

THE FREE NUCLEAR MEDICINE & MOLECULAR IMAGING EDUCATIONAL MAGAZINE AVAILABLE WORLDWIDE

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MÉDECINE NUCLÉAIRE SIMPLIFIÉE

MEDICINA NUCLEAR EN PALABRAS SENCILLAS



PANGEA PROJECT



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TECHNEGAS®

Kit for the preparation of technetium Tc 99m-labeled carbon inhalation aerosol



Cyclomedica is proud to bring its innovative technology, Technegas®, to the United States. Technegas®, referenced in

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INDICATIONS & USAGE

TECHNEGAS", when used with sodium pertechnetate Tc 99m in the Technegas" Plus System, provides technetium Tc 99m-labeled carbon inhalation aerosol (Technegas" Aerosol), a radioactive diagnostic agent for use in adults and pediatric patients aged 6 years and older for:

- visualization of pulmonary ventilation
- evaluation of pulmonary embolism when paired with perfusion imaging

DOSAGE & ADMINISTRATION

 For adult patients, the recommended activity of sodium pertechnetate Tc 99m injection to be loaded in the Technegas Crucible is 400 MBq to 1,000 MBq (10.8 mCi to 27 mCi) to achieve a lung count rate between 1,500 counts per second (cps) and 2,500 cps at the end of the last respiration. (2.2)

- For pediatric patients aged 6 years and older, a sufficient amount of Technegas Aerosol should be inhaled to achieve between 500 cps and 1.000 cps at the end of last respiration. The radioactivity to be loaded in the Technegas Crucible is a fraction of the recommended activity for aduits adjusted by body weight. (2.2)
- Administer as soon as possible following preparation and complete inhalation within 10 minutes of preparation.
 (2.2)
- For drug handling, breathing techniques, preparation, and dosimetry information, see the full prescribing information. (21, 2.3, 2.4, 2.5)

DOSAGE FORMS & STRENGTH

TECHNEGAS (kit for the preparation of technetium Tc 99m labeled carbon inhalation aerosol) is a 1.25 gram single-use black to dark grey oval shaped graphite carbon rucible (Technegas Crucible). Upon addition of sodium pertechnetate Tc 99m injection. USP to the Technegas Crucible, the Technegas Plus System provides Technegas Aerosol for oral inhalation. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS & PRECAUTIONS

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. [5.1]

Radiation Exposure Risk: Ensure safe handling and preparation procedures to protect patients and health care providers from unintentional radiation exposure. (2.1, 5.2)

ADVERSE REACTIONS

The most common adverse reaction (≥ 1%) was hypoxia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Cyclomedica Australia Pty Ltd at toll free phone number 1-888-8-586-4396 or FDA at 1-800-FDA-1088 or www.fda. gov/medwatch.

USE IN SPECIFIC POPULATIONS

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, [8,2]

¹ Bajc M, et al. Eur J Nucl Med Mol Imaging (2019) 46:2429–2451

¹ Leblanc M, et al. CANM Guidelines for V/P SPECT in PE CANM Nov 2018 ^t https://www.accessdata.fda.gov/drugsatfda_docs/ label/2023/022335s000lbl.pdf

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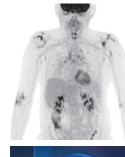
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Content



EDITORIAL BOARD



I am thrilled to introduce our outstanding editorial board members. Through our travel and NM lecturing around the globe, I have met terrific scientists and colleagues. Most, if not all of them, are really passionate about and true advocates for the field of nuclear medicine. They strongly believe in the power, usefulness and safe use of NM diagnostic and therapeutic procedures for the betterment of public healthcare worldwide. I am delighted that the following leaders

have embraced the concept of the Pangea-ePatient magazine and accepted to share their invaluable expertise and experience with patients, referring colleagues, health care administrators, government agencies and insurance companies. Dr. François Lamoureux



Dr. Akram Al-Ibraheem, M.D. President, Arab Society of Nuclear Medicine (ARSNM) Chairman, Department of Nuclear Medicine & PET/CT EANM; Director, Institute King Hussein Cancer Center, Amman, Jordan



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François Lamoureux, M.D, M.Sc., FRCP(C), ABNM

LES AVANCÉES MÉDICO-PHARMACOLOGIQUES



QUI EST DONC CE MÉDECIN NUCLÉAIRE?

Une des grandes avancées du XX^e siècle fut la maîtrise de l'énergie nucléaire. Cette avancée a permis un apport exceptionnel dans l'amélioration de la qualité de vie de l'être humain. Aujourd'hui, on retrouve dans notre vie quotidienne des applications de cette technologie souvent insoupçonnée, comme c'est le cas des alarmes résidentielles pour le feu, de la production d'électricité ou encore de l'irradiation de certains aliments pour en assurer la conservation. C'est une énergie puissante, mais invisible, insonore, incolore, inodore, et donc difficilement détectable pour l'Homme. Des détecteurs construits par l'Homme sont donc nécessaires.

Une des grandes applications de cette forme d'énergie est sans contredit son apport à la médecine, principalement dans la détection de maladies et, dans certains cas, pour leur traitement. Aujourd'hui, dans le monde, plus de 30 millions de ces examens scintigraphiques sont réalisés chaque année. C'est réellement une guerre contre des pathogènes, des cellules cancéreuses, des agressions tissulaires ou d'organes que le médecin nucléiste, ce spécialiste de la médecine nucléaire, tente de débusquer dans sa pratique médicale. Ces agresseurs sont souvent extrêmement délétères pour l'humain et, s'ils ne sont pas détectés de façon précoce, ils peuvent non seulement être source d'une grande morbidité, mais également conduire à une mort prématurée. Souvent, ces mauvais compagnons peuvent se terrer durant de longues périodes, voire des années, dans le corps humain avant de se manifester sous forme de lésions visibles (tumeurs. excroissances ou destructions cellulaires).

Mais qui est donc ce médecin nucléiste? C'est d'abord et avant tout un médecin qui, après cinq années d'études en médecine, s'est spécialisé pour au moins une nouvelle période de cinq années et parfois plus pour atteindre une meilleure maîtrise de l'anatomie humaine, de sa physiologie, des différentes pathologies et de l'interaction des différents médicaments ou traitements au niveau de ses organes.

Comme le médecin nucléiste agit au niveau cellulaire, de l'infinitésimal et des systèmes moléculaires, il doit en plus maîtriser un niveau élevé de connaissance de ses outils de travail, soient l'informatique, la physique nucléaire, le rayonnement nucléaire, les équipements très sophistiqués de détection et la radioprotection associée à l'utilisation de cette technologie de haut niveau, et ce, pour le meilleur bénéfice des patients.

Fort de ces connaissances et de la disponibilité d'équipements de détection de plus en plus sophistiqués, tels que des caméras monophotoniques ou à positrons pour la détection de rayonnements provenant du noyau d'un isotope radioactif introduit dans le corps d'un patient, le médecin nucléiste sera à même de débusquer les modifications métaboliques ou cellulaires pathologiques, souvent même avant qu'une lésion morphologique ne se manifeste. On peut donc, dans plusieurs situations, détecter précocement des lésions agressives comme des métastases osseuses, de l'ischémie cardiaque ou cérébrale, des processus neurodégénératifs ou encore des processus infectieux sournois évoluant à bas bruit. Comment est-ce possible? C'est en utilisant des radiotraceurs couplés ou non à des supports biologiques de plus en plus disponibles et agissant aux niveaux cellulaire

« On peut les qualifier de super-technologues de l'atome! Ce sont nos alliés de tous les jours et combien indispensables pour le patient, car les examens se déroulent entièrement en leur présence. » et moléculaire que l'on y arrive. C'est une véritable médecine moléculaire qui fait appel aux deux grandes avancées du XX^e siècle, soient l'énergie nucléaire et la micro-informatique.

Les renseignements obtenus sont ensuite transmis au médecin traitant sous forme de données quantitatives ou scintigraphiques, c'est-à-dire souvent en images tridimensionnelles ou encore sous forme dynamique. Ces données sont cependant toujours l'expression d'une manifestation cellulaire, métabolique, dynamique ou physiologique. Dans certaines situations, le médecin nucléiste procède à des traitements de pathologie, par exemple pour certains cancers ou encore des pathologies de la glande thyroïde ou de certaines articulations.

Pour le patient, ces investigations sont simples, rapides, sans douleur ni effraction importante et sans effets secondaires significatifs. Les phénomènes allergiques sont pratiquement inexistants. C'est une médecine très douce pour le patient et combien utile!

Le médecin nucléiste ne travaille pas seul. Il travaille en équipe avec des physiciens, des ingénieurs biomédicaux et surtout avec des technologues hautement spécialisés en médecine nucléaire qui se sont spécialisés exclusivement dans ce domaine par une formation spécifique de trois ans comme ici au Canada. On peut les qualifier de super-technologues de l'atome! Ce sont nos alliés de tous les jours et combien indispensables pour le patient, car les examens se déroulent entièrement en leur présence.

Au Canada, les patients ont facilement et gratuitement accès à ces examens.

En raison de l'évolution fulgurante de cette médecine, par l'apparition continuelle de nouveaux radiotraceurs, d'équipements de détection de plus en plus sophistiqués, d'une informatique galopante, de la découverte de nouveaux processus pathologiques, le

médecin nucléiste et ses collègues technologues doivent consacrer une part importante de leur temps au maintien de leurs connaissances ou à l'acquisition de nouvelles.

C'est une spécialité de la médecine extrêmement vivante et en continuelle évolution. Plus de 220 de ces centres existent au Canada, dont 54 au Québec. Plus de 40 résidents, de futurs médecins nucléistes, sont actuellement en formation au Canada, dont 25 au Québec.

Le volet thérapie par radiotraceurs devient le nouveau défi de la médecine nucléaire. Le Canada possède un des meilleurs systèmes de santé au monde et facilement accessible et sans frais pour le patient et la médecine nucléaire fait partie de cette excellence.



« C'est une spécialité de la médecine extrêmement vivante et en continuelle évolution. Plus de 220 de ces centres existent au Canada, dont 54 au Québec. »

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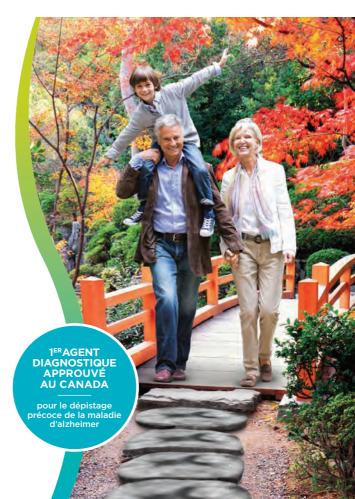
Neuraceq (florbetaben [¹⁸F]) est indiqué pour l'évaluation, par tomographie par émission de positons (TEP), de la densité des plaques séniles β -amyloïdes dans le cerveau de patients adultes atteints de troubles cognitifs, pour le diagnostic de la maladie d'Alzheimer (MA) ou d'autres causes de troubles cognitifs.













François Lamoureux, M.D, M.Sc., FRCP(C), ABNM

MEDICAL AND PHARMACOLOGICAL ADVANCES



SO, WHO IS THIS NUCLEAR MEDICINE PHYSICIAN?

One of the great advances of the twentieth century was the control of nuclear energy. This progress has made an exceptional contribution to improving the quality of life of human beings. Today, we find in our daily life applications of this often-unsuspected technology, as is the case of residential fire alarms, electricity production or even the irradiation of certain foods to ensure their conservation. It is a powerful energy, but invisible, soundless, colorless, odorless, and thus hardly detectable for the man. Man-made detectors are needed.

One of the major applications of this form of energy is undoubtedly its contribution to medicine, mainly in the detection of diseases and, in some cases, for their treatment. Today, in the world, more than 30 million scintigraphic examinations are performed each year. It is really a war against pathogens, cancer cells, tissue or organ attacks that the nuclear medicine physician tries to find in his medical practice. These aggressors are often extremely deleterious to humans and, if they are not detected early, they can not only be a source of great morbidity, but also lead to premature death. Often these bad companions can burrow for long periods, or even years, in the human body before manifesting themselves as visible lesions (tumors, growths or cellular destruction).

So, who is this nuclear medicine physician? It is first and foremost a doctor who, after spending five years in medical school, has specialized for at least a further five years, and sometimes more, to achieve a better mastery of human anatomy, its physiology, different pathologies and the interaction of different drugs or treatments in its organs.

Since the nuclear medicine physician acts at the cellular, infinitesimal and molecular systems levels, he must also master a high level of knowledge of his working tools, namely computer science, nuclear physics, nuclear radiation, very sophisticated detection equipment and radiation protection associated with the use of this high-level technology, and this, for the benefit of patients.

With this knowledge and the availability of increasingly sophisticated detection equipment, such as single-photon or positron cameras for the detection of radiation from the nucleus of a radioactive isotope introduced into the body of a patient, the nuclear medicine physician will be able to flush out pathological metabolic or cellular changes, often even before a morphological lesion occurs. Thus, in many situations, aggressive lesions such as

"They can be called super-technologists of the atom! These are our everyday allies and so essential to the patient, because the examinations are always performed in their presence." bone metastases, cardiac or cerebral ischemia, neurodegenerative processes, or devious infectious processes can be detected early. How is it possible? It is by using radiotracers coupled or not with biological supports more and more available and acting at the cellular and molecular levels that one arrives there. It is a true molecular medicine that uses the two great advances of the twentieth century, namely nuclear energy and micro-computing.

The information obtained is then transmitted to the treating physician in the form of quantitative or scintigraphic data, often in three-dimensional images or in dynamic form. This data is, however, always the expression of a cellular, metabolic, dynamic or physiological manifestation. In certain situations, the nuclear medicine physician carries out pathology treatments, for example for certain cancers or even pathologies of the thyroid gland or certain joints.

For the patient, these investigations are simple, fast, without significant pain or break-in and without significant side effects. Allergic phenomena are practically non-existent. It is a very gentle medicine for the patient and how useful!

The nuclear medicine physician does not work alone. He works in a team with physicists, biomedical engineers and especially with technologists highly specialized in nuclear medicine who have specialized exclusively in this field through a specific training of three years, as is the case here in Canada. They can be called supertechnologists of the atom! These are our everyday allies and so essential to the patient, because the examinations are always performed in their presence.

In Canada, patients have easy and free access to these tests.

Due to the rapid evolution of this medicine, the continual emergence of new radiotracers, more and more sophisticated detection equipment,

rampant computing technology, the discovery of new pathological processes, the nuclear medicine physician and his technologist colleagues must devote a significant amount of their time to maintaining their knowledge or acquiring new ones.

It is a specialty of medicine that is extremely alive and constantly evolving. More than 220 of these centers exist in Canada, including 54 in Quebec. More than 40 residents, future nuclear physicians, are currently training in Canada, including 25 in Quebec.

Radiation tracer therapy is becoming the new challenge of nuclear medicine. Canada has one of the best health care systems in the world and is easily accessible at no cost to the patient and nuclear medicine is part of that excellence.



"It is a specialty of medicine that is extremely alive and constantly evolving. More than 220 of these centers exist in Canada, including 54 in Quebec."

Knowing can help you plan your path ahead

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World Federation of Nuclear Medicine & Biology 2025-2026 President-Elect Dr. Francois Lamoureux



- MD: University of Sherbrooke
 - Board Certified in Nuclear Medicine
- M.Sc: University of London, England
- Fellow Royal College of Canada
- Medalist of the city of Paris
- Professor at the University of Montreal
- Membership: EANM, SNMMI, SFNM, CANM
- Past President of the AMSMNQ, President of the CANM
- Several presentations/lectures in Europe, North & South America
- Editor in chief of the magazines Le Patient and ePatient
- Main interests: Precision Medicine, Theranostics, NM Education and Promotion

As President-Elect of the WFNMB, I will bridge connections with you worldwide.

I currently serve as the Treasurer of the World Federation of Nuclear Medicine and Biology (WFNMB) and as the President of the Canadian Association of Nuclear Medicine (CANM). For over 30 years, the CANM has worked closely with the WFNMB. I firmly believe that the WFNMB plays a vital role globally, fostering stronger partnerships among countries to ensure the enhancement of nuclear medicine.

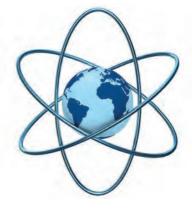
With the development of new detectors, novel radiopharmaceuticals, and the rapid expansion of theranostics, the WFNMB is needed more than ever as a key interlocutor. I have strong relationships with the International Atomic Energy Agency (IAEA) and firmly believe that through this partnership, the WFNMB can significantly increase the availability of nuclear medicine for patients worldwide, especially in emerging countries.

The WFNMB is widely regarded as a well-respected organization, and I would be delighted to work closely with the executive board to enhance access to high-quality nuclear medicine across the globe.

As a professor of nuclear medicine, I have trained many residents, authored numerous publications and presentations, and genuinely believe that nuclear medicine has a promising future.

referm

François Lamoureux M.D., M.Sc., FRCP(C). President-Elect 2025-2026 Of the WFNMB President CANM +1 (514) 889-0662 lamoureuxf@sympatico.ca Canada



DR. GISELA ESTRADA-SÁNCHEZ

The Latin American Association of Societies of Biology and Nuclear Medicine (ALASBIMN) is a Scientific Society founded in 1964, whose permanent secretariat is located in Montevideo, Uruguay. It includes the Biology and Nuclear Medicine Societies of Latin America: Argentina, Bolivia, Brasil, Chile, Colombia, Ecuador, Guatemala, México, Paraguay, Perú, Uruguay and Venezuela.

The main purpose of ALASBIMN is to promote the development of Nuclear Medicine in the region, generating spaces for exchange and learning.

Nuclear medicine is a medical specialty that uses very small amounts of radioactive tracers (radiopharmaceuticals) to diagnose and treat disease. Specially designed cameras allow doctors to track the path of these radioactive tracers. Single Photon Emission Computed Tomography or SPECT and Positron Emission Tomography or PET scans are the two most common imaging modalities in nuclear medicine.

Nuclear Medicine provides unique information that often cannot be obtained using other imaging procedures to help diagnose. Nuclear imaging shows organ and tissue structure as well as function.

SPECT scans are primarily used to diagnose and track the progression of heart disease, such as blocked coronary arteries. There are also radiotracers to detect disorders in the brain, thyroid, kidneys, parathyroids, bone, breast, lungs, gall bladder and intestinal bleeding.

The major purpose of PET/CT scans is to detect cancer and monitor its progression, response to treatment, and to detect metastases using different radiotracers, the most common is glucose.

Nuclear medicine is used to treat various pathologies. These include hyperthyroidism, thyroid cancer, lymphomas, prostate cancer, neuroendocrine cancer and bone pain due to metastasis.





Dr. Gisela Estrada-Sánchez, MD, PhD.

Nuclear Medicine Physician 18 years of experience in PET/CT. High resolution breast PET Treatments with I-131, Ra-223, Lu-177. She is the chief of the PET/CT department at Imagen Tomográfica y Molecular in Cancun, Mexico. Dr. Estrada authored numerous peer-reviewed research articles, reviews, committee publications and editorials. She co-edited The book PET and PET/CT in Oncology. Ed. Panamericana, 2013. President Mexican Board Nuclear Medicine 2018-2021. President Mexican Federation of Nuclear Medicine 2021-2023.

President of ALASBIMN 2023-2025.

Nuclear medicine physicians are strongly committed to keeping radiation exposure to patients as low as possible, giving the least amount of radiotracer needed to provide a diagnostically useful examination.

ALASBIMN has a Journal that publishes different topics in general nuclear medicine and PET/CT http://www.alasbimnjournal.net/, also organizes a meeting every two years, the next one will be in Cancún, México in April 2025.

All the updated information will be at Federación Mexicana de Medicina Nuclear e Imagen Molecular 2021 and in the ALASBIMN page https://alasbimn.net/acerca-de-alasbimn/





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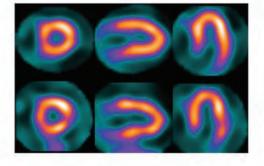
Myoview's post-reconstituted shelf life is 12 hours¹

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In a prospective study by Ravizzini:

- Myoview demonstrated significantly shorter completion time for both rest studies and total study time²
- Patients receiving Myoview required fewer repeat scans due to extra cardiac activity²

References: 1. Myoview [product monograph], February 12, 2018 (revised August 21, 2019), Control No. 211075. 2. Ravizzini GC, Hanson MW, Shaw LK, et al. Efficiency comparison between 99m Tc-tetrofosmin and 99m Tc-sestamibi myocardial perfusion studies. *Nucl Med Comm.* 2002;23:203-208.



