# LE PATIENT

LE SEUL MAGAZINE DE TOUS LES PROFESSIONNELS DE LA SANTÉ

## LES AVANCÉES MÉDICO-PHARMACOLOGIQUES

## LA MÉDECINE NUCLÉAIRE

## THÉRANOSTIQUE

JUIN 2025
VOL 19 • NO 1
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There are no contraindications associated with Technegas Aerosol.

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**Decreased Oxygen Saturation:** Decrease in oxygen saturation may occur during or after the inhalation of Technegas Aerosol. Oxygen saturation nadirs as low as 60% have been reported in a published study. In an efficacy trial, 79% of patients received supplemental oxygen or had the flow of Technegas Aerosol interrupted. Patients with compromised respiratory function may be at increased risk for decreased oxygen saturation. Monitor oxygen saturation with continuous pulse oximetry. If clinically indicated, allow patients to breathe room air throughout the procedure and consider administration of supplemental oxygen before and at any time during the procedure.

**Radiation Exposure Risk:** Technegas Aerosol contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling and preparation procedures to protect patients and health care providers from unintentional radiation exposure.

**Bronchospasm:** As with other inhaled aerosol medications, Technegas Aerosol may result in acute bronchoconstriction, especially in patients with heightened bronchoreactivity, such as patients with asthma or other lung or allergic disorders. Monitor all patients for bronchospasm.

**ADVERSE REACTIONS**

The adverse reaction occurring at ≥ 1% in patients receiving Technegas Aerosol was hypoxia (1%). Adverse reactions reported at < 1% were dizziness, dysgeusia, cough, dyspnea [not otherwise specified], throat irritation, and upper respiratory tract congestion.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy:** All radiopharmaceuticals, including Technegas Aerosol have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose.

**Lactation:** Temporarily discontinue breastfeeding. A lactating woman should pump and discard breastmilk for at least 4 hours after Technegas Aerosol inhalation to minimize exposure to the breastfed infant.

**Pediatric Use:** The safety and effectiveness of Technegas Aerosol with the patient administration set have not been established in pediatric patients less than 6 years of age.

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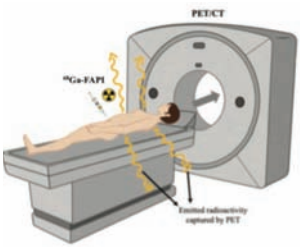
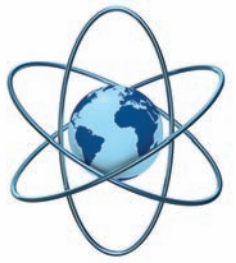
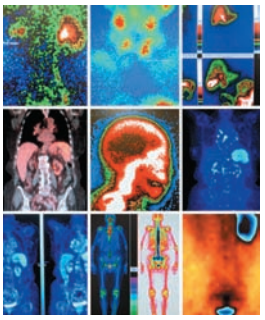
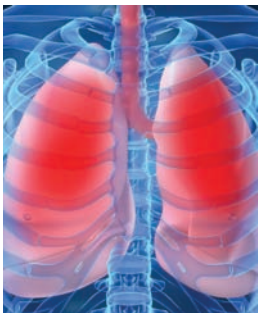
# SOMMAIRE

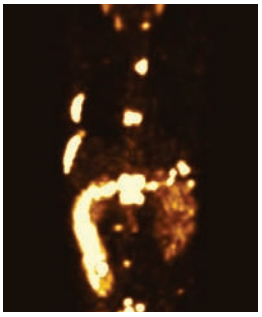


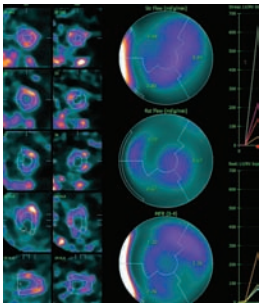









**François Lamoureux,**
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# LES AVANCÉES MÉDICO-PHARMACOLOGIQUES

## LE GRAND DÉFI DE LA MÉDECINE NUCLÉAIRE AU XXIe SIÈCLE

Devant le nouveau paradigme de l'évolution humaine, l'approche en matière d'investigation des maladies et de leurs traitements évolue dans de nombreuses situations. Avec une population croissante, tant en nombre qu'en longévité — vivre jusqu'à 100 ans est désormais envisageable — les enjeux se multiplient.

On estime qu'une personne sur deux développera un cancer, mais 40 % pourront être guéris. Certaines leucémies chez les enfants de moins de 10 ans peuvent même être complètement traitées. Par ailleurs, 20 % des personnes atteintes de maladies cardiaques ischémiques mourront subitement, souvent sans symptômes prémonitoires. Plusieurs bactéries développeront une résistance aux antibiotiques, entraînant la mort de nombreux patients. Les maladies neurodégénératives telles que Parkinson, Alzheimer, les corps de Lewy, ainsi que les tumeurs malignes, verront leur incidence et leur prévalence augmenter de manière significative.

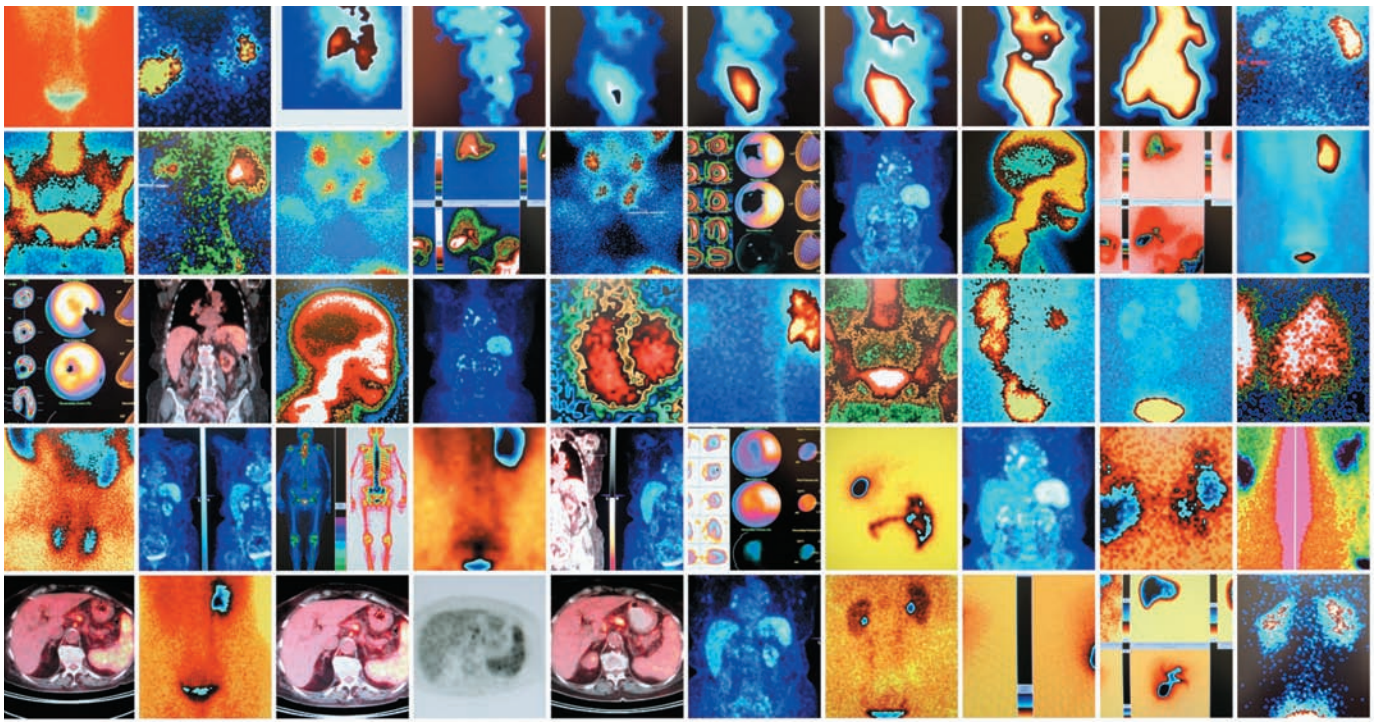
Il devient donc essentiel de réévaluer la nécessité d'investigations moins effractives, pancorporelles, et réalisées autant que possible de manière externe, afin d'éviter les examens inutiles, inappropriés ou coûteux. Les nouveaux développements en médecine nucléaire, tant sur le plan diagnostic que thérapeutique, offrent de nouveaux espoirs à ces patients.

Les examens pancorporels réalisés à l'aide de radiotraceurs externes sont désormais courants et accessibles à tous les patients. Qu'il s'agisse de tomographie par émission monophotonique couplée à la tomodensitométrie (TEMP-TDM) ou de tomographie par émission de positons (TEP-TDM), ces examens sont réalisés rapidement et sans effets secondaires. Ils fournissent une carte anatomique et fonctionnelle pancorporelle, permettant de détecter des pathologies dans les moindres recoins du corps humain.

Mais la médecine nucléaire va encore plus loin en offrant des traitements ciblés par molécules radioactives : c'est l'extraordinaire domaine de la théranostique.

En cancérologie, il est essentiel que l'évaluation initiale soit pancorporelle, afin d'identifier les métastases, même de petite taille, et parfois éloignée de la lésion primaire. La médecine nucléaire permet cette avancée. Elle permet également de diagnostiquer précocement certaines pathologies cardiaques ischémiques asymptomatiques. De plus, elle permet de confirmer et/ou de suivre l'évolution de maladies neurodégénératives comme Parkinson ou Alzheimer. La médecine nucléaire est une médecine non effractive, extrêmement sensible, à portée pancorporelle, indolore, habituellement sans effets secondaires, et applicable à tout patient, à tout âge. Oui, c'est une AVANCÉE exceptionnelle, réelle et indispensable pour l'être humain, qui aspire à vivre jusqu'à 100 ans… et plus. ■

***« En cancérologie, il est essentiel que l'évaluation initiale soit pancorporelle, afin d'identifier les métastases, même de petite taille, et parfois éloignée de la lésion primaire. La médecine nucléaire permet cette avancée. »***



Appareil de TEP/TDM Biograph Trinion doté de myExam Companion

# Conçu pour l'avenir

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- TDM de haute qualité à faible dose de rayonnement

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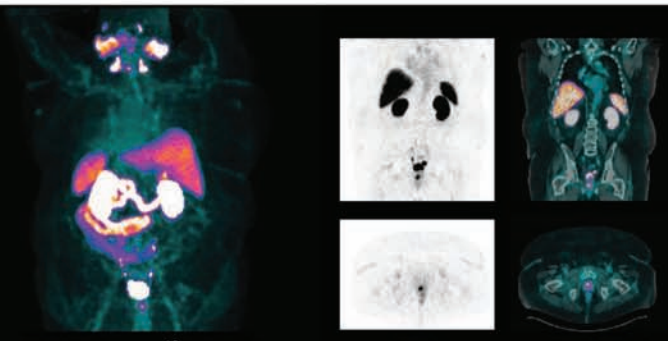
**Points saillants d'ordre clinique**

- Imagerie oncologique rapide et à faible dose
- Imagerie cardiovasculaire reproductible
- Imagerie neurologique à haute résolution
- Soins personnalisés contre le cancer grâce à la théranostique
- TDM de routine/avancée (comprend l'angiographie par TDM)

## Le temps de vol ultrarapide permet de détecter les lésions profondes

- Patient ayant un IMC élevé de 50,3
- Faible bruit et contraste net

Données fournies par le Rome Imaging Center, Rome, Géorgie, États-Unis.



TEP/TDM au $^{18}$F-PSMA | TEP | TEP/TDM

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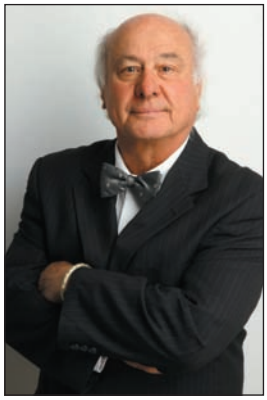

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# MEDICAL AND PHARMACOLOGICAL ADVANCES

## THE GREAT CHALLENGE OF NUCLEAR MEDICINE IN THE 21ST CENTURY

In light of the new paradigm of human evolution, the approach to disease investigation and treatment is changing in many situations. As the population grows — both in size and in longevity — the idea of living to 100 years old is becoming increasingly realistic.

It is believed that one in two people will develop cancer, but 40% can be cured. In fact, certain types of leukemia in children under the age of 10 can be completely cured. Additionally, 20% of people with ischemic heart disease may die suddenly, often without any warning signs. Several bacteria will develop resistance to antibiotics, leading to the death of many patients. Neurodegenerative diseases such as Parkinson's, Alzheimer's, Lewy body dementia, as well as malignant tumors, are expected to rise significantly in both incidence and prevalence.

It is crucial to reassess the need for less invasive, whole-body investigations, ideally conducted externally, to eliminate unnecessary, inappropriate, or costly examinations.

New developments in Nuclear Medicine, both diagnostic and therapeutic, are bringing renewed hope to these patients.

Whole-body imaging using external radiotracers has now become routine and accessible to all patients. Whether through single-photon emission computed tomography (SPECT/CT) or positron emission tomography (PET/CT), these scans are performed quickly and without side effects. They provide a complete anatomical and physiological map of the body, allowing detection of diseases in even the most hidden areas.

But Nuclear Medicine goes even further — it also offers therapeutic options using radioactive molecules. This is the extraordinary field of theranostics.

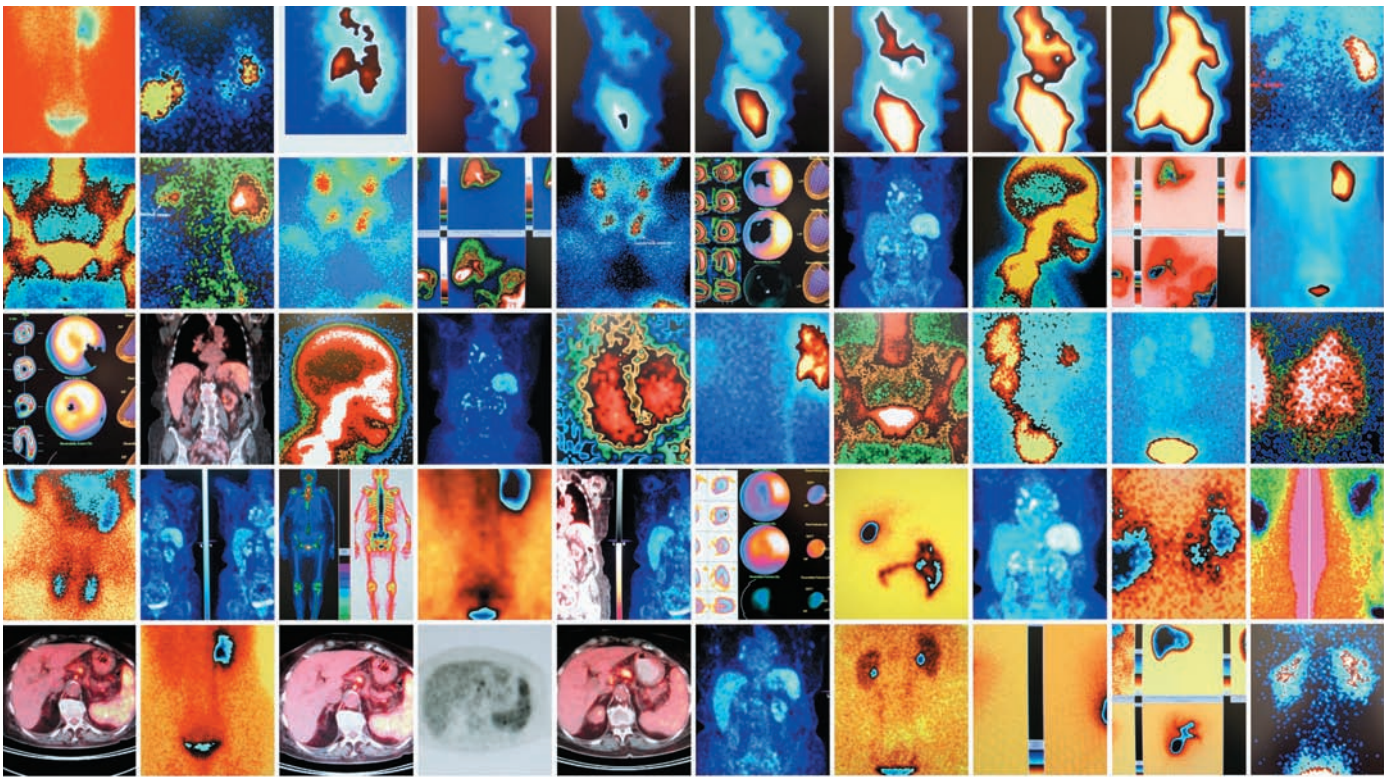
In oncology, whole-body imaging is essential at the initial diagnostic stage to detect small or distant metastases that may not be visible otherwise. Nuclear Medicine makes this advancement possible.

It can also help diagnose asymptomatic ischemic heart disease and confirm or monitor the progression of neurodegenerative conditions such as Parkinson's and Alzheimer's.

Nuclear Medicine is non-invasive, highly sensitive, whole-body, painless, usually free of side effects, and suitable for all patients of any age.

Indeed, it is an exceptional and essential ADVANCEMENT for humanity — one that can help us live well into our centennial years… and beyond. ■

***« In oncology, whole-body imaging is essential at the initial diagnostic stage to detect small or distant metastases that may not be visible otherwise. Nuclear Medicine makes this advancement possible.»***



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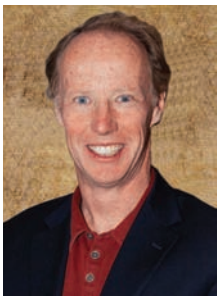
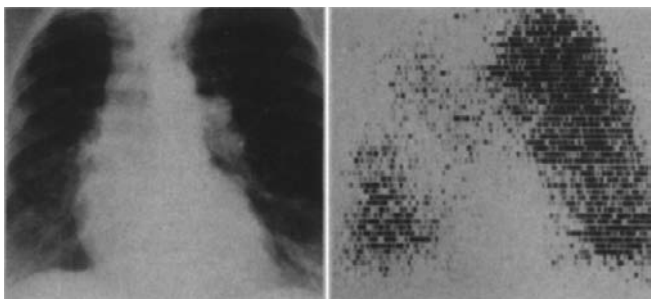


**Dr. Andrew Ross,**
Past President,
The Canadian Association
of Nuclear Medicine
Professor at
Dalhousie University

# 21ST CENTURY LUNG SCANS: WHAT'S OLD IS NEW AGAIN!

Ventilation Perfusion imaging assessing lung physiology is one of the earliest clinical applications in Nuclear Medicine, only predated by thyroid scanning as a procedure in the specialty. The earliest documented measurements of regional pulmonary perfusion using radioactive tracers were conducted by Dr. John West and his colleagues in the UK in 1961. They utilized radioactive tracers to assess gravitational differences in pulmonary blood flow, marking a significant advancement in understanding lung physiology. Building upon these foundational studies, Dr. George Taplin's group at UCLA made a pivotal contribution in 1963 by introducing the use of iodine-131-labeled macroaggregated albumin ($^{131}$I-MAA) for perfusion lung scanning. This innovation significantly enhanced the diagnosis of pulmonary embolism and facilitated more detailed studies of regional lung function. See Figure 1

**Figure 1**



**H.N. Wagner Jr., D.C. Sabiston Jr., M. Iio, et al.**
**Regional pulmonary blood flow in man by radioisotope scanning**
**JAMA, 187 (1964), pp. 601-603**

**Assessment of ventilation closely followed with Taplin introducing xenon-133 ($^{133}$Xe). They first presented their research in Canada. "Colloidal Radioalbumin Aggregates for Organ Scanning" (Authors: G.V. Taplin, E.K. Dore, D.E. Johnson, H. Kaplan) was presented at the 10th Annual Meeting of the Society of Nuclear Medicine in Montreal in 1963.**

Combination imaging of ventilation and perfusion followed and with the development of the new efficient anger camera technology, expanded use of VQ scanning with it becoming the standard of practice for evaluation of pulmonary embolism. At this time, the only other imaging method for embolism detection was direct visualization with angiography which was expensive and invasive.

