Nuclear Radiation Applications in Medicine

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Preface

Atomic nucleus radiation, as one of the essential tools in modern science and medical practices, it naturally comes well-armed with an array of effective methods for diagnosis, monitoring, and cure of diseases. No longer just in the environment or a product of nuclear power, radiation is one of the pillars of medical advancements. The ability to interact with human tissues at the atomic and molecular level gives clinicians and researchers opportunities to see internal structures in remarkable detail, measure the functioning of organs, and choose which diseased cells should be killed. The full spectrum of alpha and beta emitters, gamma emitters, and alpha and beta-emitting radioisotopes all have unique roles in medicine to advance patient care and the clinical technology that results. While historically associated with nuclear physics and environmental science, radiation itself now straddles the intersection of the physical, biological, chemical, and medical disciplines, with so many groundbreaking developments occurring that were previously unfathomable just a few decades ago.

This text addresses multiple types of ionizing radiation used in medicine, encompassing four significant chapters. The first chapter is focused on α radiation, especially with respect to its high effectiveness in target alpha therapy and cancer cell-specific killing. Chapter 2 covers beta radiation and its use in systemic and brachytherapy, thyroid diseases, and eye diseases. Chapter 3 is centred on gamma-radiation, specifically its use in diagnosis (in radionuclide imaging), and for treatment using external-beam radiotherapy. The last chapter integrates the wider context of medical radioisotopes: their production, behavior in the body and growing importance to contemporary precision medicine.

This book is intended to provide students, investigators, medical physicists, and healthcare providers with a comprehensive reference that links the science of radiation physics to advanced clinical applications. In addition to theoretical content, practical applications, safety considerations, and new trends that are shaping the future of nuclear medicine are discussed in this work.

With a systematic and comprehensive treatment, this book has the goal to accompany the next generation of medical doctors and researchers in their understanding and application of nuclear technology responsibly. I believe that the content in this book may help a further understanding of them and also motivate studies on new aspects that contribute to the safety and better utilization of radiation in medicine around the world.

ABSTRACT

The book presents an overview of the nuclear radiation sources and devices used in advanced medicine, covering ionizing nuclear radiation. It discusses the basic physical principles underlying each type of radiation, their interactions with a biological system, including clinical radiological features, and the dose /response relationship for some important pathological processes. These include targeted alpha therapy, which provides an extremely limited treatment for cancer using alpha radiation. Beta-emitting nuclides are considered for systemic therapy, thyroid, and brachytherapy. Gamma radiation is described in terms of nuclear medical imaging by SPECT or PET, and its extensive application in external beam radiotherapy. Production, characteristics, and clinical application of medical radioisotopes, as well as their incorporation into diagnostic or therapy radiopharmaceuticals, are also discussed.

Innovative applications of nuclear medicine radiopharmaceuticals and molecular imaging are also described to show possible future directions of this field. Integrating basic science, technology, and medical application, this combination updates the readers while offering a fresh view on nuclear medicine.

Keywords*: Alpha particles, beta particles, gamma ray,* radiopharmaceuticals, nuclear medicine, radition physics, and applications of nuclear medicine.

INTRODUCTION

This includes radiological and nuclear radiation, which has been part of our professional landscape for many years and has given us some of our most powerful weapons in the identification, measurement and treatment of a variety of medical conditions. As the practice of medicine moves increasingly toward personalized medical care, judicious application of ionizing radiation has been instrumental in defining and enhancing precision in clinical management and treatment. And the laws of physics are no longer just in the domain of subatomic particles and nuclear weapons but rather are indispensable instruments in hospitals, clinics, and laboratories worldwide.

In fact, ionizing radiation only refers to types of radiation that are actually several forms, all with disparate physical properties and biological consequences. Alpha- and beta-particles, along with gamma-rays, deposit their energy differently into matter and human tissue, allowing for distinct medical uses. However, alpha radiation has a higher linear energy transfer (LET), which is an advantage , especially for therapeutic purposes, where the destruction of cancerous cells would be preferred to preserve healthy tissue. Due to its short penetration range, beta radiation has been commonly used for systemic therapy, thyroid therapy, and brachytherapy. Gamma rays, due to their long-absorption range and high energy, remain an important factor in diagnosis (SPECT & PET) and in external beam radiotherapy.

Rounding out these forms of radiation are radioisotopes – radioactive atoms that decay and emit radiation, and can be incorporated as radiopharmaceuticals for accurate diagnostics and treatments. Their incorporation into nuclear medicine allows physicians to study organ function, map metabolic pathways, and deliver site-specific radiation dose to tumors. theragnostic, with the combination of diagnostic imaging and personalized radionuclide therapy, has proved to be one of the most enigmatic developments in contemporary oncology as well as personalized medicine.

The purpose of this book is to offer a straightforward but comprehensive overview of nuclear radiation and the medical applications for it. Covering alpha, beta, and gamma radiation, and the development of apparatus with medical applications and additional medicinal radioisotopes, it describes the interaction of radiation therapy with biological systems from the physics perspective to clinical practice and safety. In each chapter, the features of radiation type and interaction mechanisms with tissues are treated along with clinical applications and radioprotection. There is a strong focus on new developments and elementary processes in nuclear and radiation research.

Along the way, readers will gain insights into how nuclear radiation is used in modern health care, and why its careful useis such an integral component of

successful outcomes for health care patients. Whether a student, medical physicist, radiologist, or another specialty with an interest in nuclear physics and the practice of Nuclear Medical or related specialty (e.g., cardiology) / interested researcher - this book offers scientific credibility and understanding for a crucial part of what makes medicine so far advanced.

Chapter 1
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Application of Alpha Radiation in Medicine

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1.1 Introduction

In 1899, physicists Ernest Rutherford and Paul Villard had already determined that radiation consisted of at least two types, based on penetration into matter and the ability to cause ionization: Alpha rays Al are easily absorbed by paper or by some other material, stopping them from traveling far. Alpha radiation was determined to penetrate ordinary materials the least [1]. While far less penetrating than more energetic beta particles, alpha particles have sufficient energy to cause the production of ionization in some substances because they are relatively massive compared with other types of ionizing radiation, such as beta particles and photons. For example, a thousand alpha particles can be stopped by a single sheet of paper, and if ingested, an average alpha emitter is 20 times more dangerous when compared to an average β or γ radiation emitter (based on the relative biological effectiveness coefficient). These properties make them important tools for scientists in many areas, from medicine to forensics. (2) Showing that α particles, emitted from radium bromide, were used to bombard several substances, and by this means, leading evidence against J. J. Thomson's plum pudding model of the atom was provided by Rutherford. In the well-recognised gold foil experiment by Rutherford's students – Hans Geiger and Ernest Marsden, a narrow beam of alpha particles was targeted at an ultra-thin piece of gold foil, only a few hundred atoms in thickness. The alpha particles thus scattered were observed on a zinc sulphide screen, and the impact produced flashes of light. Indeed, the positive charge in the atom was believed to be spread out so that Rutherford actually anticipated very little scattering of alpha particles by the foil from his experience interpreting the plum pudding model (1). But the experiment's large-angle scattering did not support this prediction. This was long before the alpha particle became known to be a helium nucleus, let alone protons and neutrons. These results meant that Thomson's model was rejected in favour of the nuclear model of the atom, subsequently reformulated as the Bohr model and finally the modern wave-mechanical theory. In 1917, he also showed that the emission of alpha particles can cause the intentional transformation of one element into another. "Though the transmutation of elements by radioactivity had already been discovered in 1901, Rutherford here found that alpha particles from different radioactive sources show a new type of radiation when penetrating air. This radiation he named protons. Further investigation showed that these protons came from nitrogen in the air, and it was inferred that nitrogen being

turned into oxygen. This reaction was the first nuclear reaction experimentally verified and expressed by the corresponding reaction equation [1].

$$14N + \alpha \rightarrow 170 + p \ldots\ldots\ldots (1.1)$$

1.2 Define of Alpha Particle

It is the type of decay that Rutherford and his colleagues (Geiger and Marsden) first observed when they experimented with radiation penetrating through metal foils. This decay occurs as a nuclear reaction, in which an unstable parent nucleus (P) changes to a more stable mode of decay by emitting an alpha particle and changing into a new daughter nucleus (D). The emitted alpha particle is a helium-4 nucleus, known for its great stability that comes from a high binding energy ~of 7 MeV/n of such a nucleus [2]. During alpha decay, conservation of nucleon number and charge is also preserved by emitting a (^4_2He) nucleus. Thus, the mass number A of which the parent nucleus loses four units, and the atomic number Z is the number by which it loses two units; important considerations to remember are [2]:

$$^A_ZP \rightarrow {}^{A-4}_{Z-2}D + {}^4_2He \ldots\ldots\ldots (1.2)$$

When an alpha particle is ejected from a parent nucleus with atomic number Z and mass number A, the atomic number of the nucleus decreases by two units (isotope), and its mass number is decreased by four units (isobar). involving a daughter nucleus (Z−2, A−4). In doing so, the parent atom sacrifices two of its orbital electrons in protecting an outermost energy shell to remain electrically neutral. The emitted alpha particle slows down in the absorber material and captures two electrons, three from it's surrounding to give a neutral (^4_2He) atom primarily. Alpha particles emitted from naturally occurring radionuclides usually have kinetic energies between 4 and 9 MeV. These energies range in their ability to penetrate air from approximately 1–10 cm and biological tissue from about 10^{-3}–10^{-2} cm [2]. The α particle feels a well at the surface of the parent nucleus called the Coulomb barrier (CB), and it is in the order of 30 MeV. Classically, the alpha particles involved (with only 4–9 MeV of kinetic energy) could not have penetrated such a barrier. However, from a quantum mechanical viewpoint, there is still some finite probability of the alpha particle tunneling through the potential well and escaping confinement by the parent nucleus. The combination of a positive decay energy Q_α and the phenomenon of the tunneling effect allows alpha decay, which changes an initial nucleus P to a final one D [2].

The alpha decay, common in heavy elements, involves the emission of a helium nucleus (two protons and two neutrons), which reduces the parent nucleus's atomic number by two and its mass number by four [3].

1.3 Decay Energy in α Decay

The decay energy Q released in α decay appears as kinetic energy shared between the α particle and the daughter nucleus and is given as follows [2]:

$$Q_\alpha = \{ m(P) - [m(D) + m(^4_2He)]\}$$

$$= \{ M(P) - [M(D) + M(\alpha)] \} \ c^2 \ldots\ldots\ldots(1.3)$$

where m(P), m(D), and m (^4_2He) are the atomic rest masses and M(P), M(D) and M(α) are the nuclear rest masses of the parent, daughter, and α particle, respectively [2].
Since neither the total number of protons nor the total number of neutrons changes in the α decay, Q_α can also be expressed in terms of binding energies E_B of the parent, daughter and helium nuclei, as follows [2]:

$$Q_\alpha = E_B(D) + E_B(\alpha) - E_B(P) \ldots\ldots\ldots(1.4)$$

where $E_B(D)$ is the total binding energy of the daughter D nucleus, $E_B(\alpha)$ is the total binding energy of the α particle (28.3 MeV), and $E_B(P)$ is the total binding energy of the parent P nucleus.

For α decay to be feasible, Qα must be positive. This implies that the combined total binding energies of the daughter nucleus and the α particle nucleus must exceed the total binding energy of the parent nucleus. Or, similarly, this implies that the rest mass of the parent nucleus must exceed the combined rest masses of the daughter nucleus and the α particle [2].
Two entities are produced in α decay: the α particle and the daughter product. For decay of the parent nucleus at rest this implies that the α particle and the daughter will acquire momenta p equal in magnitude but opposite in direction and kinetic energies equal to $(EK)_\alpha = p^2/(2m_\alpha)$ for the α particle and $(EK)_D = p^2/(2M_D)$ for the daughter [2].
• α decay occurs commonly in nuclei with Z > 82 because in this range of atomic number Z, decay energies Qα given by (1) or (2) are positive and of the order of ~ 4 MeV to ~ 9 MeV.
• The Qα > 0 results mainly from the high total binding energy of the ^4_2He nucleus (28.3 MeV) that is significantly higher than for nuclei of ^3_2He, ^3_1He, and ^2_1He for which spontaneous ejection from parent nuclei energetically is not feasible.
• Ejection of a heavy nucleus from the parent nucleus is energetically possible (large Q value); however, the effect of tunneling through the potential barrier is then also much more difficult for the heavy nucleus in comparison with tunneling for the α particle.
• Emission of heavy particles from parent nuclei with Z > 92 is possible and represents a mode of radioactive decay referred to as spontaneous fission [2].
The total decay energy Q_α must be positive for α decay to occur and is written as follows [2]:

$$Q_\alpha = (E_K)_\alpha + (E_K)_D = \frac{p^2}{2m_\alpha} + \frac{p^2}{2M(D)} = \frac{p^2}{2m_\alpha}\left\{1 + \frac{m_\alpha}{M(D)}\right\}$$
$$= (E_K)_\alpha \left\{1 + \frac{m_\alpha}{M(D)}\right\} \ldots\ldots\ldots(1.5)$$

Since m_α << M(D), the α particle recoils with a much higher kinetic energy than the daughter, i.e., the α particle acquires a much larger fraction of the total disintegration energy Qα than does the daughter [2].
From (eq.5) we determine $(EK)_\alpha$, the kinetic energy of the α particle, as

$$(E_K)_\alpha = \frac{Q_\alpha}{1 + \frac{m_\alpha}{M(D)}} \ldots\ldots\ldots(1.6)$$

After inserting Qα from (eq.3) we get

$$(E_K)_\alpha = \frac{M(P)\,c^2 - M(D)\,c^2 - m_\alpha c^2}{1 + \frac{m_\alpha}{M_D}}$$

$$\approx \left\{M(P)\,c^2 - M(D)\,c^2 - m_\alpha c^2\right\}\left\{\frac{A_P - 4}{A_P}\right\} = Q_\alpha \left\{\frac{A_P - 4}{A_P}\right\} \ldots\ldots\ldots(1.7)$$

where AP is the atomic mass number of the parent nucleus; (AP − 4) is the atomic mass number of the daughter nucleus; and m_α/M(D) ≈ 4/(AP − 4).
The kinetic energy $(E_K)_D$ of the recoil daughter nucleus, on the other hand, is given as follows [2]:

$$(E_K)_D = Q_\alpha - (E_K)_\alpha = \frac{4Q_\alpha}{A_P} \ldots\ldots\ldots(1.8)$$

For historical reasons, the most important example of radioactive decay in general and α decay in particular is the decay of radium-226 with a half-life of 1600 years into radon-222 which in itself is radioactive and decays by α decay into polonium-218 with a half-life of 3.824 days as the following equation [2]:

$$^{226}_{88}Ra \rightarrow {}^{222}_{86}Rn + \alpha \ldots\ldots\ldots(1.9)$$

Radium-226 is the sixth member of the naturally occurring uranium series starting with uranium-238 and ending with stable lead-206. It was discovered in 1898 by Marie Curie and Pierre Curie and was used for therapeutic purposes almost immediately after its discovery, either as an external (sealed) source of radiation or as an internal (open) source [2].
The external use of radium-226 and radon-222 focused largely on treatment of malignant disease. In contrast, internal use of these two radionuclides was spread over the whole spectrum of human disease between 1905 through the 1930s and was based on ingestion of soluble radium salts, inhalation of radon gas or drinking water charged with radon [2].

Radon-222, a noble gas, is particularly important due to its ability to diffuse through soil and accumulate indoors, presenting a natural radiation hazard. In contrast, the thorium-232 decay series, known as the thorium series, terminates with the stable isotope lead-208, following a similar sequence of alpha and beta transitions. The similarities between these two decay chains highlight the universal tendency of heavy nuclei to move toward stability through successive transformations [4].

1.4 Physical Properties of Alpha

Among the cutest and most popular types of ionizing radiation are alpha particles, which are emitted directly in the course of the radioactive decay of heavy nuclei, such as uranium-238, radium-226, and thorium-232. These particles are nothing more than helium nuclei with two protons and two neutrons held firmly together by strong nuclear forces. It is this structure that imparts to the alpha particles unique physical and physicochemical characteristics which exert a profound influence on their interaction with matter, atomic ability to ionize, as well as the biological insult [5].

1.4.1 Charge

The alpha particle has an electric charge of +2e with e being the elementary charge (1.602×10^{-19} C). This double positive charge is a result of two protons in the particle. The alpha particles and the atoms through which they are moving are caused to interact more electrostatically by the large charge. Therefore, alpha particles produce dense ionization throughout their paths. These heavy particles have a high charge and a slower speed than light particles like beta particles or electrons (alpha particles lose their energy via Coulomb interaction at short distances due to their large charge quickly [5]), resulting in a low range in matter.

1.4.2 Mass

An alpha particle has a rest mass of approximately 6.644×10^{-27} kg, which is equivalent to about 4 atomic mass units (u). This makes it nearly 7300 times more massive than an electron. The high mass of the alpha particle means it has significant momentum at a given kinetic energy, but also a very limited deflection during collisions. Compared with other forms of radiation, such as beta or gamma radiation, the large mass of alpha particles contributes to their limited range and poor penetration ability. However, this same property makes them highly efficient at depositing energy locally within a very short distance, which explains their high linear energy transfer (LET) characteristics [6].

1.4.3 Penetration Ability

Alpha radiation exhibits extremely low penetration power due to the combined effects of its double charge and high mass as show Figure 1.1. In air, typical alpha particles travel only a few centimeters (usually between 2–10 cm depending on their initial energy). When they encounter a denser medium, such as human tissue or metal, their range decreases dramatically. For example, a sheet of paper or even the outer dead layer of human skin (approximately 40 μm thick) is sufficient to stop alpha particles completely. Despite their weak penetration, alpha particles are highly dangerous when emitted from radionuclides that enter the body through inhalation or ingestion, as they can deliver intense localized doses to biological tissues [6].

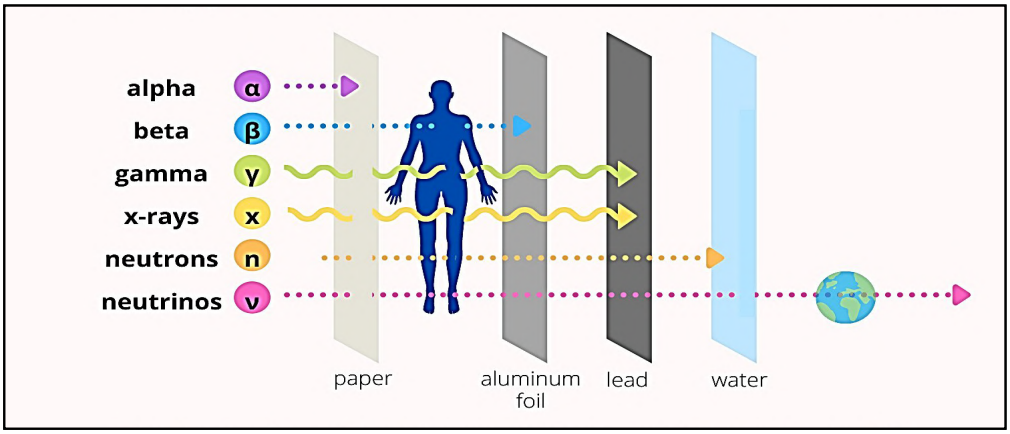

Figure 1.1: Penetrating ability of different types of radiation

The stopping power of alpha particles the ability of a material to slow and eventually halt their motion is proportional to the square of their charge and inversely proportional to their kinetic energy. This means that as alpha particles slow down, their ionization rate increases sharply until they come to rest, a phenomenon known as the Bragg peak. It has been used in medical and therapeutic applications, such as targeted alpha-particle therapy (TAT), where small doses of alpha emitters are directed to cancerous cells, resulting in minimal collateral damage to the surrounding healthy tissue. Table 1.1 provides some physical properties of the alpha particles [5].