(Kit for the Preparation of Technetium Tc99m Tetrofosmin for Injection) **PRODUCT INDICATIONS AND CLINICAL USES:** MyoviewTM (Kit for the Preparation of Technetium Tc-99m Tetrofosmin Injection) is indicated for scintigraphic imaging of the myocardium following separate administrations under stress (exercise and/or pharmacologic) and resting conditions in patients with known or suspected coronary artery disease. It is useful in the delineation of regions of reversible myocardial ischemia in the presence or absence of infarcted myocardium. Dipyridamoleinduced pharmacologic stress may be used as an alternative to exercise in patients who cannot exercise adequately.

Important Safety Information About Myoview

CONTRAINDICATIONS: None known. **WARNINGS:** In studying patients with known or suspected coronary artery disease, care should be taken to ensure continuous cardiac monitoring and the availability of emergency cardiac treatment. Myoview is not recommended for use in patients with known hypersensitivity to tetrofosmin. Severe hypersensitivity reactions and anaphylactoid reactions have been reported for Myoview. The contents of the vial of Myoview are intended for use only in the preparation of technetium Tc-99m tetrofosmin injection and are NOT to be administered directly to the patient. Pharmacologic induction of cardiovascular stress may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Caution should be used when dipyridamole-induced pharmacologic stress is selected as an alternative to exercise; it should be used when indicated and in accordance with the Product Monograph and instructions for dipyridamole (Persantine®). **PRECAUTIONS - General:** Allergic reactions and anaphylaxis may occur with Myoview. Technetium Tc-99m tetrofosmin injection, like other radioactive drugs must be handled with care, and appropriate safety measures should be used to minimize radiation exposure to clinical personnel. The contents of the kit are not radioactive.

However, after sodium pertechnetate Tc-99m is added, adequate shielding of the final preparation must be maintained to minimize radiation exposure to occupational workers and patients. Care should also be taken to minimize radiation exposure to patients, consistent with proper patient management. To minimize radiation dose to the bladder, patients should be encouraged to void when the examination is completed and as often thereafter as possible. Adequate hydration should be encouraged to permit frequent voiding. The Tc-99m labeling reactions involved depend on maintaining the tin (stannous ion) in the reduced state. Therefore, sodium pertechnetate Tc-99m-containing oxidants should not be employed. Radiopharmaceuticals should be used only by those practitioners who are appropriately qualified in the use of radioactive, prescribed substances in or on humans.

The components of the reagent vial are sterile and nonpyrogenic. It is essential that the user follows the directions carefully and adheres to strict aseptic technique. Drug Interactions: Drug interactions were not noted and were not studied in clinical studies in which Myoview was administered to patients receiving concomitant medication. Drugs such as beta-blockers, calcium channel blockers, and nitrates may influence myocardial function and blood flow. The effects of such drugs on imaging results are not known. Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies have not been conducted to evaluate carcinogenic potential or effects on fertility. Tetrofosmin sulphosalicylate was not mutagenic in vitro in the Ames test, mouse lymphoma, or human lymphocyte tests, nor was it clastogenic in vivo in the mouse micronucleus test. Use in Pregnancy: Since adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has adverse effects on the fetus, this radiopharmaceutical preparation should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards. Nursing Mothers: Technetium Tc-99m pertechnetate can be excreted in human milk. Where an assessment of the risk-to-benefit ratio suggests the use of this product in lactating mothers, formula feeding should be substituted for breastfeeding. Pediatric Use: Adequate studies do not exist to support the use of this radiopharmaceutical in children. ADVERSE REACTIONS: The following events were noted in less than 1% of study patients: Angina, hypertension, torsades de pointes, flushing, vomiting, abdominal pain/discomfort, cutaneous allergy, hypotension, dyspnea, metallic taste, burning of mouth, smelling something, abnormal vision. There was a low incidence (less than 4%) of a transient and clinically insignificant rise in white blood cell counts following administration of the agent. Postmarketing: Adverse reactions included hypersensitivity, anaphylactic or anaphylactoid shock, anaphylactic or anaphylactoid reaction, taste alteration, dizziness, tachycardia, chest pain, hypotension, dyspnea, bronchospasm, throat tightness, coughing, nausea, vomiting, abdominal pain, urticaria, pruritus, rash, erythema, and angioedema.

Prior to Myoview administration, please read the full Product Monograph, which is available by calling 1 800 654 0118 (option 2, then option 3).

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 1 800 654 0118 (option 2, then option 1), or email canadainfo@ge.com to request an adverse events form, or fax a request for a form to 905 847 5849. Adverse reactions can also be reported to Health Canada as follows:

- Online at www.healthcanada.gc.ca/medeffect
- By calling 1 866 234 2345 (toll-free)
- By completing a Canada Vigilance Reporting Form and sending it by:
- Fax to 1 866 678 6789 (toll-free)
- Mail to Canada Vigilance Program, Health Canada, Postal Locator 0701E Ottawa, ON K1A 0K9
- Postage-paid labels and the Canada Vigilance Reporting Form are available at www.healthcanada.gc.ca/medeffec



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GERO-THERANOSTICS

Nuclear Medicine & Theranostics

As the 21st century dawned, nuclear medicine faced a bleak outlook. The advent of clinical ultrasonography, computerized tomography, and magnetic resonance seemed to overshadow our field's relevance, while a dearth of investments in novel radiopharmaceuticals and relying on decades old Anger physics cast a shadow over its future.

Yet, through a series of remarkable developments intertwined with the human genome projects and the explosion of the omics knowledge and technologies, coupled with the relentless determination of pioneers, nuclear medicine has undergone a profound and fantastic resurgence. Today, it stands poised to play a pivotal role in patient management, particularly in oncology, marking a turning point marked by a shortage of nuclear professionals unprecedented in our history.

Central to this renaissance is the discovery and clinical application of a new class of radiopharmaceuticals known as Theranostics. Coined by John Funkhouser in 1998, Theranostics represents a revolutionary fusion of therapeutic and diagnostic modalities. Under Funkhouser's leadership as CEO of PharmaNetics, this vision crystallized into a paradigmshifting approach that was intending to blend therapeutics and diagnostics seamlessly.

Nuclear Theranostics, epitomized by the use of a single target binding agent to both diagnose and treat specific diseases, has sparked immense enthusiasm within the nuclear medicine community. With approximately 90 companies currently engaged developing in precision medicine radiopharmaceuticals, market analyses indicate exponential financial growth for the specialty in the years ahead. Forecasts indicate a seismic shift from an imaging-centric specialty to a therapeutic focus, with nuclear medicine projected to transition from an 85 percent imaging specialty to a 60-70% therapeutic specialty.

While Nuclear Theranostics have already made significant inroads in managing neuroendocrine tumors, prostate cancers, and select thyroid cancers, their integration of diagnostic and therapeutic components represents just the beginning of the concept of Theranostics. Across diverse fields, from Nano Theranostics to Magnetic Theranostics and Immuno-Theranostics, researchers are harnessing the power of integrated platforms to tackle a spectrum of diseases, spanning from degenerative and systemic disorders to infectious diseases.

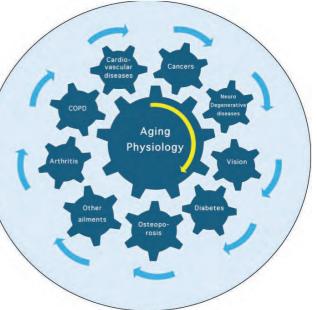


Figure 1. GeroScience: illustration of aging related conditions/diseases

In essence, the revitalization of nuclear medicine through Theranostics heralds not only a renaissance within our field but also a broader revolution in precision medicine and patients management fueled by relentless innovation and collaborative research.

GeroScience

The progress in socioeconomics, living standards, medicine, and public health has heralded a remarkable era of increased lifespan worldwide. Over centuries, life expectancy has nearly doubled from the early 19th century, a testament to humanity's strides in healthcare and societal development.

While aging itself isn't a disease, it significantly heightens the risk of various acute and chronic conditions, including cardiovascular disease, diabetes, cancer, arthritis, and degenerative disorders (Figure 1). Gerontology, coined by Ilya Ilyich Mechnikov in 1903, encompasses a broad spectrum of disciplines, addressing the societal, psychological, cognitive, and biological dimensions of aging's impact on older adults.

Recognizing the pivotal role of aging research, the National Institute on Aging (NIA), established by the U.S. Congress in 1974, has been at the forefront. In 2012, Drs. Felipe Sierra and Ronald Kohanski catalyzed the NIH-wide Geroscience initiative, consolidating efforts to understand the genetic, molecular, and cellular biology processes that underpins aging.

GeroScience endeavors to unravel the intricate mechanism of aging, viewing it as a primary driver of age-related diseases. Geroscientists delve into the fundamental physiological, pathophysiological and biological processes associated with aging, aiming to develop interventions that mitigate age-related ailments and enhance overall well-being in older populations (Figure 2).

By probing the molecular and cellular intricacies of aging, GeroScience is poised to accelerate our understanding of aging and revolutionize approaches to age-related healthcare. This interdisciplinary pursuit unites researchers across diverse fields, forging pathways to address the multifaceted challenges posed by an aging worldwide population, with the ultimate aim to foster healthier and more fulfilling lives for older adults.

GeroScience, Nuclear Medicine and Theranostics

The intersection of GeroScience, nuclear medicine, and Theranostics represents a promising frontier in understanding and managing age-related conditions and diseases. As people worldwide are living longer, addressing age-related health challenges becomes increasingly urgent. GeroScience, as a field, seeks to unravel the underlying genetic, molecular, and cellular mechanisms driving aging and age-related diseases.

Nuclear medicine, with its ability to visualize and treat diseases at the molecular level, offers a unique toolset for GeroScientists to delve into the intricacies of aging processes. The development and utilization of nuclear diagnostic and therapeutic Theranostics further enhance this capability, enabling precise detection and targeted treatment of age-related conditions (Figure 3).

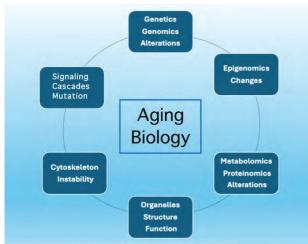


Figure 2.GeroScience: aging biology processes snapshot



Figure 3. 18-FDG PET scintigraphy performed on a 62year old patient for suspicion of a pulmonary tumor showing in fact a diffuse joint inflammatory process related to a psoriatic arthritis

By leveraging radiopharmaceuticals and Theranostics, GeroScientists can gain insights into the molecular changes associated with aging, aiding in the identification of biomarkers and pathological pathways. This knowledge not only deepens our understanding of aging but also enables the development of interventions and therapies to mitigate in not curing age-related diseases.

Additionally, nuclear medicine techniques can assist Gerontologists in patient management by providing

> personalized diagnostic and therapeutic strategies tailored to individual molecular profiles. This targeted approach enhances treatment efficacy and patient outcomes, ultimately improving quality of life for older adults.

Conclusion

As the fields of GeroScience, Nuclear Medicine, and Theranostics continue to evolve, their integration holds great promise for advancing our understanding of aging and transforming the landscape of age-related healthcare. By synergizing these disciplines, researchers and clinicians can pave the way for innovative approaches to promote healthy aging and address the complex health challenges associated with growing older.

"GeroScience endeavors to unravel the intricate mechanism of aging, viewing it as a primary driver of agerelated diseases. Geroscientists delve into the fundamental physiological, pathophysiological and biological processes associated with aging, aiming to develop interventions that mitigate agerelated ailments and enhance overall wellbeing in older populations."

CLINICAL USEFULNESS OF VENTILATION/PERFUSION LUNG SCINTIGRAPHY (V/Q scan) IN DETECTION OF PULMONARY EMBOLISMS



Raymond Taillefer MD, FRCP, ABNM Director of Nuclear Medicine, Hôpital du Haut Richelieu, St-Jean-sur-Richelieu, Québec, Canada

ulmonary embolism (PE) is a blockage in one or more of the pulmonary arteries of the lungs. Most of the time, PE results from blood clots travelling to the lungs and originating from deep veins in the legs (deep vein thrombosis) or, sometimes, from veins in other parts of the body. The lungs act as "filters" to these blood clots which can block the blood flow to the lungs. Blockage of the lung arteries can occasionally be secondary to fat from the marrow after a bone fracture, air bubbles or tumor. Depending on the size of the clots, the area of the lung involved and any underlying lung or heart diseases, PE can be a life-threatening condition, necessitating a rapid diagnosis. Prompt anticoagulant therapy (use to dissolve the blood clots) greatly reduces the risk of death and future chronic lung complications (such as chronic pulmonary hypertension).

The symptoms of PE can be quite variable, making the diagnosis of PE based only on the signs and symptoms more difficult. Most common signs and symptoms of

PE include a sudden shortness of breath which gets worse with exertion or inspiration, a chest pain (sometimes mimicking a heart attack), cough (sometimes with bloody sputum), irregular heartbeat, leg pain, leg swelling or fever, to name only the most frequent ones. Various risk factors are associated with PE such as recent surgery, estrogen supplement, pregnancy, prolonged immobility, cancer, family history, COVID-19, heart disease, smoking, and overweight are the most frequent ones.

As the clinical assessment alone is not reliable in the diagnosis of PE, objective demonstration of the presence of PE is essential. About one-third of patients with undiagnosed and untreated PE will not survive. On the other hand, incorrect diagnosis of PE unnecessarily exposes the patient to the risk of anticoagulant therapy such as potentially fatal hemorrhage. Therefore, various blood tests and imaging procedures have been developed to objectivate the presence of PE.

Discussion on all the different procedures used in the diagnosis of PE is beyond the scope of this article. Only those directly involved in the diagnosis of PE in clinical practice are presented. Various D-dimer blood tests have been developed. This is a substance derived from the coagulation process which shows increased levels in PE. This is a very sensitive test to detect PE but unfortunately increased in D-dimer blood levels is not specific to PE as it can be seen also in inflammation, cancer or aging. However, a negative D-dimer test almost completely rules-out PE.

The gold-standard method for diagnosis of PE is the pulmonary angiography which consists of injecting a contrast dye directly into the pulmonary arteries. Unfortunately, this quite invasive procedure is associated with serious side effects with a mortality rate of about 0.5%, is costly, technically challenging and sometimes difficult to interpret. The actual radiologic procedure mostly used in the diagnosis of PE is the multirow-detector computed tomographic pulmonary angiography (MD-CTPA). This consists in the use of a CT scan (Computed Tomography) with an injection of a radiologic contrast medium. This procedure can allow to visualize the main arteries as well as the lobar and segmental lung arteries. However, the diagnostic accuracy to detect subsegmental pulmonary lesions is rather low. The major advantage of CTPA is the ability to provide valuable information on diseases other than PE such as pneumonia, pleural effusion, aortic aneurysm or dissection, or tumor. Unfortunately, a significant number of patients are not illegible for CTPA due to allergy, kidney failure, critical illness, ventilator support, or recent myocardial infarction. Furthermore, up to 15-20% of CTPA are limited due to technical artifacts such as dilution effect of the contrast medium or respiratory motion artifacts. Therefore, other imaging modalities are frequently needed.

One of the most commonly used procedure nowadays in clinical practice is the ventilation/perfusion lung scintigraphy also known as V/Q scan performed in nuclear medicine. This procedure has been the witness of dramatical technical improvements in the last decade which can explain its constantly increased clinical demand. Interpretation criteria for the presence of EP has also contributed to its clinical usefulness. Many scientific societies have established criteria and technical guidelines for the realization of V/Q scans under strict conditions to allow for optimal results. The three major improvements can be summarized as follows: 1- The routine use of SPECT (Single Photon Emission Computed Tomography), 2- The use of 99mTc-Technegas for the ventilation part of the study, 3- Modifications of interpretation criteria for an abnormal V/Q lung study.

1- Routine clinical use of SPECT:

The first technical improvement includes the routine use of SPECT (Single Photon Emission Computed Tomography) for both ventilation and perfusion studies. This technique allows for a better image resolution and images of multiple slices of the lung, therefore providing better details and significant improvement in overall accuracy in comparison to the "standard" planar imaging acquisition used in the majority of published studies. In more complex cases, it is also possible to add the CT portion to the SPECT acquisition which is called SPECT-CT. The combination of these two modalities allows for simultaneous evaluation of the function with V/Q scan and the anatomical increased resolution of the CT.

2- Use of 99mTc-Technegas for the ventilation study: Ventilation study is preformed first (duration of



approximately 15-20 minutes) using the best widely available agent in Canada, 99mTc-Technegas (Cyclomedia), which consists of an aerosol of carbon nanoparticles. This radiotracer is distributed in the lungs almost like a gas (because of its very small particle size varying from 5 to 200 nm) and deposited in alveoli by diffusion where it remains stable for the duration of the lung scan using SPECT imaging. The patient rapidly inhales the 99mTc-Technegas for 2-5 deep inspirations. The administered dose varies from



0.8 to 1.4 mCi. Once the ventilation part of the study is completed, the perfusion part immediately follows. 99mTc-macroaggregated albumin (MAA) are used to perform the lung perfusion study. Approximately 400,000 albumin particles with an average size of 10-90 um are slowly injected into a vein, usually of the arm. This particle size allows them to lodge into the pulmonary small capillaries and provides a good definition of the entire lung perfusion. The standard dose is approximately 3.0-6.0 mCi of 99mTc-MAA (the activity ratio between perfusion and ventilation should be at least 4:1, preferably more). A second SPECT acquisition immediately starts and will last approximately 15-20 minutes although this time may vary according to the type of gamma camera used and the clinical situation. For example, in pregnant or lactating patient, the dosage will be significantly decreased in order to limit the radiation dose to the patient and the acquisition time will be increased in order to obtain still high quality images. 99mTc-Technegas provides a more uniform and a better overall ventilation scan in comparison to the previously used 99mTc-DTPA aerosols. Almost all the ventilation studies performed actually in Canada used 99mTc-Technegas.

3- Modifications of the diagnostic criteria for the V/Q study:

In the majority, if not all previous large studies comparing clinical assessment, radiologic procedures and nuclear medicine V/Q scans in the diagnosis of PE, interpretation criteria were based in probabilistic terms (normal, low, intermediate, and high probability) which are now unacceptable in clinical practice. Technological improvements in ventilation studies and the use of SPECT acquisition can now allow the interpreter to be more decisive, that is presence of PE or absence of PE, without gradation of probability which was very confusing to the referring physician. Equivocal or non diagnostic TOMO PER TOMO VEN TOMO PER SCINTIGRAPHIE PULMONA TOMO VENT

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studies may still be possible but should not be more than 5% of all the cases.

Interpretation criteria:

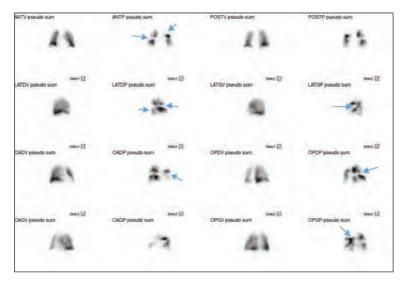
Different criteria have been proposed since the early ages of V/Q scan, the detailed discussion of which is beyond the scope of this article, but most diagnostic algorithms are derived from the same premisses. The basic principle of the lung scintigraphy is to compare the ventilation and the perfusion status of each pulmonary lobes, segments and subsegments, side by side. In a normal study, both perfusion and ventilation are homogeneous and similar (Figure 1). However, when PE occurs, only the lung perfusion is impaired by the blood clots blocking local blood circulation and preventing the radiotracer (99mTc-MAA) to travel beyond the clot, creating a "perfusion defect" on the perfusion images, while the ventilation remains normal since it is not affected by the venous clot (Figure 2). This is called vascular mismatched defects with usually clear borders, wider at the periphery of the lung and narrower more centrally, respecting the pulmonary vascular anatomy.

V/Q scans are frequently prescribed to rule-out PE in patients with chronic obstructive pulmonary disease (COPD) in whom the incidence of PE is increased and clinical presentation is very often confounding. Typically, V/Q lung scans in these COPD patients show impaired ventilation proportional to the severity of COPD (often underestimated clinically) which can be similar to perfusion defects or more prominent. Usually, both ventilation and perfusion defects are matched, meaning that they both have similar extension, pattern and localization (Figure 3).

The combination of 99mTc-Technegas for the ventilation part of the study, combined with SPECT acquisition of both ventilation and perfusion and new interpretation criteria have led to significant improvement in the overall diagnostic accuracy of

Figure 1.

Normal V/Q lung scan. The first and third column represent the ventilation study with 99mTc-Technegas while the second and fourth column represent the corresponding perfusion study performed with 99mTc-MAA in various imaging incidences. The distribution of both radiotracers is similar and relatively homogeneous.



V/Q scan for acute PE detection. The sensitivity of V/Q scan in the detection of PE varies from 90-95% with a similar specificity. The very high negative predictive value of V/Q scan varies between 97-99%, indicating that if a V/Q study is normal, combined with a normal D-dimer test virtually exclude the presence of PE. V/Q scan is highly sensitive for detection of chronic PE (90-95%) in comparison to CTPA (50-60%).

Radiation Exposure.

