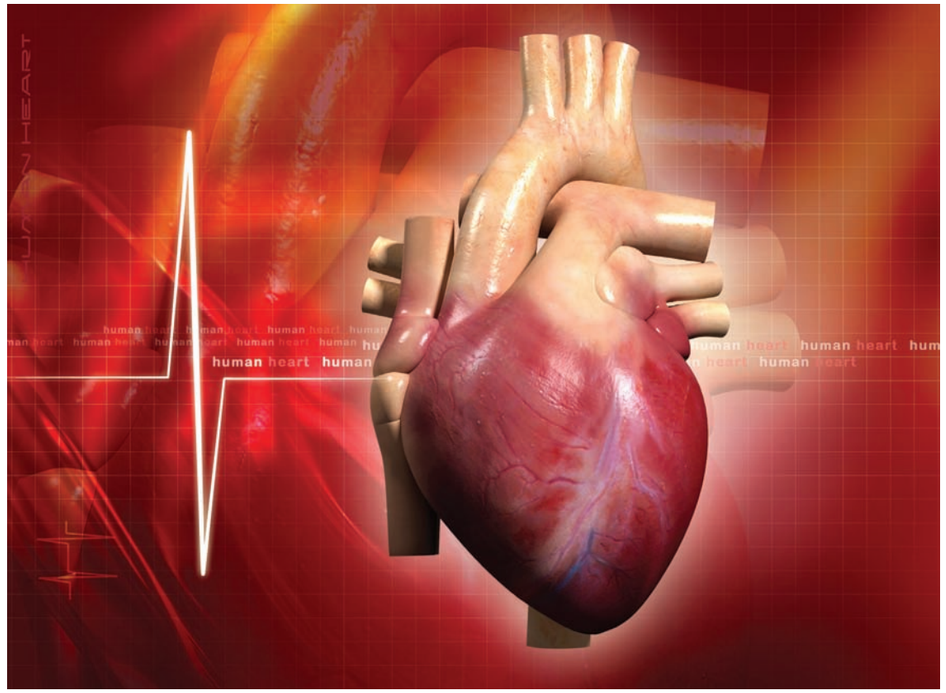


CLINICAL APPLICATIONS OF RADIONUCLIDE VENTRICULOGRAPHY

Clinical cardiac nuclear medicine began approximately 50 years ago with the introduction of radionuclide angiography. Functional cardiac evaluation with radionuclides started in 1962 with direct administration of a radionuclide into the left ventricle during cardiac catheterization, without obtaining external images. It is only in 1971 that the predecessor of radionuclide ventriculography was obtained with a noninvasive radiotracers intravenous injection in the arm, with images of the heart and synchronization of these images with the patient's electrocardiogram (ECG) signal. There are two major types of radionuclide ventriculography. The **first-pass studies** (or angiography), that is the dynamic study of the first-pass of the radionuclide into the cardiac cavities (mainly the ventricles) following its intravenous injection into the veins of the arm and **equilibrium ventriculography**, which is the study of the ventricle contractions over a representative number of cardiac cycles (therefore, the term "equilibrium" in comparison to the first-pass study where the acquisition is performed on a single cardiac cycle and not on a large number of cycles). Radionuclide ventriculography can be performed either at rest or after a stress test, either on a treadmill, on a bicycle, or following administration of pharmaceutical agents. Equilibrium radionuclide ventriculography, at rest, is by far the most common type of ventriculography used in clinical practice, and our discussion will be limited to this type of ventriculography.

RADIOTRACER

Various types of radiotracers have been used for radionuclide ventriculography, especially for the first-pass studies. The ideal radiotracer must remain in the intravascular blood pool compartment for a sufficient time to allow for image acquisition and a background activity as low as possible in adjacent organs to the heart. The most frequently used technique to achieve these goals is the labeling of patient's red blood cells with 99mTc-pertechnetate. The red blood cells labeling is a simple and easy procedure. There are various methods to label the red blood cells but the basic principle remains the same. The labeling is mediated by a reducing agent, stannous pyrophosphate, which binds both the surface of the red blood cells and the sodium 99mTc-perctechnetate, which is the radiotracer detected by the external gamma cameras. In an initial step, stannous pyrophosphate is injected intravenously, followed by the intravenous administration of 99mTc-pertechnetate (figure 1). The labeling efficiency of the red blood cells is more than 90% and is stable for several hours, allowing for longer acquisition time, especially when the cardiac rhythm of the patient is irregular.

DATA ACQUISITION

Following the patient's red blood cells labeling, the second step of the process is the scintigraphic data acquisition. This can be obtained approximately 15-30 minutes after the injection of 99mTc-pertechnetate, either with a regular planar gamma camera (usually 2 or 3 different views, thoracic anterior projection, left lateral and the best septal left anterior oblique view) or in tomoscintigraphic mode (which has been more recently introduced in clinical practice), using 32 or 64 views around the thorax, giving a better evaluation of the right ventricle and a better contrast resolution between the various cardiac chambers.

Dynamic images must be obtained in order to evaluate the contractility and to determine the ejection fraction of the left and right ventricles. These dynamic images can be obtained by the synchronization of the images with the patient's ECG. Therefore, each image from radionuclide ventriculography is synchronized to the ECG. Patient's cardiac cycle is divided into 16, 32 or 64 "frames" or image series. These frames are usually obtained over a period of approximately 10 minutes per planar projection and then, a single representative cardiac cycle is reproduced from these multiples cardiac cycles. The final image is then shown in a continuous loop and does not represent only one cardiac cycle but rather a significant number of cardiac cycles (approximately 700 cardiac cycles which are added together); this is called the representative cycle. The major advantage of this procedure is related to the fact that all parameters are not obtained from a single cycle but from a large number of cycles, which is much more representative of the patient's physiology, and allow for rejection of irregular cardiac cycles during data acquisition.

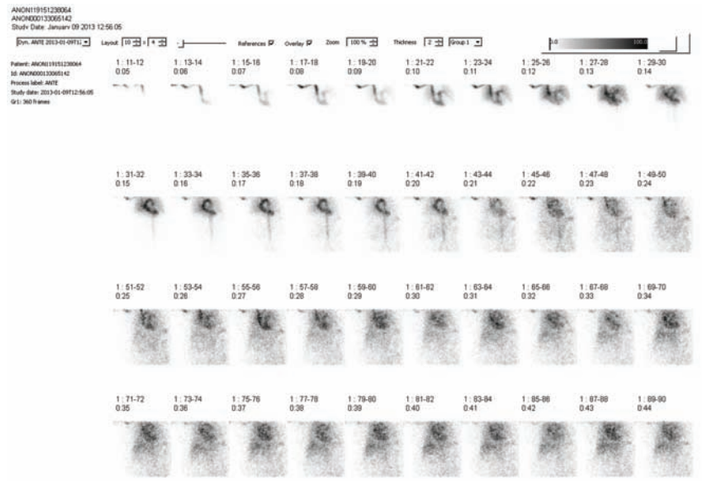


Figure 1. Example of a first-pass study of a radioactive bolus containing red blood cells radiolabeled to 99mTc-pertechnetate, through the various cardiac chambers from a simple and noninvasive antecubital vein.

DATA ANALYSIS

The major clinical advantage of equilibrium radionuclide ventriculography relies in its capacity to determine cardiac volumes, no matter the size or shape of the cardiac chambers. In contrast to geometric methods (radiologic angiology, echocardiography…), radionuclide ventriculography uses a volumetric method which is more precise and effective to determine the ejection fraction of the left ventricle (LVEF) or the right ventricle, and also ventricular volumes. This degree of precision is related to its volumetric method of calculation and the fact that the study is obtained on a large number of cardiac cycles.

The calculation of the left ventricle volume and LVEF is based on the count density detected by the gamma camera. The number of counts originating from the left ventricle is directly proportional to the number of radiolabeled red blood cells within the ventricle. A region of interest is traced on the computer over the left ventricle at end-diastole. Following this step, a specific software will automatically detect the contours of the ventricle for each frame of the cardiac cycle. The LVEF is thus precisely calculated by comparing the number of left ventricle counts at end-diastole to the number of counts at end-systole from the time-activity curve recorded by the computer (figure 2). In planar acquisition, it is more difficult to clearly delineate the right ventricle because of superimposition of other cardiac structures. Tomoscintigraphic acquisition is thus preferred because of its better accuracy to determine the ejection fraction of the right ventricle (figure 3). Tomoscintigraphic acquisition allows for a better delineation of the various cardiac chambers and their