Table 1.1: physical properties of alpha particles

No.	Property	Approximate value/ Range	Description
1	Charge	3.204×10^{-19} C	+2e
2	Mass	6.644×10^{-27} kg	4.0015 u
3	Typical energy (decay)	---	4-9 MeV
4	Velocity	---	$1.5\text{-}2.0 \times 10^{7}$ m/s
5	Range in air	Depends on energy	2-10 cm
6	Penetration in tissue	Stopped by skin or paper	Less than 100 μm

These properties drove the dualistic perspective of alpha radiation in nuclear physics and radiobiology, as both the most important isotope-specific determinant for radioactive decay series and as a possible hazard in internal exposures. Highly ionizing and minimally penetrating- a unique contrast of devastation on one hand, restraint on the other.

1.5 Interaction with matter and shielding requirements

Alpha Particles behave like charged microparticles, and the fate of alpha particles in matter is primarily determined by strong Coulomb interactions owing to their two-unit positive charge and sufficiently large mass. Alpha particles consist of heavy charged ions and, in contrast to photons or neutrons, lose most of their kinetic energy through ionization and excitation of the atoms through which they pass. Due to this strong interaction, alpha particles have a very high linear energy transfer (LET) and locally deposit energy over short distances [7].

1.5.1 Interaction Mechanisms

When the alpha particle travels through a material, it interacts with atomic electrons and deposits some of its energy each time. This leaves a trail of ion pairs—typically tens of thousands per centimeter of air. This process is repeated till the kinetic energy of the particle vanishes. This energy-loss rate per unit path length, or stopping power (−dE/dx), grows as the particle loses velocity, peaking at some distance from its origin—the so-called Bragg peak. This is of great relevance in radiation biology and medicine, as it forms the basis for targeted delivery of high LET doses by alpha-emitters to small volumes, such as radio-resistant cancer cells [7]. The total range for an alpha particle in a particular material is very dependent on its initial energy and the density of the absorbing substance. For example, a 5 MeV alpha particle has a range of approximately 4 cm in air and only about 25 μm in biological tissue. This very small distance leads to little external hazard but significant internal hazard if alpha-emitting radionuclides are inhaled or ingested [7].

1.5.2 Shielding Requirements

Because of their low penetration depth, alpha particles are the easiest form of ionizing radiation to shield. A thin barrier such as a sheet of paper, a few centimeters of air, or even human skin is sufficient to stop them completely. Laboratory environments typically use plastic, glass, or thin aluminum foils as shielding materials for alpha emitters. The purpose of shielding is less about reducing external exposure and more about preventing contamination or inhalation of alpha-emitting substances [7]. In practice, containment and ventilation measures are used more often as defense against alpha radiation rather than thick shielding. Work in alpha laboratories is generally done within fume hoods or glove boxes shielded with HEPA filters to isolate against airborne contamination. For instruments and detectors, thin windows of mica or Mylar are employed to enable alpha particles to pass into the module but still keep it contained physically [7].

Lastly, alpha particle-matter interactions are defined by a high ionization density, which results in a short range and restricted penetration. These properties render them a useful ISTI in the field of nuclear physics and medicine, as well as life-threatening participants upon internalization. The most effective protective methods

typically depend on not swallowing or inhaling, rather than consuming bulky shielding material.

1.6 Energy Transfer and Range of α-Particles

The most important energy-losing processes for alpha particles in health physics that are believed to be significant are collisions with the absorbing medium electrons. These interactions result in electronic excitation and ionization of the absorber atoms [8].

In a collision between a heavy ionizing particle and an orbital electron in an absorbing medium, the energy transferred from the ionizing particle to the orbital electron is given by [8]:

$$\Delta E = \frac{2\,(9 \times 10^9 \times Q \times q)^2}{ma^2v^2} \ldots\ldots\ldots(1.10)$$

where

Q = charge on the ionizing particle,

q = charge on the electron,

m = mass of the electron, and

a = closest distance of approach of the ionizing particle to the electron (called the impact parameter).

That is, while traversing air or soft tissue, the alpha particle on average loses 35.5 electron volts of energy for each ion pair it creates. The specific ionization produced by alpha particles is very high, at around 3.6 million ion pairs per centimeter in air. The latter, which are charged and have comparably low velocities owing to large mass, have a strong ionization potential. The slower the speed, the more the electric field of the alpha-particle is in prolonged contact with orbital electrons of atoms that compose the traversed medium; thus, energy transfer and ionization can be more effective at collisions. As the alpha particle becomes further degraded due to successive interactions, it progressively loses velocity and thus enhanced specific ionization. The longer the average time it spends per collision, the more energy is transferred along its trajectory, producing an increasing ionization density. This leads to a spectacular maximum of specific ionization towards the end of the range, called the Bragg peak. The Bragg peak is named after Sir William Henry Bragg, a British physicist who, during the early 1900s, made several groundbreaking contributions to the field of radioactivity [8].

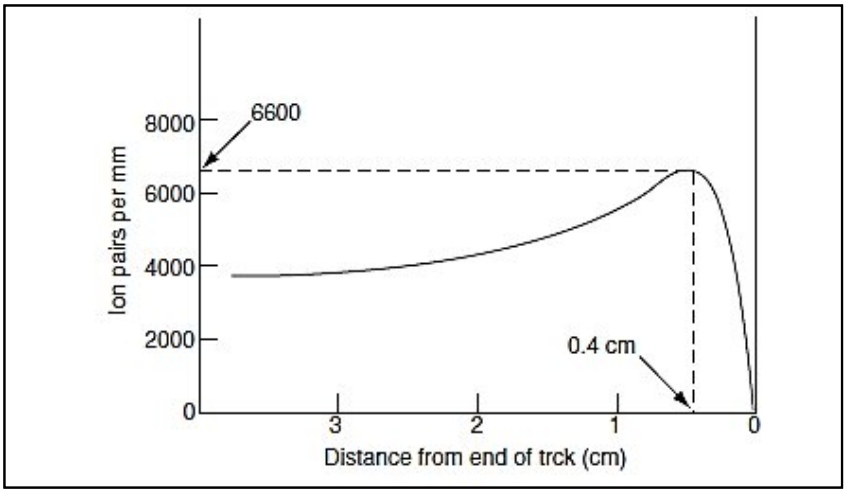

Figure 1.2: Specific ionization of a ^{210}Po alpha particle as a function of its remaining distance to the end of its range in standard air

An alpha particle loses energy at an increasing rate as it slows down until the Bragg peak is reached near the end of its range. Because of its inertia due to its heavy mass, an alpha particle undergoes very little deviation in a collision and therefore travels essentially in a straight line. Its average rate of energy loss may therefore be calculated as follows [8]:

$$\frac{d\bar{E}}{dR} = \frac{Kinetic\ energy}{Range} \ldots\ldots\ldots(1.11)$$

Very often, the unit of length used in expressing rate of energy loss is density thickness, that is, in units of MeV/g/cm^2 . This is called the mass stopping power; it is defined as the ratio of the linear stopping power to the density of the stopping medium as the following equation [8]:

$$S = \frac{dE/dx}{\rho} \ldots\ldots\ldots(1.12)$$

The mass stopping power of air for a ^{210}Po alpha particle is, according to Eq. (eq.12), is given by

$$s\ (air) = \frac{d\bar{E}/dR}{\rho\ (air)} = \frac{1.35\ MeV/cm}{1.293\ \times\ 10^{-3}\ g/cm^3} = 1.04\ \times\ 10^3 \frac{MeV}{g/cm^2} \ldots\ldots\ldots(1.13)$$

Relative Mass Stopping Power. The relative mass stopping power is used to compare quantitatively the energy absorptive power of different media. It will be shown later that the mass stopping power of different absorbers relative to that of air is important in the practice of health physics. Relative mass stopping power, ρm is defined by [8]:

$$\rho_m = \frac{S_{medium}}{S_{air}} \ldots\ldots\ldots(1.14)$$

Its mean rate of energy loss in tissue, therefore, is

$$\frac{d\bar{E}}{dR}\ (tissue) = \frac{5.3\ MeV}{5.1\ \times\ 10^{-3}\ cm} = 1.04\ \times\ 10^{3}\ \frac{MeV}{cm} \ldots\ldots\ldots(1.15)$$

and its mass stopping power, S, is

$$S\ (tissue) = \frac{d\bar{E}/dR}{\rho} = \frac{1.04\ \times\ 10^{3}\ MeV/cm}{1\ g/cm^{3}} = 1.04\ \times\ 10^{3}\ \frac{MeV}{g/cm^{2}} \ldots\ldots\ldots(1.16)$$

Using (eq.14), we calculate the relative stopping power of tissue, ρt, for 5.3-MeV alpha particles:

$$\rho_t = \frac{S_{tissue}}{S_{air}} = \frac{1.04\ \times\ 10^{3}\ \frac{MeV}{g/cm^{2}}}{1.04\ \times\ 10^{3}\ \frac{MeV}{g/cm^{2}}} = 1 \ldots\ldots\ldots(1.17)$$

Several empirical and semi-empirical formulae have been proposed to compute range of α-particles in air. For example [9],

$$R_{\alpha}^{air}\ [mm] = \begin{cases} e^{1.61\sqrt{E_\alpha}} & for\ E_\alpha\ < 4\ MeV \\ (0.05E_\alpha\ + 2.85)\ E_\alpha^{3/2} & for\ 4\ MeV\ \leq E_\alpha\ \leq 15\ MeV \end{cases} \ldots\ldots\ldots(1.18)$$

and

$$R_{\alpha}^{air}\ [mm] = \begin{cases} 0.56E_\alpha & for\ E_\alpha\ < 4\ MeV \\ 1.24E_\alpha - 2.62 & for\ 4\ MeV\ \leq E_\alpha\ \leq 8\ MeV \end{cases} \ldots\ldots\ldots(1.19)$$

Both of these equations yield almost same results as can be seen from Figure 1.3 which has been plotted for the α-particles having energy up to 8 MeV. Hence at least in this energy range one could use any one of these equations to compute the range in air.

apparent that theoretical computation of range is a difficult task. A number of experimentalists therefore turned to empirical means of measuring this quantity and modeling the behavior on the basis of their results. Bragg and Kleeman gave a formula to compute the range of a particle in a medium if its range is known in another medium.

To compute the range in some other material, (eq.20) can be used [9]:

$$\frac{R_1}{R_2} = \frac{\rho_2}{\rho_1}\ [\frac{A_1}{A_2}]^{1/2} \ldots\ldots\ldots(1.20)$$

Here ρ and A represent density and atomic mass of the materials. If we have a compound material an effective atomic mass given by [9]:

$$\frac{1}{\sqrt{A_{eff}}} = \sum_i \frac{w_i}{\sqrt{A_i}} \ldots\ldots\ldots(1.21)$$

is used instead. Here wi is the weight fraction of ith element having atomic mass Ai.

For example, at normal pressure and temperature the range of α-particles in any material x can be determined from equation:

$$R_{\alpha}^{x} = 3.37\ \times\ 10^{-4}\ R_{\alpha}^{air}\ \frac{\sqrt{A_x}}{\rho_x} \ldots\ldots\ldots(1.22)$$

Here we have used the effective atomic number of air A_{air} = 14.6 and its density ρair = 1.29×10^{-3} g/cm^3. Although it is very tempting to use Bragg-Kleeman rule, however it should be noted that the values thus obtained are only approximations and care must be taken while using them to draw conclusions [9].

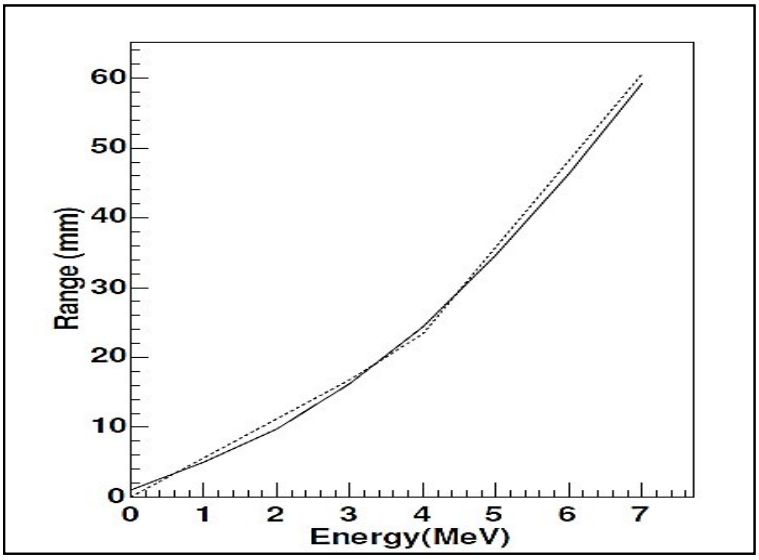

Figure 1.3: Range of α-particles in air as computed from equations 1.18 (solid line) and 1.19 (dashed line).

1.7 Sources of Alph Particles

Alpha particles, with their small penetration range1,2 have still found many uses in science and technology. As a result, much effort has been made to produce efficient and reliable sources of alpha particles. Many alpha-particle-emitting radioisotopes occur naturally in substantial amounts, and these have historically been used as primary sources. In some cases, particle accelerators are used to increase even more the kinetic energy of these particles up to the values needed for some uses. Other means to produce high alpha-particle fluxes, in addition to radioactive sources, have also been developed [9].

1.7.1 Accelerator-Based Sources

Like protons and neutrons, alpha particles can be created through an interaction between high-energy incident particles and stationary target materials. When the beam particle energy is relatively high, spallation reactions can happen by which the target nucleus is broken into its individual nucleons. Due to the high stability of the

two-proton, two-neutron system, these reactions often lead to the emission of alpha particles as well as free protons and neutrons.
One example of such a reaction is the collision of high energy neutrons (25-65 MeV) on a cobalt-59 target, which produces one or more α-particles per collision [9].

1.7.1 Radioactive Sources of α-Particles

There are numerous radionuclides that emit α-particles, some of which are listed in Table.1.2 [9].

Table 1.2: Common α emitters, the energies of their most probable emissions, and their half lives

No.	Element	Isotope	Energy (MeV)	$T_{1/2}$
1	Ameritium	$^{241}_{95}Am$	5.443 (13%), 5.486 (85.5%)	432.2 years
2	Bismuth	$^{213}_{83}Bi$	5.549 (7.4%), 5.869 (93%)	45.6 minutes
3	Curium	$^{244}_{96}Cm$	5.763 (23.6%), 5.805 (76.4%)	18.1 years
4	Californium	$^{252}_{98}Cf$	6.076 (15.7%), 6.118 (82.2%)	2.645 years
5	Radium	$^{223}_{88}Ra$	5.607 (25.7%), 5.716 (52.6%)	11.435 days
6	Thorium	$^{229}_{90}Th$	4.845 (56.2%), 4.901 (10.2%)	7340 years
7	Plutonium	$^{239}_{94}Pu$	5.144 (15.1%), 5.156 (73.3%)	24110 years
8	Polonium	$^{210}_{84}Po$	5.304 (100%)	138.376 days

1.8 Alpha Particle Spectroscopy

A large number of radionuclides emit α-particles of well defined energy. Since these particles are emitted from the nucleus of the atom, their spectroscopic parameters allow one to deduce information about the nuclear structure. This makes α-particle spectroscopy a very valuable tool for nuclear physics. The usefulness of the spectroscopy has fueled a lot of research and development into not only the techniques and methods but also the associated equipment. A typical α-particle spectroscopy setup is shown in Fig.12.2.1. It consists of a vacuumed enclosure for source and the detector, a pulse amplification system, and a pulse analyzer [9].

A vacuumed enclosure for the source and the detector is absolutely necessary to avoid parasitic absorption of α-particles in the space between the source and the detector. The reader might recall that the range of α-particles emitted by radioactive sources in air is very small, of the order of a centimeter. Even if the source and the detector are placed very near to each other, there would still be some air between

them. Since the cross section of air molecules for α-particles is very high, there would be significant absorption leading to loss of information and lowering of the signal to noise ratio. The latter effect is due to the statistical nature of α-particle interactions leading to addition of a statistical noise term in the expression for the signal to noise ratio. There are two ways to avoid the parasitic absorption of α-particles. One is to place the source inside the active volume of the detector, which would ensure total absorption of energy. This can only be done with gas filled detectors and carries handling and operational difficulties. The other technique, as shown in Figure1.4, is to place the source and the detector in a vacuumed enclosure [9].

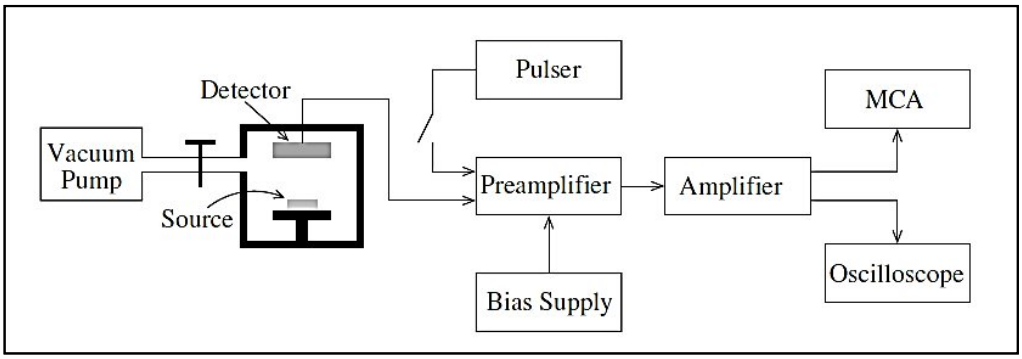

Figure 1.4: Block diagram of a typical setup for α-particle spectroscopy

Let us now move on to the types of detectors suitable for α-spectroscopy. In principle, any detector capable of detecting α-particles can be used. However, the most commonly used ones are the semiconductor detectors. In the early years of α-spectroscopy, mostly gas filled detectors were used as the semiconductor detector technology was in its infancy at that time. There are a few reasons behind preference of semiconductor detectors over their gas filled counterparts, as described below [9].