One of the most frequent and comprehensible concern when comes the time to inject a radiotracer to a patient, especially in young patients, or in breastfeeding or lactating patients, is the risk of radiation exposure to the patient. In medicine (either radiology or nuclear medicine) the millisievert (mSv) is used as a radioprotection unit which measures the radiation dose received by a specific medical procedure. While discussing the risk of radiation exposure, it is very important to consider the relative overall picture. For example, natural radioactivity occurring from cosmic rays or radon in the ground, generates between 2 to 10 mSv a year, depending on

Figure 2.

Patient with multiple perfusion defects (blue arrows) on perfusion images with corresponding normal ventilation, typical of segmental and sub-segmental acute PE (mismatches).

the location on the planet. Internal radioactivity from a human body generates approximately 0.25 mSv.

Besides natural radioactivity and radioactivity from general medical imaging procedures, regulations in almost countries in the world limit exposures related to other causes to less than 1.0 mSv per year for the general public. A trans-atlantic flight from Montreal to Paris results in a dose of 0.03mSv.

The radiation exposure from a V/Q SPECT study is approximately 2.1 mSv while for CTPA it varies from 5 to 15 mSv, depending of many technical factors. The fetal exposure in a pregnant patient is relatively the same for both procedures while the breast exposure for the CTPA is increased by a factor of 5-20 in comparison to the V/Q scan.

CONCLUSION

V/Q lung scan with its high sensitivity and specificity, low radiation exposure and no adverse reactions can be considered as a first line investigation procedure in suspected acute or chronic PE, in pediatric population, in pregnant or breast-feeding female patients or in patients with COPD.



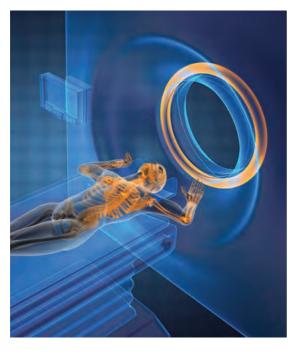
Figure 3.

Patient with moderate to severe COPD. Both ventilation and perfusion studies show similar and corresponding matched defects.

Dr. Rodrigo Jaimovich, M.D Past-President of ALASBIMN Professor, Nuclear Medicine at Clinica las Condes S.A Chili University, Chili



APORTE DEL SPECT/CT EN TÉCNICA DEL GANGLIO CENTINELA PARA CÁNCER DE MAMA



a adecuada evaluación del compromiso ganglionar axilar en cáncer de mama es de tremenda importancia tanto para el pronóstico del paciente así como para la toma de decisiones acerca de la terapia. En algunos casos puede implicar una mayor acción quirúrgica que incluya el vaciamiento ganglionar de la axila, o bien aumentar los campos a irradiar durante la radioterapia. Además muchas veces el status ganglionar define si se debe agregar quimioterapia como terapia adyuvante.

La técnica del ganglio centinela se ha transformado en la mejor forma de evaluar el compromiso axilar en cáncer de mama ya que identifica al primer ganglio tributario del drenaje linfático proveniente del tumor. Al identificar ese ganglio se puede resecar y analizar en forma exhaustiva con técnicas histoquímicas. Se ha demostrado que la capacidad predictora del status axilar a partir del ganglio centinela es muy buena, sobre el 95%, por lo que un estudio de ganglio centinela negativo predice con un alto nivel de certeza que el resto de los ganglios axilares no tienen diseminación tumoral.

Para identificar el ganglio centinela se utilizan dos técnicas que se basan en el mismo principio, una radioisotópica y otra con colorante. En ambas se inyecta una dosis de radiofármaco o colorante en la mama, generalmente en región periareolar en el cuadrante del tumor, de forma intradérmica. Posteriormente se espera a que el trazador (radioactivo o colorante) migre a través del sistema linfático hasta encontrar un ganglio SU camino donde se acumula en progresivamente. En el caso de la técnica con radioisótopos se realiza una imagen para demostrar la acumulación en el o los ganglios centinelas, se marca su ubicación para posteriormente ir a la resección guirúrgica. En pabellón se utiliza un detector portátil de radiación para ayudar a encontrar los ganglios radioactivos. En muchos centros se utilizan ambas técnicas en forma complementaria, realizando la marcación radioisotópica pre-operatoria, y en pabellón se agrega además el colorante. La combinación de ambas técnicas es la que mejores resultados ha reportado en cuanto a la correcta identificación del ganglio centinela.

Si bien la técnica radioisotópica ha demostrado excelentes resultados, existen algunas variaciones respecto a la forma original de adquirir las imágenes. En otros tumores donde también se identifica el ganglio centinela como el melanoma maligno, se ha planteado combinar las imágenes planares con una adquisición tomográfica (SPECT) a las cuales se les agrega una imagen anatómica (CT) que sirve tanto para mejorar la calidad de imagen como para dar un correlato espacial a la imagen de medicina nuclear. Esto es de particular interés en los melanomas de cabeza y cuello debido a la complejidad de las estructuras y espacios cervicales, donde se ha demostrado la superioridad de la técnica híbrida SPECT/CT sobre la planar tradicional en la detección del ganglio centinela.

La experiencia de la técnica de ganglio centinela con SPECT/CT en cáncer de mama es variada, reportándose algunas situaciones donde se obtienen beneficios con la técnica de imágenes híbridas. La indicación del SPECT/CT más común es la no visualización del ganglio centinela en las imágenes planares. Esto puede ocurrir por diversas razones, siendo la principal la superposición de la radioactividad del sitio de invección con la ubicación del ganglio centinela, quedando este último oculto. Otra causa es que la radioactividad acumulada en el ganglio centinela sea muy baja, impidiendo que sea visualizada en las imágenes planares. Las imágenes tomográficas con técnica SPECT/CT permiten identificar los sitios de radioactividad y diferenciarlos del sitio de invección. Además la reconstrucción de las imágenes con esta técnica entrega una mejor resolución, superior a la planar, por lo que se logran identificar ganglios muy pequeños y/o con baja captación. Esto ha permitido disminuir la cantidad de estudios donde no se lograba identificar los ganglios centinela mediante las imágenes preoperatorias.

Otra condición donde la técnica híbrida ha demostrado superioridad es la correcta identificación de sitios de drenaje atípico. Existe un porcentaje de pacientes donde el drenaje linfático no se dirige a la región axilar ipsilateral, siendo posible un drenaje hacia la cadena mamaria interna o a región supraclavicular. Este tipo de drenaje puede darse en forma exclusiva o concurrente con el drenaje hacia axila. La correcta identificación del territorio de drenaje permite a los cirujanos tomar decisiones acerca de la potencial resección de esos ganglios con drenaje atípico. Además, se ha postulado que la presencia de drenajes atípicos cuando no se identifica drenaje axilar puede reflejar una mayor probabilidad de que esos ganglios estén comprometidos. La explicación de este último fenómeno sería que, al infiltrarse los ganglios con metástasis tumorales, se bloquea su capacidad de captar el trazador, por lo que se "salta" a la siguiente estación ganglionar.

Se ha descrito una dificultad en la marcación del ganglio centinela en pacientes obesas, existiendo una correlación directa entre el valor creciente del índice de masa corporal y la menor tasa de detección de ganglios centinelas mediante la técnica planar tradicional. Esto se debe a la mayor atenuación que ocurre por la mayor profundidad de los ganglios. Cuando se realiza la técnica de SPECT/CT con la consiguiente corrección de atenuación, la tasa de detección de los ganglios aumenta significativamente.

Si bien no hay reportes de disminución del tiempo operatorio en pacientes que se realizan la técnica de ganglio centinela en cáncer de mama con método SPECT/CT versus planar, existe la referencia de esta disminución en casos de melanoma maligno. La información entregada por el SPECT/CT sí es apreciada por los cirujanos en términos de contar con la mayor cantidad de referencias para la exitosa localización del ganglio centinela. Lo primero es el número correcto de ganglios que muestran captación,

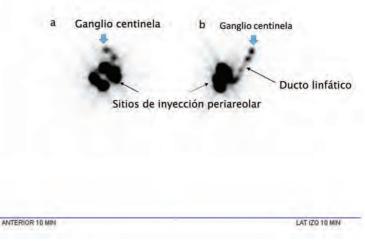


Figura 1

Proyección anterior (a) y lateral (b) de mama izquierda con sitios de inyección periareolar (4), ducto linfático y ganglio centinela.

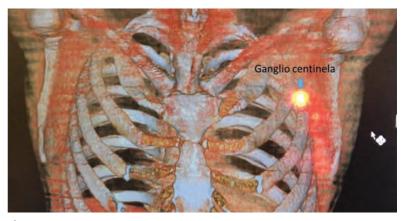


Figura 2 Misma paciente con adquisición SPECT/CT demostrando la ubicación del ganglio centinela con sus relaciones anatómicas cercanas.

diferenciarlos correctamente de captación en ductos linfáticos. Además el CT entrega una adecuada posición del ganglio, en cuanto a profundidad, relación con otras estructuras (músculos, vasos, pared costal) y eventuales ubicaciones atípicas como ya se mencionó.

La técnica del ganglio centinela se ha instalado como parte de la mejor forma del manejo de la cirugía del cáncer de mama. La correcta identificación de este ganglio permite entregar una información relevante al equipo tratante ya que permite definir el pronóstico de la paciente y su eventual tratamiento. Esta técnica se ha visto mejorada con la incorporación de las híbridas SPECT/CT, imágenes con el especialmente relevante en casos donde la técnica planar no logra detectar adecuadamente el ganglio centinela.

INTERVIEW WITH PREMIER OF ONTARIO, CANADA DOUG FORD

IN THIS INTERVIEW, THE PREMIER OF ONTARIO DISCUSSES THE PROVINCE'S SIGNIFICANT COMMITMENT TO ADVANCING AND SHARING THE EXTRAORDINARY BENEFITS OF NUCLEAR ENERGY WITH CITIZENS AROUND THE WORLD, BOTH IN INDUSTRIAL AND MEDICAL FIELDS.

A TRUE VISIONARY AND A LEADER WHO TURNS IDEAS INTO REALITY.



Ontario announced an investment of \$40 million dollars to help companies and bio manufacturers to innovate and develop the life saving medicines and technologies of tomorrow. How does an investment like this showcase Ontario's place in the life sciences sector?

"Ontario's life sciences sector is a key economic driver, employing over 72,000 people in good-paying jobs with annual exports exceeding \$12 billion dollars. We are an economic powerhouse, and we need to continue to create the conditions to attract new investments across the province.

Our \$40 million dollar investment through the Venture Ontario Fund supports our life sciences companies and bio manufacturers to innovate, grow, and compete in global markets. We want to continue leading the way in creating life-saving medicines and build our competitive economic advantage through our Venture Ontario Fund that allows businesses to succeed in the global marketplace."

- Premier of Ontario, Doug Ford

The province of Ontario has become a major supplier worldwide for one of the major radioisotopes used for patients. What's Ontario's plan for the production of medical isotopes? What do you hope to see from the expansion of isotope production? "I'm proud to support the expansion of nuclear power, which will bring safe, reliable, and affordable energy, along with cutting-edge cancer treatments, to families across Ontario. We want Ontario to be a place where medical breakthroughs and innovative life-saving products are developed to benefit the future of healthcare.

The reactors at Darlington, Bruce, and Pickering can be a long-term source of medical isotopes that can help save lives in Ontario and around the world. Bruce Power was the first commercial power reactor in the world to produce lutetium-177, putting Ontario on the map as a global leader in the production of cancer-fighting medical isotopes. We are filling the gap in the global shortage of isotopes and we hope Ontario will become more selfsufficient so we can connect people to the care they need, when they need it."

- Premier of Ontario, Doug Ford



The province of Ontario has become a major supplier worldwide for one of the major radioisotopes used for patients. What's Ontario's plan for the production of medical isotopes? What do you hope to see from the expansion of isotope production?

"We can see how nuclear energy plays a role in lifesaving technology for people across Ontario and the entire world at the intersection of medicine. As someone whose family has been affected by cancer, it is unbelievable to learn that more than 40 million medical procedures each year use nuclear isotopes. Also, Ontario produces roughly 50% of the world's supply of Cobalt-60. And we will soon be making several other isotopes that can directly treat these types of diseases. We have an ambition as a province to scale up that percentage as we want to continue helping patients worldwide in this space."

- Minister of Energy and Electrification, Stephen Lecce.

What is your government doing to bring the future of nuclear energy to Ontario?

"Energy demand is growing exponentially over the next 20 to 30 years. Under Premier Ford's leadership, our government is stepping up to ensure Ontarians have access to clean, reliable and affordable energy sources for the years to come.

We are leading the way on the nuclear front around the world. The world is watching Ontario as we build the first Small Modular Reactors (SMR) in the G7 at Darlington, with three more on the way. We are delivering nuclear refurbishment projects at Pickering and Bruce Power, all on time and on budget. These proposed refurbishments and expansions represent 18,000 megawatts (MW) of power, enough to power 18 million homes.

Part of it is our 65,000 nuclear energy workers, who have the ingenuity and bold ideas that make us the envy of the world.

Weeks into my appointment, I flew to Washington, D.C., for a Canada-U.S. nuclear summit to share our value proposition to the world: that we are your dependable source of affordable and reliable energy, displacing energy resources from authoritarian regimes who do not share our democratic values.

We look forward to expanding our nuclear energy footprint across Ontario and the world to deliver reliable energy to families and businesses."

- Minister of Energy and Electrification, Stephen Lecce.



INTERVIEW WITH JOHN O. PRIOR



John O. PRIOR, PhD MD FEBNM Professor and Head of Department Department of Nuclear Medicine and Molecular Imaging Lausanne University Hospital



Could you briefly present yourself to our readers?

I have been Professor and Head of Nuclear Medicine and Molecular Imaging at Lausanne University Hospital in Lausanne (Switzerland) since 2010. I underwent graduate studies in engineering at Swiss Federal Institute of Technology in Zurich (ETH Zurich) in Switzerland and earned a PhD in Biomedical Engineering from The University of Texas Southwestern Medical Center at Dallas (UTSW) in 1993 with a thesis on nuclear medicine instrumentation and image reconstruction. I returned to Switzerland to obtain my medical degree (MD) from the University of Lausanne and did nuclear medicine specialization training there. I was able to spend 2 years at the University of California at Los Angeles (UCLA) from 2002 to 2004. In 2018, I became President of the Swiss Society of Nuclear Medicine. Since 2019, I am the Liaison Officer between the World Health Organization (WHO) and the World Federation of Nuclear Medicine and Biology (WFNMB). In 2024, I also became President of the Section and Board of Nuclear Medicine of the European Union of Medical Specialists (UEMS), a more than 50-year-old political representative organisation of medical specialists in the European Union and associated countries aiming at obtaining comparable highest level of knowledge to allow free movement of specialists between member countries and guarantee high-quality CME programs of scientific and education excellence, free from healthcare industry influence.

As president of the Swiss Society of Nuclear Medicine could you give us an idea of the deployment of units of Nuclear Medicine in Switzerland?

Nuclear Medicine has a its origins in Switzerland with the first iron (⁵⁹F) and iodine studies (¹³¹I) by Prof. A. Vannotti in Lausanne starting as early as 1945, followed with the first radionuclides therapies (intracavitary ¹⁹⁸Au and intravascular ⁶³Zn) by J. H. Müller in Zurich in 1948–50. The first radioimmunoscintigraphy was performed in Lausanne in 1975. Interestingly, a few first world premieres happened in Switzerland, as with the first clinical ⁹⁰Y-DOTATOC in Basel in 1996, the first clinical PET/CT installed in Zurich in 2001, and the first clinical use of PSMA radioligand therapy officially approved outside any clinical trial in 2019.

Our Swiss Society of Nuclear Medicine (https://nuklearmedizin.ch) has separated in 1997 from the common Society for Diagnostic Radiology, Nuclear Medicine, and Radiation Oncology, itself originating in 1979 from the Society for Radiology and Nuclear Medicine created in 1958. Since 2000, nuclear medicine exists as an independent specialty in Switzerland. Today, we count about 90 members in the 4 Swiss linguistic regions (German-, French-, Italian-, and Romansh-speaking).

We have witnessed a rapid adoption and expansion of PET/CT in Switzerland since its beginning two last two decades ago, with 38 centres in 2024 for about 9 million inhabitants with over 80,000 yearly examinations. There are over 100 PET/CT and SPECT/CT scanners in Switzerland with only 1 PET/MR used clinically. Radioligand therapies are also rapidly increasing, but with a total of only about 60 therapy beds in the whole Switzerland and a compulsory 48-hour minimal hospital stay per law, challenges are soon lying ahead, as the number of indications is increasing as well as the number of patients-to-treat, as we are moving toward earlier lines of treatment.

How do you see the contribution of the Artificial Intelligence for the patients in Nuclear Medicine?

Artificial Intelligence (AI) is certainly going to help our patients obtaining improved nuclear medicine quality in the future. As in radiology, AI in nuclear medicine has known a rapid progression, and it is starting to be used clinically outside research studies. It will change the way we practice nuclear medicine tomorrow offering improved diagnostic and prognostic precision using image features notdirectly assessable by the human eye. It will also help the way therapeutic decision will be done using imaging information and integrating tumour heterogeneity, as well as making clinical dosimetry a clinical reality.

Also, languages models will help creating nuclear medicine reports, increasing automation, speed and reducing errors. However, we will keep on discussing with our patients like before, but AI will help tomorrow's physicians by reducing the work burden and offering more time and freedom for patient contact, taking over AI in matter of empathy. On the research side, AI will also speed up innovation progresses in radiopharmaceuticals and therapeutic regimen, as well as reducing side effects thanks to AI diagnostic and theranostic digital twins.

With the rapid development of theranostic, how will it impact the practice of Nuclear Medicine?

Although theragnostic has been practised in the last 80 years in nuclear medicine, its rapid expansion and recent frontline exposure has changed the face of not only nuclear medicine, but also medicine. We are witnessing a rapid explosion of indications and number of therapies worldwide outpacing often patient access to these novel and latest therapies in many countries. The numbers of indications will broaden, as will the number of diseases to be treated, as more clinical trials are performed, and research advances will be made. Amazingly, the theranostics sides effects are few and mild and most often predictable, allowing to adapt the administered activity accordingly. As mentioned above, this field will benefit from the progresses brought by AI to become even more efficient.

Finally, what is your greatest wish for the future of the speciality of Nuclear Medicine?

Wearing my hat as Liaison Officer between the World Health Organization (WHO) and the World Federation of Nuclear Medicine and Biology (WFNMB), my greatest wish for the future of our specialty would be to offer increased access to diagnostic and therapeutic nuclear medicine to the millions of people living in the Low- and Middle-Income Countries (LMICs) to improve health in patients with non-communicable disease including cancer, neurological diseases, and cardiovascular diseases. This goes not only through strengthening access to medical imaging equipment and radionuclides therapy, but also to training, supervision, quality management and qualified personnel. The concept of "frugal innovation" applies to low-cost technology designed specifically to LMICs addressing population needs considering the limited human resources and infrastructure from the desian start (https://doi.org/10.1016/j.jacr.2024.04.003).

With this, every investment will decrease mortality from non-communicable diseases would ensure a durable return on investment saving downstream health care costs and patient's number and guality of years left. This goes through the creation of specific WHO resolutions and their adoption by member countries in line with the WHO conceptual framework called "the triple billion targets" to be reach by 2030 as compared to the 2018 baseline, in particular with Pillar 1 "One billion more people benefitting from universal health coverage" and Pillar 3 "One billion more people enjoying better health and well-being" (https://www.who.int/about/general-programme-ofwork). We can be proud that nuclear medicine has also a role to play in health equity.

"Although theragnostic has been practised in the last 80 years in nuclear medicine, its rapid expansion and recent frontline exposure has changed the face of not only nuclear medicine, but also medicine. We are witnessing a rapid explosion of indications and *number of therapies* worldwide outpacing often patient access to these novel and latest therapies in many countries."



INTERVIEW WITH KALEVI KAIREMO



Kalevi Kairemo, MD, PhD, MSc(Eng), Professor Consultant in Nuclear Medicine, Clinical Chemistry, Pharmaceutical Medicine & Health Care Administration President 2024-5, World Association of Radiopharmaceutical and Molecular Therapy WARMTH

Dear Dr.Kalevi Kairemo 'You just have been elected President of Warthm Could you briefly present yourself to our readers?

I am now retired from the positions of chief physician/professor, in the field of molecular radiotherapy and nuclear medicine, at the Docrates Cancer Center (Helsinki, Finland) and, since 2015, I have been acting as a visiting professor in nuclear medicine at the University of Texas M.D. Anderson Cancer Center (Houston).

I graduated with an MSc (Eng) degree from the Helsinki University of Technology (Finland) in 1980 before completing my medical (1986) and doctorate (1993) degrees at the University of Helsinki. From 1989 to 1993. I had a postdoctoral research fellowship at the Memorial Sloan Kettering Cancer Center (MSKCC; New York, NY). I got medical specialist training in clinical chemistry (1994), nuclear medicine (1996), health care administration (2002), and pharmaceutical medicine (2006) at the University of Helsinki and University Central Hospital. I have had faculty leadership positions at the Norwegian University of Science and Technology (Trondheim), Uppsala University Hospital (Sweden), and the Docrates Cancer Center in Helsinki. I have been active in transitioning new agents and techniques through the developmental pipeline and authored more than 250 peer-reviewed publications.