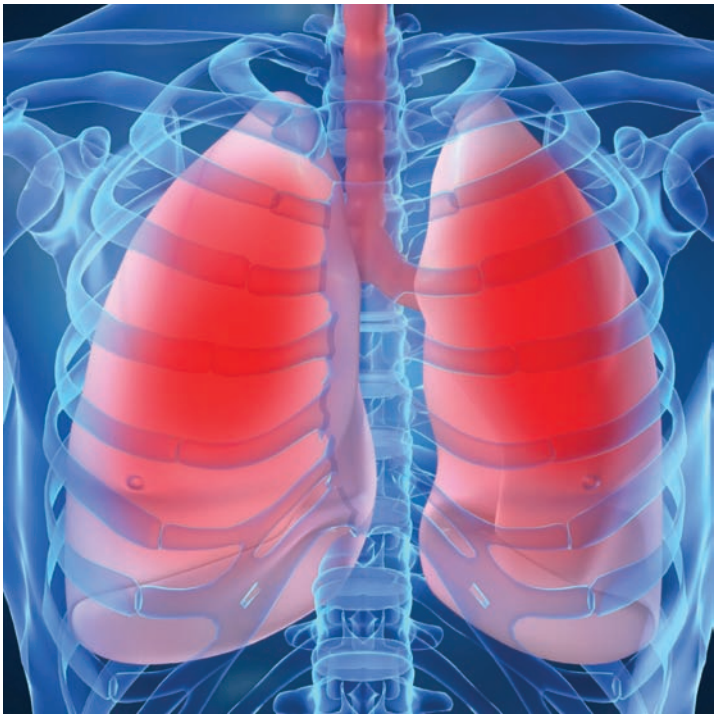
The development of the Molybdenum generator for Nuclear Medicine departments led to the incorporation of Technetium-99M based tracers. In the late 1960s, $^{99M}$Tc MAA was developed and quickly replaced the iodine-based product which had worse imaging characteristics as well as higher radiation dose to the patient. The development of Technetium-99M aerosols occurred in the late 1970's and saw increased use thereafter although Xenon remained as an agent even until today.

Despite all these advancs, the major limitation of VQ scanning was it's indirect assessment of the lung parenchyma and resultant issues with specificity. As well, it's nonstandard reporting led to concerns regarding reproducibility. Efforts to address these issues continued and culminated in the publication of the PIOPED criteria in 1990. Although addressing standardization, there were issues with this study, most significantly a high rate of inconclusive studies (up to 40%). As well, the utilization of probability based reporting, although scientifically sound, was an area of clinical frustration with the test. Concurrently, the fast evolution of helical CT scanning and its incorporation into evaluation of pulmonary imaging was occurring. The issues of a difficult to understand and somewhat nebulous system of reporting based on probability versus the CT direct visualization of clot and binary reporting of either embolism positive or negative led to the decline of VQ scanning in this clinical scenario.

However, even with these issues, there was still clinical use in situations such as patients with CT availability, contrast allergy or renal impairment which negated the ability to use CT scanning. Further, increasing concern about radiation exposure with the wide proliferation of CT technology led to further development of lung scanning. VQ scanning was shown to have significantly lower doses particularly to the female breast and thyroid.

Through the 1990s, further advances were occurring for ventilation perfusion imaging. Most significantly was the adoption of SPECT aquisition. This method provided 3D visualization which demonstrated a significant improvement in terms of diagnostic accuracy of lung scanning. Overall, clinical validity was demonstrated to equal CTPE. This was cemented in guidelines adopted by the EANM in 2007 with SPECT as the standard for this procedure. Furthermore, these guidelines provided a binary system of reporting with either "pulmonary embolism present" or "pulmonary embolism absent" doing away with the probabilistic system. This dramatically reduced the number of indeterminant scans to a level on par with CT.

As well during this period, advances occurred in ventilation imaging agents. While xenon 133 was effective it had drawbacks including high radiation



dose and contamination. Another radioactive gas, Krypton 81, with better imaging characteristics and dose, developed in the UK had seen some use over the decades although was limited because of availability and cost. Although these gases possess theoretical advantages of ideal physiologic behaviour, they are dynamic with changing distribution over time within the lungs which negates the ability to perform SPECT. Utilization of nebulizers with technetium agents partially addressed these problems; however, administration of such was time consuming and led to potential contamination and other technical issues. Moreover, in patients with breathing difficulties, the agent provided less than ideal images and in many such patients, SPECT imaging was technically suboptimal.

These limitations were overcome by the development and marketing of another technetium based ventilation agent called Technegas in Australia in the 90's. This involves superheating (1500°C) a droplet of technetium in a small carbon cup in pure argon environment. The result is a technetium based "pseudo gas" which can be administered to patients in 3-5 breaths and provides very high quality stable imaging. The agent allowed for SPECT imaging in virtually all patients. The EANM guidelines adopted it as the ventilation agent of choice (if Krypton was unavailable) and was further endorsed by the Canadian Association of Nuclear Medicine guidelines in 2018 as the imaging agent of choice.

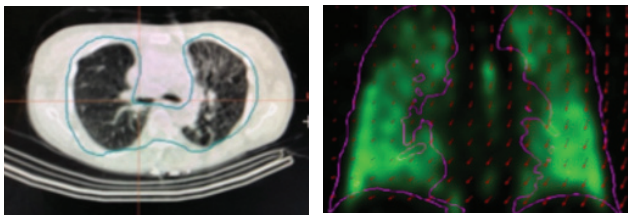
These 21st century technological adoptions cemented ventilation perfusion imaging as an imaging technique comparable to CT for pulmonary embolism evaluation but more significantly providing robust physiologic assessment of the lungs. The imaging technical advancement of full ring digital gamma imaging systems provides even more opportunity in terms of faster image exams and integration of new analysis software with the incorporation of artificial intelligence.

These factors have led to a resurgence of investigation and articles assessing ventilation perfusions imaging. Our center has been investigating ventilation perfusion imaging utilizing Technegas in patients who have undergone lung and stem cell transplants. This group is prone to significant pulmonary complications including Bronchiolitis Obliterans Syndrome. The current clinical evaluation assessing for this are pulmonary function tests which are insensitive until the later stages of the process which delays the institution of therapy. Utilizing data from the VQ SPECT/CT with Technegas and software which provided measures of ventilation distribution and changes over time, patients developing the complication demonstrate deterioration with increasing degrees of heterogeneity of ventilation which was more sensitive than PFTs. (Figure 2)

***« The imaging technical advancement of full ring digital gamma imaging systems provides even more opportunity in terms of faster image exams and integration of new analysis software with the incorporation of artificial intelligence. »***

**Figure 2**

**A** **B**



**Low dose CT with automated lung segmentation (green outline) (A) applied to Technegas ventilation data (B) to assess regional ventilation for quantitative assessment.**

Others have investigated similar protocols in common pathologies such as COPD and asthma. These patterns of changes of ventilation as well have shown the ability to better predict lung status than current evaluation methods such as pulmonary function tests. With this data, follow up VQ studies show potential to provide more sensitive and clinically important information about response to treatment. So, as the specialty of Nuclear Medicine has seen a 21st century renaissance along with it has come one of its oldest studies. Fueled by technical innovation including SPECT, digital detectors, software and newer ventilation agents, it is being utililized in old and new indications.

# PLUVICTO IN PROSTATE CANCER: A NEW FRONTIER IN THERANOSTIC RADIOLIGAND THERAPY

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Director of Nuclear Medicine Department, McGill university
Assistant Professor at McGill University Health Centre (MUHC), McGill University
Adjunct Professor at Department of Nuclear Medicine, University of Ottawa

*« In Canada, public access to medications like Pluvicto is determined at the provincial and territorial level. Each jurisdiction evaluates the clinical efficacy, cost-effectiveness, and healthcare impact before listing a drug in its public formulary. »*

## Introduction: Theranostics and the Rise of Targeted Radioligand Therapy

Modern oncology is increasingly defined by precision medicine — treating disease based not just on its location, but on its unique molecular characteristics. Among the most promising advances in this space is the field of theranostics, a portmanteau of "therapy" and "diagnostics." Theranostics uses a shared molecular target to first diagnose and then treat cancer, often by pairing radiopharmaceuticals for imaging with therapeutic counterparts.

This concept has revolutionized prostate cancer management, particularly in cases of metastatic castration-resistant prostate cancer (mCRPC). A key molecular target in this context is prostate-specific membrane antigen (PSMA) — a transmembrane glycoprotein overexpressed on the surface of most prostate cancer cells, especially in aggressive and metastatic disease.

Using PSMA-targeted PET imaging agents (e.g., Ga-68-PSMA-11 or F-18-DCFPyL), clinicians can detect and stage disease with high sensitivity. If lesions are shown to be PSMA-positive, the patient may be eligible for treatment with a therapeutic agent such as Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) — a PSMA-targeted radioligand therapy (RLT) that exemplifies the theranostic paradigm. Approved by the FDA, Health Canada, and other international agencies, Pluvicto is rapidly becoming a cornerstone in the treatment of advanced prostate cancer.

## What Is Pluvicto?

Pluvicto is a radioligand therapy that combines two critical components:

- Lutetium-177 (Lu-177): A beta-emitting radioisotope that delivers ionizing radiation.
- Vipivotide tetraxetan: A PSMA-targeting ligand that directs the therapy to prostate cancer cells.

Once administered intravenously, Pluvicto circulates through the bloodstream, binds to PSMA-expressing tumor cells, and is internalized. The Lu-177 component then emits short-range beta particles, causing lethal double-stranded DNA breaks — effectively killing cancer cells while minimizing off-target toxicity.

This highly targeted mechanism distinguishes Pluvicto from systemic chemotherapy and underscores its role in theranostic treatment.

## Regulatory Approvals and Indications

Pluvicto received:

- FDA approval (March 2022) for use in adult patients with PSMA-positive mCRPC who had previously received at least one androgen receptor pathway inhibitor (ARPI) and taxane-based chemotherapy.
- Expanded FDA approval (March 2025) for patients with PSMA-positive mCRPC who have received prior ARPI therapy and are either appropriate to delay chemotherapy or have already received taxane-based chemotherapy.

It has also been approved by the European Medicines Agency and Health Canada.

Health Canada approved Pluvicto on August 25, 2022, as the first targeted radioligand therapy for treating PSMA-positive mCRPC in adults who had received at least one ARPI and taxane chemotherapy.

Following national approval, the pan-Canadian Pharmaceutical Alliance (pCPA) negotiated reimbursement terms with the manufacturer, leading to public funding agreements in several provinces. Ontario was the first to implement public access, with the first patient receiving treatment at London Health Sciences Centre in December 2024. Alberta and Nova Scotia subsequently announced public reimbursement as well.

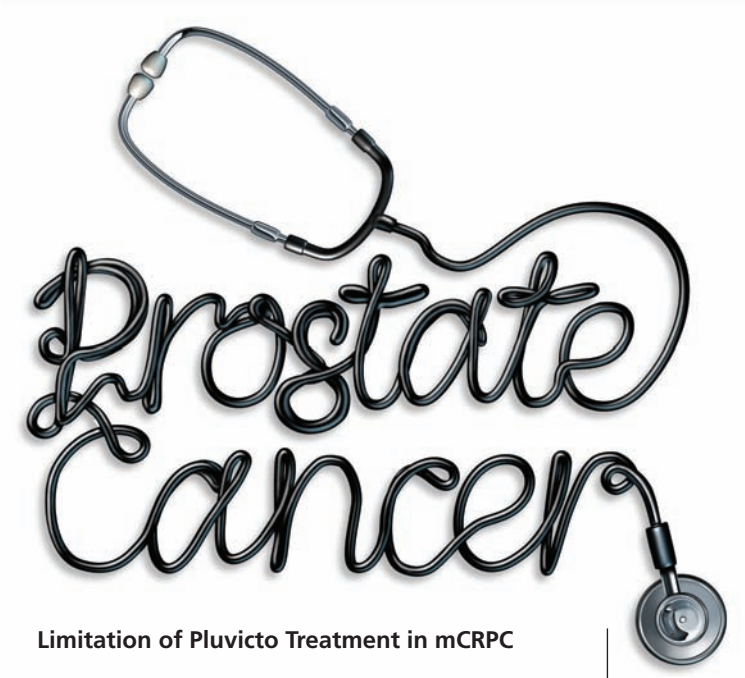
In Canada, public access to medications like Pluvicto is determined at the provincial and territorial level. Each jurisdiction evaluates the clinical efficacy, cost-effectiveness, and healthcare impact before listing a drug in its public formulary. The pCPA plays a central role in price negotiations, but final coverage decisions are made independently by each province.

## Mechanism of Action: The Theranostic Cycle in Action

Pluvicto complements PSMA PET imaging agents used in diagnosis. The theranostic workflow involves:

1. Diagnosis: PSMA PET/CT confirms PSMA expression in metastatic lesions.
2. Treatment: Pluvicto targets and delivers radiation to the same PSMA-positive lesions.
3. Monitoring: Therapeutic response is tracked via imaging and biomarkers (e.g., PSA levels).

Lu-177 delivers cytotoxic beta radiation over a short range (1–2 mm), inducing DNA damage and cancer cell death, while sparing surrounding healthy tissue.




### Clinical Trial Evidence

1. VISION Trial (NEJM, 2021)

- Design: Phase 3, randomized, open-label, multicenter
- Population: 831 patients with PSMA-positive mCRPC post-ARPI and chemotherapy
- Results:
- Median overall survival: 15.3 vs. 11.3 months
- Radiographic progression-free survival: 8.7 vs. 3.4 months
- Objective response rate: 30% vs. 2%

2. PSMAfore Trial (2024)

- Design: Phase 3, pre-chemotherapy
- Results: rPFS: 9.5 months (Pluvicto) vs. 5.6 months (alternative ARPI)

3. TheraP Trial (2021)

- Design: Phase 2, randomized controlled trial in Australia
- Comparison: Pluvicto vs. cabazitaxel in mCRPC patients post-docetaxel
- Results: PSA ≥50% reduction: 66% (Pluvicto) vs. 37% (cabazitaxel)
- Fewer grade 3–4 adverse events: 33% vs. 53%
- Overall survival similar: 19.1 vs. 19.6 months

### Administration and Monitoring

- Dose: 7.4 GBq (200 mCi) IV every 6 weeks
- Cycles: Up to 6, based on response and tolerance
- Eligibility: Confirmed PSMA-positive disease on PET/CT
- Monitoring: Hematology, renal and liver function, PSA, and imaging

### Side Effects and Safety

Common Side Effects of Pluvicto

Fatigue: 43%
Dry mouth (xerostomia): 38%
Nausea: 35%
Anemia: 31%
Decreased appetite: 21%
Constipation: 18%
Thrombocytopenia: 13%
Neutropenia: 8–10%

Renal toxicity is rare but monitored due to urinary excretion. Long-term data are still being evaluated.

### Treatment options comparison

| Therapy | Type | Role in mCRPC | Notes |
|---|---|---|---|
| Enzalutamide/Abiraterone | ARPI | 1st/2nd line | Resistance eventually develops |
| Docetaxel/Cabazitaxel | Chemotherapy | Later line | More toxic, systemic side effects |
| Radium-223 | Bone-targeted radiotherapy | Bone-only disease | No soft tissue effect |
| Pluvicto | Radioligand therapy (RLT) | PSMA+ mCRPC | Systemic reach, well tolerated |

### Limitation of Pluvicto Treatment in mCRPC

While promising, Pluvicto faces several implementation hurdles:

- Access and Infrastructure: Requires nuclear medicine facilities and trained personnel
- Tumor Heterogeneity: Not all lesions express PSMA uniformly
- Resistance Mechanisms: Under ongoing investigation

### Ongoing and future studies include:

- PSMAddition: Pluvicto in metastatic hormone-sensitive disease
- LuPARP: Pluvicto + olaparib (PARP inhibitor)
- Checkpoint inhibitor combinations
- Next-generation alpha therapies (e.g., Actinium-225)

### Conclusion

Pluvicto represents a paradigm shift in prostate cancer management, embodying the full potential of theranostics — from precise diagnosis to targeted treatment. Its approval in multiple jurisdictions, including Canada, and integration into provincial healthcare systems, highlights its growing clinical significance.

As clinical evidence continues to support its efficacy and safety, and as infrastructure and funding improve, Pluvicto is set to become a mainstay in the treatment of advanced prostate cancer and a model for theranostic strategies in other cancers.

***« Pluvicto represents a paradigm shift in prostate cancer management, embodying the full potential of theranostics — from precise diagnosis to targeted treatment. Its approval in multiple jurisdictions, including Canada, and integration into provincial healthcare systems, highlights its growing clinical significance. »***

**Dr. Steven Burrell**
**MD, FRCPC**
Head of Nuclear Medicine
QEII Health Sciences Centre
Halifax, Nova Scotia,
Canada

# A PARADIGM SHIFT IN NUCLEAR MEDICINE SCANNING

A new breed of high-tech body scanner is revolutionizing nuclear medicine, bringing better patient care, a better patient experience, and a more efficient use of health care resources: a big win-win-win.

Nuclear Medicine is an impactful field of medicine that uses tracers to image and diagnose a wide range of medical diseases, including cancer, cardiac disease, and many more. The tracers are called radiopharmaceuticals and have 2 properties, a molecule with a specific physiologic property such as seeking and binding to cancer, and a tiny radioactive component that emits energy detected by scanners, creating an image of the distribution of the tracer in the body. While the past several years have seen major advances in other pillars of Nuclear Medicine -- Positron Emission Tomography (PET)scanning, and radioisotope therapy – the scanners used for most Nuclear Medicine tests had changed little in many years. However, a new state-of-the-art class of scanners has been developed, raising the bar to a new level. There are two such scanners, the StarGuide by GE and the Veriton by Spectrum Dynamics. In June 2024, with the support of donors and the QEII Foundation, we installed the first of 2 planned StarGuide scanners in our department, immediately ushering in improvements in diagnostic accuracy and confidence, patient experience, and departmental efficiencies.

*« The CZT detectors are more efficient than conventional detectors, creating images of comparable quality in significantly less time. Further, acquiring 3-D images shortens the overall scan time in some studies that traditionally would acquire both 2-D and 3-D images. »*

## TECHNOLOGICAL ADVANCES

At the core of the scanners are 2 major innovations. One is the arrangement of the detectors in a 360° ring-configuration around the patient (Figure 1B). Traditional Nuclear Medicine scanners have always had a flat-panel of detectors, which created 2-dimensional (2-D) images of individual organs or the whole body. Those scanners could be slowly rotated around the patient to create 3-D images, known as SPECT scanning (Single Photon Emission Computed Tomography).

However, this took time and was often impractical to add to the 2-D images for large portions of the body. With the ring-detector approach all images are automatically acquired as 3-D images of the body, providing more precise assessment. The second major advantage is the use of high-tech detectors comprised of Cadmium-Zinc-Teluride (CZT). CZT is much more efficient at detecting the energy emitted by the radiopharmaceuticals, allowing excellent quality images to be obtained in less time or with a lower amount of radiopharmaceutical.

While CZT detectors are not new, they were previously used in only a small number of Nuclear Medicine scanners, and not in a ring-detector configuration. Another important technological consideration, although this is not unique to the new scanners, is that they have a built in Computed Tomography (CT) scanner. CT scans are the workhorse of advanced medical imaging, providing assessment of anatomy in fine detail. By combining a Nuclear Medicine scanner with a CT scanner, this "hybrid imaging" provides simultaneous assessment of disease processes (Nuclear Medicine) and anatomy (CT), a powerful construct (Figure 2B).