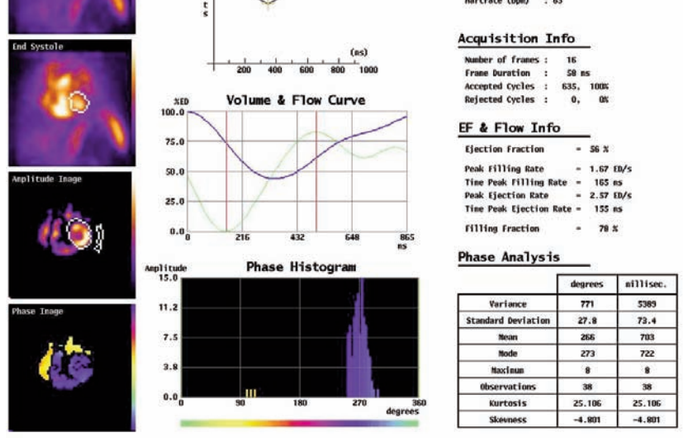
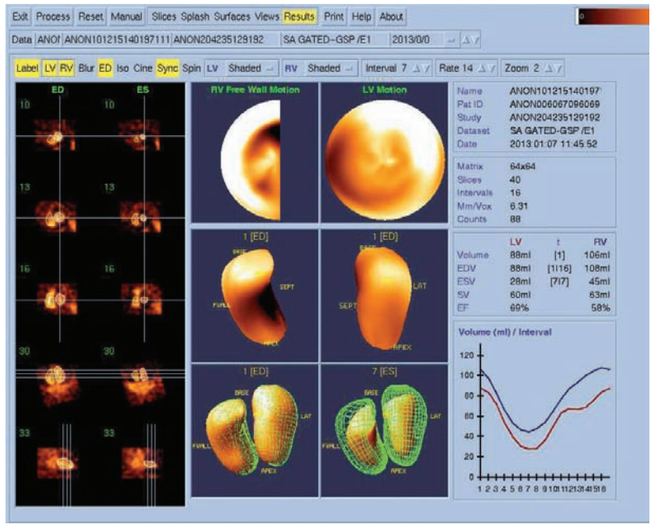
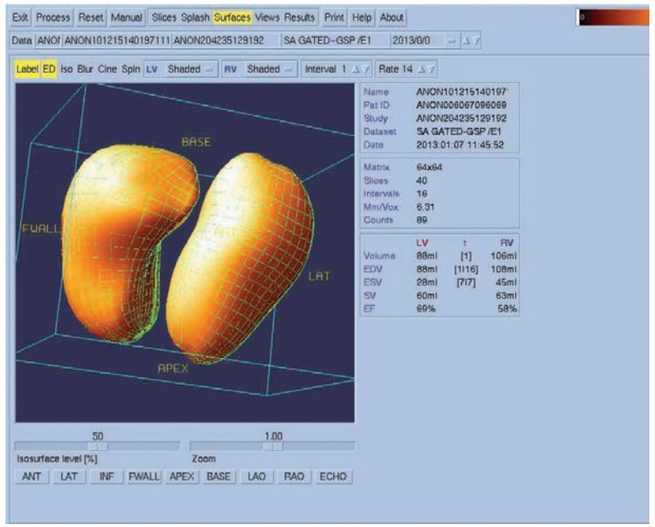


Figure 2. Regions of interest in end-diastole obtained from a planar study to precisely determine the LVEF (in this case 56%, from a time-activity curve derived from a representative cardiac cycle). Many other parameters can be obtained as well from the time-activity curve such as filling rates, ejection rates etc…





Figures 3a, b. Tomoscintigraphic radionuclide ventriculography allowing for a clear delineation of the right from the left ventricle and thus having a more accurate determination of the LVEF and RVEF.

superimposition, the result being a better contour evaluation of the right ventricle and its activity during the cardiac cycle.

The high resolution of the computer generated time-activity curve allows for calculation of LVEF and RVEF, as well as other parameters such as ventricular volumes, peak filling rate, ejection rate… just to name a few. Furthermore, planar and mostly tomoscintigraphic studies provide a very good evaluation of the global and regional contractility status of both right and left ventricles

CLINICAL APPLICATIONS

Radionuclide ventriculography has been used in the evaluation of almost all types of cardiac diseases. This procedure does not have the high anatomic resolution of echocardiography or magnetic resonance necessary to evaluate the ventricular mass or anatomic details of the cardiac valves. However, radionuclide ventriculography is recognized as the gold standard to precisely evaluate the LVEF. The LVEF remains, to date, one of the best and most effective predictors of a patient's outcome with coronary artery disease, cardiac valvular disease or cardiomyopathies.

Table 1 summarizes the major clinical indications of radionuclide ventriculography as described in the guidelines from the American College of Cardiology, American Heart Association and American Society of Nuclear Cardiology. These indications are not limited but are established from studies demonstrating the clinical usefulness of both planar and tomoscintigraphic radionuclide ventriculography in the determination of LVEF and the study of global and regional contractility of both right and left ventricles.

The great accuracy of radionuclide ventriculography in the evaluation of LVEF makes it a very important diagnostic and follow-up tool in patients treated with cardiotoxic chemotherapy. The determination of the LVEF is important since an early decrease of it allows for an early diagnosis of cardiotoxicity and a subsequent change in the treatment to avoid irreversible cardiac damage. Radionuclide ventriculography is the best and most accurate method to perform a follow-up of these patients. Radionuclide ventriculography is the gold standard used in clinical research to follow cardiotoxicity.

The various parameters obtained from radionuclide ventriculography (especially LVEF, RVEF, and global and regional contractility) can be noninvasively and easily obtained in the diagnosis, prognosis and follow-up of various cardiac diseases.

CONCLUSIONS

Planar radionuclide ventriculography and more recently tomoscintigraphic ventriculography is a simple, reliable and accurate procedure allowing for precise determination of the ejection fraction of both the right and the left ventricles and global and regional cardiac contraction as well. This is an important and complementary diagnostic tool to echocardiography and magnetic resonance. ■

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DATSCAN FOR DIAGNOSING PARKINSON'S DISEASE AND DEMENTIA WITH LEWY BODIES (DLB)

DaTSCAN (I^{123} ioflupane) is a radiolabelled tracer which is used for differentiation of Parkinson's disease from Essential tremor and also in differentiation of Dementia with Lewy bodies (DLB) from Alzheimer's dementia.

Parkinson's disease (PD) is one of the most common chronic neurological disorders affecting over 127,000 people in the UK, a million in the USA and, 100,000 in Canada. Its prevalence is set to rise by around 25% by the year 2020 using available population trends. The condition is caused by degeneration and loss of neurons in substantia nigra in the brain. These cells send tentacle (axons) to another part of the brain called striatum (compromised of Caudate and Putamen, figure 1), where dopamine (a neurotransmitter) is produced and stored. Dopamine is a signalling chemical in the brain which regulates complex functions including voluntary and involuntary movements. The brain has a huge compensatory capacity so the symptoms of Parkinson's disease are not detected until approximately 60% of these neurons and their associated axons are lost. Patients may then present with one or more of the clinical features of tremor, slowness of movement and stiffness (rigidity). The condition progresses over a period of years, resulting in progressive disabilities including freezing, difficulty in walking, pain, eye problems, communication problems, expressionless face and depression. The diagnosis of Parkinson's disease can be difficult as the symptoms may initially be subtle and also occur in other neurological conditions, such as essential tremor (a common and benign condition). Misdiagnosis is not uncommon even by clinicians who specialize in movement disorders. Correct diagnosis of this condition is important for the patient, the carers and for correct treatment of symptoms.

Dementia is another global challenge with increasing recognition of its devastating effect on people's lives and that of their carers. Over 800,000 people in the UK, 5.2 million in the USA and 700, 000 in Canada are diagnosed with dementia, and this number is increasing with growth in the elderly population. Alzheimer's dementia is the most common form of dementia (50-70%) and DLB accounts for 10-15% of dementias. DLB is thought to be underdiagnosed. It is important to get an accurate diagnosis as there are drugs which can benefit and also drugs to be avoided in patients with DLB. DaTSCAN can be used for distinguishing DLB from other forms of dementia.

DaTSCAN (also known as ioflupane & FP-CIT) was first licensed for clinical use in Europe in July 2000, and was approved by the FDA (USA) in August 2009. It is currently licensed and used in 34 countries and has so far been used in more than 300,000 patients worldwide. DaTSCAN binds to dopamine transporters in dopaminergic nerve terminals in the striata (caudate and putamen). As mentioned earlier, there is substantial loss of dopaminergic nerve terminals (>60%) in both Parkinson's disease and DLB before the clinical signs and symptoms are seen. DaTSCAN imaging can detect this loss of neurons and nerve terminals with minimal symptoms, enabling earlier and more accurate diagnosis of these conditions. There is often a preferential loss of these nerve terminals in the putamen, changing the normal comma shaped appearance of the striata (figure 2) to that of a dot appearance in Parkinson's and DLB patients (figure 3). Quantification can help to further confirm this in earlier and in more difficult cases.

DaTSCAN is a nuclear medicine investigation and comes in a ready-to-inject solution containing 185 MBq (5 mCi) of I^{123}-ioflupane. This is injected intravenously. No special preparations are necessary and there is no need to stop most of the anti-Parkinson's/Dementia medication. The patient undergoes SPECT imaging 3 to 6 hours later using a standard SPECT gamma camera available in most nuclear medicine departments. The images take around 30 minutes to produce, during which time the patients' head is kept still. Images are then appropriately processed using standard software and reported by a nuclear medicine physician. The accuracy of this test is shown to be more than 95% for both indications.

