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Nuclear and Radiological Safety Principles and Practice of Nuclear Pharmacy

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Abbreviations

Abbreviation	Description
ALARA	As Low As Reasonably Achievable
Al^{3+}	Aluminium
ALT	Alanine transaminase
ANC	Absolute neutrophil count.
APhA	American Pharmacists Association
ASHP	American Society of Health-System Pharmacists
BAT	Brown Adipose Tissue
BCNU	1,3-bis (2-chloroethyl)-1-nitroso-urea (also known as carmustine)
BSC	Biological Safety Cabinet
BUD	Beyond-Use Date
CT	Computerized Tomography
DNA	Deoxyribonucleic Acid
DTP	Drug Therapy Problem
DUE	Drug use Evaluation
DUR	Drug use Review
ECOG	Performance Status Assessment by Using ECOG (Eastern Cooperative Oncology Group)
EPVC	Egyptian Pharmaceutical Vigilance Centre
FDA	The Food and Drug Administration
GBq	Gigabecquerel (radioactive unit)*
GFR	Glomerular filtration rate
GM	Geiger-Muller Counters
GMP	Good Manufacturing Practice
Gy	Gray (Unit of radiation absorbed dose)**
HAMA Reaction	Human Anti-Mouse Antibody Reaction
HEPA	High-Efficiency Particulate Air
IAEA	The International Atomic Energy Agency
ISO	International Organization for Standardization
IV	Intravenous
kBq	kilobecquerel (radioactive unit)*
keV	kilo electron volt (unit of energy used in atomic and nuclear physics)
LAF	Laminar Air Flow
LAFW	Laminar Air Flow Workbench
LFC	Laminar Flow Cabinet
MAA	Macro Aggregated Albumin
Mab	Monoclonal antibody
MBq	Megabecquerel (radioactive unit)*
mCi	Millicurie (radioactive unit)*
mCRPC	Metastatic Castration-Resistant Prostate Cancer
Mg^{2+}	Magnesium
mGy	Milligray (Unit of radiation absorbed dose)*
MRI	Magnetic Resonance Imaging
NHL	Non-Hodgkin's Lymphoma

PEC	Primary Engineering Control
PET	Positron Emission Tomography
PPE	Personal Protective Equipment
PSMA	Prostate-Specific Membrane Antigen
P&T committees	pharmacy-and-therapeutics (P&T) committees
QA	Quality Assurance
QC	Quality Control
rad	Unit of radiation absorbed dose**
RBC	Red Blood Cell
RDRCs	The Radioactive Drug Research Committee
rem	(Roentgen equivalent man) unit of dose equivalent of radiation**
RES	Reticuloendothelial system
RIT	RadioImmunoTherapy
RPO	Radiation Protection Officer
SC	Sub-Cutaneous
SPECT	Single-Photon Emission Computed Tomography
SOPs	Standard Operating Procedure
SRPA	Segregated Radiopharmaceutical Processing Area
SSKI	Saturated Solution of Potassium Iodide
Sv	(The sievert) unit of radiation equivalent dose **
TSH	Thyroid Stimulating Hormone
ULN	Upper limit normal
Vs	Versus

*** Radioactive units.**

1 millicurie (mCi) = 37megabecquerels (MBq)

1 curie = 3.7 x 10^{10} Bq.

Note:

kBq (kilobecquerel), MBq (megabecquerel), and GBq (gigabecquerel).

1 kBq = 1000 Bq, 1 MBq = 1000 kBq, 1 GBq = 1000 MBq.

****Radiation absorbed and equivalent doses.**

1Sv=100 rem

1rem =1rad

1Gy=100 rad

Glossary

Term	Definition
Administration	"The direct and immediate application of a radiopharmaceutical to a patient by injecting, infusing, ingesting, or otherwise providing a radiopharmaceutical in its final form".
Approved or Registered radiopharmaceuticals	"Radiopharmaceuticals approved or registered by competent authorities, for example, the Food and Drug Administration (FDA), and national authorities, should not be compounded".
Aseptic processing or preparation	"A process by which separate, sterile components (e.g., drugs, containers, or closures) are brought together under conditions that maintain sterility".
Becquerel (Bq)	"The unit of radioactivity. One becquerel equals one disintegration per second".
Beyond-use date (BUD)	"The assigned date and time beyond which the radiopharmaceutical must not be administered".
Biological half-life	**"**The taken time for the quantity of material in a specified tissue, organ, or region of the body (or any other specified biota) to half as a result of biological processes".
Biological Safety Cabinet (BSC) Class II	"A ventilated cabinet with an open front and inward and downward unidirectional HEPA-filtered airflow and HEPA-filtered exhaust".
Cold kit-based radiolabeling	"It is considered a closed procedure, consisting of preparing a sterile radiopharmaceutical by adding a sterile eluate to a sterilized close vial containing a set of sterile, lyophilized ingredients via a system close to the atmosphere".
Curie (Ci)	"The radioactivity unit defined as 3.7×10^{10} disintegrations per second".
Dispensing	"The manipulation or labeling of a radiopharmaceutical to render it in its final form for administration, typically obtained from a single-dose or multiple-dose container (e.g., withdrawing a volume of finished product or preparation from a vial into a syringe)".
Expiration date	"The specified date (and time) beyond which the product must not be administered. The manufacturer determines the expiration date".
High-efficiency particulate air (HEPA) filtration	**"**Using a tested and certified air filter designed to remove 99.97% of airborne particles measuring 0.3-micron or greater diameter from the air passing through it".
Hot lab	"A laboratory designed for the safe handling of radioactive materials. Usually contains one or more hot cells".
Individual dose (unit dose)	"A radiopharmaceutical in its final form is ready for administration (e.g., capsule, sterile solution in a syringe) consisting of the amount (dose) prescribed, ordered, or intended for an individual patient or research subject".
ISO class	"A quality classification from the International Organization for Standardization based on the quantity and size of particles per air volume".
Multiple-dose container	"A container of radiopharmaceutical for administration designed to contain more than one patient dose".

Negative-pressure area	"An area is maintained at a lower pressure than the adjacent spaces; therefore, the net airflow is into the area. This area is appropriate for volatile or gaseous radionuclides and radiopharmaceuticals and is intended to lend protection for the radiation workers and the general public".
Nuclear pharmacy or Radiopharmacy	**"**A clinical service that procures, prepares or compounds dispenses radiopharmaceuticals and assures safety and quality for diagnostic or therapeutic use in patients referred to the nuclear medicine service of a hospital".
Nuclear pharmacist or Radio pharmacist	"A professional with the authority license as a pharmacist or nuclear pharmacist (as applicable), who meets local/international training requirements".
Primary engineering control (PEC)	"A device or zone that provides an ISO Class 5 air quality environment for sterile processing".
Quality assurance (QA)	"The procedures, activities, and oversight system ensures that radiopharmaceutical processing consistently meets quality standards".
Quality control (QC)	"The sampling, testing, and documentation of results, taken together, ensure that specifications have been met before the release of the radiopharmaceutical".
Radioactive half-life ($t_{1/2}$)	"The time required for the one-half quantity of a radionuclide to decay".
Radioactive isotopes, radioisotopes, or radionuclides.	"The unstable form of an element emits radiation to transform it into a more stable form. Radiation is easily traceable and can cause changes in the substance it falls upon. These special attributes make radioisotopes useful in medicine, industry, and other areas".
Radioimmunotherapy	"Engineered monoclonal antibodies paired with radioactive materials. When injected into the bloodstream, they bind to cancer cells and deliver a high radiation dose directly to the tumor".
Radiolabeled	"The process of radiopharmaceutical formation".
Radiopharmaceutical	"Radioactive pharmaceutical/medicinal product for clinical use (diagnostic or therapeutic)".
Radiopharmaceutical Compounding	"Formulation of radiopharmaceutical reagent kits from raw ingredients for the preparation of radiopharmaceuticals by the addition of radioisotopes, adding reagents to commercial kits to modify or enhance the performance of radiopharmaceuticals and/or synthesis from raw materials"**.**
Radiopharmaceutical Manufacturing	"Competent authorities issue the manufacturing license; The manufacturers have approval from the government to supply products that are registered or approved for safety, quality, and efficacy. The manufacturer should follow national or international good manufacturing practice (GMP) guidelines".
Radiopharmaceutical Reagent Kit	"Sterile and pyrogen-free reaction vials (s) containing non-radioactive material are required to compound or produce a specific radiopharmaceutical".
Shielding	**"**Barriers of appropriate radiation attenuating material, used for radiopharmaceuticals, to protect the personnel. These barriers can be general to afford protection from a radiation field, or specific to a container used to hold a particular radiopharmaceutical (e.g., syringe shield, vial shields)".

Segregated radiopharmaceutical processing area (SRPA):	"A designated, unclassified space, area, or room with a defined (by facility procedures) perimeter that contains a PEC. An SRPA is only suitable for radiopharmaceutical preparation (with and without minor deviations), dispensing, and repackaging".

This chapter helps you to uncover the following:

This chapter will discuss

Nuclear pharmacist Responsibilities

- Safe handling, preparation, dispensing, and regulatory responsibilities
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Nuclear pharmacy

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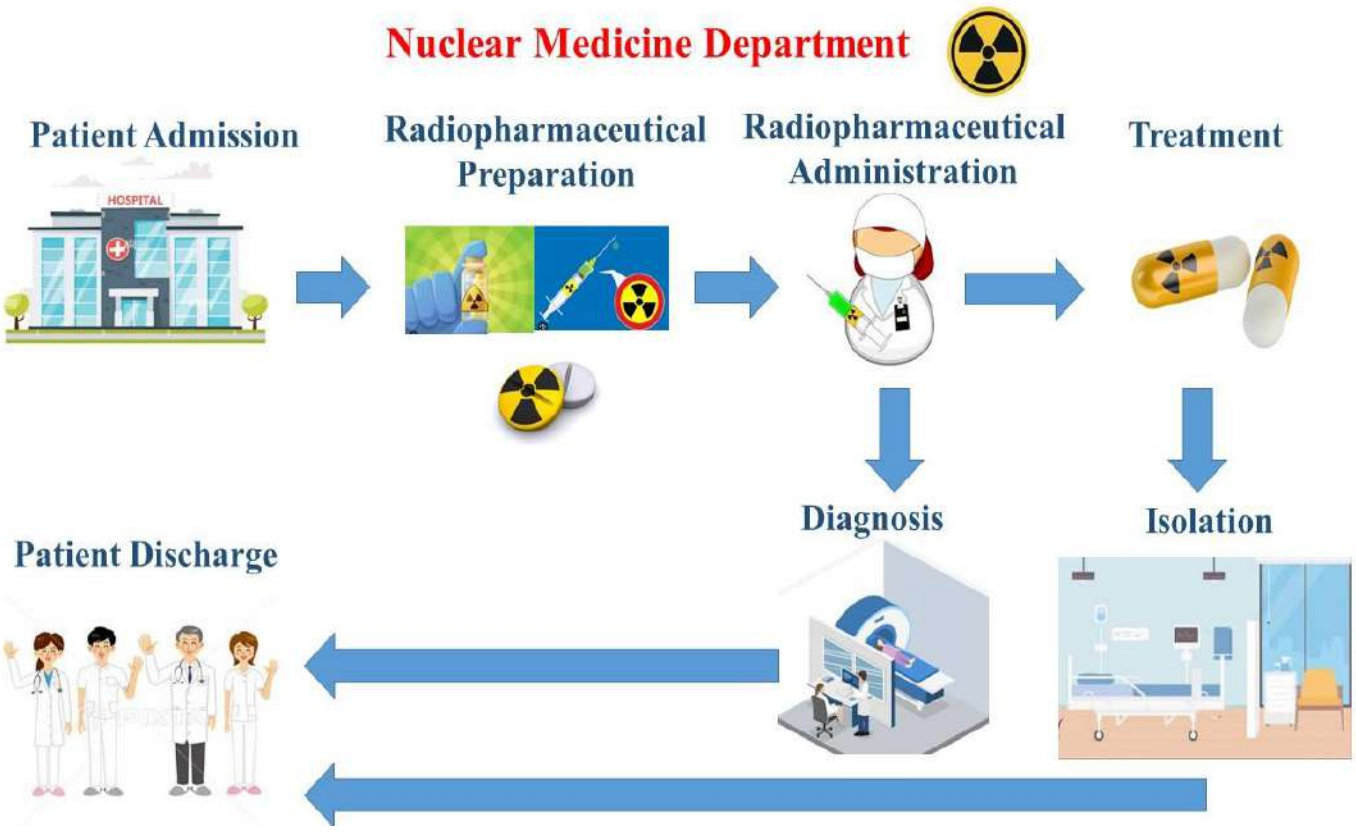

Introduction

Background:

Nuclear medicine and radiotherapy are vital in diagnosing and treating major non-communicable diseases, especially cancer and heart disease. The IAEA, one of the major organizations working toward the Sustainable Development Goals, is committed to helping its member states, including Egypt, use nuclear science and research to decrease morbidity and mortality in non-communicable diseases. Identification, resolution, and prevention of radiopharmaceutical and medication-related problems is vital for the pharmacist. Drug-related problems are an essential challenge that may affect morbidity and mortality, the patient's quality of life, and support to the health care team.

Nuclear medicine is a field that uses radiopharmaceuticals, or unsealed sources of radiation, in medicine for diagnosis, staging of disease, therapy, and monitoring the response of a disease process. It is also a powerful tool in sciences such as biology, drug discovery, and pre-clinical medicine. Nuclear medicine is a multidisciplinary science that includes physics, chemistry, biology, computing, mathematics, and pharmacology.

Radiotherapy is the use of radiation via sealed sources to treat a variety of cancers and a few non-cancerous diseases. Internal radiation therapy (brachytherapy) uses sealed sources like seeds, wires, or rods implanted in the patient's body. External radiation (e.g. teletherapy and Intesnisty-Modulated Radiation Therapy (IMRT)) is delivered from a distant source outside the patient's body to the cancer tissue, including orthovoltage x-ray machines, Cobalt-60 machines, linear accelerators, and proton and neutron beam machines.

Nuclear pharmacy (also referred to as Radiopharmacy) is a specialized area of pharmacy practice concerned with compounding and dispensing radioactive materials to enhance and promote health, where radioactive medications are utilized to identify and treat a particular disease accurately. It has different practices and combines the expertise of manufacturing radioactive, pharmacological effects, pharmaceutical preparation, clinical research, and the skills needed to handle radioactive substances. The radiopharmaceutical practices include large-scale industrial manufacturing and small-scale hospital radio-pharmacy.

The nuclear pharmacist always seeks to improve and promote health by safely and effectively using radioactive drugs for diagnosis and therapy during preparation, quality control, and dispensing. The nuclear pharmacist provides an exciting, challenging, and rewarding environment for pharmacy practice. Being a nuclear pharmacist requires the learning and practical knowledge of physics, chemistry, clinical pharmacy practice, and pharmaceutical care, as well as the skills needed for the interaction with experts from various fields and the healthcare team for participation in the institution's mission of patient care service, professional development, and research.

Scope:

Nuclear pharmacy has been an area of specialty pharmacy that has grown enormously over the past 50 years, so this document provides general knowledge and helps nuclear pharmacists regarding the radio-pharmacy service. It also draws clear lines between the various levels of radio-pharmacy operation to provide more definitive guidance on staff qualifications, training, facilities, equipment, types of procedures, record keeping, quality assurance, and quality control. This chapter encourages hospital pharmacists to maintain their skills. There aren't many hospitals in Egypt that have nuclear pharmacists among the staff of nuclear medicine. Nuclear pharmacy needs to expand and grow in government and private hospitals, this is why the chapter was created.