1.8.1 Resolution

Resolution is a very important parameter as far as spectroscopy is concerned. By resolution we mean how well the detector can differentiate between two particles depositing unequal energies into its active volume. Note that we are not talking about the electronics resolution yet. The resolution of the detector is a separate issue and is concerned with how well the deposited energy corresponds to the pulse height [9].

1.8.2 Linearity

It is an established fact that semiconductor detectors show better linearity for particles of low to moderate energies [9].

1.8.3 Parasitic Absorption

A big issue with gas filled detectors is that they need an enclosure to contain the filling gas. The enclosure is generally made of a metal with an entrance window for the radiation. One can make such a window very thin, of the order of a few microns, provided the gas is kept at approximately normal temperature. However, even in such thin windows there is a high probability of α absorption. Of course, this parasitic

absorption leads to signal loss and non-linearity in the response. A way around this problem is to place the source inside the active volume of the detector, which is associated with handling and operational difficulties. Semiconductor detectors do not share this problem since they do not have any entrance windows. The incident α-particles directly interact with the material in the active volume and deposit their energies [9].

The analog signal from the detector has to be amplified and shaped before being processed by the pulse height analyzer. These analog units are generally installed very close to the detector output. The output of the amplifier/shaper is a well shaped pulse with height proportional to the energy deposited by the incident α-particle [9].

The shaped pulse is then input into a pulse height analysis system. In brief, an MCA first digitizes the analog pulses and then increments the counts of its channels according to the height of the pulse. The channels of an MCA, also called bins, span its whole dynamic range. These bins are divided into intervals or bin widths. In general all the bin widths are of equal size but some modern MCAs allow the user to manually set different bin widths as well. The bin width used in the analysis and the overall MCA resolution set the limit on peak resolution capability of the system. This concept is graphically depicted in Figure 1.5. As shown in the figure, if the peaks are too close together, they can not be resolved and hence appear as a single peak in the MCA spectrum [9].

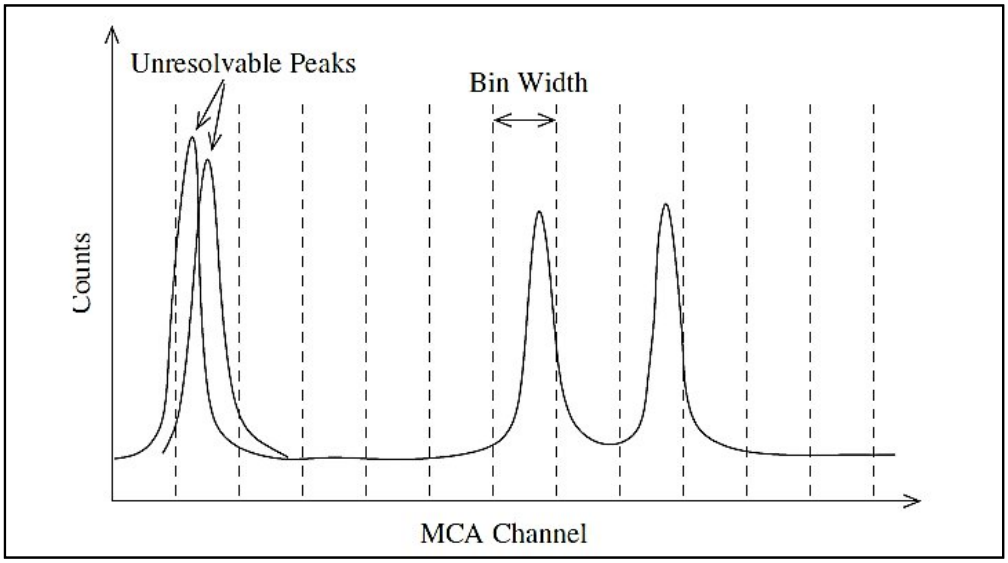

Figure 1.5: Effect of bin width of an MCA on its energy resolution

1.9 Health Effects

The Bethe–Bloch equation describes the energy loss of charged particles as they traverse matter, and for alpha particles it shows that their stopping power is proportional to the square of their charge and inversely proportional to their velocity.

As they slow down, they produce dense ionization tracks that can lead to molecular damage in biological systems, especially DNA double-strand breaks. The high LET of alpha radiation makes it particularly destructive at the cellular level, which is why its use in targeted alpha therapy must be carefully controlled to prevent unwanted tissue damage [10]. Alpha particles can also cause nuclear reactions in light elements if the energy of the alpha particle is high enough. For instance, alpha particles can cause (α,n) reactions that form neutrons in beryllium or boron targets. Some early sources of neutrons utilized this property, and it is of continued use in some research reactors and radiation laboratories [10]. Alpha particles are not dangerous outside of the body due to their poor penetrative ability, but they are very harmful when inhaled or absorbed into the body via wounds. When inside the body, alpha emitters may release their energy within a short range in vulnerable organs, resulting in damage to cells and DNA mutations with an increased potential for cancer. Large case–control epidemiological studies of radon-exposed uranium miners have shown increased rates of lung cancer, mainly as a result of alpha radiation from inhaled radon daughters [9]. Alpha radiation is much more biologically effective than beta or gamma radiation. Its Relative Biological Effectiveness (RBE) may rise as high as 20, in contrast to typical X-rays, making any management of alpha-emitting substances extremely strict. Preventive measures are provided by protective procedures aiming at preventing internal contamination through good ventilation, tight seals, and adequate personal protection gear (PPG) like gloves and respirators [10]. Alpha particles are a good example of this double-natured role they embody in nuclear physics and radiobiology; while being a cut that can produce effects at a distance, the high linear energy transfer (LET) and short pathlength make them very useful for targeted therapy despite their danger if internal exposure happens. The use of this fact in medicine, industry, and research is weighed against strict safety and protection measures to minimize health hazards and maximize uses beneficial to life.

1.10 Application in Medicine

Alpha particles are high (LET) radiation with very limited penetration capability in biological tissues. These characteristics make alpha particles in general well-suited for medical applications, and particularly in cancer treatment (i.e., where intense but localized dosage is required). In medical science, there are alpha-emitting radionuclides to specifically kill cancer cells, while keeping normal surrounding tissues low-damaged. Targeted alpha therapy for cancer treatment is the most vital use of alpha particles as explained in the following subsections **[***7*,11**].**

1.10.1 Targeted Alpha Therapy (TAT)

Targeted Alpha Therapy (TAT) is an advanced form of radionuclide therapy that utilizes alpha-emitting radionuclides conjugated to biological targeting vectors to selectively destroy malignant cells. This therapeutic approach exploits the unique

physical and radiobiological properties of alpha particles, particularly their high linear energy transfer (LET) and extremely short tissue penetration range, which typically spans only a few cell diameters (50–100 μm). These characteristics allow alpha particles to deliver highly localized and lethal radiation doses to cancer cells while minimizing damage to surrounding healthy tissues [7,11].

An alpha particle is a helium nucleus (two protons and two neutrons) with a +2 charge, with a mass being high relative to beta particles. Their high LET causes alpha particles to transfer a great deal of energy over a very short track, resulting in dense clusters of ionization in tissue. This highly ionizing dense crossing causes mainly hard-to-repair complex DNA lesions, including double-strand breaks. Therefore, alpha particles are considered extremely cytotoxic and effective even at very low absorbed doses [7]. TAT relies on the targeted delivery of alpha-emitting radionuclides to tumor cells using molecular recognition methods. These include in general, monoclonal antibodies, peptides, or other biomolecules that specifically recognize a tumor-associated antigen or receptor overexpressed on cancer cells. After being trapped, the alpha-emitting radionuclide emits cytotoxic radiation in proximity to the cancer cell and its surrounding area [7,11]. TAT has a unique advantage in that, compared to the traditional external beam radiotherapy and β-emitting radionuclide therapy, it is less affected by oxygenation status and cell cycle phase. Many of the standard therapies in radiation do not work well in hypoxic regions within tumors and the slow growth of cancer cells. Direct DNA damage caused by alpha particles, though, does occur to a great extent independently of oxygen concentration [7,11], and this may explain why TAT is especially efficacious against radioresistant tumors and micrometastases. Other alpha-emitting radionuclides have been studied and used in targeted alpha therapy. Among the most widely studied are astatine-211 (^{211}At), bismuth-213 (^{213}Bi), actinium-225 (^{225}Ac), radium-223 (^{223}Ra), and thorium-227 ^{227}Th). Properties of radionuclides A unique set of physical and chemical properties exists for each radionuclide; these attributes dictate the potential clinical applications and include half-life, decay scheme, daughter products, and radiochemical compatibility with targeting molecules [11]. Actinium-225 has been of interest in recent years because of its half-life (~10 days) and decay chain yielding multiple alpha particles. This feature could greatly improve the anti-tumor efficacy of ^{225}Ac-labeled agents. However, the recoil energy of daughter radionuclides presents a challenge, as it may cause the release of radioactive daughters from the targeting vector, potentially increasing toxicity to non-target tissues [7,11]. Radium-223 dichloride represents a notable clinical success of targeted alpha therapy and has been approved for the treatment of metastatic castration-resistant prostate cancer with bone metastases. Radium-223 behaves as a calcium mimetic and selectively localizes to areas of increased bone turnover, delivering alpha radiation to metastatic lesions while sparing surrounding soft tissues. Clinical studies have demonstrated that radium-223 therapy improves overall survival and reduces skeletal-related events with a relatively favorable safety profile [11]. From a radiobiological

perspective, the high LET of alpha particles results in a relative biological effectiveness (RBE) significantly greater than that of low-LET radiation such as X-rays or gamma rays. Reported RBE values for alpha particles range from 3 to 7, depending on the biological endpoint and experimental conditions. This higher RBE is responsible for the improved anti-cancer potency of TAT, especially in killing single cancer cells and small tumor masses [7]. Targeted alpha therapy (TAT) dosimetry faces additional complexity because the alpha particles are of a microscopic range and radionuclides are heterogeneously distributed at the subcellular and cellular levels. Most traditional macroscopic dosimetry formulations are inadequate to accurately predict biological response in TAT. Hence, microdosimetric and nanodosimetric methods have been developed for a more accurate estimation of absorbed dose at the level of individual cells, as well as for establishing correlations with biological effects [7,11]. Nevertheless, like many therapeutic approaches, targeted alpha therapy does have limitations and challenges. barrier Reasons for our limited success include the scarcity of appropriate alpha-emitting radionuclides, difficult radiochemistry, toxicities from redistributing daughter radionuclides, and accurate targeting to avoid damage to normal organs. Additionally, technical and economic challenges still exist to produce these alpha-emitting radiopharmaceuticals in a large-scale manner, followed by regulatory approval [11]. At present, the key subject of targeted alpha therapy is to enhance targeting specificity and to optimise radionuclide choice, radiochemical stability, and vectors for uptake. It is anticipated that with the advances of molecular biology, nanotechnology, and radiopharmaceutical chemistry, more clinical applications of TAT will be developed. In addition, combination treatments with TAT and chemotherapeutic agents [7], immunotherapy [11], or beta-emitting radionuclide therapies are under development to enhance the therapeutic potential of TAT. In summary, targeted alpha packing is a powerful and hopeful field in current cancer therapy. Because of these characteristics (high LET and short range), alpha particles from TAT offer the possibility of a specific attack on tumor cells with less peripheral effects on normal tissues. With further technological and clinical development, TAT is likely to become more integral in precision oncology.

1.10.2 Cancer Treatment

The therapeutic use of alpha radiation in the context of cancer is thus a special application issue for nuclear medicine, and those involved in tumor therapy seek to maximize tumor control while minimizing normal tissue damage. In contrast to standard external beam radiotherapy, in which ionising radiation is applied from outside the body, cancer therapy with alpha-particles involves the use of radionuclides that are given internally, exposing preferentially tumor tissue. This is an approach that allows for accurate radiation of the cancer cells and is most successful in diseases that is widesprea,d microscopic or refractory to conventional treatments [11].

The use of alpha-emitting radionuclides for cancer therapy is particularly important in solid tumors, which are often characterized by heterogeneous cellular distribution and limited accessibility. Solid tumors frequently contain hypoxic, necrotic, and irregularly vascularized regions that degrade the efficacy of X-ray and beta radiation treatment. Alpha radiation deliverable directly to tumor-associated targets when a radionuclide is used, can efficiently kill cancer cells in such settings as well because of its very short-range energy deposition [7,11]. Treatment of bone metastases is one of the most successful clinical applications of alpha radiation for cancer therapy. Bone metastasis is a typical feature of advanced prostate, breast, and lung cancers with complications including severe pain, fractures a, nd decreased quality of life. A-emitting radionuclides with calcium metabolism reducing maps concentrate in sites of increased bone turnover, hence delivering radiation to metastatic lesions and conserving the function of the bone marrow. This therapeutic approach has indeed shown great clinical efficacies such as pain control and increased survival [11]. Alpha radiations have also been promising for the treatment of micrometastatic disease and minimal residual cancer. These are tiny, comma-shaped groups of cancer cells or single related malignant (cancer) cells that can remain in the body after treatment, usually too small to be seen by ordinary imaging tests. Because of their short range and high cytotoxicity, alpha particles can efficiently kill such small cancer cell populations after only a few radioactive decays without inducing much tissue toxicity. This renders α-particles an especially appropriate form of radiation for inhibiting cancer re-growth [7,11].

Alpha-emitting radionuclides have been considered for selective treatment of hematological malignancies like leukemia and lymphoma, ie malignant cells in the blood, bone marrow and lymphatic tissues. These diseases are characterized by high levels of widespread cancer cell distribution and thereforeexternal radiation therapy is ineffective. Alpha radiation is characterized by the ability, when delivered in a targeted manner, to produce selective cell killing with lower systemic toxicity than conventional chemotherapy [11]. Another relevant clinical application of alpha particles in cancer treatment is daring exploitation toward advanced or refractory disease. Most of the cancers acquire resistance to chemotherapy, hormone therapy or low-LET radiation with chronological progression. Alpha radiation causes complex cellular damage that is mostly unrelated to the biological processes of resistance. Therefore, therapies that are alpha-emitting can still be efficacious in cases where all other treatment has failed, and they can potentially allow for the possibility of treating patients with advanced-stage disease [7,11]. Clinically, the treatment planning for alpha radiation is substantially different from that of external beam radiotherapy. Shielding is less of a challenge clinically since focus is on the sub-mm scale radionuclide distribution, targeting efficiency and biological effective dose. Other patient-dependent factors like disease burden, organ status, and metabolism pathway

should also be considered to achieve the maximal therapeutic aim without untoward effect [11]. Safety profile of alpha-based cancer therapy is an important consideration for clinical application. Since alpha-emitting nuclides do not penetrate tissues deeply, high level of control and organ at risk monitoring is necessary when using them for internal exposure. Clinical considerations, including patient selection, dosimetry considerations, and post-therapy follow-up, are also addressed to ensure safe and effective therapy. These are relatively well recognized in nuclear medicine [7]. Preclinical research: the use of combination therapies has been identified as a new field in alpha treatment for cancer. Alpha-emitting radionuclide therapy combined with surgery, chemotherapy, or immunotherapy, or beta-emitting radiopharmaceuticals could potentially improve the overall treatment efficacy. Combined approaches like that would complement each other and leverage the strengths of TERT and PMCAs by neutralizing their

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Chapter 2
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Application of Beta Radiation in Medicine

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2.1 Introduction

Beta particles are high-energy, high-speed electrons or positrons emitted by certain types of radioactive nuclei such as potassium-40. They are a type of ionizing radiation and are one of the three primary types of radioactivity originating from radioactive decay processes, the other two being alpha (α) and gamma (γ). Beta particles, which are ejected from a (β^-) or gained by a (β^+) nucleus according to the nuclear reaction. Both natural and artificial radioactivity depend on beta radiation. Background radiation in the environment and living organisms is also due to naturally-occurring beta emitters like carbon-14, potassium-40, and tritium. Artificial beta emitters (such as phosphorus-32, strontium-90, yttrium-90, and fluorine-18) are used in many applications, such as medical therapy, industrial tracers, and topological tracing. Beta particles are electrically charged, so they deposit their nucleon(s) at a relatively uniform density as they traverse matter, causing ionization and excitation of atoms in the materials through which they pass. They have a moderate penetrating power (climaxing, in the case of standard smoke detectors, just enough to pass through paper) but are usually effectively stopped by a few millimeters of aluminum or plastic. Beta emitters are important for levels of nuclear stability, radioactive decay series, and radiation protection [1].

2.2 Basic of Beta Theory

Beta radiation Beta (β) are streams of fast-moving electrons or positrons. β decay is a type of decay in which an unstable nucleus without an excess of neutrons transforms by converting a neutron to a proton (β−) or a proton to a neutron (β+), via the weak interaction. “Strong” nuclear force prevents instability and further decays but is overcome when it reaches practical limits. Beta decay is mediated by the weak nuclear force and can be used to obtain valuable information on nuclear structure and fundamental interactions. The nucleus that emits the beta is now made of different nucleons. In beta-minus decay (β−), the neutron changes into a proton, an electron, and an electron antineutrino ($\bar{\nu_e}$): $n \rightarrow p + e^- + \bar{\nu_e}$. For beta-plus (β+) decay (positron emission), a proton converts to a neutron, emitting a positron and an electron neutrino (ν_e): $p \rightarrow n + e^+ + \nu_e$. The continuous energy spectrum of beta particles arises because the decay energy (Q-value) is shared between the

beta particle and the (anti)neutrino. Consequently, beta spectra are characteristic but continuous, not monoenergetic (except in special cases like bound-state beta decay). The maximum beta energy E_{max} corresponds to the Q-value (neglecting recoil) and defines practical penetration and shielding behavior [2].

2.3 Sources of Beta Radiation

Natural sources include cosmogenic and primordial radionuclides. Cosmogenic radionuclides such as carbon-14 (^{14}C) and tritium (^{3}H) are produced by cosmic ray interactions in the atmosphere and undergo beta decay ($^{14}C \rightarrow {}^{14}N + \beta- + \bar{\nu_e}$; $^{3}H \rightarrow {}^{3}He + \beta^- + \bar{\nu_e}$). Primordial beta emitters like potassium-40 (40K, which decays partly via beta emission) exist in earth materials, foods, and biological tissue. Natural background radiation therefore contains a beta component that contributes to external and internal dose. Artificial sources are widespread in medicine, industry, research, and nuclear technology. Medical radionuclides include ^{32}P (therapy), 90Y (radiotherapy and radiopharmaceuticals), ^{131}I (thyroid treatment — β and γ emissions), and ^{18}F (positron emitter used in PET imaging). Industrial sources include fission products (e.g., $^{90}Sr \rightarrow {}^{90}Y$), activation products, and sealed beta sources used in thickness gauges and radiotracers [3].