From the beginning of this year I became President of the World Association of Radiopharmaceutical and

Molecular Therapy (WARMTH), which I consider a great honor.

I am licensed physician in Sweden, Norway and Estonia besides Finland. I have also been working pharmaceutical industry; CTT Cancer Targeting Technologies, Imanext and Advanced Accelerator Applications. Additionally, I have been involved with therapy tourism to Finland (patients traveled to Helsinki to get radionuclide treatments) and I have been active in setting up targeted therapies in neighbouring (e.g. Estonia) and European countries (e.g. Greece, Ireland) and some African countries.

What is WARMTH and how it is implicated in the investgation and the treatment of patients in Nuclear Medicine?

The World Association of Radiopharmaceutical and Molecular Therapy (WARMTH) has heen established in 2009 after initiatives from its predecessor World Radiotherapy Council in 1999 at the SNMMI meeting. In the beginning it had very strong connection with IAEA and its member states in promoting the medical use of radionuclides globally. It is the only worldwide organization founded to promote the use of radionuclide molecular therapy, and the relatively novel paradigm of 'Thera(g)nostics.' was in use from the very beginning. WARMTH is a voluntary non-profit organization of individuals specifically associated for the purposes, and for using the means, to

"From the beginning of this year I became President of the World Association of Radiopharmaceutic al and Molecular Therapy (WARMTH), which I consider a great honor." achieve the following research and educational objectives: Advance science and education of therapeutic nuclear medicine and radiopharmaceutical therapy including dosimetry, treatment evaluation, radiation physics, radiation biology and radiation protection for the benefit of public health and humanity; Work towards worldwide access to radionuclide therapy by harmonizing good practice; Educating nuclear medicine professionals in the use of radionuclide therapies and to facilitate research in this area.

WARMTH has conducted three major global trials which were published in high-ranked journals. There were two retrospective trials using Lu-177-PSMA-617 (the same compound as Pluvicto®), both published in the European Journal of Nuclear Medicine and Molecular Imaging. In these studies, there were more than 400 patients treated and factors predicting outcome and excellent results could be confirmed before official registration trials, using real-world evidence data. The third WARMTH trial was published this year in Lancet Oncology, describing targeted alpha therapy using Ac-225-PSMA-617. In this retrospective study with 488 patients from four continents the excellent outcome, more than half of the advanced stage patients responded and limited adverse effects were observed, and multiple factors affecting response could be identified. Additionally, Lancet Oncology asked for a commentary from me.

What do you think will be in the next future the great developments in Nuclear Medicine?

My own research has been based on multiomics, making discoveries at the nexus of genomics, transcriptomics, proteomics, metabolomics, microbiomics, epigenomics, imaging, and precision medicine. And my research has focused on theragnostics from the very beginning.

The prime examples of great developments are NET and especially prostate cancer theragnostics. Additionally, there are multiple new specific tracers for oncology; the best example is prostate cancer, 20 years ago there was nothing available, now there are more than 10 tracers. Similarly, the diagnostics in neurology, for example in movement disorders and dementias, has improved substantially. Actually, the diagnostics in many aspects in this field is ahead treatments. But more precise diagnostics will help the discovery of new medication. I will have great expectations in this field eventhough functional MRI is very potent, but unfortunately not that sensitive as nuclear medicine methods. The newest developments in oncology, speak very much for targeted treatment. Therefore, there will be new findings in the field of theragnostics. Mutation-driven cancers can

sometimes be treated with specific "blockers"; theragnostics may offer an ideal diagnosis/ therapy treatment combination possibility. Very often these treatments are based on the use of radiopharmaceuticals.

With this incredible expansion of Nuclear Medicine either in the diagnostic or in the therapeutic fields whow will Nuclear Medicine will be able to cope with the shortages of medical nuclear medicine specialists and technologists?

The shortage of labor is a problem in almost all sectors within medicine. We have to make nuclear medicine attractive; the discipline speaks for itself, but we have to increase awareness to the target populations. This nuclear medicine is such a fascinating field: a person has to understand cell and atomic nuclear behavior and make a clear difference between nuclear physics and cell biology. The radioactive atoms decay in a way which is known very precisely, but how they behave in organisms is not that easy to understand, but they can be tracked in a quantitative and dynamic manner. With nuclear medicine methods we can follow online physiology.

Finally what is your greatest wish for wish for the patients needing Nuclear Medicine ?

I have been a patient, too. Some of my minor health issues have been diagnosed with nuclear medicine techniques. From my own experience, I know that there is no need for an irrational fear of nuclear medicine imaging or therapy studies, because of radiation. In the world there has always been radiation (e.g. soil, cosmic) and a human body has multiple mechanisms to repair radiation damage. Radionuclide therapies are designed to overcome this resistance and these treatments can be planned with a targeted accuracy. These therapies can therefore be powerful, even in resistant conditions. Diagnostic radionuclide methods are very sensitive, therefore they are here to stay, especially becuse of depth resolution (imaging) and reasonable acquisition times.

Because of their sensitivity, specificity, time factors, and depth resolution in imaging, radionuclide methods cannot be replaced. Relevant therapy products can be designed for targeting and optimal kinetic constants. I have believed in this method for more than 30 years, and now we have products such as Pluvicto that have changed the treatment paradigm. Theranostics are here to stay.

"The World Association of Radiopharmaceutica l and Molecular Therapy (WARMTH) has been established in 2009 after initiatives from its predecessor World **Radiotherapy** Council in 1999 at the SNMMI meeting. In the beginning it had very strong connection with IAEA and its member states in promoting the medical use of radionuclides globally."

"Because of their sensitivity, specificity, time factors, and depth resolution in imaging, radionuclide methods cannot be replaced. Relevant therapy products can be designed for targeting and optimal kinetic constants."

Wei He, M.D., PH. D.,

Director of nuclear medicine departement and PET/CT Center Fu Dan University, affiliated with Shanghai Hua Dong Hospital China



不同TSH抑制治疗对分化型甲状腺癌术后 TSH、FT3、FT4的影响

【摘要】目的: 探讨不同促甲状腺激素 (TSH) 抑制对分治 疗化型甲状腺癌术后 TSH、游离三碘甲状腺原氨酸(FT3)、 血清游离甲状腺素 (FT4) 的影响。方法:选取 2018 年 8 月 -2019 年 2 月本院收治的分化型甲状腺癌患者 80 例为 观察对象,按随机数字表法将其分为对照组(n=40)与试验 组(n=40),两组均给予甲状腺癌根治术治疗。术后,对照 组给予常规剂量左旋甲状腺素治疗,试验组给予抑制剂量左 旋甲状腺素治疗。比较两组治疗前后甲状腺功能、骨生化指 标、心血管与骨骼系统不良事件发生及复发情况。结果:治 疗后,试验组 TSH 低于对照组, FT3、FT4 均高于对照组(P<0.05)。治疗后,两组血钙、血磷及碱性磷酸酶(alkaline phosphatase, ALP) 比较, 差异无统计学意义 (P>0.05)。对照组心血管与骨骼系统不良事件发生率为 17.50%,复 发率为 7.50%; 试验组不良事件发生率为 12.50%, 复发率为 5.00%,试验组心血管与骨骼系统不良事件与复发率稍低于对 照组,但两组比较差异均无统计学意义(P>0.05)。结论: 对分化型甲状腺癌术后患者实施抑制剂量左旋甲状腺素治疗 可改善甲状腺功能,且不良事件发生风险较低,临床应用 价值显著。

【关键词】 促甲状腺激素 抑制治疗 分化型甲状腺癌 游 离三碘甲状腺原氨酸 血清游离甲状腺素

甲状腺癌根据组织学分类可分为分化型、非分化型,其中分 化型甲状腺癌(differentiated thyroid carcminoma, DTC) 在甲状腺癌中占比可达95%,是一种常见的内分 泌恶性肿瘤,具有恶性程度较低,手术效果较好的特征[1]。术后多采用促甲状腺激素

(Thyroid stimulating hormone, TSH) 抑制或替代治疗、 放射性 131I 治疗等辅助方式,以提高手术治疗效果,改善预后。尤其是 TSH 抑制治疗不仅能抑制垂体分泌 TSH,还能 维持甲状腺功能,以发挥其维持与抑制的双重作用 [2]。但 有临床研究认为,甲状腺激素会促使骨量丢失与骨代谢,继 而引发骨折或骨质疏松等不良事件 [3]。因此,在本次研究 观察中,选取本院 2018 年 8 月 -2019 年 2 月收治的60 例 DTC 患者手术治疗后实施 TSH 抑制治疗,并对 TSH、FT3、 FT4 水平及用药安全性展开讨论与分析,现报道如下。

1 资料与方法

1.1 一般资料 选取 2018 年 8 月 -2019 年 2 月本院收治的 DTC 患者 80 例为 观察对象。纳入标准:均符合《甲状腺 结节和分化型甲状腺癌诊治指南》[4]诊 断标准,且经甲状腺超声或甲状腺发射 单光子计算机断层扫描(ECT)检查诊断 为甲状腺实性、冷结节,术后病理诊断 为 DTC;既往无甲状腺功能亢进或减低 病史;术后行放射性 1311 清除残余甲 状腺

组织。排除标准:既往行颈部放射治疗 ;术前口服甲状腺素制剂或口服碘制剂 ;合并下丘脑垂体轴方面疾病;合并术 后并发症如感染、乳糜漏等;术前合并 骨质疏松或影响骨代谢疾病者。按随机 数字表法将患者分为对照组与试验组, 每组 40 例。所有患者及家属均知情同 意并签署知情同意书,本研究已经医院 伦理委员会批准。

1.2 方法 两组均行甲状腺癌根治术治疗 ,所有患者均于全身麻醉下实施甲状腺 癌根治术,对于术中快速病理提示淋巴结转移患者,给予颈 部淋巴结功能性清扫术。经颈部 CT 检查以及颈部彩色多普 勒超声检查均未见残余甲状腺组织者视为清甲治疗成功。对 照组给予常规剂量左旋甲状腺素治疗。每天口服 2.0 μg/kg 左旋甲状腺素钠(生产企业:常州康普药业有限公司,批准 文号:国药准字 H20030502,规格:50 μg)。试验组给予 抑制剂量左旋甲状腺素治疗。每天口服 2.5 μg/kg 左旋甲 状腺素钠。治疗中密切监测患者甲状腺功能,其中对照组需 要维持 TSH 水平在 2⁻¹⁰ mU/L、游离三碘甲 状 腺 氨 酸 (free triiodothyronine-3, FT3)水平在 2.8^{-7.1} pmool/L 血清游离甲状腺素 (serum free thyroxine, FT4) 水 平 在 10.3^{-31.0} pmol/L; 试 验 组FT3、FT4 维持水平同对照 组,TSH 指标水平则低于0.3 mIU/L。两组术后均持续治疗 6 个月。

1.3 观察指标与判定标准 (1)比较两组治疗前后的甲状腺功能。于治疗前后清晨空腹状态下采集两组静脉血 5 mL,行抗凝与离心处理,应用血清自动免疫分析仪(瑞士罗氏公司Roche Cobas e411)检测患者 TSH、FT3、FT4 水平。(2)比较两组治疗前后骨生化指标。采用上海索莱宝生物科技有限公司生化试剂盒对血清钙、磷、碱性磷酸酶(alkaline phosphatase, ALP)水平采用比色法检测。比较两组患者治疗后心血管及骨骼系统不良事件发生与术后 1 年复发情况,包括心悸、心绞痛、心动过速、钙丢失、骨质疏松等。

1.4 统计学处理 采用 SPSS 21.0 软件对所得数据进行统计 分析,计量资料用 $(x-\pm s)$ 表示,比较采用 t 检验;计数 资料以率 (%)表示,比较采用 字2 检验。以 P<0.05 为差 异有统计学意义。

2 结果

2.1 两组一般资料比较 对照组男 17 例,女 23 例;年龄 46[~]73 岁,平均(59.50±13.50) 岁;平均术后 1311 用量 (109.85±12.55) mCi。试验组男 15 例,女 25 例;年龄 45[~]74 岁,平均(59.35±14.35) 岁,平均术后 1311 用量 (110.45±12.85) mCi。两组一般资料比较,差异均无统计 学意义(P>0.05),具有可比性。

2.2 两组治疗前后甲状腺功能比较 治疗前,两组各项甲状腺功能指标比较,差异均无统计学意义(P>0.05)。治疗后,试验组 TSH 低于对照组,FT3 与 FT4 均 高 于 对 照 组,差 异 均 有 统 计 学 意 义(P<0.05)。见表 1。</p>

		表1 两组治	行前后甲状腺功能出	b较(ī±s)		
组别	TSH mIU/L		FT ₃ pmol/L		FT ₄ pmol/L	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组(n=40)	4.11 ± 0.56	2.71 ± 0.34	2.25 ± 0.30	4.34 ± 0.61	11.27 ± 3.15	18.50 ± 3.78
试验组(n=40)	4.15 ± 0.59	0.39 ± 0.08	2.28 ± 0.32	6.56 ± 0.74	11.30 ± 3.16	26.17 ± 4.01
ı 值	0.311	42.009	0.433	14.641	0.043	8.803
Р值	0.757	0.000	0.667	0.000	0.966	0.000
		表2 两组》	的方前后骨生化指标的	と 貌(x ± s)		
组列	血学	5 mmol/L	血	🛱 mmol/L	A	LP U/L
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组(n=40)	2.15 ± 0.36	2.20 ± 0.42	1.10 ± 0.27	1.09 ± 0.24	87.52 ± 15.28	84.49 ± 15.23
试验组(n=40)	2.16 ± 0.38	2.17 ± 0.40	1.12 ± 0.26	1.11 ± 0.25	87.60 ± 15.31	85.12 ± 15.26
1 值	0.121	0.327	0.338	0.365	0.023	0.185
Р值	0.904	0.744	0.737	0.716	0.981	0.854
	表3	两组心血管与骨骼	系统不良事件发生与	夏发情况比较 例(%)	
组别	心血管与骨骼系统不良事件					复发
	心悸	心动过速	钙丢失	骨质硫松	合计	发及
试验组(n=40)	1 (2.50)	2 (5.00)	1 (2.50)	1 (2.50)	5 (12.50)	2 (5.00)
对照组(n=40)	2 (5.00)	1 (2.50)	2 (5.00)	2 (5.00)	7 (17.50)	3 (7.50)
x ² 值	0.866	0.866	0.866	0.866	0.980	0.533
P值	0.352	0.352	0.352	0.352	0.322	0.465

2.3 两组治疗前后骨生化指标比较 治疗前,两组 各 项 骨 生 化 指 标 比 较, 差 异 均 无 统 计 学 意 义 (P>0.05)。治疗后,两组血钙、血磷及 ALP 指标比较,差异均无统 计学意义 (P>0.05)。见表 2。

2.4 两组心血管与骨骼系统不良事件发生与复发情况比较 试验组心血管与骨骼系统不良事件发生率与复发率均稍低于对照组,两组比较差异均无统计学意义(P>0.05),见表 3。 3 讨论

DTC 作为甲状腺癌最为常见的类型,近年来,其发生率在 全球均呈现出增高趋势,但死亡率无明显变化 [5]。DTC 是 起源于甲状腺滤泡上皮的恶性肿瘤,临床表现单一,为无痛 性甲状腺结节、颈部肿块,其质地坚硬 [6]。但随着病情发 展,肿瘤逐渐增大会对邻近器官、组织造成压迫和侵犯,继 而并发面容潮红、心动过速、吞咽困难、呼吸困难等症状 [7]。目前临床中对甲状腺癌确切病因仍未完全明确,但认为 癌基因、电离辐射、性别、碘摄入及遗

传等影响因素均与 DTC 发生、发展有着直接关系 [8]。甲状 腺癌根治术作为治疗 DTC 的主要方式, TSH 抑制治疗则是术 后治疗首选方法,通过联合治疗可提高患者生存质量。因 DTC 患者癌细胞表面存在可被 DTC 刺激受体,术后容易增生 或复发,经抑制TSH,则能够控制术后肿瘤复发 [9]。TSH 是 一种由腺垂体分泌的激素,经由与 TSH 受体相互结合,经 cAMP 信号通路对 Tg、TPO、NIs 水平表达进行调节,从而对 细胞增生分化调控,利用甲状腺反馈性抑制 TSH 水平,达到 抑制残留甲状腺癌组织生长的积极效果 [10]。

虽然 TSH 抑制治疗效果得到公认, 但长时间TSH 抑制治疗 会影响患者机体内环境变化,将成骨细胞与破骨细胞之间的 动态平衡打破,从而干扰骨代谢过程,致使患者术后并发骨 质疏松症状 [11-12]。且邱海江等 [13] 研究认为, TSH 水 平与治疗时间存在交互作用,尤其是中、高危女性患者,TSH 治疗会引发骨质疏松,且绝经后女性影响更明显,分析原因 得知,其一在于绝经后女性运动能力降低,自身骨骼重建速 率下降; 其二为绝经后性激素变化, 雌激素分泌减少导致垂 体分泌的 FSH 呈代偿性增加,将原有骨代谢平衡打破,因此 临床中对于 TSH 剂量选择一直存在争议 [14]。马超 [15] 研究报道中显示, DTC 患者行甲状腺癌根治术后给予常规剂 量 TSH 对于甲状腺激素无明显抑制作用,可能诱发甲状腺特 异性蛋白表达水平增高,促使残留甲状腺肿瘤组织增生。而 给予抑制剂量用药干预后则提示 TSH 水平降低, FT3、FT4 水平增高,表明 TSH 抑制治疗有助于帮助患者术后甲状腺功 能维持在亚临床甲亢状态,降低癌灶增殖风险 [16]。

在本次研究中,通过对试验组实施 TSH 抑制治疗后甲状腺 功能得到明显改善,骨代谢情况则与治疗前差异不明显,表 明抑制剂量的甲状腺激素对于患者骨生化在短期内无明显影 响,但 ALP 指标水平稍有上调,提示患者破骨与成骨细胞活 性提高,这可能与 TSH 信号传导改变相关,对于骨重建有一 定影响;同代瑞等 [17]研究结果基本一致。本研究试验组 术后心血管及骨骼系统不良事件发生率及术后 1 年复发率较 对照组降低,但两组差异不明显,这是因长期使用超生理剂 量甲状腺激素,可导致心脏负荷加重与心肌缺血,严重情况 下可致使心律失常;而 TSH 抑制治疗则能减轻对心脏与骨代 谢影响,再次证实,TSH 抑制治疗对于避免肿瘤复发,降低 病死率有着积极作用 [18-19]。但需注意,骨密度与骨代谢 变化是一个缓慢过程,在短期内虽未发现其对于骨骼系统影 响,但还需延长观察时间,并在行

TSH 抑制治疗同时展开抗骨质疏松初级预防,确保钙离子摄入,加强对 DTC 患者术后辅助治疗过程中风险评估 [20]。

综上所述,对分化型甲状腺癌术后患者实施抑制剂量左旋 甲状腺素治疗,可改善甲状腺功能,且不良事件发生风险较 低,临床应用价值显著。

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INTERVIEW WITH DR LIZETTE LOUW



Dear dr. Lizette Louw has president of the WORLD FEDERATION OF NUCLEAR MEDICINE AND BIOLOGY (WFNMB) could you present yourself to our readers?

I am the current president of the World Federation of Nuclear Medicine and Molecular Biology (WFNMB) and past president of both the South African Society of Nuclear Medicine and the South African Association of Nuclear Physicians.

I'm passionate about the entire field of nuclear medicine, but my special interest lies in oncology imaging and therapy. As such I attend several weekly tumour board meetings and serve as an advisor to medical insurance companies in South Africa. Through my platform as WFNMB president, I am an active participant in various international collaboration projects.

What do you think will be in the next three years the most important developments in Nuclear Medicine? Further improvements in imaging resolution and hybrid imaging, expansion of Theranostic applications, and expansion of the tracers available for molecular imaging.

How Artificial Intelligence (AI) will impact the practice of Nuclear Medicine in the emerging countries?

Unfortunately emerging countries can often not afford advanced technologies and special software packages. Equipment is also more expensive due to import costs, lower patient numbers and lower reimbursement amounts. These factors will limit the implementation of AI. However, ideally AI should be utilised to improve and streamline the workload in areas with staff shortages.

What will be the challenges to make available THERANOSTICS to the emerging countries?

Theranostics often require prior imaging with PET/CT. There is currently limited availability of PET/CT scanners in emerging countries, and few cyclotrons due to financial constraints. Due to additional logistical challenges of delivering short half-life tracers such as F-18, PET/CT services are limited to major centers. Nuclear Medicine as a speciality will have to grow and expand in various emerging countries, and become more widely accepted by governments and health funders to enable successful implementation of Theranostics.