Objective:

As a part of the Egyptian Guide for Oncology Pharmacy Practice, this nuclear chapter aims to provide operational information to hospital nuclear pharmacy staff which covers the skills, competencies, and fundamental knowledge required to work safely and effectively as a hospital nuclear pharmacist in the hot laboratory or as a clinical nuclear pharmacist.

1. Impact and Responsibilities of a Nuclear Pharmacist

1. Impact and responsibilities of a nuclear pharmacist

Nuclear pharmacy practice is quite complex, this is mainly due to the nature of radiopharmaceuticals being radioactive materials and pharmaceutical products. So the nuclear pharmacist provides patient-focused pharmaceutical services, literature reviews, pharmacodynamic and pharmacokinetic information to reduce radiopharmaceutical and drug-related problems and prevent adverse events. Furthermore, the nuclear pharmacist contributes to the optimal efficacy and safety of radiopharmaceuticals that guarantee both clinical benefits and better economic outcomes.

"The American Pharmaceutical Association -Nuclear Pharmacy Practice Group (APhA)" and "the American Society of Health-System Pharmacists (ASHP)" have provided a list of responsibilities for nuclear pharmacists who have a distinctive personality, expertise, and skills to reflect a high level of professionalism, as compared to other pharmaceutical services. This responsibility is multi-dimensional and can be described in 4 parts:

1. A. The safe handling, preparation, dispensing, and regulatory responsibilities

- Receiving, storing, and managing the supply and records of radioactive drugs (radiopharmaceuticals), additional medications, and associated supplies used in nuclear medicine.
- Preparing radiopharmaceuticals not readily available on the market by compounding them using reagent kits and radioisotopes.
- Conducting functional tests on tools, devices, and equipment and assessing the purity and quality of radiopharmaceuticals in the radio-pharmacy (also known as hot lab).
- Dispensing prescriptions on demand (filling step).
- Radiopharmaceutical packaging, labeling, and supervising transportation.
- Handling dangerous chemicals with special care.
- Disseminating knowledge about radiopharmaceuticals to others.
- Ensuring correct patient preparation before radiopharmaceutical administration and resolving unexpected consequences.
- Assuring that new radiopharmaceuticals and chemicals are being tested in laboratories.

1. B. Clinical responsibilities

- Review the patient's medical and medication history and current medication to identify potential modifications to the treatment's protocol, delays, adjustments to the radiopharmaceutical's biodistribution, or other significant interferences with diagnostic or therapeutic outcomes.
- Collect and analyze patient information and review evidence-based therapeutic radiopharmaceutical regimens.
- Provide patient education and recommendations for radiopharmaceutical and other related supportive medication, such as premedication before radiopharmaceutical use (for either investigation or therapeutic purposes), stopping any potentially interfering medications, restarting them after the study, and managing patients during discontinuing them.
- Calculate the appropriate dosage of the radiopharmaceutical for a specific patient before, during, and after the administration of radiopharmaceuticals, and make sure that patients with special requirements or issues (such as dialysis patients, pediatric patients pregnant women, and nursing mothers) are given the proper consideration.
- Monitor the patients after administering radiopharmaceutical to determine if the proper response was achieved, to prevent complications or intervene with the necessary therapy, and to monitor any potential adverse effects.
- Radiation safety recommendations for patients either used therapeutic or diagnostic radiopharmaceuticals.

1. C. Indirect clinical responsibilities

- Nuclear pharmacist participates in radiation safety committees and “Radioactive Drug Research Committees (RDRCs)” to develop institutional policies, protocols, and guidelines for using radiopharmaceuticals and related drugs.
- Provide information or literature reviews on radiopharmaceutical and particular drugs or dosage forms.
- Drug use evaluation (DUE) or drug use review (DUR).
- Research and development including laboratory testing of new radiopharmaceuticals, new compounding procedures, or new quality control methods, and participation in clinical trials of radiopharmaceuticals.

1. D. Research responsibilities

- The RDRC seeks to ensure that patients participating in research procedures or clinical trials are as radioactive and pharmaceutically safe as possible.
- To approve and oversee the use of radiopharmaceuticals by researchers to study their kinetics, distribution, localization, biochemistry, physiology, etc., RDRC consists of an authorized user, a radiochemist or radiopharmacist qualified to formulate radioactive drugs, a person with radiation safety and dosimetry experience, as well as at least two other members.

2. Radiation

2. Radiation

Radiation is the energy released by matter as particles (alpha or beta particles) or electromagnetic waves (gamma or X-ray). Atoms are the building blocks of all matter; the nucleus of an atom contains subatomic particles called protons and neutrons, and the outer shell of an atom contains additional particles called electrons. The nucleus is positively charged, whereas the electrons are negatively charged. These forces within the atom destroy excess atomic energy (radioactivity) to maintain a strong, stable balance. Radiation is the word used to describe the energy released by unstable nuclei throughout the process.

2. A. Types of Radiation

- **Non-ionizing radiation** is a type with a lower energy that is insufficiently potent to separate electrons from atoms or molecules, whether they are part of matter or living things. However, its power can cause those molecules to vibrate, generating heat. Non-ionizing radiation includes microwaves, radio waves, radiofrequency energy from cell phones, and visible light.
- **Ionizing radiation** is high-energy radiation that can remove an electron (a negative particle) from an atom or molecule. Ionizing radiation can disrupt cellular chemistry and cause DNA damage. This may increase the risk of some diseases, such as cancer. Cosmic rays from space are natural sources of ionizing radiation. Radioactive materials and medical imaging technologies such as X-rays, CT scans, and PET scans may also contribute to it. Ionizing radiation is released as a result of radioactive decay.

Alpha, beta, gamma, and/or X-rays are some of the emitted ionizing radiation.

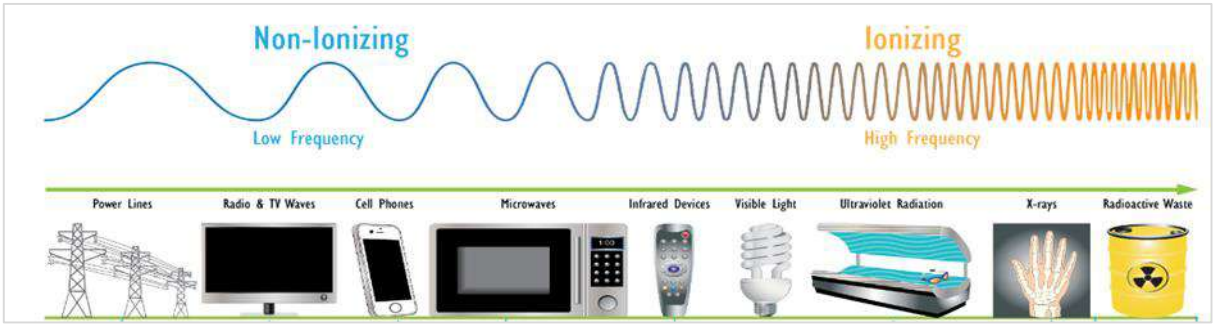

Figure 1: Electromagnetic waves spectrum
The penetrating power of the radiation increases from left to right as the Frequency rises.

2.A.1. Types of Ionizing Radiation in Medical Applications (Radioactive Emissions)

Common types of radioactive decay are used mainly in medical applications are the following:

a. <u>Alpha particles</u>

- Alpha particles are heavy positively charged particles consisting of two protons and two neutrons with large mass and are emitted by radionuclides of heavy elements to become more stable.
- Alpha particles travel only a few centimeters in the air and are blocked by a sheet of paper.
- Alpha particles have a very low ability to penetrate other materials and cannot penetrate the skin.
- Alpha particles are potentially dangerous if inhaled, swallowed, or absorbed through open wounds, but external exposure generally does not pose a danger.

b. <u>Beta Radiation or β^- Decay</u>

- Beta particles consist of electrons, which are much smaller than alpha particles and can penetrate deeper.
- Beta particles can pass through the “germinal layer” of human skin. Beta emitters can potentially harm the skin if left on it for an extended time.

- In general, beta particles have a more remarkable ability to penetrate the tissue, have a less destructive effect than alpha particles, and can be used in therapy.

c. Electromagnetic Waves (Gamma and X-Rays)

- Gamma radiation have no mass or charge, and it has a high penetration ability of the deep tissue of organs. Hence, they are used for diagnosis by imaging using a gamma camera.
- X-ray radiation is created intentionally by blasting a metal target with electrons in a vacuum (in an X-ray tube).

Gamma rays are frequently employed in sterilizing medical equipment and other diagnostic and therapeutic uses. X-rays are commonly employed to provide static pictures of body regions.

d. Positrons or β^+Decay

- A positron (electron anti-particle) has the same mass as an electron but is positively charged.
- The positron annihilates with an electron; the positron and electron masses are split into two 511 keV photons traveling in opposite directions during this annihilation event. These photons can penetrate living tissues and are used in Positron Emission Tomography (PET) to diagnose medical abnormalities.

Low energy (diagnostic) gamma rays and positrons, in particular, are helpful for various diagnostic imaging applications. The alpha and beta particles are used for therapeutic applications.

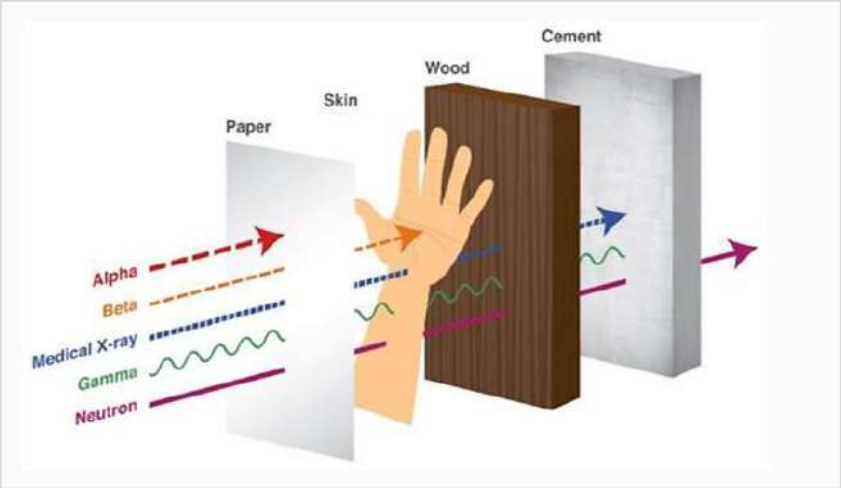

Figure 2: The five Major types of ionizing radiation and their penetrative abilities

Radiological Half-life

The half-life of a radioactive isotope is the time it takes for one-half of the radioactive isotope to decay. When a radioactive atom decays, it becomes a stable product. Each radioisotope has a unique half-life, which is a distinguishing feature. Depending on the stability of the nucleus, the half-lives can be anything from a millionth of a second to billions of years.

For Example, carbon-12 and carbon-13 are stable, but carbon-14 is unstable, radioactive and will decay into a stable product.

2.A.2. Radiation Units

- **Radioactivity units:** Radioactivity represents how many atoms in the material decay in a given time (second). The units of measure for radioactivity are the curie (Ci), and the system international (SI) unit for radioactivity is the becquerel (Bq).

$$1\ curie\ (Ci) = 3.7\ \times\ 10^{10}\ disintegrations\ per\ second\ (dps)$$

$$1\ becquerel\ (Bq) = 1\ dps$$

- **Absorbed dose**: describes how much radiation is absorbed by living or nonliving things (Joule/Kilogram). The radiation absorbed dose (rad) and Gray (Gy) are the units for absorbed dose.
- **Dose equivalent (or effective dose)**: combines the dose of radiation received and the radiation's impact on health. The roentgen equivalent man (rem) and Sievert (Sv) are the units used to measure dose equivalent.
- **Internal dosimetry** is the science of internal radiation dose assessment because of interference of radionuclides inside the human body. Internal dosimetry provides estimates of the amount of radiation that is absorbed by different organ systems. Physical and biological parameters affect internal dose, such as physical and biological half-life, intake route, tissue sensitivity, etc. The calculated radiation doses are an essential element of balancing the risks and benefits of the proposed administration.

2.A.3. Biological Effects of Radiation

Radiation causes damage to living cells, affecting the health of all living things. This effect is determined by the amount of radiation absorbed, the type used, and the afflicted organ or body tissue. There are two types of radiation-related health effects: deterministic and stochastic.

2.A.3.a Deterministic effects

This is characterized by the existence of the threshold dose, which means that radiation exposure below this dose has no evident effect; however, radiation exposure over this dose generates effects in which many cells degenerate, and the incidence rate grows. A predictable effect with a threshold dose of approximately 3 Gy (300 rad) is starting from skin reddening (erythema). Examples: tissue reactions, e.g., hair loss, cataracts, skin injury, etc.

2.A.3.b Stochastic effects

There is no threshold as the probability of the effect increases with the dose, but the severity of the effect is independent of the dose received. The effects of radiation exposure at specific doses are unclear because of the influence of other cancer-promoting variables such as smoking and dietary habits. Examples: cancer, leukemia, hereditary effects, etc.

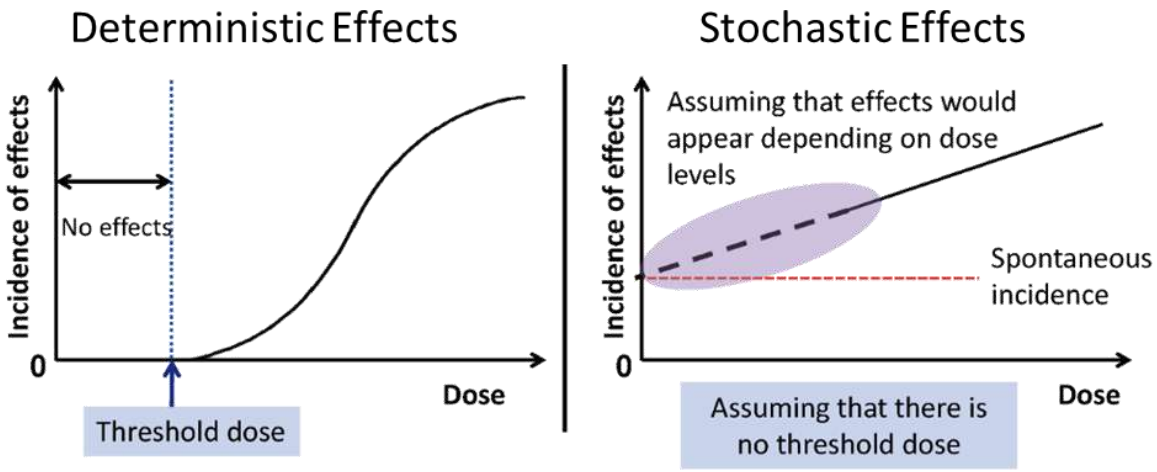

Figure 3: Radiation dose-related deterministic and stochastic health effects

Table 1: Comparison between radiation dose-related deterministic and stochastic effects

Items	Deterministic Effects	Stochastic Effects
Description	Damage occurring above a threshold dose.	Delayed damage due to DNA damage or injury (genetic level).
Cause of the Damage	Killing or dysfunction of numerous cells	Individual altered cells' mutations and subsequent replication.
Dose Dependence	With increasing radiation dose, radiation damage becomes more severe.	Radiation damage is more likely to occur with larger radiation doses.
Dose Threshold Value	threshold dose for erythema is <3 - 6 Gy (<300 - 600 rad) to skin	Non-existent
Examples	Skin reddening, hair loss, infertility	Cancer, hereditary effects

2. B. Radiation Protection and Safety Principles

The IAEA identified three safety categories for ionizing radiation. This categorization reflects an international consensus on what constitutes a high level of safety for safeguarding people and the environment.

