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Radioactive Isotopes in Medicine: Handling, Applications, and Safety Measures: A Review

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النظائر المشعة في الطب: التعامل والتطبيقات وإجراءات السلامة: مراجعة

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ABSTRACT

Many elements on Earth occur in various atomic configurations called isotopes, which have identical atomic numbers but vary in atomic mass. Un-stable elements undergo disintegration through energy emission; isotopes that emit radiation are termed radioisotopes. The application of these isotopes in sectors including manufacturing, farming, medical services, and research institutions is presently of considerable significance. In the medical field, these isotopes are employed in nuclear medicine for diagnostic and therapeutic uses. Radionuclide imaging, or functional imaging, represents a medical specialty that uniquely enables the evaluation of physiological changes resulting from biochemical abnormalities, utilizing the radiotracer technique.

Radioisotopes play a pivotal role in modern medicine, being widely used in diagnosis and therapy, contributing to improved disease detection accuracy and treatment effectiveness. In diagnostics, isotopes like technetium-99m (Tc) have been utilized in organ imaging via single-photon emission computed tomographic (SPECT), whereas fluorine-18 (F) was a crucial component in positron emission tomography (PET), facilitating the high-resolution identification of metabolic alterations within tissues. In therapy, isotopes like iodine-131 (I) were utilized to address thyroid diseases, while lutetium-177 (Lu) is an effective targeted therapy for some cancers. Despite the significant benefits of radioisotopes, challenges related to their availability, high cost, and radiation risks remain, necessitating the development of safer technologies and the production of isotopes using more efficient methods. The future of nuclear medicine depends on continued progress in targeted radiation therapy, improved imaging methods, and enhanced safety measures to ensure maximum therapeutic benefit with the least possible risks.

Keywords: Radioisotopes, Nuclear Medicine, Positron Emission Tomography, Radiopharmaceuticals.

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INTRODUCTION

Nuclear medicine constitutes a specialized medical discipline that utilizes radionuclides for diagnosis or treatment purposes. Radionuclides employed for diagnostic purposes that emit β+ particles in Positron Emission Tomography (PET) and γ rays in Single Photon Emission Tomography (SPECT)[1]. In the treatment of cancer, radionuclides emitting energetic α, β−, and Auger electrons are employed[2]. These particles are localized within a limited tissue range (from nanometers to millimeters, depending on particle mass and power), allowing them to destroy cells linked to diseases through the biological impacts of the emitted radiation, thus ensuring maximum effectiveness of treatments restricted to the cancerous region [3]. Radionuclide therapy is currently attracting considerable interest in the treatment of cancer because of multiple causes: (1) radioactivity has become selectively directed at the targeted tumor, safeguarding surrounding healthy tissue; (2) low doses of radiopharmaceuticals enable swift and easily performed procedures; (3) every tissue and organ can be effectively reached from within the body, unlike the whole-body irradiation used in external- beam radiotherapy. The primary therapeutic radionuclide were iodine-131 (131I); strontium-89 (89Sr) and samarium-153 (153Sm); and rhenium-186,188 (186Re, 188Re), yttrium-90 (90Y), and lutetium-177 (177Lu) [4]. This article is to present an overview of radioisotopes utilized in medical applications, the chemical-physical properties that render these radioisotopes highly appealing for tumor therapy is provided, with a special focus on clinical trials advocating the use of radiopharmaceuticals.

1. Definition and characteristics of radioisotopes

Radiopharmaceuticals, or radioisotopes, consist of two primary elements: pharmaceutical carriers and radioactive isotopes[5]. Radioactive isotopes decay, releasing different types of radiation, such as alpha, beta, and gamma rays. This decay process finally results in the stabilization of the isotope's nucleus. An essential characteristic of radiopharmaceuticals was their half-life, which signifies the time necessary for half of a radioactive atom in a sample to decompose[6]. This attribute is essential in assessing a particular radioisotope's appropriateness for diagnostic and therapeutic medical uses. Also, radioisotopes have unstable nuclei due to an imbalance among neutrons and protons, causing them to decay radioactively to reach a more stable state. The radiation emitted by radioisotopes affects the materials they pass through, allowing them to be used in medical imaging, sterilization, and industrial testing[7]. However, they can cause damage to living cells under intense exposure. Despite their radioactivity, radioisotopes share the same chemical properties as their stable isotopes, making them suitable for tracking biological and chemical processes.

1.1. Types of radioisotopes used in medicine

Radioisotopes serve as a powerful tool in modern medical treatment. More than 100 unique isotopes, each with specific decay properties, enable various diagnostic and therapeutic applications[8]. Technetium-99m (99mTc) is preeminent in nuclear medicine, accounting for

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approximately 80% of all procedures. Iodine-131 (131I) is essential for diagnosis and treatment, particularly in thyroid disorders. Fluorine-18 (18F) powers positron emission tomography (PET) scans, facilitating the visualization of metabolic processes. Iodine-123 (I-123) provides a shorter half-life alternative to Iodine-131 (I-131), which is especially beneficial for pediatric imaging. Gallium-67 (67Ga) is essential for imaging infections and inflammation, facilitating diagnosis and therapeutic management. This selection underscores the significant potential of radioisotopes in contemporary medicine, with each isotope presenting distinct characteristics to enhance diagnosis, treatment, and research across several medical fields[9]. Table 1, show common medical isotopes according to half-life, energy, and use.

Table 1. Show common medical isotopes (half-life, energy, and use).