How THE WFNMB works in close partnership with the World Health Organisation (WHO)?

Many emerging countries rely on recommendations from WHO regarding minimum therapy, diagnostic and imaging procedures that should be available to the population. WFNMB, together with the Lancet Oncology Commission, has been actively working with the WHO to adopt Nuclear Medicine into imaging and diagnostic recommendations.

As president of the WFNMB what is your greatest wish for the patients in need of Nuclear Medicine all over the World?

It would be a dream come true if all patients had easy access to Nuclear Medicine imaging and therapy services, without having to spend excessive time and money to travel for these services. Access to Nuclear Medicine services should be just as easy as it is to go for a chest X-ray!

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INTERVIEW OF DR. KGOMOTO MOKOALA



Dear Dr Kgomoto Mokoala could you present yourself to our readers?

I am Prof. Kgomotso Mokoala, currently honoured to serve as the President of the South African Society of Nuclear Medicine. In addition to my role as president, I am a Nuclear Medicine Physician and an Associate Professor in the Department of Nuclear Medicine at Steve Biko Academic Hospital, the University of Pretoria and Nuclear Medicine Research Infrastructure (NuMeRI). My work is centred around advancing research and education in this expanding and interesting field, with a commitment to both clinical excellence and innovative research.

As President of the South African Society of Nuclear Medicine, I lead efforts to promote the integration of cutting-edge technologies and best

practices within the field. My work involves collaborating with healthcare professionals, policymakers, and international organizations to enhance the availability and quality of nuclear medicine services. My goal is to address the unique challenges faced by our region, enhance professional development, and improve patient care through collaboration with local and international experts.

In my academic role, I am dedicated to nurturing the next generation of nuclear medicine professionals and conducting research that pushes the boundaries of current knowledge. My aim is to contribute to the development of effective, personalized diagnostic and therapeutic approaches that can make a significant impact on patient outcomes.

As the president of the South African Society of Nuclear Medicine what are the three major issues Nuclear Medicine will have to deal with in the next three years in the World and also more specifically in Africa?

I believe the three major issues that nuclear medicine will face over the next three years are related to:

1. Radiopharmaceutical Supply and Demand especially with the boom in theragnostics with the use of alpha particles. Currently there are few facilities capable of producing high-quality alphaemitting isotopes. Many of these facilities face capacity constraints leading to supply shortages, ultimately resulting in inability to deliver these therapies to patients that need them. Ensuring a stable and reliable supply is critical for patient care and research.

2. There are rapid advancements in imaging technologies, such as hybrid PET/MRI systems, and integration with artificial intelligence and machine learning are transforming the field. Adapting to these changes requires significant investment in training and infrastructure. While these advancements offer improved diagnostic capabilities, they also present challenges in terms of cost, implementation, and maintaining expertise.

3. Regulatory frameworks and safety standards may not be as developed or uniformly enforced as in other regions. This can lead to variability in practice and potential safety issues. Ensuring consistent and high standards of practice across diverse regions can be challenging but is crucial for patient safety and effective treatment.

Issues Specific to Africa

• Many African countries face challenges related to the infrastructure required for nuclear medicine, including outdated or limited imaging equipment, and lack of maintenance facilities. Additionally, advanced technologies access to and radiopharmaceuticals often is restricted. Additionally, there is often a shortage of trained professionals in nuclear medicine in Africa. Training programs may be limited, and retaining skilled personnel can be challenging due to economic and logistical factors. A lack of trained professionals can impede the effective implementation of nuclear medicine techniques and limit the quality of patient care.

Addressing these issues will require a collaborative effort involving policymakers, healthcare professionals, and international organizations to ensure that advancements in nuclear medicine benefit patients worldwide, including those in Africa.

What will be the contribution of Artificial Intelligence (AI) in Nuclear Medicine?

Artificial Intelligence (AI) is set to revolutionize nuclear medicine in several transformative ways. AI algorithms, particularly those based on machine learning, can significantly enhance the accuracy of diagnostic imaging by improving image quality and aiding in the detection of subtle abnormalities that might be missed by the human eye. Advanced AI tools can also optimize the analysis of complex datasets, leading to more precise and personalized treatment planning. In addition, AI can streamline workflow processes by automating routine tasks such as image analysis and reporting, thereby reducing the burden on medical professionals and increasing efficiency. Predictive analytics driven by Al can also aid in patient management by forecasting disease progression and tailoring treatments to individual patient profiles.

What will be the next major development in Theranostics?

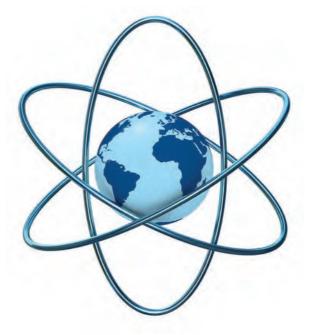
The next major development in theragnostic is likely to be the integration of more advanced and targeted radiopharmaceuticals combined with precision medicine techniques. This involves enhanced imaging techniques that provide more detailed and accurate visualization of disease which will provide imaging precision for better localization and characterization of disease, facilitating more effective and personalized treatment plans. Secondly, the use of personalized dosimetry to optimize radiation doses. There are ongoing efforts in this space and we look forward

to dosimetric calculations and algorithms for alpha particles which is particularly critical given the high linear energy transfer and short range of these particles. While we have had some great successes with radiopharmaceutical therapies, we cannot ignore tumour heterogeneities which result in inconsistencies in outcomes. There is a need for multidisciplinary approach with integration of other therapies as well as consideration of genomics and biomarkers. Combining theragnostic with genomic profiling and advanced biomarker identification will help tailor treatments based on individual genetic and molecular profiles. Lastly, the development of novel drug delivery systems, such as nanoparticle-based carriers, that can more precisely deliver theranostic agents to targeted sites within the body will help advance theragnostics. These developments collectively aim to make theragnostics more precise, effective, and personalized.

Finally dear dr. Kgomotso Mokoala what is your greater wish for patients in need of those new developments in Nuclear Medicine?

My greatest wish for patients in need of the latest advancements in nuclear medicine is to see a future where every patient benefits from truly personalized and effective care.

I hope for a future where the integration of advanced imaging, sophisticated radiopharmaceuticals, and artificial intelligence ensures that each patient receives tailored treatments designed to meet their unique medical needs. This would not only enhance the quality of life for patients but also provide them with the best possible chance for recovery and long-term health. In essence, my wish is for a world where the promise of innovation in nuclear medicine translates into tangible, positive impacts on the lives of patients, making advanced, personalized care a reality for everyone in need.





SPEAKING NUCLEAR MEDICINE **"THERANOSTICS"**

Prof. Mark Tulchinsky

Tenured Professor of Radiology and Medicine, Chief of Nuclear Medicine Section, Department of Radiology, PennState College of Medicine, PennState Health, Milton S. Hershey Medical Center

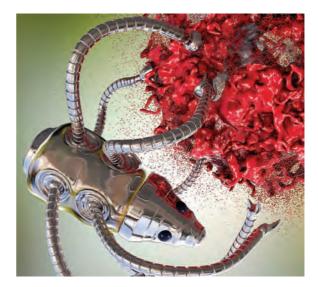
t is common for professionals to use specialty terms before defining them. While a professional may be familiar with them, a patient or a layperson needs an explanation. For example, "theranostic" or "theranostics" are often used with the presumption that readership and audiences will understand them intuitively or know their origins and meanings. The same can be said about other terms to describe nuclear medicine tests and treatments. Henceforth, the term theranostics is explained without assumptions, and the discussion will expand to other relevant terms.

As a concept in nuclear medicine, theranostics proposes using similar or the same radiolabeled chemical to identify and treat a disease. What you see (on diagnostic nuclear medicine imaging) is what you can get (using therapeutic nuclear medicine). The original application of this concept was recorded on March 31st, 1941, by Dr. Saul Hertz at the Massachusetts General Hospital. He used radioactive iodine to show avid absorption in the thyroid gland of a patient with Graves' Disease and then used the radioactive iodine to treat it successfully. He did not use the term theranostics, but he invented the concept before the term was applied to describe it. In 1942, Dr. Hertz was invited to present the thennovel treatment for Graves' Disease at the 34th Annual Meeting of the American Society for Clinical Investigation. In the abstract for his presentation, Dr. Hertz wrote: "Information which we have obtained by careful study of the radioactive iodine uptake by the goiters and the urinary excretion studies is presented and discussed in relation to the problem of finding the best means for the administration of this new therapeutic agent."

However, the published stories about the origin of "theranostics" seem mostly fiction upon factchecking. One published origin for the term "theranostics" is that a consultant to the pharmaceutical company "Cardiovascular Diagnostics" in the U.S.A., John Funkhouser, coined it in August 1998 to describe a material that allows the combined diagnosis, treatment, and follow-up of heart diseases. This was reportedly published in the company's press release. However, Mr. Funkhouser's professional biography on LinkedIn

lists no such company, the term does not appear on his LinkedIn site, and the year he purportedly published it corresponds to his work in a nonmedical industry. Another article recounted that Funkhouser coined the term "theranostics" while working as Chief Executive Officer of PharmaNetics in 2002 to describe his company's business model for developing diagnostic tests directly linked to the application of specific therapies. However, there is no published evidence to support this story either. Besides, the term "theranostics" had already appeared in a 2001 publication (submitted for publication in 2000) by a different author, Dr. Jefferys, who worked at the U.K. Medical Devices Agency and used the term without offering a definition - another example of presumptive use. All published accounts of the origins of "theranostics" agree that it is a portmanteau word, which means creating a new word by fusing two words. In the case of "theranostics," it is a fusion of "therapy" with the guiding power encapsulated in the word "diagnostics."

However, the unknown origin and lack of a clear definition at the turn of the century did not prevent a linguistic debate among its users. While the most common spelling of the term is "theranostics," others argue that the second part of the term comes from the Greek root "gnostic," while "nostic" is not a linguistically correct version. So, some argue that the linguistically accurate term should include the additional letter "g" to spell "theragnostics" instead of "theranostics." But it may be just human nature that compels us to take a shortcut sometimes and, as in this case, to shorten a word by skipping a letter. Regardless of why the foreshortened term became widely used, it may be more critical for Nuclear





Medicine specialists to recognize that many fields and medical specialties ubiquitously use "theranostics." To date, the use of the term peaked in 2020 when it appeared in 1,986 medical articles, while "theragnostics" appeared only in 41.

It is essential to recognize that nuclear medicine is not the only specialty of this diverse group of theranostics enthusiasts. For example, nanoparticle sciences incorporated the theranostics concept, and this emerging subspecialty is called "nanotheranostics." They use various indicators incorporated in a nanoparticle for diagnostic purposes (paramagnetic metals for MRI, radioisotopes for nuclear medicine imaging, etc.) and incorporate various drugs (chemotherapeutics, genetic vectors, radioisotopes, etc.) in similar nanoparticles for subsequent therapy. The concept is also applied to developing novel cardiovascular drugs. While the theranostics concept is becoming ubiquitous among specialties, theranostic nuclear

medicine (TNM) is uniquely centered on incorporating radioisotopes in diagnostic and therapeutic pharmaceuticals, i.e., radiopharmaceuticals (RPs). When an RP is used to treat a disease, it is called radiopharmaceutical therapy (RPT). There is a Journal named "Theranostics," which includes all specialties using this general concept.

New terms analogous to RPT are introduced into the expanding literature on the subject, including "Radioligand Therapy (RLT)," "Targeted Radiopharmaceutical Therapy (TRT)," and "Peptide Receptor Radionuclide Therapy (PRRT)." This terminological variety could be confusing and may not make good common sense. For example, there is an essential difference between a ligand or a radioligand and a pharmaceutical or a radiopharmaceutical. The former is clearly defined in chemistry, biochemistry, and pharmacology as an ion, molecule, or part of a molecule responsible for forming complexes or binding with other elements or molecules. These ligands can be labeled with an indicator, such as radioisotopes, when they become radioligands for use in bioassays, laboratory assays, and autoradiography. However, these radioligands are not approved for human diagnostic or therapeutic use. When a chemical is authorized by regulatory agencies (in the USA, it is the Food and Drug Administration) for human medical use, it becomes a pharmaceutical drug. In nuclear medicine therapy, we use an approved radioactive drug, a radiopharmaceutical, which was called a radioligand during its pre-approval development. However, when we treat patients, only approved radiopharmaceuticals can be used.

Radiopharmaceutical therapy is a broadly accepted term that makes good sense—it is performed utilizing a radiopharmaceutical for therapy. However, some add a specific descriptor or qualifier, for example, "Targeted Radiopharmaceutical Therapy." The "targeted" is inherent to every radiopharmaceutical therapy, and stating it is redundant—just like saying "wet" before "water."

The term "peptide receptor radionuclide therapy" came with the development of somatostatin analogs for delivering radiation doses to neuroendocrine tumors with abundant expression of somatostatin receptors. But it is a radiopharmaceutical that binds with the receptor, not a radionuclide mentioned in this term. It is not a therapy of a peptide receptor, as the name would suggest, but a treatment of the disease. Using this approach to naming treatments, radioactive iodine therapy should be a sodiumiodide symporter radionuclide therapy. Therefore, each radiopharmaceutical therapy application will require a different term. This can significantly complicate communication with patients and their primary doctors. On these pages, we will try to follow the advice of Albert Einstein, "Make everything as simple as possible, but not simpler."

INTERVIEW OF RUDI DIERCKX



Dear Prof. Dr. Rudi A.J.O. Dierckx, as President of the European Association of Nuclear Medicine (EANM), could you introduce yourself to our readers?

As a teenager, I decided to become the first physician in my family. After completing gymnasium, I pursued the traditional seven-year medical program at the University of Brussels, with the first year focused on physics, biology, chemistry, and anatomy. My strong interest in neuropsychiatry led to board certification after five years of training. I was also fortunate to receive a small stipend that allowed me to spend a year of my training (third year) at a large neurological referral center in Innsbruck, Austria. During this time, I gained expertise in clinical work and neuro-CT, earning a formal certificate of proficiency. Upon returning to Brussels, I additionally performed two years of in vitro work at the Institute of Molecular Biology, alongside my neuropsychiatry training.

My growing interest in imaging as well as in vitro receptor binding studies naturally led me to Nuclear Medicine (NM), where both fields converged. After fulfilling my military service as a medical lieutenant in a Military Hospital in Cologne, Germany, I completed a second specialty training in NM at Middelheim General Hospital in Antwerp. During this period, I also earned a PhD with a dissertation titled 'Brain SPECT Quantification: Clinical and Methodological Studies' from the University of Antwerp in 1994. Later, in 2004, I obtained an MBA (cum laude) from the Leuven Gent Vlerick School for Management.

At 36, I became the head of NM at the University Hospital of Gent in 1995, a full professor at Gent University (UG) in 2002, and later an extraordinary professor. I was appointed as a full professor at the University of Groningen and head of the Department of Nuclear Medicine and Molecular Imaging in 2005 till now, later also leading the Radiology Department from 2013 to 2022. My teams and I strive to provide the highest standard of care to patients in Flanders and the North of the Netherlands (and beyond), to educate and inspire the next generation, and to contribute to research according to international standards. Our multidisciplinary imaging research and training program has hosted over 40 nationalities, including participants from Canada and the USA.

In the European context, I served as the Belgian national delegate to the EANM and the World Federation of Nuclear Medicine and Biology (WFNMB) between 1998 and 2001. I chaired the EANM Task Group on Quality Assurance and Standardization, introducing the first European guidelines, and contributed to redefining the EANM's vision and strategy as part of its Strategy Committee (1998-2000). In 2021-2022, I was elected EANM President-Elect, and I have served as EANM President since 2023. My term of office will be ending at the end of the year.

The EANM includes 40 national societies as defined by the European Council, but its influence extends globally. The last EANM congress in Vienna attracted over 7,000 participants, marking it as the premier annual event in NM. The European School of Multimodality Imaging and Therapy (ESMIT) continues to provide ongoing education, with free webinars also available to non-members upon registration.

For more information, please visit the EANM website or follow the EANM LinkedIn account.

What do you think will be the major developments in Nuclear Medicine in the next three years?

Theranostics, particularly radioligand therapy, is currently a rapidly evolving field. NM has a longstanding tradition in this area, beginning with iodine therapy and later expanding to treatments such as MIBG therapy, radioligand therapy for neuroendocrine tumors, and liver cancer treatment following selective catheterization. The Vision trial and its findings marked a significant global breakthrough in clinical practice and have sparked a surge in research for broader applications in urology and other fields. This momentum has led to an increased focus on expanding the scope of radionuclides beyond beta-emitters, to include alpha emitters, Auger electrons, and theranostic pairs for both NM diagnosis and therapy. In a broader sense, theranostics also involves therapy navigation and, hopefully, increasingly includes therapy prediction to personalize new, effective, and often costly immune and targeted therapies.

Beyond oncology, we can expect the growing demand for precision medicine to extend into other areas such as infection-inflammation, cardiology, neurology, and psychiatry, driven by new therapies based on molecular insights and the significant socio-economic impact of diseases in these fields.

The validation implementation and of methodological and technical advancements and new possibilities in clinical practice are crucial. While radiochemistry and radiopharmacy represent the beating heart of NM, medical physics may be considered its backbone, facilitating the translation of signals into clinically meaningful images and accurate metrics for diagnosis and therapy. The equipment and software industries, along with many colleagues in the field, have significantly contributed to major technological developments. From rectilinear scans to SPECT, PET, hybrid systems like SPECT-CT, PET-CT, or PET-MR, and most recently, Total Body PET, along with software advancements such as iterative reconstructions, radiomics, and artificial intelligence, we see continuous improvements in sensitivity, resolution, and accuracy. Optical imaging is another rapidly growing branch in molecular imaging, with NM providing the ideal foundation to support its methodological and clinical development in collaboration with users, i.e. surgeons, and gastroenterologists. NM-trained physicians understand molecular pathways, our medical physicists are experts in quantification, and our chemists excel in labeling. For those interested, further details are available in this editorial.

As we move towards biological rather than symptomatic characterization, there is much to be gained from an integrated diagnostic approach, including multi-omics, such as biomics or genomics, alongside imaging data. This will require further standardization and quantification for both diagnosis and therapy, underscoring the importance of accreditation programs and interdisciplinary collaboration. effect of the increasing clinical demand for molecular imaging and therapy in the precision medicine era, alongside the impact of significant investments from major pharmaceutical companies in NM for both therapy and related diagnostics. This acceleration in NM comes amidst a broader European trend of a declining healthcare workforce, while the number of patients continues to rise.

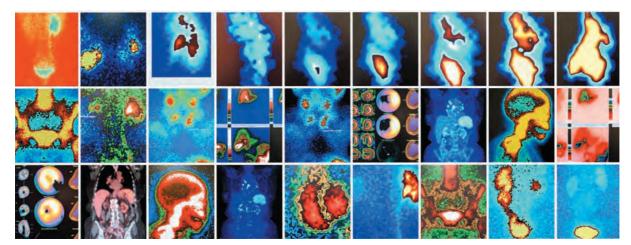
This challenge affects all disciplines within NM. Therefore, we need to attract more attention to our specialty, which the late H. Wagner once described as 'Nuclear Medicine is the best-kept secret in Medicine'. Although our visibility has improved with the advent of PET scans, hybrid imaging, and radioligand therapy, much remains to be done to meet the growing demand. In response, the EANM supported by its stakeholders has established a Young Professionals Council, which focuses on increasing awareness of NM's strengths and opportunities, and also an INSPIRE program focused on the next generation. While primarily serving its member states and individual members, the EANM collaborates closely with sister societies like SNMMI to achieve synergistic outcomes.

What will be the contribution of Artificial Intelligence (AI) in the practice of Nuclear Medicine?

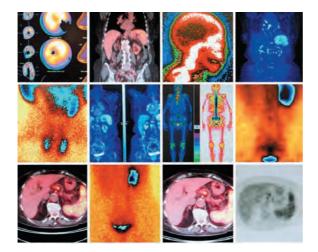
To explore the future of nuclear medicine, one might look at radiology, which, due to its larger volume of examinations and professionals, is already years ahead in focusing on and driving research developments. Despite high expectations, the number of CE-marked applications in clinical settings until now remains quite limited and primarily confined to niche areas, such as breast cancer screening. Practical challenges to widespread adoption include standardization across different equipment, protocols, and populations. Additionally, issues such as updating, transparency, and liability need to be addressed.

Addressing workforce challenges is another critical issue. In the next three years, we are likely to see the

There is no doubt that the future of medical imaging will involve artificial intelligence (AI). It is crucial for nuclear medicine to catch up by



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understanding this evolving field and tailoring AI applications to meet the specific needs of the specialty, which encompasses not only diagnosis but also subdomains like dosimetry, operational planning, and tracer development. A deep understanding of AI's opportunities, challenges, and risks within our domain is essential for meaningful discussions with stakeholders, including health authorities, hospital management, referring physicians, patients, and students.

