## **Radiopharmaceuticals-Emerging Trends and Applications in diagnostic Imaging and Therapy**

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#### ABSTRACT

The landscape of nuclear medicine is undergoing a profound transformation, driven by the rapid evolution of radiopharmaceuticals. These innovative agents are redefining the boundaries of diagnostic imaging and targeted therapy, offering unprecedented opportunities for precision medicine. This comprehensive review article provides a cutting-edge overview of the emerging trends and applications of radiopharmaceuticals in diagnostic imaging and therapy. We delve into the latest advancements in radiopharmaceutical design, synthesis, and application, including the development of novel isotopes, peptides, and antibodies. The article highlights the growing importance of Theranostics, immuno-PET, and alpha-particle therapy in cancer diagnosis and treatment, as well as their potential applications in neurology, cardiology, and infectious diseases. Furthermore, we examine the challenges and future directions in radiopharmaceutical development, including the need for standardized manufacturing processes, improved regulatory frameworks, and enhanced radiation safety measures. We also discuss the role of artificial intelligence, machine learning, and big data analytics in accelerating the development and application of radiopharmaceuticals.

This review article aims to provide a roadmap for the future development and application of radiopharmaceuticals in diagnostic imaging and therapy, highlighting the vast potential of these innovative agents to revolutionize the field of nuclear medicine and improve patient outcomes.

*Keywords:* Radiopharmaceuticals, Nuclear medicine, Diagnostic imaging, Therapy, Oncology, Neurology, Cardiology, Infectious diseases, Theranostics, Immuno-PET, Alphaparticle therapy, Precision medicine, Personalized medicine, Artificial intelligence, Machine learning, big data analytics, Radiopharmaceutical development, Regulatory frameworks, Radiation safety, Molecular imaging.

#### **INTRODUCTION**

Recent years have seen tremendous developments in the field of nuclear medicine, particularly in the area of radiopharmaceuticals.<sup>[1]</sup> These substances, which are made up of physiologically active chemicals and radio nuclides, are essential

for both therapeutic and diagnostic imaging procedures. This review's title, "Radiopharmaceuticals-Emerging Trends and Applications In diagnostic Imaging and Therapy," captures the ever-changing environment in which new advancements

are redefining nuclear medicine's potential and uses.

As we continue this investigation, it becomes clear that new opportunities are being created by the convergence of biology, chemistry, and medical imaging. In addition to being essential instruments for diagnostics, non-invasive radiopharmaceuticals play a key role in targeted therapy giving medicine methods. a more individualized touch. By illuminating the underlying ideas of the most recent advancements in radiopharmaceuticals and their revolutionary effects on healthcare, this review seeks to map the course of these discoveries.

This overview will traverse the complex web of developments, from state-of-the-art imaging modalities like positron emission tomography (PET) and single photon emission computed tomography (SPECT) to the growing range of radiotracers. Furthermore, it will explore the practical uses that make use of these advancements, forming a sophisticated comprehension of their effectiveness in many medical specialties.

We hope to discover not just the present status of the field but also hints at its bright future as we set out on our exploration of developments radiopharmarecent in This ceuticals. field's integration of technology, chemistry, and medical research is an example of how teamwork is being used to push the limits of therapeutic effectiveness and diagnostic accuracy.<sup>[2,3]</sup>

## Historical Background

An interesting journey spanning several decades is the historical development of radiopharmaceuticals and their uses in diagnostic imaging and therapy. Significant turning points, innovations in technology, and an increasing comprehension of the complex interrelationship between radioactive elements and medical science have all contributed to the development of this subject.

## **Early Beginnings:**

The discovery of radioactivity in the early 20th centurv created new research opportunities. which where is radiopharmaceuticals got their start. Understanding the characteristics of radioactive elements was made possible by the groundbreaking work of scientists like Marie and Pierre Curie. The ultimate use of radioisotopes in medicine was made possible by their pioneering studies of polonium and radium.

## World War II and Technetium-99m:

The development of nuclear technology during World War II is directly linked to the discovery of technetium-99m (Tc-99m).

Technetium-99m is a radioactive isotope of technetium that was discovered in 1937 by Emilio Segrè, an Italian researcher. But it was not until the Manhattan Project in the 1940s that Tc-99m production took precedence.

The United States conducted a covert research and development operation during World War II called the Manhattan operation with the goal of creating atomic bombs. Tc-99m is one of the radioactive isotopes that scientists and engineers developed as part of this effort.

The Manhattan Project's creation of nuclear reactors made it possible to produce Tc-99m on a wide scale. Chicago Pile-1, the first nuclear reactor, was constructed in 1942. Subsequent reactors were made to generate radioactive isotopes for use in scientific and medical research.

Tc-99m manufacturing changed from military to medical uses after the war. The most often used radioactive isotope in nuclear medicine nowadays is Tc-99m, which is employed in imaging and diagnostic processes for a variety of illnesses. <sup>[4,5,6]</sup>

The nuclear technology created during World War II is directly related to the discovery and development of technetium-99m. The extensive use of Tc-99m in nuclear medicine today was made possible

by the Manhattan Project's emphasis on creating radioactive isotopes.

#### Advancement in Positron Emission Tomography (PET): A growing field

Positron-emitting radioisotopes were added to the focus in the second part of the 20th century, which resulted in the creation of Positron Emission Tomography (PET). A notable accomplishment was the creation of fluorodeoxyglucose (FDG), a radiopharmaceutical used in PET imaging that improved the visibility of bodily metabolic processes.

Recent years have tremendous seen improvements Positron Emission in Tomography (PET) imaging, making it a potent diagnostic tool in contemporary medicine. The development of new technology, radiotracers, and therapeutic applications are responsible for the growth of PET imaging.

#### Advancements in PET Technology

**1. Improved Spatial Resolution:** Clinicians may now see tiny lesions and cancers thanks to improvements in spatial resolution brought about by advancements in detector technology and reconstruction algorithms.