Isotope	Half-life	Radiation / Energy	Main Medical Applications	Ref.
Technetium-99m (Tc-99m)	6 hours	Gamma (140 keV)	Widely used in nuclear medicine imaging (bone scan, cardiac scan, renal imaging, thyroid scan)	[10].
Iodine-131 (I-131)	8 days	Beta (606 keV) & Gamma	Treatment of hyperthyroidism and thyroid cancer; also diagnostic in small doses	[11]
Iodine-123 (I-123)	13 hours	Gamma (159 keV)	Thyroid imaging and functional studies	[12]
Fluorine-18 (F-18)	110 minutes	Positron (β^+, 635 keV)	PET imaging, especially FDG-PET for oncology and neurology	[13]
Cobalt-60 (Co-60)	5.27 years	Gamma (1.17 & 1.33 MeV)	External beam radiotherapy, sterilization of medical equipment	[14]
Cesium-137 (Cs-137)	30 years	Gamma (662 keV)	Radiotherapy (less common now), calibration source	[15]
Strontium-89 (Sr-89)	50.5 days	Beta (1.46 MeV)	Palliative treatment of bone metastases pain	[16]
Yttrium-90 (Y-90)	64 hours	Beta (2.28 MeV)	Targeted radiotherapy (radioimmunotherapy, liver cancer microspheres)	[17]
Gallium-67 (Ga-67)	78 hours	Gamma (93, 185, 300 keV)	Tumor detection, infection and inflammation imaging	[18]
Thallium-201 (Tl-201)	73 hours	Gamma (69-83 keV, X-rays)	Myocardial perfusion imaging (heart scans)	[19]
Carbon-11 (C-11)	20 minutes	Positron (β^+, 960 keV)	PET imaging for brain function and oncology	[20].

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1.2. Properties that make radioisotopes suitable for medical applications

Radionuclides, unstable atomic nuclei with excess energy, undergo radioactive-decay, converting to stable nuclei while emitting radiation (β-, γ-, or α-particles). This process, characterized by a specific "half-life" (t1/2), allows diverse biomedical applications, including cancer and tumor treatment: targeted radiation therapy. Imaging: for visualizing physiological processes and anatomical structures. Biochemical tests: quantifying biomolecules and their interactions[21]. Biological labeling: tracking molecules in biological systems. Sterilization: eliminating microorganisms from medical equipment and materials. Clinical diagnostics: diagnosing various diseases using radiolabeled tracers. Radioactive dating: determining the age of geological and archaeological objects. Thus, radionuclides offer a powerful toolset in biomedicine with diverse applications [22].

2. Radiopharmaceuticals Approved by the FDA

A Previous study indicates that 67 radiopharmaceuticals are presently licensed globally, with 54 utilized for illness diagnosis and 13 for therapeutic intervention (Fig. 1)[7]. Diagnostic agents are classified into six groups based on their indications. Various agents are employed in the treatment of different disorders (such as [18F]FDG) and are primarily classified according to their main indicators. Each beneficial radiopharmaceuticals was utilized in cancer treatment. Radionuclides used in PET represent 37.0%, while those utilized in SPECT account for 63%. [23]. Table 2 show of FDA-approved radiopharmaceuticals [7].

Table 2. FDA-approved radiopharmaceuticals

Radionuclides	Category	Purpose / Indication
Fluorine-18 (^{18}F-FDG), Gallium-68, Carbon-11, Nitrogen-13, Copper-64, Rubidium-82	PET Diagnostic Agents	Cancer, neurology, cardiology
Technetium-99m, Iodine-123, Indium-111, Gallium-67, Iodine-125, Thallium-201	SPECT Diagnostic Agents	Multi-organ imaging, cardiology, thyroid, infection
Iodine-131, Yttrium-90, Lutetium-177, Phosphorus-32, Strontium-89, Samarium-153, Radium-223	Therapeutic Agents	Cancer, hyperthyroidism, bone metastases
Gallium-68 DOTATATE, Lutetium-177 DOTATATE	Peptide-based Agents	Diagnosis & treatment (neuroendocrine tumors)
Radiolabeled monoclonal antibodies (e.g., Zevalin® [Y-90 Ibritumomab tiuxetan])	Antibody-based Agents	High-affinity targeting in vivo (oncology & immunology)
Radiopharmaceuticals derived from serum albumin, protein tracers	Protein/Albumin-based	Diagnostics & therapeutic carriers