2.4 Interaction of Beta Particles with Matter

Beta particles interact with matter primarily through inelastic collisions with atomic electrons (ionization and excitation) and, at higher energies, via bremsstrahlung (radiative losses) in the Coulomb field of nuclei. The stopping power dE/dx describes the rate of energy loss per unit path length and depends on particle energy, atomic number Z of the absorber, and density. At non-relativistic and low-relativistic energies, collisional losses dominate and produce dense ionization tracks. For high-Z absorbers and higher beta energies, bremsstrahlung becomes significant and produces secondary photons that can penetrate further and contribute to dose. Positrons (β^+) lose energy similarly to electrons until they reach thermal energies, at which point they annihilate with electrons producing two 511 keV gamma photons emitted nearly back-to-back [4].

2.5 Range and Penetration

Practical range in matter (commonly in units of g/cm² or mm in a given material) is often estimated empirically. A rule-of-thumb for maximum range R_{max} in g/cm² for beta particles in many materials is approximately: $R_{max} \approx 0.412 \times E_{max}^{1.265} - 0.0954$ (with E_{max} in MeV) Although empirical formulas vary, a simpler estimate often used in shielding practice is that a beta particle of energy E (MeV) has a range in millimeters in water roughly equal to $0.5 \times E^{(1.5)}$ to a few mm per MeV depending on the source [2].

2.6 Detection Methods for Beta Radiation

Beta detection strategies depend on the measurement objective: qualitative presence, count rate, spectrometry, surface contamination, or imaging. Common detectors include [1,4]:

a. Gas-filled detectors (Geiger-Müller and proportional counters): GM tubes detect beta particles with thin entrance windows (mica) for low-energy betas; proportional counters can provide energy information and pulse-height analysis when designed appropriately.

b. Scintillation detectors: Plastic scintillators and inorganic scintillators (e.g., NaI(Tl) for mixed β/γ, or specialized scintillators coupled to photomultiplier tubes or photodiodes) detect beta-induced scintillation light. Liquid scintillation counting (LSC) is widely used for low-energy beta emitters (^{3}H, ^{14}C) where the sample is mixed with cocktail to transfer energy efficiently to scintillator molecules.

c. Semiconductor detectors: Silicon surface-barrier and PIN diodes provide excellent energy resolution for beta spectrometry and surface contamination monitoring. They require vacuum or thin-window arrangements for low-energy betas.

d. Cherenkov counting: High-energy beta particles (e.g., from ^{32}P and ^{90}Y) traveling faster than the phase velocity of light in a medium generate Cherenkov radiation that can be detected optically; useful for quick assays without scintillants.

e. Beta spectrometers and magnetic spectrometers: For high-resolution studies, magnetic spectrometers and electrostatic analyzers separate beta particles by momentum/energy for fundamental studies. Surface contamination monitors and portable instruments are optimized for beta sensitivity and ease of use; they commonly combine thin-window GM tubes or scintillators with counting electronics and background subtraction.

2.7 Beta Spectrum

The beta spectrum is the distribution of the energy levels of the beta particles emitted in radioactive beta decay. Unlike alpha and gamma emissions, beta particles have a continuous energy spectrum rather than discrete lines (see Figure 3-1). This continuous behavior occurs because the allowed total energy of the beta particle and daughter nucleus varies: The electrons emitted by H or He are at

endpoint energies below 0.1 MeV, but uranium decays to a series of nuclei with relatively high decay energies per nucleon. This results in beta particles being emitted with a spectrum of energies that peaks at nearly zero and ends at a maximum energy called the endpoint. The beta spectrum is of characteristic shape; at low energies, the intensity rises steeply to a most probable energy which is well short of the endpoint and thereafter falls off with approximately exponential decay. The exact shape of the spectrum depends on several quantities, such as the charge of the daughter nucleus, the beta decay (allowed versus forbidden transitions), and interaction with the nuclear electric field for emitted beta particles. These determine the probability of emission at different energies, which result into overall modifications to the detected spectra when dealing with various radionuclides. The beta spectrum was one of the topics that contributed significantly to the development of nuclear physics and it proved to be very important in order to prove the existence of neutrinos, thus demonstrating again, the weak interaction as a genuine force. The study of the beta spectrum gives information on nuclear levels, decay schemes and various conservation laws relating to radioactive processes [1,5].

Figure 3-1 is a generic beta energy spectrum, in which the number of beta particles (Count), along the vertical axis, and the kinetic energy of beta particles (Beta Particle Energy) is plotted on the horizontal axis.

At low energy, the number of beta particles detected is low because of a lack of phase space and detector efficiency. As the energy decreases, however, the count rate increases and peaks at a most probable beta emission energy that is established by each specific type of emitter. This energy is much less than the maximum decay energy possible. Above the most probable energy, the count rate tapers off at higher energies approaching the endpoint energy (E_{max}). The endpoint energy is the maximum kinetic energy a beta particle can have when the neutrino carries off practically no momentum. At this value, the count rate drops steeply to zero, indicating that no particles above E_{max} are emitted.

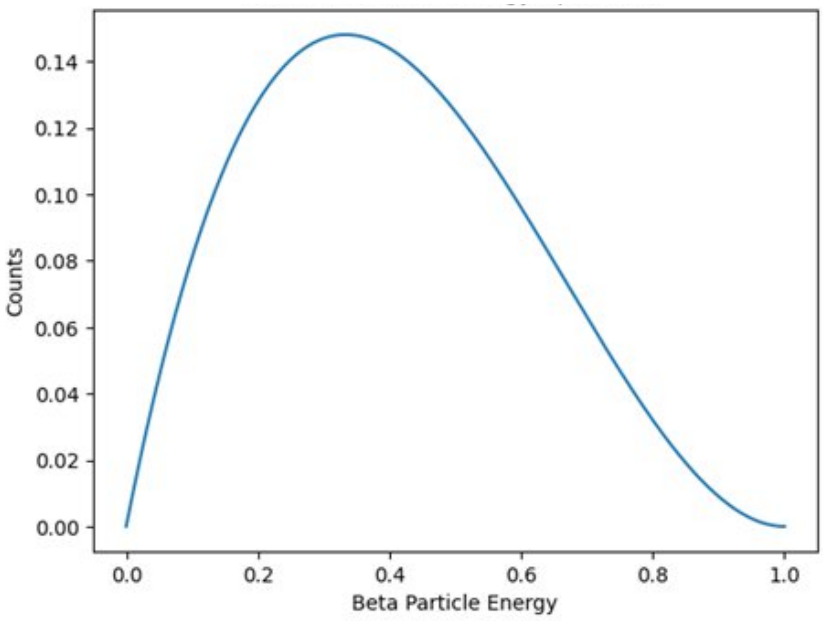

Figure 3-1. Schematic beta energy spectrum [1].

2.8 Beta Spectroscopy

Beta spectroscopy is the experimental analysis of a beta energy spectrum. This requires measuring beta particles and their energy distribution at a high enough resolution to be able to analyze spectral features (such as the endpoint energy and complete shape). The primary aim of beta spectroscopy is to obtain nuclear and decay information from data not accessible by simple activity measurements. Several detection arrangements are used in beta spectrometry according to the measured energy range and resolution. Magnetic and electrostatic spectrometers can separate beta particles according to their momentum or energy, allowing for the accurate measurement of spectral endpoints and spectroscopic features. One type of semiconductor detector is one based on silicon, which is easily used and has excellent energy resolution for low- to medium-energy beta particles. The scintillation detectors, generally composed of plastic materials, are also applied in beta spectroscopy with high counting efficiency and fast timing (but less sensitive energy resolution) [5].

2.9 Health Effects of Beta Radiation on Humans

Beta rays include electrons and positrons that are ejected during radioactive decay. As a result of their low mass and electric charge, beta particles are strongly affected by electric and magnetic fields, thus behave with a great deal of energy loss through ionizing material such as gas and lose energy in each collision until their forward velocity is higher than the speed of light in that material. In biological tissues, such interactions can result in localized as well as systemic health effects, depending on the beta particle energy, time of exposure, and pathway. Beta radiation is primarily an external hazard, but exposure can lead to radiation burns if extensive skin or body surface area is involved, particularly as beta particles are not deeply penetrating and can be stopped by less dense materials such as a few millimeters of plastic. Long-term or high-dose external exposure results in damage to the skin, which may present as erythema, burns, ulceration, and, when more severe, radiation dermatitis. Eyes are the most sensitive to beta radiation, and overexposure may result in cataract formation because of injury to the lens epithelium. Within the body, beta radiation is a much greater health risk than gamma radiation when an equivalent activity is inhaled, ingested, or absorbed into the body. Beta emitters will, after entering the body, irradiate the surrounding tissue for a prolonged period until decaying or being removed. The ionization disrupts cellular structures, particularly DNA, and can give rise to mutations or kill cells. Organs with a concentration of radioisotopes, such as the thyroid, bone or GI tract are particularly susceptible to focal radiation damage. On a cellular level, beta radiation can directly cause damage to the cell's DNA due to high-energy ionization of the DNA molecules as well as other possible methods causing further indirect damage. These mechanisms can lead to DNA single-strand and double-strand breaks. If this damage is not correctly repaired, it can result in longer-term biological consequences such as an increased risk of cancer or genetic changes that are inherited [6].

Health consequences are highly dependent on absorbed dose and dose rate. Deterministic effects, including skin burns and tissue necrosis, occur with acute high-dose exposure, whereas stochastic effects, particularly increased cancer incidence, arise from chronic low-dose exposure. Stochastic effects on the other hand, have no threshold dose and their probability increases with cumulative dose. In medical and industrial environments, beta is a health risk because of the ability of continuous exposures to exceed their tolerable doses, due to human error or equipment failure. The biological consequences of beta radiation, and particularly their validity and accuracy in establishing safety guidelines for radiation exposure as well as in the practice of medicine when using such radionuclides, are very important to both patients, workers, and the public.

2.10 General Applications of Beta Radiation

Beta radiation (β-radiation) is a type of ionizing radiation that consists of high-energy electrons or positrons and is released from the process of beta decay. Intermediate in penetrating power and ionizing capability, beta particles are ideal for surface or near-surface applications. One of the main industrial applications of beta emission is the measurement of thickness and density. They are frequently employed in the paper, plastic films, rubber sheet , and metal foil industries. Beta particles lose energy when they penetrate a substance, and the intensity of the transmitted beta rays depends on the thickness and density of the material. Production processes are thus able to be controlled in real time with the accurate detection of transmitted beta radiation.

Beta radiation is commonly used in industrial process monitoring and quality control. Perhaps the most common beta monitoring application is in the production line, using automated controls to measure thickness, uniformity, and material composition of coating. These no-contact measuring methods increase productivity, minimize material loss and promote consistent product quality. In environmental science, beta radiation is used for the measurement of radioactive contamination in water, air, and soil. Beta-counting methods are employed in the monitoring of beta-emitting radionuclides such as 90 Sr, which is used to investigate levels of environmental radioactive contamination and radiological safety following nuclear activities or incidents. A significant use of beta radiation is in radioisotope tracers. Beta-emitting tracers are also employed for material flow, mixing and leakage detection studies in industrial systems. Due to the limited range of beta particles, they are well-suited for monitoring processes in thin materials or near surfaces without undue perturbation of neighboring systems. Beta radiation is also used in scientific research and material analysis. Beta decay studies are carried out in nuclear physics research to study the properties of the nucleus, the weak interaction, and basic conservation laws. In material science, beta radiation is commonly used to modify properties and induce cross-linking of polymers in a process known as Irradiation Crosslinking, and to disrupt the molecular structure by foreign atoms (radiation damage). Furthermore, beta rays are used for static electricity elimination. Beta emitters are employed for the neutralization of static charges on material surfaces in the printing, textile, and electronics industry by ionizing molecules of the ambient air. This application minimizes the picking of dust, enhances ease of handling, and prevents electrostatic damage to delicate objects.

On the whole, beta radiation provides convenient and effective solutions in various non-medical fields. Controlled use of it provides accurate measurement of materials and the change in their properties, along with optimization of processes, while obviously keeping safe distance for workers & the environment [7].

2.11 Applications of Beta Radiation in Medicine

Contents Beta (β-) radiation refers to energetic electrons or positrons emitted during a type of radioactive decay known as beta decay. In medical applications, beta radiation is used primarily for its reduced penetration depth, which enables deposition of radiation energy inside a targeted tissue. This property makes beta emitters particularly desirable for therapeutic purposes so that surrounding healthy tissue is not damaged.

Beta-emitting radionuclides are of medical relevance as a consequence of their low penetration depth and high ionizing capacity. They are primarily implemented in medicine, targeting and eradicating living tissues such as tumors and irregular thyroid cells through short-range beta radiation exposure with minimum adverse effects on the adjacent healthy tissue. In diagnostic medicine, indirectly with beta emitters, especially in PET scanners, where the isotope used (positron emitter) undergoes positron decay that produces detectable gamma rays. Beta radiation is also used in sterilization, particularly for the irradiation of surface and thin medical products, which effectively inactivates microorganisms [8-11].

2.11.1 Diagnostic Applications

Beta emitters occupy a niche, but nonetheless crucial, role in diagnostic Nuc. Med. practice, predicated mainly on positron- emitting radionuclides (β^+ emitters). β particles are weakly penetrating in biological tissues and are inefficient for detection externally, but certain β-emitting radionuclides permit imaging through secondary radiation. It renders beta emitters much more desirable for functional and molecular imaging than anatomical imaging. For positron emission tomography (PET) imaging, radiotracers incorporating β^+-emitting radionuclides, such as Fluorine -18, Carbon-11, Nitrogen-13, and Oxygen-15, are employed. Following emission, the positron travels a few millimeters in tissue before annihilation with an electron, emitting two gamma photons of 511 keV that are emitted almost in opposite directions. These photons are detected coincidentally by PET scanners so that the tracer distribution in the body can be reconstructed precisely. Chemical agents: Reagents labeled with beta-emitting radionuclides are commonly used in nuclear medicine to measure metabolic activity, blood flow, oxygen consumption, and receptor expression. For instance, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is widely employed for imaging of glucose metabolism and plays an important role in the diagnosis, staging, and monitoring of response in cancer as well as neurological and cardiac applications. This feature can result in early tumor detection, at the cellular level, even before structural changes are visible. Some β-emitting isotopes whose gamma radiation is also relatively easy to detect, like Iodine-131, can be used diagnostically in a few specific clinical indications (e.g., thyroid uptake studies). In these cases, little imaging is performed with beta particles, and their associated gamma rays are detected externally. These radionuclides are used for diagnostic purposes as well as to assist in therapy planning.

In summary, although beta particles are not directly utilized for external imaging, the beta-emitting radionuclides are essential in contemporary medical imaging with emphasis on PET. Their capability to follow through on physiological and biochemical processes yields a very sensitive, quantitatively relevant diagnostic information; the beta emitters are essential for functional imaging in nuclear medicine.

2.11.2. Therapeutic Applications

Beta-emitting radionuclides remain central to current therapeutic nuclear medicine since high radiation doses can be deposited over distances somewhat greater than the size of cells. The short range of beta particles enables targeted destruction of cancerous cells while preserving adjacent healthy tissues. Beta Radiation in Therapy. The uses of beta radiation. In this chapter, we consider the therapeutic applications of beta radiation and include radionuclide therapy with beta emitters, treatment for thyroid disorders, targeted cancer radiotherapy, and palliation for bone pain from metastatic disease. These applications reflect the medical significance of beta emitters for local and efficient treatment and personalized medicine.

a) Radionuclide Therapy Using Beta Emitters

Beta therapy with a radionuclide is internal radiation therapy in which the radioactive beta emitter is delivered to the patient, selectively binding to disease tissue. The therapy is based on the fact that beta particles penetrate tissues only a few millimeters, permitting high radiation intensity to be given to the target cells and minimal damage to neighbouring nontumor tissue. In this method, beta-emitting radionuclides can be administered in at least three forms: orally, intravenously, or directly inserted into the diseased tissue. When in place at the target site, the beta particles from the radionuclide ionize atoms and molecules near and around their paths through tissue, inducing DNA damage, preventing cell division, and death of individual cells. This local cytotoxic effect is the basis for successful treatment of, e.g., cancer, overactive thyroid tissue, and bone metastases. Examples of therapeutic beta emitters used in nuclear medicine today are Iodine-131 (^{131}I) for therapy of thyroid disease, other Yttrium-90 (^{90}Y) preparations used to treat liver cancer and lymphoma, Strontium-89 (^{89}Sr) or Samarium-153 (^{153}Sm) for palliation of bone pain. Choice of a particular radionuclide depends on its physical half-life, beta particle energy, and chemical character so that it is deposited preferentially in the target tissue and minimizes systemic exposure.

In general, beta-emitter radionuclide therapy is an accurate, less-invasive, and highly efficient disease-specific protocol of nuclear medicine, which can be targeted to the treatment where external beam radiation may not have rendered adequate control or at the cost of normal tissues.

b) Treatment of Thyroid Disorders

Beta-emitting radionuclides, in particular Iodine-131 (1 3 1I), have been successfully employed in thyroid disease treatment to treat conditions such as hyperthyroidism and differentiated thyroid cancer. The thyroid gland will normally concentrate iodine metabolically to synthesize the thyroid hormones, and this characteristic is utilized in therapy. When ^{131}I am ingested, it accumulates specifically in the thyroid tissue and emits beta particles that deliver focused radiation and kill hyperactive or cancerous cells while minimizing harm to neighboring tissue. In ligaments ^{131}I treatment decreases the excess production of thyroid hormones by destroying part of the gland, in most cases obtaining a sustained remission without surgery. In thyroid carcinoma, ß radiation emanating from ^{131}I respectively attack remaining thyroid tissue or metastases after a total thyroidectomy, suppressing further malignant manifestation. Low-energy beta emissions mean only a short distance that energy will travel in the body, and the high doses that can be delivered to a small, localized area (thyroid), maximizing efficacy for thyroidal tissues while also providing enough penetration so as to allow either imaging or dosimetry. This treatment is known to be very effective, minimally invasive, and safe when radionuclide dosage is appropriate, making beta-emitting substances the most widely used treatments for thyroid diseases.

c) Cancer Therapy and Targeted Radiotherapy

Beta-emitting radionuclides are important in cancer therapy, particularly where tumor treatment is localized. The high-energy beta particles do not travel far and, thus, can deliver cytotoxic radiation directly to the cancer cells with minimal exposure to healthy tissues. This property is very useful for targeted radiotherapy by conjugating a tumor-targeting radionuclide to molecules that specifically bind to the cancer cells. TRT, also known as TRN for Targeted Radionuclide Therapy, is based on the use of beta emitters bound to monoclonal antibodies, peptides, or microspheres in order to direct radioactivity to cancer cells.

For example:

^{90}Yttrium (^{90}Y)-labeled antibodies are employed in non-Hodgkin's lymphoma patients, targeting β-radiations to malignant B cells. ^{90}Y microspheres are used for the treatment of liver cancer (radioembolization) where they embolize the tumor vascular bed and deliver radiation specifically to the tumor while preserving normal liver tissue.