In conclusion, DaTSCAN imaging is a safe and effective new addition to the nuclear medicine portfolio, accurately diagnosing patients with Parkinson's disease and DLB and confidently excluding the disease in those patients who actually do not have the disease, improving the management of patients with dementia and with movement disorders. ■

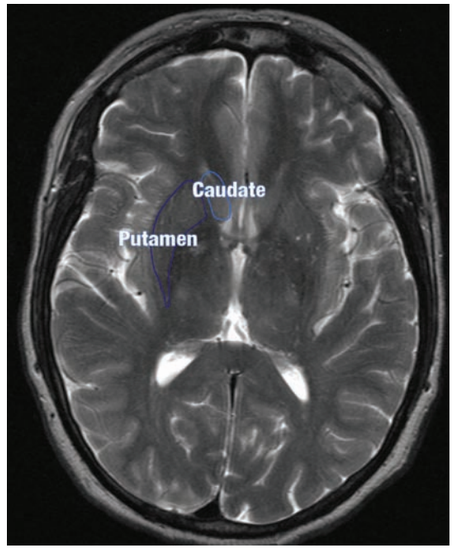

Figure 1:
MRI section of brain showing caudate and putamen (striata). The dopaminergic nerve terminals in these structures are affected in Parkinson's Disease and in DLB. There is DaTSCAN uptake in these structures in a healthy individual. In PD and DLB, DaTSCAN uptake is progressively reduced in these structures.

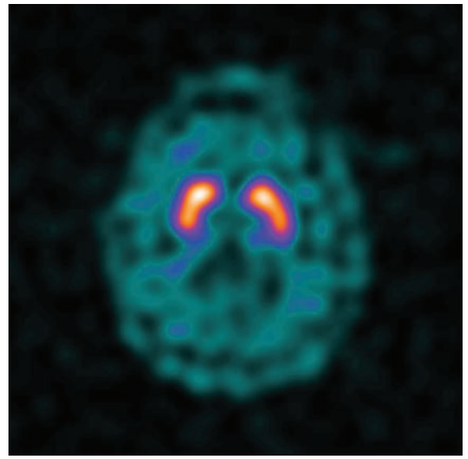

Figure 2:
DaTSCAN normal uptake in striata showing the typical comma shaped appearance on both sides. The "head" of the comma is the caudate and tail of the comma is the putamen uptake in the striata.

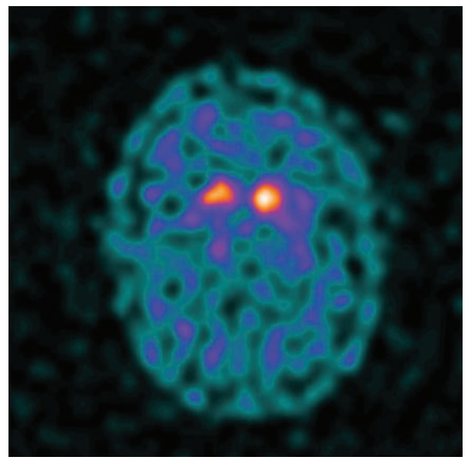

Figure 3:
DaTSCAN uptake in a patient with idiopathic Parkinson's disease. There is preferential loss of uptake in putamen in a patient with idiopathic Parkinson's disease, producing the typical dot appearance of the striatum (with only caudate uptake remaining). Furthermore, note the increased relative background activity in the image, also indicating that there is loss of uptake in the remaining caudate.

NUCLEAR MEDICINE IN THE DIAGNOSIS OF OSTEOMYELITIS

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Osteomyelitis is a diagnostic problem because significant bone destruction must occur before it can be seen on regular x-rays or CT scan. MRI is a sensitive test, but is not routinely available in most Canadian hospitals. MRI, also, is not particularly good at whole-body imaging where an infection other than osteomyelitis is being considered.

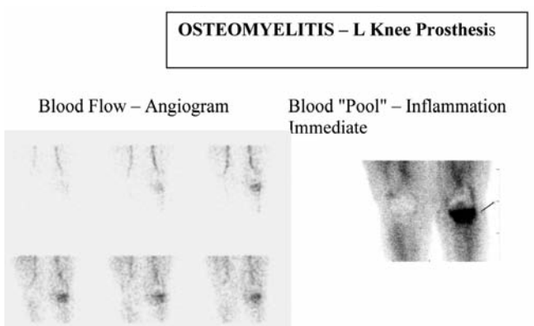
Nuclear medicine tests – namely bone scans, gallium scans and white cell scans, on the other hand, are widely available, relatively inexpensive, can do whole-body survey for other sites of infection, and are still considered the most sensitive and specific tests for bacterial bone infections, especially if combined with SPECT (Single Photon Emission Computed Tomography) as shown in the table below.

Procedure	Sensitivity(%)	Specificity(%)	Accuracy(%)
Bone Scan			
3Phase	36	92	67
Planar	73	31	50
SPECT	73	69	71
Bone/Gallium			
Planar	64	85	75
SPECT	91	92	92
Gallium Scan			
Planar	82	77	79
SPECT	91	92	92
MRI	91	77	83

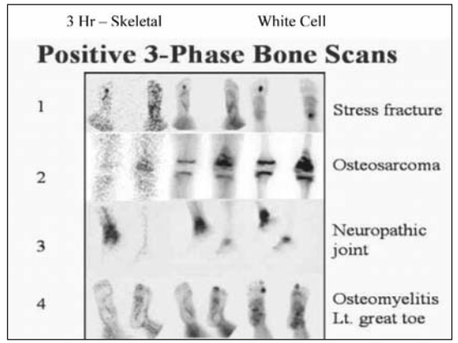
Love et al. Clin Nucl Med, 2000

A bone scan is a 2-3 hour test available in all hospital nuclear medicine departments in Canada, and is done in three phases:

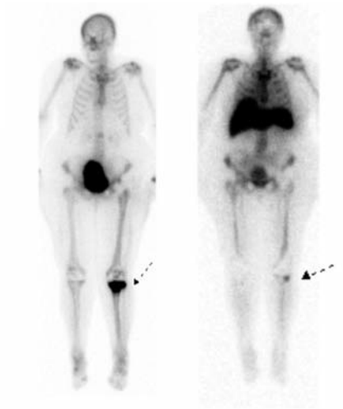
1. Blood Flow or low resolution nuclear angiogram;
2. Blood Pool – or inflammation scan done immediately after the flow images as blood is "pooled" in the capillaries, mostly the muscles and organs, and which corresponds to a low resolution T2 MRI image; and
3. Bone delay images at 1.5-3 hours and corresponds to a "mini-skeleton" showing areas of active bone deposition.

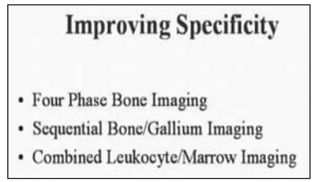


The bone scan is very sensitive and specific for osteomyelitis, and is positive as early as 24 hours after infection is suspected when standard x-rays of the bones are often negative. However, since it only sees bone inflammation and "repair", other conditions, such as fracture, tumor, osteoarthritis or rheumatoid arthritis can cause false positives, and certain areas, such as the spine, which are difficult to evaluate on planar nuclear medicine, can be missed in early osteomyelitis.

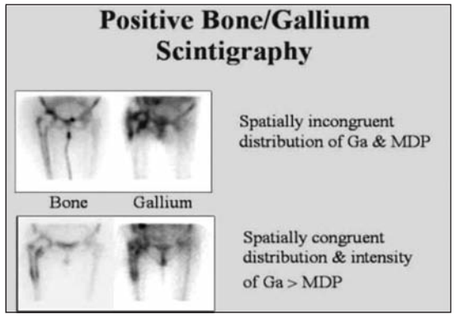


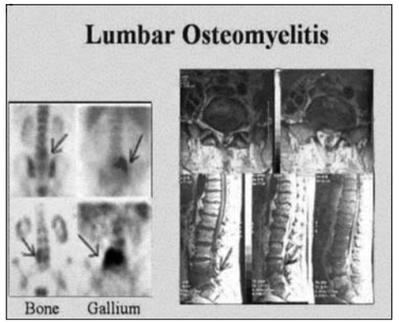
Often, the patient history, raised white count, and later x-ray changes are enough in the presence of a positive bone scan to make the diagnosis of osteomyelitis. However, in difficult or confusing cases, in order to increase the specificity of the bone scan, other more specific, but also more expensive and time-consuming, nuclear medicine tests can be added. The easiest is the 24 hour bone scan – or "four-phase" bone scan, which can occasionally help in the certainty of increased uptake. However, the two most widely available tests in nuclear medicine for improving sensitivity for bone infection are the gallium scan, using the radioactive tracer Gallium-67, and the labeled white cell scan.