**2. Time-of-Flight (TOF) PET:** By more precisely localizing positron annihilation events, TOF PET technology has enhanced image quality.

**3. Digital PET:** Traditional analog PET scanners have been superseded by digital ones, which provide better image quality, sensitivity, and spatial resolution.

**4. Total-Body PET:** With the development of total-body PET scanners, medical professionals may now image the complete body in a single scan, increasing diagnostic precision and lowering radiation exposure.

## New Radiotracers and Clinical Applications

**1. Amyloid PET:** Alzheimer's disease can now be diagnosed and tracked by amyloid PET imaging.

**2. PSMA PET:** Prostate cancer diagnosis and treatment have been enhanced by prostate-specific membrane antigen (PSMA) PET imaging.

**3. Immuno-PET:** A promising method for identifying and tracking cancer immunotherapy is immuno-PET imaging.

**4. Cardiovascular PET:** For the diagnosis and follow-up of cardiovascular conditions such coronary artery disease and cardiomyopathy, cardiovascular PET imaging has grown in significance.

## **Prospects for the Future**

**1. Artificial Intelligence (AI) in PET Imaging:** AI algorithms are being created to enhance the processing, interpretation, and reconstruction of PET images.

**2. Personalized Medicine:** It is anticipated that PET imaging will be essential to personalized medicine, allowing physicians to customize treatment plans for each patient.

**3. Combination of PET with Other Imaging Modalities:** The integration of PET with other imaging modalities, including as MRI and CT, is predicted to improve diagnostic accuracy and patient outcomes.

The development of new technology, radiotracers, and therapeutic applications are responsible for the growth of PET imaging. PET imaging is anticipated to become more and more significant in contemporary medicine as research advances.<sup>[7,8,9]</sup>

## Therapeutic Radiopharmaceuticals:

While the early emphasis was on diagnostic imaging, the latter part of the 20th century witnessed the advent of therapeutic radiopharmaceuticals. Radioactive isotopes iodine-131 vttrium-90 like and find applications in the treatment of different medical problems, including thyroid disorders and certain types of cancer.

## Molecular Imaging and Targeted Radiopharmaceuticals:

Radiopharmaceuticals Targeted and Molecular Imaging: In recent decades, there has been a paradigm shift toward the creation of targeted radiopharmaceuticals and molecular imaging. Compounds that are precisely made to target and bind with receptors or biomarkers linked to specific diseases have been made possible by developments in biochemistry and molecular biology. This has created new opportunities for more precise illness detection and therapy as well as tailored medication.

## **Imaging Modalities**

Numerous imaging modalities have greatly improved diagnostic capacities in the field of nuclear medicine, and they are essential for both therapeutic treatments and medical imaging.

This section examines the fundamentals and many uses of several important imaging modalities, such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT).

#### Single Photon Emission Computed Tomography (SPECT)

Single Photon Emission Computed Tomography (SPECT) is a nuclear medicine imaging modality that creates threedimensional images of the body using gamma rays. It is commonly used in clinical practice to diagnose and track a number of diseases, such as neurological disorders, cardiovascular disease, and cancer.

## Principle

The foundation of SPECT imaging is the detection of gamma rays released by intravenous injections of radioactive tracers. When the tracers build up in particular organs or tissues, they release gamma rays that a gamma camera can detect. Multiple projections of the gamma ray emissions are captured by the rotating gamma camera. A computer program is then used to

reassemble these projections into a threedimensional image.

#### Instrumentation

A SPECT system consists of several key components:

**1. Gamma Camera:** A gamma camera is a device that detects gamma rays emitted by the radioactive tracer. It consists of a crystal scintillator, photomultiplier tubes, and a collimator.

**2. Collimator:** A collimator is a device that focuses the gamma rays onto the gamma camera, allowing for better spatial resolution.

**3. Computer System:** A computer system is used to reconstruct the SPECT images from the acquired projections.

#### **Clinical Applications**

SPECT imaging has a wide range of clinical applications, including:

**1. Oncology:** Breast, lung, and thyroid cancer are among the many cancer forms that can be detected and tracked using SPECT imaging.

**2. Cardiology:** Cardiomyopathy and coronary artery disease are two conditions that can be diagnosed and tracked by SPECT imaging.

**3.** Neurology: Numerous neurological conditions, such as epilepsy, Parkinson's disease, and Alzheimer's disease, can be diagnosed and tracked by SPECT imaging.

**4. Infection and Inflammation:** Osteomyelitis and abscesses are among the inflammatory illnesses and infections that can be detected and tracked with SPECT imaging.

#### **Advantages and Limitations**

SPECT imaging has several advantages, including:

**1. High sensitivity:** Due to its extraordinary sensitivity, SPECT imaging can detect even minute amounts of radioactive tracer.

**2. Good spatial resolution:** Due to its extraordinary sensitivity, SPECT imaging can detect even minute amounts of radioactive tracer.

**3. Wide range of clinical applications:** SPECT imaging is a flexible imaging technique with a broad variety of therapeutic uses.

## However, SPECT imaging also has several limitations, including:

**1. Limited spatial resolution:** A versatile imaging method, SPECT imaging has several therapeutic applications.

**2. Radiation exposure:** Patients and medical professionals may be concerned about the radiation exposure associated with SPECT imaging.

**3. Availability and accessibility:** SPECT imaging might not be accessible or generally available in all healthcare settings, especially in places with limited resources. [10]

#### **Positron Emission Tomography (PET)**

Positron-emitting radiotracers are used in Positron Emission Tomography (PET), a nuclear medicine imaging technique, to show the body's metabolic activities. In contemporary medicine, PET imaging has become an essential technique, especially in the domains of neurology, cardiology, and oncology.

## **Principle of PET**

The foundation of PET imaging is the detection of positron-electron annihilation events: a positron-emitting radiotracer is injected into the body and accumulates in particular tissues or organs, where it decays and releases positrons that travel a short distance before colliding with electrons, annihilating the positron and electron, and creating two gamma photons that travel in opposite directions.