**Figure 1. (A) QEII Nuclear Medicine technologists with the new StarGuide SPECT-CT scanner. (B) Two technologists prepare a patient for a scan, as viewed through the bore of the StarGuide. Note the ring of detectors (arrow pointing to one) in a ring configuration around the bore of the scanner, providing 3-D image acquisition.**

## FASTER SCANNING BRINGS MULTIPLE BENEFITS

Nuclear Medicine scans take a considerable amount of time to acquire, many close to a half hour, and some an hour or even more. With the StarGuide scan times are significantly reduced for many types of studies, due to the 2 major technological advances discussed above. The CZT detectors are more efficient than conventional detectors, creating images of comparable quality in significantly less time. Further, acquiring 3-D images shortens the overall scan time in some studies that traditionally would acquire both 2-D and 3-D images. Shorter scan times means patients better tolerate the scans, particularly patients with pain or claustrophobia. This also means there is less patient motion during the imaging, leading to better quality scans and therefore more accurate diagnoses. Finally, the shorter scan times means that more patients can be scanned in a day, which is critical in a time of limited health care resources including Nuclear Medicine technologist staffing. This in turn leads to shorter wait lists for these important scans.

## OVERALL PATIENT EXPERIENCE

In addition to less time in the scanner, patients often find the ring-detector configuration less claustrophobic than conventional scanners. At our centre, patients who have had scans on both types of scanners have stated they prefer their experience in the StarGuide. A further advantage is that, because of the greater sensitivity of the CZT detectors, a lower amount of radiopharmaceutical can be used, resulting in a lower radiation exposure to the patient, as well as to the Nuclear Medicine staff.

## MORE DIAGNOSTIC SCANS ACROSS A WIDE RANGE OF MEDICAL CONDITIONS

Ultimately the main purpose of the test is to obtain the most diagnostic scan possible, and that is achieved with the StarGuide. Greater sensitivity and 3-D imaging lead to more accurate diagnoses, made with greater confidence, across a wide variety of scans and disease states. At our centre the greatest change has been in bone scans obtained to assess the spread of cancer (metastases) to bone. These scans are now obtained fully in 3-D, with anatomic correlation through the simultaneous CT, resulting in a more diagnostic scan. With the additional detail they take more time for our Nuclear Medicine physicians to interpret them, but the improved accuracy in cancer assessment warrants it. Bone scans are also commonly obtained to assess more localized bone abnormalities such as fractures or infection, and the 3-D assessment is fast and precise.

In cardiac imaging, myocardial perfusion studies with $^{99m}$Tc-Sesta-MIBI have long made major contributions to the management of patients with known or suspected heart disease. Images obtained with the StarGuide are highly diagnostic, and obtained more quickly: these detailed heart assessments are particularly affected by patient motion during the scan, so the faster scan times are important. Highest level image quality is also obtained with $^{99m}$Tc-PYP scans used to diagnose a form of amyloidosis in the heart, reliably distinguishing activity in the heart muscle from activity in the blood pool.

The advantages of the new scanning paradigm have also been realized in lung Ventilation-Perfusion scans to assess for blood clots, a potentially fatal condition, and in $^{111}$Indium-labelled white blood cells scans to assess for infection. In neurology, very high-quality scans of brain perfusion are obtained with $^{99m}$Tc-HMPAO to assess epilepsy, and of dopamine transporters with $^{123}$I-ioflupane to assess for Parkinsonism. The neck is imaged in exquisite detail on StarGuide with $^{99m}$Tc-Sesta-MIBI to identify parathyroid adenomas in patients with hyperparathyroidism, with greater sensitivity than before, and there is more.

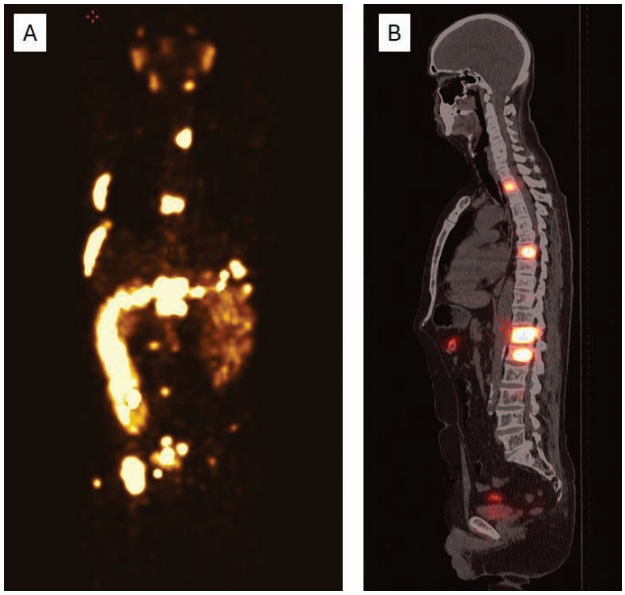



**Figure 2. StarGuide scan of a patient who underwent nuclear medicine therapy with $^{177}$Lu-PSMA (PluvictoTM) for prostate cancer 3 days earlier.**

**(A) Frontal view of the StarGuide scan demonstrates the distribution of the therapy within the body.**

**(B) Sagittal SPECT-CT cross-section through the midline of the body shows the delivered therapy radiopharmaceutical (yellow) in sites of prostate cancer in the spine. Patients undergo 6 such treatments each 6 weeks apart, and the scans provide accurate depiction of the delivered therapeutic, a unique capability in cancer care, allowing monitoring of the disease throughout treatment.**

***« Images obtained with the StarGuide are highly diagnostic, and obtained more quickly: these detailed heart assessments are particularly affected by patient motion during the scan, so the faster scan times are important. »***

*« Theranostics is a rapidly expanding field of Nuclear Medicine wherein molecules have been designed which bind to certain types of cancer and are labelled with radioisotopes that are then imaged in a scanner showing the distribution of the tumours throughout the body, or deliver treatment radiation to those tumours ("theranostics" = therapeutic + diagnostic). »*

## NEW APPLICATIONS: CORONARY FLOW RESERVE

So far we have reviewed the advantages the StarGuide has brought to existing Nuclear Medicine tests. However, the state-of-the-art technological advances also bring new capabilities. This includes the measurement of coronary flow reserve. This is an adjunct to the well-established myocardial perfusion studies performed with $^{99m}$Tc-Sesta-MIBI mentioned above. Although uncommon, a limitation of the existing studies is an underestimation of heart disease through visual assessment alone in patients with widespread coronary artery disease. CZT scanners can perform a flow reserve analysis in these patients, effectively detecting and quantifying such multi-focal disease, a further contribution of the new technology.

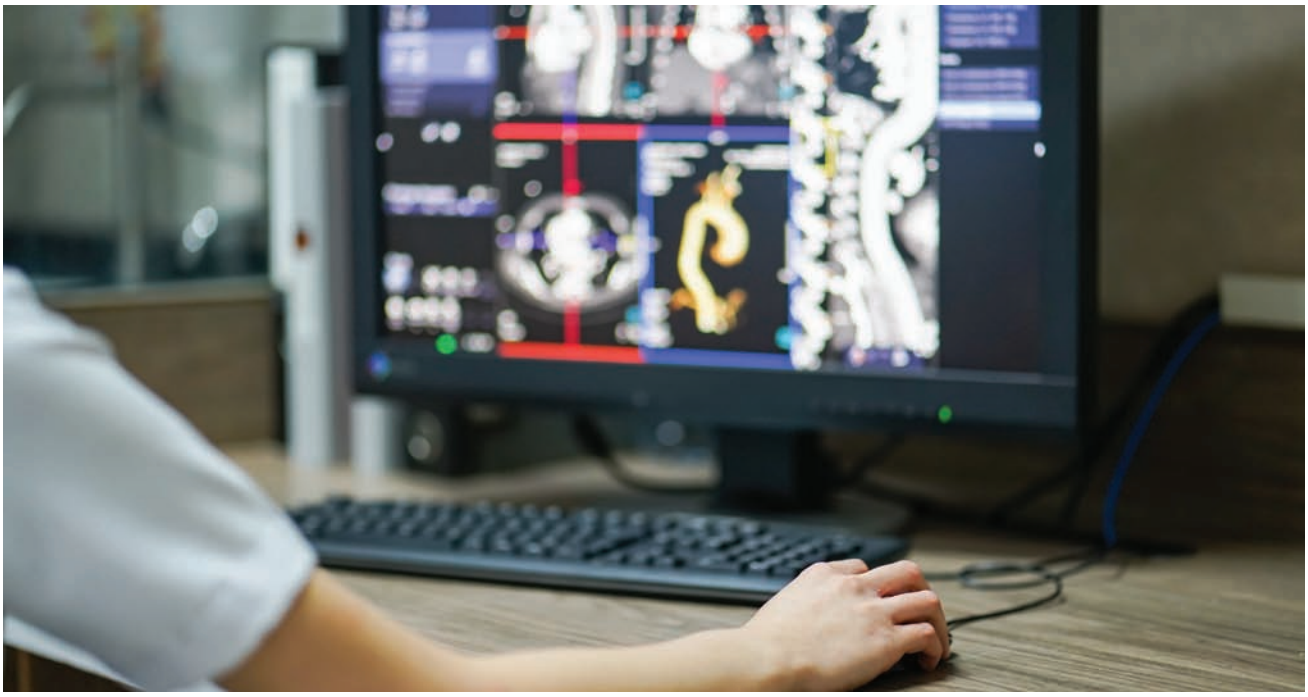
## PUSHING THE BOUNDARIES: THERANOSTICS

Theranostics is a rapidly expanding field of Nuclear Medicine wherein molecules have been designed which bind to certain types of cancer and are labelled with radioisotopes that are then imaged in a scanner showing the distribution of the tumours throughout the body, or deliver treatment radiation to those tumours ("theranostics" = therapeutic + diagnostic). Recent radiopharmaceutical cancer treatments include Lutathera™ for neuroendocrine tumours and Pluvicto™ for prostate cancer. This paradigm has proven so effective that many more theranostic radiopharmaceuticals are under development for other cancers. The therapeutic dose of these treatments is accurately imaged with the StarGuide hours or days after it has been administered in the patient, depicting the distribution of the treatment in tumour sites within the body, a unique and powerful concept in cancer treatment. This allows confirmation that the treatment has gone to all sites of known disease, and monitoring of the disease throughout the course of therapy (Figure 2). The technological advances of the new breed of scanners does this accurately and efficiently, in many cases better than with conventional scanners. It also facilitates dosimetry, calculating how much of the therapeutic radiopharmaceutical goes to each tumour site and to normal tissue, which is exploited in some centres to deliver patient-individualized doses, a form of personalized medicine.

In our centre our Interventional Radiology team treats liver tumours with Therasphere™, glass microspheres labelled with radioactive $^{90}$Yttrium delivered through a catheter in an artery to the liver. To ensure it will be safe to deliver the planned dose, a mock treatment is performed in advance, injecting a non-therapeutic radiopharmaceutical $^{99m}$Tc-MAA. The patient is then imaged in the StarGuide scanner to assess whether the tracer has gone to organs which might be damaged when the treatment dose is administered. As with the other theranostics discussed above, accurate quantitative measurements with the StarGuide can contribute to individual patient dosimetry.

## CONCLUSION

The new breed of scanners has revolutionized the imaging of many diseases, with accurate and more efficient imaging leading to better patient care and a more effective use of health care resources. Along with recent major advancements in the other pillars of Nuclear Medicine, PET and radioisotope therapies, the new scanners are solidifying Nuclear Medicine as a state-of-the-art, impactful, specialty contributing to best patient care. ■



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**Yuting Zhao, Yaqi Zheng, Xiaoli Zhang, MD, PhD*.**
Department of Nuclear Medicine, Molecular Imaging Lab, Beijing Anzhen Hospital, Capital Medical University, Beijing, China

# CLINICAL APPLICATIONS AND ADVANCES OF PET/CT IN CARDIOLOGY

## INTRODUCTION

Positron Emission Tomography/Computed Tomography (PET/CT) has emerged as a cornerstone of precision medicine in cardiovascular disease, offering unparalleled insights into myocardial physiology and pathology, including myocardial perfusion, metabolism, and viability. By integrating functional PET imaging with anatomical CT data, PET/CT enables precise diagnosis, risk stratification, and evidence-based therapeutic decision-making for complex cardiovascular diseases.

## PET/CT MYOCARDIAL BLOOD FLOW QUANTIFICATION: FROM DIAGNOSIS TO PROGNOSIS

*« By integrating functional PET imaging with anatomical CT data, PET/CT enables precise diagnosis, risk stratification, and evidence-based therapeutic decision-making for complex cardiovascular diseases. »*

PET/CT enables absolute quantification of myocardial blood flow (MBF) and myocardial flow reserve (MFR) using low-dose and short half-life radiotracers. Compared to SPECT, PET/CT offers superior spatial resolution, enhancing detection of myocardial ischemia in patients with microvascular disease, balanced multivessel disease and obesity (Figure 1). Therefore, it is highly effective in diagnosing and ruling out coronary artery disease (CAD). 2019 European Society of Cardiology (ESC) guidelines on chronic coronary syndromes underscore the evidence of myocardial ischemia for treatment strategy of revascularization and optimal medical therapy, recommending non-invasive functional imaging to detect myocardial ischemia. However, the widespread adoption of PET myocardial perfusion imaging is constrained by technical requirements, high costs for onsite cyclotron, and the necessity for skilled professionals. Clinicians must balance clinical likelihood of CAD, patient characteristics, technical availability, and cost-effectiveness when selecting non-invasive functional imaging techniques.

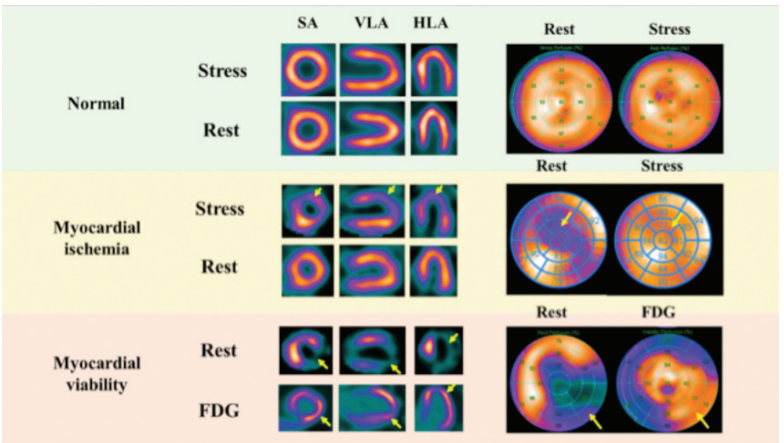



**Figure 1. Typical imaging of normal myocardium, myocardial ischemia, and myocardial viability.**

## MYOCARDIAL VIABILITY ASSESSMENT: FROM MECHANISMS TO CLINICAL DECISION-MAKING

In pathophysiology, myocardial viability refers to those cardiomyocytes that are "alive", characterized by the maintained metabolism activity in dysfunctional myocardium at rest. In a clinical context, viability is defined as perfusion reduction but normal or high myocardial glucose metabolism activity, which has the potential for functional recovery once restoration of coronary blood flow supply. Both hibernation and stunning are the primary subdivisions of viable myocardium, each exhibiting distinct yet overlapping characteristics. $^{18}$F-FDG PET/CT myocardial metabolism imaging is an established technique, and is recognized as the "gold standard" for noninvasive diagnostic myocardial viability. This modality identifies viable myocardium by revealing a characteristic perfusion-metabolism mismatch pattern, which shows reduced perfusion alongside preserved glucose metabolism for energy supply (Figure 1). Furthermore, gated cardiac PET/CT imaging allows for simultaneous multiparametric functional evaluation, including global function (end systolic volume, diastolic volume, left ventricular ejection function), regional ventricular wall motion and wall thickening, and mechanical dyssynchrony.

Substantial evidence demonstrated that coronary revascularization combined with optimal medical therapy may improve left ventricular (LV) function, heart failure symptoms and long-term outcomes in patients with ischemia cardiomyopathy and myocardial viability (Figure 2). This establishes viability assessment as a crucial determinant in therapeutic decision-making for ischemic cardiomyopathy. Although landmark trials such as PARR-2, STICH, and REVIVED-BCIS2 failed to establish universal benefits of viability-guided revascularization, some subgroup analyses suggest that ischemic cardiomyopathy patients with more than 10% of viable myocardium may benefit from revascularization. Consensus statements from the American Heart Association and the European Association of Cardiovascular Imaging continue to endorse this approach clinically.

Notably, therapeutic decision-making strategy and prognosis in patients with ischemic cardiomyopathy and heart failure with reduced ejection fraction should integrate factors such as ischemic burden, scar burden, degree of LV remodeling, the presence of comorbidities (e.g., severe arrhythmias, significant valvular heart disease), and multivessel disease. Future investigation should focus on developing multivariate predictive models to enhance the precision of PET/CT-guided personalized therapy.

## $^{18}$F-FAPI PET/CT: A NOVEL PERSPECTIVE IN CARDIOVASCULAR MOLECULAR IMAGING

Fibroblast activation protein (FAP), a type II transmembrane serine protease with dipeptidyl peptidase and endopeptidase activities. FAP is overexpressed by activated fibroblasts in damaged myocardium, where its expression levels can vary significantly. This characteristic allows molecular probes targeting FAP to exhibit low background signals and high target-to-non-target contrast, demonstrating considerable potential for diagnosis and treatment of cardiovascular diseases. Consequently, fibroblast activation protein inhibitor (FAPI) labeled with radiotracers, such as fluorine 18 ($^{18}$F), can be utilized for non-invasive visualization of activated fibroblasts in different pathologies in patients with cardiovascular disease.

Following an acute myocardial infarction, $^{18}$F-FAPI PET/CT quantifies myocardial fibroblast activation, which can predict adverse LV remodeling and long-term outcomes though the mechanism is not very clear and warrant further investigation. $^{18}$F-FAPI PET/CT can also detect early cardiac damage caused by chemotherapeutic agents or immune checkpoint inhibitors, thereby aiding in treatment optimization. Furthermore, in patients with hypertrophic cardiomyopathy, $^{18}$F-FAPI PET/CT can evaluate myocardial fibrosis, offering critical information for risk stratification. Additionally, $^{18}$F-FAPI PET/CT demonstrates unique value in assessing disease activity and monitoring treatment response in vasculitis.

## WHOLE-BODY PET IMAGING

### Atherosclerotic Plaque Imaging

Novel tracers such as $^{18}$F-NaF, $^{68}$Ga-DOTATATE, and $^{68}$Ga-pentixafor target plaque microcalcification or chemokine receptors, quantifying plaque uptake activity to assess plaque vulnerability and predict cardiovascular events. A clinical role for molecule-targeted plaque imaging has not yet been established, highlighting the need for further investigation with combination of molecular imaging and therapy of vulnerable atherosclerosis.

### Large-Vessel Vasculitis and Aortic Pathologies

For Takayasu or giant cell arteritis, $^{18}$F-FDG PET/CT not only aids in assessing disease activity and the extent of vascular involvement but also monitors treatment response by quantifying changes in FDG uptake activity. Aortic aneurysm and dissection have also become targets for molecular imaging, focusing on microcalcification or inflammatory activity, which may predict disease progression and complications, as well as guide endovascular repair.

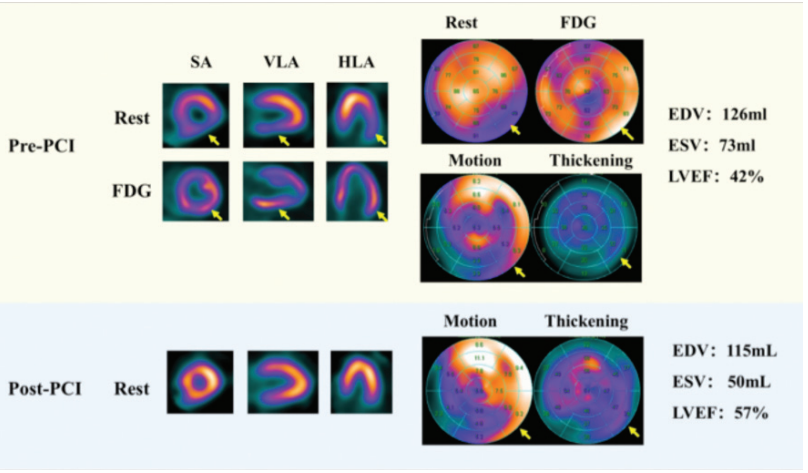



**Figure 2. Evaluation the therapeutic effects in patients with coronary heart disease treated by percutaneous coronary intervention (PCI). EDV, end-diastolic volume; ESV, end-systolic volume; LVEF, left ventricular ejection fraction.**

### Other Applications

In patients with cardiac sarcoidosis, PET/CT can detect areas of active inflammation by visualizing the increased myocardium FDG uptake activity, thereby for diagnosis and monitoring treatment response. PET/CT molecular imaging has important value in patients with cardiac tumor and pulmonary artery sarcoma, which may precede structural changes detecting by other imaging modalities. Additionally, PET/CT helps identify regions of metabolic abnormality in patients experiencing chemo-therapeutic cardiotoxicity or radiation-induced cardiac injury.