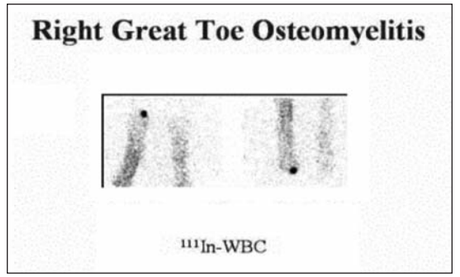


Gallium-67, when injected into patients, binds to transferring which is incorporated into white cells and bacteria. It is widely available in almost all Canadian nuclear departments, quite specific for infection (although it also localizes in certain tumors), and fairly inexpensive. However, because it is cyclotron-produced, it usually must be ordered specially for each patient, and imaging of gallium is done over 2-4 days. Also, because it localizes in all inflammation, the patterns of uptake can be increased even in non-infections,

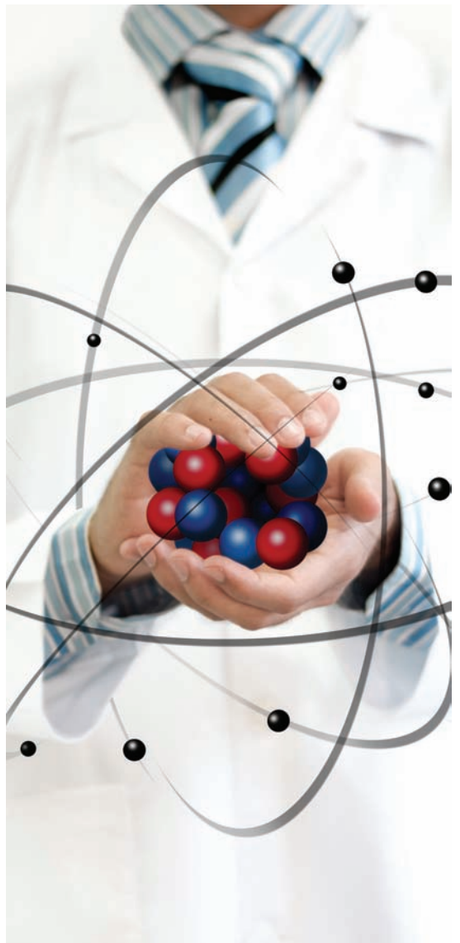




The other technique in nuclear medicine is to use labeled white cells, using the patient's own cells as the infection-seeking vehicle, with either Tc-99m or In-111 as the radioactive "tracer", which follows the cells to the site of infection. This is highly specific for osteomyelitis, although in some cases yet another nuclear test must be added. This is because labeled white cells also target normal marrow, and in some patients, such as those with infected prostheses, the marrow-expansion resulting from the surgery can confuse whether the patient has an infection or simply a normal variation resulting from the surgery. One particularly useful area for white cell scanning is in diabetic patients, where because of poor vascularity, there is increased risk for infection, particularly in the peripheral tissues such as the hand and foot. Diabetics often, however, have peripheral neuropathies and Charcot injuries to the feet or hands. In this setting, a bone-scan and white cell scan are frequently the only way, short of frank pus coming out of the extremity, of making the diagnosis.



In conclusion, nuclear medicine offers a number of highly sensitive and specific tests for the presence of osteomyelitis to Canadian doctors, which are cost effective, widely available, and inexpensive. ■



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LOWER GASTROINTESTINAL BLEED: A FOCUS ON RADIONUCLIDE SCINTIGRAPHY

Gastrointestinal (GI) bleed refers to any bleed originating from the gastrointestinal tract and is a potentially life threatening disorder. It can be divided into upper and lower GI bleeds. Upper GI bleed occurs proximal to the ligament of Treitz and lower GI bleed occurs distal to the ligament of Treitz. Lower GI bleeds account for approximately 20% of episodes of GI hemorrhage and are usually due to diverticular disease, angiodysplasia or, less commonly, after polypectomy.

An indication of the site of the GI bleed is the color of the stool. The presence of melena, which is known as black tarry stools, is indicative of blood that has been in the GI tract for at least 8 hours. The presence of melena indicates that the source of bleed is much more likely to be in the upper GI tract than in the lower GI tract. On the other hand, the presence of hematochezia, which is known as bright red blood per rectum, is indicative that the source of bleed is much more likely to be from the lower GI tract than the upper GI tract. A nasogastric (NG) aspirate can be done to differentiate an upper from lower GI bleed. The presence of blood in the aspirate reliably confirms upper GI bleed. However, an upper GI bleed may be missed if the bleed has stopped or arises beyond a closed pylorus. If the NG aspirate shows the presence of bilious fluids, this indicates that the pylorus is open and, in that circumstance, a negative lavage would reliably exclude an active upper GI bleed and indicate a lower GI bleed.

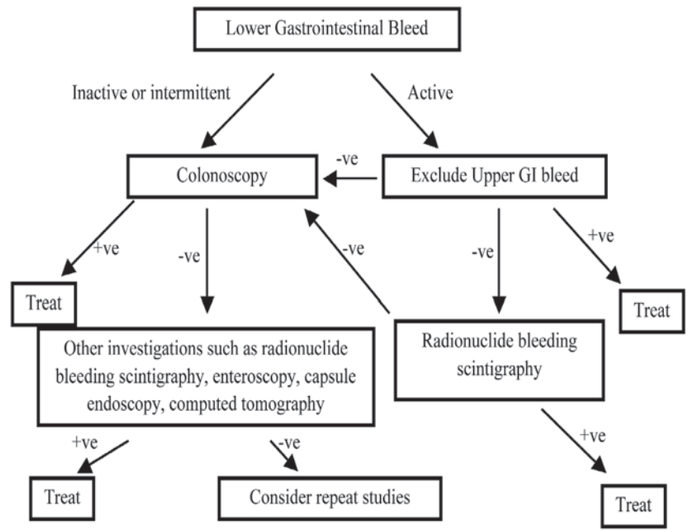
Radionuclide scintigraphy is an easy non-invasive diagnostic tool to evaluate lower GI bleed, which can detect hemorrhage at rates as low as 0.1 to 0.5 mL/min. It does not only detect a bleed but also can localize the site of the bleed. This can be done by two methods: the "pulse" method using 99mTc sulphur colloid and the "blood pool" method using 99mTc labeled red blood cells. With both of these techniques, no preparation is necessary for the patient.

In the first method, the rapid clearance of the tracer from the blood circulation into the reticuloendothelial system allows a detection of very low bleeding rates (0.1 ml/min in animal experiments). The disadvantage with that technique is that it detects bleeding that only occurs within up to 10 minutes after the radiotracer injection, and the bleeding sites in the upper abdomen may be obscured by the intense physiologic accumulation of the tracer in the liver and in the spleen. Using this method, imaging begins immediately following injection of 99mTc sulfur colloid and dynamic images are generated over 20 minutes. Once the bleeding site is visualized, additional time must be allowed to see the passage of the tracer and determine whether it is of small bowel or large bowel origin.

In the second method, 99mTc labeled red blood cells remain in the vascular space to make continuous monitoring of the entire GI tract for a long time. The in vitro technique of labeling RBCs is the preferred method to label RBCs over the in vivo and modified in vivo techniques because of the highest labelling efficiency. With radionuclide imaging using 99mTc labeled red blood cells, dynamic images are acquired over 60 minutes initially to allow the identification of the bleeding site and the intraluminal motion of the labeled RBCs. Longer imaging times are possible to increase the sensitivity for the detection of intermittent bleeds and allow sufficient time to see the passage of the tracer and determine whether it is of small bowel or large bowel origin.

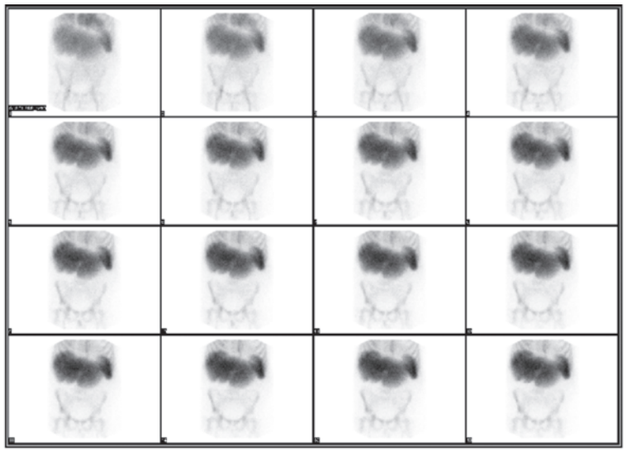
Radionuclide imaging requires active bleeding to detect a source and is indicated for severe (high risk) GI bleed. Patients with intermittent or inactive (low risk) bleed can be scheduled for colonoscopy. Difficulty of localization of bleed can occur with radionuclide imaging, particular with redundant transverse or sigmoid colon. However, this difficulty can be overcome by obtaining SPECT/CT imaging.

Algorithm for investigation of lower gastrointestinal bleed



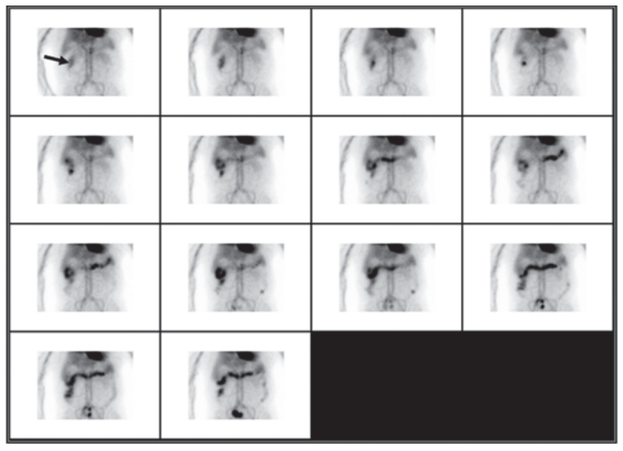
Case 1:
Radionuclide bleeding study was done using 99mTc sulphur colloid. Images demonstrated clearance of the radiotracer from the blood circulation into the reticuloendothelial system (liver, spleen and bone marrow) within 10 minutes after injection. No active bleed was demonstrated on that study.