#### Instrumentation

A PET scanner consists of several key components:

**1. Detector Rings:** The gamma photons generated by positron-electron annihilation events are detected by PET scanners using detector rings. Usually, scintillator materials like gadolinium oxyorthosilicate (GSO) or

lutetium oxyorthosilicate (LSO) are used to make these detector rings.

**2. Coincidence Detection:** The gamma photons generated by positron-electron annihilation events are detected by PET scanners via coincidence detection. This entails observing two gamma rays arriving at opposing detectors simultaneously.

**3. Reconstruction Algorithm:** In order to recreate the PET images from the detected gamma rays, PET scanners employ reconstruction algorithms. Iterative reconstruction methods like ordered subset expectation maximization (OSEM) are frequently used in these algorithms.

## **Clinical Applications**

PET imaging has a wide range of clinical applications, including:

**1. Oncology:** In oncology, PET imaging is frequently used for cancer diagnosis and staging, therapy response monitoring, and recurrence detection.

**2. Neurology:** In neurology, PET imaging is used to diagnose and track neurological conditions such epilepsy, Parkinson's disease, and Alzheimer's disease.

**3. Cardiology:** In cardiology, PET imaging is used to diagnose and track cardiovascular conditions, such as cardiomyopathy and coronary artery disease.

## **Advantages and Limitations**

PET imaging has several advantages, including:

**1. High sensitivity:** Due to its high sensitivity, PET imaging can detect even minute amounts of radiotracer.

**2. High spatial resolution:** Because PET imaging has a great spatial resolution, tiny structures can be seen.

**3. Quantitative imaging:** Quantitative imaging made possible by PET imaging makes it possible to measure the body's metabolic activities.

## However, **PET imaging also has several limitations, including:**

**1. Radiation exposure:** Patients and medical professionals may be concerned

about the radiation exposure associated with PET imaging.

**2.** Cost: Due to its relatively high cost, PET imaging is not always readily available or accessible in some healthcare settings.

**3. Availability:** Not all healthcare settings have access to PET imaging, especially those with limited resources. <sup>[11-15]</sup>

## Hybrid Imaging: SPECT/CT and PET/CT

Combining two or more imaging modalities to create a single, comprehensive image is known as hybrid imaging. Hybrid imaging in nuclear medicine usually combines Computed Tomography (CT) with Single Photon Emission Computed Tomography (SPECT) or Positron Emission Tomography (PET).

## SPECT/CT

SPECT/CT hybrid imaging integrates the anatomical information from CT with the functional information from SPECT, allowing physicians to:

- 1. Increase the precision of diagnosis by integrating functional and anatomical data.
- 2. Improve the staging and identification of tumors
- 3. Track the course of the disease and the response to treatment.
- 4. Use smaller dosages of radiotracer to lessen radiation exposure.

## PET/CT

The functional information from PET and the anatomical information from CT are combined in PET/CT hybrid imaging. With this combination, physicians can:

- 1. Improve diagnostic accuracy by correlating functional and anatomical information
- 2. Enhance tumor detection and staging
- 3. Monitor treatment response and disease progression
- 4. Reduce radiation exposure by using lower doses of radiotracer

## **Clinical Applications**

Hybrid imaging with SPECT/CT and PET/CT has a wide range of clinical applications, including:

**1. Oncology:** tumor identification, staging, and therapy response tracking.

**2. Neurology:** identifying and keeping track of neurological conditions like Parkinson's and Alzheimer's.

**3. Cardiology:** identifying and keeping track of cardiovascular conditions, such as cardiomyopathy and coronary artery disease.

**4. Infection and inflammation:** identifying and keeping track of inflammatory illnesses and infections.

#### **Advantages and Limitations**

Hybrid imaging with SPECT/CT and PET/CT offers several advantages, including:

- 1. Enhanced precision in diagnosis.
- 2. Improved tumor staging and detection.
- 3. Improved tracking of illness development and response to treatment.
- 4. Decreased exposure to radiation.

## However, hybrid imaging also has several limitations, including:

- 1. Increased cost
- 2. Limited availability
- 3. Radiation exposure
- 4. Complexity of image interpretation

#### Radiopharmaceuticals

Products used for research, treatment, or diagnosis that contain radioactive isotopes are known as radiopharmaceuticals. These products enable accurate imaging or therapy of a variety of disorders since they are made to target particular cells, tissues, or organs.

#### **Types of Radiopharmaceuticals:**

**1. Diagnostic radiopharmaceuticals:** These goods, which are used for imaging and diagnosis, include radioactive isotopes that release positrons or gamma rays that imaging equipment like PET scanners and gamma cameras can detect.

**2.** Therapeutic radiopharmaceuticals: These items are used to treat cancer by containing radioactive isotopes that release gamma, beta, or alpha radiation that either kills cancer cells or reduces their symptoms.

**3. Research radiopharmaceuticals:** These items are used in research to create new diagnostic or therapeutic agents or to examine the behavior of particular cells, tissues, or organs. <sup>[16-20]</sup>

#### Some Examples of Radiopharmaceuticals: 1. Technetium-99m (Tc-99m) Radiopharmaceuticals:

As a gamma-emitting, metastable nuclear isomer, technetium-99m (Tc-99m) is a perfect radionuclide for medical imaging. In nuclear medicine, Tc-99m radiopharmaceuticals are frequently employed for disease monitoring and diagnosis.

#### **Properties of Tc-99m**

- ✓ Half-life: With a half-life of 6.02 hours, Tc-99m provides ample time for imaging procedures.
- ✓ Gamma energy: The 140 keV gamma rays that the Tc-99m generates are perfect for gamma camera imaging.
- ✓ Chemical properties: Numerous ligands can readily complex with Tc-99m, enabling the creation of a broad variety of radiopharmaceuticals.

## **Production of Tc-99m**

Molybdenum-99 (Mo-99), which is created by nuclear fission events, decays to yield Tc-99m. Technetium generators are the most often used technique for creating Tc-99m.