- **Safety Fundamentals:**

Establish the foundation for safety standards by outlining the fundamental safety objective, protection, and principles.

- **Safety Requirements:**

A comprehensive and consistent set of safety regulations must be met to ensure the protection of people and the environment in the present and the future.

- **The Safety Guides:**

Provide global best practices, which are increasingly reflective to assist users in pursuing the highest safety standards.

All employees who work with radiation must receive protection and safety training and the necessary education, training, and credentials to understand their roles and carry them out competently, wisely, and following hospital radiation protection committee rules and the handling specifications set forth by the national regulatory authority.

By making patient information available to multiple users, digital information systems can, when appropriately utilized, aid in helping to reduce the performance of unneeded or unsuitable tests and repeated studies. The information from such monitoring can improve security and safety for imaging processes. These systems can also assist in monitoring doses to patients and image receptors.

The guiding principle of radiation safety is "ALARA," which stands for **"As Low As Reasonably Achievable"**. ALARA minimizes or prevents unnecessary radiation exposure when working with or near radiation.

2.B.1. Three key factors for radiation protection

Time:

Personnel exposure to radiation is closely correlated with the level of radiation handled and the handling period. Radiation exposure will be reduced by minimizing the handling time. The alarming dosimeters can help minimize the amount of time in an area with elevated radiation levels.

Distance:

Radiation exposure follows the inverse square law; increasing the distance between the operator and the radiation source will decrease radiation exposure to personnel by the square of the distance; For example, using tongs or forceps when handling vials containing radioactive medications allows for increasing the distance between the hands of the operator and the radioactive source.

Shielding:

It reduces the personnel's exposure to radiation. As a result, those who handle radiopharmaceuticals may utilize a variety of high atomic number (Z) materials that absorb radiation and can be used in different ways as shielding materials (such as lead). The handling of radiopharmaceuticals frequently necessitates the use of shielding, such as bottle and syringe shields. First responders can be shielded from alpha and beta particles by protective clothes, but gamma rays cannot be avoided.

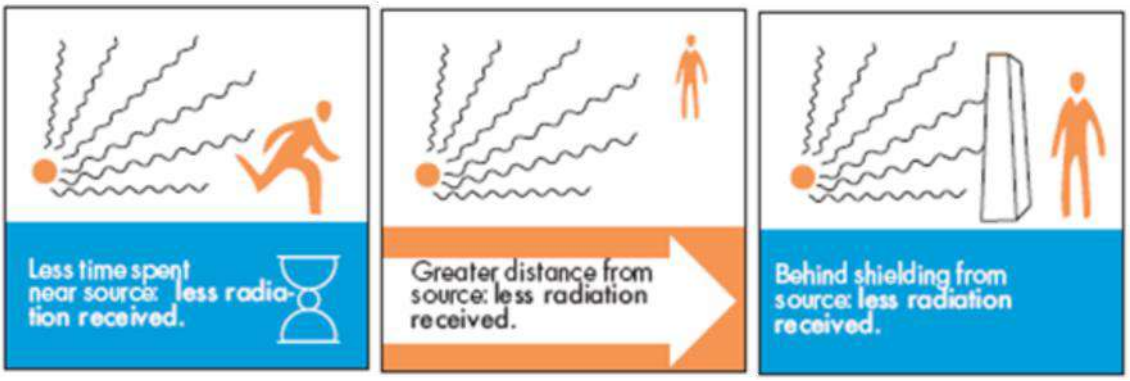

Figure 4: Time, distance, and shielding principles to minimize exposure to radiation

Occupational and public dose limits are 20 mSv per year and 100 mSv per five years for occupational exposure and with a 1 mSv per year limit for public exposure.

Note: Pregnant Workers

A pregnant employee may not be allowed to spend much time in the radio-pharmacy or deal with radioiodine solutions. This is its most significant concern since radioiodine crosses the placental barrier and concentrates on the developing fetal thyroid.

2.B.2. Security Requirements

All radiation-producing equipment and radioactive materials must be protected from theft or unauthorized use, and the regulatory body must be notified immediately if any of these items are lost or stolen.

2.B.3. Warning Signs and Labels

- The radioactive labels warn people, especially handlers, that the container contains radioactive material and could need certain handling and storage precautions.
- **Radioactive– White I**: "The maximum allowable radioactivity is 0.5 mrem/hr (0.005 mGy/hr) on the package surface".
- **Radioactive – Yellow II:** "The maximum allowable radioactivity is 50 mrem/hr (0.5 mGy/hr) on the package surface and one mrem/hr at three feet (1 meter) from the package".
- **Radioactive – Yellow III:** "Maximum allowable radioactivity is 200 mrem/hr (2 mGy/hr) on the package surface and 10 mrem/hr at three feet (1 meter) from the package".

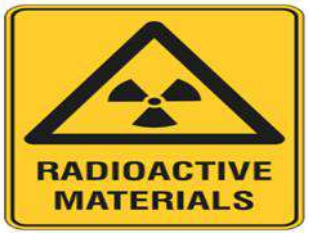

Figure 5: Radiation sign

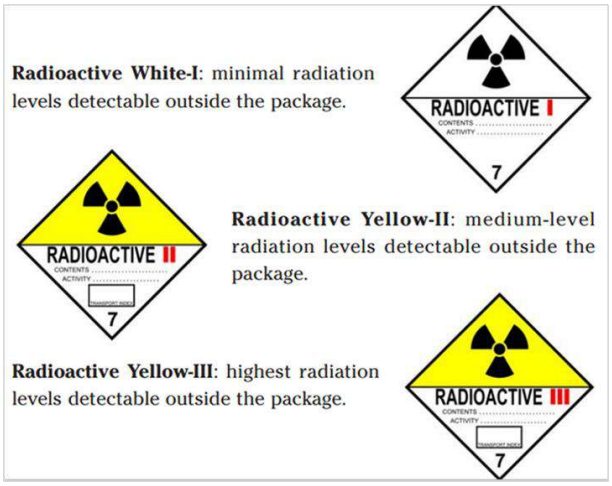

Figure 6: Labels for radioactive material transport packages

2.B.4. Radiological safety precautions for workers

- Examine the processes for handling radioactive materials to ascertain any risks associated with exposure, and contamination, also with volatile compounds, and/or aerosols. Reduce radiation exposure effectively.
- After handling radioactive materials, employees should wash their hands, examine their hands and shoes for radiological contamination, and keep radioactive waste containers covered or capped when not in use.
- Never consume, drink, smoke, store food, or apply cosmetics in an area designated for using or storing radioactive materials. Never locate devices in this area, and constantly check work surfaces and equipment for radiological contamination.
- Using volatile radioactive materials in biosafety cabinets that circulate air back into the environment is not advised. Also, never pipet radioactive solutions into your mouth.
- Before repairing or disposing of any equipment or materials used to handle or store radioactive material, they must be free of radioactive contamination.
- Nursing staff and other hospital personnel should spend as little time as possible in the patient's room while providing all essential care.

2. C. Radiological Contamination Control

Radiological contamination, such as spills, drips, sprays, and volatility, is a severe issue for radiation protection. Because of this, radiopharmaceutical handlers can reduce radioactive contamination by using various techniques and materials.

For example, container contents are maintained at neutral or negative pressure because positive pressure in a container is a common cause of radioactive contamination. Vertical airflow, not horizontal, in primary engineering control, is used to control contamination.

The nuclear pharmacist should implement the policies to minimize radiological contamination of radiopharmaceuticals according to the national regulatory authority during these steps: ordering, transporting, and receiving radiopharmaceuticals, along with unpacking and storage; preparing and administration of radiopharmaceuticals to patients; examining, treating, and caring for patients who are receiving a lot of radioactive materials; and storing and handling radioactive wastes.

Decontamination of the working staff

- After completing work with unsealed radioactive materials, hands should be washed on a separate sink.
- In some situations, the employee's movements through the work areas should be restricted to prevent the spread of contamination through the laboratory, and hands should be washed before leaving a place that is classified as controlled because of possible contamination.
- Using a surfactant or chelating agent for hand wash should be tailored to the chemical form of the contaminating agent to be more effective if detectable radioactive contamination is still present on the hands after simple washing.
- When radioactive contamination of body parts other than the hands is suspected, or the decontamination procedures for the hands are unsuccessful, the Radiation Protection Officer (RPO) should be consulted. When decontaminating the face, extra care should be taken to prevent internal contamination by limiting the entry of radioactive material into the eyes, nose, or mouth.
- Suppose a wound or break in the skin occurs in an environment with a chance of radioactive internal contamination. In this case, the injury or break should be cleansed with water as soon as possible, without washing contamination into the wound. Once first aid has been administered, the person should seek additional medical attention, including decontamination if required.
- Training in handling spills, accidents, and contaminated people should be provided initially to every employee who works with unsealed sources, with periodic refresher training. The instructions should also include proper showering and eye-washing techniques.

2. D. The Radioactive Waste

- Radioactive wastes are stored to avoid radiation exposure to the public or causing environmental pollution, and radioactive waste from the nuclear pharmacy is disposed-of according to the national regulatory authority.
- Segregating radioactive waste according to its form into solid waste, liquid waste, and gaseous waste.
- Segregating radioactive waste according to half-life into short-half-life waste and long-half-life radionuclides.
- Segregating radioactive waste according to the level of activity into high-level waste, medium-level waste, and low-level waste.
- Records must be maintained as to the date of waste storage, the amount stored and disposed of, and the date of disposal.

Radiation Section Summary

- There are two types of radiation: ionizing and non-ionizing radiation.
- Alpha particles have a positive charge; beta particles have a negative charge; and gamma or x-rays (photons), which are neutral in electrical charge, are among the most common types of ionizing radiation used in medical applications.
- The half-life of a radioactive isotope is the time it takes for half of the radioactive isotope to decay.
- There are two types of health effects associated with radiation: deterministic and stochastic.
- The fundamental of radiation safety is "ALARA," a term for "As Low As Reasonably Achievable."
- Radiation protection is regulated by three key factors: time, distance, and shielding.
- It is essential to follow radiological safety precautions to protect personnel.
- Contamination should be monitored and regulated regularly, and decontamination should be set for employees and work areas.
- To avoid radiation exposure to workers, members of the public, and the environment, radioactive waste should be correctly stored, separated, and disposed-of following national regulatory authority regulations.

3. Radiopharmaceuticals

3. Radiopharmaceuticals

Radiopharmaceuticals (radioactive drugs) are the type of medication that contains both a radionuclide (emits radiation) and a pharmaceutical component. The pharmaceutical component is a biologically active molecule, such as a protein or a small molecule drug, specifically designed to target an organ or tissue in the body. The physiochemical characteristics of the medication, its stability, purity of the radiopharmaceutical preparation, the patient's pathophysiologic condition, and the presence or absence of interfering medications all affect the distribution of the radiopharmaceutical inside the body.

Diseases can be detected, followed up on, and treated using radiopharmaceutical medications. The body is exposed to minute doses of radiation, for instance, during diagnostic procedures employing radiopharmaceuticals to monitor organ function. Radiopharmaceuticals utilized for therapeutic purposes are typically supplied at higher levels to give therapeutic doses to specific disease areas.

Radioactive drugs generally have short half-lives (hours to a few days), so they must reach the patient for administration soon after they are produced.

The radiopharmaceuticals of choice should be safe and non-toxic for human administration, radiation from the radionuclide of choice should be easily detected by nuclear instruments, and the radiation dose to the patient should be minimal.

3. A. Ideal Radiopharmaceutical

Because radiopharmaceuticals are delivered to humans, radiopharmaceuticals should have a few fundamental properties. Below are some details on the optimal properties of radiopharmaceuticals:

Simple Accessibility

The radiopharmaceutical needs to be affordable and accessible at any nuclear medicine institution. Complex radionuclide production processes or tagged chemicals increase the price of radiopharmaceuticals.

Short-Effective Half-Life

Humans who receive radiopharmaceuticals experience biological system removal via perspiration, fecal or urine excretion, or other processes.

$T_{1/2}$ biological stands for the biological half-life. It is the time needed for half of the radiopharmaceutical to disappear from the biological system. Some radioisotopes used in nuclear medicine have short half-lives, which means they decay quickly and are suitable for diagnostic purposes; others with longer half-lives take more time to decay, which makes them suitable for therapeutic purposes.

Decay by Electron Capture or Isomeric Transition

The diagnostic radionuclides utilized should decay via electron capture or isomeric transition without any internal conversion since radionuclides releasing particles are less desired. For diagnostic purposes, the radionuclide must emit radiation with energy preferably between 30 keV and 300 keV, regardless of the decay mechanism.

High Target-to-Non-Target Activity Ratio

For a diagnostic purpose, the target-to-non-target ratio should be very high. Any administered radiopharmaceutical not extracted by the target organ/ tissue should be eliminated from circulation and completely from the body.

A perfect radiopharmaceutical would possess all the characteristics listed above to diagnose diseases as effectively as possible while exposing patients to the least amount of radiation possible. However, achieving all of these requirements with a particular radiopharmaceutical is challenging.

Technetium-99m is employed in more than 80% of nuclear imaging operations and meets many of the requirements for the ideal radionuclide.

In nuclear medicine, nearly 90% of the radiopharmaceuticals are used for diagnostic purposes, while the rest are used for treatment. Radiopharmaceuticals usually have a minimal pharmacologic effect because they are generally used in tracer quantities. Therapeutic radiopharmaceuticals can cause tissue damage due to radiation.

3. B. Diagnostic Radiopharmaceuticals

Nuclear medicine diagnostic radiopharmaceuticals are also referred to as radioactive tracers that produce gamma radiation inside the body. The camera creates an image from the locations where a different mechanism emits radiation. On a computer, this image is magnified, and the abnormalities are visible on a monitor, as in the following examples:

- Passive diffusion: **Technetium^{99m}Tc-DTPA** in brain and renal imaging, **Technetium ^{99m}Tc-DTPA** aerosol for suspected pulmonary embolism, **Xenon ^{133}Xe** in ventilation imaging for lung problems, and **Indium ^{111}In-DTPA** in cisternography for the brain and spinal column.
- Ion exchange: uptake of **Technetium ^{99m}Tc-**phosphonate complexes to detect bone abnormalities.
- Capillary blockage: **Technetium ^{99m}Tc-**macro aggregated albumin (MAA) particles trapped in the lung capillaries scanning.
- Phagocytosis: removal of **Technetium ^{99m}Tc-**sulfur colloid particles by the reticuloendothelial cells in the liver, spleen, and bone marrow.
- Active transport: **Iodine ^{131}I** uptake in the thyroid, **thallium ^{201}Tl** uptake to detect recurrent lesions or metastatic lesions from thyroid cancer, lung cancer, brain tumor, breast cancer, mediastinal tumor, bone and soft tissue tumor, pancreas cancer, and colon cancer.
- Cell sequestration: sequestration of heat-damaged **Technetium ^{99m}Tc-**labeled red blood cells detecting ectopic or accessory splenic tissue.
- Metabolism: **fluorine 18 fluorodeoxyglucose (**^{18}**F-FDG**) uptake in metastatic colorectal cancer. *(FDG will be discussed later).*
- Receptor binding**: raclopride ^{11}C-**dopamine binding to the dopamine receptors in the brain study.
- Compartmental localization: **Technetium ^{99m}Tc-**labeled red blood cells used in the gated blood pool study diagnostic agent.
- Antigen-antibody complex formation: **Iodine ^{131}I-, Indium^{111}In-,** and **Technetium ^{99m}Tc-**labeled monoclonal antibodies for the immuno-imaging of cancers such as malignant melanoma, colorectal and ovarian cancer**.**
- Chemotaxis: **Indium ^{111}In-**labeled leukocytes imaging to localize infections.
- **Metaiodobenzylguanidine (MIBG)** for imaging the adrenal medulla and its abnormalities. MIBG, a guanethidine analog, is taken up by an active mechanism in the neuroendocrine cells because of its similarities with nor-epinephrine.