Figure 1



Case 2:
71 year old patient presented with bright red blood per rectum. Radionuclide imaging using RBCs (Figure 2) showed extravasation initially in the right side of the abdomen (arrow) at the first minute of the study. Later images showed that the distribution of the radiotracer activity framed the abdomen with the radiotracer present in the regions of the ascending, transverse and descending colon.

Figure 2



Case 3:
90 year old patient presented with hematochezia. Radionuclide imaging using RBCs (Figure 3) showed extravasation initially in the left upper quadrant of the abdomen, which tracked inferiorly. SPECT/CT clearly showed a convoluted distribution of the tracer in the left aspect of the abdominal cavity on the maximal intensity projection image (wide arrow, Figure 4A) rather than framing of the abdomen that would be seen in a large bowel bleed.

The tomographic images demonstrated absence of the radiotracer throughout the large intestines and rectum, in the descending colon (short arrow, Figures 4B1-3, 4C1-3 and 4D1-3) and the radiotracer was in loops of intestines anterior to the descending colon (long arrow, Figures 4B1-3, 4C1-3 and 4D1-3). These findings indicated that the site of the bleed was in the jejunum rather than the descending colon.

Figure 3

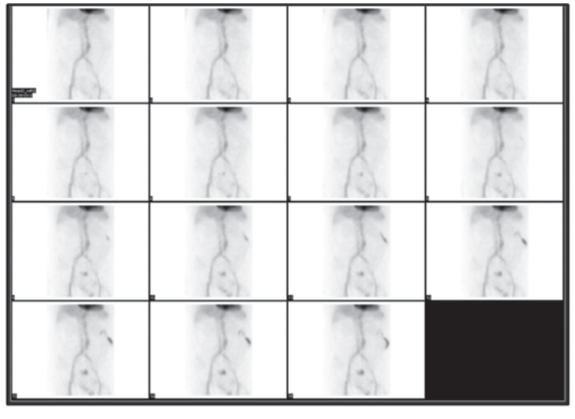
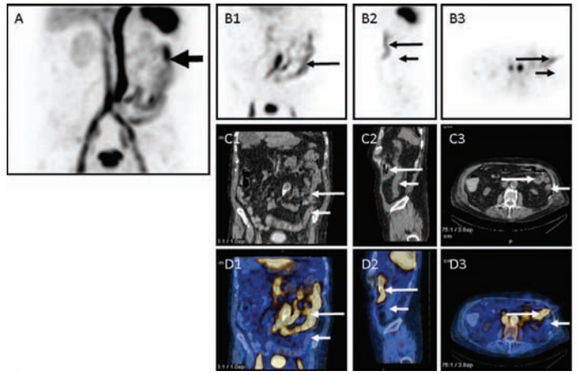


Figure 4



Case 4:
71 year old patient presented with hematochezia. Radionuclide imaging using RBCs (Figure 5) showed extravasation (small arrow) in the right lower quadrant of the abdomen. SPECT/CT confirmed that the location of the bleed was in the ascending colon (large arrow) on the maximal intensity projection image (Figure 6A) and tomographic images (Figure 6B, 6C and 6D).

Figure 5

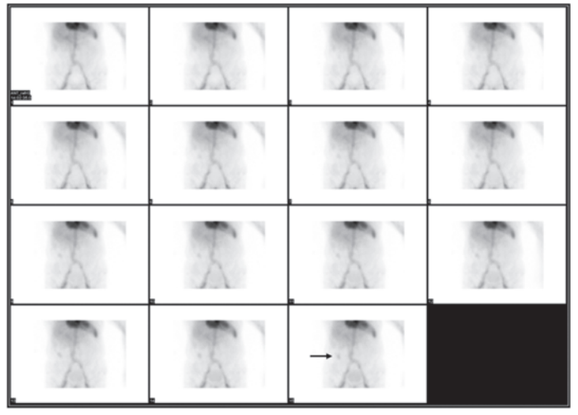
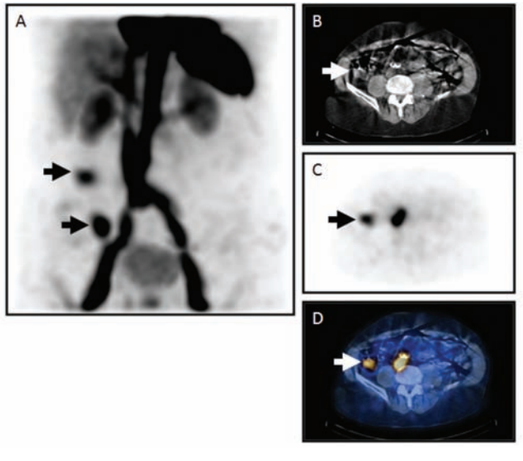


Figure 6



BRAIN IMAGING
IN NUCLEAR MEDICINE

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When visiting a patient with atypical cognitive defects or movement disorder, refractory epilepsy or, during follow-up of a brain neoplasm, brain imaging studies in nuclear medicine might help you to accurately evaluate your patient's disorder.

Cerebral blood flow studies with Ceretec® or Neurolite®, as well as brain metabolism studies with ^{18}FDG (fluorodeoxyglucose) (table 1) can help determine the cause of dementia (Alzheimer's disease (AD), fronto-temporal dementia (FTD) or dementia with Lewy body disease (DLBD)) and/or a movement disorder unresponsive to medications (multiple system atrophy, corticobasal degeneration or supranuclear palsy). In addition, these same exams can also help localize an epileptic focus in case of refractory epilepsy. Furthermore, the degree of glucose hypermetabolism with ^{18}FDG helps determine the aggressiveness of a tumor and, later on, to evaluate the responsiveness to treatment and to look for recurrence when conventional imaging cannot distinguish post-irradiation changes from recurrence.

The brain nuclear imaging possibilities are multiple, and this is without taking into account the possibilities of more specific tracers that could eventually reach clinical availability, such as dopaminergic tracer (Datscan®), tumoral tracer (^{18}FET) or amyloid tracer used in dementia diagnosis.

The most frequent and recognized use remains dementia imaging, which will be the subject of this article.

ALZHEIMER'S DISEASE

According to the most recent statistics, approximately 500,000 Canadians suffer either from AD or a similar dementia. By 2038, this number will double. Currently, the medications available to decrease or slow down the progression of cognitive symptoms are useful only in AD, justifying the need to obtain a precise diagnosis whenever possible before giving such medications, which cost is not negligible. Furthermore, having the right diagnosis is helpful when discussing with families about the disease and prognosis.

SPECT VS PET? WHAT IS THE DIFFERENCE?

Depending on different hospitals, two types of brain nuclear imaging are available. SPECT (Single Photon Emission Computed Tomography) is a tomographic test (3 D slices) available in all nuclear medicine departments since it's done with conventional gamma cameras. It uses a blood flow tracer with technetium-99m to image brain *perfusion*.

Brain FDG PET (positron emission tomography) is available in different PET centers in Quebec (table 1). It uses glucose to study brain *metabolism*. With regards to dementia, the bio-distribution of the two types of radiotracers is similar. PET studies are somewhat more accurate, however, when not available, SPECT is a good alternative. (Note: to simplify reading in the following paragraphs, the term hypometabolism will be used when referring to a PET exam, while the term hypoperfusion will be used when referring to SPECT).

Table 1

Study	Tracer		Mechanism	Indication	Availability
	Commercial name	Radiotracer			
PET	Gludef ®	^{18}FDG	Glucose metabolism	dementia movement disorder tumors epilepsy (interictal)	PET Centers: Chicoutimi, Gatineau, Montréal, Québec, Rimouski, Sherbrooke, Trois-Rivières
SPECT	Ceretec ®	^{99m}Tc-HMPAO	Blood flow	dementia movement disorder epilepsy (ictal and interictal)	All nuclear medicine departments
	Neurolite ®	^{99m}Tc-ECD	Blood flow		

Table 2

Hypometabolism/hypoperfusion	Parietal	Temporal	Frontal	Occipital
Alzheimer's disease	x	x	If advanced	
Fronto-temporal dementia	If advanced	x	x	
Lewy body disease	x	x	If advanced	x

METABOLIC PATTERNS OF DIFFERENT TYPES OF DEMENTIA

Distinguishing AD from FTD is sometimes difficult in clinical routine, especially when a frontal syndrome complicates the presentation. With nuclear brain imaging, this distinction is usually easy to make. In early AD, bilateral parieto-temporal hypometabolism (figure 1B) is seen, often asymmetrical, which will eventually progress toward dorsolateral frontal regions. There will also be an early involvement of the posterior cingulate gyrus and precuneus. By opposition, FTD will show a predominantly bilateral frontotemporal hypometabolism, most marked in their frontal aspect (figure 1C). DLBD will show defects similar to AD, with further extension to the occipital region (table 2). Vascular dementia is rather a conventional imaging diagnosis, with focal asymmetrical defects that can be seen.