To boost global interest and critical mass in the nuclear medicine community, the NM department in Groningen organized the 'First International Network Symposium on Artificial Intelligence in Nuclear Medicine' in 2023, with contributions from many experts and researchers. For those interested, I recommend reading the related EJNNMI editorial. Meanwhile, within the EANM, a pilot group led by Margarita Kirienko has advised the EANM Board on the role that EANM should play in AI within the European context. This group has now been transformed into a permanent overarching committee, which is addressing the top priorities. Of course, this EANM initiative needs to be part of a larger international effort, in collaboration with other societies such as SNMMI.

How will Nuclear Medicine physicians be able to cope with the rapid expansion of Theranostics in their day-to-day practice?

Addressing this question involves considering two key components: capacity and expertise. Capacity includes the necessary infrastructure, equipment, and workforce, while expertise across all involved disciplines remains crucial. Significant investment will be required in infrastructure and tools, such as for example upgrading the number of SPECT systems in departments to support radioligand therapy or increasing the number of nurses in the setting or radioligand therapy.

In terms of expertise, following the trend of hybridization in recent years, considerable effort in NM has been made to acquire more radiological expertise. This has even led to the establishment of a common training path in Nuclear Medicine within Radiology (RX) in the Netherlands, aiming to produce nuclear radiologists. As Ken Herrmann, who leads the EANM project group on this topic, aptly puts it, the current challenge is 'how to oncologize NM?' In other words, how do we also become nuclear oncologists, balancing the two sides of theranostics in NM?

This challenge may be even greater for our American colleagues, given the impact of their chosen training programs on the NM workforce. A seemingly straightforward solution might be to allocate NM diagnostic imaging to radiologists and radioligand therapy (RLT) to radiation oncologists. However, this approach could undermine the inherent link between diagnosis and therapy in NM, diminish the motivation to pursue NM due to its opportunities for translational research and integrated therapy, and compromise the necessary knowledge of internal radiation oncology

What is your greater wish for patients in need of Nuclear Medicine?

In the Netherlands, medical education, specialty training, and postgraduate learning are all structured around the CanMEDS framework (Canadian Medical Education System). This framework emphasizes that expertise alone is not sufficient; healthcare professionals must also embody other essential roles such as health advocate, communicator, collaborator, leader, and scholar to effectively meet the needs of the people they serve. In other countries, this comprehensive approach might be referred to as personal leadership development.

This multifaceted skill set is becoming increasingly crucial as Nuclear Medicine (NM) continues to evolve, requiring the communication of its expanding capabilities and the necessary resources to deliver optimal patient care in healthcare systems often constrained by limited resources. It is vital to provide decision-makers with the data that demonstrate within the broader healthcare continuum the positive effects of our interventions on downstream costs in the chain and on patient outcomes.

Fortunately, we are more connected than ever with various stakeholders, making this an opportune time to work in NM, given the numerous new opportunities to help alleviate patient suffering. Eventually, we will all find ourselves as patients, and when that time comes, I would hope to be cared for by an empathetic physician and team who have demonstrated a commitment to quality and excellence in their NM department, ready to address and resolve my medical concerns.



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The VISION trial demonstrated a statistically significant improvement in both major efficacy outcome measures of OS and rPFS by BICR with PLUVICTO[™] plus BSoC compared to treatment with BSoC alone, respectively.^{1‡}

- OS: estimated 38% reduction in the risk of death based on the HR (HR=0.62; 95% CI: 0.52, 0.74; P<0.001); median OS 15.3 months vs. 11.3 months¹
- rPFS: HR for progression or death, 0.40; 99.2% CI, 0.29 to 0.57; P<0.001 (significance level, 0.008); median rPFS 8.7 months vs. 3.4 months³

Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm.¹ Refer to the page in the bottom-right icon for additional safety information and for a web link to the product monograph discussing

- Most serious warnings and precautions regarding healthcare professional qualifications pertaining to use of radiopharmaceuticals; severe and life-threatening myelosuppression and renal toxicity including severe renal injury
- Other relevant warnings and precautions regarding location of use; compliance with regulations and good safety practices
 related to radiopharmaceuticals; contamination including special precautions such as bladder catheterization in incontinent
 patients; radiation exposure including long-term cumulative radiation exposure and increased risk for cancer; patient
 counselling on consumption of oral fluids and voiding to reduce bladder radiation; patient education regarding minimizing
 radiation exposure; hematology laboratory tests to assess myelosuppression; dose adjustments and discontinuation
 related to severity of myelosuppression; renal toxicity; kidney function laboratory tests; dose adjustments and
 discontinuation based on the severity of renal toxicity; male reproductive health; risk of temporary or permanent infertility;
 use effective contraception; no indication in pregnant women and risk of fetal harm in pregnant women
- · Conditions of clinical use, adverse reactions, drug interactions, and dosing instructions.

In addition, the page contains the reference list and study parameters relating to this advertisement.

PSMA=prostate-specific membrane antigen; mCRPC=metastatic castration-resistant prostate cancer; BSoC=best standard of care; BICR= blinded independent central review; HR=hazard ratio; OS=overall survival; rPFS=radiographic progression-free survival † Comparative clinical significance has not been established.



Indication and clinical use:

 $PLUVICTO^{TM}$ (lutetium [¹⁷⁷Lu] vipivotide tetraxetan injection) is indicated for the treatment of adult patients with PSMA-positive mCRPC who have received at least one androgen receptor pathway inhibitor (ARPI) and taxane-based chemotherapy.

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use. Geriatrics (\geq 65 years of age): No clinically relevant differences in efficacy were observed between patients \geq 65 years and those younger than 65 years.

Most serious warnings and precautions:

Healthcare professional qualifications: Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

Myelosuppression can occur in patients treated with PLUVICTO[™]. PLUVICTO can cause severe and life threatening myelosupression including anemia, thrombocytopenia, leukopenia and neutropenia.

Renal toxicity can occur in patients treated with PLUVICTO[™]. Cases of severe renal injury have been reported.

Other relevant warnings and precautions:

- · Location of use; compliance with regulations and good safety practices related to radiopharmaceuticals
- Contamination: the following measures should be taken for 2 days after receiving the radiopharmaceutical product:
- Toilet should be used instead of urinal
- Toilet should be flushed several times after use
- Contamination: special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination
- Radiation exposure including long-term cumulative radiation exposure is associated with an increased risk for cancer
- Radiation exposure to patients, medical personnel, and household contacts should be minimized during and after treatment
- Encourage patients to increase consumption of oral fluids and voiding to reduce bladder radiation
- Patient education regarding minimizing radiation exposure to patient and others including instruction about close contact, sexual activity and sleeping location
- Hematology laboratory tests before and during treatment to assess myelosuppression; PLUVICTO[™] should be withheld, dose
 reduced, or permanently discontinued and patients should be clinically managed as deemed appropriate based on the severity
 of myelosuppression
- Renal toxicity; maintain hydration; frequent urination before and after administration; perform kidney function laboratory tests before and during treatment; withhold, reduce dose or permanently discontinue based on the severity of renal toxicity
- Male reproductive health; risk of temporary or permanent infertility; use effective contraception during treatment with PLUVICTO™ and for 14 weeks after the last dose
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For more information:

Consult the Product Monograph at **https://www.adacap.com/wp-content/uploads/pluvicto-pm-20220825-en.pdf** for adverse reactions, drug interactions and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-363-8883.

‡ VISION was an international, prospective, open-label, multicenter, randomized phase 3 clinical trial evaluating PLUVICTO[™] in 831 adult patients with PSMA-positive mCRPC previously treated with at least 1 ARPI and 1 or 2 taxane regimens. Participants were randomized in a 2:1 ratio to receive PLUVICTO[™] (7.4 GBq every 6 weeks for up to 6 cycles) + BSoC or BSoC alone.

References: 1. PLUVICTOTM Product Monograph. Advanced Accelerator Applications USA, Inc. August 25, 2022. 2. Data on file. 3. Sartor O et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. NEJM 2021;385:1091-103.

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INTERVIEW OF MARK VINEIS COUNTRY PRESIDENT, NOVARTIS PHARMACEUTICALS CANADA INC.

Could you briefly introduce yourself to our readers?

With over 25 years of experience in the pharmaceutical industry, I'm excited and honoured to be leading our team in Canada as we continue to develop innovative healthcare solutions. I'm deeply committed to Novartis' mission of reimagining medicine for patients.

Like many members of our highly talented and dedicated team, I have a personal connection to cancer that motivates me to bring my best to work every day. My own family has been impacted by prostate cancer, fueling my passion to advance novel therapies like radioligand therapy (RLT) that can improve the lives of those suffering with cancer.

Behind each patient is a real person with a story like you or I - a family member, a colleague, a friend, a neighbour. That is why each decision we make at Novartis Canada, big or small, begins with the interests and needs of patients in mind.

How does Novartis see the development of Nuclear Medicine over the next three years?

We envision a future where nuclear medicine, particularly radioligand imaging (RLI) and therapy, plays a pivotal role in unlocking the next generation of cancer care.

Increasing access to existing and novel RLIs will further enhance diagnosis and management decisions at various disease stages. Building on the promising results seen in treating neuroendocrine tumors and prostate cancer, we aim to expand the indications for RLT and pursue its significant potential for other cancer types.

By investing in nuclear medicine research and development, and collaborating closely with healthcare professionals and government, we believe that both RLI and RLT are poised to become new standards of care for Canadian patients.

How does Novartis see the development of Theragnostics in Nuclear Medicine and its impact?

Theragnostic approaches, which combine diagnostic imaging and therapy, are at the forefront of the theragnostic revolution. At Novartis Canada, we envision a future where both imaging and diagnostic agents are widely available, enabling personalized and targeted treatment for Canadian patients with a variety of cancer types. By leveraging the power of theragnostics, we can optimize treatment plans, minimize side effects, and significantly improve



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overall patient outcomes. The supporting evidence to date has been remarkable, and we've only scratched the surface.

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

Artificial intelligence is having significant impacts across the entire healthcare system. Within the sphere of nuclear medicine alone, it has the potential to enhance the efficiency and effectiveness of both RLI & RLT. By analyzing vast amounts of data, AI can more accurately detect disease, aid in diagnosis, optimize treatment planning and accelerate the development of new therapies. We are actively exploring new AI applications to help ensure that Canadian patients have access to some of the most advanced and personalized care approaches.

What is your greatest wish for patients in need of Nuclear Medicine?

My greatest wish is for every eligible Canadian patient to have equitable access to nuclear medicine, notably radioligand imaging and therapy.

At Novartis Canada, we are committed to further developing the potential of theragnostics for patients with advanced cancers while keeping patient safety at the forefront. Every day, we are building upon the positive momentum in our healthcare system to expand infrastructure, train personnel, and ensure equitable access for patients.



fostering collaboration By between industry, government, and healthcare professionals, we can continue to enhance what the healthcare system has to offer and further prioritize patient-centered care and innovation. Together, we can ensure that Canadian patients, irrespective of their circumstances, have the same opportunity to benefit from the life-changing potential of nuclear medicine.









COMPOSITION and ELECTION

The Executive Board is the highest executive level of the Federation. It shall create a vision for the future of the Federation and develop strategies to fulfil them as well as to develop strategies regarding the cooperation with partner societies for the future of the medical specialty and the benefit of its Members and national Member societies.

It shall execute and supervise the execution of operational goals along the strategic lines as developed together with the different Integral Parts of the Federation. The Executive Board represents the Federation legally and is responsible for its financial management according to the Statutes and legal regulations.

Candidates for the position of President Elect, Secretary General and Treasurer will be proposed by the Members and elected during the General Assembly.



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INTERVIEW OF DR. NADIA WITHOFS MD, PHD



 Nuclear Medicine Physician & Expert in PET/CT Imaging and Radioligand Therapy, Division of Nuclear Medicine and Oncological Imaging, Institut de Cancérologie Arsène Burny (ICAB), CHU of Liège, Liege, Belgium

• Professor in Clinical Medicine, University of Liège, Liege, Belgium

• Core Principal Investigator, GIGA-Laboratory of Experimental Nuclear Medicine, ULiège

• President (2024-2025) of the Belgian Association of Nuclear Medicine (BELNUC)

• National Delegate for Belgium and Chair of the Health Technology Assessment (HTA) Piloting Group, European Association of Nuclear Medicine (EANM)

• Member of the Scientific Council (WAC), SCK CEN (Belgian Research Center on Nuclear Applications)

• Associate Editor, Médecine Nucléaire, the official publication of the main francophone societies in the field, including Société Française de Médecine Nucléaire et Imagerie Moléculaire (SFMN).

Dear Dr. Nadia Withofs could you present yourself to our readers?

I am a dedicated Nuclear Medicine physician at the Cancer Institute of the University hospital of Liège in Belgium and a researcher in the GIGA-Laboratory of Experimental Nuclear Medicine at the University of Liege. My mission is to ensure that patients have access to the highest standard of care in nuclear medicine imaging and radioligand therapy.

Currently, I serve the Belgian Nuclear Medicine community as the 2024-2025 President of the Belgian Association of Nuclear Medicine (BELNUC: https://www.belnuc.be) and am actively involved with the European Association of Nuclear Medicine (EANM: https://eanm.org/the-eanm-community/ about-us/). Additionally, I share my expertise as a member of the Scientific Council of the Belgian nuclear research centre SCK CEN (https://www.sckcen.be/en/about-sckcen-0), which plays a significant role in the production of radioisotopes for medical imaging and therapy.

My work is driven by a commitment to bridging the gap between cutting-edge research and patient care, ensuring that innovations in nuclear medicine translate into tangible benefits for patients. I strive to push the boundaries of nuclear medicine, with the ultimate goal of improving patient outcomes and quality of life through my engagements.

What do you think will be within the next three years the 3 major developments in Nuclear Medicine?

Over the next three years, I foresee three significant advancements in the field of Nuclear Medicine:

Prof. Dr. Nadia Withofs, Nuclear Medicine physician, holds the position of Professor at ULiege (Liege, Belgium), is a core PI of the GIGA-Laboratory of Experimental Nuclear Medicine at the University of Liege, Belgium and is a staff member in the Division of Nuclear Medicine and Oncological Imaging at the "Institut de Cancérologie Arsène Burny" (ICAB), CHU of Liege. Her expertise lies in PET/CT imaging and radioligand therapy, with a focus on hematological malignancies, uro-oncology, and neuro-oncology. Prof. Withofs is the current 2024-2025 President of the Belgian Association of Nuclear Medicine (BELNUC).

She is actively involved with the European Association of Nuclear Medicine (EANM) as the National Delegate for Belgium and Chair of the Piloting Group responsible for assessing the potential integration of Health Technology Assessment (HTA). She is a member of The Scientific Council (WAC) of the SCK CEN, the Belgian Research Center on nuclear applications. She is associate editor of the Journal Médecine Nucléaire, the official publication of the main francophone societies in the field, including Société Française de Médecine Nucléaire et Imagerie Moléculaire (SFMN).

1. The expansion of radiotheranostics:

Radiotheranostics is the combination of a cancer target imaging using positron emission tomography (PET) and therapy using the corresponding therapeutical radioligand. This therapeutical strategy has already demonstrated efficacy in treating metastatic neuroendocrine tumors and prostate cancer with the radioligands 177Lu-DOTATATE and 177Lu-PSMA-ligand, respectively. The beauty of radioligand therapy lies in the combination of efficacy and the preservation of the patient's quality of life.1,2 Moreover, radioligand therapy will likely expand to other types of cancers. As these treatments become more established, their application across a broader range of cancers could reshape cancer care by offering targeted, effective, and patient-centered therapies.

2. Integration of artificial intelligence (AI) in Nuclear Medicine:

There are growing European and national initiatives aiming at integrating effective, reliable, and safe AI systems into nuclear medicine practice. By enhancing diagnostic accuracy, optimizing treatment planning, and improving workflow efficiency, AI will make nuclear medicine even more precise and personalized, benefiting both patients and healthcare providers.

3. Advances in total-body PET/CT systems:

Long field-of-view PET/CT systems covering the total body (TB) are being installed in a growing number of nuclear medicine departments. These systems enable to visualize the biodistribution of a radiopharmaceutical throughout the whole-body, facilitating the development of new radioligands, at lower radiation dose thanks to the higher sensitivity of these systems. However, the high cost of these systems has been a limiting factor. To address this, Prof. Stefaan Vandenberghe's research group at the University of Ghent (Medical Image and Signal Processing, MEDISIP, Department of Electronics and Information Systems, Faculty of Engineering and Architecture) has developed a novel walk-through total-body PET scanner with flat panel detectors, similar to an airport security scanner (https://physicsworld.com/a/walk-through-petscanner-made-for-high-throughput-imaging-atlower-cost/).3 This innovative design reduces costs while maintaining high performance, making advanced imaging more accessible. Additionally, it accelerates the imaging process, enhancing patient comfort and streamlining the work of technologists.

These developments will collectively push the boundaries of what is possible in Nuclear Medicine, with the ultimate goal of improving patient outcomes and enhancing the quality of care.

In Belgium how the Nuclear Medicine physicians are involved in the incredible expansion of Theranostics?

In Belgium, Nuclear Medicine physicians play a pivotal role in the expansion of radiotheranostics and radioligand therapy (RLT), supported by the country's extensive experience and unique ecosystem in nuclear medicine and radioligand therapy. Belgium is well-equipped to implement both current and future radioligand therapies. The therapeutic radioligands 177Lu-DOTATATE and 177Lu-PSMAligand have been reimbursed in Belgium, with the reimbursement process being notably fast. To maintain and strengthen Belgium's leadership in this field, a comprehensive 'RLT action plan' (RLT4BE, https://www.inovigate.com/media/filer public/ e5/5f/e55f7371-b79c-4f24-bab2-bb75c1b765ec/ a_radioligand_therapy_plan_for_belgium_final-11062024.pdf) has been developed. This plan, created through collaboration among government bodies like the Belgian healthcare system (RIZIV/INAMI), the Belgian Nuclear Research Centre SCK CEN (https://www.sckcen.be/en), healthcare professionals, hospitals, universities, scientific societies including BELNUC and patient associations, is designed to future-proof the healthcare system for radioligand therapy. This initiative will enhance the collaboration across the entire Belgian RLT ecosystem.

Finally dear dr Nadia Withofs what is your greater wish for patients in need of Nuclear Nedicine?

My greatest wish for patients is to ensure they have access, through reimbursement, to radioligand therapies that have proven to be effective while preserving quality of life. I also hope that this therapeutic strategy can be expanded to other types of cancer. I am encouraged by the commitment of researchers and pharmaceutical companies in advancing radiotheranostics, which I believe will play an increasingly significant role alongside other oncology treatments. Furthermore, I am confident that Nuclear Medicine will continue to drive more precise and personalized approaches, offering tailored care that meets each patient's individual needs.

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INTERVIEW WITH TOM FRANCKE



Where do you see Nuclear Medicine and Molecular Imaging heading to, and what is Hermes Medical Solutions' contribution to it?

I strongly believe in the new developments we see in theranostics and neurology for degenerative diseases. There are new tracers and treatments available, and the pharma companies invest heavily in these fields. We see new therapies and diagnosis methods being developed almost guarterly, and an ever-growing share of these therapies and diagnoses use nuclear medicine and molecular imaging. The treatment of cancer and degenerative diseases is becoming more and more personalized. This trend goes hand in hand with the advancement of quantitative SPECT, which enables precision medicine in new geographical areas by its better availability in developing countries. At the same time with a strong trend towards precise, patient-centric methods.

Hermes Medical Solutions positions itself as the flagship for safe, personalized molecular radiotherapy and confident diagnosis. Hermia dosimetry software is not only used in clinical practice, but also by the research community developing new clinical workflows and by pharmaceutical companies developing new tracers. Olinda/EXM, the most widely used organ dosimetry software, is exclusively provided by Hermes Medical Solutions. The fast pace of our development as a small, streamlined company is second to none in this field of huge corporations with years-long development cycles, so we can adapt to our customers' ever-changing needs.

What makes Hermes Medical Solutions so unique?

We dedicate all efforts to developing software for Nuclear Medicine and Molecular Imaging. We are unique in the world with this focus. This helps us build up expert knowledge in the field and work closely both with pharma companies and medical research leaders. We do not compete with the pharma companies; we are a supporting resource for them.

Our remote access possibility is much appreciated by our users. You can work equally well from any location: the hospital, at home, or while travelling.

Our expertise and size allow us to follow every trend and rapidly integrate new methods into our MDR-certified and FDA approved software. We are a nuclear medicine/molecular imaging software company. Nothing else.

Where do you see the advantages of vendor neutral software?

Our primary focus is to provide the most advanced and easiest to use software for analysing images in nuclear medicine and molecular imaging. We see the Hermes workstation as the primary tool for the clinicians. Good software makes the all the difference, no matter the camera.