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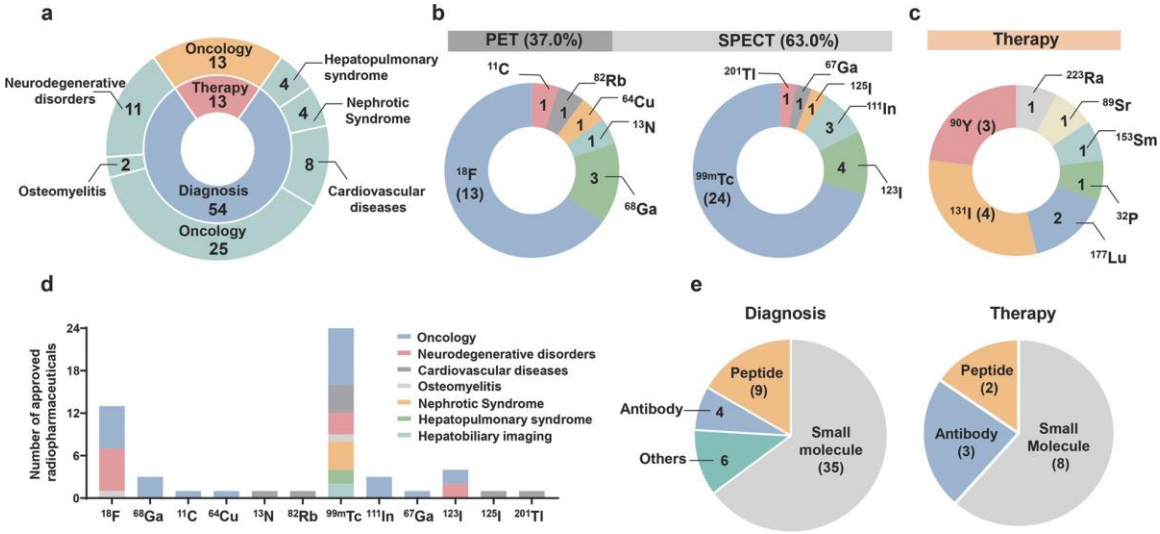

Figure 1. Radiopharmaceuticals Approved by the FDA [7]

3.Application of radioisotopes

3.1 In diagnostic aspects

Radioisotopes play a vital role in medical diagnosis through their use in imaging various organs and tissues to detect diseases with high accuracy[24]. Their working principle is based on the injection or administration of specific radioisotopes that interact with body tissues and emit radiation that can be tracked using advanced imaging techniques.

3 .1.1 Positron Emission Tomography (PET)

Positron emission tomography is considered one of the most advanced nuclear imaging modalities, as it provides high sensitivity and quantitative accuracy for detecting biochemical and metabolic changes in vivo. Its principle relies on the use of positron-emitting radionuclides such as fluorine-18, gallium-68, or carbon-11, which undergo annihilation reactions that release two 511 keV photons traveling in opposite directions[25]. These photons are simultaneously detected by a ring of detectors, allowing for precise image reconstruction. Clinically, PET has become indispensable in oncology for tumor detection, staging, and monitoring therapeutic response, as well as in neurology for evaluating brain metabolism and in cardiology for assessing myocardial viability and perfusion. The integration of PET with computed tomography (PET/CT) has further enhanced diagnostic accuracy by combining functional and structural information in a single scan. PET is highly accurate in detecting pathological changes early before they appear in conventional scans[26]. The amalgamation of PET and CT scans into a singular device provides simultaneous structure and biochemical information (fused images) under almost equal conditions, thus minimizing temporal and spatial disparities between the two

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imaging modalities, known as fusion imaging [22]. Figure 2 illustrates the sequential steps of PET imaging: radionuclide production in a cyclotron or generator, radiosynthesis into a biologically active tracer, quality control, injection into the patient, followed by in vivo positron decay and photon emission. The coincidence detection system records these signals, and the acquired data are processed into high-resolution images that provide precise insights into physiological and pathological processes.[27]. The coincidence recognition system records these paired photons, and the collected data are reconstructed into detailed images reflecting tissue metabolism and function. This process enables PET to provide highly sensitive and quantitative information about physiological and pathological processes[28].

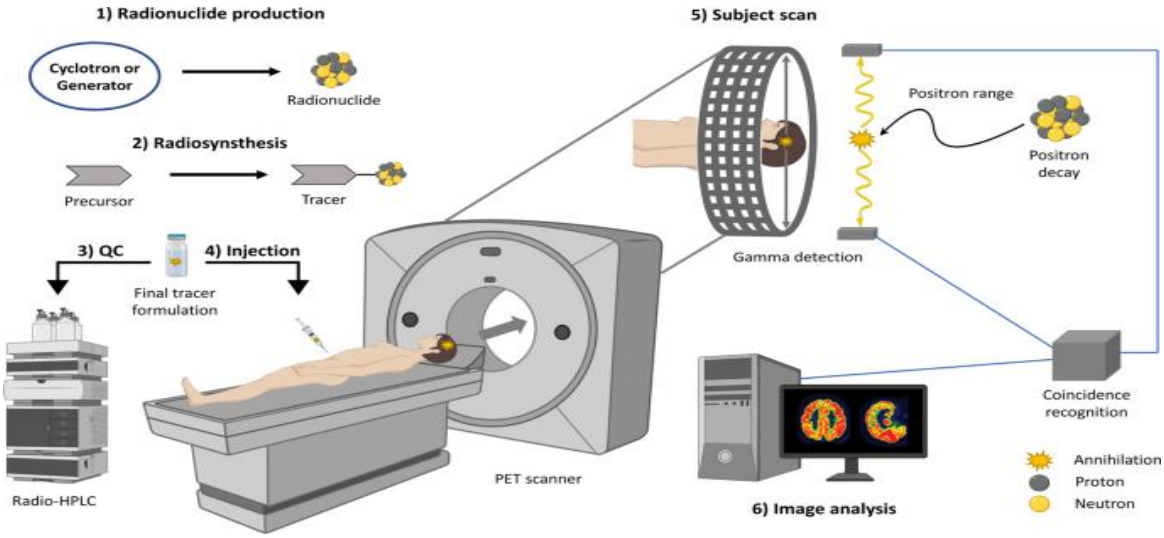

Figure 2. Principle of positron emission tomography (PET) imaging[27]