BEFORE PRESCRIBING A BRAIN IMAGING STUDY!

There are confounding factors important to know. For example, uncontrolled hypothyroidism and major depressive disorder can cause hypometabolism similar to AD. It is thus essential to establish that TSH is normal before sending your patient for a brain study. Besides, TSH detection is rarely a problem. Likewise, it is as important to wait for the resolution of a depressive episode to avoid misinterpretation of the results, necessitating the need to repeat the exam at a later date and, of course, incurring unnecessary costs and stress. This is also true for any psychiatric syndrome. It is also worth mentioning that DLBD and Parkinson's dementia have similar metabolic patterns and therefore cannot be distinguished from one another by either PET nor SPECT.

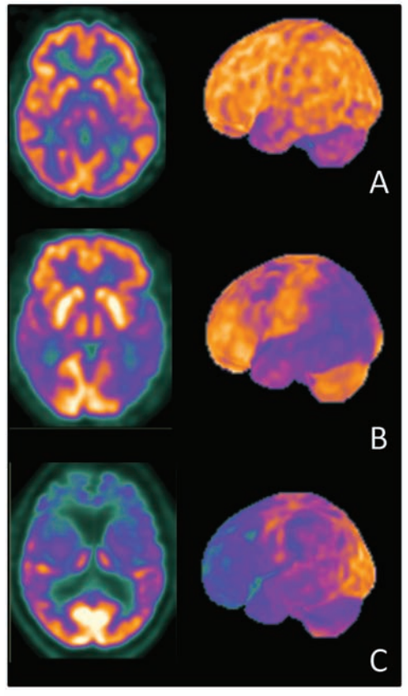

Figure 1
Transaxial slices and 3D reconstructions of ^{18}FDG PET studies

A-Normal: homogeneous cortical distribution.

B-Alzheimer's disease: mainly bilateral parieto-temporal hypometabolism.

C-Fronto-temporal dementia: mainly bilateral fronto-temporal hypometabolism.

In conclusion, when would it be best to request for these exams? Well, mainly whenever there is uncertainty between the diagnosis of AD and FTD. On the other hand, the use of SPECT or PET is not recommended when one wants to differentiate DLBD from Parkinson's dementia, since these have the same metabolic pattern. Finally, it is imperative to wait for the resolution of a depressive or psychiatric syndrome before requesting such tests. ■

V/Q SPECT IN PULMONARY EMBOLISM

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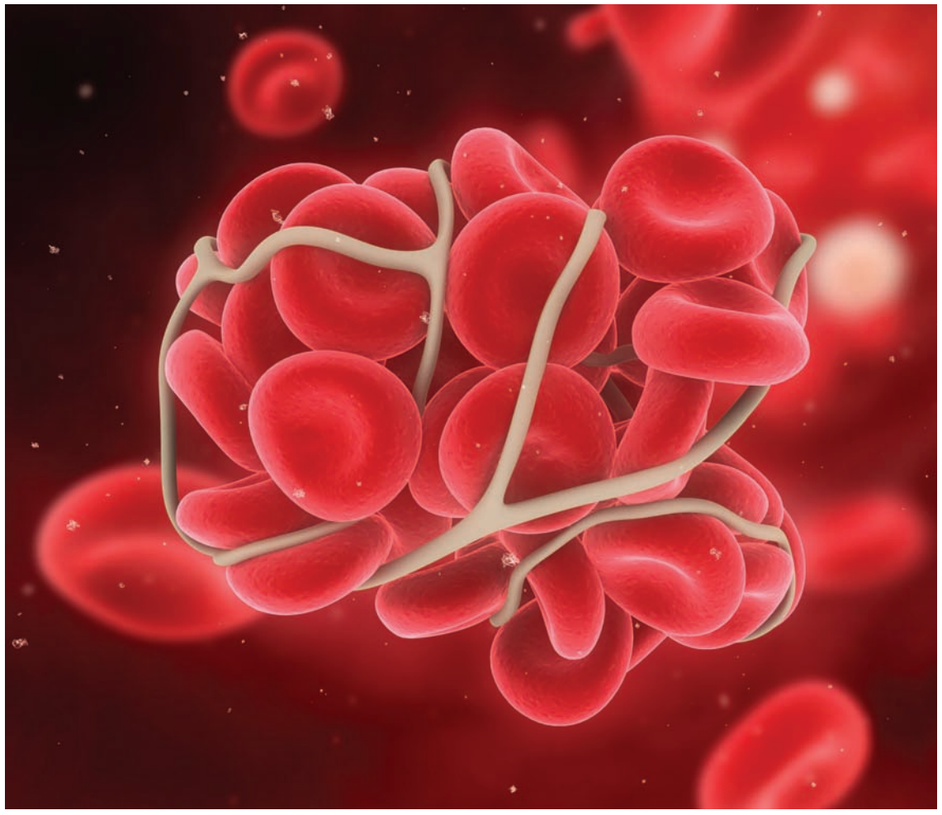
Clinical professor, University of Montreal
Clinical professor, University of Sherbrooke



Pulmonary embolism (PE) is a frequent and potentially lethal disease caused by a loose thrombus, originating most frequently from the lower limbs, migrating to the lungs and causing occlusion of a part of the pulmonary circulation. The diagnosis of pulmonary embolism is difficult because no combination of signs and symptoms is sensitive or specific. Different strategies have been devised to evaluate the clinical probability, for example, Wells score. They are usually combined with D-Dimer measurements and, if the resultant probability is moderate or high, further investigation is warranted.

Therefore, imaging tests are often required to establish the diagnosis. Traditionally, it was mainly based on planar ventilation and perfusion scintigraphy ("lung scan"). When it showed one or several areas of poorly perfused but adequately ventilated lung, it was considered compatible with PE. However, because of the high rate of indeterminate readings, especially within the PIOPED scheme of interpretation, it was progressively replaced in most settings by computerized pulmonary tomographic angiography (CTPA).

Within the last few years, the availability of a highly performing nuclear medicine ventilation agent (technegas) enabled the emergence of a major technical enhancement, tomographic tridimensional analysis of ventilation and perfusion, mainly known as Ventilation Perfusion Single Photon Emission Computed Tomography (V/Q SPECT). This technique has major advantages over traditional planar ventilation perfusion imaging.

Using tomographic imaging improves sensitivity for PE and drastically reduces indeterminate readings (< 5% of cases) due to better contrast and 3D visualisation of perfusion defects. This enables classification of defects into vascular or non-vascular origin, with much more accuracy than with conventional planar imaging. Matching or mismatching of ventilation with perfusion is easily determined (much better than with xenon gas) in 3D. Therefore, a probabilistic interpretation of results is totally discarded in favor of a binary interpretation (embolism present or absent), even though the basis of the diagnosis remains the same: embolism is deemed present when a vascular type perfusion defect is ventilated. Figure 1 shows a normal exam, while figures 2 to 4 show embolism of increasing size.

Available studies show that V/Q SPECT and CTPA have very similar accuracies, with V/Q SPECT being slightly more sensitive, but slightly less specific. Besides a very high sensitivity and a negative predictive value over 95%, V/Q SPECT has several benefits over CTPA, namely a much lower radiation dose, absence of allergic reactions or contrast nephropathy and a more reliable detection of subsegmental embolism. This profile makes it the imaging test of choice for most of the usual indications, especially if the chest X-ray is not severely abnormal. CTPA can be used as a first line study for more complex cases, specifically those who would require a chest CT anyway for a complete evaluation of their symptoms. CTPA is also a good choice for unstable patients, as it can be completed much quicker than a V/Q SPECT. Table 1 compares characteristics of V/Q SPECT to those of CTPA.

In the last few years, concern has been raised about the radiation dose incurred to patients by the rising use of CT in clinical practice. Table 2 compares the radiation dose given by both imaging tests. As can be seen, dose levels are much lower for V/Q SPECT, which is much more appropriate for widespread use in a large population, including low to moderate clinical probabilities. The dose to the breasts is very high for CTPA, representing the equivalent of 10-25 mammograms. Even if we take into account special low dose protocols for CTPA, the difference with V/Q SPECT is still substantial. Fetal dose is very low for both tests (negligible risk in both cases), but the high total and breast doses incurred by CTPA to young mothers make V/Q SPECT a much better option for this group.