#### Clinical Applications of Tc-99m Radiopharmaceuticals

Tc-99m radiopharmaceuticals have a wide range of clinical applications, including:

Bone imaging: To detect and track bone disorders like osteoporosis and bone

cancer, Tc-99m-methyl diphosphonate (MDP) is utilized in bone imaging.

- Cardiac imaging: Cardiomyopathy and coronary artery disease are diagnosed and tracked by cardiac imaging using Tc-99m-sestamibi.
- Renal imaging: Kidney illnesses like renal failure and kidney cancer are diagnosed and tracked via renal imaging using Tc-99m-mercaptoacetyltriglycine (MAG3).
- Infection and inflammation imaging: White blood cells labelled with Tc-99m are used to detect and track infections and inflammatory conditions such abscesses and osteomyelitis.

## 2. Fluorine-18 (F-18) Radiopharmaceuticals:

A common radioactive isotope of fluorine used in positron emission tomography (PET) imaging is fluorine-18 (F-18). Nuclear medicine has undergone a F-18 revolution because to radiopharmaceuticals, which make it possible to diagnose and track a variety of illnesses.

## **Production of F-18**

Usually, a cyclotron is used to bombard oxygen-18 with protons in order to create F-18. The desired radiopharmaceutical is then created by chemically processing the resultant F-18.

#### Clinical Applications of F-18 Radiopharmaceuticals

F-18 radiopharmaceuticals have a wide range of clinical applications, including:

- Oncology: F-18-fluorodeoxyglucose (FDG) is frequently utilized in cancer monitoring and diagnosis.
- Neurology: Alzheimer's disease, Parkinson's disease, and other neurological conditions are diagnosed and tracked with F-18-FDG.
- Cardiology: Cardiovascular disease is diagnosed and tracked with F-18-FDG.

Infection and inflammation: Infections and inflammatory disorders are diagnosed and tracked with F-18-FDG. [21,22,23]

## 3. Gallium-68 (Ga-68) Radiopharmaceuticals:

A common radioactive isotope of gallium used in positron emission tomography (PET) imaging is gallium-68 (Ga-68). Ga-68 radiopharmaceuticals have attracted a lot of interest lately because of their possible uses in neurology, oncology, and other disciplines.

#### **Production of Ga-68**

Usually, a cyclotron is used to bombard zinc-68 with protons in order to create Ga-68. The necessary radiopharmaceutical is subsequently created by chemically processing the resultant Ga-68.

#### Clinical Applications of Ga-68 Radiopharmaceuticals

Ga-68 radiopharmaceuticals have a wide range of clinical applications, including:

- Oncology: Neuroendocrine cancers are diagnosed and tracked with Ga-68-DOTATATE.
- Neurology: Additionally, Ga-68-DOTATATE is utilized to monitor and diagnose neurological conditions like Parkinson's disease.
- Infection and inflammation: Ga-68citrate is used to monitor and diagnose inflammatory disorders and infections. [24,25,26]

## 4. Iodine-131 (I-131) Radiopharmaceuticals:

A common radioactive isotope of iodine used for both diagnostic and therapeutic reasons in nuclear medicine is iodine-131 (I-131). After more than 60 years of usage, I-131 radiopharmaceuticals are still a vital tool in the treatment of many illnesses.

#### **Production of I-131**

Usually, uranium-235 is fissioned in a nuclear reactor to make I-131. The necessary radiopharmaceutical is

subsequently created by chemically processing the resultant I-131.

### Clinical Applications of I-131 Radiopharmaceuticals

I-131 radiopharmaceuticals have a wide range of clinical applications, including:

- Thyroid cancer: I-131 is used to treat thyroid cancer, specifically to remove any remaining thyroid tissue following surgery.
- Hyperthyroidism: I-131 is used to treat hyperthyroidism, especially in people who do not respond to antithyroid drugs.
- Thyroid nodules: Thyroid nodule diagnosis and treatment are accomplished with I-131.
- Cancer therapy: For the treatment of solid tumors, leukemia, lymphoma, and other cancers, I-131 is being researched. [27,28]

#### 5. Yttrium-90 (Y-90) Radiopharmaceuticals:

A common radioactive isotope of yttrium utilized for therapeutic purposes in nuclear medicine is yttrium-90 (Y-90). For more than two decades, Y-90 radiopharmaceuticals have been a vital component in the treatment of numerous illnesses.

#### **Production of Y-90**

Y-90 is usually created by utilizing a cyclotron to attack strontium-89 with protons. The appropriate radiopharmaceutical is subsequently created by chemically processing the resultant Y-90.

#### Clinical Applications of Y-90 Radiopharmaceuticals

Y-90 radiopharmaceuticals have a wide range of clinical applications, including:

Cancer therapy: Leukemia, lymphoma, and liver cancer are among the cancers that are treated using Y-90 radiopharmaceuticals.

## \* Radioembolization:

Radioembolization, a less invasive

technique for liver cancer treatment, uses Y-90 radiopharmaceuticals.

- Radiation synovectomy: Radiation synovectomy, a treatment for rheumatoid arthritis, uses Y-90 radiopharmaceuticals. <sup>[29-31]</sup>
- 6. Lutetium-177 (Lu-177) Radiopharmaceuticals:

A common radioactive isotope of lutetium utilized for therapeutic purposes in nuclear medicine is lutetium-177 (Lu-177). The prospective uses of Lu-177 radiopharmaceuticals in oncology have drawn a lot of attention recently.

## **Production of Lu-177**

Usually, a cyclotron is used to bombard ytterbium-176 with protons in order to create Lu-177. The appropriate radiopharmaceutical is subsequently created by chemically processing the resultant Lu-177.