3.1.2 Single-Photon Emission Computed Tomography (SPECT)

Single-photon emission computed tomography represents an evolution of planar nuclear imaging, providing three-dimensional localization of radionuclide distribution within the body[29]. Single photon emission computed tomography (SPECT) is a nuclear imaging technique that delivers three-dimensional insights into the functional and molecular processes occurring within the patient's body[30]. In SPECT, one or many gamma cameras are employed to detect mostly gamma radiation from the injected radioactive tracer. The detectors rotate around the subject, obtaining projections from various angles for subsequent three-dimensional reconstruction of the radioactive tracer distribution [31]. This technology is fundamentally established in the advancement of nuclear medicine imaging. The initial demonstration of SPECT was conducted by Kuhl and Edwards, but the first commercial scanner utilizing a spinning gamma camera was not created until the late 1970s at Searle Radiographics[32]. Currently, SPECT imaging is a fundamental diagnostic procedure in nuclear medicine, with the gamma camera serving as the primary instrument because to its versatility in executing both planar and tomographic imaging [33]. Clinically, SPECT is widely used in cardiology to

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evaluate myocardial perfusion and ischemia, in endocrinology for thyroid imaging, and in infectious disease for identifying sites of inflammation or infection. Its widespread application is supported by the relative ease of radiopharmaceutical production [34]. The fundamental working principle of nuclear imaging systems can be better understood through schematic representations. Figure (3) illustrates the basic design and function of gamma cameras and SPECT systems, as well as the underlying mechanism of PET imaging. This diagram highlight how gamma rays or annihilation photons are detected, converted into electrical signals, and subsequently reconstructed into diagnostic images.

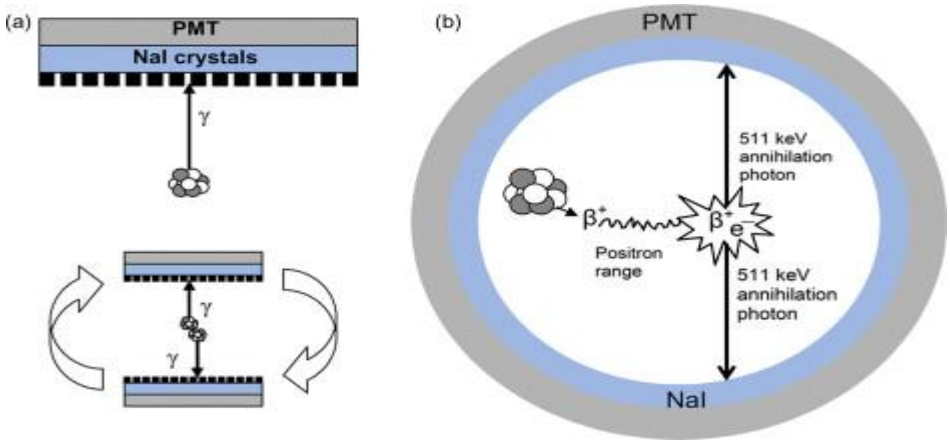

Figure 3. (a) A schematic overview of gamma camera function (upper) and SPECT imaging (lower). In this system, gamma rays penetrate the lead collimator and reach the scintillation crystal, where they ionize iodine atoms, generating light photons that are subsequently converted into electrical signals by photomultiplier tubes (PMTs). Planar scintigraphy employs a single stationary gamma camera (top), whereas SPECT acquires tomographic data using two or three rotating cameras (bottom). (b) Diagram of the PET principle. After emission, a positron travels a limited distance before undergoing annihilation with an electron, resulting in the release of two photons with an energy of 511 keV in opposite directions. These photons are detected externally by arrays of scintillation crystals coupled to PMTs. Image reconstruction is based only on photon pairs detected in temporal coincidence[35].

3.1.3 Advantages and Limitations

While both PET and SPECT are integral to nuclear medicine, they differ significantly in performance and clinical application. **PET** provides higher spatial resolution, superior sensitivity, and quantitative accuracy, which enables early detection of subtle metabolic and functional changes, particularly in oncology, neurology, and cardiology[34]. The main limitations of PET lie in the short half-lives of most positron-emitting tracers and the need for costly infrastructure, including cyclotron facilities, which restricts its availability. In contrast, **SPECT** is more widely accessible and cost-effective, using radionuclides with longer half-lives that simplify distribution and routine clinical use. Its diverse tracer repertoire supports

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applications in cardiology, thyroid evaluation, and infection imaging[29]. However, SPECT generally suffers from lower resolution, reduced sensitivity, and limited quantitative accuracy compared to PET, making it less effective for detecting early or small-scale pathological changes. Thus, PET is favored where precision and quantitative assessment are critical, whereas SPECT remains valuable for its affordability, versatility, and clinical practicality[30].

3.2 Physical Half-Life

The physical half-life of a radioisotope means the duration necessary for its radioactivity to diminish to fifty percent of its initial value due to radioactive decay, unaffected by physical and chemical conditions, and typically determined with great precision .This concept is one of the fundamental properties of radioisotopes, as it determines the persistence of radioactivity and its impact in various applications, whether medical, industrial, or environmental [36]. Half-life varies greatly from one isotope to another. It can be very short, such as carbon-11 (C), has a half-life of around 20 minutes, rendering it appropriate for imaging purposes in medicine methods such as PET scanning. It can also be very long, such as uranium-238 (U), has a half-life of 4.5 billion years, rendering it significant in geologic and cosmological investigations of the Earth [37].