## CONCLUSIONS AND FUTURE PERSPECTIVES

In summary, PET/CT integrating both anatomical and functional information offers a novel approach and optimize the entire workflow of diagnosis, risk stratification, evaluation therapeutic effects, and prognosis assessment. Advances in artificial intelligence further enhance the diagnostic capabilities. Additionally, progress in radio-pharmaceuticals and molecular imaging supports targeted imaging and therapies, ensuring that the appropriate treatment strategy reaches the right patient at the right time. As multimodal imaging and precision medicine evolve, PET/CT will remain as the forefront of innovation in precision cardiovascular medicine. ■

*« Advances in artificial intelligence further enhance the diagnostic capabilities. Additionally, progress in radio-pharmaceuticals and molecular imaging supports targeted imaging and therapies, ensuring that the appropriate treatment strategy reaches the right patient at the right time. »*


**John Lebland,** MD, FRCPC, FASNC, CCD

# THE NUCLEAR MEDICINE SERVICE AT THE CHALEUR REGIONAL HOSPITAL

*« We offer the full range of conventional Nuclear Medicine diagnostic and therapeutic services to our population and occasionally to other patients referred within our health authority, the Vitalite Health network, which primarily serves the Acadian population. »*

The Nuclear Medicine Service at the Chaleur Regional Hospital is situated in Bathurst, New Brunswick, at the base of the beautiful Bay of Chaleur, nestled between the Gaspe and Acadian Peninsulas where fresh seafood and great people are plentiful. Our region is a haven for outdoor activities and quality of life. Our department has historically been one of the busiest in the province serving most of northern New Brunswick as well as part of the Matapedia region of Quebec. We offer the full range of conventional Nuclear Medicine diagnostic and therapeutic services to our population and occasionally to other patients referred within our health authority, the Vitalite Health network, which primarily serves the Acadian population.

We currently have 2 functional gamma cameras (GE cardiac 530 and a GE 670 SPECT-CT) as well as GE lunar BMD unit whereas a third unit, a GE StarGuide, the second bought in Canada in December 2023 to replace an inoperative, obsolete system, is currently being stored at our facility awaiting to be installed.
Our team has always been in the forefront of innovation and seeks to offer our population the latest state of the art technology and studies. We strive that all our examinations are performed to the highest of standards; at the suggestion of one of our technologists, our department undertook and completed the OAR Canadian Bone Densitometry Facility Accreditation Program, becoming the first site east of Ontario to do so.

Some of the following are some of the enhancements we have made to the conventional NM studies we perform:

## CARDIAC STUDIES

Myocardial perfusion studies have over the past few years come under increased competition from other imaging modalities; with the goal of remaining relevant, our department has embraced new technologies and protocols to provide added value to our studies.

Under the crucial guidance of Drs Terrance Ruddy and Glenn Wells at the University of Ottawa Heart Institute (1), our department has been able to offer our population myocardial flow reserve evaluations on a good portion of our myocardial prefusion studies performed on our dedicated GE 530 CZT system. Our chief technologist was able to incorporate the Ottawa Heart Institute's protocols with those of Dr. Mathieu Bailly at the CHUM in Orleans, France (2). This has allowed us to identify high risk patients (left main or multi-vessel disease), provide important prognostic information and to distinguish between obstructive and non-obstructive coronary artery disease. It has also allowed us to single out dipyridamole non-

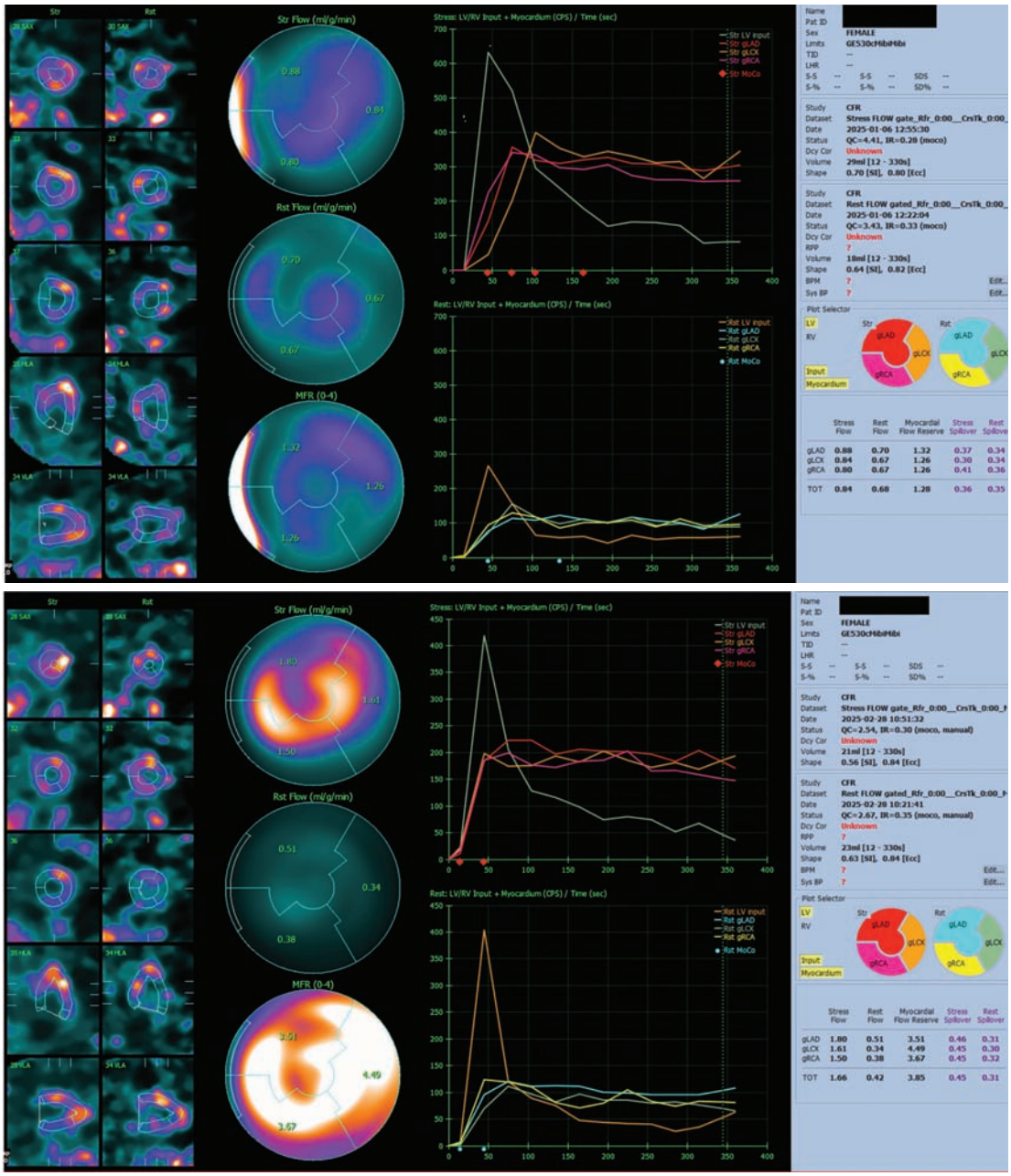



**Figure 1**
**65 year old female with previous history of STEMI in 2022, referred for positive troponins and chest pains. No significant perfusion defects were seen on the Dipyridamole stimulated myocardial perfusion study which showed acceptable BP (137/84 to 123/68)) and heart rate (93 to 101 bpm) changes suggestive of a good pharmacologic response. The myocardial flow reserve (MFR) values were however very attenuated (global MFR 1.19). The study was repeated 2 weeks later under Dobutamine stimulation which showed normal global MFR values at 3.85.**

responders or patients that did not adhere to their caffeine-free preparation as well as to spot potential CMD in patients with INOCA or ANOCA (3,4) (figure 1). Patients also appear to enjoy the convenience of having to spend just over an hour under the camera for a complete MPI-MFR study as opposed to 2-3 hours in our department for a conventional MPI study.

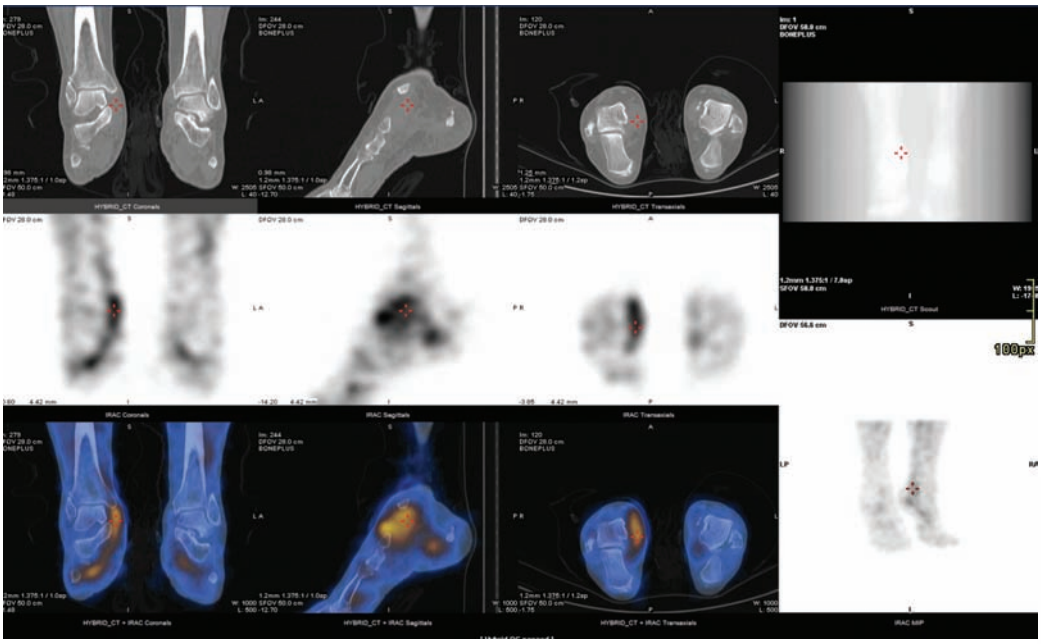
To our knowledge, we are one of the very few if not the only department in our province to adhere to the ASNC 2010 goals of reducing patient exposure during myocardial perfusion studies while maintaining an increased throughput on our system. When it was available, we were fervent users of Tl-201 in selected patients (standard dose administered 0.5- 0.7 mCi).

When indicated, we perform coronary calcium scoring to our referred patients.

**RAPID SPECT- CT BP STUDIES**

We have been performing Rapid SPECT-CT blood pool studies since 2019. Our first case involved a young woman referred for foot pain for which an occult stress fracture was suspected; late planar and SPECT images were normal. The Rapid SPECT-CT BP study was diagnostic and showed severe soft tissue activity at the level of the peroneus brevis tendon, the site of her pain.

To date, we have performed hundreds of these studies; we have been incorporating this technique not only when performing bone scans for evaluations of occult fractures, infection and inflammation but also on patients with painful orthopedic implants and in those with occult GI bleeding. Other than increasing the sensitivity, specificity and diagnostic yield of our studies, Rapid SPECT-CT BP acquisitions



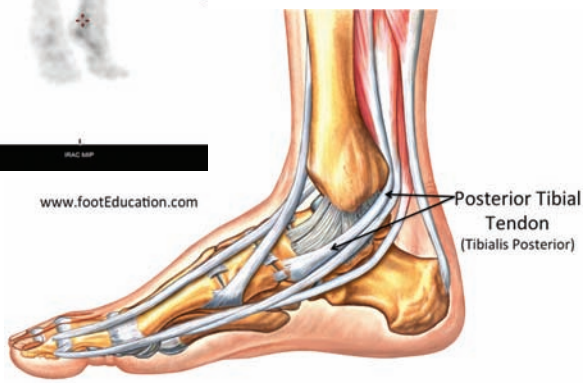



**Figure 2**
**57 year old female with pain in the medial aspect of the right ankle. The flow and post-flow portions of the bone scan showed slight increased vascularisation and hyperemia at the level of the medial malleolus region of the right ankle. A rapid BP SPECT-CT however showed significant hyperemia at the level of the tibialis posterior and flexor dig. longus tendons and their common sheaths. Late bone scan images were normal.**

improve localization of the underlying pathology, enhances diagnostic confidence all within an acceptable imaging time frame (5). Being able to combine a CT to an otherwise anatomy poor BP pool SPECT has opened for us a new imaging frontier (figures 2,3).

*« Our department was the second in Canada to acquire the GE StarGuide in 2023 to bolster our imaging program; it is unfortunately in storage awaiting room renovations. This new unit will allow our department to offer our population faster innovative studies with an emphasis on patient comfort, dose reduction, speed and multiple energy window acquisitions. »*

## EVALUATION OF FUNCTIONAL GASTRO-INTESTINAL DISEASE (FGIDS)

Functional gastrointestinal disorders (FGIDs) are a group of conditions characterized by chronic symptoms without demonstrable pathology, often involving altered gut sensitivity, motility and brain-gut communication. The diagnosis of FGIDs is often challenging as conventional structural tests (endoscopy, blood tests, radiology) are often negative and frequently repeated when the patient re-consults. Furthermore, different FGID conditions may have similar clinical presentations whereas several conditions may be present in the same patient.

Nuclear Medicine does have a role to play in the evaluation of FGIDs but requires enhancing the pre-test probability for each condition and following a proper diagnostic algorithm; we accomplish this by incorporating the Rome IV criteria (6). Depending on the condition being evaluated (Functional dyspepsia, Hepato-biliary dysfunction, motility disorders), we perform C-14 Urea Breath tests, single or double isotope gastric emptying (with or without whole gut scintigraphy) as well as hepato-biliary studies with CCK. We have also developed and perform gastric accommodation studies. We have been cataloging our NM GI studies since 2018 with the goal of gaining insight into the strengths and limitations of our studies and how to better utilize them in the diagnostic algorithm for the investigation of these disorders.

## WHOLE-BODY SPECT AND QUANTIFICATION

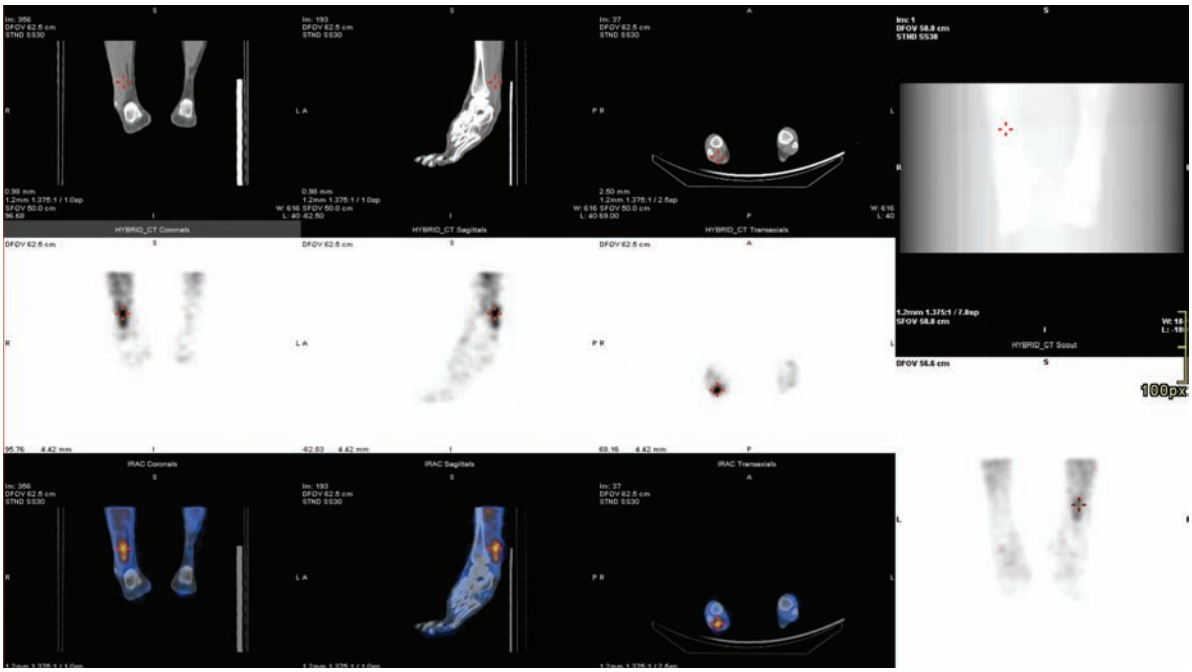
Whole-body bone SPECT studies for oncology workups have been the standard in our department since 2008; when indicated, we have over the years gradually incorporated low dose CT anatomic correlation and quantification (SUVs) to our studies which we have found to be useful in following the evolution of malignant, infectious and orthopedic processes over time. As per our department philosophy, we have done this with an eye on the future to position ourselves for the age of theranostics and PET imaging.

## STARGUIDE

Our department was the second in Canada to acquire the GE StarGuide in 2023 to bolster our imaging program; it is unfortunately in storage awaiting room renovations. This new unit will allow our department to offer our population faster innovative studies with an emphasis on patient comfort, dose reduction, speed and multiple energy window acquisitions. The StarGuide is expected to make our department more efficient and cost-effective while being the catalyst for next wave of development and innovations.

## THERANOSTICS

Historically, our department has been a leader in our province for the various theranostic therapies of the thyroid and painful bone metastases. Like many departments in Canada, we have been preparing and positioning ourselves to be able to offer our



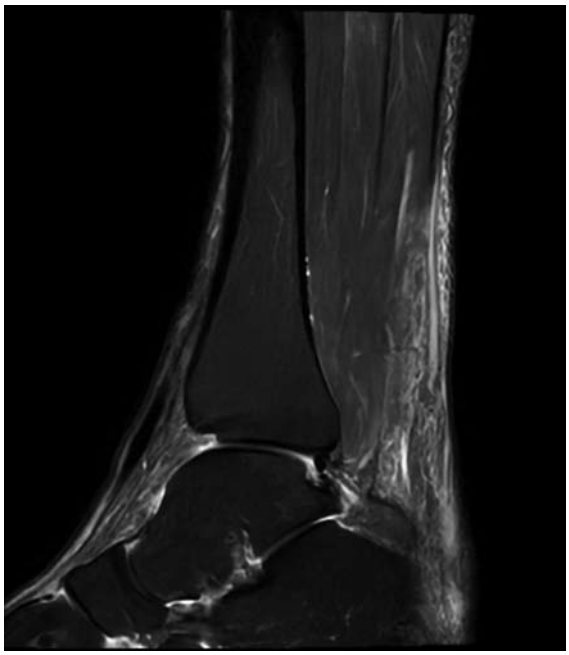


**Figure 3**
**46 year old female runner was referred for episodes of cellulitis and swelling at the level of the lateral malleolus of the right ankle despite repeat antibiotic therapy. A bone scan was performed to rule out underlying osteomyelitis. A rapid BP SPECT-CT showed very significant hyperemia at the level of the distal right Achilles tendon. Late bone scan images were normal. A subsequent MRI study of this region showed diffuse fatty infiltration around the Achilles tendon consistent with an Achilles tendinopathy in the absence of any obvious associated tear.**

population base the next chapter of innovative diagnostics and treatments, all this while advocating Nuclear Medicine's mandatory and critical role in the theranostic multidisciplinary treatment team in which certified trained NM specialists and technologists take center stage (7).