^{18}F-FDG PET /CT Imaging

PET/CT is an imaging modality in nuclear medicine that uses positron-emitting radiopharmaceuticals to measure radiotracer distribution within tissues. Positron-emitting radionuclides like F-18, C-11, and Cu-64 are produced in cyclotrons. A cyclotron is a particle accelerator that uses a constant electromagnetic field to hold charged particles in a circular spiral pattern to produce radioisotopes.

The most widely used radiopharmaceutical in PET imaging is 2-[F-18] fluoro-2-deoxy-D-glucose (FDG) (also referred to as Fluorodeoxyglucose) and has a short half-life (109.7 min).

The success of FDG as a tumor tracer is based on its ability to be a metabolic marker and allow for the assessment of metabolic functions in vivo. The FDA authorized ^{18}F-FDG for brain imaging tests for epilepsy patients in 1995. The FDA provided ^{18}F-FDG-wide approval in 2000 to diagnose all malignancies and cardiovascular conditions.

The FDA has approved Netspot, the first product for producing gallium Ga 68 dotatate injection, a radioactive diagnostic agent for PET imaging. This radioactive agent will aid in locating neuroendocrine tumors (NETs) in adults and children with somatostatin receptor-positive NETs.

Gallium 68 PSMA-11 (Ga-68 PSMA-11) is the first FDA-approved medication for PET imaging of prostate-specific membrane antigen (PSMA)-positive lesions in males with prostate cancer.

Pylarify (piflufolastat F-18), a medication for PET imaging of prostate-specific membrane antigen (PSMA)-positive lesions in prostate cancer patients, has been approved by the FDA. With Pylarify's clearance, confident men with prostate cancer will have easier access to PSMA-targeted PET imaging, which can help doctors diagnose prostate cancer.

3. C. Therapeutic Radiopharmaceuticals

Radiopharmaceutical therapy is becoming increasingly popular as a targeted, safe method of treating many cancers. Radiopharmaceutical therapy aims to provide high radiation doses to specific cancerous spots in target organs or tissues while reducing radiation doses to nearby healthy cells.

Radionuclides emitting beta particles are widely used. They include phosphorus-32, strontium-89, and iodine-131, which might be considered the "first generation" of therapeutic radionuclides. And Alpha emitting radionuclides are also used in therapeutic applications like astatine-211, actinium-225, bismuth-213 and radium-223. However, the use of α-emitting radionuclides includes production and availability limitations. Also, high cytotoxic effects of α-particles have been reported after administration to patients.

It is typically advised to avoid using radiopharmaceuticals on patients who are or may become pregnant during treatment. Female patients should be informed that breastfeeding is usually not suggested after receiving some radiopharmaceuticals due to the possibility of excreting radioactivity through breast milk and external irradiation to the sucking infant.

Radionuclides coupled to particular biological substances, such as immunoglobulin molecules (monoclonal antibodies), are used worldwide in medical studies. Some disorders may eventually regress or even be cured due to the therapeutic radiation dose that will subsequently be applied to these cells.

Table 2: Examples of therapeutic radionuclides in nuclear medicine

Radionuclides	Emitting	Half-Life	Indication
Iodine (I-131)	β	8.02 days	Medullary thyroid cancer, thyroid cancer, hyperthyroid cancer, radioimmunotherapy (RIT) for NHL and neuroblastoma
Strontium-89 (^{89} Sr)	β	50.53 days	Bone pain palliation
Yttrium-90 (^{90}Y)	β	64.10 days	RIT for NHL, neuroendocrine tumor, liver metastasis, and hepatocellular carcinoma,
Lutetium-177 (^{177}Lu)	β	6.73 days	Synovitis and RIT for various cancers, such as prostate cancer
Astatine-211 (^{211}At)	α	7.2 hour	RLT prostate cancer, RIT leukemia, and brain tumor
Bismuth-213 (^{213}Bi)	α	46 mins	RIT leukemia, brain tumor
Radium 223(^{223}Ra)	α	11.44 days	Bone pain palliation

Sodium Phosphate-32 or Orthophosphate is an older radiotherapeutic agent used in the palliation of bone pain in patients not responsive to the usual analgesics, for example, pain palliation agents in the prostate cancer, breast cancer patients, and multiple areas of skeletal metastases.

Yttrium-90 radioembolization has shown clinical effectiveness for unresectable hepatocellular carcinoma in people with locally advanced hepatocellular carcinoma.

Yttrium-90 ibritumomab tiuxetan is a radio-immunotherapeutic agent used for the treatment of non-Hodgkin's lymphoma (NHL). It is approved for treating relapsed or refractory low-grade, follicular, or CD20+ transformed non-Hodgkin's lymphoma (NHL).

Pretargeted radioimmunotherapy, the monoclonal antibody (Mab) construct that has an affinity for the tumor-associated antigen on the one hand and a radiolabeled hapten on the other is used to target the tumor. The radiolabeled is delivered later, preferably after the Mab has cleared the circulation.

On January 26, 2018, the FDA approved lutetium Lu 177 dotatate, a radiolabeled somatostatin analog, for the treatment of individuals with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

Major Therapeutic Application

A. Sodium iodide ^{131}I for well-differentiated thyroid carcinoma

The ability to concentrate ^{131}I makes well-differentiated thyroid tumors, such as papillary and follicular tumors, responsive to treatment. Since ^{131}I is not focused on anaplastic or medullary thyroid tumors, therefore ^{131}I therapy is useless for their management.

- **Physical characteristics for ^{131}I and dose**

  Iodine-131 is available as a stabilized aqueous solution or solid capsule forms for oral administration with a physical half-life of 8.04 days. It decays by beta and gamma emission, and the dose starts from the low dose of 30 mCi. In moderate and high-risk patients, the administered dose must be escalated to a maximum of around 250 mCi.

- **Therapeutic indications for Sodium Iodide ^{131}I**

  Sodium Iodide (^{131}I) therapy solution is indicated in treating hyperthyroidism, detecting and ablating residual functioning thyroid tissue in differentiated thyroid carcinoma.

- **Pharmacokinetic properties of Sodium Iodide ^{131}I**

  When taken orally, sodium iodide (^{131}I) is quickly absorbed from the gastrointestinal tract into the bloodstream and dispersed in the extracellular fluid. A percentage is localized in thyroid tissue, where beta radiation is primarily responsible for its therapeutic impact. Additionally, the stomach and salivary glands trap iodine. A small amount is excreted via sweat and saliva, while most leftover material is eliminated through renal excretion.

B. Lutetium-177–Prostate-Specific Membrane Antigen (PSMA)-617 for Metastatic Castration-Resistant Prostate Cancer (mCRPC)

For patients with mCRPC who have undergone specific previous treatments (androgen receptor pathway targeting drugs and taxane-based chemotherapy), ^{177}Lutetium-PSMA-617 (Lu-PSMA) is now FDA-approved. Patients also need to have a PSMA PET scan that is positive.

Physical Properties of ^{177}Lu

- ^{177}Lu PSMA is a targeted beta-emitting radionuclide therapy that selectively binds to PSMA receptors on prostate cancer cells, and it has a long physical half-life of 6.73 days.
- ^{177}Lu PSMA is easily administered with no significant symptoms during intravenous injection. It undergoes renal excretion in the first 48 hours following injection, and the rapid renal excretion of ^{177}Lu needs 2–4 hr.
- Dose calculations for individual patients have been determined from a combination of disease burden, patient weight, and renal function.
- One dosage consists of 7.4 GBq [^{177}Lu] Lu-PSMA-617 intravenously injected every six weeks for up to six doses.

C. Radium-223 Dichloride for Metastatic Prostate Cancer

Radium-223 was the first targeted alpha therapy approved by the FDA in May 2013. It was approved as an effective therapy for patients with castration-resistant prostate cancer that had metastasized to bone and had a half-life of 11.4 days.

The indication of Radium-223 dichloride

- Patients with symptomatic bone metastases and castration-resistant prostate cancer.
- Patients having symptomatic or bulky soft tissue metastases (lymph nodes, local disease, etc.) but no known liver, lung, or brain metastases.
- Patients must be in good physical condition (ECOG 0-2).
- Radium-223 is administered at a 55 kBq/kg dose every six weeks.

3. D. Theranostics (Dual-Functioning Radiopharmaceuticals)

The term "theranostic" refers to combining focused therapy with a targeted diagnostic, commonly known as the "see and treat" strategy.

A theranostic may be an isotope such as iodine-131, or it may be a mixture of isotopes with various emission properties, as in the instance of lutetium-177 and galium-68 used in conjunction to detect and treat neuroendocrine tumors.

Radiopharmaceuticals Summary

- Radiopharmaceuticals, often known as radioactive drugs, are a type of medications that combines a radionuclide that emits radiation with a pharmaceutical component.
- An ideal radiopharmaceutical should have easy accessibility, a short and effective half-life, decay by electron capture or isomeric transition, and a high target-to-non-target activity ratio.
- Technetium-99m, used in more than 80% of nuclear diagnostic procedures, fulfills several criteria needed for an ideal radionuclide.
- In nuclear medicine, approximately 90% of radiopharmaceuticals are used for diagnostic purposes, with the rest used for therapeutic procedures.
- Radiopharmaceuticals are typically used in tracer levels; they often have minimal pharmacological effects. Radiation may result in tissue damage when therapeutic radiopharmaceuticals are administered.
- Diagnostic radiopharmaceuticals, also known as radioactive tracers, are compounds in the human body that emit gamma radiation. The camera creates an image based on the locations from which radiation is released. When viewed on a computer, the image is magnified, allowing any anomalies on the monitor to be detected.
- Iodine-123 (^{123}I), technetium-99m (^{99m}Tc), xenon-133 (^{133}Xe), thallium-201 (^{201}Tl), and indium-111 (^{111}In) radioisotopes are examples of radiopharmaceuticals used in Single Photon Emission Computed Tomography (SPECT) imaging.
- The radiopharmaceutical substance ^{18}F-FDG is widely utilized in positron emission tomography (PET) imaging. The PET/CT imaging modality is a nuclear medicine approach that uses radiopharmaceuticals that produce positrons to examine the distribution of radiotracers within biological tissues.
- Gallium Ga-68 dotatate injection is a PET imaging radioactive diagnostic agent. This radioactive substance can help detect and locate somatostatin receptor-positive neuroendocrine tumors in adult and pediatric patients.
- Gallium 68 PSMA-11 (Ga-68 PSMA-11) is the first medicine approved by the FDA for PET imaging in males with prostate cancer, specifically targeting lesions positive for prostate-specific membrane antigen (PSMA).
- Pylarify (piflufolastat F-18), a pharmaceutical drug used for PET imaging of PSMA-positive lesions in men with prostate cancer, has been approved by the FDA. Pylarify clearance allows increased access to PSMA-targeted PET imaging for selecting individuals with prostate cancer, assisting physicians in diagnosing this disease.

Radiopharmaceuticals Summary (Continued)

- Therapeutic radiopharmaceuticals are gaining support as a precise and safe technique for treating several forms of cancer. Radiopharmaceutical therapy aims to provide concentrated radiation doses to specific cancer areas within target organs or tissues while exposing healthy cells around them to the least amount of radiation.
- This response will include cases of therapeutic radiopharmaceuticals, a pharmaceutical agent used for medicinal purposes in nuclear medicine. These agents combine radioactive isotopes with pharmaceutical substances to achieve their goals.
- The first therapeutic approach is sodium iodide-131 delivery, commonly employed to treat well-differentiated thyroid cancer.
- The second alternative to treat Metastatic Castration-Resistant Prostate Cancer (mCRPC) is using Lutetium-177- PSMA-617.
- Radium-223 dichloride is used to treat metastatic prostate cancer.
- Therapeutic radiopharmaceuticals are becoming increasingly popular as a targeted, safe method of treating many cancers. Radiopharmaceutical therapy aims to provide high radiation doses to specific cancerous spots in target organs or tissues while reducing radiation doses to nearby healthy cells.

Examples of therapeutic radiopharmaceuticals

- Sodium iodide ^{131}I for well-differentiated thyroid carcinoma
- Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer (mCRPC)
- Radium-223 dichloride for metastatic prostate cancer
- Theranostics, also known as dual-functioning radiopharmaceuticals, combines targeted therapeutic with diagnostic capabilities, sometimes known as the "see and treat" method.
- A theranostic agent can be a single isotope, such as iodine-131, or a mixture of isotopes with differing emission properties, as shown by the use of lutetium-177 and gallium-68 in conjunction for neuroendocrine tumor diagnosis and treatment.

4. The Hospital Nuclear Pharmacy (Radio-pharmacy)

4. The Hospital Nuclear Pharmacy (Radio-pharmacy)

Depending on the clinical services and choice to purchase or prepare radiopharmaceuticals, radiopharmacy, often known as "hot labs," is necessary for the nuclear medicine department.

The national regulatory authorities typically authorize access to these radio-pharmacies and is usually secure (i.e., trained individuals with authorization to work with radioactivity and medicines). Most radio-pharmacies are located within existing nuclear medicine facilities to eliminate radiation hazards due to transferring radioactive materials. Areas that can be shared with the main building should be (administration areas, computers, restrooms, etc.).

To simplify cleaning and disinfection, the radiopharmacy ceiling, walls, floors, benches, tables, and seats must be smooth and non-absorbent.

4. A. Operational levels for nuclear pharmacy

The hospital's decision to "purchase or prepare" radiopharmaceuticals is based on clinical requirements, which also influence operational and quality control levels.

Operational levels 1, 2, and 3 are the three major categories into which IAEA guidelines and references are divided for distinct clinical practice levels to assure the safety of patients and operators responsible for handling radiopharmaceuticals. The relevant guidance on staff qualifications, training, facilities, equipments, types of processes, record-keeping, Quality Assurance (QA), and Quality Control (QC) necessary for each level can be found in each category's additional subcategories.

Operational Level 1a

Dispensing radiopharmaceuticals acquired or supplied in their finished form from reputable and/or recognized producers or centralized radio pharmacies are considered operational level 1a. This includes radiopharmaceuticals manufactured in unit doses or bulk for which no additional tampering or pharmaceutical compounding is necessary.

Operational Level 1b

Radioiodine and other ready-to-use radiopharmaceuticals are distributed for radionuclide therapy or palliation at operational level 1b. Samarium and strontium injections that are ready to use for pain relief are included in this.

Operational Level 2a

Nuclear medicine facilities at operational level 2a prepare radiopharmaceuticals using a technetium Tc-99m generator and authorized reagent kits following a "closed aseptic procedure". In a closed aseptic method, transferred material is not exposed to the outside environment since the manufactured product is confined in a sealed vial with a rubber septum.

Operational Level 2b

Autologous blood cell radiolabeling falls under operational level 2b. Red blood cells, platelets, and white blood cells frequently used for imaging infections or inflammation are radiolabeled as part of this. (It would be ideal to have an additional LAF or isolator for this function).

Operational Level 3a

Operational level 3a is the compounding of radiopharmaceuticals from ingredients and radionuclides for diagnostic application (including open procedure), modification to existing commercial kits, and individualized and tailored patient diagnostics. The compounding should be performed in a class II LAF cabinet/isolator placed in an aseptic environment and have better air quality, depending on national regulations. It is used in research and development.