The appropriate physical half-life for a specific pharmacological use is contingent upon various parameters, mostly associated with the pharmacokinetics in target tissues that put adjacent normal tissues at risk. After a radiopharmaceutical is administered, its activity within the body's tissues is constantly changing, resulting in a continuous fluctuation in the absorbed dose rate over time. Most radiation treatments, particularly those administered intravenously, undergo two phases: uptake and washout. The speed of these phases varies from tissue to tissue, depending on the kinetics of each tissue[38].

When using radionuclide therapy, the absorbed dose of radiation within each tissue known as the self-dose—is determined by calculating the total number of nuclear disintegrations per unit mass and multiplying it by the amount of energy deposited locally in the tissue[39]. This dose is directly dependent on the amount of radionuclide absorbed in the tissue and the duration of its presence there. Although adjacent tissues or organs may contribute to the total absorbed dose through what is known as cross-dose, these contributions are often much lower than the dose absorbed by the specialized tissue itself due to selective absorption of the radioisotope. With regard to brachytherapy, it relies on radioactive sources available in various shapes and sizes, and using multiple types of radioisotopes, depending on the type of radiation and the radiation energy required [40].

When it comes to the treatment of cancers with metastases, a relatively new area of focus is targeted alpha therapy (TAT) and alpha radio-immunotherapy. Using a radionuclide-labeled carrier, like a monoclonal antibody, the narrow range of extremely intense alpha emissions is focused towards cancer cells[41]. Cancers of the pancreas, ovaries, and skin (melanoma) are treated with lead-212 using targeted alpha therapy. The experimental treatment known as boron

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neutron capture therapy (BNCT) makes use of boron-10, a radioactive element that builds up in cancerous brain tumors. Refractory diseases have become easier to manage with the use of radionuclide therapy while minimizing hazardous side effects[42].

3.3 Properties of Imaging

When imaging the radiotherapeutic distribution after treatment, it's essential to check if the absorption patterns matche expectations and, in many cases, to evaluate the dosages absorbed by target tissues and other organs that could be injured [43]. Radiation therapy's pharmacokinetics and distribution, the number of photons produced by disintegrations, and the radionuclide's given activity all have a role in imaging's effectiveness. Photons' source, yield, and energy, as well as the camera's settings, affect the final product's quantitative properties and image quality[44]. To enable gamma camera imaging, the majority of beta- and auger-emitters generate gamma photons. The in vivo distribution of 177Lu and 131I can be easily tracked owing to their gamma emissions corresponding to energy and yields [45]. Other beta-emitters provide greater hurdles; for example, 90Y was formerly considered impossible to shoot accurately. Nevertheless, bremsstrahlung imaging and subsequently PET have been shown to be feasible, and these techniques have achieved extensive utilization following SIRT [46]. The treatment itself is localized; nonetheless, systemic administration of 90Y presents significant hurdles for imaging, as demonstrated by studies on [90Y]Y-ibritumomab tiuxetan and [90Y]Y-DOTA-DPhe1-Tyr3-octreotide ([90Y]YDOTATOC) [47]. Companion diagnostics—similar carrier molecules with diagnostic emitters—can predict the distribution pattern of a radiotherapeutic; however, potential inconsistencies among the radiopharmaceuticals remain to be investigated. Additionally, the half-lives of the diagnostic emitters must closely correspond with the ones for the therapeuticradionuclides for dosimetric purposes.

4.Treatment of Diseases with Radiopharmaceuticals

Radiopharmaceuticals have revolutionized modern medicine by offering both diagnostic and therapeutic solutions for various diseases. These specialized compounds contain radioactive isotopes that can be precisely targeted to specific organs or tissues, making them invaluable in nuclear medicine[48]. Their applications range from treating cancers to managing bone pain and even diagnosing neurological and cardiovascular disorders. The ability to selectively deliver radiation to diseased cells while sparing healthy tissues makes radiopharmaceuticals an essential tool in personalized medicine[49].

One of the most well-known uses of radiopharmaceuticals is in the treatment of thyroid disorders. Iodine-131 (I-131) is widely used to treat hyperthyroidism and thyroid cancer due to its ability to accumulate in thyroid tissue and emit beta radiation, effectively destroying overactive or malignant cells. This targeted approach ensures minimal damage to surrounding healthy tissues while offering an efficacious therapy alternative with comparatively benign side

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effects [50]. Lutetium-177 (Lu-177) was discovered as a revolutionary treatment for neuroendocrine tumors, selectively binding to cancer cells expressing somatostatin receptors and delivering radiation directly to the tumor site. This therapy has significantly improved survival rates in patients with advanced neuroendocrine tumors[51].

Beyond thyroid and neuroendocrine cancers, radiopharmaceuticals play a critical role in treating metastatic prostate cancer and bone metastases. Radium-223 (Ra-223) is very useful for men whose cancer of the prostate has spread to their bones, as it mimics calcium and integrates into bone tissue, emitting alpha particles that selectively destroy cancerous cells while sparing healthy bone marrow[52]. Similarly, Actinium-225 (Ac-225) has gained attention for its effectiveness in targeting prostate-specific membrane antigen (PSMA)-expressing tumors, offering potential treatment to patients with advanced cancer of the prostate. These therapies not only help reduce tumor size but also improve the quality of life by alleviating pain and slowing disease progression[53].