Like all Nuclear Medicine departments in Canada, we suffer from the same radiopharmaceutical, personnel and equipment issues which limits timely access to our services. For the longest time, Nuclear Medicine in New Brunswick was considered an offshoot of Radiology with only the departments in the northern regions being staffed by certified nuclear medicine specialists. Recently however, there has been an influx of several dual trained specialists in other departments, enhancing and strengthening our community. Our department will continue striving to be in the forefront of our field, harnessing the talents and resiliency of all our members to offer enhanced innovative care to our service population. ■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# A NEW AND PROMISING THERANOSTIC AGENT: FAPI

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According to the Canadian Cancer Society, 247,100 new cases of cancer were diagnosed in Canada only in 2024, and 88,100 people died from cancer. These statistics highlight the importance of research and development of new therapies for each cancer to reduce the associated mortality rates and improve the survival of patients with cancer. For nearly two decades, various radioligand therapies have been developed in nuclear medicine, such as $^{68}$Ga/$^{177}$Lu-Dotatate (targeting gastroenteropancreatic neuroendocrine tumors) and $^{68}$Ga/$^{177}$Lu-PSMA (targeting metastatic prostate cancer). These theranostic agents have the advantage of being able to image the targeted cancer with PET/CT and treat the same imaged cancer with an intravenous radioactive treatment that will precisely target the cancer cells with very few side effects on healthy cells. Since 2018, a promising new theranostic agent for PET imaging and the treatment of new cancers has been developed: FAPI, which stands for fibroblast activation protein inhibitor.

## WHAT IS FAPI?

Several types of cancer originate in different cell layers that line the various tissues and organs of the body, called carcinomas. For example, if the cancer cells that develop originate in the breast, this cancer will be called breast carcinoma, whereas if the cancer cells originate in the lung, the cancer will mostly be lung carcinoma. Of course, there are also several more specific subtypes of carcinomas by organ. Generally, cancer is characterised by an uncontrolled cell replication following damage to its DNA and by poor or absence of DNA repair, thus causing this newly cancerous cell to grow into a cancer, or carcinoma.

Fibroblasts are a type of cell present in the various tissues and organs of the body, overexpressed in very large numbers in the muscles. It is understandable that cancer-associated fibroblasts (CAFs) can be carcinomas. More than 90% of cancers are carcinomas, and CAFs are present in many of these cancers. When fibroblasts are inactive, they do not cause any harm, as seen in normal muscles. However, when activated by a pathological process like cancer does, these activated fibroblasts produce a protein that enables the abnormal fibroblast to develop into a cancerous mass. This protein is called fibroblast activation protein (FAP). It is to this same protein that FAPI binds to as a theranostic agent, enabling PET imaging and cancer treatment in nuclear medicine (Figure 1).

*« Since 2018, a promising new theranostic agent for PET imaging and the treatment of new cancers has been developed: FAPI, which stands for fibroblast activation protein inhibitor. »*

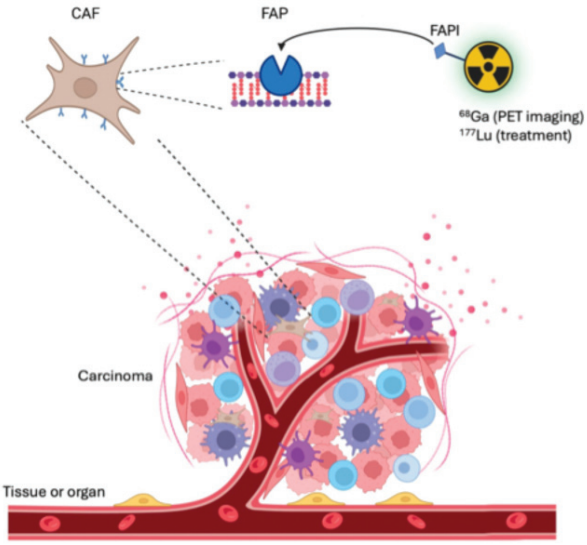


**Figure 1. Mechanism for FAPI binding to the CAFs.** Most carcinomas are rich in fibroblasts, a type of cell in the body (beige cell with blue receptors on the surface of the cell membrane). These carcinomas are CAFs because the fibroblasts that make up these cancers are activated and express FAP (blue receptor) on the surface of the cancer cell membranes. To be able to image these cancers by PET/CT and treat them in nuclear medicine, a FAPI has been developed in the laboratory and is bound to a radioisotope that emits radioactivity. Depending on the rays emitted by the chosen radioisotope, $^{68}$Ga-FAPI will produce PET/CT images of the cancer and $^{177}$Lu-FAPI will be able to treat the imaged cancer.

Image: Privé BM, Boussihmad MA, Timmermans B, et al. Fibroblast activation protein-targeted radionuclide therapy: background, opportunities, and challenges of first (pre)clinical studies. Eur J Nucl Med Mol Imaging. 2023;50(7):1906-1918.

## $^{68}$GA-FAPI PET/CT

Thanks to FAPI, it is possible to image the CAFs by binding to the FAP present on the surface of the cancer cells (Figure 1). FAPI being bound to a specific radioisotope, gallium-68 ($^{68}$Ga), which emits rays that make it possible to capture an image. The radioactivity emitted by $^{68}$Ga is captured by PET/CT (Figure 2). The integrated CT is used for anatomical imaging and localization. The anatomical images obtained by CT help the nuclear medicine physician to precisely localize the cancer and metastases, which are seen as intense uptake foci on PET imaging (Figure 3). $^{68}$Ga has a short half-life, ideal for examinations lasting less than two hours. This means

that the patient has almost no radioactivity left in his body when the $^{68}$Ga-FAPI PET/CT is completed, and he leaves the clinic. The radioisotope is injected intravenously in liquid form prior to the PET/CT imaging. It is important to know that $^{68}$Ga-FAPI is not iodinated contrast media (ICM). Patients known to be allergic to ICM can therefore have this test without any concern, but some centers may indeed use intravenous ICM to enhance contrast in the vascular compartment on anatomical images of the CT component. If known for ICM allergies, PET/CT will be performed without an intravenous ICM, and is therefore not a contraindication to the test. In addition, although 68Ga-FAPI is eliminated by the kidneys, renal impairment of any grade is also not a contraindication to $^{68}$Ga-FAPI PET/CT.

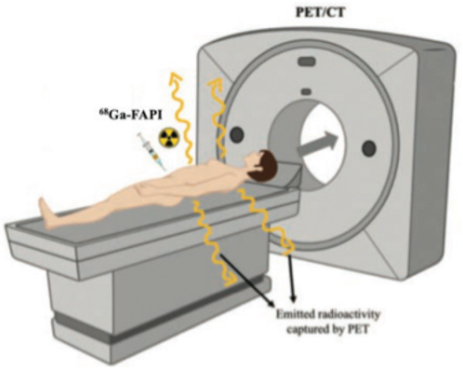


**Figure 2. PET/CT imaging.**

The radioactivity emitted by the radioisotope $^{68}$Ga bound to FAPI is captured by PET/CT, enabling images to be obtained. $^{68}$Ga-FAPI is injected 10 to 60 minutes prior to PET/CT imaging. Most centers acquire images 60 minutes after the injection, but images obtained 10 minutes after the injection allow a quality diagnosis. As there are several different PET radiotracers, it is more practical for departments to make images at 60 minutes, like other PET radiotracers (e.g. $^{68}$Ga-PSMA and $^{18}$F-FDG). The patient lies under the camera for less than 20 minutes.

As shown in Figure 3, CAFs in gastric carcinomas are rich in FAP, and there is very intense cancer uptake with $^{68}$Ga-FAPI. This corresponds to the presence of high levels of radioactivity ($^{68}$Ga) bound to FAPI in CAFs.

As previously mentioned, it is normal to see radioactivity in muscles and urinary tracts, due to the presence of non-activated fibroblasts and the rapid elimination of radioactivity, respectively. This low or even non-existent uptake in other organs makes FAPI very attractive.

### $^{18}$F-FDG PET/CT

$^{18}$F-FDG is the most widely used radiotracer in PET oncology and has been in use for over 20 years. One of the problems encountered with $^{18}$F-FDG is that it sometimes does not show up very well in certain types of cancer (Figure 3).

As $^{18}$F-FDG is sugar that is radioactive ($^{18}$F), some types of cancer cells do not eat the sugar, making it difficult to image the cancer with $^{18}$F-FDG PET/CT. In these specific clinical cases, $^{68}$Ga-FAPI PET/CT is a relevant complementary imaging test that allows for a more accurate diagnosis and assessment of the extent of the disease. $^{68}$Ga-FAPI PET/CT does not replace $^{18}$F-FDG PET/CT, but it is a very useful complementary tool when available.

### WHO IS ELIGIBLE FOR A $^{68}$GA-FAPI PET/CT?

All patients known with a cancer in centers where $^{68}$Ga-FAPI is available. Table 1 shows a summary of cancers that have intense uptake of $^{68}$Ga-FAPI. Certain types of cancer, such as thyroid cancer, multiple myeloma, and lymphoma, have relatively low uptake on $^{68}$Ga-FAPI PET/CT, but $^{18}$F-FDG PET/CT is better for these three types of cancer.

***« These theranostic agents have the advantage of being able to image the targeted cancer with PET/CT and treat the same imaged cancer with an intravenous radioactive treatment that will precisely target the cancer cells with very few side effects on healthy cells. »***

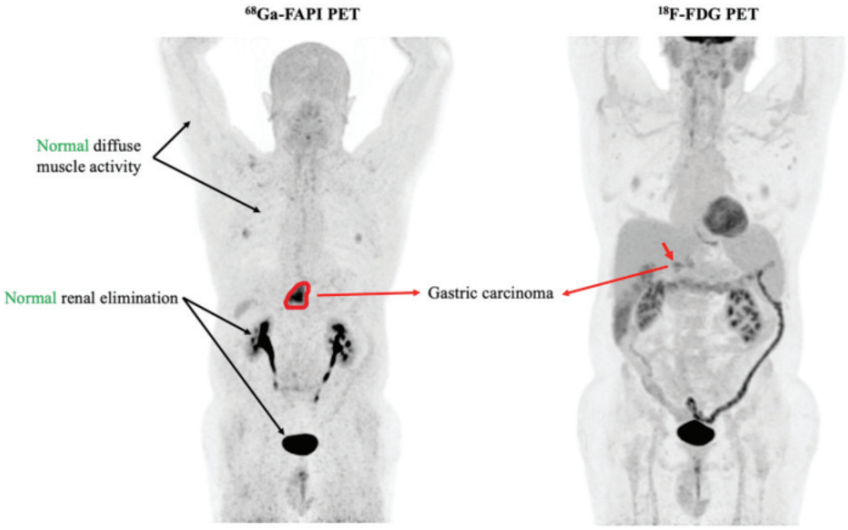


**Figure 3. Gastric carcinoma imaged with $^{68}$Ga-FAPI PET vs. $^{18}$F-FDG PET.**
The image on the left shows gastric carcinoma (red circle) imaged with $^{68}$Ga-FAPI PET. The cancer shows as intense black foci of uptake, indicating that it is highly FAP-positive. Furthermore, as there are normal, non-activated fibroblasts in the muscles, the image on the left shows very low diffuse muscle uptake. Significant activity can also be seen in the kidneys and bladder, as $^{68}$Ga-FAPI is eliminated from the body via the kidneys and urine. The image on the right shows the same gastric carcinoma (red arrow), but imaged using $^{18}$F-FDG PET, the most used PET radiotracer. $^{18}$F-FDG is radioactive glucose that is absorbed by many cancers. This image highlights the added value of $^{68}$Ga-FAPI PET for more accurate diagnosis of certain cancers.

*« Radioligand therapy with $^{177}$Lu-FAPI can be administered on an outpatient or inpatient basis. This depends on the regulations of each country. In Canada, this treatment can be administered on an outpatient basis. The patient arrives at the nuclear medicine department to receive their dose of $^{177}$Lu-FAPI, which takes between 1 and 30 minutes, and then returns home to isolate themselves for 48 hours in accordance with Canadian radiation protection rules. »*

**Table 1: Cancers and malignant presentations with $^{68}$Ga-FAPI uptake**

| |
|---|
| **Glioblastoma** |
| **Head and neck cancers** |
| **Lung cancer** |
| **Breast cancer** |
| **Pancreas cancer** |
| **Cholangiocarcinoma** |
| **Peritoneal carcinomatosis (all cancers)** |
| **Ovarian cancer** |
| **Bladder cancer** |
| **Prostate cancer** |
| **Sarcomas** |
| **Oesophageal cancer** |
| **Gastric cancer** |
| **Colorectal cancer** |

$^{68}$Ga-FAPI PET/CT is not widely available. Several countries already use it routinely in clinical research, including in Europe, Asia, and the United States of America. However, $^{68}$Ga-FAPI is not used routinely in clinical practice as it is still being studied, given that it is a recent PET radiotracer (2018), as is the case in Canada.

## RADIOLIGAND THERAPY WITH $^{177}$LU-FAPI

Radioligand therapy with $^{177}$Lu-FAPI is an intravenous treatment used in nuclear medicine for the treatment of metastatic CAFs (Table 1) that strongly express FAP, previously imaged by PET/CT with $^{68}$Ga-FAPI. One of the major differences between PET/CT and the treatment is that FAPI is bound to a long-half-life radioisotope, lutetium-177 ($^{177}$Lu), enabling radioactivity to be delivered to metastases over a longer period.

Compared to $^{68}$Ga (half-life of 68 minutes), $^{177}$Lu has a half-life of 6,5 days. The mechanism binding the radioisotope to cancer cells for $^{177}$Lu-FAPI and $^{68}$Ga-FAPI is the same (Figure 1). By giving several cycles of $^{177}$Lu-FAPI spaced at a given time interval of approximately 4 weeks, it is possible to achieve a significant response and disease control in metastatic CAFs. As radioactivity is distributed locally to metastases, side effects are few and treatment is generally well tolerated.

The most common side effects are fatigue and mild abdominal tenderness. They occur within the first 48 hours and are dure to acute radiation syndrome; they disappear after 1-2 weeks. The $^{177}$Lu is an attractive radioisotope, because in addition to treating metastases CAFs with β- emission, it also emits ɣ-rays. These ɣ-rays can be imaged using scintigraphy and SPECT (single photon emission computed tomography), and the images show where the $^{177}$Lu-FAPI treatment is distributed throughout the body (Figure 4). Post-treatment scintigraphy with $^{177}$Lu-FAPI is performed from hours to a few days after receiving an injection. This scintigraphy is used to monitor therapy response.

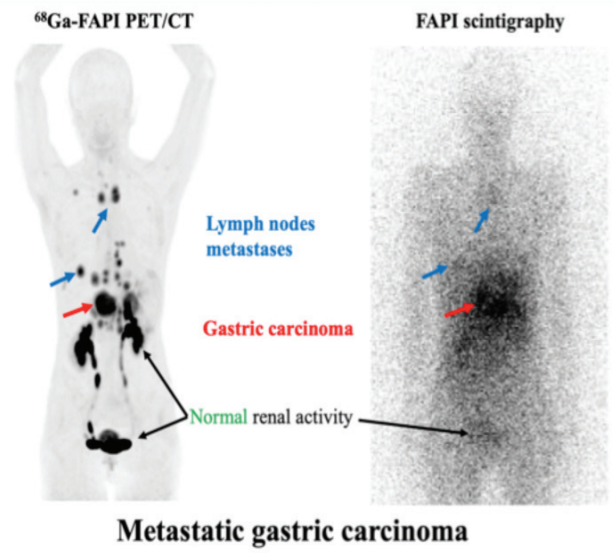


**Figure 4.**
**Metastatic gastric carcinoma imaged with $^{68}$Ga-FAPI PET/CT and post-treatment FAPI scintigraphy.**

The image on the left shows gastric carcinoma (red arrow) with multiple lymph node metastases (blue arrows) in the thoracic and abdominal regions on $^{68}$Ga-FAPI PET/CT. The gastric carcinoma and its lymph node metastases show very intense uptake of $^{68}$Ga-FAPI, making the patient a good candidate for radioligand therapy with $^{177}$Lu-FAPI.

The image on the right shows the patient's first post-treatment FAPI scintigraphy, showing the gastric carcinoma (red arrow) and some thoracic and abdominal lymph node metastases (blue arrows).

Radioligand therapy with $^{177}$Lu-FAPI can be administered on an outpatient or inpatient basis. This depends on the regulations of each country. In Canada, this treatment can be administered on an outpatient basis. The patient arrives at the nuclear medicine department to receive their dose of $^{177}$Lu-FAPI, which takes between 1 and 30 minutes, and then returns home to isolate themselves for 48 hours in accordance with Canadian radiation protection rules.

However, as radiation acts over a longer period, the patient must follow a few additional precautions to

limit radiation exposure of those around him. For example, as $^{177}$Lu-FAPI is eliminated in the urine, sitting urination and flushing the toilet twice are recommended to contain radioactivity to a minimum for 48 hours.

Radioligand therapy with $^{177}$Lu-FAPI consists of four cycles spaced four weeks apart. The dose administered is a standard dose of 7,4 MBq of $^{177}$Lu-FAPI every cycle. Side effects are rare, but blood samples are taken every 2-4 weeks to ensure the absence of significant bone marrow toxicity (anemia, reduced immune system, excessive bleeding). These side effects occur in less than 5%. During blood tests, the renal function is checked to ensure that there is no renal insufficiency, which could impair the elimination of $^{177}$Lu-FAPI.

Radioligand therapy with $^{177}$Lu-FAPI is still in its early stages, mainly used in clinical research in Germany for less than five years. Currently, radioligand therapy with $^{177}$Lu-FAPI is reserved for metastatic CAFs that have progressed despite several lines of treatment and when no other treatment is available. Table 2 shows the eligibility criteria for $^{177}$Lu-FAPI.