Being vendor neutral, we put much effort into ensuring that the Hermia software works with images from all camera brands equally well. We give hospitals the freedom to use a single workstation to support all their cameras, regardless of manufacturer, and to purchase new cameras independent of the processing software. Our reconstruction software allows accurate quantitative comparisons between SPECT images taken with different camera brands.

We also see an interest in extending the lifetime of the camera by using a workstation that support all cameras, regardless of age. This saves the hospital money.



How do you ensure that the software fits all needs and all imaging equipment in such a heterogeneous world?

We have been developing software for nuclear medicine and molecular imaging for 48 years. Our product portfolio is complete. We have all the functionality a NM/MI department needs, as well as support for the forefront of scientific research. We have long experience in integrating images from new cameras into our software. The medical community often helps us push the camera manufacturers to support us in this work. We are contributing to new standards in the field. All our support and training personnel are clinical specialists from NM departments. Our continuous recruitment of clinical professionals constantly adds experience and expertise to the company.

What is your vision for Nuclear Medicine/ Molecular Imaging?

Hermes Medical Solutions does everything in its power to support the precise diagnosis and treatment of our most common diseases, especially in oncology and neurology. If we are successful, there will be completely new ways in the future to diagnose and treat cancer, Alzheimer's disease, Parkinson's disease and more.

We welcome the latest advancements in SPECT imaging, allowing a large variety of tracers, faster image acquisition times, and lower equipment cost. Not least in the less wealthy regions of the world, where the most people are in need.



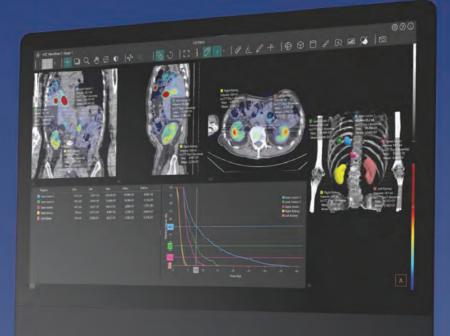


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About HERMIA

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 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 healthcare providers and their patients worldwide.

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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.

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INTERVIEW WITH PROFESSOR KAREN JONES

Dear Professor Karen Jones, President of the Australian and New Zealand Society of Nuclear Medicine (ANZSNM) could you present yourself to our readers?

I am very pleased to be interviewed for ePatient. I have been President of the ANZSNM since April this year. As the peak body in Australia and New Zealand representing all professions in nuclear medicine, this position (and my former role as Vice President) has provided me with the opportunity to interact more closely with individual special interest groups: physics, radiopharmacy, medical specialists, technologists and nuclear medicine students, so I now better understand their challenges, current priorities and future initiatives. I am a passionate advocate for students and recent graduates and was instrumental in establishing a Student Representative Council and Mentorship Programme within the ANZSNM. I believe that highguality mentorship is essential to building a successful and motivated workforce.

My background is unconventional. - I trained as a nuclear medicine technologist at the University of South Australia before embarking on a PhD at the University of Adelaide (the first nuclear medicine technologist in Australia to do so) and have subsequently established a career as an independent clinical researcher. - As the famous American baseballer/coach, Yogi Berra, once said 'It's tough to make predictions, especially when it is about the future' and that is certainly true in my case. I had intended to work in a research role for only a short period of time and then return to full-time clinical work - but my curiosity, and the challenges of research, drew me in, and it was soon evident that I was destined to be a career researcher. I may be even more enthusiastic about research today than I was more than 30 years ago when I embarked on my research journey. My research activities continue to capitalise strongly on my background in medical imaging, so that my research is very much crossdisciplinary (i.e. nuclear medicine, endocrinology, gastroenterology, pharmacology and cardiology) and my research group is also multidisciplinary, which, from my perspective, stimulates both innovation and interest. A particular focus continues to be the use of nuclear medicine and ultrasound techniques to evaluate the role of the gut, particularly gastric emptying, in the blood glucose and blood pressure responses to food in humans. The outcomes of my work have proved to be of major relevance to the management of diabetes, where good control of blood glucose levels is essential to minimise the risk of potentially devastating complications (i.e. eye, kidney and nerve damage). With my colleagues, I demonstrated that the rate of gastric emptying, which



Professor Karen Jones, DipAppSc (Nuclear Medicine), PhD, MANZSNM President, ANZSNM William T Southcott Senior Research Fellow in Nuclear Medicine The University of Adelaide

is not widely recognised to exhibit a substantial variation between healthy individuals that is even greater in people with diabetes (where emptying is often either abnormally slow or rapid), is a major determinant of the magnitude of the rise in blood glucose following meals. This recognition has stimulated the development of, now widely used, dietary and pharmacological approaches (e.g. most recently, so-called, GLP-1 receptor agonists) to improve blood glucose control following meals, markedly by slowing gastric emptying. GLP-1 receptor agonists were also shown to lead to weight loss and are effective in the management of obesity. It has been remarkable (and humbling) to witness the progressive translation of work I initiated in my PhD to clinical practice today. My research in the underrecognised field of postprandial hypotension (PPH), a substantial fall in blood pressure induced by eating, that occurs in ~15% of healthy older people over 65 years of age and ~25% of people with type 2 diabetes, and predisposes to falls, has pioneered the concept that PPH can be regarded broadly as a 'gastrointestinal', rather than 'cardiovascular', disorder (i.e. the fall in blood pressure is initiated by the interaction of nutrients with the gut, leading to a substantial increase in intestinal blood flow). Accordingly, strategies which target slowing of gastric emptying are likely to be therapeutically beneficial and I have recent evidence that this is the case. Underpinning much of my work has been measurement of gastric emptying using scintigraphy, which was largely developed in the late 1970s, but remains the 'gold standard' technique. - I think even Yogi Berra would be surprised! So, I have learnt that nuclear medicine techniques can have important, broad-based research, and clinical, applications particularly if you have colleagues who can facilitate this.

You will not be surprised to learn that I continue to do my best to support research relating to nuclear medicine. I established the first postgraduate research programs in medical radiations in South Australia and have supervised ~40 higher degree research students from a variety of backgrounds, including pharmacy, science, endocrinology, intensive care, gastroenterology, radiology, nursing, dietetics, radiography, radiation therapy and nuclear medicine. My connection to the ANZSNM is longstanding, (I joined as a student member) and I have held key positions in several committees, including as Chair of both the Technologist Special Interest Group and the Executive Committee of the Australasian Radiopharmaceuticals Trials Network (ARTnet). as well as both Vice President and President roles on Federal Council. In addition to the ANZSNM, I now sit on the Governing Board of the National Imaging Facility, which is responsible for the distribution of government funding for key imaging infrastructure for research in Australia. - When I'm not working, I enjoy spending time with my 4 children (aged 13 - 24 years) and my husband, along with our enthusiastic spoodle (cockapoo), Maisie, and our tabby cat, Dolly.

What do you see will be the three most important developments in Nuclear Medicine in the next few years?

1. The recent, rapid development of novel radiopharmaceuticals already represents a 'game changer' for the diagnosis, staging, and personalised management, of cancer and other diseases. The expansion of PET and theranostics will inevitably continue to grow substantially with the development of novel targeted radiopharmaceuticals.

2. Technological advances in imaging systems will lead to improved diagnostic accuracy, earlier detection of disease and shorter imaging times – so I am confident that tests will continue to become better, and the patient experience enhanced.

3. As we are all aware, artificial intelligence (AI) is rapidly being integrated into society, perhaps disconcertingly rapidly, with inherent major benefits for healthcare and more personalised medicine. The development of machine learning algorithms to recognise patterns of disease will certainly lead to the integration of AI in nuclear medicine practice, where the use of AI is likely to reduce reporting times, as well as enhance diagnostic accuracy. The rate at which this technology is evolving is phenomenal. These are very exciting times, and it will be interesting to witness the magnitude of the impact in the next few years.

What are the biggest challenges facing nuclear medicine in the coming years?

I see the major challenges, perhaps surprisingly, as very much practical, rather than technical – we are doing exceptionally well with the latter. The increased demand for nuclear medicine services, particularly PET and theranostics, is already placing increased pressure on our workforce, with shortages across all nuclear medicine professions, particularly technologists. I am well aware that these workforce shortages are not unique to Australia and New Zealand - it is very much a global issue, where, areas that do not have training programs, and rural and regional locations, are particularly vulnerable. In 2023, the ANZSNM held a successful Nuclear Medicine Technologist Workforce Summit to bring together stakeholders from a number of areas (i.e. nuclear medicine technologists from metropolitan and regional areas, private and public health systems, Chief Allied Health Officers, Education providers, regulatory bodies and professional associations) from both Australia and New Zealand to identify challenges and potential solutions. The Summit identified several key themes to be considered in moving forward, including: 1. 'Telling our story well': promoting nuclear medicine to the wider community to attract and retain nuclear medicine students; 2. 'Creating rich and diverse learning experiences', including the provision of scholarships and other incentives to make clinical placements more affordable for students; 3. 'Achieving more through partnerships': sharing resources and strengthening industry and university relationships; 4. 'Investing in our workforce': defining and promoting career pathways with appropriate renumeration, implementing mentorship programs; 5. 'Exploring different models of care', including the 'assistant' model; 6. 'Data gathering for informed decision making': collecting accurate data for sector forecasting and modelling, and 7. 'Evolving to endure': understanding the role of emerging technologies and the potential impacts on the profession.

The ANZSNM has implemented a mentorship program for nuclear medicine technologists and recently introduced Student Placement Grants, the latter, in partnership with the Australasian Association of Nuclear Medicine Specialists (AANMS). These are modest, but important, steps forward - but there is much more to be done. I see the strengthening of relationships between international 'sister societies' as very important. It will allow us to share our experiences – what we have tried, what has worked and what hasn't. It is essential that we address workforce shortages in nuclear medicine in a unified manner to enable high quality care to be delivered when, and where, people require it.

What is your greatest wish for patients in need of Nuclear Medicine?

My wish is, again, a practical one. Australia is a vast country (approximately 80% of the land size of the USA or Canada) with a population of ~26 million of whom some 7 million people (~27%), live in rural or regional areas. The latter are linked to much poorer health outcomes when compared to urban metropolitan areas, as attested to by higher rates of hospitalisations, death and more limited access to primary health care services. People living in rural and regional areas also often have to travel long distances for procedures. The future for nuclear medicine is so bright. – I want nuclear medicine services to be readily accessible and affordable for all individuals that require them, including those in rural and regional areas.



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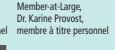


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THE PANGEA PROJECT



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The Canadian Association of Nuclear Medicine Association canadienne de médecine nucléaire

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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.





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James McBrayer Managing Director and CEO of Cyclopharm/ Cyclomedica

"The nuclear medicine landscape of lung imaging has undergone a remarkable evolution, from the early days of planar imaging to contemporary techniques of SPECT (Single-Photon **Emission Computed** Tomography) and **SPECT CT** (Computed Tomography) with quantification."

A NEW ERA IN NUCLEAR PULMONOLOGY: EVOLUTION, IMPACT, AND FUTURE PROSPECTS

Summary:

This article reviews the history of diagnostic lung imaging and explores the pivotal shift towards the burgeoning field of nuclear pulmonology.

The nuclear medicine landscape of lung imaging has undergone a remarkable evolution, from the early days of planar imaging to contemporary techniques of

SPECT (Single-Photon Emission Computed Tomography) and SPECT CT (Computed Tomography) with quantification.

In recent years, the ventilation imaging challenges specific to COVID-19 have only served to accelerate the progression and utility of nuclear medicine in lung imaging. This progression has hastened in an exciting new era of novel diagnostic and therapeutic avenues well beyond pulmonary diseases - and with it the prospect of improved patient outcomes.

Introduction: The Evolution of Lung Imaging

The history of diagnostic lung imaging in nuclear medicine is a testament to the pursuit of precision medicine. Planar imaging, though a cornerstone in early lung diagnostics, lacks the depth and detail offered by the modern techniques using SPECT and SPECT CT. At the next level of progression, evolving nuclear pulmonology techniques, supported by a growing body of peer reviewed clinical evidence, is revolutionizing our understanding of pulmonary physiology and pathology.

Nuclear medicine lung imaging is historically best known for diagnosing acute pulmonary embolism (PE). Drawing insights from the seminal works of Roach, Bailey, Leblanc, Bajc, Le Roux, King, Gibson and others, this article briefly discusses the expanding role of nuclear medicine in diagnosing and managing pulmonary diseases Beyond PE, such as chronic thromboembolic pulmonary hypertension (CTEPH), asthma, COPD, lung cancer, lung transplant evaluations, and interventions in respiratory medicine.

A crucial aspect of this progression is the rapid advances in nuclear medicine compared to imaging with computed tomographic pulmonary angiography (CTPA). While CTPA remains the frontline modality for diagnosing acute PE, nuclear medicine techniques offer unique advantages, especially in scenarios where CTPA may be inconclusive, contraindicated or where concerns exist about the high radiation dose in patient populations including paediatrics¹⁹ and young women. CTPA, for example, delivers up to 20 times higher radiation to the breast dose than a nuclear medicine ventilation perfusion (V/Q) study.^{23,40}

Despite the widespread use of CTPA for determining acute PE, present-day nuclear medicine methods are delivering improved sensitivity, specificity, negative predictive values, positive predictive values and accuracy at a fraction of CTPA's radiation dose⁴⁰. The following diagram provides a comparison of the expected clinical outcomes between CTPA versus the various ventilation perfusion (V/Q) techniques available via nuclear medicine.^{1,2,3}

In the case of a ventilation perfusion SPECT CT study, where a low dose of non-contrast CT is also performed with the nuclear medicine study, the ability of nuclear imaging to provide metabolic insights, complemented by anatomical referencing from CT and automated analytical tools^{13, 27}, is paving the way for a potential subspecialty in nuclear medicine.

Introduction: The Evolution of Radiopharmaceuticals in Lung Imaging

Essential to any nuclear medicine study is a radiopharmaceutical or tracer that has an affinity for a disease state, a metabolic process or organ system. By combining ventilation and perfusion images, clinicians can evaluate lung function, identify areas of ventilation-perfusion mismatch (which can indicate conditions like pulmonary embolism or other lung diseases), and make other diagnostic and treatment decisions.

Perfusion imaging is achieved with Technetium-99m labelled macroaggregated albumin (Tc-99m MAA). These particles are injected into a vein and become trapped in the small blood vessels of the lung, allowing imaging of blood flow distribution.

Radiopharmaceuticals used in ventilation imaging have evolved over time and are being leveraged to drive some of the advancements in this field. There are four tracers used in nuclear medicine ventilation studies. They are; inert gases, Krypton-81m and Xenon-133; Tc99m based agents, to include 99mTcdiethylenetriaminepentaacetic acid aerosol (Tc99m-DTPA) and the ultrafine 99mTc-carbon dispersion of Technegas. Kr-81m's use is limited by availability, cost, and its short half-life, and is less practical for SPECT imaging. Xenon-133, due to its low energy, long administration time and inability to be utilized with SPECT, has progressively been displaced globally in favour of the Tc99m based agents. ^{3, 4, 5, 36, 37, 38}

99mTc-DTPA has aerosolized droplets with varying sizes $(0.5-2 \,\mu\text{m})$, with distribution dependent on the aerodynamics of gas flow. As a result, 99mTc-DTPA aerosol ventilation studies can be confounded by deposition in large airways, and this issue is exacerbated in patients with respiratory symptoms. The ultrafine Tc99m-Technegas particles with greater than 80% that are less than .92 μ m, by contrast, have a gaslike distribution, particle-like retention, and the attractive properties of 99mTc to allow high-quality imaging, including SPECT. Internationally, Technegas is considered the best alternative for the ventilation portion of the V/O scan. 3, 4, 22, 36, 37, 38

Furthermore, according to the recently published Canadian Guidelines for ventilation/perfusion (V/P SPECT) in pulmonary embolism state, "For ventilation, 99mTc-Technegas is the best radio-aerosol, particularly in patients with COPD. Liquid aerosols produced in nebulizers such as 99mTc-DTPA are inferior for SPECT and should not be used unless Technegas is not available." 3

Technegas was approved by the United States Food and Drug Administration on 29 September 2023, making the USA the 65th country in which Technegas is available. ³⁹

Impact of COVID-19 on Lung Imaging

The COVID-19 pandemic brought unprecedented challenges to the realm of diagnostic imaging, particularly in nuclear medicine ventilation imaging. At the onset of the pandemic, the lack of personal protection equipment saw a reduction in procedures across all modalities. However, due to the perceived contamination risk associated with long administration times of Xenon-133 and Tc99m-DTPA, a return to previous levels of procedures has been slower in countries where the choice of agents was limited to Xenon-133 and Tc99m-DTPA.

In markets where Technegas was available during the pandemic, citing the limited risk associated specifically with the product and the clinical importance of the ventilation procedure, lung ventilation imaging was either maintained during the pandemic or has fully recovered to pre-pandemic levels. The importance of continuing ventilation imaging during the pandemic was highlighted in a multicentre study conducted 2021 in France in a population of COVID-19 patients assessed with lung scintigraphy. Based on the results of the study PE could confidently be excluded without the ventilation imaging in only 57% of patients. Importantly, ventilation imaging was required to confidently rule out PE in 31% of patients.³³

It was this concern about false positives leading to unnecessary anticoagulation, which in turn places those patients at risk of severe associated adverse effects, that led the French Society of Nuclear Medicine to recommend that the routine performance of ventilation studies be maintained despite the pandemic on the basis that the clinical importance of the

"The history of diagnostic lung imaging in nuclear medicine is a testament to the pursuit of precision medicine. "

"Essential to any nuclear medicine study is a radiopharmaceutical or tracer that has an affinity for a disease state, a metabolic process or organ system."

Diagnosing Pulmonary Embolism: VQ Planar vs V/Q SPECT +/- CT vs CTPA

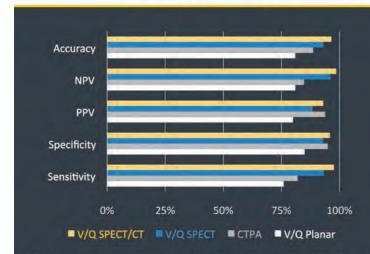


Table: Diagnostic ability of V/Q SPECT/CT¹, V/Q SPECT¹, CTPA¹ and V/Q Planar² to detect PE (adapted from Hess et al, 2016¹ and from Reinartz et al, 2004²)

V/Q SPECT and V/Q SPECT/CT have shown that V/Q SPECT/CT is superior in most clinical settings with better overall diagnostic performance¹.

In situation of acute PE, chronic PE pregnancy, paediatrics and the COPD population, V/Q SPECT, with or without low-dose CT, can be considered as a first-line investigation to detect PE³ due to:



Nuclear medicine delivers higher accuracy, sensitivity and negative predictive value when compared to CTPA³

Nuclear medicine is low radiation and has no known serious adverse reactions³

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ventilation study far outweighs the concern of viral contamination, particularly when risks can be mitigated by appropriate personal protective equipment.³³

Expanding Horizons: Nuclear Pulmonology Beyond PE

"The COVID-19 pandemic brought unprecedented challenges to the realm of diagnostic imaging, particularly in nuclear medicine ventilation imaging."

"Historically, lung ventilation imaging in nuclear medicine played a crucial role almost exclusively in the diagnosis of acute pulmonary embolism. Technological strides have, however, expanded the procedure's horizons to encompass a broader spectrum of pulmonary diseases." Historically, lung ventilation imaging in nuclear medicine played a crucial role almost exclusively in the diagnosis of acute pulmonary embolism. Technological strides have, however, expanded the procedure's horizons to encompass a broader spectrum of pulmonary diseases. Multimodality imaging, coupled with artificial intelligence (AI), has unlocked new frontiers in nuclear pulmonology including, but not limited to:

• CTEPH and Congestive Heart Failure: Nuclear imaging plays a pivotal role in identifying perfusion defects characteristic of chronic thromboembolic pulmonary hypertension and congestive heart failure, aiding in early diagnosis and management. ^{25,40}

• Asthma and COPD: Functional imaging techniques provide valuable insights into airflow dynamics, inflammation, and ventilation-perfusion matching, aiding in personalized treatment strategies. ^{7,9,14,16,18,20,26,28,29}

• Lung Transplantation: Pre-transplant evaluations and post-transplant monitoring benefit from nuclear imaging's ability to assess graft function, perfusion, and potential complications. ^{8, 32}

• Interventional Respiratory Medicine: Nuclear imaging guides interventions such as lung volume reduction, offering a quantitative assessment of treatment efficacy and patient response. ^{10, 11, 12, 13, 30, 31}

• Occupational Hazard Screening: Risks associated with particulates to include silicosis, mining and other work related toxic exposures.^{21, 42}

Indeed, the translational work that is being driven by the collaboration between nuclear medicine and respiratory medicine is growing rapidly. An example of this alliance is the recently published study by Radadia N, et al entitled Comparison of ventilation defects quantified by Technegas SPECT and hyperpolarized 129Xe MRI where, "observations indicate that, despite substantial differences between the imaging modalities, assessment of ventilation defects using established quantification practices for Technegas SPECT and 129Xe MRI are comparable" thus opening a pathway from research initiatives using 129Xe MRI, with its limited availability and high cost, to clinical practice through nuclear medicine.⁸

Towards Precision Medicine: The Era of Treatable Traits

The paradigm shift towards precision medicine in pulmonary care is epitomized by the concept of "treatable traits."³⁵ By leveraging advanced imaging modalities, clinicians can identify and target specific pathophysiological traits in individual patients, tailoring

therapies for optimal outcomes. Here, lung imaging transcends mere diagnosis to become a predictive tool, guiding therapeutic decisions and enhancing patientcentric care.