#### **Clinical Applications of Lu-177 Radiopharmaceuticals**

Lu-177 radiopharmaceuticals have a wide range of clinical applications, including:

- Cancer therapy: Prostate, breast, and neuroendocrine tumors are among the cancers that can be treated with Lu-177 radiopharmaceuticals.
- Peptide receptor radionuclide therapy (PRRT): Lu-177 radiopharmaceuticals are utilized in peptide receptor radionuclide therapy (PRRT), a targeted treatment for neuroendocrine cancers.
- Radiation synovectomy: To treat rheumatoid arthritis, radiation synovectomy is performed using Lu-177 radiopharmaceuticals. <sup>[32,33]</sup>
- 7. Radium-223 (Ra-223) Radiopharmaceuticals:

Radium-223 (Ra-223) is a radioactive isotope of radium that is used in nuclear medicine for the treatment of certain types of cancer. Ra-223 radiopharmaceuticals have gained significant attention in recent years due to their potential applications in oncology.

## **Production of Ra-223**

Ra-223 is typically produced through the bombardment of radium-226 with alpha particles, using a cyclotron. The resulting Ra-223 is then chemically processed to produce the desired radiopharmaceutical.

#### Clinical Applications of Ra-223 Radiopharmaceuticals

Ra-223 radiopharmaceuticals have a wide range of clinical applications, including:

- Cancer therapy: Certain cancers, such as osteosarcoma, breast cancer, and prostate cancer, can be treated with Ra-223 radiopharmaceuticals.
- Bone metastases: Bone metastases, especially in patients with prostate cancer, are treated with Ra-223 radiopharmaceuticals.
- Pain palliation: Patients with bone metastases can have their pain managed using Ra-223 radiopharmaceuticals.

## 8. Copper-64 (Cu-64) Radiopharmaceuticals:

Nuclear medicine uses the radioactive copper isotope copper-64 (Cu-64) for both diagnostic and therapeutic applications. Cu-64 radiopharmaceuticals have attracted a lot of interest lately because of their possible uses in neurology and oncology.

## **Production of Cu-64**

Usually, a cyclotron is used to attack nickel-64 with protons in order to create Cu-64. The necessary radiopharmaceutical is subsequently created by chemically processing the resultant Cu-64.

#### Clinical Applications of Cu-64 Radiopharmaceuticals

Cu-64 radiopharmaceuticals have a wide range of clinical applications, including:

Cancer detection and treatment: Cu-64 radiopharmaceuticals are used to detect and treat a number of cancers,

including as prostate, lung, and breast cancer.

- Neurological disorders: Alzheimer's and Parkinson's diseases are among the neurological conditions that can be diagnosed and treated with Cu-64 radiopharmaceuticals.
- Infection and inflammation: Infections and inflammatory illnesses are diagnosed and treated with Cu-64 radiopharmaceuticals. <sup>[34-37]</sup>

## **Clinical Applications**

## 1. Oncology:

Advancements: application of new radiopharmaceuticals, such as PSMA-targeted medicines for prostate cancer, for targeted cancer imaging and treatment.

**Application:** Personalized treatment plans are guided by precision oncology, which uses PET/CT or SPECT/CT to identify particular molecular markers.

## 2. Neurology:

Advancements: creation of radiotracers to enhance the imaging of neurodegenerative illnesses, such as Alzheimer's disease amyloid imaging agents.

**Application:** Better patient treatment is facilitated by the early identification and tracking of neurological problems using cutting-edge imaging techniques.

## 3. Cardiology:

Advancements: Myocardial perfusion imaging using new radiopharmaceuticals to accurately diagnose coronary artery disease.

**Application:** enhanced cardiac condition diagnostics that enable accurate assessment of cardiac function and early identification.

## 4. Rheumatology:

Advancements: imaging of rheumatoid arthritis and other autoimmune diseases using radiopharmaceuticals that target particular inflammatory processes. **Application:** improved visualization of disease activity and treatment response, which facilitates the creation of tailored treatments.

## 5. Endocrinology:

Advancements: creation of radiolabelled hormones to help locate endocrine malignancies more precisely.

**Application:** Endocrine abnormalities can be accurately diagnosed and staged, allowing for prompt and focused therapies.

## 6. Theranostic:

Advancements: integration of theranostic techniques, which use the same radiopharmaceutical to combine targeted therapy and diagnostic imaging. **Application:** customized therapy regimens based on each patient's unique more response, resulting in individualized and successful therapeutic interventions.

## 7. Infectious Diseases:

Advancements: creation of radiopharmaceuticals to help monitor and detect infectious diseases early by imaging infection sites.

**Application:** enhanced comprehension of how illnesses develop and how antimicrobial therapies affect patients.

## 8. Pediatrics:

Advancements: introduction of radiopharmaceuticals tailored to children that require less radiation exposure.

**Application:** better and safer imaging for young patients, guaranteeing a precise diagnosis without endangering their well-being.<sup>[38-40]</sup>

## Challenges and Future Directions Challenges:

# I. Radiopharmaceutical Design and Optimization:

Developing radiopharmaceuticals with improved targeting specificity and reduced side effects remains a

significant challenge. Optimization of radiotracer design to enhance imaging resolution and accuracy.

### **II.** Production and Supply Chain:

Ensuring a consistent and reliable supply of radiopharmaceuticals, particularly those with short half-lives, poses logistical challenges. Addressing issues related to the global distribution and accessibility of radiopharmaceuticals. <sup>[41,42]</sup>

#### III. Radiation Safety and Dosimetry:

Striking a balance between maximizing the therapeutic effect and minimizing radiation exposure to healthy tissues. Establishing standardized dosimetry protocols for different radiopharmaceuticals.

#### **IV.** Regulatory Hurdles:

Navigating regulatory processes for approval and ensuring compliance with evolving standards in different regions. Developing streamlined approval pathways for innovative radiopharmaceuticals. <sup>[43,44]</sup>

#### V. Integration with Multimodal Imaging:

Integrating nuclear medicine with other imaging modalities for comprehensive diagnostic assessments presents technical and interpretational challenges.

#### **Future Directions:**

#### I. Personalized medicine:

creating radiopharmaceuticals that can be customized to meet the needs of specific patients by utilizing methods like companion diagnostics and precision medicine.

## **II.** Theranostics:

Integrating diagnostic and therapeutic capabilities into a single radiopharmaceutical, enabling simultaneous diagnosis and treatment.