In addition to cancer treatment, radiopharmaceuticals are also used for managing bone pain caused by metastatic diseases. Strontium-89 (Sr-89) and Samarium-153 (Sm-153) are widely employed for this purpose, accumulating in bone tissues where they emit radiation that helps relieve pain and slow tumor growth. This targeted approach has been especially beneficial for patients suffering from multiple bone metastases, reducing their dependency on opioid pain medications and improving their overall comfort[54].

Moreover, radiopharmaceuticals have proven valuable in non-cancerous conditions, such as cardiovascular and neurological disorders. Technetium-99m (Tc-99m) is extensively used in myocardial perfusion imaging to assess blood flow to the heart, helping in the early detection of coronary artery disease. Meanwhile, fluorodeoxyglucose (F-18 FDG) is instrumental in diagnosing neurodegenerative diseases like Alzheimer's and Parkinson's by detecting abnormal metabolic activity in the brain. These applications highlight the versatility of radiopharmaceuticals in both diagnostics and treatment, making them indispensable in modern medicine[55].

5.Radiopharmaceuticals in medication

All throughout the world, there are currently thirteen therapeutic radiopharmaceuticals that have been approved, each and every one of them is utilized. In the realm of cancer treatment, radiopharmaceuticals are garnering a growing amount of attention due to their being able to release both α-rays and β-rays, hence having the ability to destroy the DNA of tumor cells that are specifically targeted. Radiopharmaceuticals that are currently in the early stages of development and have been sold for therapeutic purposes, such as [223Ra] RaCl2, [32P] Sodium orthophosphate, and [89Sr] SrCl2, have a mechanism that is based on organ accumulation; nevertheless, they do not have tumor specificity, which results in instability in vivo. To enhance

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tumor uptake and retention, new targeted radionuclide-conjugated antibodies, peptides, and small compounds have been found. The compounds included in **Table (3)** include [131I] MIBG, [177Lu] Lu-DOTA-TATE, and [90Y]Y-DTPA-Ibritumomab tiuxetan, among others [7].

Table 3. Radiopharmaceutical therapy agents approved wordwide

Radionuclides	Type	Agent	Targets	Indication
Radium-223	α	[^{223}Ra]$RaCl_2$	As a calcium mimic accumulating in bone[554]	Prostate cancer bone metastases
Phosphorus-32	β	[^{32}P]Sodium orthophosphate	Major bone deposition[69]	Palliation of bone pain due to metastases
Strontium-89	β	[^{89}Sr]$SrCl_2$	As a calcium mimic accumulating in bone[69,70]	Prostate cancer bone metastases
Samarium-153	β	[^{153}Sm]Lexidronam	As a calcium mimic accumulating in bone[71]	Relieving pain associated with bone metastasis
Lutetium-177	β	[^{177}Lu]Lu-PSMA-617	PSMA	mCRPC
		[^{177}Lu]Lu-DOTA-TATE	SSTR	NETs
Yttrium-90	β	[^{90}Y]Resin microspheres	Selective internal radiation therapy	Hepatocellular carcinoma
		[^{90}Y]Glass microspheres	Selective internal radiation therapy	Hepatocellular carcinoma
		[^{90}Y]Y-DTPA-ibritumomab tiuxetan	CD20	Non-Hodgkin's follicular lymphoma
Iodine-131	β	[^{131}I]MIBG	Norepinephrine tansporter[73]	NETs
		[^{131}I]Sodium iodinate	Sodium Iodide Symporter[555]	Hyperthyroidism and thyroid carcinoma
		[^{131}I]Metuximab	CD147[556]	Hepatocellular carcinoma
		[^{131}I]Tositumomab	CD20	Non-Hodgkin's follicular lymphoma

5.1 Radium-223, also known as [223Ra]RaCl2, represents the only radiopharmaceutical permitted to release α-radiation. It was licensed by the FDA in 2013 for the treatment of bone metastases caused by cancer of the prostate. Cancerous cells' DNA can be irreparably damaged by the α-particles' inherent features, which include a limited range and high energy. As a result, research into developing new treatments that target α-particles has been a key focus. There are 68 The therapeutic radiopharmaceuticals that are left apart from [223Ra]RaCl2 are β-particle-emitting agents that damage cancer cells' DNA in a way that can be reversed [56].

5.2 Phosphorus-32, Samarium-153, and Strontium-89: Alongside [223Ra]$RaCl_2$, three more radiopharmaceuticals utilized for the treatment of bone metastases are [32P], Sodium orthophosphate [153Sm] Lexidronam, and [89Sr]SrCl2. Similar to radium-223, these radiopharmaceuticals, like radium-223, function as calcium analogues and can be embedded in the skeleton as hydroxyapatite crystal components with calcium and the hydroxyl group [57].

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5.3 Iodine-131 served as inaugural radioactive isotope utilized in cancer therapy. Iodine-131 Sodium iodinate may seem significantly absorbed as well as concentrated in the thyroid gland, which then releases particles with high energies through β-decays to eradicate cancerous cells. Seventy-two [I-131] MIBG is a 131I-iodinated small molecule applicable for adult pheochromocytoma and paediatric neuroblastoma. Furthermore, 131I-iodinated antibodies, specifically [I-131] Metuximab and [I-131] Tositumomab have been utilized in the treatment of hepatocellular carcinoma (HCC) and non-Hodgkin's follicular lymphoma, correspondingly. [131I] omburtamab is a radiolabeled antibody therapy that specifically targets the tumor antigen B7-H3 in the treatment of central nervous system and softer meningeal metastases in paediatric neuroblastoma individuals. Seventy-four Unfortunately, it failed to satisfy the requirements for priority consideration through the FDA's Biologics License Application (BLA) owing to inadequate proof indicating an improvement in overall survival[58].