Operational Level 3b

It includes compounding radiopharmaceuticals from chemicals and radionuclides for therapeutic applications, including open procedures. Depending on national requirements, the compounding should be done in a class II LAF cabinet/isolator located in an aseptic environment with improved air quality. It is applied to development and research.

Operational Level 3c

The creation of PET radiopharmaceuticals is operational level 3c. This includes the ^{18}FDG injections, which are growing in popularity. Research and development primarily involve compounding radiopharmaceuticals from unlicensed or long-lived generators, like gallium ^{68}Ga.

4. B. The Routine Activities of Nuclear Pharmacy

The facilities and procedures for preparing, using, and storing radiopharmaceuticals are subject to licensing by national regulatory authorities. All steps of operation require full records (hard or electronic copies), including policies and standard operating procedures (SOPs), that must be maintained for all activities which are: personnel training, hygiene, equipment/environment cleaning and disinfecting, testing, and monitoring of environmental controls, equipment maintenance and cleaning/disinfecting, end product radiochemical purity and another testing, validation of stability testing, repackaging, preparing, preparing with minor deviations, compounding, and dispensing radiopharmaceuticals.

The daily operations of a nuclear pharmacy include the following:

- Radiation protection and safety principles
- Receiving of radioactive materials
- Storage
- Preparation of radiopharmaceuticals
- Dispensing
- Quality control tests of radiopharmaceuticals
- Radioactive waste disposal

It's crucial to have accurate patient information and thorough records. The patient's name, hospital number or identity number, sex, birthdate, desired investigation, radiopharmaceutical utilized, dose activity measured, measurement time, the administering person, the checking person, and the date and time of administration must all be included in the records.

Radiopharmaceutical adverse effects should be noted and reported to the responsible doctor, the radio-pharmaceutical manufacturer, and the EPVC Egyptian Pharmacovigilance Center.

The nuclear pharmacist must ensure that all of the nuclear pharmacy's equipment, including the dose calibrator, survey meter, and Well counter, are in good working conditions before the day's operations start. The nuclear pharmacist must also ensure that all employees are committed to following safety regulations, such as wearing PPE when handling radioactive materials and high-activity materials with a pair of long tongs, preferably concealed behind a lead barrier shield.

The nuclear pharmacist plays a very important role in all the following aspects of radiopharmaceuticals:

- Procurement and Monitoring of Radioactive Packages
- Storage of Radiopharmaceuticals
- Ordering and Transcribing of Radiopharmaceuticals

- Preparation of Radiopharmaceuticals
- Dispensing of Radiopharmaceuticals
- Labeling
- Quality Control of Radiopharmaceuticals
- Radiopharmaceutical Waste Disposal
- Administering and Monitoring of Radiopharmaceuticals

4.B.1. Procurement and Monitoring of Radioactive Packages

Institutions are authorized to possess and use radioactive materials upon issuance of a radioactive material license by the national authority. Radioactive supplies are delivered directly to the nuclear medicine department or nuclear pharmacy. The nuclear pharmacist reviews and audits product invoices, including description, quantity, product number, unit price, and half-life. Feedback and input provided to the nuclear medicine leadership as warranted. In some institutions, radioactive supplies are delivered to the radiation safety office, which then is dispensed to the respective user after properly monitoring the package for external exposure and radioactive contamination.

Radiopharmaceuticals shortage: planning and communication are essential in appropriately managing short-supply situations.

Nuclear medicine departmental management systems: can significantly facilitate compliance with health system medication management programs. This software system allows the nuclear medicine department to store and retrieve relevant information about orders, deliveries, and individual patient cases.

4.B.2. Storage of Radiopharmaceuticals

Radiopharmaceutical storage policies will require review and approval by the P&T committee and inspection by a nuclear pharmacist, the same as other medications. Pharmacy follow-up brings added emphasis to medication labeling, including expiration dates and warnings. All radiopharmaceuticals must be stored appropriately according to the instructions on the radiopharmaceutical monograph for temperature or light storage to prevent degradation; for example, ^{99m}Tc-labeled macro aggregated albumin should be held at 2–4ºC to avoid any bacterial growth and denaturation of proteins, whereas ^{99m}Tc-sulfur colloid should be stored at room temperature**.**

- **Beyond Use Dating**

The staff must routinely inspect all medications and radiopharmaceuticals used in nuclear medicine at the time of use. Patients should not receive radiopharmaceuticals that have expired, been damaged, or are contaminated. Some medications are still radioactive even though they are expired; they may require decay-in-storage handling in the nuclear medicine department before disposal.

- **Look-Alike, Sound-Alike**

Storage issues: because they resemble other products and may even share a name, imaging agents with similar labeling but differing dosages may induce dispensing errors—possibly radiopharmaceuticals with similar looks and sounds, such as 99mTc-macroaggregated albumin and 99mTc-mercaptoacetyltriglycine. Caution should be exerted to prevent such errors.

4.B.3. Ordering and Transcribing of Radiopharmaceuticals

Radiopharmaceutical department follows a procedure rather than a specific prescriber order. Medication management standards permit nuclear pharmacy to follow the procedure, ensuring proper and safe use.

The nuclear medicine department manager and medical director, a pharmacist, and the P&T committee examine and approve nuclear medicine protocols regularly and whenever new information affects the safety or efficacy of the procedures.

A protocol for a specific diagnosis or treatment should have a policy defining what information must be accessible and taken into consideration before administering any radiopharmaceuticals. Age, sex, diagnoses, allergies, sensitivities, current medications, and any additional information, as necessary, like height, weight, pregnancy/lactation status, and relevant lab results are included in this information to allow an appropriateness-of-use review, drug interaction, and allergy screening, and other steps for each case.

The P&T committee approves the dose ranges in each protocol, and there is a clinical reason to utilize a dose that falls outside the range.

4.B.4. Preparation of Radiopharmaceuticals

Personnel must be trained to work with radiopharmaceuticals as per the approved policies and SOPs, the timing of reevaluation, personal hygiene, and requalification by the national regulatory authority.

All formulations should be handled in an aseptic condition. Compounded preparations (sterile and nonsterile) should depend on maintaining appropriate quality and purity, including radiochemical and radionuclides purity, as clinically relevant by the national regulatory authority and following manufacturer instructions.

- Nonsterile Radiopharmaceuticals: include oral capsules and oral solutions.
- Sterile Radiopharmaceuticals: include injectables (e.g., intravenous, intrathecal, intraperitoneal, subcutaneous, and intradermal), inhalation, ophthalmic, and intra-organ installations.

Radiolabeling of blood components requires special attention to biological risks and must be handled with standard precautions using an aseptic technique to prevent microbial contamination. It must be administered no later than 6 hours.

A decontamination kit containing absorbent material, decontamination solutions or sprays, gloves, coveralls, plastic sheets, tape, and bags to hold contaminated products should be available to cope with an unintentional radioactive spill. The staff must be trained and knowledgeable about its use, which should be checked regularly.

A description of the product, including the radionuclide, a product identification number, the activity at the time of patient administration, the volume, the time of dispensing, the patient's name, the date, the operator's identification, and the checker's identification should all be recorded for manufactured radiopharmaceuticals. The same information must be visible on a label affixed to the patient's dose.

Proper placement of the PEC is critical to ensuring an ISO Class 5 environment for preparing radiopharmaceuticals (**Particulate Matter in Area ISO Class 5 < 3520 Particle Count/m3).**

Types of PECs and Placement:

1. **Laminar Airflow Workbench (LAFW):** An LAFW for preparing radiopharmaceuticals must provide vertical unidirectional HEPA-filtered airflow.
2. **Class II Biological Safety Cabinet (BSC):** A Class II BSC cabinet has an open front, inward airflow, and downward unidirectional HEPA-filtered airflow and HEPA-filtered exhaust.

3. **Placement of PEC:** The PEC needs to be placed away from air currents in the room and traffic patterns that might interfere with the PEC's planned airflow patterns. The ISO Class 5 PEC may be installed in an unclassified **Segregated Radiopharmaceutical Processing Area (SRPA)** and is only used to prepare, prepare with minor variations, dispense, or repackage sterile radiopharmaceuticals. The PEC must be situated in an ISO Class 7 or better buffer area with an ISO Class 8 or better ante-room if used to manufacture sterile radiopharmaceuticals.

The nuclear pharmacist must take into account all potential interactions between the components, such as solubility, altered chemical stability, radiochemical stability, or other parameters (such as osmolality or pH), to ensure that the final preparation complies with pre-established standards or acceptance criteria for identity, quality, and purity.

Material identified by a label includes details on the concentration, total activity, calibration time, and nuclear pharmacy control number. The generator control sheet should provide this information.

- Intravenous: cannula PPE absorbent sheets
- Capsule: cup gloves
- Ventilation Study: vaporization set**.**

Most compounding and dispensing of radioactive material are done behind leaded glass shielding, with the radioactive material being held in lead containers and protected by leaded glass syringe shields.

4.B.5. Dispensing of Radiopharmaceuticals

- The dispensing area must adhere to national safety regulations and be clean and in good working order. The dispensing process begins with a doctor's prescription for a patient's nuclear medicine protocol.
- Each prescription must be signed by the licensed user physician and include the following elements: patient's name, identifying number (such as a clinic or hospital number), age, date, kind of study, dose and dosage form of a radiopharmaceutical, and signature.
- Each radiopharmaceutical must complete many quality control checks before being prescribed for human use.
- At the time of administration, the doses drawn should not depart from the authorized doses by more than 20%.

Figure 7: Different types of lead syringes for transporting radioactive material

Radiopharmaceuticals can be dispensed from single-dose or multiple-dose containers prepared with slight variations, compounded, or produced. The dispensing process may also involve changing the needles,

putting on a sterile cap, or diluting the radiopharmaceutical (for example, adding 0.9% sodium chloride injection to the final container).

Taking one capsule out of a container with one or more capsules is an example of dispensing non-sterile radiopharmaceuticals. One example of withdrawing a volume of solution from a single-use or multiple-dose container into a syringe pertains to sterile radiopharmaceuticals. The dosage syringe is labeled with its composition and quantity before being put in a lead syringe holder.

The quality assurance of the dose calibrator should comprise daily consistency checks, quarterly linearity checks, and annual accuracy checks.

For each dose of a radiopharmaceutical dispensed in a centralized nuclear pharmacy, the institution must enter all relevant data in the record book. This includes the patient's name, the doctor's name, and a prescription number.

The implementation of the recall procedures policy must be reported to appropriate regulatory bodies according to the severity of the problem (such as the wrong administration of radiopharmaceuticals or overdose of radiopharmaceuticals) and the urgency for the implementation and completion of the recall.

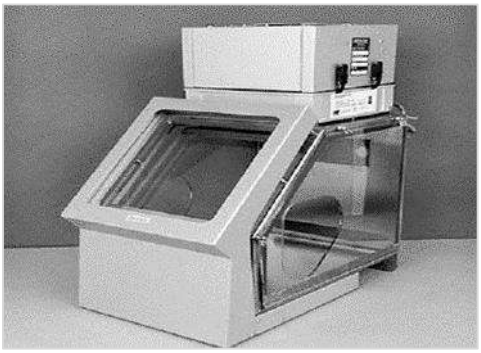

Figure 8: Dose dispensing hoods

4.B.6. Labeling

The minimal standards for labeling the outer shielding (such as a syringe or vial shielding) and the inner container (such as a syringe or vial) are needed for radiopharmaceuticals. All employees who distribute and/or dispense radiopharmaceuticals must ensure that all labeling complies with the national regulatory authority's regulations.

The outer shielding must be labeled with the following:

- The patient name/identifier, for all therapeutic and blood products
- Radionuclide and chemical form (generic name)
- Radioactivity at the date and time of calibration
- Volume or number of units dispensed (e.g., 2 capsules), as applicable
- The product's expiration date or beyond-use date (BUD, if appropriate)
- Any unique handling or storage recommendations for usage that are not immediately necessary (such as refrigeration or resuspension)
- Route of administration
- Standard radiation symbol
- The words "Caution—Radioactive Material"

4.B.7. Quality Control of Radiopharmaceuticals

Before releasing the radiopharmaceutical(s), QC ensures that the requirements have been completed by sampling, testing, and documenting results.

QA for radiopharmaceutical processing establishes a system of:

1. Procedures should be followed as outlined in the SOPs.
2. Errors and other quality issues should be prevented and detected.
3. Adverse events and complaints should be assessed.
4. Appropriate investigations should be conducted, and corrective measures should be taken.

Radiopharmaceuticals must pass several QC tests (To ensure the quality of a radiopharmaceutical product, various tests are conducted such as radionuclide purity control, radiochemical purity control, chemical purity control, biological control, and physical inspection, before dispensing for human administration. Regular checks should be made for all labeled products' sterility, biological safety, potency, efficacy, and radiochemical purity.

- Discard any preparations with incorrect labeling.
- The particle size of colloidal and macro-aggregated preparations must be checked, and any inappropriate items must be discarded.
- All radiopharmaceuticals should have a suitable hydrogen ion concentration or pH for stability and integrity.
- Radionuclide purity varies over time and is based on the amounts of the target radionuclide and other contaminants and their relative half-lives.
- SOPs for managing complaints must be created and implemented by radiopharmaceutical plants. A specific radiopharmaceutical quality, container labeling, or potential adverse responses may be the subject of complaints.
- A designated individual must review all complaints to see if they point to possible issues with the radiopharmaceutical's quality.
- All testing devices must be appropriate for their intended application and capable of generating reliable results. To guarantee that equipment is regularly maintained, calibrated, and qualified and that these operations are documented, each laboratory should have and adhere to written procedures.
- Radionuclides that can be traced to national standards should be utilized for routine calibration of radionuclides, containers, and sample volume. It is recommended to do quarterly linearity checks on the dose calibrator response throughout the entire spectrum of activities monitored.
- The facility must keep an easily accessible record (written or electronic) of every complaint, regardless of how it was submitted (e.g., via e-mail, phone, or letter).

4.B.8. Radiopharmaceutical Waste Disposal

Radiopharmaceutical wastes are disposed of under the proper circumstances without harming humans or the environment. Most hospitals produce solid radioactive, liquid, biological, sharp, and airborne wastes, which are disposed of following the national regulatory body's regulations.

- **Solid Radioactive Wastes**

Empty radiopharmaceutical containers, such as bottles, injectors, inhalation apparatus, PET end-result wastes, and injection-related gloves, are included in this category of wastes. Sharp-tipped wastes, such as needles, are collected in separate containers. These containers' lids, covers, and bases are shielded with the necessary material, and an international radiation mark is placed on the outside of the container. Foot pedals are used to open and close these.

The containers should be suitable for the waste, considering its physical, chemical, biological, and radioactive properties, and segregate wastes according to their half-life.

Waste bins shouldn't be overfilled to the point that they compromise their structural integrity. The radiation dose rate is then calculated using a Geiger Müller (GM) detector once these containers are gathered in a different location. The trash is considered routine medical waste and is disposed of immediately according to national regulations.

Suppose the measured value exceeds the released threshold. In that case, the accumulation container is retained in lead-shielded storage and left to stand for ten times the physical half-life before being measured again with the GM instrument.

- **Liquid Radioactive Wastes**

Radiopharmaceuticals fluids waste and urine and stools of patients containing radionuclides waste should be collected, segregated, and characterized, as far as possible, at the point of origin according to its physical, chemical, biological, and radiological properties.