Finally, $^{68}$Ga-FAPI PET/CT and radioligand therapy with $^{177}$Lu-FAPI are two promising new diagnostic and therapeutic tools for CAFs. Above all, this is a promising new therapy with few side effects for several types of cancer that can be identified and visualized using $^{68}$Ga-FAPI PET/CT. In the coming months, $^{68}$Ga-FAPI PET/CT and $^{177}$Lu-FAPI radioligand therapy will be available in Canada under clinical research protocols for certain types of cancer, including breast cancer and colorectal cancer, to name a few! Stay tuned! ■

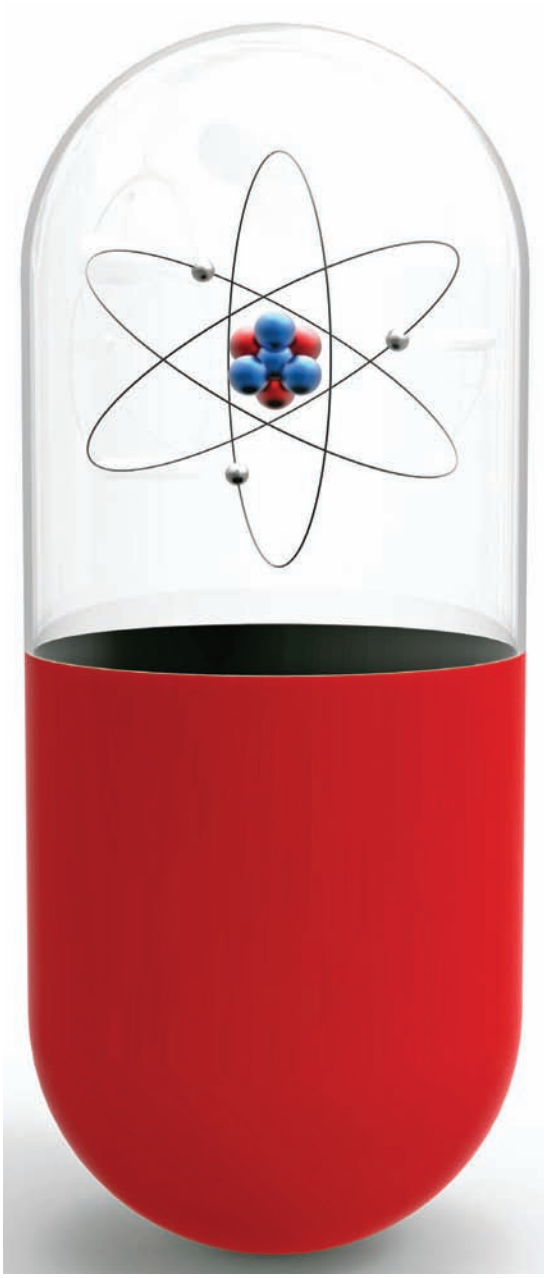

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**Table 2: Eligibility criteria for radioligand therapy with $^{177}$Lu-FAPI**

| ELIGIBILITY CRITERIA FOR $^{177}$LU-FAPI | |
|---|---|
| **Clinical parameters** | **Imaging and biochemical parameters** |
| Progressive metastatic solid tumor | Strong FAP expression: SUVmax >10 in more than 50% of tumor lesions on $^{68}$Ga-FAPI PET/CT |
| Exhaustion of approved therapies | $^{18}$F-FDG PET-CT to rule out discordant disease (FAPI- / FDG+) |
| Decision by the interdisciplinary tumor board | Adequate bone marrow<br>- Leukocytes >2,5/nL<br>- Hemoglobin >8,0 mg/dL<br>- Platelets >75/nL<br>*Exception: Patient stable on transfusion |
| Clinical condition that allows standing for more than 50% of the day (ECOG ≤ 2) | Adequate renal function<br>- $^{99m}$Tc-MAG3 renal scintigraphy to rule out urinary tract obstruction<br>- GFR >45 ml/min/1,73m$^2$ |

# FUNCTIONAL IMAGING: THE GATEAWAY FOR THERANOSTICS

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***" FDG allows us to map out the extent of pathology in vivo based on cellular metabolism, with intensity of uptake proportional to metabolic demand. This has permitted clinicians to stage and follow up multiple various malignancies, inflammatory disorders, as well as certain infections. "***

Molecular imaging has made great strides in the two decades. Until recently, the greatest of these was the clinical approval of 2-fluorodeoxyglucose (FDG) for positron emission tomography (PET). FDG allows us to map out the extent of pathology in vivo based on cellular metabolism, with intensity of uptake proportional to metabolic demand. This has permitted clinicians to stage and follow up multiple various malignancies, inflammatory disorders, as well as certain infections. However, FDG fell short in select pathologies, one of those being neuroendocrine tumours (NET). NET falls on a spectrum from well differentiated to poorly differentiated, with neuroendocrine carcinoma (NEC) at the extreme end of this spectrum. This phenomenon is commonly encountered in endocrine cancers, thyroid cancer being a classic example. Well-differentiated thyroid cancer does not typically demonstrate increased metabolic activity on FDG PET, yet poorly differentiated or anaplastic thyroid cancers are typically very hypermetabolic. For this reason, well-differentiated thyroid cancer is imaged and treated with radioactive iodine. To that effect, the behaviour of NET on molecular imaging conforms to that of thyroid cancer and other endocrine cancers.

From a pathology standpoint, NET is classified according to a grading system that is defined by cellular proliferation rate, with the most indolent, well-differentiated tumours defined as grade 1, the most aggressive as grade 3, and grade 2 for everything in between. NET can develop nearly anywhere in the body, but this grading system has been formally endorsed for gastroenteropancreatic NET (GEP-NET). Historically, somatostatin receptor imaging was used in nuclear medicine to stage disease for NET. This functional imaging has been largely supplanted by newer PET molecular radiotracers using somatostatin analogs bound to Gallium-68 (Ga68). Several variations of this imaging molecule exist, however the only one that is currently approved for clinical use in Canada is Ga68-DOTATATE. DOTATATE PET has revolutionized functional imaging for NET as the spatial resolution and sensitivity for detecting disease is far greater than with conventional functional imaging. As a result, it is being streamlined into the market particularly at tertiary University hospital centers as standard of care. Typically, grade 1 NET is positive on DOTATATE PET and negative on FDG PET. Grade 2 NET is often positive on both DOTATATE and FDG, although this may vary. Lastly, FDG PET is more often positive in grade 3 NET as compared to DOTATATE. This spectrum of findings on PET imaging reflects the varying biology across the different grades of disease.

Disease specific functional imaging has opened the gateway for theranostics, a paradigm that is based on imaging and treating disease using a common biologically active molecule. In the case of NET, the biologically active molecule of interest is the somatostatin receptor analog, called octreotate. In fact, DOTATATE is derived from the covalent bonding of a chelator (DOTA, or dodecane tetraacetic acid) with octreotate. The DOTA chelator traps heavy metals, such as Ga68, to form Ga68-DOTATATE. The Gallium-68 is an unstable radionuclide which decays via positron emission and whose annihilation gamma rays are captured by the PET camera to produce images using computational algorithms. On the other hand, the DOTA chelator can also traps other radionuclides such as Lutetium-177 (Lu177) which primarily decays via beta particle emission. This type of decay deposits energy locally into surrounding tissues making it a prime candidate for therapy. Therefore, using a common molecule (DOTATATE), both imaging (i.e. Ga68-DOTATATE) and therapeutic (Lu177-DOTATATE) radiopharmaceuticals can be employed to diagnose and treat the patient thereby making it an ideal theranostic agent.

Lu177-DOTATATE has also been recently approved by Health Canada for treatment of midgut GEP-NET. This is also known as peptide receptor radionuclide therapy (PRRT), the peptide receptor being the somatostatin receptor in this case. Lu177-DOTATATE is approved for unresectable or metastatic GEP-NET that are progressing on somatostatin therapy. Since Lu177 radioactive decay also emits small amount of gamma radiation, it allows for imaging at the time of therapy. Furthermore, the longer half-life of Lu177 permits imaging over several days which is ideal of dosimetry calculations. At our center, these types of calculations are performed using Hermes voxel dosimetry which allows for prediction of dose distribution using patient specific anatomy from computed tomography (CT), and time dependent activity distribution from single photon emission computed tomography (SPECT). Monte Carlo based energy deposition models provide a voxelized dose map which is segmented to determine dose distribution in volumes of interest.

In conclusion, theranostic agents such as Ga68-DOTATATE for imaging and Lu177-DOTATATE for PRRT have had a big impact on patient care and quality of life. Our center has had a very positive experience with PRRT since its inception. DOTATATE is just one example of many possible theranostic agents that will help shape the future of personalized medicine. ■

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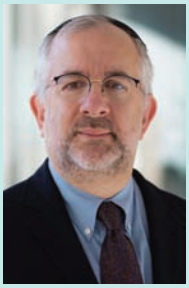

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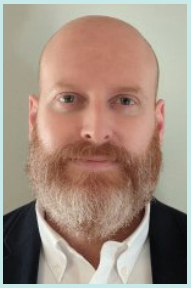

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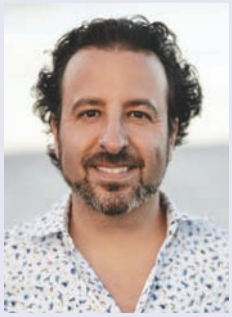
## VENEZ CONSULTER : https://www.facebook.com/AMSMNQ/

Venez consultez la page Facebook de l'association des médecins spécialistes en médecine nucléaire du Québec. Vous y trouverez de multiples informations concernant principalement la médecine nucléaire québécoise.

Nous y partageons des événements à venir, des articles intéressants et toutes nouvelles susceptibles d'intéresser la communauté de médecine nucléaire d'ici et d'ailleurs. Nous sommes aussi très fier de présenter les réalisations exceptionnelles de certains de nos membres.

N'hésitez pas à nous contacter si vous souhaitez nous partager une bonne nouvelle, une information, ou un article d'intérêt.

## Message du président de l'AMSMNQ



**President AMSMNQ**
**Chief of the Department of Medical Imaging**
**Chu Québec**

Un peu plus de six ans. C'est le temps que ça aura pris entre le moment où le Dr Norman Laurin m'appela afin que je me présente comme conseiller à l'Association des médecins spécialistes en médecine nucléaire du Québec (AMSMNQ) et le moment où il m'a passé le flambeau pour la présidence de l'Association.

Tout d'abord comme conseiller, puis comme trésorier, officier et délégué de l'Association aux assemblées de la Fédération des médecins spécialistes du Québec, j'ai eu l'occasion de parfaire mes aptitudes et habilités de gestion sur de nombreux dossiers. Le style de gestion instauré au sein du CA de l'Association sous la présidence de Dr Laurin est très ouvert, participatif, et surtout dans la transparence. Un style qui me rejoint; un style par lequel je compte entreprendre mon mandat en continuité avec le conseil d'administration qui a été reconduit, sans oublier l'arrivée de Dre Virginie Bruneau comme conseillère. Et je le dis sans aucune gêne, j'ai la chance d'être supporté par une équipe extraordinaire, et une directrice générale en or!

Ma voie jusqu'ici n'était certes pas tracée d'avance. Diverses opportunités et défis qui se sont présentés à moi m'ont permis d'en arriver là où j'en suis. C'est un peu par hasard que j'ai été dirigé vers l'une des plus belles spécialités médicales qu'est la médecine nucléaire au moment même où mon frère Christian était pris en charge par l'équipe de médecins spécialistes en médecine nucléaire du CHUM. Il a d'ailleurs su quelques semaines avant moi que j'étais accepté en cette spécialité!

J'entrevois la présidence de l'AMSMNQ comme un défi de taille, mais Norman me laisse les rênes d'une Association en bonne posture. La médecine nucléaire est florissante au Québec. Je suis fier de dire que la population bénéficie d'une médecine personnalisée de pointe digne des plus grands établissements de santé au monde. On a su pivoter à l'arrivée de la tomographie par émission de positrons (TEP). On vit le changement de paradigme avec l'émergence de la théranostique, alliant examen diagnostique fonctionnel, indispensable à une approche thérapeutique personnalisée.

Je souligne au passage que le CHU de Québec a été le premier établissement au Canada reconnu comme centre d'excellence en thérapie par radiopharmaceutiques décerné par la SNMMI. Le département de médecine nucléaire du CHUM a été le site désigné pour quelques premières mondiales dans le développement de paires théranostiques. Le CHUS travaille à l'accessibilité pour une médecine nucléaire de pointe à un autre ordre de grandeur. Collectivement, nous collaborons sur quelques dizaines de protocoles de recherche permettant aux malades un accès rapide à des traitements émergents. Par parrainage, l'éventail de développement professionnel continu se trouve bonifiée. Et tout ça ne serait pas possible sans la contribution de toutes et tous. Les patients nécessitant des soins en médecine nucléaire sont entre bonnes mains au Québec!

C'est donc avec un profond sens de l'honneur, sous la confiance de mes collègues, que j'entame ma présidence à l'AMSMNQ. Engageons-nous ensemble à joindre nos talents afin de tendre vers l'excellence, mettre à contribution l'innovation au service des patients.

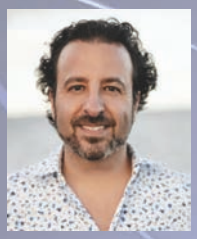
AMSMNQ

# ASSOCIATION DES MÉDECINS SPÉCIALISTES EN MÉDECINE NUCLÉAIRE DU QUÉBEC

## L'IMAGERIE PERSONNALISÉE PAR LA MÉDECINE NUCLÉAIRE

**« La mission du comité de développement professionnel continu (DPC) de l'Association des médecins spécialistes en médecine nucléaire du Québec (AMSNMQ) est de soutenir les médecins nucléistes à acquérir et à préserver leur expertise médicale, ainsi qu'à améliorer leurs compétences de collaboration et de communication dans le but de prioriser la qualité des soins aux patients. »**

### COMITÉ EXÉCUTIF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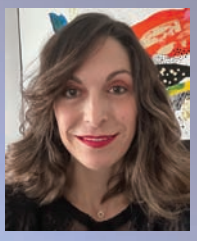
Dre. Virginie Bruneau
Conseillière


Dr. Norman Laurin
Membre honoraire

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# INTERVIEW WITH JOHANN L. FERNANDO

**DEAR MR FERNANDO, COULD YOU PRESENT YOURSELF TO OUR READERS ?**

With pleasure! I'm Johann Fernando, Ph.D., Executive Vice President of Marketing at Spectrum Dynamics Medical. Spectrum Dynamics is a global leader in digital SPECT/CT innovation, pioneering the next generation of nuclear medicine imaging. Our technologies are redefining scanner design, workflow efficiency, and diagnostic capabilities—setting a new standard for the field.

I joined the company in 2024, bringing nearly 25 years of experience in Nuclear Medicine and Medical Imaging. I earned my Ph.D. from The University of Texas Southwestern Medical Center at Dallas (UTSW) in 1996, with a dissertation focused on nuclear medicine instrumentation. My career began at UTSW as a post-doctoral fellow before transitioning into industry, where I held roles including Senior R&D Manager. Over the past two decades, I have gained extensive experience across product development, marketing, sales, and business leadership in corporate environments. This diverse background has significantly enriched my professional journey and strengthened my ability to lead Spectrum Dynamics Medical's global marketing efforts effectively.

**WHAT DO YOU SEE WILL BE THE THREE MOST IMPORTANT DEVELOPMENTS IN NUCLEAR MEDICINE IN THE NEXT FEW YEARS?**

**1. Expansion of Theranostics**
Theranostics—combining targeted diagnostics with personalized radiopharmaceutical therapies—is rapidly transforming oncology care, particularly for prostate cancer (e.g., PSMA-targeted agents) and neuro-endocrine tumors. The next few years will likely see:

- **New radioisotopes and ligands:** Expanding beyond Lutetium-177 and Gallium-68 to include Actinium-225 and other alpha emitters for higher efficacy.
- **Broader indications:** Moving from niche applications to more widespread cancer types like breast, lung, and pancreatic.
- **Increased integration:** Closer alignment between diagnostic imaging and therapy for truly personalized treatment protocols.

**2. Advancements in Digital Detector Technology**
Digital SPECT/CT and PET/CT systems with solid-state detector technology (e.g., CZT) are driving a major shift in image quality, acquisition speed, and workflow:

- **Higher sensitivity and resolution:** Enables earlier and more accurate detection of disease.
- **Lower dose imaging:** Enhances patient safety and broadens the eligible patient population.
- **Faster throughput:** Improves efficiency in busy clinical settings and increases access to nuclear medicine procedures.

**3. AI and Data Integration**
Artificial Intelligence (AI) and machine learning are starting to play a transformative role in nuclear medicine:

- **Image reconstruction and interpretation:** AI is improving lesion detection, segmentation, and quantitative analysis.
- **Workflow optimization:** Intelligent scheduling, patient positioning, and scanner operation will reduce bottlenecks and enhance productivity.
- **Predictive analytics:** Using imaging and clinical data to predict patient outcomes and guide therapeutic decisions.

**Johann L. Fernando, Ph.D.**
Executive Vice President, Global Marketing
Spectrum Dynamics Medical
Sarasota, Florida

*« Theranostics—combining targeted diagnostics with personalized radiopharmaceutical therapies—is rapidly transforming oncology care, particularly for prostate cancer (e.g., PSMA-targeted agents) and neuroendocrine tumors. »*

*« Spectrum Dynamics Medical can play a vital role in advancing the use of theranostics—by leveraging its expertise and innovation in digital SPECT/CT technology. »*

These developments are not only improving the precision and effectiveness of nuclear medicine but also positioning the field as central to the future of personalized and value-based healthcare.

**WHAT IS THE CONTRIBUTION OF ARTIFICIAL INTELLIGENCE IN NUCLEAR MEDICINE?**

Artificial Intelligence (AI) is making transformative contributions to nuclear medicine across the entire clinical and operational workflow. Here are the key areas where AI is having the greatest impact:

**1. Image Reconstruction and Enhancement**

• Faster, higher-quality imaging: AI-based algorithms, such as deep learning reconstruction (DLR), can significantly reduce scan times or radiation dose while maintaining or even improving image quality.

• Noise reduction and resolution improvement: Enhances the visibility of small lesions, improving diagnostic confidence.

**2. Automated Image Analysis and Interpretation**

• Lesion detection and segmentation: AI tools assist radiologists by automatically identifying and delineating tumors, organs, or abnormalities.

• Quantification: AI improves the accuracy and reproducibility of standardized uptake values (SUVs) and other functional biomarkers, critical for monitoring therapy response.

• Pattern recognition: AI models can identify complex disease patterns and support differential diagnosis, especially in oncology and neurology.

**3. Workflow Optimization**

• Patient scheduling and scanner utilization: AI can predict no-shows, optimize patient flow, and suggest ideal scan protocols based on patient and exam data.

• Protocol selection: Automatically selects the most appropriate scan parameters tailored to patient characteristics and clinical indications.

**4. Operational Efficiency and Decision Support**

• Clinical decision support systems (CDSS): Integrate imaging, EHR, and lab data to guide clinical decisions and flag potential issues.

• Training and standardization: AI provides decision support to less experienced clinicians, improving consistency across different institutions and levels of expertise.

In essence, AI is helping nuclear medicine evolve from a manual, subjective, and time-intensive specialty into a more automated, accurate, and patient-centric field.

**HOW A COMPANY LIKE SPECTRUM-DYNAMICS COULD HELP THE USE OF THERANOSTIC FOR OUR PATIENTS?**

**Spectrum Dynamics Medical** can play a vital role in advancing the use of **theranostics**—by leveraging its expertise and innovation in digital SPECT/CT technology. Here's how Spectrum Dynamics could help expand and support theranostic applications for patients:

**1. Providing Advanced Imaging Technology for Theranostics**

• **High-sensitivity digital SPECT/CT systems**, like the **VERITON-CT**, offer superior image resolution, speed, and quantitative accuracy, which are critical for:

- Accurate patient selection for targeted radionuclide therapies.

- Dosimetry planning and post-therapy follow-up.

- Monitoring treatment response and disease progression.

• **360° CZT detector design** improves localization and characterization of disease, especially in complex cases like neuroendocrine tumors and prostate cancer—key targets for theranostic agents.

**2. Enabling Personalized Dosimetry**

• Spectrum Dynamics' systems support **quantitative SPECT**, which is essential for **patient-specific dosimetry**:

- Ensures safe and effective dosing of therapeutic radiopharmaceuticals.

- Helps tailor treatments to individual patient needs, improving outcomes and minimizing toxicity.

- Facilitates repeatable and standardized workflows across treatment centers.

**3. Collaborating with Key Opinion Leaders and Institutions**

• By partnering with **leading theranostic centers and research hospitals**, Spectrum Dynamics can:

- Co-develop new clinical protocols.

- Validate novel radiopharmaceuticals and workflows.

- Share clinical evidence and best practices that expand theranostics into mainstream practice.

• These collaborations help bridge the gap between cutting-edge research and widespread clinical adoption.

**4. Driving Innovation in Software and AI Integration**

• **Intelligent imaging solutions** can integrate diagnostic, therapeutic, and clinical data to:

- Automate lesion detection and quantification.

- Streamline therapy planning and documentation.

- Support clinicians with decision-making tools based on AI and machine learning.

• Spectrum Dynamics can develop **integrated theranostic platforms** that combine imaging, dosimetry, and therapy tracking into a seamless user experience.

**5. Supporting Education and Training**

• Spectrum Dynamics can play a leadership role in:

- **Educating physicians, physicists, and technologists** on how to use advanced imaging tools in theranostics.

- Hosting workshops, webinars, and user forums to disseminate knowledge.

- Helping establish **standardized protocols** that accelerate the safe and effective use of theranostics globally.

**6. Expanding Access and Market Penetration**

• With a global presence, Spectrum Dynamics can:

- Equip more centers, including community hospitals, with the necessary imaging infrastructure.

- Support emerging markets in adopting theranostics.

- Help build a more equitable ecosystem for precision cancer care.