5.4 Yttrium-90: As radiopharmaceuticals, [90Y] Resin microspheres and glass microspheres have been authorised for the treatment of hepatocellular carcinoma (HCC) by selective internal radiation therapy (SIRT). Seventy-five SIRT was based on the vascular features of hepatocellular carcinoma tissues in the liver, where tumour growth results in arterial thickness, hence aiding interventional treatments. To treat liver cancer, a technique called superselective intubation is used. Millions of radioactive [90Y] resin microspheres or glass microspheres are injected into the artery that supplies blood to the tumor. This ensures that the tumor cells receive a large dosage of radiation[59].

5.5 Lutetium-177: 177Lu-labeled peptide-targeted radionuclide treatment has been successfully employed in clinical studies subsequent to the approvals of [177Lu]Lu-DOTA-TATE in 2018 and [177Lu]Lu-PSMA-617 in 2022. Both radiopharmaceuticals are manufactured by companies affiliated with Novartis. The PSMA-targeting radiopharmaceutical [177Lu]Lu-PSMA-617 has been authorised for the treatment of individuals with metastatic castration-resistant prostate cancer. This radiopharmaceuticals was based on the glutamate-urea pattern originally characterized by Alan P. Kozikowski and demonstrates considerable potential for improving the survival of mCRPC patients. [177Lu]Lu-DOTA-TATE is a therapeutic agent targeting somatostatin receptors, employed in the treatment of patients with neuroendocrine tumours (NETs). It's an equivalent of somatostatin, a natural peptide that engages with SSTR2, which is increased in neoplastic cells. [60, 61].

6. Radiopharmaceuticals in Theranostics Administration

Radiopharmaceuticals are compounds containing radioactive isotopes used in medical diagnosis and therapy, playing a fundamental role in nuclear medicine. Theranostics are primarily utilized in the management of neoplastic and contaminated regions. Due to its diagnostic and therapeutic capabilities, theranostics mitigate treatment adverse effects and

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enhance patient compliance and survival rates[62]. This strategy integrates molecular imaging by merging diagnostic and therapeutic procedures with a diagnostic agent that possesses the same or a comparable chemical structure as the treatment agent. Prognoses of therapy responses are offered. This method enables the classification of disorders based on molecular phenotype, observation of molecular biodistribution, and monitoring of therapy response. The relationship between diagnostic and therapeutic procedures can be categorized into three divisions. These factions are -Diagnostic and therapeutic molecules are identical, -Diagnostic and therapeutic molecules are analogous, -Diagnostic and therapeutic molecules are distinct, however their mechanisms of action are comparable. Identical Diagnostic and Therapeutic Agents The most exemplary instance for this category is the application of I-131[63].

7. Advancements and Future Directions

7.1. Emerging radioisotopes in medical research

The unique power of isotope tracers lies in their ability to differentiate atoms of the same element based on their origins and pathways within intricate systems. The exceptional sensitivity of modern detection techniques further enhances this. Combining these qualities, radioactive isotopes excel as tracers, and their application is anticipated to expand due to increased availability through cyclotron bombardment. However, stable isotopes like 13c, 15n, and 18o are gaining traction for several reasons. First, their nonradioactive nature eliminates environmental and sample contamination concerns, particularly in biological studies[64]. Second, ERURJ 2024, 3, 4, 1680-1694 1690 their infinite shelf life allows for extended research durations. Despite their past high cost and limitations in detection sensitivity (requiring expensive or imprecise techniques like optical devices or mass spectrometers), progress is being made. Lower detection limits (well below the parts-per-million threshold) are now achievable, paving the way for wider adoption of stable isotopes as powerful tracers[65].

7.2 Potential applications of novel radioisotopes in medicine

Nuclear medicine utilizes radiopharmaceuticals' unique properties to explore the human body's metabolic, physiological, and pathological landscape. This powerful imaging modality excels at detecting abnormalities at the earliest stages of the disease, enabling prompt initiation of treatment. Its unparalleled strength lies in the ability to monitor in vivo anatomical and physiological processes, a capability unparalleled by other modern imaging modalities such as magnetic resonance imaging (MRI), CT, or ultrasound waves. Nuclear medical therapy additionally offer a spectrum of therapeutic applications, effectively managing diverse conditions such as hyperthyroidism, rheumatoid arthritis, Hodgkin's disease, and a range of cancers (liver, colon, lung, breast, ovarian, prostate)[66]. Notably, it has been extensively employed in treating leukemia, cardiac diseases, and the debilitating pain associated with metastatic bone cancer (das, n.d.). Future research may focus on differentiating metastatic tumor volume by organ system to assess tumor heterogeneity and varying metastatic aggressiveness. This involves longitudinally

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tracking individual metastasis volume, potentially in response to therapy. Additionally, combining tracers like fdg and psma pet, or fap pet and psma pet, could help evaluate intralesional tumor heterogeneity in vivo. Furthermore, dynamic pet acquisitions (4d pet) could provide valuable insights as whole-body pet scanners become more widespread. Finally, image denoising techniques will be crucial to enable "ultra-low-dose" pet acquisitions [67]