Lutetium-177 (^{177}Lu) releases b-particles and g-photons, which makes it ideal for use as a therapeutic radioisotope since the emitted particles enable both therapy and imaging of surprising tumors in patients with neuroendocrine tumors (NETs), termed peptide receptor radionuclide therapy (PRRT).

Beta rays, which are electrons and positrons, cause ionization of cellular DNA with production of strand breaks in the DNA, cells arrested in mitosis, and

death by apoptosis of cancer cells. Selection of the radionuclide is based on half-life, beta energy, reactivity and tumor uptake. High-energy beta emitters such as ^{90}Y may be used for larger tumors, whereas the low-energy emitters such as ^{177}Lu are favored for small tumors or metastatic lesions.

Beta emitter-based cancer therapy is less invasive, selective, and therapeutically active compared to the conventional method of external beam radiotherapy or chemotherapy. It is particularly useful for metastatic disease, inoperable tumors, or when healthy tissue must be spared. Rapid radiopharmaceutical development is broadening the use of beta- emitting radionuclides in oncology, with a promise to enhance patient survival while minimizing toxicity.

d) Bone Pain Palliation

Beta-emitting radionuclides are used to treat profound bone pain from metastatic cancer, especially due to prostate, breast, or lung malignancies. Metastasis of cancer to the bones commonly results in osteoblastic lesions, or metabolically active sites of bone production that accumulate specific radionuclides. Beta-emitting radiopharmaceuticals take advantage of this by preferentially accumulating in such lesions and emitting beta radiation, thus producing the therapeutic radiation dose directly to the tumor-invaded bone.

Some of the widely used beta-emitting radionuclides for pain relief in malignant disease involving bone:

Strontium-89 (^{89}Sr) – radioactive strontium that behaves like calcium and deposits in areas of bone metastases, particularly where osteoblastic activity is increased.

Samarium- 153 (^{153}Sm-EDTMP) – binds to bone-phosphate, putting the radiation source in metastatic sites.

The beta-emitting radionuclides emit radiation a few millimeters into the adjacent tissue, resulting in local cytotoxic effects, which decrease tumour activity and inflammation and hence cause pain reduction. These radionuclides are systemically delivered and home in on bone lesions due to their natural habits, being of low invasiveness.

The palliation of bone pain with beta-emitting isotopes is safe, efficacious, and quality of life (QOL) enhancing, ideal for the non-surgical patients who cannot undergo radiotherapy. The treatment yields striking analgesic effects one to four weeks after delivery and can be repeated when desired, frequently in conjunction with other measures for pain control.

2.11.3 Sterilization Applications

Beta radiation is often used in sterilizing medical devices, pharmaceuticals, and some foods for its ability to kill microorganisms effectively. Beta particles are

energetic electrons that interact with matter primarily through ionization and excitation of atoms and molecules by them to cause DNA breakage and disruption of cell structures of bacteria, viruses, fungus which leads to their death. The most significant advantage beta radiation has for sterilization purposes is that depositing this energy takes place over a very narrow 'zone' (that extends ~1 millimetre into the target material). This makes beta-emitting sources or electron beams of accelerators capable of sterilizing thin or surface layers of the material, but being less invasive in altering the structure and chemical integrity of the product.
Common applications include:
Medical instruments, including syringes, surgical gloves, catheters, and tubing. Heat-sensitive pharmaceutical products, which may not be sterilized by autoclaving. Packaging materials with prior art. The growing use of the laboratory test has created a need to pre-sterilize any surface on which the sample is cultured.

Beta radiation is less penetrating than gamma, therefore not as effective in sterilizing large volumes or thick materials. Nevertheless, it is suitable for surface sterilization, seed-sterilization, or clinical treatment and adds easily to the conveyor-type electron beam systems that can accomplish mass processing. Beta-radiation radionuclides or electron accelerators also offer a no temperature, non-chemical method for sterilization to minimize product degradation. Moreover, sterilization by beta radiation is rapid, effective, and ecologically feasible and thus represents a more convenient method than chemical or thermal procedures.

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Chapter 3
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Application of Gamma Radiation in Medicine

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3.1 Introduction

Gamma radiation (γ-rays) is a form of electromagnetic radiation characterized by extremely short wavelengths (typically < 0.01 nm) and high photon energies (above 100 keV) [1]. It arises from transitions within atomic nuclei and subatomic particles, and plays a central role in nuclear physics, astrophysics, and radiation protection. Unlike alpha and beta particles, gamma rays are massless and electrically neutral, allowing them to penetrate matter deeply and interact primarily through electromagnetic processes.

Gamma rays have neither mass nor electric charge, and they travel through space at the speed of light. The most energetic photons in the electromagnetic spectrum are gamma rays, as their wavelength is very short. They have good penetration power and can penetrate most substances, but they mainly interact with matter through the photoelectric effect, Compton scattering, and pair production. Yet although it ionizes rather weakly directly, the secondary charged particles produced when such radiations interact with matter often amount to a tremendous degree of ionization. These special properties of the gamma rays make them interesting for science and suitable for diverse technical applications, such as nuclear physics, medical diagnostics and therapy, radiation protection, and industrial control [2].

3.2. General Application of Gamma ray

Gamma radiation is a form of ionizing electromagnetic radiation which is produced by radioactive materials, nuclear reactions, and other high-energy astrophysical processes, and for this reason, it has become one of the most interesting subjects to be researched in different fields such as physics, medicine and engineering from which has led to many applications in medical imaging (for example), treatment of cancer either curative or as palliative care e.g., through gamma knife radiotherapy that can prevent unwanted side effects which are usually shown with other invasive procedures) and the sterilization of clinical equipment. Furthermore, gamma radiation finds widespread industrial use in applications ranging from food sterilization and wastewater treatment to inspection of the structural integrity of welding seams, for which non-destructive testing is a priority issue in many industrial fields [3]. Furthermore, the unique properties of gamma radiation, such as its high penetration and ionizing capabilities, make it an ideal tool

for various scientific research, including probing the structure of materials, analyzing the composition of substances, and studying the behavior of subatomic particles, which has led to significant advancements in our understanding of the fundamental laws of physics, particularly in the fields of nuclear and particle physics, where researchers continue to explore the intricacies of nuclear reactions, particle decay, and the behavior of antimatter, all of which have far-reaching implications for our understanding of the universe, from the smallest subatomic particles to the vast expanse of cosmic phenomena, including the birth and evolution of stars, the expansion of the universe, and the mysteries of dark matter and dark energy, driving scientists to continue pushing the boundaries of human knowledge, as they strive to unravel the secrets of the universe, and in doing so, have led to breakthroughs in various fields, including medicine, where gamma radiation is used in cancer treatment, sterilization of medical instruments, and imaging techniques such as posit ron emission tomography (PET) scans, which have revolutionized the way doctors diagnose and treat diseases, enabling them to pinpoint the exact location of tumors, track the progression of diseases, and develop targeted treatments that have significantly improved patient outcomes and saved countless lives, while also inspiring new areas of research, such as radiation oncology, nuclear medicine, and advanced medical imaging, which have become essential components of modern healthcare

3.3 Origin of Gamma Radiation

Gamma radiation is most commonly emitted during the de-excitation of atomic nuclei. After undergoing alpha or beta decay, a nucleus may remain in an excited state [1]. To reach its ground state, it emits a gamma photon: $E\_excited - E\_ground = hv$, where h is Planck's constant and v is the frequency of the emitted photon. For example, the decay of Cesium-137 involves beta decay followed by gamma emission:

$$^{137}Cs \rightarrow {}^{137}Ba^{*} + \beta^{-} \rightarrow {}^{137}Ba + \gamma$$

Gamma transitions are classified by their multipolarity, which reflects changes in angular momentum and parity: Electric (E) and Magnetic (M) multipoles: E1, M1, E2, etc. Higher multipolarity transitions are less probable and correspond to lower transition rates. In some cases, instead of emitting a gamma photon, the nucleus transfers energy to an orbital electron, causing it to be ejected from the atom. This process, known as internal conversion, competes with gamma emission and is significant in low-energy transitions.

3.4 Sources of Gamma Radiation

There are many sources of gamma ray as following [2,3]:

3.4.1 Gamma Radiation from Nuclear Reactions

Gamma rays are also produced during nuclear reactions such as:

Neutron capture: $n + {}^{14}N \rightarrow {}^{15}N^* \rightarrow {}^{15}N + \gamma$

Fusion reactions in stellar cores: ${}^{2}H + {}^{3}H \rightarrow {}^{4}He + n + \gamma$

Fission fragment de-excitation: Fission products are often highly excited and emit gamma rays as they stabilize.

3.4.2 Particle-Antiparticle Annihilation

Gamma radiation is a direct product of matter-antimatter annihilation. The most notable example is electron-positron annihilation: $e^- + e^+ \rightarrow 2\gamma$. Each gamma photon carries 511 keV of energy, equivalent to the rest mass of the electron.

3.4.3 Meson and Hadron Decay

Unstable subatomic particles such as neutral pions decay into gamma photons: $\pi^0 \rightarrow \gamma + \gamma$. The electromagnetic interaction mediates this decay and occurs with a lifetime of approximately 8.4×10^{-17} seconds.

3.4.4 Astrophysical Sources of Gamma Radiation

a) Supernovae and Stellar Nucleosynthesis: Radioactive isotopes produced in supernovae (e.g., ${}^{56}Ni$, ${}^{56}Co$) emit gamma rays during decay, contributing to the observed gamma-ray spectra of remnants.

b) Gamma-Ray Bursts (GRBs): GRBs are among the most energetic events in the universe, believed to result from neutron star mergers or hypernova. They emit intense gamma radiation over short durations (milliseconds to minutes).

c) Active Galactic Nuclei and Quasars

Particles accelerated near supermassive black holes emit gamma rays via synchrotron radiation and inverse Compton scattering.

d) Cosmic Ray Interactions

High-energy cosmic rays interacting with interstellar matter produce neutral pions, which decay into gamma photons.

3.4.5 Terrestrial Gamma Radiation

Gamma radiation is also observed on Earth from natural and Terrestrial sources: Natural radioisotopes: Isotopes such as ${}^{40}K$, ${}^{238}U$, and ${}^{232}Th$ emit gamma rays during decay.

Terrestrial gamma-ray flashes (TGFs): Produced by lightning and thunderstorms via bremsstrahlung from relativistic electrons. As well as, Gamma-emitting isotopes like ${}^{60}Co$ and ${}^{99}mTc$ are used in radiotherapy and imaging.

3.5 Gamma Interactions with Matter

Usually gamma-ray will interact with material in one of three different ways: photoelectric absorption, Compton scattering, and pair production. These different interactions change their probability of occurring depending on the energy of the gamma-ray and the atomic number of the matter. As can be seen from Figure (3-1), the photo electric effect is dominant for low energy photons and high Z materials. The Pair production is dominant for high energy photons and high Z materials. The Compton scattering interaction is dominant for moderate energies [2].

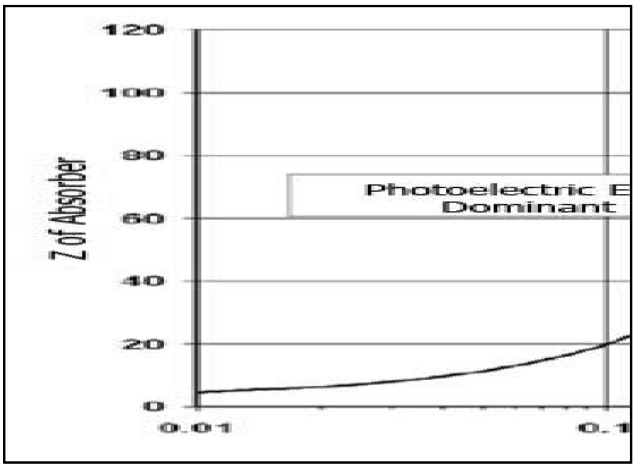

Figure 3-1:A graph depicting the various regions where the different gamma-ray interact ions are dominant [2].

3.5.1 Photoelectric Effect

In this process the photon interacts with electron in an atom. The electron of the material will eject from its shell with kinetic energy E_e , as in Figure (3-2) [3].

$$Ee -= hv - Eb \qquad \textbf{(3-1)}$$

the binding energy of the electron in its shell represented by E_b, is the hv, photon energy. The vacancy in the electron shell is quickly filled by electron rearrangement. The Photoelectric process causes the binding energy, E_b, to be liberated as well. This energy is liberated in the form of a characteristic (X-ray) or an Auger electron. The photon which interacts with absorber atom is completely disappeared, this process is enhanced for absorber with high atomic number (Z).

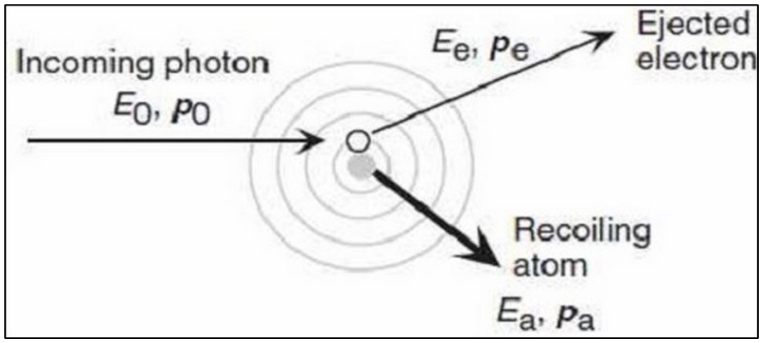

Figure 3-2 **: Schematic diagram of photoelectric effect [3].**

3.5.2 Compton Scattering

The incoming photon does not disappear after a Compton scattering. The change occurs Only in direction of motion and energy. (Figure 3-3) The energy of the photon is reduced by a certain amount that is given to the electron. Therefore, the conservation of energy given assumes the electron stationary before the collision [4].

$$\mathbf{T} = \mathbf{E}_{\gamma} - \mathbf{E}_{\gamma'} \qquad \textbf{(3-2)}$$

The energy of the scattered photon as a function of the scattering angle θcan be obtained by equation (3-3).

$$E_{\gamma'} = \frac{E_{\gamma}}{1+(1-\cos\theta)E_{\gamma}/mc^2} \qquad \textbf{(3-3)}$$

photon energy. The incoming photon does not disappear after a Compton scattering. The change occurs Only in direction of motion and energy. The energy of the photon is reduced by a certain amount that is given to the electron. Therefore, the conservation of energy given assumes the electron stationary before the collision.

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$$E_{\gamma'} = \frac{E_{\gamma}}{1+(1-\cos\theta)E_{\gamma}/mc^2} \qquad \textbf{(3-4)}$$

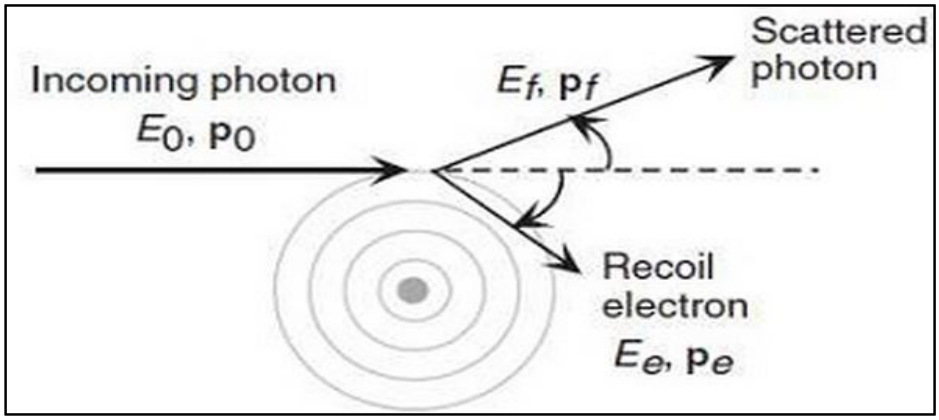

Figure 3-3: process of the Compton Scattering [4]

3.5.3 Pair Production

The Pair production happen in the Coulombe field of the nucleus, creating in the transformation of a gamma-ray to "electron–positron" pair. This process occurs in a puff of quantum mechanical smoke, where gamma-ray vanishes and the pair of electrons–positron will evidence. The main condition for the occurrence of this phenomenon is that the energy of the gamma ray coming is not less than twice the rest mass of the 2 particles which about 511 keV each1022 kilo eV in all. the Scientific exercise guide of this process is only visible through gamma ray spectrum where energy extra than 1022 keV as express in Figure (3-4) [3]. The pair production may be taking place beneath the effect of the field electron but the contingency be very lower also the threshold of the energy is four electron rest masses, where it be omitted as a considerate on in normal zero into 3MeV gamma spectrometry.

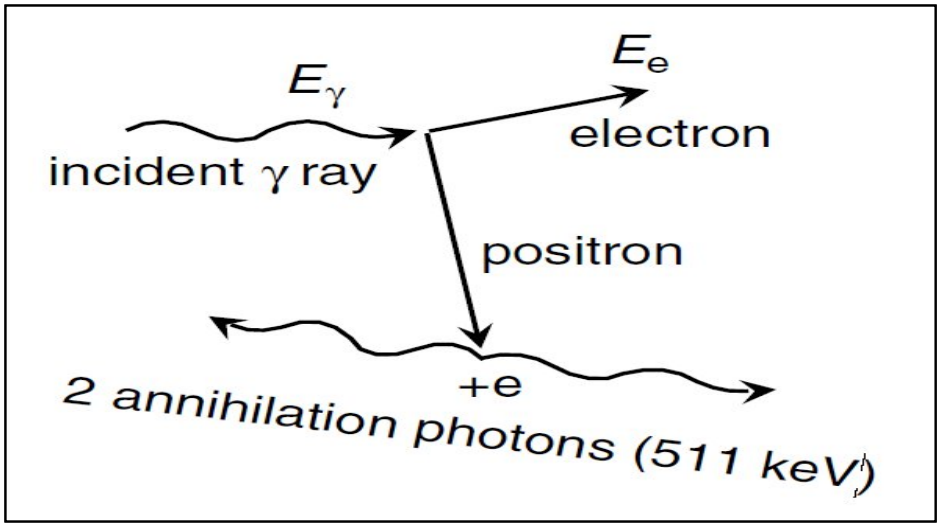

Figure 3-4: Schematic diagram of pair production interaction [3].

3.6 Gamma-ray spectroscopy

Gamma-ray spectroscopy is one of the basic and widely applied nuclear analytical techniques to measure and analyze the energy distribution of gamma radiation that comes from radioactive sources. Because gamma radiation is produced by transitions between well-defined energy levels in an atomic nucleus, the energies are specific and characteristic of a given radionuclide. Using a gamma energy spectrum, one can investigate radioactive isotopic composition, activity and nuclear structure and decay schemes [4].