One recent example is the publication by Gibson, P, et al. entitled Ventilation Heterogeneity is a Treatable Trait in Severe Asthma, The Journal of Allergy and Clinical Immunology: In Practice. The study concludes that in a population of severe asthmatics that Ventilation Heterogeneity, as diagnosed using Ventilation SPECT with Technegas, is "clinically significant, measurable, and treatable, which establishes Ventilation Heterogeneity as a treatable trait in severe asthma". ³⁵

Conclusion: A Vision for the Future

The fusion of nuclear medicine with pulmonology heralds a new era characterized by precision, innovation, and personalized care. In tandem with the continuing evolution of technology, the role of nuclear pulmonology will undoubtedly expand, encompassing novel diagnostic and therapeutic avenues. The pathway from imaging to patient management is no longer linear but holistic, reflecting the transformative impact that nuclear medicine is already having on shaping the future of respiratory medicine. ^{13, 24}

The author, James McBrayer, is a Nuclear Pharmacist and CEO of Cyclopharm/Cyclomedica the manufacturer of Technegas[®]. For more information about Technegas please direct inquires to info@technegas.com.

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"The paradigm shift towards precision medicine in pulmonary care is epitomized by the concept of "treatable traits."35 By leveraging advanced imaging modalities, clinicians can identify and target specific pathophysiological traits in individual patients, tailoring therapies for optimal outcomes."

"The fusion of nuclear medicine with pulmonology heralds a new era characterized by precision, innovation, and personalized care. In tandem with the continuing evolution of technology, the role of nuclear pulmonology will undoubtedly expand, encompassing novel diagnostic and therapeutic avenues. "



OCCLUSION AND ORTHODONTIC TREATMENT IN CHILDREN AND TEENS

Victoria Kuzina DMD (docteure en médecine dentaire) de l'UdeM Fello en Orthodontie Invisalign Premier Provider

Parents of young children and adolescents often ask me when it is necessary to straighten their children's teeth. This is a question that worries many parents.

Allow me to shed more light on this conundrum about the occlusion and the dental alignment in children and adolescents.

Currently, there is a huge difference between dentists and orthodontists in their opinion about when it is appropriate to start orthodontic treatments in young patients.

The diagnosis and treatment must begin with the evaluation of the temporomandibular joints and the respiratory tract of children.

We must find the CAUSE of dental malalignment in children.

It's the most harmonious development as well as a predictable occlusion in young children and adolescents that must be sought after.

As this will avoid problems in the future such as dental destruction (decay, dental interference, fractures, losses, attrition), inflammation of the gums and periodontium (the base of teeth and bones), masticatory dysfunctions (chewing, swallowing), muscle tension ("trigger" points, headaches, pain, tension, trismus).

"All analysis of occlusion begins with TMJ" (temporomandibular joints) (Dr Peter Dawson).

The key to success is simple: as soon as a child begins an interceptive orthodontic treatment (i.e., repositioning of the jaws, space regaining leading to proper functioning of the oro-facial structures, airways, tongue, alignment of the permanent teeth), the sooner this child will have a desirable and long-term result.

In addition, the treatment duration will be much shorter than at adolescence or adulthood and will cost less.

I would like to explain the most common cases without getting carried away in the rare exceptional cases.

Let's look at the 2 age groups:

- 1. Children with primary and mixed dentition from 3 to 12 years old.
- 2. Adolescents aged 12 or children with all permanent teeth present in their mouths before this age.

THE PRIMORDIAL IMPORTANCE of orthodontic correction relates to the development of the airways in a young age.

It must always be remembered that the child's bones are very malleable and bad habits or dental interference (such as a crossbite) can prevent the proper development of the cranio-masticatory system having a lasting impact on the child's facial appearance and psychology.

At the age of 4-5 years we can foresee oral problems related to dental interferences and crossbites as they alter the growth and anatomical position of the condyles of the temporomandibular joints.

In addition, these crossbites reduce the space for the tongue which encroaches good nasal breathing.

All these factors can lead to faulty growth and development of the masticatory system as well as malocclusion and lack of space for the permanent teeth of children.

Genetics plays a 50% probability of malocclusion. However, with new early detection methods (visits to the dentist checking the eruption of the child's first teeth) and new advanced technologies (dental appliances at the base of digital technologies), the developmental problems and malocclusions can be prevented and/or corrected. Early intervention is suggested around the age of 6-7 years, more rarely before.

Simple mechanotherapy (wearing removable or fixed devices) can correct the initial problem.

The eyes do not see what the brain does not know (Dr A.Aubé).

The signs often arrive before the symptoms (Dr A.Aubé).

It is at this age that your dentist must observe the child's breathing and the development of the masticatory systems (temporomandibular joint, tongue, palate, dental arches, upper and lower jaws) and suggest orthodontic treatment if necessary.

Many children experience physical trauma at an early age. Trauma to the face, head or jaws may be one of the factors that can cause developmental abnormalities in the future.

Occlusion is the first step in digestion. Digestion gives nutrition and nutrition gives health (Dr Aubé).

Orthodontics is not just about aligning your teeth. This involves a fairly complex system called functional and dynamic occlusion.

Including temporomandibular joints, muscles, tongue, lips, cheeks, ligaments and all other structures in the oral cavity.

If occlusion is healthy, all functions such as phonetics, chewing, musculoskeletal balance and aesthetics will be healthy.

For the most part, orthodontists (specialists for straightening teeth) focus on correcting the jaws and teeth.

Few of them give importance to the temporomandibular joint which is very often the cause and origin of dental misalignment problems. Some developmental problems can wait until adolescence or adulthood.



We can see more and more teenagers wearing braces. It is at the age of 12 that a child/teenager has all their permanent teeth erupted. Our teenagers are the carriers of potential problems that were not corrected at a young age!

The duration of orthodontic treatment after 12 years of age will be longer than in young people because of timing failure and development and growth outpace time!

It is longer and more painful because the child's "bone matrix" is constantly growing and developing. Additionally, between ages 9 and 12, hormonal changes in our teens speak for themselves!

In conclusion, here are the benefits of intercepting in a young age:

- promote the development of the respiratory tract
- promote the development of the temporomandibular joints
- avoid extracting permanent teeth
- influence balanced jaw growth
- reduce or eliminate the need for surgery
- have enough room for permanent teeth to erupt
- reduce trauma and potential damage to permanent teeth
- avoid and shorten definitive orthodontic treatments (at adolescent age)
- improve facial appearance and facial aesthetics

This is why your dentist must have a more critical, more "interceptive" look regarding the development of malocclusion in children.

Your dentist should have an understanding of what is harmonious growth and development, and a knowledge of the importance of the balance of masticatory functions and the correct position of the temporomandibular joints, have to see the cause of the problem.

The ideal treatment of malocclusions in young children and adolescents is PREVENTION, hence the importance of consulting your dentist as early as possible.

This way, parents are reassured that the development of their child's occlusion is under dental control and is will be taken care of in due time.



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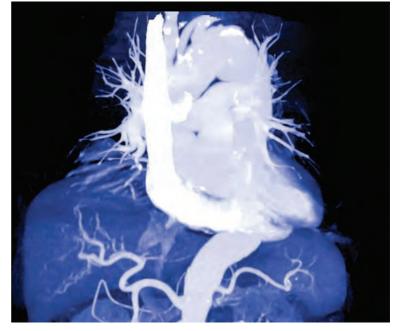
Symptomatic severe aortic stenosis presents an ominous prognosis, for this reason have increased the interest in the management of asymptomatic patients.

We included a retrospective evaluation in a population with asymptomatic severe aortic stenosis (aSAS) to assess the role of Radionuclide Ventriculography (RNV).

Sixty patients included with aSAS, referred to undergo RNV. Vascular (blood pool) imaging was conducted by red blood cells tagging technique, and subsequently, intravenous (IV) 99mTc. Information was obtaining images in rest, stress and post-stress. The presence of symptoms, STsegment depression, sustained ventricular tachycardia and/or drop equal or greater than 5 points of left ventricular ejection fraction (LVEF) during stress were considered an abnormal result. In a 16-month follow-up median, the role of the study and the variables that influenced on the decision of valve intervention (VI) by the attending physician were evaluated. The evaluation between variables was made with Pearson's chi-squared test.

The average age was 66 ± 13 years and 73% were men. Twenty-seven percent (n=16) presented abnormal RNV and 30% (n=18) were referred to VI. Eighty-one percent of patients with abnormal RNV and 11% with normal RNV were referred to VI (p<0.0001). Between the target variables of the study, LVEF drop during stress presented the highest relationship with the decision of VI; with 86% of patients presenting LVEF drop versus 23% with normal LVEF (p<0.001).

ROLE OF RADIONUCLIDE VENTRICULOGRAPHY IN ASYMPTOMATIC SEVERE AORTIC STENOSIS PATIENTS



The findings in this study show the probable role of RNV in patients with aSAS, as an usefull diagnostic tool for decision-making in this clinical scenario.

Keywords: Radionuclide Ventriculography ; Asymptomatic patiens; Severe Aortic Stenosis.

Aortic stenosis (AS) affects 5% of adults older than 65 years¹⁻², with a prevalence expected to increase during the next decades in relation to an ageing

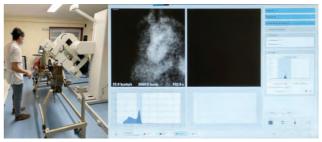


Figure 1- Exercise stress testing. Dual-head SPECT gamma camera (QuantumCam, DDD Diagnostic, Denmark), synchronized with the ECG R-wave, until reaching number of kcts needed.

population³. Symptomatic severe AS presents an ominous prognosis, with mortality close to 50% in a 1 to 2-year follow-up⁴⁻⁵. Aortic valve replacement (AVR), whether surgical or by transcatheter approach, is the only management that has proven to improve survival⁶⁻⁷.

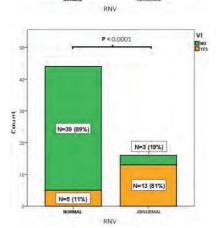
A greater knowledge on the pathophysiology and natural history of patients with AS, together with advancements on imaging diagnosis and the excellent evolution associated with transcatheter aortic valve replacement (TAVR), have increased the interest in the management of asymptomatic patients with severe aortic stenosis (SAS)⁸. A less invasive therapy than conventional surgery may justify preventive percutaneous replacement in a certain subgroup of patients, instead of waiting for the appearance of symptoms or left ventricular dysfunction to decide on valvular intervention (VI)⁹. Clinical experience has shown that symptoms can be difficult to determine in sedentary and/or elderly patients with physical limitations,¹⁰ and data based on imaging studies may potentially modify the existing decision-making paradigms^{8,11}. In this sense, the evaluation of individuals with SAS through stress tests combined with the evaluation of left ventricular ejection fraction (LVEF) during exercise may change the patterns of clinical practice and reduce the intervention threshold⁸.

Current guidelines recommend exercise stress testing (ESTs) to reveal concealed symptoms in individuals classified as asymptomatic during initial evaluation¹²; however, only about 6% of them are submitted for a bicycle or treadmill stress test. This could be due to many reasons, including a residual concern about the safety and tolerability of the test ¹³⁻¹⁴⁻¹⁵.

Through the use of rest, stress and post-stress radionuclide ventriculography (RNV), nuclear medicine offers the opportunity for simultaneous assessment of the clinical and hemodynamic consequences of valve behavior on ventricular function¹⁶.

The aim of our study was to evaluate the usefulness of RNV to reach a decision on VI in patients with asymptomatic SAS, with no other criteria for AVR indication.

Our work-team analized between April 2017 and March 2020, a total of 64 patients older than 18 years underwent RNV at the Nuclear Medicine Service of the Sanatorio San Gerónimo. The mean follow-up was 16 months. A questionnaire was filled at admission to the nuclear medicine ward to rule out the presence of spontaneous symptoms or left ventricular dysfunction that would justify VI, in order to evaluate the coexistence of moderate valvulopathy, or whether patients presented some incapacity to perform exercise due to concomitant Figure 2. Proportion of patients submitted to VI according to RNV result.



P<0.0001

N=3 (19%)

N=13 (81%)

VI

NO YES

Figure 3. Proportion of VI according to LVEF result.

comorbidities such as peripheral vascular disease, chronic obstructive pulmonary disease, anemia, immobility or significant joint disease.

tount -

N=39 (89%)

N=5 (11%)

For RNV, cardiovascular (blood pool) imaging was preceded by red blood cells tagging following an in vivo technique, with 1 to 2 mg stannous chloride administered intravenously followed by 99mTc injection (925-1110 MBq) after 20 minutes. Patients were placed on an ergometric stretcher in supine position, with the camera detector over the thorax in a left anterior oblique position at 45° +/-5° allowing the best visualization and separation of both ventricles. Information was acquired using a mobile dual-head SPECT gamma camera (QuantumCam, DDD Diagnostic, Denmark), synchronized with the electrocardiographic (ECG) R-wave, using 24 frames per cardiac cycle with a 20% acceptance window, until reaching 4,800 kcts at rest.

Subsequently, graduated ESTs was performed in the same position and images were acquired at maximum stress and one minute post-exercise using the same conditions than rest acquisition (Fig. 1). ESTs were performed according to the American College of Cardiology/American Heart Association guidelines on clinical practice using a modified Bruce protocol. ESTs was supervised by a cardiologist assisted by a nuclear medicine technologist, and were only started if the patient Table 1. Analysis of relationship between VI and predictor variables.

Variables	Vascular Intervention. P		P value*
	NO	YES	
Symptoms [%(N)]			
No	82 (40)	18 (9)	0.0001
Yes	18 (2)	82 (9)	
ST-depression [%(N)]			
No	79 (38)	21 (10)	0.002
Yes	33 (4)	67 (8)	
PBPB [%(N)]			
No	77 (40)	23 (12)	0.003
Yes	25 (2)	75 (6)	
Abnormal LVEF [%(N)]			
No	77 (41)	23 (12)	0.001
Yes	14 (1)	86 (6)	

In bold letters: Statistically significant p values. * Value of p in Pearson's chi-squared text or continuity correction. PBPB: Paradoxical blood pressure behavior.

was asymptomatic. Besides continuous recording of symptoms, hemodynamic and ECG parameters were recorded at baseline, at the end of each stage, at peak stress, and 3 min post-stress. Exercise was stopped early if any of the following appeared: symptoms (significant shortness of breath or any chest discomfort or dizziness), ventricular ectopy >3 beats, new atrial fibrillation, sustained systolic blood pressure (BP) drop >20 mmHg from the previous stage, or fatigue with physiological dyspnea. Time of exercise, exercise capacity in metabolic equivalents (METs), maximum increase in systolic BP and maximum decrease in peak ST-T segment depression in millimeters were recorded. RNV was considered abnormal when a symptom appeared (shortness of breath, chest constriction or dizziness), drop in systolic BP >20 mmHg compared to the previous stage, horizontal or descending ST-T segment depression ≥ 2 mm, sustained ventricular tachyarrhythmia and/or drop \geq 5 points in LVEF during stress.

The assessment criteria recorded during follow-up were AVR (whether surgical or by transcatheter approach) and mortality by cardiovascular cause. This information was obtained by reviewing the electronic clinical records or by contacting the patient or his/her family members. The time of follow-up was estimated from baseline RNV until AVR, death or one year after admission to the nuclear medicine service.

Statistical analysis was conducted by using the IBM SPSS software, v 23.0. Normality of quantitative variables was evaluated by the Kolmogorov-Smirnov test. To describe quantitative variables, mean as central tendencv measure and standard deviation as corresponding dispersion measure were used. Qualitative variables are presented as absolute frequencies and rates. To evaluate differences in proportions between qualitative variables, Pearson's chi-squared test or Fisher's exact test was used when there were expected frequencies < 5. Confidence intervals of 95% were reported along with parameters when considered necessary. Statistical significance α was established in 0.05

Our results showed that seventythree percent (n=44) of patients were men. The average age of the population was 66 ± 13 years; there was no significant age

difference between males and females (p>0.05). Twenty-seven percent (n=16) presented abnormal RNV, 95% CI (15-38) %. Thirty percent (n=18) was referred to VI, 95% CI (18-42) %. No medical complications were observed in a total of 60 ESTs, and a single death (by non-cardiovascular cause) was verified on follow-up.

Among individuals with abnormal RNV, 81%underwent VI, compared to 11% of those with normal RNV (X2=17.2; gl=1; p < 0.0001). (Fig. 2). A higher percentage of patients referred to valve replacement was observed in the subgroup

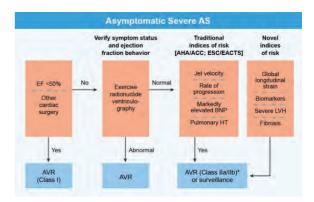


Figure 4. Management of patients with aSAS. Role of RNV.

showing LVEF drop during stress (86% in patients with abnormal RNV vs. 23% in those with normal RNV) (X2=11.7; gl=1; p<0.001). (Fig. 3).

Both a pathological EST result and the presence of abnormal LVEF behavior were related to the decision to perform VI (Table 1). Stress RNV revealed symptoms in 18% of patients. As seen in Table 2, elective valve replacement showed differences according to RNV results, verifying that VI was chosen in 14% of patients with a normal EST and in 54% of those with abnormal EST.

while when both abnormalities were present, 86% was submitted to VI (X2=18.4; gl=2; p<0.0001).

There are several reasons for which patients may appear as asymptomatic in the clinical history, but present symptoms triggered by stress RNV. Some may have too sedentary a lifestyle to experiment a spontaneous clinical manifestation, while others may reduce their level of activity in order to prevent symptoms. Also, mild dyspnea or reduced exercise capacity may sometimes be self-attributed to advanced age and not to SAS. Additionally, some patients with cognitive impairment may forget they have experienced clinical symptoms spontaneously ¹⁰. On the contrary, there is concern

Table 2: Contingency table with proportions of VI according to RNV results (N, %).

	Valve Intervention		Total
	NO	YES	
Normal EST	36	6	42
	86%	14%	100%
Abnormal EST	5	6	11
	46%	54%	100%
Abnormal EST +	1	6	7
Abnormal LVEF	14%	86%	100%
behavior			

that some symptoms manifested during EST are too subjective and do not represent a valid reason to indicate VI. However, the addition of left ventricular systolic function deterioration demonstrated by RNV would exclude this hypothesis in many cases.

A significant proportion of individuals with clinical manifestations triggered by EST develop cardiac events or spontaneous symptoms within a year¹⁴. Since the appearance of clinical manifestations is associated with a strong increase in death risk, RNV could thus be positioned as an essential diagnostic test to guide a timely referral to VI.



Some of the significant risk characteristics in asymptomatic patients include echocardiographic response to exercise. In the study by Maréchaux S et al¹⁷, twenty patients had an abnormal LVEF response to exercise with a mean decrease in LVEF from 64 +/- 10 to 53 +/- 12% while 30 patients had a normal LVEF response to exercise with a mean increase in LV EF from 62 +/- 7 to 70 +/- 8%. Patients with an abnormal LVEF response during exercise were more likely to develop symptoms during ESTs than patients with a normal LVEF response: 80% versus 27% (P< 0.0001). The survival free of cardiac events was significantly lower in patients with abnormal LVEF response to EATs than in patients with a normal LVEF response (P = 0.03).

The authors concluded that exercise echocardiography provides objective data that facilitate interpretation of exercise elicited symptoms in patients with aSAS. In addition, an

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abnormal LVEF response to EATs may predict a poor outcome. Others parameters as the excessive increase in aortic velocity estimated by cardiac Doppler echocardiography, rate of AS progression, pulmonary hypertension unexplained by other reasons, and markedly elevated brain natriuretic peptide levels. There is also an increasing interest in the potential use of global longitudinal strain indices and the detection of myocardial fibrosis by nuclear magnetic resonance imaging.⁸ We hereby propose to add RNV to these risk markers described in the literature. (Figure 4).

We believe that the stress test is safe and well tolerated in cases of aSAS and may reveal symptoms not recorded in the clinical history. The addition of LVEF evaluation during EST may improve the performance of the test and contributes incremental prognostic information to decide on VI.

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