It is necessary to segregate liquid wastes by taking the following criteria into account:

- Radionuclide content and activity
- The half-life of radionuclides and suitability for decay storage
- Organic/aqueous liquids
- Non-homogeneity of waste
- Infectious hazard
- Chemical hazards
- Flammability

Liquid radioactive waste that meets clearance levels can be discharged directly to an approved drainage/sewage system, such as a municipal sewer, according to the approval of the national regulatory authority.

When radioactive material is poured into the sink, the sink should be washed with plenty of water. It should then be checked with the Survey Meter.

The toilet should be double flushed after being used by the radioactive patient (and cover the toilette seat before flushing).

Chemically toxic or carcinogenic waste is incompatible with environmental release and must be collected separately to avoid uncontrolled chemical reactions.

This waste should be sent for appropriate waste treatment as the national regulatory authority requires.

Biologically contaminated radioactive liquid waste must be collected separately and treated to deactivate (e.g., autoclaving, chemical disinfection). All infectious contaminants follow the national regulatory authority regulations.

- **Gaseous Radioactive Waste**

Laminar airflow systems should be effective in hospitals that use radioactive gases. Within the parameters of the regulations established during the design and licensing of the hospital, these wastes are released into the atmosphere by the licensee.

4.B.9. Administering and Monitoring of Radiopharmaceuticals

Before administration, it is necessary to confirm the patient's identity, the identity of the radiopharmaceutical, and the administration route. Syringes and exterior shields or containers must be labeled to verify the contents.

The nuclear pharmacist takes part in screening for potential drug interactions and contraindications particular to the agent to be used, checks for dosage adjustments such as those required by renal or liver function, and educates the patient about the medication to be taken.

This patient education covers the name of the radiopharmaceutical, its risks and advantages, potential adverse effects, post-procedure instructions, and answers to patient inquiries.

Monitoring the patient after radiopharmaceutical administration, if there is any complication, the nuclear medicine physician is notified.

The reporting process is essential for an error or adverse effect in radiopharmaceutical administration.

Summary of Fundamental Features and Objectives of Nuclear Pharmacy in the Hospital Setting

- Clinical requirements influence operational levels in the field of nuclear pharmacy, which in turn affects the scope of operating procedures and quality control methods.
- The IAEA's guidelines and references are divided into three primary operational levels: 1, 2, and 3. These guiding principles aim to ensure the safety of patients and operators involved in radiopharmaceutical handling in various clinical practice conditions.

Nuclear pharmacy routine duties include the following:

- Procurement and monitoring of radioactive substances.
- Policies for storing radiopharmaceuticals will need to be thoroughly reviewed and approved by the P&T committee, like the approach used for other pharmaceuticals within the unit. The pharmacy's involvement in handling these prescriptions highlights the importance of proper labeling, including expiration dates and suitable warnings.
- To avoid degrading conditions, all radiopharmaceuticals must be stored per the guidelines specified in the radiopharmaceutical monograph, particularly regarding temperature and light storage requirements.
- The preparation and documentation of radiopharmaceuticals.
- The preparation of radiopharmaceuticals is classified into two types: sterile and nonsterile.
- Radiopharmaceutical administration must adhere to national safety standards, which require purity and proper procedure. The dispensing process begins with the issue of a medical practitioner's prescription for a patient's nuclear medicine examination.
- Providing descriptive or identifying information, labeling the outer shielding (e.g., syringe or vial shielding), and the interior container must meet minimal requirements.
- QC methods for radiopharmaceuticals include sampling, testing, and documenting results to ensure all standards are met.
- The disposal of radiopharmaceutical waste, specifically in solid, liquid, and gaseous forms, should be considered.
- It is critical to validate the patient's identity and the identity of the radiopharmaceutical product being used and to ensure adherence to the prescribed administration route when delivering and monitoring radiopharmaceuticals. To facilitate the verification of their contents, appropriate labels must be placed on syringes and exterior shields or containers.

5. Instrumentation and Equipment

5. Instrumentation and Equipment

5. A. Radiation Personal Protective Equipment (PPE)

- The first step to optimizing safe radiation practices is educating hospital staff on radiation best practices by following the ALARA principle.
- PPE is used to prevent workers from becoming contaminated with radioactive material. It can prevent skin contamination with particulate radiation (alpha and beta particles) and avoid inhalation of radioactive materials.
- Different PPE may protect against external and internal radiation exposures; PPE should protect large areas of the wearer's body or individual organs, such as the eye (full face shielded or leaded-safety glasses) against external irradiation.
- Respirators will protect from inhalation of radioactive contamination (internal radiation).
- Laboratory coats (lab coats) made of cotton or synthetic fibers are commonly used where there is a risk of minor radioactive contamination.
- Protective footwear and gloves against radioactive contamination.
- A lead apron with X-ray and fluoroscopy machines workers at least 0.25 mm lead equivalence (0.5 mm is recommended) will reduce scattered X-rays by 95%. A thyroid collar and leaded eyewear (or "radiation glasses") are also recommended.
- Alarming dosimeters help you stay on time and track your accumulated doses in areas with elevated radiation levels.
- The employees who enter and leave the hot lab area are the subject of surveys to detect radioactive contamination.
- Gloves are removed from patient to patient by a unique technique to avoid transferring radiological contamination.
- Taps and soap dispensers that are operable without direct hand contact and disposable towels or a hot air dryer.
- An emergency eyewash, installed near the hand washing sink.
- An emergency shower for decontamination of persons.

5. B. Dosimeters

A dosimeter is an instrument used to measure ionizing radiation for individuals who work in radiation-exposed institutions (via alpha or beta particles, neutrons, gamma rays, or x-rays). According to the international requirements, it is recommended to assess monthly.

Types of dosimeters

- **The film badge:**

The film badge is the most used for personnel monitoring, which offers precise radiation exposure readings from X, gamma, and other sources. A radiation-sensitive film is enclosed in a plastic holder to make up the film badge. When a film has been exposed and developed, its optical density is measured using a densitometer, and the results are contrasted with the optical density of a calibrated film subjected to known radiations. Radiation technicians typically swap out film badges once a month.

- **Thermoluminescent Dosimeter (TLD):**

When inorganic crystals (chips) like lithium fluoride are subjected to radiation, they become excited and emit light when heated to temperatures between 300 and 400 °C. This is how TLDs work. The radiation energy absorbed in the TLD directly correlates with the amount of light emitted.

- **Pregnancy and fetal dosimeters:**

A dosimeter is worn on the abdomen of a Declared Pregnant Woman to monitor the radiation dose to the embryo/fetus under the lead apron (if used).

Lost or damaged dosimeter:

Contact the badge coordinator or the RSO immediately if your dosimeter is broken or missing so that a replacement can be provided.

General information:

- Dosimeters do not protect you.
- It should be kept in a location apart from radiation sources.
- Don’t share your dosimeter with anybody else; never wear someone else’s.
- Avoid using your dosimeter for any personal medical treatments requiring nuclear medicine isotopes or diagnostic X-rays.

5. C. Dose Calibrators

One of the most essential tools in nuclear medicine is the dose calibrator, which measures the activity of radionuclides used to prepare and administer radiopharmaceuticals.

Figure 9: Dose calibrators

5. D. Geiger–Müller Counters (GM)

The GM Counters, also known as survey meters, are the most sensitive detectors (analogue or digital) with quick response times that are most frequently used for measuring radiation exposure supplied by a source.

Figure 10: Geiger-Müller counter

5. E. Well Counter

Well Counters are scintillation crystals that have been highly insulated. They are used to measure and identify minute levels of radioactivity—mainly gamma rays—found in limited volumes, like a test tube. A Well counter is utilized for highly sensitive counting of radioactive specimens, such as blood or urine samples or contamination survey wipes. They are highly intrinsically efficient and geometrically efficient and can count activities up to about 37 kBq.

5. F. Calibration

All radiation detection equipment, such as radionuclide detectors (non-imaging radiation detection) and radiological contamination monitors, should be calibrated regularly.

All equipment, including air handling units, isolators, laminar flow cabinets (LFCs), and radionuclide calibrators, should have the performance and maintenance outcomes documented and reviewed regularly. Refrigerator and freezer temperatures should be recorded each day using a maximum and minimum temperature gauge or a computerized central measurement.

5. G. Diagnostic Equipment

5.G.1. Single-Photon Emission Computed Tomography (SPECT)

Nuclear imaging tests like SPECT scans use spinning detectors around the body while recording events at each detector position to find single photons or energy generated by the radioactive chemical inside the body. Using a computer, the radioactivity measured is shown in three dimensions (or tomogram).

The gamma rays' information is captured by the computer and converted into 2D cross-sections. To create a 3D image, these cross-sections can be joined back together.

Iodine-123 (^{123}I), technetium-99m (^{99m}Tc), xenon-133 (^{133}Xe), thallium-201 (^{201}Tl), and indium-111 (^{111}In) radioisotopes are frequently employed in SPECT to label tracers.

For 180° or 360° angular sampling, the detector head spins around the patient's long axis in small angle increments.

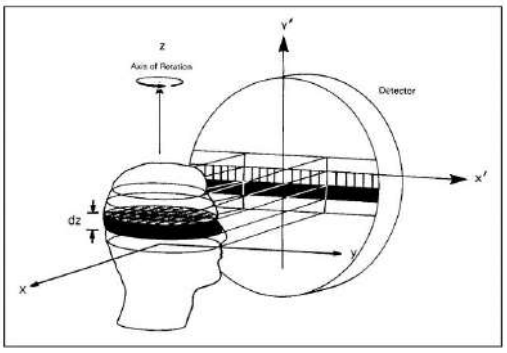

Figure 11: Single-Photon Emission Computed Tomography (SPECT) system
The system consists of a gamma camera viewing the three-dimensional (x, y, z) object as a stack of two-dimensional (x, y) slices of a finite thickness

5.G.2. Positron Emission Tomography (PET)

The three-dimensional distribution of radiotracers that emit positrons is measured using the tomographic technique known as PET. PET enables non-invasive quantitative assessment of biochemical and functional processes.

PET measures physiological function by examining blood flow, metabolism, neurotransmitters, and radiolabeled medicines. It combines nuclear medicine and biochemical analysis.

One frequent application of PET is determining the glucose consumption rate in various body regions. Accumulation of the radiolabeled glucose analog 18-FDG enables the determination of the glucose consumption rate. This can be used clinically to differentiate between benign and malignant tumors since the latter metabolizes glucose more quickly than the former.

Other uses for PET include examining blood flow and oxygen consumption in various brain regions, for example, to understand strokes and dementia better. This method can also track chemical neurotransmitters, such as dopamine, in Parkinson's disease.

Indications for ^{18}F-FDG PET/CT include but are not limited to the following:

- Differentiating benign from malignant tumors.
- When a patient exhibits a paraneoplastic syndrome or metastatic disease found to be the first sign of cancer, searching for an unidentified tumor source may be necessary.
- Staging known cancers.
- Tracking the impact of treatment on known cancers.
- Whether post-treatment tumors, post-treatment fibrosis, or necrosis represent lingering abnormalities discovered on physical examination or through other imaging investigations.
- Identifying tumor recurrence, particularly when tumor markers are elevated.
- Deciding which part of a tumor will most likely provide diagnostic information for biopsy.
- Aiding in the planning of radiation therapy to provide more conclusive information on malignant (cancerous) tumors and other lesions. PET may also be utilized in conjunction with other diagnostic procedures like computed tomography (CT) or magnetic resonance imaging (MRI). The PET/CT scanner, a more recent innovation, combines PET and CT technologies.

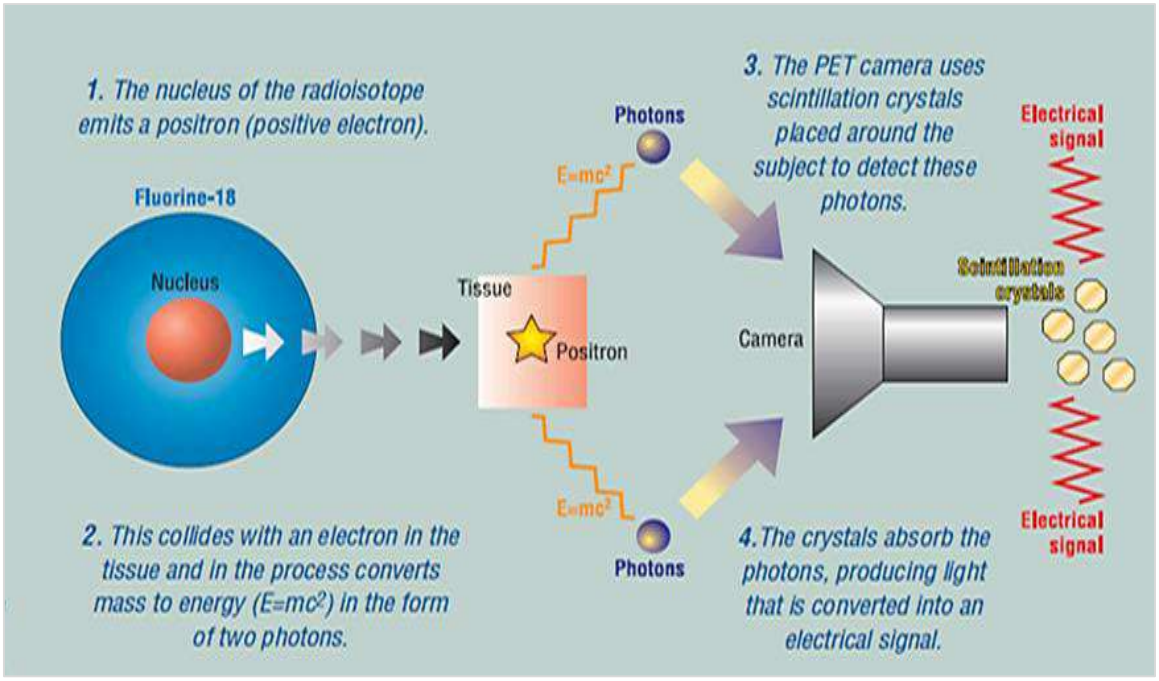

Figure 12: PET Techniques

The main difference between SPECT and PET scans

Due to the longer half-life of single-photon emitters, radiopharmaceuticals used for SPECT are more affordable and convenient to distribute. Under certain circumstances, they provide more precise targeting abilities of the biologically active compounds. Positron-emitting radioisotopes have high costs because of their short half-lives, better resolution, and sensitivity.

SPECT scans are based on **gamma-emitting** radioisotopes, and the decay of the radiotracers used with PET scans produces positive electrons **called positrons.**

5.G.3. Hybrid Multimodality Imaging

PET/CT (MRI) or SPECT/MRI images, which are particularly helpful in evaluating the efficacy of tumor treatments, are frequently created by fusing PET or SPECT images with CT or MR images. By aligning the two pictures for the matrix size, the voxel intensity, and the rotation, this technique allows functional PET or SPECT scans to be categorized with anatomical CT or MR images. These scans can detect cancer and provide information on its stage, metastasis, therapy options, and effectiveness.

The combination of PET and SPECT with MRI is motivated by clinical applications where MRI is preferred to CT (e.g., neuroimaging and pelvic cancer).