When PE is diagnosed, it is important to obtain a follow-up exam three months later to assess the degree of reperfusion. This control will also serve as a baseline in case of recurrence and will identify patients with chronic embolism at risk of

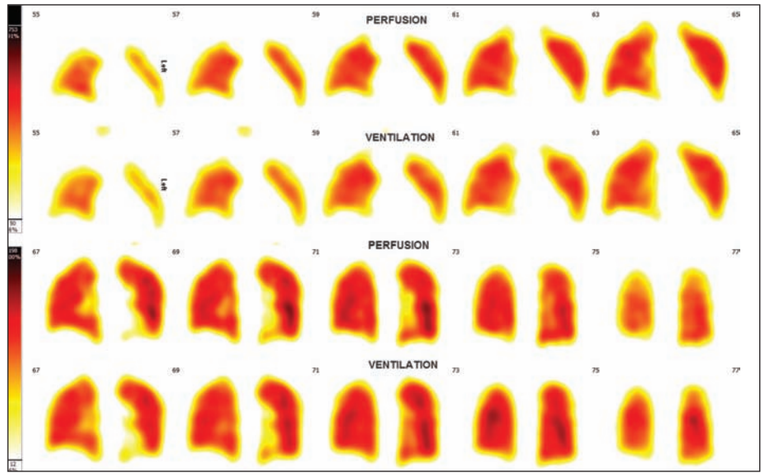


Figure 1:
Normal V/Q SPECT, coronal slices. Note homogenous distribution in both ventilation and perfusion.

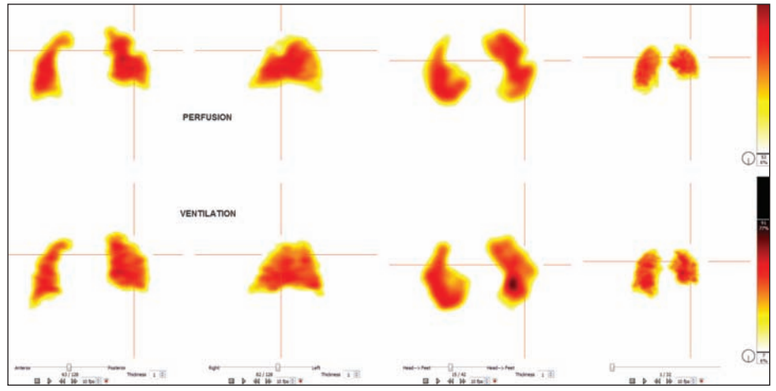


Figure 2:
Sub-segmental PE. Small typical vascular type perfusion defect with normal ventilation, viewed in triangulation mode (coronal, sagittal and transverse slices).

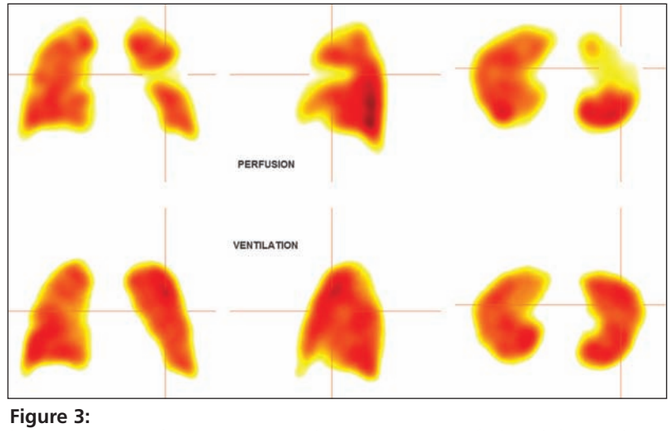


Figure 3:
Large segmental PE. Large typical vascular type perfusion defect with normal ventilation, viewed in triangulation mode (coronal, sagittal and transverse slices).

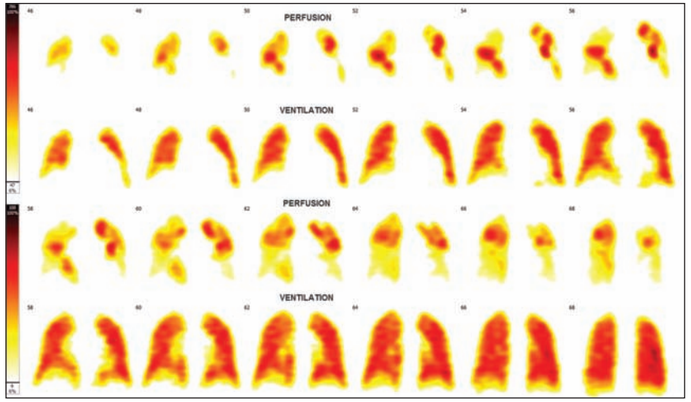


Figure 4:
Extensive PE. Multiple and extensive perfusion defects, both complete and partial, with normal ventilation.

pulmonary hypertension. In case of massive initial embolism, a first follow-up exam is obtained 7-10 days after the initial episode, which will serve as provisory baseline image in case of early symptom recurrence.

CONCLUSION

V/Q SPECT has superseded traditional planar ventilation perfusion imaging for the evaluation of pulmonary embolism. It is a highly accurate test that can be used as a first line procedure in most usual clinical scenarios. ■

	CTPA	V/Q SPECT
Sensitivity	May be lower	May be higher
Specificity	May be higher	May be lower
Possible allergies	Yes	No
Contrast induced nephropathy	Yes	No
Radiation dose	Higher	Lower
Non-related incidental findings requiring follow-up	Yes, frequent	Rare or nonexistent
Useful alternate diagnosis	Yes, frequent	Less frequent
Availability	Better availability out of hours	Less available out of hours
Accuracy with abnormal X-ray	Probably unaffected	May be affected in cases with moderate to severe changes
Accuracy in pregnancy	Strongly affected	Unaffected
Accuracy in chronic PE	Low	High
Ease of follow-up	More difficult, with higher radiation dose	Easier, with lower radiation dose
Performance in COPD	Probably not affected	May be affected in severe cases
Technical failure rate	Higher	Lower

Table 1:
Summary of advantages and limitations of CTPA and V/Q SPECT

	CTPA	V/Q SPECT
Whole body	15-20 mSv	3-4 mSv
Breasts	10-70 mSv	< 1.5 mSv
Lungs	± 10 mSv	± 10 mSV
Foetus	< 1 mSv	< 1 mSv

Table 2:
Summary of typical radiation doses incurred from CTPA and V/Q SPECT (mSv = millisievert)

SCINTIMAMMOGRAPHY AND CANCER OF THE BREAST

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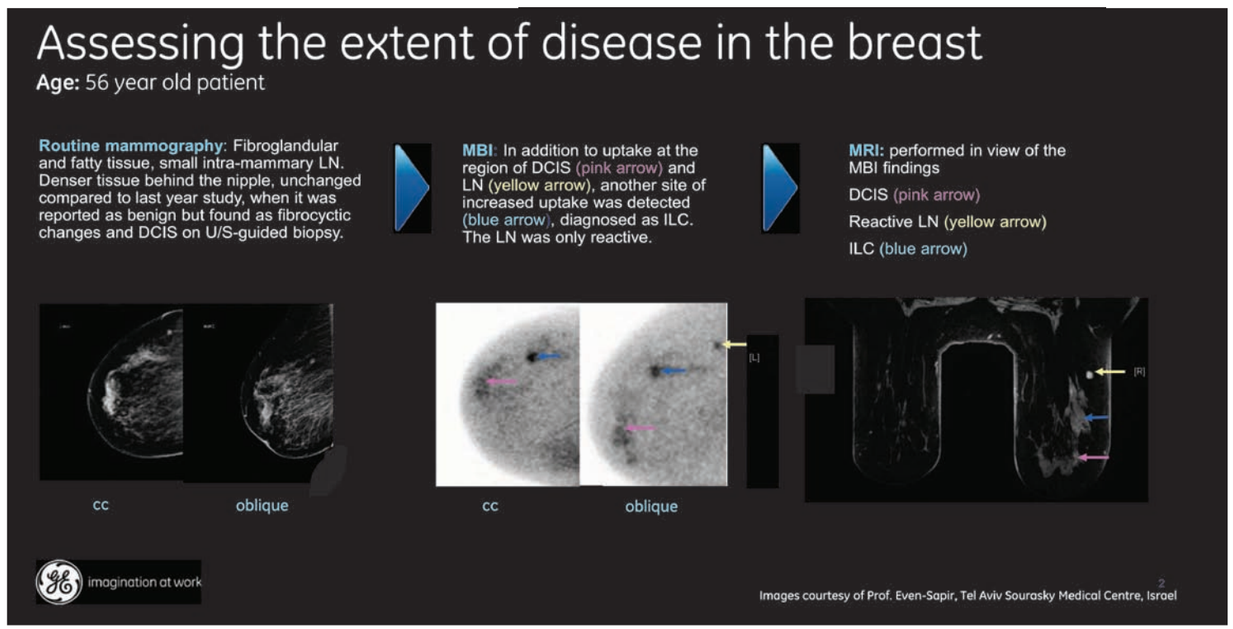
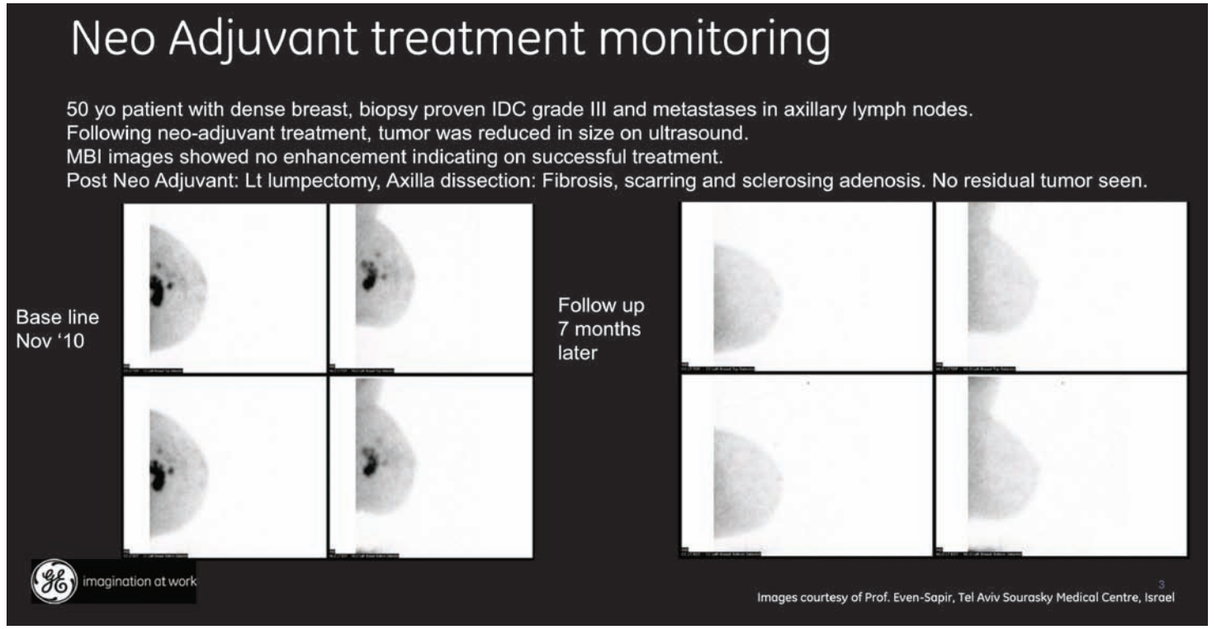
There are various goals to breast imaging. In patients with no known malignancy, breast imaging is performed with the aim of early detection of cancer, as well as assisting in separating benign lesions and premalignant or malignant lesions. Morphology of the breast is individual. It may vary from one patient group to another, may vary in the same individual during the menstrual cycle and may change with age. So is the risk for malignancy and the performance of the different imaging modalities. Mammography, which is the most readily available screening modality, may be satisfactory in patients with fatty breasts, but its lesion detect ability deteriorates the denser the breast tissue is.