By doing so, Spectrum Dynamics Medical empowers healthcare providers to offer **more precise, personalized, and effective treatments**—improving outcomes and quality of life for patients with complex diseases like cancer.

**WHAT ARE THE BIGGEST CHALLENGES FACING NUCLEAR MEDICINE IN THE COMING YEARS?**

Nuclear Medicine is poised for transformative growth, especially with the rise of theranostics, advanced imaging technologies, and AI. However, several significant challenges must be addressed for the field to realize its full potential. Here are the biggest challenges facing Nuclear Medicine in the coming years:

**1. Radiopharmaceutical Supply Chain and Availability**

Shortages and inconsistent availability of key isotopes (e.g., Mo-99, Lu-177, Ga-68) impact patient care and research. There are several reasons including the aging reactors, limited global production sites, complex logistics, and increasing demand from theranostic applications.

**2. Theranostic Infrastructure and Access**

While theranostics is revolutionizing cancer care, its adoption is uneven across regions. One of the key reasons is the high costs of infrastructure (e.g., advanced imaging systems, hot labs), lack of trained personnel, and limited reimbursement frameworks.

**3. Workforce Shortage and Training Gaps**

There is a growing shortage of nuclear medicine specialists, including technologists, physicians, and medical physicists. Aging workforce, limited training programs, and insufficient emphasis on nuclear

*« Nuclear Medicine is poised for transformative growth, especially with the rise of theranostics, advanced imaging technologies, and AI. However, several significant challenges must be addressed for the field to realize its full potential. »*

*« My greatest wish for patients in need of Nuclear Medicine is that they receive timely, accurate, and personalized care—no matter where they live or their financial situation. »*

medicine in medical curricula are some of the main reasons for the workforce shortage.

**4. Regulatory and Reimbursement Hurdles**

Complex and inconsistent regulatory requirements across countries can delay innovation and market entry. For example, new theranostic agents and procedures are often introduced before reimbursement pathways are in place, limiting access.

**5. Integration with Precision Medicine and AI**

While AI, big data, and personalized medicine hold promise, integration into clinical practice is still nascent. Some of the barriers facing the industry are data interoperability, physician skepticism, ethical concerns, and validation of algorithms. To overcome these barriers the development of robust, clinically validated AI tools and integration into existing workflows to support clinical decisions may be required.

**6. Cost and Economic Pressures**

High costs associated with imaging systems, radiopharmaceuticals, and facility upgrades can limit adoption. The need for demonstration of cost-effectiveness and improved outcomes through health economics data to support investment and reimbursement may be required.

By addressing these issues, Nuclear Medicine can fully realize its role in **personalized, precision-based**, **and outcome-driven healthcare** in the coming decade.

**WHAT IS YOUR GREATEST WISH FOR PATIENTS IN NEED OF NUCLEAR MEDICINE?**

**My greatest wish for patients in need of Nuclear Medicine** is that they receive timely, accurate, and personalized care—no matter where they live or their financial situation.

I wish for a world where:

• **Early and precise diagnosis** is the norm, not the exception.

• **Access to life-saving theranostic therapies** is equitable and widespread.

• **Innovations in imaging, radiopharmaceuticals, and AI** work seamlessly together to improve outcomes and quality of life.

• Patients and families are not burdened by delays, lack of information, or barriers to care—but are empowered by a compassionate and effective healthcare system.

Ultimately, I hope that Nuclear Medicine continues to evolve into a fully integrated, frontline tool in the fight against cancer and other serious diseases—**delivering hope, healing, and dignity to every patient.**

Thank you and best wishes, Johann.

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# INTERVIEW WITH CÉLINE LANDIE

**Céline Landie**
General Manager & Vice-President
Novartis - ESSEC Business School
Canada

**COULD YOU BRIEFLY INTRODUCE YOURSELF TO OUR READERS?**

I'm privileged to lead the radioligand therapy (RLT) team at Novartis Canada, working to bring this promising class of targeted treatments to patients with advanced cancers. I've spent the past decade in various leadership roles across Europe, Asia, and North America, and today I'm proud to work alongside the nuclear medicine community here in Canada. Our efforts are deeply collaborative — engaging with health systems, clinical leaders, and, of course, the nuclear medicine community. Canada has the opportunity to be a global leader in radioligand therapy, and I'm thrilled to play a part in making that vision a reality for the benefit of Canadian patients.

**HOW DOES NOVARTIS CONTRIBUTE TO NUCLEAR MEDICINE?**

At Novartis, we're building on decades of experience in oncology to help shape the future of nuclear medicine. Understanding the complexity and diversity of cancer, we're focused on developing targeted therapies that treat disease more precisely — with the goal of improving outcomes and quality of life. We introduced the first approved RLTs in Canada for advanced forms neuroendocrine tumours and prostate cancer and are actively investigating how RLT could benefit patients with other types of cancer. By working closely with healthcare professionals and the nuclear medicine community, we are working to integrate RLT into routine clinical practice to improve outcomes for Canadians living with cancer.

**WHAT DO YOU CONSIDER TO BE THE 3 MAIN CHALLENGES FOR NUCLEAR MEDICINE IN THE NEXT THREE YEARS?**

We see nuclear medicine — especially RLT — playing an increasingly integrated role in the cancer care pathway. To fully realize this potential, we must work together to address key challenges:

NOVARTIS

1. Access and equity: Ensuring that patients across Canada, regardless of location or socioeconomic status, have timely access to the latest advancements in nuclear medicine, such as RLT.

2. Integration into clinical practice: Ensuring that healthcare institutions are prepared to integrate advancements as nuclear medicine innovations continue to evolve.

3. Prioritizing expertise: To meet the increasing demand for nuclear medicines like RLT and unlock their full potential, ensuring education and specialized training for healthcare professionals is essential to building confidence in these treatments and driving greater interest and adoption across the healthcare landscape.

**HOW DO YOU SEE THE CONTRIBUTION OF ARTIFICIAL INTELLIGENCE TO NUCLEAR MEDICINE?**

AI holds considerable promise across nuclear medicine — from imaging interpretation to predicting treatment response. In the RLT space, we see opportunities to enhance patient selection, optimize end-to-end delivery, and support centres in managing therapy demand. While much of this is still in early stages, we're actively working with academic and clinical partners to explore meaningful, validated AI applications.

**HOW IS NOVARTIS INVOLVED IN RLT?**

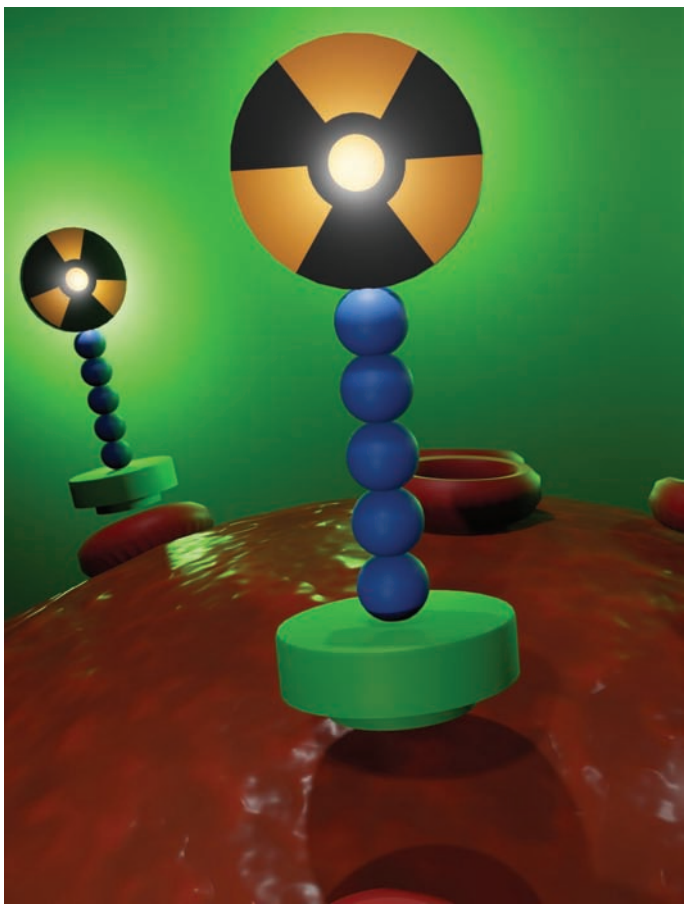
Novartis is driving advancements RLT by combining diagnostic and therapeutic approaches to enhance patient care. Through our work in RLT, we aim to provide targeted treatments that deliver directly to cancer cells while minimizing effects on healthy tissue. This "see it, treat it" integrated approach to cancer care seeks to improve both diagnostic accuracy and therapeutic outcomes. Our current RLT treatments include metastatic castration-resistant prostate cancer and certain advanced gastroenteropancreatic neuroendocrine tumours. Building on this foundation, we continue to explore novel medical isotopes and combinations to expand the potential of RLT within oncology.

**WHAT IS YOUR GREATEST WISH FOR PATIENTS IN NEED OF NUCLEAR MEDICINE?**

We understand how important it is to consider the patient perspective throughout the cancer journey — and the need to improve quality of life during and after treatment. At its core, this is about enabling patients to spend more meaningful time with the people they love. My greatest wish is for all eligible Canadian patients — regardless of the province they live in — to have timely access to RLT.

To achieve this requires strong collaboration across the healthcare system to scale up capacity with a view to leaving no patients behind. We're committed to being a reliable partner in helping to expand access and ensure that the promise of science matches real-world availability for Canadians.

***« At Novartis, we're building on decades of experience in oncology to help shape the future of nuclear medicine. Understanding the complexity and diversity of cancer, we're focused on developing targeted therapies that treat disease more precisely — with the goal of improving outcomes and quality of life. »***



# Reimagining Medicine

# INTERVIEW WITH JEFFREY BUNDY

**Jeffrey Bundy, Ph.D**
**Chief Executive Officer, UIH Solutions**

**Jeffrey Bundy is CEO of UIH Solutions LLC, leading North American sales, service, and overall operations. Jeffrey is a proven leader with experience managing large, multi-functional, global healthcare teams to measurable success. He is recognized for fostering the value of each employee and empowering team members resulting in product innovation and the creation of new marketing and business strategies.**

**Dear Jeffrey could you introduce yourself and United Imaging to our readers?**

United Imaging is a leader in Diagnostic Imaging and Nuclear Medicine and specifically, Molecular Imaging PET/CT, and has been working hard in 70 countries across the globe to change the industry by focusing on getting the best technology to patients everywhere. We have brought to market a new class of PET/CT systems that the rest of the industry is following, and we have also gone to market specifically in North America with an all-digital portfolio with industry-leading 2.9mm resolution, so physicians can see even the smallest lesions We also made it available across the USA, including in a mobile unit to make sure it can reach even the most rural locations.

For me personally, I have been in the medical imaging industry since the 1990s when I started working on my Ph.D. in cardiac MRI. I have led several businesses for one of the other industry players, both in the USA and globally. I have a personal focus and motivation because I have a family history of cancer. In addition to this, I believe my family history of growing up in a small business that cared for children and their families, matched with my industry experience, has put me in a great place to build a new and different business that puts patients at the center of focus, where employees and customers find a unique environment and culture.

**How does United Imaging see the development of Nuclear Medicine over the next three years?**

It is a great time to be in Nuclear Medicine. There is innovation everywhere in the industry. We are innovating in hardware performance, software automation, and AI tools from patient positioning to image analysis and reporting. Our academic partners are pushing us to provide new and innovative protocols and the pharma companies in our industry are also innovating at an exciting pace. And those developments are capitalizing on imaging to provide answers to physicians that can truly impact patient outcomes (e.g. visualize disease earlier for diagnosis, therapy delineation, and intervention). I am excited because I believe that innovation that makes a difference to patients is coming. I also believe that our mission "Equal Healthcare For All" which aims to provide top level care to everyone, no matter their zip code nor the demographics of their communities, comes at a great time to bring these life changing things to all patients.

**How does United Imaging see the development of Theranostics in Nuclear Medicine and what will be its impact to the patients?**

My life has been profoundly affected by cancer, as I lost both parents to cancer over the past 20 years. When I joined United Imaging in 2018, there was a lot of discussion about "theranostics" and all the new imaging agents. I was new to the Nuclear Medicine world at that time, but it did seem like something special was really happening. And that has certainly been the case over nearly the last decade. New treatments and imaging agents are in the market and some of the cases and patient results are amazing and truly remarkably life changing. In


the next three years we expect more of the same, as there is so much investment, research and focus in these areas. That is why we focus our innovation in MI around the foundation of spatial resolution which is important for physicians to see more, but also for improving accuracy, sensitivity, and longer axial FOV for organ-based to total-body coverage. As a leading innovator, we shoot to lead the field in every meaningful specification to try to see greater details in less time, with less dose.

I also think we will need to continue finding ways to do more with the same capacity scanners, because the demand will likely go up faster than the scanner capacity can keep up. That is why we are focusing on so much software innovation, including AI. We have also committed to our customers that they will receive all of those new software innovations as a part of our Software Upgrades For LifeTM program.

**How do you see the contribution of Artificial Intelligence to Nuclear Medicine?**

Where do I begin? I think artificial intelligence offers something for everyone in the picture. It offers something for physicians, technologists, administrators and patients. For the physician and technologist, they will be able to protocol and perform scans faster with less dose, and get better image quality. But it is also important to talk about how AI can make it easier for technologists to set up, scan, and process patient exams.

This is very important due to the critical shortage of technologists in Nuclear Medicine and Radiology as a whole. For administrators, we have many solutions that enable the efficient use of the scanner, such as our program which will keep a scanner state-of-the-art for its lifetime and help keep the investment more secure. For patients, we have solutions that allow them shorter exams, and we have evidence of finding lesions missed by prior equipment. Earlier diagnosis, in less time and with less dose, may seem too optimistic, but I think not. I think it's more and more real every day.

**Dear Jeffrey what is your greatest wish for patients in need of Nuclear Medicine?**

Having spent much of my adult life watching my parents fight cancer, my greatest wish is that the people who come in for an exam receive good news from the best quality exam possible. If they aren't so fortunate, then I wish that we as an industry will have done our job to put top performing technology near the best physicians and technologists and near the majority of patients, and that patients can get a quick and definitive diagnosis so that those who work to heal them know exactly what to do and can get to work on that ASAP. ■

***« United Imaging is a leader in Diagnostic Imaging and Nuclear Medicine and specifically, Molecular Imaging PET/CT, and has been working hard in 70 countries across the globe to change the industry by focusing on getting the best technology to patients everywhere. »***

# INTERVIEW WITH TOM FRANCKE


**Tom Francke, Assoc. Prof.**
**CEO of Hermes Medical Solutions**

## IMAGERIE MOLÉCULAIRE À L'ÉPREUVE DU FUTUR : LA VOIE DE L'INNOVATION

*« L'évolution vers la médecine personnalisée engendre de nouvelles exigences en imagerie moléculaire. En oncologie, le théranostique permet une approche ciblée en associant diagnostique et traitement, permettant aux médecins d'adapter les thérapies à chaque patient. »*

L'imagerie moléculaire est à la pointe de la médecine moderne et joue un rôle crucial dans le diagnostic et le traitement des maladies complexes. Face aux avancées technologiques, il est essentiel de garantir l'adaptabilité et l'efficacité des systèmes d'imagerie. Les professionnels de santé ont besoin de solutions performantes aujourd'hui, mais aussi évolutives avec les innovations futures. Flexibilité, interopérabilité et intégration transparente entre différentes plateformes d'imagerie sont essentielles pour optimiser la valeur des investissements en imagerie moderne.

L'imagerie moléculaire exige précision et exactitude, notamment dans des domaines comme l'oncologie, la neurologie et la cardiologie. Face à la généralisation du théranostique, les solutions logicielles avancées doivent prendre en charge une quantification et une dosimétrie précise pour une planification thérapeutique individualisée. Les nouveaux traceurs d'imagerie et les nouvelles thérapies exigent une adaptation continue, d'où l'importance cruciale des mises à jour et améliorations continues des plateformes d'imagerie. La possibilité de comparer les données de différents systèmes d'imagerie et à différents moments permet aux cliniciens de prendre des décisions éclairées, basées sur les informations les plus précises disponibles.

L'évolution vers la médecine personnalisée engendre de nouvelles exigences en imagerie moléculaire. En oncologie, le théranostique permet une approche ciblée en associant diagnostique et traitement, permettant aux médecins d'adapter les thérapies à chaque patient. Cela nécessite des logiciels d'imagerie capables d'effectuer des calculs dosimétriques précis pour garantir un dosage optimal et une efficacité thérapeutique optimale. En neurologie, les avancées thérapeutiques dans les maladies d'Alzheimer et de Parkinson soulignent la nécessité d'outils d'imagerie précis permettant aux cliniciens de détecter, de suivre et de quantifier la progression de la maladie. Face à l'évolution de ces domaines, les institutions doivent disposer d'une plateforme d'imagerie adaptée aux avancées médicales.

Les écosystèmes d'imagerie traditionnels limitent souvent l'utilisation de systèmes propriétaires par les établissements, limitant ainsi leur capacité à intégrer les nouvelles avancées logicielles. Une approche véritablement indépendante des fournisseurs sup-

prime ces obstacles et permet aux hôpitaux et aux cliniques d'intégrer plusieurs appareils d'imagerie sans souci de compatibilité. Cette flexibilité prolonge la durée de vie des équipements existants, permettant aux établissements de santé de prendre des décisions stratégiques en fonction des besoins cliniques plutôt que des limitations logicielles. La standardisation des flux de travail d'imagerie entre les différents sites favorise la collaboration, améliore l'accessibilité des données et optimise la prise en charge des patients.

Avec l'essor des collaborations à distance et multicentriques, le besoin de solutions d'imagerie centralisées n'a jamais été aussi grand. Une plateforme évolutive permettant un accès en temps réel aux données d'imagerie favorise le diagnostic à distance, la collaboration interdisciplinaire et l'optimisation des flux de travail. Les établissements doivent s'assurer que leurs logiciels d'imagerie s'adaptent à l'évolution des modèles de soins de santé, facilitant ainsi une intégration fluide avec les autres technologies de santé numérique. En adoptant la transformation numérique, les prestataires de soins peuvent optimiser leur efficacité opérationnelle et les résultats des patients. Le partage sécurisé des données et l'interopérabilité avec les dossiers médicaux électroniques rationalisent encore davantage les flux de travail, garantissant ainsi une intégration complète de l'imagerie moléculaire dans l'écosystème de santé.

Un autre facteur essentiel pour pérenniser l'imagerie moléculaire est le maintien de la conformité aux exigences réglementaires et à l'évolution des normes industrielles, avec l'introduction constante de nouvelles directives cliniques. Un logiciel évolutif permet aux établissements de rester conformes tout en leur permettant de bénéficier des dernières avancées technologiques.

Depuis près de 50 ans, Hermes Solutions Médicales se consacre au développement de l'imagerie moléculaire. Contrairement à d'autres entreprises d'imagerie qui se concentrent sur plusieurs modalités, nous nous spécialisons exclusivement en médecine nucléaire et en imagerie moléculaire. Cette vocation unique garantit que nos logiciels évoluent avec les besoins du domaine, intégrant les dernières avancées en imagerie, quantification et dosimétrie.

Hermia, notre plateforme logicielle indépendante des fournisseurs de caméras, permet aux établissements de rendre leurs capacités d'imagerie moléculaire à l'épreuve du futur en prenant en charge toutes les marques de caméras, en prolongeant la durée de vie des équipements et en facilitant l'accès à distance et la collaboration multicentrique. En privilégiant l'innovation et l'excellence clinique, Hermes Solutions Médicales s'engage à fournir les outils les plus avancés pour accompagner l'avenir de la médecine personnalisée. Ensemble, nous façonnons la nouvelle ère de l'imagerie moléculaire. ■

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## FUTURE-PROOFING MOLECULAR IMAGING: THE PATH TO INNOVATION

Molecular imaging is at the forefront of modern medicine, playing a crucial role in diagnosing and treating complex diseases. As technology advances, ensuring that imaging systems remain adaptable and efficient is essential. Healthcare providers need solutions that are not only powerful today but can also evolve with future innovations. Flexibility, interoperability, and seamless integration across different imaging platforms are key to maximizing the value of modern imaging investments.