Instrumentation and Equipment Section Summary

- Personal Protective Equipment (PPE) of various forms can protect against both external and internal radiation exposures.
- PPE is used as a means of prevention to protect employees from potential contamination caused by radioactive substances. This precaution is intended to reduce the risk of skin contamination caused by particulate radiation, especially alpha and beta particles, and prevent radioactive substances from being inhaled.
- Respirators, in particular, are effective in protecting individuals from inhaling radioactive pollutants, an example of internal radiation.
- A dosimeter measures ionizing radiation exposure of workers who perform their jobs in radiation-exposed environments (e.g., the film badge and Thermoluminescent Dosimeter (TLD)).
- Monthly assessments are recommended as a type of assessment following international standards.
- The dose calibrator is an essential device in nuclear medicine since it is used to quantify the activity of radionuclides used in the production and administration of radiopharmaceuticals.
- The GM Counters, often called survey meters, are susceptible detectors with quick response times. These tools often quantify radiation exposure originating from a specific source.
- Well counters are scintillation crystals that have been extensively separated. These tools are used to quantify and detect minute levels of radioactivity.
- It is advised that radiation detection equipment, such as radionuclide detectors (particularly non-imaging radiation detection devices) and radiological contamination monitors, be calibrated regularly.
- Single-Photon Emission Computed Tomography (SPECT) scans use spinning detectors around the body to detect and record the occurrence of single photons or energy released by radioactive chemical substances.
- PET is a medical imaging technology that visualizes and measures physiological processes in the body by detecting positron-emitting radioactive tracers. PET, a tomographic imaging technique, determines the spatial distribution of positron-emitting radiotracers in three dimensions.
- PET imaging enables the non-invasive and quantitative examination of biochemical and functional processes.

- PET is a scientific technique used to evaluate physiological function by examining blood flow, metabolism, neurotransmitters, and the delivery of radiolabeled drugs. This approach combines nuclear medicine and biochemical examinations.
- Combining multiple imaging techniques to get a full and detailed assessment of a certain subject or phenomenon is called hybrid multimodality imaging. The fusion of PET/CT (MRI) or SPECT/MRI images is a standard method for assessing tumor treatment efficacy.
- Combining PET or SPECT images with CT or MR images results in comprehensive and informative visual representations.

6. Patient-Related Aspects

6. Patient-Related Aspects

6. A. Radiological Precautions for Patient Safety During Administration

- Bathrooms with separate sinks and toilets should be provided in rooms allocated for patients receiving radiopharmaceutical therapy. To achieve appropriate dilution of pooped radioactive materials and to reduce radiological contamination, a sign encouraging patients to flush the toilet at least twice (and cover the toilette seat before flushing) and wash their hands should be put up.
- Preventing the spread of radioactive contamination by patient excreta and vomit requires special attention.
- After administering radiopharmaceutical therapy, a protocol for patient discharge should be implemented.
- Avoiding sexual interaction during the designated restricted period should be discussed with both male and female patients.

6. B. Radiopharmaceutical Administration Errors

Following the national regulatory authority, errors in administering radiopharmaceuticals involving discrepancies from the authorized user's prescription must be documented and reported:

- Administration errors include administering the radiopharmaceutical to the incorrect patient, administering the incorrect radiopharmaceutical, doing the incorrect activity, or inappropriately examining pregnant or nursing patients.
- Before administering radiopharmaceuticals, confirm the patient's identity, the radionuclide dose, the chemical form, the activity, and the method of administration with a documented order from the authorized user physician.
- Administration errors of therapeutic or diagnostic dose differing from the prescribed dose by >20%.
- Use the following website to share and report any radiopharmaceutical administration errors: https://shorturl.at/aqsMZ of the NO HARMe program (National Office for Handling And Reduction of Medication errors) at the Egyptian Drug Authority.

6. C. Adverse Events Reporting

The adverse events potentially associated with the diagnostic or therapeutic radiopharmaceuticals on the patient must be reported to the Egyptian Pharmacovigilance Center (EPVC) and the national regulatory authority.

The adverse events of radiopharmaceuticals may occur due to poor transport and storage conditions and can also result from a substandard product when the formulation has changed and the product expired. Products from a different manufacturer or supplier should be monitored more closely.

Adverse reactions to diagnostic radiopharmaceuticals are rare, frequently momentary, and of generally mild severity.

Adverse events of therapeutic radiopharmaceuticals may include hypersensitive reactions and a wide range of physiologic and systemic symptoms. The most frequent side events are nausea, dyspnea, bronchospasm, lowered blood pressure, itching, flushing, hives, chills, coughing, bradycardia, muscular cramps, and dizziness. Some adverse events take longer to manifest than others.

Share and report in case of any adverse event of the radiopharmaceuticals through the following link: https://shorturl.at/bouB7 to the Egyptian Pharmacovigilance Center at the Egyptian Drug Authority.

Table 3: Reported adverse reactions from radiopharmaceuticals

Radiopharmaceuticals	Adverse reactions
^{99m}Tc - pertechnetate	Nausea, pruritus, headache, hives, chills, chest pain
^{99m}Tc - sulfur colloid	Cardiopulmonary arrest, seizures, hypotension, dyspnea, chills, nausea, fever, pruritus, dizziness
^{99m}Tc - pyrophosphate	Flushing, hypotension, fever, chills, nausea, vomiting, dizziness, pruritus
^{99m}Tc - DTPA	Pyrogenic and allergic reactions
^{99m}Tc - MAA	Hypersensitivity to albumin
^{99m}Tc - mebrofenin	Urticaria/hives, chills, nausea
^{99m}Tc - M AG3	Nausea, dyspnea, tachycardia, itching, seizures, chills, fever, wheezing
^{99m}Tc - sestamibi	Headache, chest pain, angina, nausea, metallic taste
^{99m}Tc - tetrofosmin	Angina, vomiting, dyspnea, respiratory arrest, flushing, abdominal pain, hypotension, metallic taste
^{99m}Tc - DMSA	Nausea, rash, flushing, syncope, fever
^{201}TI - thallous chloride	Fever, rash, pruritus, tremors, dyspnea, blurred vision, diarrhea, sweating
^{123}I - MIBG	Dizziness, rash, pruritus, flushing, headache
^{123}I - ioflupane	Headache, nausea, vertigo, dry mouth, rash, pruritus
^{123}I - NaI capsules	Pruritus, vomiting, hives, chest pain
^{131}I - NaI	Nausea, vomiting, chest pain, rapid heart rate, itching skin, rash
^{111}In - octreotide	Fever, nausea, flushing, dizziness, headache, hypotension, tiredness
^{111}In - DTPA	Vomiting, pruritus, headache, meningitis, pyrogen reactions
^{111}In - capromab pendetide	Hypotension, hypertension, pruritus, fever, headache, increase in bilirubin, rash, elevated liver enzyme, asthenia, HAMA reaction, shortness of breath
^{67}Ga - citrate	Allergic reactions, skin rash, nausea
^{18}F - fluorodeoxyglucoset	Rash on face and trunk

6. D. Drug-Induced Changes in Radiopharmaceutical Bio-distribution

It has long been acknowledged that one essential aspect in interpreting scintigraphic images is how different medications affect the bio-distribution of radiopharmaceuticals.

Numerous medications that patients take tend to obstruct the in-vivo distribution of the radiopharmaceutical employed in a later nuclear medicine procedure. While some drugs inhibit the radiopharmaceutical uptake, others help it localize in the target organ.

Table 4: Iatrogenic alteration in the bio distribution of common radiopharmaceuticals

Imaging	Drug	Effect on localization
Bone imaging with ^{99m}Tc – phosphonate compounds	Melphalan	Increased bone uptake
	Chemotherapeutic agents, dextrose, iron	Increased renal activity
	Cytotoxic therapy	Increased uptake in calvarium
	Meperidine	Soft tissue uptake
	Iron dextran	Increased uptake at the injection site
	Phospho – soda, corticosteroids	Decreased bone uptake
RES imaging with ^{99m}Tc – SC	Al^{3+}, Mg^{2+}	Increased lung activity
	Anesthetics	Increased splenic uptake
	Estrogens	Focal areas of decreased uptake in the liver
	BCNU	Decreased splenic uptake
Myocardial perfusion imaging with ^{201}Tl chloride	Dipyridamole	Increased myocardial uptake
	Propranolol, digitalis glycosides	Decreased myocardial uptake
	Furosemide, isoproterenol	Increased myocardial uptake
Hepatobiliary imaging with ^{99m}Tc – IDA derivatives	Cholecystokinin	Increased gall bladder contraction
	Narcotic analgesics	Prolonged liver-to-duodenum transit time
	Atropine	Prolonged gall bladder activity
	Nicotinic acid	Decreased hepatic uptake
Prostatic imaging with ^{111}In – capromab pendetide	Androgen ablation	Decreased uptake in prostatic tumor
Parkinson's disease detection with ^{123}I – ioflupane	Amoxapine, amphetamine, benztropine, bupropion, buspirone, cocaine, selegiline, mazindol, methamphetamine, sertraline, methylphenidate, norephedrine, phentermine, phenylpropanolamine	Decreased uptake

Imaging	Drug	Effect on localization
Thyroid uptake and imaging with ^{123}I – NAI and ^{131}I – NAI	TcO_4^-, Br^-, ClO_4^-, SCN^-, iodine-containing preparations (Lugol's solution, SSKI, cough medicine, kelp …etc.), contrast media, antithyroid drugs (methimazole, propylthiouracil), natural or synthetic thyroid preparations (liothyronine, levothyroxine)	Decreased uptake
Tumor and inflammatory process imaging with ^{67}Ga-citrate	Iron dextran, deferoxamine (before ^{67}Ga injection)	Decreased uptake
	Iron dextran, deferoxamine (after ^{67}Ga injection)	Increased uptake
	Chemotherapeutic agents	Diffuse lung uptake
	Antibiotics	Uptake in colon and kidneys
	Estrogens	Uptake in mammary tissue
^{123}I – MIBG for imaging neuroendocrine tumors	Amitryptiline and derivatives, imipramine and derivatives, antidepressants, antihypertensives, sympathomimetic amines, and cocaine	Decreased uptake in tumor
In-vivo ^{99m}Tc – labeling of RBCs	Heparin, dextran, doxorubicin, penicillin, hydralazine	Poor labeling

Pharmacist Recommendations

The nuclear pharmacists' recommendations are means of solving the drug and radiopharmaceutical therapy problems identified in pharmaceutical care; the outcomes of the recommendations include drug regimen modification, drug dose adjustment, resolving of errors, and prevention of potential drug therapy problems (DTPs) that have positive outcomes on drug therapy and patient satisfaction.

For instance, the audiovisual intervention can reduce false positive ^{18}F-FDG uptake in muscles or brown adipose tissue (BAT) without the drawbacks of pharmacological therapies (e.g. diazepam) and minimize patient anxiety in the PET uptake room.

6. E. Clinical Nuclear Pharmacist Role in Patient Safety

6.E.1. FDG-PET/CT Examination

- **Receiving the request for FDG examination**

  The request for the examination should at least include the diagnosis and questions to be answered.

- **Review of the medical history for the FDG examination**

  ✓ Review the patient's medical history, paying close attention to the diagnosis (cancer type and known sites), oncological history, and other comorbidities (infections, inflammation, and diabetes mellitus). It

is essential to consider relevant laboratory tests and make previous imaging study data available for evaluation.

- ✓ Height and weight should be measured before each FDG PET examination.
- ✓ Review of used medications, especially but not limited to sedatives, corticosteroids, growth factors, and diabetes medications.
- ✓ The outcomes of additional imaging tests, preferably with dates and complete reports (mainly CT, MRI, and prior PET or PET/CT).
- ✓ Allergy and renal function (creatinine and/or glomerular filtration rate) should be evaluated if an intravenous contrast agent is used.
- ✓ History of claustrophobia (fear of enclosed spaces) and patient's ability to lift arms overhead.
- ✓ The referring physician can start the protocol for prevention of nephrotoxicity if renal function is suboptimal and an FDG PET/CT examination with intravenous CT contrast agent is required (the physician prescribes adequate IV fluids, repeat the blood test, and prescribe medication for prevention of nephrotoxicity if necessary).
- ✓ The physician uses iso-osmolar contrast agents, waits at least 72 hours between investigations using contrast agents, and provides appropriate hydration to at-risk patients to prevent contrast agent-induced nephropathy. Renal failure induced by contrast agents can be reduced by stopping aminoglycosides, diuretics, and nonsteroidal anti-inflammatory drugs.

- **FDG examination instructions for non-diabetic patients**

To maintain uptake in target tissues, pretreatment aims to reduce radiopharmaceutical uptake in healthy tissues such as the heart, skeletal muscle, and brown fat. These pretreatments include:

- ✓ Telling patients to avoid intense activity 24 hours before receiving the FDG injection.
- ✓ Low-carbohydrate meals are advised, 24 hours before the FDG injection.
- ✓ Avoiding the use of caffeine, alcohol, or nicotine, 12 hours before FDG injection.
- ✓ Giving instructions of minimum 4-hour fasting and for the same period to avoid drinking oral or receiving intravenous fluids containing sugar or dextrose. No sugar-containing over-the-counter medications, gum, mints, or sweets. Even "sugar-free" products can have sugar residues in them.
- ✓ Before administering ^{18}F-FDG, the blood glucose level should be tested. In hyperglycemic conditions, there is a reduction in ^{18}F-FDG tumor uptake.
- ✓ Encouraging oral hydration with a target of one liter two hours before the visit.
- ✓ Prescription drugs must be taken exactly as prescribed.
- ✓ Stop taking metformin 48 hours before the experiment.
- ✓ If a contrast-enhanced CT scan is required, request renal function tests and see if there is a history of iodinated contrast allergy.
- ✓ Individual and institutional policies should be followed if a patient needs sedation or general anesthesia.
- ✓ Personal and institutional procedures should be followed if a patient requires general anesthesia or sedation.

- ✓ For the entire examination (20 to 45 minutes), the patient should be able to lie still inside the PET/CT equipment.
- ✓ The patient should undergo brain imaging in a quiet, low-light environment during the administration of ^{18}F-FDG and the ensuing uptake period.
- ✓ The patient should be seated or lying down during the administration of ^{18}F-FDG and the subsequent uptake period to prevent muscular uptake during body imaging.
- ✓ The FDG PET/CT investigation can be carried out if the plasma glucose level is less than 200 mg/dL. The FDG PET/CT study must be postponed if the plasma glucose level exceeds 200 mg/dL.
- ✓ Insulin shouldn't be given to lower blood sugar levels because doing so increases the amount of FDG absorbed by muscles unless there is at least a 4-hour gap between giving insulin and giving FDG. Subcutaneous injections are the recommended method of delivery of insulin.

- **FDG examination instructions for pregnancy (suspected or confirmed)**
  - ✓ When necessary, conduct pregnancy tests, following the institutional policies, and, whenever possible, confirm if a female patient is pregnant before proceeding with any diagnostic treatment.
- **FDG examination instructions for breastfeeding**
  - ✓ Since minimal FDG is excreted in milk following FDG injection, the International Commission on Radiological Protection (ICRP) does not advise discontinuing breastfeeding. To lower the radiation exposure, it is recommended by the (ICRP) that contact between mother and child be restricted for 12 hours after the injection of FDG.
- **FDG examination instructions for diabetic patients**
  - ✓ As most diabetic patients have their lowest blood glucose levels in the late morning, this is the ideal time to conduct the FDG PET/CT examination.
  - ✓ Patients must follow the above-listed requirements for fasting.
  - ✓ To control their blood sugar, patients continue taking oral medications.
  - ✓ Patients with diabetes should take their regular dose of insulin the day before. Patients should fast (except for water) after midnight.
  - ✓ You can choose to have the examination at noon or in the late morning. It can be planned for early morning when the patient should consume a typical meal and administer the usual insulin dose. The PET/CT scan shouldn't be affected by the intermediate-acting insulin given the previous evening, and glycaemia will likely still be under control.
  - ✓ If a patient uses an insulin pump, it is best to switch off four hours before the examination; however, if this is not possible, it should be set to the night/basal setting during the PET scan. Setting adjustments can be made as needed after the PET scan.
  - ✓ Patients should be urged to eat dinner as soon as the PET scan is over. Patients might benefit from taking half their morning insulin dose and their post-PET meal.
- **Examination FDG considered premeditations:**
  - ✓ Patients experiencing anxiety or claustrophobia may be given anxiolytics.
  - ✓ To reduce physiologic brown fat uptake, oral beta-blockers (such as propranolol 20 mg) or benzodiazepines (such as diazepam 5 mg) might be taken 60 minutes before injection.