Once breast cancer in diagnosed, imaging of the breast is no longer aimed for screening but is rather diagnostic, assessing the local extent of the disease and monitoring response to therapy. Based on the extent of the disease, the patient may be referred for lumpectomy, mastectomy, neo-adjuvant therapy, etc. During the course of the disease, assessment of tumor viability and detection of local recurrence are common indications for breast imaging. After treatment, morphology of the breast becomes even more variable.

The use of MRI (magnetic resonance imaging) has overcome many of the limitations of mammography, even when combined with sonography in screening of high-risk patients and patients with dense breasts, as well as in patients with proven malignancy. But MRI is not





always the optimal solution. MRI may be less available. There are contraindications for MRI and it may be difficult to perform a study in claustrophobic patients. MRI may be of compromised specificity leading to a high rate of futile biopsies and it is not always sensitive for assessment of tumor viability.

In recent years, novel functional techniques, dedicated for breast imaging with radiotracers have emerged in clinical practice of breast health. Breast cancer can be detected on PET, preferably on Positron Emission Tomography (PEM), in places where there are nearby cyclotrons and for FDG-avid tumors.

^{99}Tc-MIBI technetium-99m (Tc-99m) sestamibi is a single-photon emitter tracer routinely used in most departments of nuclear medicine for myocardial perfusion studies and, therefore, is readily available. It concentrates in cells with increased mitochondrial density, a common condition in malignant breast disease. This tracer was used two decades ago for breast imaging using the general routine gamma cameras, which are suboptimal for detection of small tumors in breasts, which are approximately 15 cm from the collimators and up to 25 cm from the region of interest. Currently there are small breast gamma-cameras designed as organ-specific cameras, including devices composed of the routine NaI(Tl) detectors (breast-specific gamma imaging, BSGI) and MBI – molecular breast imaging devices composed of the novel dual-head cadmium zinc telluride (CZT) detectors, improving resolution and allowing for the detection of smaller lesions.

Using a dual-head cadmium zinc telluride (CZT) detectors cameras (Molecular Breast Imaging, MBI), researchers in the Mayo clinic have found small malignant lesions of 3 mm and calculated a sensitivity of 90% in tissue abnormalities, with diameters of 5 mm to 20 mm. Screening 936 at-risk women, Rhodes et al of the Mayo Clinic reported that the sensitivity of mammography alone for these difficult-to-image patients was 27%, while the sensitivity of combined mammography and MBI was 91%. Recently at the RSNA, the group in Mayo Clinic have reported good performance of MBI with low-dose Tc-99m sestamibi of 8mCi having an ongoing dose-reduction work aiming to perform MBI with 4 mCi Tc-99m sestamibi, with an effective dose comparable to a screening mammogram.

18 months ago, an MBI system (Discovery* NM750b, GE healthcare) has been installed in the department of Nuclear Medicine at the Tel Aviv Medical Center. We approached our clinicians; breast surgeons and oncologists as well as breast radiologists, conducting research aimed at understanding the potential complementary role of MBI. We offered the physicians to refer for MBI women in whom it was felt that additional non-invasive imaging was clinically indicated. In addition to patients with no malignancy but high- risk for cancer, dense breast or equivocal breast imaging, over 100 patients with already proven cancer were referred, assisting in building a range of indications for the use of MBI as a breast diagnostic modality. These indications included determining the extent of disease in patients referred for lumpectomy in whom clinically, or on other imaging, the possibility of more extensive disease could not be ruled out, patients prior to and post neo-adjuvant therapy, assessing the presence of viable tumor tissue post-surgery and patients with axillary metastatic lymph node spread and occult primary. Sensitivity of MBI in these complicated cohorts was 88%. Causes for false negative were low- grade DCIS, microscopic remnant disease after treatment and lactating breast within a week from delivery. In patients who had MRI, MBI and MRI resembled for the majority of pre-malignant and malignant lesions. These preliminary findings encourage further accumulation of data. ■

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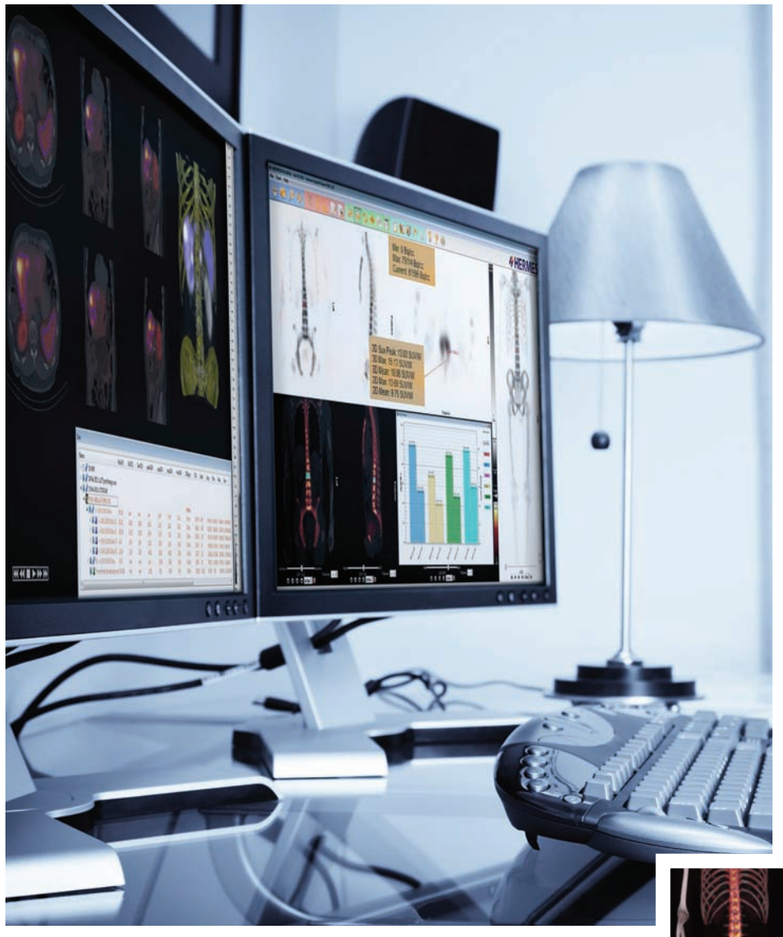

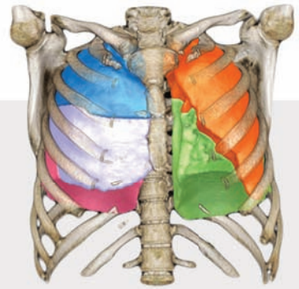

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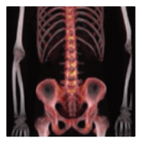

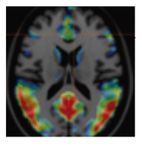

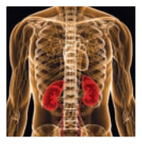

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