8. Considerations for Radiation Protection

8.1 Radiation Protection Strategies

Patient exposure to radiation depends on the radionuclide's photon yield and energy, the activity, and the radiopharmaceutical's pharmacokinetics. One European directive sets the annual effective dose limit for the general population at 1 mSv, and it also requires that all member states limit the exposure of informed and willing companions or carers. A consensus statement on 131I treatment states that thresholds of 1 mSv are generally used for children, 3 mSv for adults, and 15 mSv for those over 60 years old [77]. Nonetheless, discrepancies in suggested precautions may arise among nations, shaped by divergent stated thresholds and computation methods[68]. Treatments employing 131I are traditionally associated with elevated external radiation exposure due to substantial photon emission (Tab 2) necessitating separation protocols and other restrictions to mitigate exposure to the public, healthcare personnel, caregivers, and family members[69]. Different beta- emitters can similarly influence other radiation protection methods, contingent upon their characteristics. Therapies such as [177Lu]Lu-DOTATATE may be delivered in both outpatient and inpatient settings, subject to specific restrictions[70].

For beta-emitter with negligible photon production (such as 90Y) and most alpha-emitters, exposure to outside radiation from sufferers will be of diminished concern. However, the management of chemicals before patient administration, especially for prolonged durations (such as for labelling), may still raise difficulties. Healthcare facilities may have significant challenges regarding managing waste, particularly in storing and disposing of radioactive materials[71].

Patient fluids can pollute the environment, requiring vigilance on excretion in urine, feces, blood and saliva, and breast milk. The stability of radiopharmaceuticals, the potential discharge of radioactive offspring, and the existence of fluid or gases radionuclides have significance in this setting. The biokinetics from numerous distinct nuclides were elaborated in a collection of The international commission on radio articles[72].

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CONCLUSION

Radioactive isotopes have revolutionized modern medicine, offering unmatched precision in diagnosis and treatment. While their benefits are undeniable, safety concerns and isotope availability remain key challenges. The future of nuclear medicine lies in technological advancements, particularly AI integration, novel radiopharmaceuticals, and alternative isotope production methods. Continued research and regulatory oversight are essential to ensure safe and effective medical applications of radioactive isotopes. However, handling these materials requires strict safety procedures. This includes adherence to the guidelines of international organizations such as the International Atomic Energy Agency (IAEA) to control radiation exposure levels through the use of protective shielding, radiation monitoring systems, and specialized training for medical personnel. Safe disposal of radioactive waste also poses a challenge that requires advanced solutions to protect the environment and public health.

Limitations

This review is primarily centered on isotope-based applications in diagnosis and therapy, without detailed coverage of regulatory aspects, large-scale manufacturing, or supply chain challenges. . Future reviews could integrate these perspectives to provide a more holistic view of the field and its translational challenges.

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There are non-conflicts of interest.

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الخلاصة

توجد العديد من العناصر على الأرض في تكوينات ذرية متنوعة تُسمى النظائر، وهي متطابقة في أعدادها الذرية ولكنها تختلف في كتلها الذرية. تخضع العناصر غير المستقرة للتفكك من خلال انبعاث الطاقة؛ وتُسمى النظائر التي تُصدر إشعاعات بالنظائر المشعة. يكتسب استخدام هذه النظائر في قطاعات تشمل التصنيع والزراعة والخدمات الطبية ومؤسسات البحث أهمية بالغة في الوقت الحالي. في المجال الطبي، تُستخدم هذه النظائر في الطب النووي لأغراض التشخيص والعلاج. يُمثل التصوير بالنويدات المشعة، أو التصوير الوظيفي، تخصصًا طبيًا يُمكّن بشكل فريد من تقييم التغيرات الفسيولوجية الناتجة عن التشوهات الكيميائية الحيوية، باستخدام تقنية التتبع الإشعاعي. تلعب النظائر المشعة دورًا محوريًا في الطب الحديث، إذ تُستخدم على نطاق واسع في التشخيص والعلاج، مما يُسهم في تحسين دقة الكشف عن الأمراض وفعالية العلاج. في التشخيص، استُخدمت نظائر مثل التكنيشيوم-99م (Tc) في تصوير الأعضاء عبر التصوير المقطعي المحوسب بإصدار فوتون واحد (SPECT)، بينما كان الفلور-18 (F) عنصرًا أساسيًا في التصوير المقطعي بالإصدار البوزيتروني (PET)، مما سهّل تحديد التغيرات الأيضية داخل الأنسجة بدقة عالية. أما في العلاج، فقد استُخدمت نظائر مثل اليود-131 (I) لعلاج أمراض الغدة الدرقية، بينما يُعد اللوتيتيوم-177 (Lu) علاجًا فعالًا وموجهًا لبعض أنواع السرطان. على الرغم من الفوائد الكبيرة للنظائر المشعة، لا تزال هناك تحديات تتعلق بتوفرها وتكلفتها المرتفعة ومخاطر الإشعاع، مما يستلزم تطوير تقنيات أكثر أمانًا وإنتاج نظائر باستخدام أساليب أكثر كفاءة. يعتمد مستقبل الطب النووي على استمرار التقدم في العلاج الإشعاعي الموجه، وتحسين أساليب التصوير، وتعزيز إجراءات السلامة لضمان أقصى فائدة علاجية بأقل قدر ممكن من المخاطر.

الكلمات المفتاحية: النظائر المشعة، الطب النووي، التصوير المقطعي بالإصدار البوزيتروني، المستحضرات الصيدلانية المشعة.