The quantum mechanical foundation of gamma-ray spectroscopy is the interaction of photons with a detector material, in which photon energy is transferred to charged particles, partly or wholly, by mechanisms including the photoelectric effect, Compton scattering and pair production. These processes produce electrical signals corresponding to the deposited energy. The signals are amplified, treated, and their pulse height is discriminated so that the events are ordered according to that magnitude: a spectrum in which the number of photons detected in function of the energy.

Contemporary detection techniques of gamma rays make use of high efficiency and good energy resolution detectors. Scintillation detectors, including sodium iodide activated with thallium (NaI(Tl)), are used to a large extent because they are efficient and simple on the other hand semiconductor detectors, especially high-purity germanium (HPGe) based ones, possess better energy resolution and offer accurate identification of close-lying gamma-ray lines. The accurate energy calibration is

necessary for the typical gamma standards source. The corresponding gamma-ray spectrum usually includes full-energy peaks, Compton continua, backscatter peaks and for higher energies pair-production lines.

Figure (3-5) presents the entire gamma-ray spectroscopy, beginning from radiation generation to spectrum analysis, and can be divided into three sections. The experimental arrangement is illustrated on the left-hand side. Gamma rays from a radioactive source impinging upon the radiation detecting unit (which can be, in practice, for instance, a NaI(Tl) scintillation detector or HPGe) enter inside it. In the detector, the incident gamma photons collide with the material of the detector and lose some or all their energy there. The electrical pulses produced as a consequence of the above process are amplified and supplied to a multichannel analyzer (MCA), which sorts them according to their amplitudes, thus building the gamma-ray energy spectrum. The central portion of the figure describes basic gamma-ray interaction processes, which lead to signal creation inside the detector. In the photoelectric effect, the gamma ray delivers all of its energy to an atomic electron and generates a full-energy event. It is a partial energy transfer process in which the incoming photon transfers some of its energy to an electron, thus producing a recoiling electron (Compton recoil electron) and a scattered photon. At higher photon energies (greater than 1.022 MeV), pair production is possible, wherein the gamma energy is converted into an electron–positron pair; the positron annihilates to produce two 511 keV photons [4].

An example of a gamma-ray energy spectrum shown as counts versus energy is found on the right of the figure. The photopeak (full-energy peak) is the most distinctive feature and is used for radionuclide identification since it represents full energy absorption of the gamma photon. The Compton continuum is generated by the partial energy deposition in Compton scattering at the maximum single energy transfer, called the Compton edge. The backscatter peak is generated by photons that have been scattered outside of the detector and then, due to Compton scattering in at least one other layer from the scatter point (with energy above approximately 200 keV), pass a second time through the detector. In the case of high-energy gamma rays, escape peaks and pair-production related peaks, such as the 511 keV annihilation peak, may also occur [3,4].

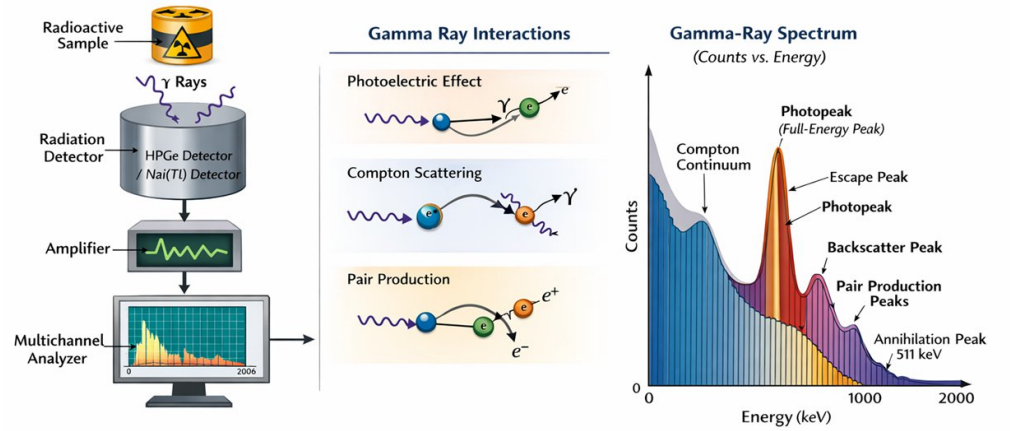

Figure 3-5: Gamma ray spectroscopy process

Quantitative estimates of radionuclide composition, photon energies, and emission probabilities can be made by the analysis of these spectral features. Therefore, gamma-ray spectroscopy is an essential technique in many areas such as nuclear physics research, environmental radioactivity monitoring, medical diagnostics and therapy applications, radiation protection practice, homeland security and industrial non-destructive testing.

3.7 Health Effects of Gamma ray

Gamma rays are a type of ionizing electromagnetic radiation, and are very high-energy, resulting in extremely-deep penetration through body tissues and posing health concerns to humans when they penetrate past the appropriate levels. As gamma rays have high energy and no charge, they travel deep inside the human body and affect the cells in it at a cellular/molecular level. The mechanism of interaction is mainly through ionization, which results in the formation of free radicals and high linear energy transfer secondary charged particles that are capable of causing damage to vital biological molecules, especially DNA [5]. Gamma rays at the cellular level can cause single- or double-strand breaks in DNA, as well as oxidative damage to bases and deoxyribose, crosslinking of DNA strands, induction of point mutations or chromosomal breakage leading to translocations, deletions, and inversions. And unless this damage is precisely fixed by cellular machineries, it can lead to mutations, cell death or cancer. They tend to do so at a faster pace than

normal cells and tissues, such as the bone marrow, lining of the gastrointestinal tract, and reproductive organs, which are known for exhibiting marked sensitivity to gamma radiation, causing these tissue types to suffer radiation-induced injury. Effects on health from gamma radiation are generally divided into two categories: deterministic effects and stochastic effects. High doses above a threshold level cause deterministic effect, such as skin burns, radiation sickness, depression of the bone marrow, and damage to various organs. In contrast, there is no threshold level for the effect of stochastic effects, such as cancer or genetic effects, and the risk that these will occur increases with the dose but not with their severity. Short-term exposure to large doses of gamma radiation can cause the first symptoms of radiation sickness, which include headache, nausea, vomiting, and lack of energy, even hair loss in some cases. If present is likely to last for a few months. Chronic or protracted exposures to lower doses can also increase the risk of developing cancers (e.g., leukemia, thyroid cancer, lung & other solid tumors) that tend to develop years after exposure [5]. However, gamma radiation also has significant beneficial uses in medicine (e.g., cancer radiotherapy and diagnostic imaging) under controlled conditions. Thus, radiation protection values, justification, optimization (ALARA), and dose limitation principles are important to minimize health hazards that may be caused by ionizing gamma radiation exposure in the occupational, medical, or environmental fields.

3.8 Application of Gamma ray in Medicine

Gamma rays are also extensively used throughout the field of medicine. These properties make gamma radiation suitable for both diagnostic imaging and treatment applications, particularly in cancer diagnosis and treatment. The implementation of gamma rays, in carefully controlled circumstances, has turned out to be a clinical gift and is also consistent with safe application within the radiation protection principles.

3.8.1 Gamma Rays in Diagnostic Medicine

Gamma rays are used in diagnostic medicine because they can pass through the body and give a functional image of an organ or physiologic process. In contrast to X-rays, which provide structural imaging, gamma rays are governed by the field of nuclear medicine (although developed for analysis with X-ray or see history of cats lifter), relying on the decaying process and having intrinsic surgical applications as Hanzi [6].

A) Nuclear Medicine Imaging

Nuclear medicine imaging is a method that allows the determination of the physiological and metabolic function(s) of various organs for which gamma-emitting radionuclides have been used for diagnosis. While conventional radiology offers morphological images, i.e., pictures of the anatomy rather than its functions, nuclear medicine provides functional imaging and hence gives the opportunity for early

disease recognition at the level of the molecule and cell. In this method, a patient is injected with a radiopharmaceutical, which comprises a biologically active moiety labeled with a gamma-emitting radioisotope. The drug is formulated for selective uptake by an organ or tissue of interest, according to its metabolic or physiological performance. Decaying radionuclide subatomic particles emit gamma photons, which will leave the body and be imaged externally. The spatial distribution of the observed gamma-rays mirrors the efficacy of the organ being analyzed. Increased tracer uptake shows increased metabolism, whereas decreased uptake suggests reduced function, ischemia, or tissue necrosis. Nuclear medicine imaging plays a significant role in cardiology, oncology, neurology, endocrinology, and renal studies because of its high sensitivity to detect disease before structural changes are evident [6].

B) Gamma Camera

The gamma camera is the main imaging tool in nuclear medicine for imaging the distribution of gamma-emitting radiotracers or radionuclides ([99mTc]) within the patient. It detects the gamma photons and transforms them into an electrical signal, which is then processed to give a two-dimensional image of radiopharmaceutical distribution. A common gamma camera includes a collimator, scintillation crystal, photomultiplier tubes, and an electronic processing system. The collimator is a lead plate perforated with a large number of parallel holes that only allow gamma rays from well-defined directions to reach the detector, providing spatial information. 'Thallium-activated sodium iodide (NaI(Tl)) is placed behind the collimator to convert interacting gamma photons into pulses of visible light. These flashes of light are picked up by photomultiplier tubes that amplify the signals and turn them into electrical pulses. The coordinates and energy of each gamma event are calculated by electronic circuits in order to locate the photon interaction accurately. The cumulative detection of all these events yields a planar image representing the location of the radiopharmaceutical in the body. Gamma cameras are extremely sensitive and can image even very small amounts of radioactivity, giving them a broad range of uses for diagnosis [6,7].

C) Single Photon Emission Computed Tomography (SPECT)

Single Photon Emission Computed Tomography (SPECT) is an advanced nuclear imaging method that allows 3-dimensional functional images to be obtained beyond the ability of a conventional gamma camera. At the 2nd step, one or several gamma cameras are rotated around the patient, and thus a series of two-dimensional projections from different views is taken in SPECT. These projections are then mathematically reconstructed using reconstruction algorithms that allow for obtaining cross-sectional images of the distribution of radiotracer within the body. The

reconstructed tomographic images give better contrast for the lesion, less overlap of tissue, and more accurate lesion localization. It is most useful in cases where a particular function needs to be evaluated, as coincident with the NL functions, such as heart-muscle activity and brain blood flow. Due to its high sensitivity and 3D imaging capability, SPECT has become an indispensable diagnostic facility in contemporary nuclear medicine [7].

3.8.2 Gamma Rays in Cancer Therapy

Gamma rays have high energy and great penetrating power; they can irradiate biological tissues with a deep penetration capability for deposition. Cytotoxic gamma rays are employed in cancer treatment to kill the DNA of cancerous cells, which causes them to lose their reproductive capabilities and die. Since cancer cells are generally less effective at repairing DNA than normal cells, dead tumor cells with fewer side effects can be the goal when applying gamma rays in a targeted manner. In oncology, two clinical applications of gamma rays are External Beam Gamma Radiotherapy and Gamma Knife Radiosurgery [8].

A) External Beam Gamma Radiotherapy

External beam gamma irradiation is a commonly used standard method for cancer therapy. In this technique, gamma-radiation is produced by an external radioactive source and aimed at the tumour within the patient. Cobalt-60 is the most widely used radionuclide for this purpose, as it has emissions of two gamma rays (each with an energy of 1.17 and 1.33 MeV). These gamma rays can go inside the body; therefore, it is useful in treating tumours near the surface of the body as well as deep-seated tumours. With external beam gamma radiotherapy, the patient is properly aligned on a treatment couch and the radiation beam is shaped and directed with collimators to conform to the size and volume of the tumor. For modern treatment, planning CT, MRI, and PET scans are used to accurately delineate the tumor volume and surrounding critical structures. With the help of these images, a treatment planning system computes an optimal distribution of radiation dose that achieves maximum tumor control with minimal radiation exposure to normal tissue [8].

B) Gamma Knife Radiosurgery

The Gamma Knife radiosurgery is a very sophisticated, highly focused approach for using gamma-radiation in the treatment of cancer. Compared with standard external beam radiotherapy, Gamma Knife radiosurgery involves the administration of a deeply penetrating dose of radiation to a focal target during one session or over a small number of treatments. Though it's called "radiosurgery," there is no actual surgical cut. Instead, it is based on the accurate crossing of several gamma-ray

beams at the same point within the brain. The Gamma Knife unit is usually based on 192- or 201-Cobalt-60 sources distributed in a hemispherical shape surrounding the patient's head. Each single source emits a relatively low-dose gamma-beam, which does very little harm to normal tissue on its own. Jet's activation signal is transmitted to Dryden's false leg by highly accurate electromagnetic displacement: Shape of the field beam distribution, Beam aperture. As the target lesion, it receives that each particle contributed to the desired dosage and that all beams were delivered, focusing on this intersection. This distinct design provides a steep dose gradient, i.e, the dose drops off significantly outside of the tumor. The stereotactic localization enables sub-millimetric accuracy with the Gamma Knife radiosurgery. A rigid stereotactic frame or a thermoplastic mask is used to fixate the patient's head, and high-resolution imaging such as MRI (MR) or CT is used. The images are then fused with computerized planning, which allows the precise 3D coordinates of the lesion to be calculated. This high-level of accuracy provides for treatment to be performed on tumors, as well as vascular malformations, with little impact upon critical structures, including the optic nerves and brainstem. The biological action of the Gamma Knife surgery is mainly caused by massive DNA injury and radiation-induced vascular damage to the tumor. In the long term, it results in loss of tumor cell viability, decreased vascularity, and progressive tumor shrinkage or growth cessation. GK radiosurgery is commonly employed as a treatment for brain metastasis, meningioma, acoustic neuroma, arteriovenous malformation, and select functional disease states, including trigeminal neuralgia [9].

3.8.3 Therapeutic Nuclear Medicine (Radionuclide Therapy)

Medical applications of gamma rays are wide-ranging because of their high penetration capability and capacity to provide ionizing radiation into deep tissue. Gamma radiation is also used in medical therapy, such as radiation therapy to kill off malignant cells, and process control measures in the food industry. Its high physical characteristics provide a proper dose delivery, along with the higher demand for imaging and treatment control, have established gamma-rays as an indispensable element in modern nuclear medicine. One of the major medical uses for gamma-rays is in nuclear medicine, specifically when using various radioactive isotopes to treat thyroid cancers with iodine-131 therapy. For this purpose, gamma rays permit post-therapy imaging and whole-body scanning, which makes it possible to verify precise localisation and dose rate control of the iodine uptake by thyroid tissue or metastases. While beta radiation is responsible for most of the therapeutic effect, gamma rays are important for monitoring the treatment and ensuring safety. Gamma rays also find applications in the field of external beam radiotherapy, such as cobalt-60 therapy units and gamma knife radio surgery. In gamma knife radiosurgery, numerous individuals, focused beams of gamma rays are precisely directed at intracranial targets with the intention of delivering a high therapeutic dose to brain tumors, arteriovenous malformations, or functional disorders caused by abnormal

nerve pathways, while minimizing damage to surrounding healthy tissue. This method works best for relatively small and well-circumscribed lesions. In brachytherapy, radionuclides that emit gamma-rays like cesium-137 and iridium-192, are implanted in or around the tumor [8]. The gamma radiation delivered leaves doses in the vicinity, for example at dose levels suitable for the treatment of gynecological cancers or prostate cancer or head and neck tumors. This technique permits high tumor doses and low exposure of neighboring normal structures. Treatment planning and dosimetry. Treatment planning and dosimetry are other significant uses of gamma-emitting radionuclides in therapeutic nuclear medicine. Gamma radiation permits visualization with gamma cameras and single-photon computed emission tomography (SPECT), through which clinicians can estimate radiopharmaceutical distribution, determine patient-specific absorbed doses, and adapt therapy. This theragnostic strategy enhances therapeutic efficacy and minimizes radiation toxicity.

Gamma rays also deliver palliative therapy, being used in patients with metastatic disease. Gamma-emitting radionuclides for localizing tumor extent and monitoring therapeutic effects in the optimization of symptomatic therapy and palliative care [9].

3.8.4 Sterilization and Infection Control

Gamma-rays are important for sterilisation and infection control as they can also penetrate other forms of ionizing radiation. Medical and health-care applications: Gamma radiation is commonly employed for the sterilisation of heat-sensitive, single-use medical disposables. Dose requirements here depend on specific characteristics of the product, which has been directly or indirectly loaded with microorganisms, and tolerance to radiation dose (vaccines being treated differently from organ transplant material), but rough rules of thumb have been developed. Such a method will provide a high degree of microbial kill without physical damage to the sterilized articles. Gamma sterilization is effective by the creation of ionization and excitation in biological molecules, such as DNA. When gamma photons are absorbed by microorganisms, water radiolysis occurs and the generation of free radicals results in irreversible damage to DNA and cellular structures in microorganisms. This damage also inactivates the reproduction of the microorganisms, thus sterilizing them. Gamma rays are lethal to a wide variety of pathogens, from bacteria and viruses to fungi and spores. One of the major benefits of gamma sterilization is the deep penetration and uniform dose through packaged products. This makes it possible to sterilize medical instruments in the final packaging, reducing the risk of re-contamination. Frequently sterilized items with gamma rays are needles, disposable medical instruments, prosthetic and orthotic devices used in human bodies (comprising bone implants), as well as the aforementioned food. Gamma rays are being utilized for sterilization in hospitals, medical facilities, and the food industry. It

is frequently used for sterilizing laboratory equipment, biological tissues, pharmaceuticals, and vaccines, where no heat or other thermodynamic process would be desirable. In blood banks, gamma irradiation is used to deactivate lymphocytes in donated blood components so as to lower the risk of transfusion-mediated graft-versus-host disease. Gamma-ray sterilization has several potential advantages over chemical and thermal methods (e.g., low processing temperature, high reliability, and accurate dosimetry). However, stringent radiation safety measures must be considered to ensure the safety of operators and the environment, and some materials may suffer from radiolytic degradation at high doses [10].