#### **III.** Alpha-particle therapy:

creating radiopharmaceuticals that produce alpha particles for targeted cancer treatment, which may have fewer adverse effects and be more effective. [45,46]

#### IV. Immuno-PET:

creating radiopharmaceuticals for immuno-PET imaging, which will allow immune cells and their interactions with cancer cells to be seen. <sup>[47,48]</sup>

## V. Artificial intelligence and machine learning:

using machine learning and artificial intelligence methods to imaging, therapy, and radiopharmaceutical development order increase in to precision, effectiveness, and patient outcomes.

#### VI. Understanding Radiobiology:

expanding our knowledge of how radiopharmaceuticals affect healthy and malignant tissues radiobiologically. Studies on enhancing treatment regimens to achieve better therapeutic results. <sup>[49-53]</sup>

#### CONCLUSION

The recent advancements in radiopharmaceuticals have ushered in a transformative era in nuclear medicine, revolutionizing the field of diagnostic imaging and therapy. The rapid evolution of novel radiotracers and targeted therapies has not only enhanced the precision of diagnostic imaging but also opened new avenues for personalized and targeted treatment strategies.

The integration of cutting-edge technologies, such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT), transformed imaging capabilities, has enabling early disease detection and more accurate diagnosis. Moreover, the expanding repertoire of radiopharmaceuticals in therapeutic applications, including targeted radionuclide therapy, holds great promise for the management of various conditions, from cancer to neurological disorders.

These developments underscore the potential to move beyond traditional approaches and embrace a more

personalized and effective approach to patient care. As we celebrate these achievements, it is essential to acknowledge the challenges that lie ahead, including regulatory considerations, costeffectiveness, and the need for widespread accessibility.

To overcome these hurdles, collaborative efforts among researchers, clinicians, and policymakers will be crucial. This may involve developing innovative funding models, streamlining regulatory pathways, and promoting education and awareness about the benefits and risks of radiopharmaceuticals.

As we embark on this exciting journey, it is clear that the future of radiopharmaceuticals holds immense promise. With continued innovation, collaboration, and dedication, we can unlock the full potential of these powerful tools and transform the lives of patients around the world.

Ultimately, the strides recent in radiopharmaceuticals mark a transformative era in nuclear medicine, one that is poised to continue with enthusiasm and dedication from the scientific and medical communities. As we look to the future, we are filled with excitement and anticipation possibilities for the that radiopharmaceuticals hold, and we are committed to working together to realize their full potential.

#### **Declaration by Authors**

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#### REFERENCES

- Goldsmith, S.J. Targeted Radionuclide Therapy: A Historical and Personal Review. *Semin. Nucl. Med.* 2020, *50*, 87– 97. [Google Scholar] [CrossRef] [PubMed]
- Yeong, C.H.; Cheng, M.H.; Ng, K.H. Therapeutic Radionuclides in Nuclear Medicine: Current and Future Prospects. J. Zhejiang Univ. Sci. B 2014, 15, 845–863. [Google Scholar] [CrossRef] [PubMed]

- Ercan, M.T.; Caglar, M. Therapeutic Radiopharmaceuticals. In *Current Pharmaceutical Design*; Bentham Science Publishers: Sharjah, United Arab Emirates, 2000; Volume 6, pp. 1085–1121. [Google Scholar]
- Gabriel, M. Radionuclide therapy beyond radioiodine. *Wien.* Med. Wochenschr. 2012, 162, 430–439. [Google Scholar] [CrossRef] [PubMed]
- Sgouros, G.; Bodei, L.; McDevitt, M.R.; Nedrow, J.R. Radiopharmaceutical therapy in cancer: Clinical advances and challenges. *Nat. Rev. Drug Discov.* 2020, *19*, 589–608. [Google Scholar] [CrossRef] [PubMed]
- Kramer-Marek, G.; Capala, J. The role of nuclear medicine in modern therapy of cancer. *Tumor Biol.* 2012, *33*, 629–640. [Google Scholar] [CrossRef] [PubMed]
- Herrmann, K.; Schwaiger, M.; Lewis, J.S.; Solomon, S.B.; McNeil, B.J.; Baumann, M.; Gambhir, S.S.; Hricak, H.; Weissleder, R. Radiotheranostics: A roadmap for future development. *Lancet Oncol.* 2020, *21*, e146–e156. [Google Scholar] [CrossRef]
- Kumar, C.; Shetake, N.; Desai, S.; Kumar, A.; Samuel, G.; Pandey, B.N. Relevance of radiobiological concepts in radionuclide therapy of cancer. *Int. J. Radiat. Biol.* 2016, *92*, 173–186. [Google Scholar] [CrossRef]
- Elliyanti, A. Radioiodine for Graves' Disease Therapy. In *Graves' Diseas*, 1st ed.; Gensure, R., Ed.; Intechopen: London, UK, 2021. [Google Scholar] [CrossRef]
- 10. Slonimsky, E.; Tulchinsky, M. Radiotheragnostics Paradigm for Radioactive Iodine (Iodide) Management of Thyroid Differentiated Cancer. Curr. Pharm. Des. 2020, 26, 3812. [Google Scholar] [CrossRef] [PubMed]
- Kendi, A.T.; Moncayo, V.M.; Nye, J.A.; Galt, J.R.; Halkar, R.; Schuster, D.M. Radionuclide therapies in molecular imaging and precision medicine. *PET Clin.* 2017, *12*, 93–103. [Google Scholar] [CrossRef] [PubMed]
- Pouget, J.P.; Navarro-Teulon, I.; Bardiès, M.; Chouin, N.; Cartron, G.; Pèlegrin, A.; Azria, D. Clinical Radioimmunotherapy— The role of radiobiology. *Nat. Rev. Clin. Oncol.* 2011, 8, 720–734. [Google Scholar] [CrossRef]