Molecular imaging requires precision and accuracy, particularly in areas such as oncology, neurology, and cardiology. As theranostics become more prevalent, advanced software solutions must support precise quantification and dosimetry for individualized treatment planning. New imaging tracers and therapies demand continuous adaptation, making it crucial for imaging platforms to provide ongoing updates and enhancements. The ability to compare data across different imaging systems and time points ensures that clinicians can make informed decisions based on the most accurate information available.

The shift toward personalized medicine is driving new demands in molecular imaging. In oncology, theranostics enable a targeted approach by combining diagnostics with treatment, allowing physicians to tailor therapies to individual patients. This requires imaging software capable of performing accurate dosimetry calculations to ensure optimal dosing and treatment effectiveness. In neurology, breakthroughs in Alzheimer's and Parkinson's disease treatments highlight the need for precise imaging tools that allow clinicians to detect, track, and quantify disease progression. As these fields evolve, institutions must have an imaging platform that keeps pace with advancements in medicine.

Traditional imaging ecosystems often limit institutions to proprietary systems, restricting their ability to incorporate new software advancements. A truly vendor-neutral approach removes these barriers, allowing hospitals and clinics to integrate multiple imaging devices without compatibility concerns. This flexibility extends the lifespan of existing equipment, enabling healthcare facilities to make strate-

***« The shift toward personalized medicine is driving new demands in molecular imaging. In oncology, theranostics enable a targeted approach by combining diagnostics with treatment, allowing physicians to tailor therapies to individual patients. »***

# INTERVIEW WITH TOM FRANCKE

*« For nearly 50 years, Hermes Medical Solutions has been dedicated to advancing molecular imaging. Unlike other imaging companies that divide their focus among multiple modalities, we specialize exclusively in nuclear medicine and molecular imaging. »*

gic decisions based on clinical needs rather than software limitations. Standardized imaging workflows across locations enhance collaboration, improve data accessibility, and optimize patient care.

With the rise of remote and multi-center collaborations, the need for centralized imaging solutions has never been greater. A scalable platform that enables real-time access to imaging data supports remote diagnostics, interdisciplinary collaboration, and improved workflow efficiency. Institutions must ensure that their imaging software keeps pace with evolving healthcare models, facilitating seamless integration with other digital health technologies. By embracing digital transformation, healthcare providers can enhance operational efficiency and improve patient outcomes. Secure data sharing and interoperability with electronic health records further streamline workflows, ensuring that molecular imaging is fully integrated into the broader healthcare ecosystem.

Another critical factor in future-proofing molecular imaging is maintaining compliance with regulatory requirements and evolving industry standards with new clinical guidelines constantly being introduced. Software that evolves with these changes helps institutions remain compliant while ensuring they can take advantage of the latest technological advancements.

For nearly 50 years, Hermes Medical Solutions has been dedicated to advancing molecular imaging. Unlike other imaging companies that divide their focus among multiple modalities, we specialize exclusively in nuclear medicine and molecular imaging. This singular dedication ensures that our software evolves with the needs of the field, integrating the latest advancements in imaging, quantification, and dosimetry.

Hermia, our vendor-neutral software platform, allows institutions to future-proof their molecular imaging capabilities by supporting all camera brands, extending equipment lifespan, and facilitating remote access and multi-center collaboration. By prioritizing innovation and clinical excellence, Hermes Medical Solutions remains committed to providing the most advanced tools to support the future of personalized medicine. Together, we are shaping the next era of molecular imaging. ■

HERMES MEDICAL SOLUTIONS

HERMIA

# Software that makes a difference

Unify clinical workflows across facilities with ONE Molecular Imaging/Nuclear Medicine software platform that enables secure access – anytime and anywhere. Staff can work just as efficiently from remote locations, enabling you to create a flexible workplace with 24-hour coverage. Hermia also provides smooth connectivity to your existing systems. What will you do with the time you save?

HERMES MEDICAL SOLUTIONS

hermesmedical.com

HERMIA

# THE ALL-IN-ONE MOLECULAR IMAGING SOFTWARE

## About HERMIA

Hermia is a state-of-the-art software suite that supports all clinical scenarios in NM/MI on all cameras. Powerful tools enable clinicians to simplify their workflow, increase consistency and quality and keep pace with the fast development of scanners, tracers and procedures in nuclear medicine.

HERMES MEDICAL SOLUTIONS

Hermes Medical Solutions continuously innovates to enable faster and more personalized diagnosis and therapies in molecular imaging. We empower physicians and healthcare professionals with state-of-the-art software for all clinical scenarios into ONE vendor-neutral platform. The result is improved quality in patient management and decision support for thousands of health-care providers and their patients worldwide.

# HERMIA

## Osteology

*Bone Metastasis*
*Joint pain*
*Infection/Inflammation*

Whole Body SPECT/CT
Fused Volume Render
Whole Body Bone Scan
Dynamic 3-Phase
DEXA Results Review

## Gastroenterology

*Gastric Motility*
*Salivary Function*
*Bile Acid Malabsorption*

Gastric Emptying
Colonic Transit
Oesophageal Reflux
Salivary Gland Analysis

## Hepatology

*Hepatobiliary Function*
*Surgical Planning*
*Gallbladder Functionality*

HIDA Hepatic Uptake
Gallbladder Ejection Fraction
Remnant Liver Function
SeHCAT Analysis

## Nephrology

*Relative Function*
*Urinary Tract Obstruction*
*Renal Transplant*

Rutland Patlak Method
Duplex Kidney
DMSA
Renogram
Advanced Renal Analysis

## Endocrinology

*Hyperthyroidism*
*Hyperparathyroidism*
*Thyroid Nodules*

Thyroid Uptake
Parathyroid Subtraction
(Planar and SPECT)

## Pneumology

*Pulmonary Embolism*
*COPD*
*Surgical Planning*

Lung V/Q SPECT(/CT)
Lung Lobe Quantification
AI Lung Lobe Segmentation
Planar Reprojection

## Cardiology

*Ischaemia*
*Myocardial Infarction*
*LVEF, CFR, Ca-Scoring*

Invia 4DM
Cedars-Sinai QGS/QPS
FUGA/MUGA
Cardiac MPI Splash
AI Myocardium Detection
AI Motion Correction
First Pass Shunt

## Neurology

*Parkinsonism*
*Alzheimer's Disease*
*Epilepsy Focus*

FDG vs Normal
DaTSCAN vs Normal
Ictal/Interictal
Amyloid SUVR (Amyvid™, Vizamyl™, Neuraceq™)

## Oncology

*Cancer Diagnosis*
*Tumor Staging*
*Treatment Response*

AI Data Loading
Automatic Registration
AI Lesion Tracking
AI Foci Segmentation
PERCIST
WHO criteria

## Dosimetry

*Neuroendocrine Tumors*
*Thyroid Cancer*
*Metastatic Prostate Cancer*

OLINDA/EXM v2
Organ-Based
Voxel-Based
Single Time Point
Quantitative SPECT

## Theranostics + Therapies

*Workflows for Theranostics & Radionuclide Therapy*
*Organ At Risk and Target Dose Assessment*
*Dose Prediction from imaging*

Fully Approved Dosimetry for 1000+ isotopes including Lu-177, Y-90, I-131
DOTA-peptide, PSMA, Microspheres Bremsstrahlung
SPECT Y-90 Reconstruction
Full Monte-Carlo Collimator modelling

## AI-Driven

Our software is designed with efficiency in mind and leverages the power of Artificial Intelligence and automation, where it makes sense, together with the latest computing technology, to accelerate your workflow and reporting.

## Reporting tools

Patient browser, Workflow builder, Quantitative SPECT reconstruction, Alignment & co-registration, Multi-modality fusion of CT/PET/SPECT/MR, Real-time 3D visualization of fused data and ROI, Automated segmentation, Statistics dashboard, RT-structure export for RadOnc, NIFTI export for post-processing and much more!

## With HERMIA you benefit from:

- Consistent and high-quality quantitative reconstruction SUV SPECT™
- Improved camera flexibility for easier patient scheduling
- Simplified workflow and training
- Proven tools tailored to your clinical needs
- Best-in-class dosimetry tools
- Fast and secure remote access
- Seamless connectivity and integration to your existing systems and workflows
- Local and dedicated support with NM experts
- 45+ years of leading innovation in NM

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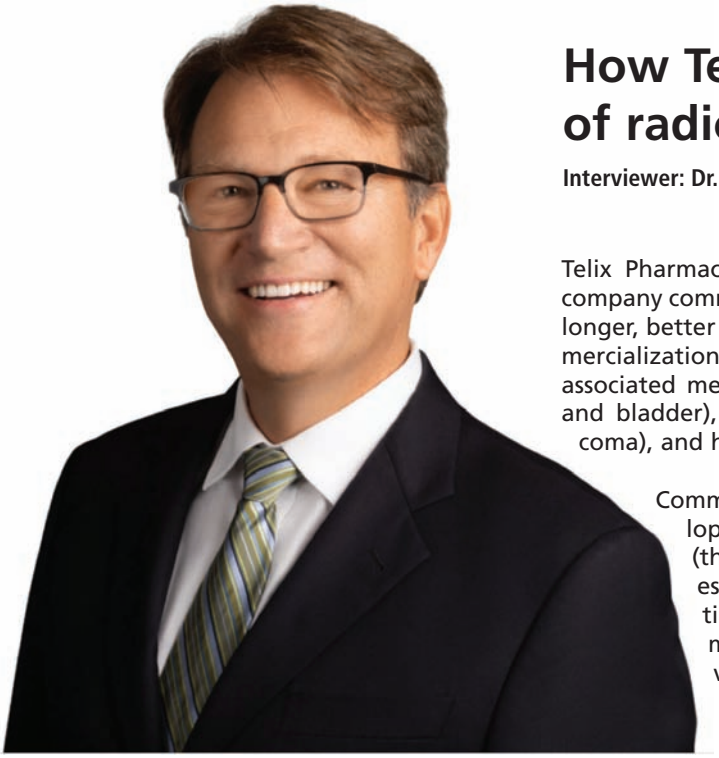

# How Telix is defining the future of radiotheranostics

**Interviewer: Dr. Francois Lamoureux**

Telix Pharmaceuticals is a global, commercial-stage biopharmaceutical company committed to helping patients with cancer and rare diseases live longer, better quality lives. Telix is focused on the development and commercialization of therapeutic and diagnostic radiopharmaceuticals and associated medical technologies in urologic oncology (prostate, kidney, and bladder), neuro-oncology (glioma), musculoskeletal oncology (sarcoma), and hematologic oncology.

Committed to the principles of precision medicine, Telix is developing and commercializing innovative theranostic approaches (therapeutic and diagnostic modalities) for patients. As an established leader and innovator in the field, Telix is differentiated by its patient-centricity, deep expertise in radiopharmaceutical drug development and commercialization, innovative pipeline that spans the cancer care continuum, and ability to deliver patient outcomes globally.

**Kevin Richardson**
**CEO of Precision Medicine Telix**

*« Telix is a global, commercial-stage biopharmaceutical company committed to helping patients with cancer and rare diseases live longer, better-quality lives. We specialize in developing and commercializing targeted radiopharmaceuticals designed to enhance precision medicine. »*

**Tell us a little about Telix and its role in the radiotheranostics space.**

Telix is a global, commercial-stage biopharmaceutical company committed to helping patients with cancer and rare diseases live longer, better-quality lives. We specialize in developing and commercializing targeted radiopharmaceuticals designed to enhance precision medicine. Our focus spans urologic oncology (prostate, kidney, and bladder cancers), neuro-oncology (glioma), musculoskeletal oncology (sarcoma), and hematologic oncology.

Radiotheranostics is at the heart of what we do. We are set apart by our patient centricity and our differentiated radiopharmaceuticals, coupled with our innovative medical technologies and vast manufacturing and distribution network, allowing us to deliver on our promise to our patients and their families and transform clinical practice and healthcare.

**How is Telix redefining precision medicine and radiotheranostics?**

We are redefining precision medicine by making radiotheranostics a standard of care in oncology and beyond. By pairing highly targeted molecular imaging with therapeutic radiopharmaceuticals, we offer confidence to physicians and patients in their decision making, leading to optimized patient stratification, dosing, and treatment responses. In clinical practice, this means reducing unnecessary treatments, minimizing side effects, and ultimately improving survival and quality of life for patients. As we continue to develop next-gen radiotheranostics, we anticipate expanding access to these transformative therapies and driving a paradigm shift in how patients with complex diseases are diagnosed, treated, and managed.

**What are the most innovative aspects of your theranostic agents that differentiate Telix's offerings from others?**

Telix's theranostic agents are designed to push the boundaries of precision medicine by offering highly targeted treatment options to support patients throughout their continuum.

A great example of our differentiated approaches is our lead prostate cancer therapeutic candidate, TLX591 ($^{177}$Lu-rosopatamab tetraxetan), which is currently being evaluated in our Phase 3 ProstACT Global study. Unlike currently available radioligand therapy, TLX591 offers a patient-friendly dosing schedule of 2 treatments given 14 days apart, while delivering a high therapeutic index and lower off-target effects like salivary gland toxicity.

We are also pioneering development of novel targeted alpha therapies. $^{225}$Ac-PSMA-RADmAb® is our "next generation" targeted alpha therapy candidate for the treatment of prostate cancer, which utilizes our proprietary RADmAb engineered antibody technology. RADmAb technology accelerates blood clearance and

reduces bone marrow residence time compared with standard monoclonal antibodies, while retaining target selectivity, internalization, and retention.

Further strengthening our capabilities, Telix has now added lead-212 ($^{212}$Pb) isotope production capacity. $^{212}$Pb is a promising isotope for targeted alpha therapy, but its relatively short half-life (10.6 hours, compared with 9.9 days for actinium-225, $^{225}$Ac) and lack of production scale has limited commercial potential. By securing our own $^{212}$Pb supply chain, we are accelerating innovation in alpha-emitting radiopharmaceuticals and ensuring global access to this promising new class of therapies for patients.

**How is Telix leveraging emerging technologies, such as artificial intelligence, to improve radiotheranostics?**

At Telix, we have a business unit committed to medical technology, supporting the integration of AI solutions to further augment our highly accurate radiopharmaceuticals.

One exciting example is our recent partnership with Subtle Medical to integrate AI-enabled SubtlePET™ software for use with our PSMA PET agents. We know there is a high demand on the healthcare system and workers in the U.S., which can have downstream negative impacts on patient access. We are delivering a solution here to help reduce this burden and optimize workflow with potential to reduce scan acquisition times, thereby improving patient comfort and allowing greater scheduling flexibility.

**How is Telix working to improve patient access to radiopharmaceuticals?**

We have successfully leveraged novel innovations and built an internal infrastructure that allows large-scale production and distribution of radiopharmaceuticals to enhance patient access globally.

A major milestone in this effort is the recent FDA approval of Gozellix® ($^{68}$Ga-PSMA-11), making us the only company with two approved PSMA imaging agents. When used with our ARTMS QUANTM Irradiation System® (QIS®) cyclotron technology, which produces multi-curie volumes of gallium-68, Gozellix® will push the envelope for geographic distribution capabilities, supporting expanded patient access.

We are dedicated to serving patients across their continuum. To do this, we are radioisotope agnostic, which allows us to find the best "tool for the job" and find complementary treatment approaches. Our work in advancing $^{212}$Pb isotope production capacity is an exciting example.

Our novel investigational prostate cancer therapy (TLX591) allows for a patient-friendly dosing regimen - 2 treatments given 14 days apart. The short regimen can allow patients without access to reasonably travel across continents even to receive care in a short time frame.

We are working to expand access of PSMA imaging to patients in regions with limited radiopharmaceutical manufacturing infrastructure or in remote locations via our spinoff Rhine Pharma, formed in collaboration with Heidelberg University Hospital. The RHINO study aims to explore safety and efficacy of RHN001, a next-generation theranostic compound targeting PSMA, labeled with either $^{99m}$Tc for SPECT imaging or $^{188}$Re for therapy, offering a highly-differentiated solution since $^{99m}$Tc and $^{188}$Re can each be produced using on-site generators.

Lastly, to further ensure widespread availability, Telix has acquired an extensive network of radiopharmacies, strengthening our distribution capabilities and reducing delays in patient care. Through these initiatives, we remain committed to breaking barriers in radiopharmaceutical access, making cutting-edge theranostics available to more patients worldwide.

**In the last year, what has been exciting at Telix?**

This past year has been a transformative one for Telix, marked by two new drug applications accepted for filing (Zircaix® and Pixclara®), and one new drug to market (Gozellix in US). Illuccix® has also been approved in Brazil (the first full approval for PSMA-PET imaging in Latin America), the United Kingdom and a number of European Economic Area member states, bringing us closer to addressing critical unmet needs for patients with cancer and rare diseases.

Our ZIRCON Phase 3 study successfully demonstrated the ability of Zircaix PET to detect and characterize clear cell renal cell carcinomas. With limited diagnostic options currently available, this represents a major step forward in improving early and accurate detection for patients who often face uncertainty about their diagnosis and treatment path.

We are also excited to bring Pixclara, a PET agent for the characterization of progressive or recurrent glioma from treatment related changes, subject to approval. This is addressing a critical unmet need in the US. We are also leading development of theranostic approaches with Pixclara as a "companion" diagnostic for TLX101, our therapy for patients with gliomas, with promising results to date.

Our recent acquisition of fibroblast activation protein (FAP)-targeting theranostic candidates is a game-changer. FAP is a pan-cancer marker expressed in the

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tumor microenvironment of epithelial cancers and on the surface of some specific cancer types, including sarcomas and mesotheliomas. We believe this acquisition strengthens our ability to develop novel radiopharmaceuticals that could provide new hope for patients with limited imaging and treatment options. Ultimately, our goal is to not only expand access to these innovative solutions but also to reduce the emotional burden patients face by providing clearer answers and improving physician confidence in clinical decision-making. Knowing the full extent of disease—or confirming its absence—can significantly reduce the fear of the unknown, empowering both patients and their care teams with the information needed to make the best possible treatment decisions.

**In the next 5 years, how do you see the future of radiotheranostics evolving, and what role will Telix play in shaping it?**

The future of radiotheranostics is incredibly promising, with broader applications not only within oncology but also in other disease areas. AI-driven imaging and personalized dosimetry will enhance precision, while novel radionuclides have the potential to improve treatment efficacy and expand therapeutic options.

In the next 5 years, we anticipate having a first-in-class radio antibody-drug conjugate (TLX591) available for patients with prostate cancer, as well as novel theranostic pairs for patients with brain and kidney cancers available, delivering on critically unmet needs. We aim to have further established the complementary role of our alpha- and beta-emitting radiopharmaceuticals, supporting patients across their continuum. We aim to also have unlocked the full potential of FAP-targeted theranostics, expanding treatment options for a wider range of cancers.

Additionally, we are committed to bringing the accuracy of our PSMA imaging to patients earlier in their disease, supporting early and accurate diagnosis and treatment planning and optimizing potential positive patient outcomes. For CAIX imaging, the full potential of Zircaix for metastatic lesion detection and myriad clinical utilities will be elucidated.

We will remain at the forefront by remaining focused on our mission – our commitment to our patients. Telix is reshaping the future of precision oncology and ensuring patients receive the right treatment at the right time, throughout their experience.

ISOLOGIC
SOINS DE QUALITÉ FIABLE

# Vous faites confiance à Isologic pour des radiopharmaceutiques de haute qualité afin d'optimiser les soins aux patients. Mais nous offrons bien plus encore.


FIER MEMBRE DE LA COALITION

MorePETs

DISTRIBUTION À L'ÉCHELLE DU CANADA

Galli Eo

NeuraCeq^MC
injection de florbétaben F18

illuccix
(Trousse pour la préparation du gallium [68Ga] gozetotide injectable)

## Radiopharmacies TEMP et sites de production TEP à travers le Canada à votre service

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