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Chapter 4
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Application of Radioisotopes in Medicine

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4.1 Introduction

Medical radioisotopes constitute the foundational backbone of modern nuclear medicine, enabling clinicians to transform the invisible processes of cellular metabolism, organ perfusion, receptor expression, and molecular signaling into quantifiable diagnostic images or potent therapeutic actions. A medical radioisotope is an unstable nuclide that emits ionizing radiation typically gamma photons, positrons, beta particles, or alpha particles allowing physicians to track physiological processes or selectively destroy pathological tissues. Combo PC The coupling of a radionuclide to a biologically active molecule allows real-time imaging of organ function, detection of disease at the molecular level, and targeting tumors with irradiation that can be focused to sub-millimeters with minimal collateral damage [1]. The use of radioisotopes, as it developed in medicine soon after the discovery of radioactivity, is a paradigm example for the migration process that began from simple tracer studies to molecular imaging techniques. In the 1960´s, with the implementation of technetium-99m (^{99m}Tc) a new era in functional imaging was initiated, and cyclotron-produced positron emitters brought PET into routine use for both metabolic and biochemical characterization of disease to an extent not possible before. Now, the modality has evolved to hybrid imaging (SPECT/CT, PET/CT, PET/MRI) and to theranostics with the matching of diagnostic and therapeutic isotopes for individualized treatment [2]. The clinical utility of any particular radioisotope is dependent on the nuclear decay characteristics (half-life, photon energy, emission type), as well its chemical properties in vivo. Short-half-life positron emitters, e.g. ^{18}F, provided detailed resolution in metabolic imaging and beta or alpha isotopes emitting radioisotopes (e.g. ^{131}I, ^{177}Lu and ^{225}Ac) were used in therapy due to its spectacular specificity towards cancerous cells. Radiopharmaceuticals are prepared by sophisticated radiochemical procedures which guarantee high purity, stability and specific biodistribution, so the radiopharmacy or nuclear medicine discipline is multidisciplinary in nature, involving nuclear physics, chemistries of living organisms (medicinal chemistry), radiobiology, and clinical pharmacology [3]. Three primary clinical uses of medical radioisotopes are in use that include:

1. Functional Imaging: Images of disease through what it is doing.
2. Quantitative analysis of organs' function, perfusion, or metabolic rate.

3. Selective irradiation of only pathological tissue while sparing healthy surrounding tissue with targeted radionuclide therapy.

With the growing tendency of precision medicine and personalized medicine in global health care systems, the requirements for advanced radioisotopes are more and more urgent. Their fundamental value is reflected through their applications in oncology, cardiology, neurology, endocrinology, and advanced molecular therapies. Production, classification, diagnostics, therapeutics, and biodistribution of medical radioisotopes will be discussed in detail in the further sections of this chapter [3].

4.2 Radiopharmaceutical Production and Quality Control

Radiopharmaceuticals manufacture is a highly technical and safety-critical activity in contemporary medical practice. These entities are cointegrates of a radioactive nuclide and a naturally occurring biologically active molecule, which is able to be directed at particular physiological pathways, meaning their clinical activity will entirely depend on the accuracy, make-up, and reproducibility in synthesis. Given that radiopharmaceuticals are administered directly to patients, typically by intravenous injection, and that they include radionuclides, which are inherently unstable and undergo decay while in storage, production processes must adhere to extremely stringent standards of nuclear physics, radiochemistry, drug manufacturing, and regulation all at the same time [1].

4.2.1 Sources of Radioisotopes:

Sources of medical radioisotopes are mainly nuclear reactors or particle accelerators (cyclotrons), both having nuclides with specific characteristics relevant for clinical purposes (Figure 4-1) [3]. Reactor-produced isotopes like ^{131}I, ^{99}Mo (the parent of ^{99m}Tc), or ^{177}Lu are generally produced by neutron activation, meaning that stable atoms have to take up neutrons and be transformed into radioactive ones. These isotopes generate primarily beta and gamma radiation, for therapeutic and diagnostic purposes, respectively [3]. Cyclotron produced isotopes, in contrast, are generated when charged particles (e.g., protons or deuterons) bombard a target nucleus. This method enables production of short-lived positron emitters like ^{18}F, ^{11}C, ^{13}N, and ^{15}O, which are essential for PET imaging. Because of their extremely short half-lives minutes in many cases cyclotrons must be located near the imaging facilities, supported by automated radiochemical modules capable of synthesizing compounds within very constrained time frames [3].

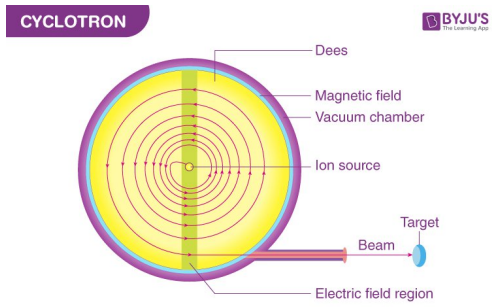

Figure (4-1). Schematic Diagram of Cyclotron Structure and Target System

4.2.2 Radiochemical Synthesis and Labeling:

Once the radionuclide is generated, it must be incorporated into a suitable carrier molecule. This process may involve chelation (as in ^{99m}Tc-based compounds), covalent bonding (as in ^{18}F-FDG), or encapsulation in nano or micro-particles. The chemical stability of the radiolabeled compound determines the accuracy of imaging or therapy, as any in vivo breakdown can lead to mis distribution of radioactivity [3].

Automated synthesis modules are used to minimize radiation exposure to workers and to ensure reproducibility. These “hot cells” (see Figure 4-2) maintain negative pressure, shielding, isolation airflow, and lead-glass viewing panels conditions required for working safely with high-activity radionuclides [3].

Figure (4-2). Automated Radiopharmacy Hot Cell for Radiochemical Synthesis

4.2.3 Good Manufacturing Practice (GMP) in Radiopharmaceutical Production

Radiopharmaceuticals are produced under Good Manufacturing Practice (GMP) conditions, ensuring that each batch is consistent in quality, safety, and efficacy (Figure 4-3). These GMP standards require [3]:

- **Classified clean room environments** with strict particle and microbial controls.
- **Aseptic handling techniques** because radiopharmaceuticals are sterile injectable drugs.
- **Validated production workflows**, ensuring every synthesis step is reproducible and traceable.
- **Batch record documentation**, providing a complete history of each produced dose.
- **Environmental monitoring** to prevent contamination by particulates or microorganisms.

Because of the short half-lives involved, radiopharmaceutical GMP emphasizes rapid testing, real-time release mechanisms, and automated quality control systems [3].

Figure (4-3). "GMP-Certified Radiopharmacy Clean Room Layout

4.2.4 Quality Control (QC) Testing of Radiopharmaceuticals:

Quality control is essential to ensure that each radiopharmaceutical meets regulatory standards before being released for patient administration Core QC parameters include [6] (Figure 4-4).

a. Radiochemical Purity (RCP)

Ensures that the administered dose contains the intended chemical compound, not free radionuclide or unwanted byproducts. High performance liquid chromatography (HPLC), thin layer chromatography (TLC), and electrophoresis are commonly used [6].

b. Radionuclidic Purity

Confirms that only the desired isotope is present, with no contaminating nuclides Gamma spectroscopy is employed to analyze the emitted energy peaks [7].

c. Chemical Purity

Assesses the concentration of non-radioactive impurities, residual solvents, heavy metals and precursor molecules [7].

d. PH Measurement & Osmolality

Ensures patient safety during injection and compatibility with blood components [7].

e. Sterility and Endotoxin Testing

All parenteral radiopharmaceuticals must be sterile and pyrogen free. Because results for sterility testing require days, radiopharmacies use parametric release procedures that allow doses to be administered immediately after other QC parameters are satisfied [1].

f. **Specific Activity and Concentration**

Monitors the amount of radioactivity per unit mass of carrier molecule, essential for receptor-based imaging [1].

Figure (4-4). Radiopharmaceutical QC Setup Including HPLC

4.2.5 Packaging, Dispensing and Radiation Safety

After QC approval, the radiopharmaceutical is dispensed into lead shielded containers (Figure 4-5) using calibrated dose calibrators. Each dose is labeled with [8]:

- Radionuclide name
- Activity and calibration time
- Volume
- Expiration time
- Patient or batch identification

Radiation protection principles are applied rigorously during dispensing, including time minimization, distance maximization, and shielding. Dose calibrators and survey meters ensure accurate activity measurement and radiation containment [8].

Figure (4-5). Lead-Shielded Dose Vial and Dose Calibrator Station

4.2.6 Regulatory Oversight and International Standards

Radiopharmaceutical production is governed by multiple regulatory organizations, such as [3]:

- **IAEA** (International Atomic Energy Agency)
- **FDA** (Food and Drug Administration) for the United States
- **EMA** (European Medicines Agency)
- **Pharmacopoeias** (USP, EP, BP)

These bodies define purity criteria, allowable limits of impurities, and all mandatory testing procedures. Because of their radioactive nature, radiopharmaceuticals also fall under nuclear regulatory frameworks, requiring secure handling, waste management, and detailed activity logs [3].

4.3 Diagnostic Radioisotopes in Nuclear Medicine

Gamma-emitting diagnostic radioisotopes are the cornerstone of nuclear medicine imaging technology and have provided clinicians with the capability to visualize physiological, metabolic , and molecular processes with unprecedented sensitivity. The advantage is that, unlike anatomical imaging with CT or MRI, diagnostic radionuclides allow visualization from function rather than structure, and the visualization of disease very early in the course of its development, even before any structural abnormalities may occur. These have several attributes of interest for imaging, but the key to the suitability of a diagnostic isotope includes: emission of photons that can be detected externally, a half-life long enough to carry out and complete imaging, but not so long as to limit patient exposure, chemically amenable for radiolabeling, and predictable biodistribution [1]. SPECT imaging employs gamma emitters (e.g., technetium-99m, iodine-123), whereas positron emitters are used in the formation of PET images (e.g., fluorine-18, carbon-11, nitrogen-13, oxygen-15). The decay characteristics of each radionuclide dictate its use within an imaging system and for what clinical purpose [3].

4.3.1 Technetium-99m Applications

Technetium-99m (^{99m}Tc) is the most widely used diagnostic isotope in the world, accounting for nearly 80% of all nuclear medicine procedures. Its dominance arises from a unique combination of favorable physical and chemical characteristics. With a half-life of 6 hours and a pure 140 keV gamma emission (Figure 4-6), it provides excellent imaging quality with low radiation dose. Additionally, ^{99m}Tc can be attached to a wide range of pharmaceuticals through diverse chelation chemistries, enabling targeting of the skeleton, brain, kidneys, liver, myocardium, and tumor tissues [4].
Common clinical applications include:

- Bone scintigraphy using ^{99m}Tc-MDP or HDP to detect fractures, metastases, and infection.
- Myocardial perfusion imaging with ^{99m}Tc-sestamibi or tetrofosmin.
- Renal imaging using ^{99m}Tc-MAG3 or DTPA.
- Hepatobiliary imaging with ^{99m}Tc-HIDA tracers.

- Detection of sentinel lymph nodes in oncology.

Technetium's chemistry makes it adaptable to numerous targeting molecules which explains its continued relevance even with the expansion of PET technologies [5].

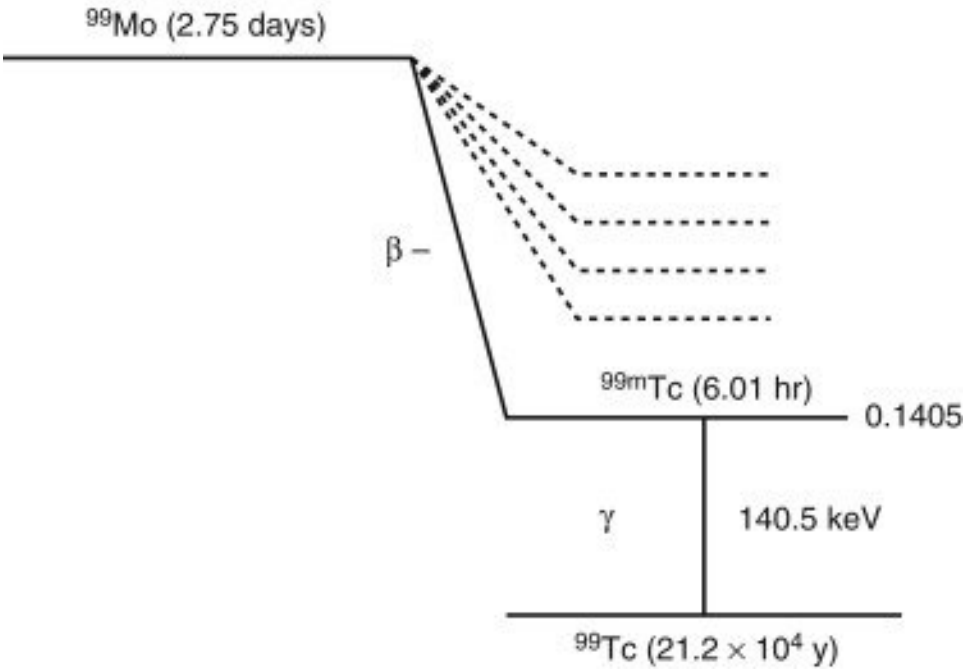

Figure (4-6). Technetium-99m Decay Scheme and ^{99}Mo/^{99m}Tc Generator

4.3.2 PET Isotopes:

Positron emitting isotopes underpin the technology of positron emission tomography (PET) (Figure 4-7), a modality known for extremely high sensitivity and quantitative accuracy. After positron emission, annihilation photons form a pair of 511 keV gamma rays detected in coincidence, yielding precise localization of radiotracer distribution [8].

4.3.2.1 ^{18}F (Fluorine-18):

With a half-life of 110 minutes and favorable nucleophilic substitution chemistry, ^{18}F is ideal for producing metabolic tracers such as ^{18}F-FDG, the global standard for

oncologic PET imaging. ^{18}F-labeled compounds also target cardiac viability, brain glucose metabolism, inflammation, and neurodegenerative disorders [6].

4.3.2.2 ^{11}C (Carbon-11):

^{11}C has a very short half-life (20 minutes), requiring on site cyclotron production. It integrates seamlessly into biomolecules because carbon is a universal element in organic chemistry This allows synthesis of physiologic tracers including ^{11}C-methionine, ^{11}C-acetate, and ^{11}C-raclopride, essential in neuroimaging and metabolic studies [23].

4.3.2.3 ^{13}N (Nitrogen-13):

Produced as ^{13}N-ammonia, this isotope plays a central role in myocardial perfusion PET Its rapid uptake and enzymatic trapping in myocardial tissue make it a gold standard marker of coronary flow reserve and ischemia [1].

4.3.2.4 ^{15}O (Oxygen-15):

With a half-life of just 2 minutes, ^{15}O is used for cerebral blood flow, oxygen metabolism, and perfusion studies. Its biological relevance oxygen being essential to cellular respiration allows unparalleled quantitative assessment of brain physiology [3].

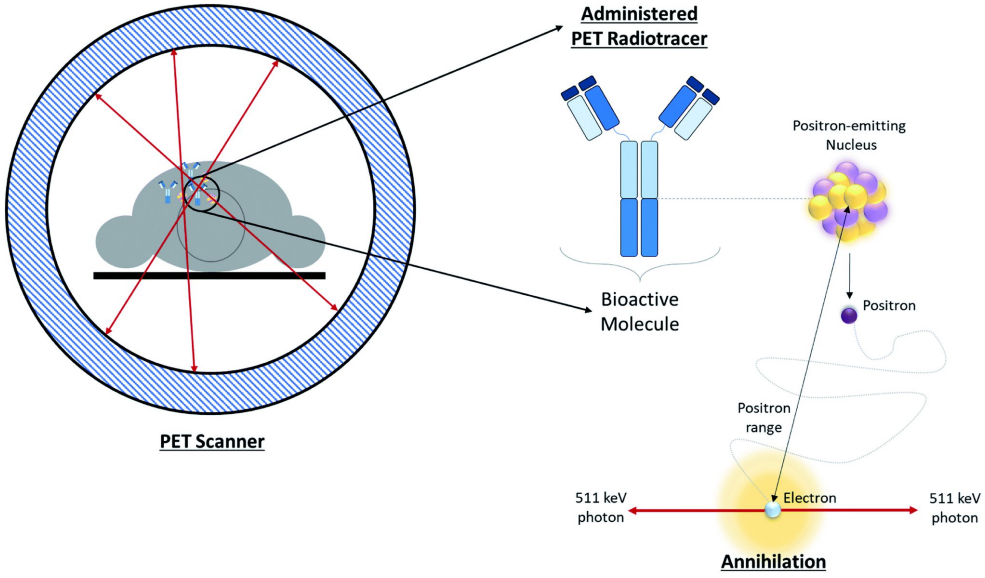

Figure (4-7). PET Isotopes Production Scheme and Annihilation Coincidence Detection

4.4 Therapeutic Radioisotopes:

Therapeutic radioisotopes have emerged as a hallmark of contemporary nuclear medicine approaches that offer localized radiation treatment of diseased tissues with relatively low exposure to nearby healthy tissue. The therapeutics produce beta particles (β^-), alpha particles (α), Auger electrons or conversion electrons, and are, as opposed to the diagnostic isotopes, not producing photons that can be used for external imaging. These releases result in DSBs, oxidative stress, and apoptosis, thereby preferentially eliminating tumoral or hyperfunctioning tissue [9].

The selection of a therapeutic isotope is influenced by several factors, which include half-life, particle energy, range, chemical stability, and potential for specific binding to molecular targets such as receptors, antigens, or metabolic pathways. Recent progress in radiochemistry and molecular oncology has accelerated the development of radiotherapeutic agents and converted some earlier 'incurable' cancers into lesions that can be locally controlled or treated systemically with radionuclide therapy (TRT) [10].

4.4.1 Radioiodine Therapy (^{131}I):

Radioiodine therapy using iodine-131 (^{131}I) is one of the oldest and most successful forms of targeted radionuclide therapy. Due to the thyroid gland's natural ability to trap and organify iodine, ^{131}I selectively concentrates within thyroid tissue, enabling precise treatment of hyperthyroidism and differentiated thyroid cancer[11].

4.4.1.1 Physical and Radiobiological Properties:

Iodine-131 has a half-life of 8.02 days and emits both β^- particles (average energy 192 keV) and γ-rays (364 keV). The β^- emissions produce therapeutic action by inducing local cellular damage, while the γ emissions allow for post-therapy imaging and dosimetry [11].

4.4.1.2 Clinical Applications:

a. Hyperthyroidism:

^{131}I is the treatment of choice for Graves' disease, toxic multinodular goiter, and toxic adenoma. The administered dose results in selective destruction of hyperfunctioning thyroid tissue, restoring euthyroid status in most patients [12].

b. Differentiated Thyroid Cancer (DTC):

Post-thyroidectomy ^{131}I ablation is used to eliminate residual thyroid tissue and treat metastatic lesions, with demonstrated improvements in recurrence-free survival and long-term disease control [13]. The therapy targets:

- residual thyroid remnants,
- cervical lymph-node metastases,
- pulmonary metastases,
- osseous metastatic lesions.