- Jia, Z.; Wang, W. Yttrium-90 radioembolization for unresectable metastatic neuroendocrine liver tumor: A systematic review. *Eur. J. Radiol.* 2018, *100*, 23–29. [Google Scholar] [CrossRef]
- Waldmann, T.; White, J.; Carrasquillo, J.; Reynolds, J.; Paik, C.; Gansow, O.; Brechbiel, M.; Jaffe, E.; Fleisher, T.; Goldman, C. Radioimmunotherapy of interleukin-2R alpha-expressing adult T-cell leukemia with yttrium-90-labeled anti-Tac. *Blood* 1995, *86*, 4063–4075. [Google Scholar] [CrossRef] [PubMed]
- Nisa, L.; Savelli, G.; Giubbini, R. Yttrium-90 DOTATOC therapy in GEP-NET and other SST2 expressing tumors: A selected review. *Ann. Nucl. Med.* 2011, 25, 75–85. [Google Scholar] [CrossRef] [PubMed]
- Kang, L.; Li, C.; Rosenkrans, Z.T.; Huo, N.; Chen, Z.; Ehlerding, E.B.; Huo, Y.; Ferreira, C.A.; Barnhart, T.E.; Engle, J.W.; et al. CD38-Targeted Theranostics of Lymphoma with <sup>89</sup>Zr/<sup>177</sup> Lu-Labeled Daratumumab. *Adv. Sci.* 2021, *8*, 2001879. [Google Scholar] [CrossRef]
- Da Silva, T.N.; van Velthuysen, M.L.F.; van Eijck, C.H.J.; Teunissen, J.J.; Hofland, J. Successful neoadjuvant peptide receptor radionuclide therapy for an inoperable pancreatic neuroendocrine tumour. *Endocrinol. Diabetes Metab. Case Rep.* 2018, *11*, 18-0015. [Google Scholar] [CrossRef]
- Guerra Liberal, F.D.C.; O'Sullivan, J.M.; McMahon, S.J.; Prise, K.M. Targeted Alpha Therapy: Current Clinical Applications. *Cancer Biother. Radiopharm.* 2020, *35*, 404–417. [Google Scholar] [CrossRef]
- 19. Goyal, J.; Antonarakis, E.S. Bone-targeting radiopharmaceuticals for the treatment of prostate cancer with bone metastases. *Cancer Lett.* 2012, *323*, 135. [Google Scholar] [CrossRef] [PubMed]
- Filippi, L.; Chiaravalloti, A.; Schillaci, O.; Cianni, R.; Bagni, O. Theranostic approaches in nuclear medicine: Current status and future prospects. *Expert Rev. Med. Devices* 2020, *17*, 331–343. [Google Scholar] [CrossRef] [PubMed]
- 21. McDevitt, M.R.; Sgouros, G.; Sofou, S. Targeted and nontargeted α-particle therapies. *Annu. Rev. Biomed.*

*Eng.* 2018, *20*, 73–93. [Google Scholar] [CrossRef]

- 22. Reissig, F.; Wunderlich, G.; Runge, R.; Freudenberg, R.; Lühr, A.; Kotzerke, J. The effect of hypoxia on the induction of strand breaks in plasmid DNA by alpha-, beta- and Auger electron-emitters <sup>223</sup>Ra, <sup>188</sup>Re, <sup>99m</sup>Tc and DNA-binding <sup>99m</sup>Tc-labeled pyrene. *Nucl. Med. Biol.* 2020, 80–81, 65– 70. [Google Scholar] [CrossRef] [PubMed]
- Persson, L. The Auger electron effect in radiation dosimetry. *Health Phys.* 1994, 67, 471–476. [Google Scholar] [CrossRef] [PubMed]
- Widel, M. Radionuclides in radiationinduced bystander effect; may it share in radionuclide therapy? *Neoplasma* 2017, 64, 641–654. [Google Scholar] [CrossRef] [PubMed]
- Kirsch, D.G.; Diehn, M.; Kesarwala, A.; Maity, A.; Morgan, M.A.; Schwarz, J.K.; Bristow, R.; DeMaria, S.; Eke, I.; Griffin, R.J.; et al. The Future of Radiobiology. *J. Natl. Cancer Inst.* 2018, *110*, 329–340. [Google Scholar] [CrossRef]
- 26. Paillas, S.; Ladjohounlou, R.; Lozza, C.; Pichard, A.; Boudousq, V.; Jarlier, M.; Sevestre, S.; Le Blay, M.; Deshayes, E.; Sosabowski, J.; et al. Localized irradiation of cell membrane by auger electrons is cytotoxic through oxidative stress-mediated nontargeted effects. *Antioxid. Redox Signal.* 2016, 25, 467–484. [Google Scholar] [CrossRef]
- 27. Pandit-Taskar, N. Targeted Radioimmunotherapy and Theranostics with Alpha Emitters. J. Med. Imaging Radiat. Sci 2019, 50, S41–S44. [Google Scholar] [CrossRef]
- White, J.M.; Escorcia, F.E.; Viola, N.T. Perspectives on metals-based radioimmunotherapy (RIT): Moving forward. *Theranostics* 2021, *11*, 6293–6314. [Google Scholar] [CrossRef]
- Fendler, W.P.; Rahbar, K.; Herrmann, K.; Kratochwil, C.; Eiber, M. 177Lu-PSMA Radioligand Therapy for Prostate Cancer. J. Nucl. Med. 2017, 58, 1196–1200. [Google Scholar] [CrossRef]
- Nevedomskaya, E.; Baumgart, S.J.; Haendler, B. Recent advances in prostate Cancer treatment and drug discovery. *Int. J. Mol. Sci.* 2018, *19*, 1359. [Google Scholar] [CrossRef] [PubMed]