4.4.1.3 Mechanism of Action:

- Uptake through the sodium-iodide symporter (NIS), see Figure 4-8.
- Organification and storage in thyroglobulin
- Local emission of β^- particles leading to cell death via DNA damage

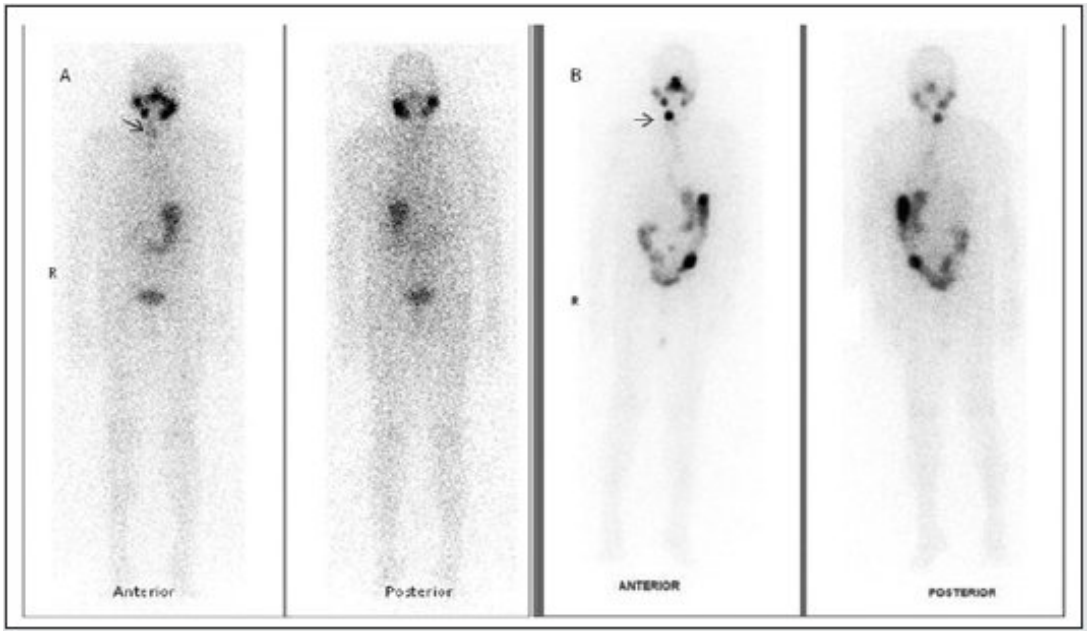

Figure (4-8). 131-I uptake and distribution inside thyroid follicles showing NIS-mediated transport.

4.4.2 Radiopharmaceuticals for Cancer Therapy:

Therapeutic radiopharmaceuticals have expanded dramatically beyond iodine, with multiple isotopes now used for tumor-targeted therapies. These agents exploit

molecular markers, tumor perfusion metabolic pathways or receptor overexpression to deliver cytotoxic radiation directly to cancer cells [14].

4.4.2.1 β-Emitting Therapeutic Isotopes:

a. Lutetium-177 (^{177}Lu)

^{177}Lu is widely used in peptide receptor radionuclide therapy (PRRT), especially for neuroendocrine tumors (NETs). It binds to somatostatin receptors (SSTR2) via radiolabeled peptides such as ^{177}Lu-DOTATATE, delivering β-radiation with a tissue penetration of 0.2–2 mm—ideal for small tumors [15].

Applications:

- Gastroenteropancreatic NETs
- Pheochromocytomas/paragangliomas
- Metastatic SSTR-positive tumors

b. Samarium-153 (^{153}Sm-EDTMP):

^{153}Sm is used for bone pain palliation in patients with metastatic prostate, breast, or lung cancer. Its affinity for hydroxyapatite allows targeted delivery to skeletal metastatic lesions [16].

c. Yttrium-90 (^{90}Y):

Used in radioimmunotherapy (e.g., ^{90}Y-ibritumomab tiuxetan for lymphoma) and selective internal radiation therapy (SIRT) for liver tumors. The high-energy β emissions are effective for bulky tumors [17].

4.4.3 α-Emitting Therapeutic Isotopes:

Alpha therapies have gained prominence due to their high linear energy transfer (LET) and extremely short tissue range (50–100 μm), enabling destruction of individual cancer cells while sparing surrounding tissue [18].

a. Radium-223 (^{223}Ra):

^{223}Ra is FDA-approved for metastatic castration-resistant prostate cancer (mCRPC) with bone metastases. It mimics calcium and localizes in regions of active bone turnover [18].

b. Actinium-225 (^{225}Ac)

^{225}Ac-labeled agents (e.g., ^{225}Ac-PSMA-617) show remarkable promise in treating prostate cancer, including cases resistant to β-emitter therapy [19].

4.5 Biodistribution and Pharmacokinetics of Medical Radioisotopes

The biodistribution and pharmacokinetics of medical radioisotopes define how radiopharmaceuticals behave inside the body: how they are absorbed, transported, accumulated, metabolized, and ultimately eliminated. Understanding these parameters is essential for optimizing diagnostic image quality, maximizing therapeutic effectiveness, and ensuring radiation safety for both patients and healthcare workers [20].

Unlike conventional pharmaceutical agents, radiopharmaceuticals possess a *dual nature*:

1. **A chemical/drug component**, which determines biological targeting and organ specificity.
2. **A radionuclide component**, which contributes physicochemical properties that dictate radioactive decay, penetration range, and dosimetric distribution.

This duality makes pharmacokinetic modeling unique for radiopharmaceuticals, requiring integration of molecular biology, physiology, nuclear physics, and tracer kinetics [21].

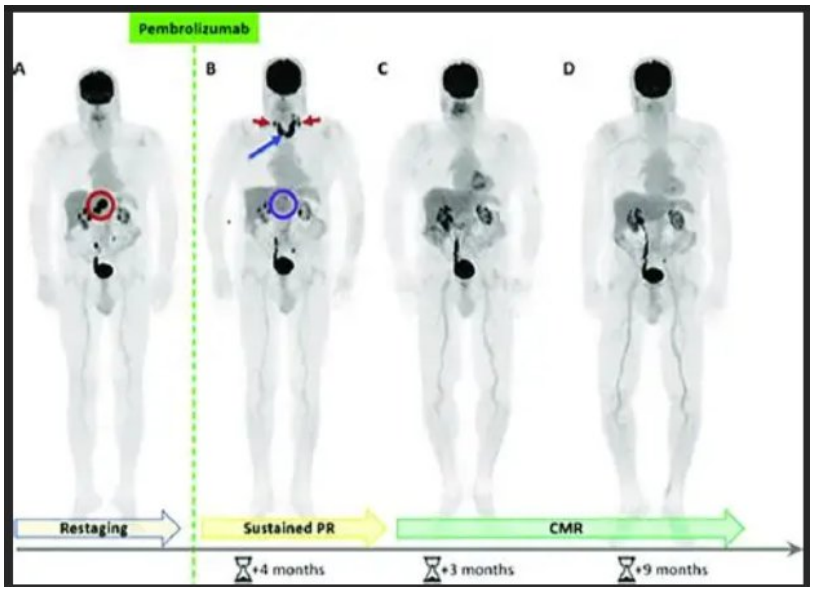

Figure (4-9). distribution of radiopharmaceuticals in major organs

4.5.1 Mechanisms of Radiopharmaceutical Distribution:

Biodistribution is primarily governed by the biochemical characteristics of the ligand and its interaction with specific cellular or molecular targets. Several mechanisms influence how radioisotopes accumulate in various tissues:

a. Receptor-Mediated Targeting:

Many therapeutic agents such as ^{177}Lu-DOTATATE or ^{90}Y-ibritumomab bind to overexpressed receptors on tumor cells. These ligand–receptor interactions enable selective targeting, internalization, and high tumor uptake [22].

b. Metabolic Incorporation:

Some radiotracers mimic natural substrates and become incorporated into metabolic pathways.

Example: ^{18}F-FDG, which follows glucose metabolic pathways and accumulates in high-glycolytic tumors [14].

c. Ion Transport Systems

Isotopes resembling physiological ions follow endogenous transport mechanisms. Example: ^{131}I, which is trapped by the sodium iodide symporter (NIS) in thyroid tissue [11].

d. Physiologic Perfusion and Capillary Permeability

Highly vascular organs (kidneys, liver, lungs) rapidly receive circulating radiotracers, demonstrating perfusion-dependent early uptake [11].

4.5.2 Pharmacokinetic Modeling:

Pharmacokinetic modeling for radiopharmaceuticals seeks to quantify how a tracer moves between physiological compartments blood plasma, target tissue, non-target organs and elimination pathways and to translate those kinetic behaviors into meaningful parameters for imaging interpretation and dosimetry The two principal modeling approaches are compartmental modeling and non-compartmental analysis, each serving different clinical and research needs [11].

4.5.2.1 Compartmental Models

Compartmental models conceptualize the body (or a region of interest) as a system of interconnected compartments through which tracer exchanges occur at definable rates. In its simplest form a one-tissue compartment model describes tracer transfer from plasma into a single tissue compartment and back; a two-tissue (or multi-tissue) model subdivides the tissue space into reversible and irreversible binding or metabolite compartments. Rate constants commonly denoted as K_1 (influx from plasma to tissue), k_2 (efflux back to plasma), k_3 (binding or trapping), and k_4 (dissociation) parameterize these flows. Estimating these constants requires solving sets of differential equations that describe tracer mass balance over time and fitting them to dynamic imaging data (time activity curves) obtained from serial PET or SPECT frames [22].

The input function (typically arterial plasma activity vs. time) is essential for absolute quantification; where arterial sampling is impractical, image-derived input functions or population-based curves are used with appropriate corrections. From the fitted rate constants we derive physiologically interpretable metrics: K_1 often reflects tissue perfusion and extraction; k_3 may represent irreversible metabolic trapping or receptor internalization; residence time (the integral of activity over time in a compartment) links directly to absorbed dose calculations. Compartmental

modeling supports advanced analyses such as Patlak graphical methods (for irreversible tracers) and Logan plots (for reversible systems), enabling both kinetic insight and improved quantification beyond simple standardized uptake values (SUVs). Because compartmental models map kinetic parameters to biological processes, they are invaluable in tracer development, therapy planning and individualized dosimetry [22].

4.5.2.2 Non-Compartmental Analysis

Non-compartmental analysis (NCA) provides a model-independent approach appropriate when tracer behavior is complex, heterogeneous, or when a mechanistic compartmental description is unwarranted. NCA concentrates on summary measures extracted directly from the observed time–activity curves, avoiding explicit assumptions about compartment number or inter-compartmental flows. Key parameters include the area under the curve (AUC), which represents the total exposure of tissue to radioactivity over time; the mean residence time (MRT), indicating the average time a tracer molecule resides within the body or a specific organ; and the effective half-life, which combines the physical decay of the radionuclide with biological clearance to indicate how quickly activity decreases in vivo [22].

4.5.3 Biokinetics of Diagnostic vs. Therapeutic Radioisotopes

Biokinetics how a radiopharmaceutical is taken up, retained and cleared differs fundamentally between diagnostic and therapeutic agents because their clinical goals diverge: diagnostics aim for rapid, high-contrast imaging with minimal dose, while therapy aims for prolonged, high-absorbed dose in target tissue [9].

Diagnostic radiopharmaceuticals are engineered for quick delivery to target organs followed by rapid clearance from non-target tissues to maximize target to background ratios. Short effective half-lives reduce radiation burden and allow repeated studies or outpatient workflows. For example, Tc-99m exhibits fast blood clearance and renal or hepatobiliary elimination depending on the ligand, which yields clear organ images within hours and limits whole-body dose PET tracers such as ^{18}F-FDG are designed to be taken up into glucose-metabolizing cells and then trapped intracellularly, providing a practical imaging window within a few hours after injection [9].

Therapeutic radiopharmaceuticals, by contrast, require extended residence within the tumor or diseased tissue to deposit sufficient ionizing energy to kill cells. This may be achieved by using radionuclides with longer physical half-lives (e.g., ^{131}I, ^{177}Lu), by selecting vectors that internalize and are retained in cells (e.g., peptide-receptor internalization for PRRT), or by leveraging high LET emitters (alpha particles) whose dense energy deposition yields effective cytotoxicity even with shorter physical half-lives. A therapeutic agent such as ^{177}Lu-DOTATATE

demonstrates prolonged tumor residence and favorable tumor-to-kidney ratios when appropriately dosed and administered, enabling effective PRRT while allowing predictable organ dosimetry [14].

Understanding these biokinetic differences is essential for timing imaging windows, selecting radionuclide properties, determining patient preparation (e.g., fasting, hydration, thyroid blockade), and for accurate dosimetry required by regulatory and clinical protocols [14].

4.5.4 Routes of Excretion

Routes of excretion determine both the duration of organ exposure and strategies for radiation protection of patients, caregivers and wastewater systems. The three primary elimination pathways renal, hepatobiliary (fecal), and respiratory/exhalation each carry distinct implications (Figure 4-10) [24]:

- Renal excretion: Small, hydrophilic radiotracers are filtered and/or secreted by the kidneys and eliminated in urine. Rapid renal clearance reduces background activity and often lowers whole-body dose, but it increases urinary radioactivity that requires patient hydration and, in some protocols, voiding regimens to minimize bladder dose. Examples include ^{18}F-FDG and many ^{68}Ga-labeled peptides. Renal impairment markedly prolongs residence time and elevates absorbed dose to both kidneys and bladder, necessitating dose adjustments and careful monitoring.
- Hepatobiliary excretion: Lipophilic tracers or larger molecules that undergo hepatic metabolism are secreted into bile and eliminated via feces. This pathway prolongs gastrointestinal residence and can complicate interpretation of abdominal imaging due to intestinal activity (e.g., Tc-99m-MIBI shows hepatobiliary clearance). Hepatobiliary excretion also poses different environmental release considerations because fecal waste may contain radioactivity requiring controlled disposal.
- Respiratory/exhalation routes: Volatile radionuclide species or tracers that yield gaseous metabolites may be partially exhaled. An example is ^{13}N-ammonia, which can be eliminated via the lungs. Respiratory elimination has implications for room ventilation, airborne contamination control in radiopharmacies and imaging suites, and staff protection.
- Gastrointestinal excretion (specific context): For large particulates or radiolabeled embolic agents used in liver SIRT, fecal excretion can be slow and variable, affecting both dosimetry and patient-to-environment transfer of activity.

Each excretion route informs clinical protocols for patient preparation (hydration, bowel cleansing), timing of imaging, post therapy radiation safety instructions (time to avoid close contact with vulnerable individuals), and environmental controls to limit radioactive release into sewage and the biosphere.

Regulatory guidance (e.g., ICRP) prescribes monitoring and constraints tailored to these pathways [24].

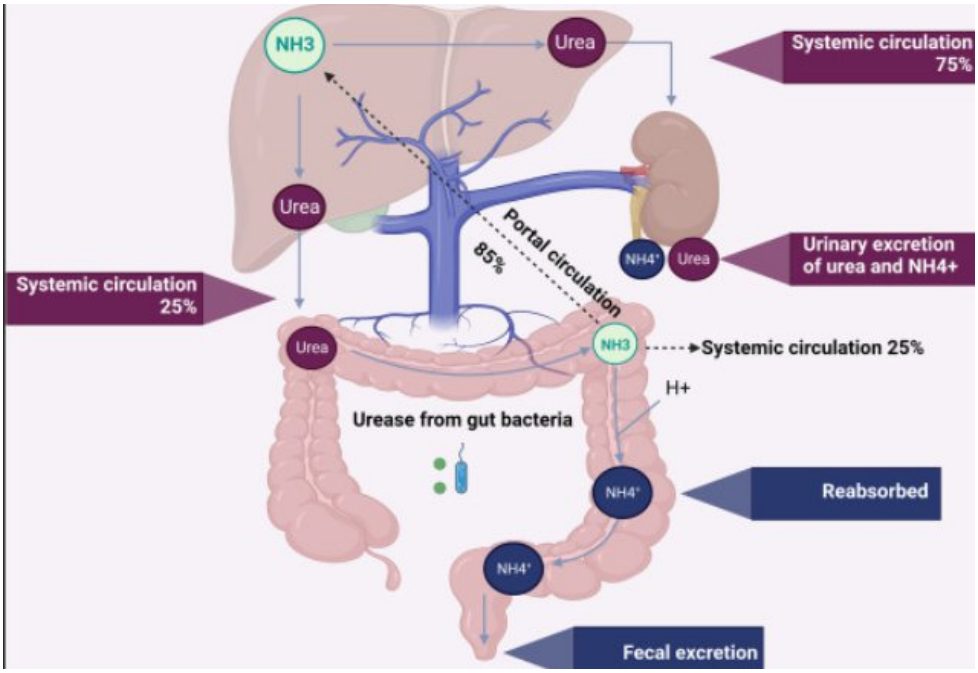

Figure (4-10). Major excretion pathways for therapeutic and diagnostic radioisotopes

4.5.5 Factors Affecting Biodistribution

Biodistribution is not static; it is shaped by an interplay of physicochemical properties of the radiopharmaceutical, patient physiology, and disease characteristics. A mechanistic appreciation of these factors enables rational tracer selection and individualized dosimetry:

- **Molecular size and conformation:** large molecules (antibodies, nanoparticles) remain intravascular longer, exhibit slower extravasation into interstitial spaces, and often have prolonged circulation times that favor certain targeting strategies (e.g., radioimmunotherapy). Small molecules reach tissue compartments more rapidly but may clear faster, impacting both imaging windows and therapeutic dosing [14-24].
- **Charge and lipophilicity:** Ionized or highly polar compounds have limited membrane permeability and may distribute primarily in extracellular fluids.

Lipophilic agents cross membranes more readily, may undergo hepatic metabolism, and often show higher non-specific binding, which can both help and hinder imaging contrast [14-24].

- **Plasma protein binding:** High protein binding increases apparent circulation time and reduces free fraction available for target uptake, altering apparent K_1 and effective bioavailability. In therapeutic settings, protein binding can either sequester radioactivity away from targets or provide a depot effect prolonging exposure [14-24] .
- **Disease states and organ function:** Renal failure, hepatic dysfunction, inflammation and ischemia modify tracer clearance and uptake. For example, reduced renal clearance increases systemic residence, which raises radiation dose to non-target organs and may necessitate altered administered activities [14-24].
- **Tumor heterogeneity and microenvironment:** Variations in perfusion, hypoxia, interstitial pressure, and receptor expression across tumor regions affect tracer delivery and retention. Heterogeneous uptake complicates dosimetry and may require voxel based or lesion-level analyses to capture true absorbed dose distribution [14-24].
- **Physiological competition and dietary factors:** Endogenous substrates or dietary iodine can compete with radiotracers. A classic example is high dietary or pharmaceutical iodine intake reducing thyroidal uptake of ^{131}**I**, thereby diminishing therapeutic efficacy; hence, iodine restriction and preparation protocols (e.g., low-iodine diet, thyroid hormone manipulation) are standard before radioiodine therapy [14-24].
- **Pharmacogenomics and receptor polymorphisms:** Individual genetic differences may alter receptor density, enzyme activity, or transporter function, producing interpatient variability in biodistribution that has implications for personalized radionuclide therapy [14-24].

Understanding and, where possible, controlling these factors improves image interpretation, optimizes therapeutic indices, and reduces unintended radiation to healthy tissues. Pre-administration assessments (renal/liver tests, medication review, dietary guidance) and patient-specific dosimetry are recommended best practices to account for these variables [14-24].

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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