- Lunger, L.; Tauber, R.; Feuerecker, B.; Gschwend, J.E.; Eiber, M. Narrative review: Prostate-specific membrane antigenradioligand therapy in metastatic castrationresistant prostate cancer. *Transl. Androl. Urol.* 2021, *10*, 3963–3971. [Google Scholar] [CrossRef] [PubMed]
- Kairemo, K.; Joensuu, T. Lu-177-PSMA treatment for metastatic prostate cancer: Case examples of major responses. *Clin. Transl Imaging* 2018, *6*, 223–237. [Google Scholar] [CrossRef]
- Sathekge, M.; Bruchertseifer, F.; Knoesen, O.; Reyneke, F.; Lawal, I.; Lengana, T.; Davis, C.; Mahapane, J.; Corbett, C.; Vorster, M.; et al. <sup>225</sup>Ac-PSMA-617 in chemotherapy-naive patients with advanced prostate cancer: A pilot study. *Eur. J. Nucl. Med. Mol. Imaging* 2019, *46*, 129–138. [Google Scholar] [CrossRef] [PubMed]
- 34. Khreish, F.; Ebert, N.; Ries, M.; Maus, S.; Rosar, F.; Bohnenberger, H.; Stemler, T.; Saar, M.; Bartholomä, M.; Ezziddin, S. <sup>225</sup>Ac-PSMA-617/<sup>177</sup> Lu-PSMA-617 tandem therapy of metastatic castrationresistant prostate cancer: Pilot experience. Eur. J. Nucl. Med. Mol. 721-728. Imaging 2020, 47, [Google Scholar] [CrossRef]
- 35. Kratochwil, C.; Haberkorn, U.; Giesel, F.L. <sup>225</sup>Ac-PSMA-617 for Therapy of Prostate Cancer. *Semin. Nucl. Med.* 2020, *50*, 133–140. [Google Scholar] [CrossRef]
- 36. Basu, S.; Parghane, R.V.; Chakrabarty, S. Peptide Receptor Radionuclide Therapy of Neuroendocrine Tumors. *Semin. Nucl. Med.* 2020, *50*, 447–464. [Google Scholar] [CrossRef]
- Kunikowska, J.; Królicki, L. Targeted α-Emitter Therapy of Neuroendocrine Tumors. Semin. Nucl. Med. 2020, 50, 171– 176. [Google Scholar] [CrossRef]
- Elliyanti, A.; Rustam, R.; Tofrizal, T.; Yenita, Y.; Susanto, Y.D.B. Evaluating the Natrium iodide Symporter expressions in thyroid Tumors. *Open Access Maced. J. Med. Sci.* 2021, *9*, 18–23. [Google Scholar] [CrossRef]
- Elliyanti, A.; Rusnita, D.; Afriani, N.; Susanto, Y.D.B.; Susilo, V.Y.; Setiyowati, S.; Harahap, W.A. Analysis natrium iodide symporter expression in breast cancer subtypes for radioiodine therapy response. *Nucl. Med. Mol.*

*Imaging* 2020, *54*, 35–42. [Google Scholar] [CrossRef]

- 40. Liu, J.; Liu, Y.; Lin, Y.; Liang, J. Radioactive Iodine-Refractory Differentiated Thyroid Cancer, and Redifferentiation Therapy. *Endocrinol. Metab.* 2019, *34*, 215–225. [Google Scholar] [CrossRef]
- Mirshojaei, S.F.; Ahmadi, A.; Morales-Avila, E.; Ortiz-Reynoso, M.; Reyes-Perez, H. Radiolabelled nanoparticles: Novel classification of radiopharmaceuticals for molecular imaging of cancer. *J. Drug Target.* 2016, 24, 91–101. [Google Scholar] [CrossRef]
- 42. Ting, G.; Chang, C.H.; Wang, H.E.; Lee, T.W. Nanotargeted radionuclides for cancer nuclear imaging and internal radiotherapy. *J. Biomed. Biotechnol.* 2010, 2010, 953537. [Google Scholar] [CrossRef]
- 43. Farzin, L.; Sheibani, S.; Moassesi, M.E.; Shamsipur, M. An overview of nanoscale radionuclides and radiolabeled nanomaterials commonly used for nuclear imaging and therapeutic molecular functions. J. Biomed. Mater. Res. A 2019, 107, 251–285. [Google Scholar] [CrossRef]
- 44. Wong, C.H.; Siah, K.W.; Lo, A.W. Estimation of clinical trial success rates and related parameters. *Biostatistics* 2018, 20, 273–286. [Google Scholar] [CrossRef]
- 45. Jadvar H. (2018). Molecular Imaging Theranostics: Evolving Role of PET in Targeted Imaging and Therapy. Expert Review of Medical Devices, 15(3), 241– 246.
- Paudyal B., Paudyal P., Oriuchi N., et al. (2018). Recent Advances in Nuclear Medicine in Thyroid Cancer. Seminars in Nuclear Medicine, 48(1), 22–35.
- 47. Zhang J., Mao F., Niu G., et al. (2020). Molecular Imaging of Theranostic Radiopharmaceuticals. International Journal of Molecular Sciences, 21(10), 3672.
- Kostelnik T. I., Orvig C. (2018). Radioactive Main Group and Rare Earth Metals for Imaging and Therapy. Chemical Reviews, 118(2), 902–947.
- 49. Elgqvist J. (2019). Therapeutic Radiopharmaceuticals in Modern Medicine

  Current Status and Future Development.
  European Journal of Nuclear Medicine and Molecular Imaging, 46(3), 261–277.

- 50. Ballinger J. R. (2017). Theranostic Radiopharmaceuticals: Established Agents in Current Use. British Journal of Radiology, 90(1073), 20160678.
- Zeglis B. M., Lewis J. S. (2018). The Bioconjugation and Radiosynthesis of 89Zr-DFO-labeled Antibodies. Journal of Visualized Experiments, 137, e57389.
- Pandey M. K., Byrne J. F., Jiang H., et al. (2019). Recent Advances in (68) Ga-Based Radiopharmaceuticals. European Journal of Nuclear Medicine and Molecular Imaging, 46(4), 860–877.
- Kurth J., Krause B. J. (2018). Monoclonal Antibodies in Nuclear Medicine: Clinical Applications Beyond Oncology. Journal of Nuclear Medicine, 59(8), 1207–1213.

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