- **FDG examination dose**
  - ✓ The approved range for administered FDG activity in humans is between 185 and 740 MBq (5-20 mCi).
  - ✓ A minimum administered activity for pediatric FDG should be 26 MBq (0.7 mCi) for the body and 3.7 MBq/kg (0.10 mCi/kg), with a minimum of 14 MBq (0.37 mCi) for the head.
- **Protocol for imaging**
  - ✓ The radiopharmaceutical should be intravenously delivered far from any known or suspected disease locations. A central line can be utilized if peripheral IV access is impossible, but it must be sufficiently flushed with normal saline.
  - ✓ Images of the emission should be taken 60 minutes following the radiopharmaceutical injection.
  - ✓ Based on the administered activity, patient body weight, and the sensitivity of the PET device, the average emission picture capture time for body imaging ranges from 1 to 5 minutes or longer per bed position. In some clinical circumstances, an acquisition time can be changed to deliver higher-count images in a specific anatomic region.
  - ✓ Report any issues with FDG administration, and if extravasation is suspected, image the injection site.
  - ✓ Ask patients to sit or lie as quietly as possible without talking. Give out cozy seats or beds. Five minutes before the FDG PET/CT examination starts, instruct patients to visit the restroom to empty their bladder.
- **Nuclear clinical pharmacy interventions for FDG examination**
  - ✓ Intense urinary bladder tracer activity decreases image quality and can confound the interpretation of findings in the pelvis. Hydration and a loop diuretic, with or without bladder catheterization, may reduce accumulated urinary tracer activity in the bladder. Bladder catheterization with a 3-way flushing catheter running a continuous bladder flush after injection until imaging successfully clears bladder activity.
  - ✓ Especially in cold locations and air-conditioned environments, keeping the patient in a warm room for 30 to 60 minutes before the injection of ^{18}F-FDG will aid in reducing brown fat uptake. Before administering ^{18}F-FDG, lorazepam or diazepam may lessen the amount of ^{18}F-FDG taken up by brown adipose tissue or skeletal muscle. B-blockers may also reduce brown fat uptake.
- **Sources of error in FDG examination**

  Other processes could result in false-positive and false-negative outcomes. The most typical causes are included in the following list, which is not exhaustive but does contain them:

  1. **False-negative findings in FDG examination**
     - Small size (>2 times the resolution of the system)
     - Tumor necrosis
     - Hyperglycemia and hyperinsulinemia
     - Some low-grade malignancies (such as brain tumors, sarcomas, and lymphomas)
     - Recent high-dose steroid therapy
     - Recent chemotherapy or radiotherapy
     - Tumors with significant mucinous components
     - Prostate carcinoma, especially well-differentiated tumors
     - Some genitourinary carcinomas, especially well-differentiated tumors
     - Some skeletal metastases, especially osteoblastic or sclerotic tumors

- Some osteosarcomas
- Some neuroendocrine tumors, especially well-differentiated tumors
- Some thyroid carcinomas, especially well-differentiated tumors
- Some hepatocellular carcinomas, especially well-differentiated tumors
- Some bronchioloalveolar carcinomas
- Some lobular carcinomas of the breast

2. **False-positive findings in FDG examination**
   - Physiologic uptake may lead to false-positive interpretations.
   - Inflammatory processes
   - Ischemia
   - Hyperplasia or dysplasia
   - Benign neoplasms
   - Artifacts: Misalignment between PET and CT data can cause attenuation correction artifacts

- **Instructions after a PET-CT scan**
  - ✓ After the PET-CT scan, the patient can resume regular routines for eating, exercising and driving. Getting plenty of water is recommended as it aids in washing any remaining color and radioactive material from your body.
  - ✓ The radiotracer typically leaves the patient's body naturally after a few hours and rapidly loses radioactivity.
  - ✓ After having a PET scan, the patient might be told to stay away from young children, pregnant women, and babies for a while. This is because the patient will be slightly radioactive at this time.

6.E.2. Iodine -131pre-examination specifications

A review of the patient's medical history for tumor pathology included information on thyroidectomy, the number and location of removed lymph nodes, if possible, cervical compartment assignment, menstrual history, pregnancy status, breastfeeding status in post-pubertal females, and family planning status.

Physical exam and laboratory tests include TSH, serum thyroglobulin (Tg) including recovery test, quantification of anti-Tg antibodies or both, urinary stable iodine excretion if there is suspicion of iodine excess, creatinine, calcium, calcitonin (post-surgery, if medullary thyroid cancer has not been ruled out), parathyroid hormone, and differential complete blood count.

The following should also be reviewed: history of diagnostic whole-body scan (radioisotope, activity, date, and results). Results of a neck ultrasound and additional imaging tests, such as computed tomography (CT) without contrast or, if necessary, magnetic resonance imaging, with an approximate measurement of the thyroid remnant size. Results of pulmonary function tests, if essential.

- **Sodium iodide ^{131}I is classified as Category X in pregnancy**

  A beta-human chorionic gonadotropin test must rule out pregnancy a few days before each radioiodine therapy because sodium iodide (^{131}I) can induce severe, potentially irreversible hypothyroidism in newborns.

- **Sodium iodide ^{131}I and lactation**

  Breastfeeding must be stopped at least 8 weeks before sodium iodide (^{131}I) injection to give the body enough time to go through involution and to prevent an excessive buildup of sodium iodide [^{131}I] in breast tissue. Once breastfeeding has been stopped, it should not be resumed.

- **Sodium iodide ^{131}I precautions**

The following safety precautions should be followed to maximize the safety and effectiveness of radioiodine therapy and reduce its side effects:

- ✓ Retention and uptake of physiological radioiodine are minimized. Using lemon juice, sour candies, or chewing gum enhances salivary flow and lowers radiation exposure to the salivary glands 24 hours after radioiodine administration.
- ✓ Management and prevention of neck compression symptoms; if an inflammatory reaction develops in the lower neck, ice packs, and non-steroidal anti-inflammatory medicine should be taken.
- ✓ Before receiving ^{131}I treatment, most patients have a total or nearly total thyroidectomy, in which the malignant tissues and some normal tissues are removed, in such circumstances a 10–14 days iodine restriction diet is advised.
- ✓ A review of recent clinical history indicates the absence of the following: current iodinated contrast delivery, amiodarone medication within the previous year, or long-acting iodine pollutants.
- ✓ Additionally, it would be best to avoid daily multivitamins with iodine and fish oil during this time.
- ✓ To boost the level of TSH, all oral thyroid hormone (T4) prescriptions must be stopped six weeks before treatment.
- ✓ There shouldn't be any radiographic contrast examinations for six to eight weeks before therapy. Lithium is occasionally given before ^{131}I treatment, as it prevents ^{131}I from being released by thyroid tumors.

- **The complication of radioiodine therapy**
  - ✓ Both acute and chronic damage to the salivary glands may occur, occlusion of the nasolacrimal duct, and late consequences such as secondary cancers and gonadal dysfunction.
  - ✓ Bone marrow depression (thrombocytopaenia/leukocytopenia)
  - ✓ Radiation-induced pulmonary fibrosis
  - ✓ Second primary malignancy (leukemia and solid tumor)

- **Radioiodine therapy intervention**
  - ✓ Antiemetic agents can be used for nausea and vomiting.
  - ✓ Corticosteroids can be used for chest pain, tachycardia, itching skin, and rash for several days after radioiodine administration.
  - ✓ Corticosteroids can also be used for tumor swelling for several days after radioiodine administration.

6.E.3. Radium-223 Dichloride Contraindications

- ✓ Active inflammatory bowel disease or significant fecal incontinence.
- ✓ Creatinine clearance less than 30 mL/min.
- ✓ Chemotherapy, radiotherapy, bone-targeted radioisotope, or other myelosuppressive therapy within the last month.
- ✓ For initial dose: hemoglobin less than 100 g/L, platelets less than 100 x 10^9/L, and ANC less than 1.5 x 109/L
- ✓ ECOG performance status >2 (which is assessment by using Eastern Cooperative Oncology Group).

- **Radium-223 dichloride therapy prerequisite (required data)**
  - ✓ Patient data (age, weight)
  - ✓ Inclusion criteria for treatment with radium-223; therapy is indicated in castration-resistant prostate cancer, symptomatic bone metastases, and no known visceral metastases.
  - ✓ Baseline: differential CBC, platelets count, serum creatinine, sodium, albumin, bilirubin, alkaline phosphatase, ALT, and Prostate-Specific Antigen.
  - ✓ A complete blood count should be performed within 10 days before radium-223 administration.
  - ✓ Before starting therapy, patients should be informed verbally and written about the procedure. Depending on national legislation, at least 24 hours before the first scheduled administration of radium-223, a patient information sheet/consent form must be signed by the patient and the doctor in charge of the patient in the same session. The patient should be aware that this therapy will likely regulate their disease rather than cure it.
  - ✓ Fasting is not required before therapy. The patient should be well-hydrated.
  - ✓ Patients must be informed of the potential side effects of therapy, and should receive a contact card to be carried at all times after each injection.
  - ✓ As usual, medications should be taken. Exceptions: It is recommended to stop taking calcium, phosphates, or vitamin D supplements 4 days before and 4 days after each injection of radium-223.
  - ✓ An appropriate monitoring of radioactive surface contamination must be performed to check for contamination in the space where the injection was administered.
- **Radium-223 dichloride precautions**
  - ✓ Extravasation: radium-223 should be administered slowly, and the patient should be observed for extravasation symptoms.
  - ✓ Diarrhea; the patient needs to be monitored to prevent dehydration.
  - ✓ Vomiting; the patient should be kept under observation to prevent dehydration.
- **Radium-223 dichloride dose modifications**

  No known dose adjustments for age, hematologic parameters, liver functions, or renal functions have been recommended. Doses need to be postponed until counts recover.

6.E.4. Lutetium-177 PSMA Contraindications

Contraindications to Lutetium-177 PSMA include the following:

- ✓ Life expectancy is less than six months (ECOG performance status > 2) unless the main objective is alleviating suffering from disease-related symptoms.
- ✓ Unmanageable urinary tract obstruction or hydronephrosis in patients diagnosed or at high risk of urinary retention.
- ✓ Progressive deterioration of organ function (GFR < 30 mL/min or creatinine > 2-fold upper limit of normal (ULN); liver enzymes > 5-fold ULN).
- ✓ Myelosuppression
- ✓ Total white cell counts less than 2.5×10^9 /L
- ✓ Platelet counts less than 75×10^9 /L
- ✓ Lu-177–PSMA-617 is not recommended in patients with dominant PSMA-negative lesions. PSMA-negative lesions are a metastatic disease lacking PSMA uptake, including bone and soft tissue.

- **177Lu-PSMA administration**
  - ✓ 177Lu PSMA is applied by slow intravenous injection (30–60 sec) in a volume of 5 mL (diluted with 0.9% sterile sodium chloride solution), followed by a flush of sterile 0.9% sodium chloride. It is recommended that the patients are hydrated pre- and post-administration of 177Lu PSMA with 1–1.5 L of water and encouraged to void the urinary bladder as frequently as possible.
  - ✓ Lu-177–PSMA-617 is typically administered IV every 6 weeks for 2- 6 treatment cycles depending on the response, prognosis, and renal risk factors.
- **177Lu-PSMA precautions**
  - ✓ Diuretics and moderate laxatives can be given to support clearance of unbound 177Lu-PSMA.
  - ✓ Prophylactic antiemetic therapy, e.g., ondansetron.
  - ✓ Corticosteroids one day before and up to several days after 177Lu-PSMA in case of cerebral, spinal, or other metastases with risk of painful or obstructive swelling.
- **Lutetium-177 PSMA follow-up**
  - ✓ Every 2–3 weeks (depending on baseline conditions), blood cell count should be checked for up to 12 weeks after each cycle.
  - ✓ Every 6–8 weeks, primary liver and kidney profiles should be assessed.
  - ✓ A physical exam should be performed before each treatment.

6.E.5. Patient Discharge Instructions

- ✓ The radiopharmaceutical's name, risks and advantages, predicted side effects, post-procedure instructions, answers to patient questions, and discharge instructions are all included in patient education.
- ✓ The radioactive diagnostic study needs radiation-specific discharge instructions to be provided. On the contrary, patients who have received radioactive therapy are a little different because there is significantly more activity; a dose limit of 1 mSv/y for the public, and a dose constraint of 5 mSv/episode for caregivers (not including workers) has been proposed as acceptable limits.
- ✓ To reduce radiation exposure to caregivers and the general public, direct assessment of patient activity before discharge is frequently done and can be used as a patient-specific recommendation.

Patient Instruction Card

At the time of discharge, the patient should be given an information card, which he should always keep as long as the hospital advises.

- **Patient instructions information:**
  - ✓ Until the date (following the biological and physical half-life of the radiopharmaceutical), the patient should avoid any close contact with children or pregnant women.
  - ✓ Until (date), the patient should avoid having extended personal interaction with adults at home.
  - ✓ Until (date), the patient should avoid having sustained close personal interaction with adults away from home.
  - ✓ The patient may start working again on (date).
  - ✓ Until (date), the patient should avoid sharing a bed with an adult.

Patient-Related Aspects Section Summary

- The importance of the provided pharmacist recommendations, including patient education, and applying the role of clinical nuclear pharmacists in improving patient safety is urgently demanding.
- Radiological precautions for patient safety protocols must be followed during the administration process.
- Separate sinks and toilets should be provided in rooms for patients with radiopharmaceutical therapy. To achieve the necessary amount of dilution for radioactive waste and avoid radiological contamination, it is recommended that patients flush the toilet at least twice, cover the toilet seat before flushing, and thoroughly wash their hands.
- Special care must be taken to prevent the spread of radioactive contamination caused by patient excreta and vomit.
- Following the administration of radiopharmaceutical therapy, developing all the details for patient discharge is critical.
- The concept of avoiding sexual activity within the specified restricted period should be discussed with both male and female individuals.
- Radiopharmaceutical administration errors, also known as mis-administration, include unintentionally administering radiopharmaceuticals to the wrong patient, administering an incorrect radiopharmaceutical, incorrectly determining the radiopharmaceutical's activity, or inadequate examination of pregnant or breastfeeding patients.
- It is critical to verify the patient's identity, the prescribed radionuclide dose, the chemical composition, the level of activity, and the designated method of administration before administering radiopharmaceuticals. This verification procedure should comply with a written order issued by the authorized user physician.
- Medication errors related to the diagnostic or therapeutic use of radiopharmaceuticals must be reported to the NOHARMe at EDA and the national regulatory body.
- Adverse events related to the diagnostic or therapeutic use of radiopharmaceuticals must be reported to the EPVC center and the national regulatory body.
- There is a high number of medications that can reduce radiopharmaceutical in vivo diffusion in subsequent nuclear medicine procedures. Some drugs can prevent radiopharmaceutical absorption, while others can aid localization inside the intended organ.
- PET/CT examination is a diagnostic imaging procedure that combines PET with computed tomography (CT).

Patient-Related Aspects Section Summary (Cont.)

The following variables must be considered when providing pharmacist advice and patient counseling concerning the FDG examination:

1. Patient preparation for FDG examination.
2. Evaluation of the medical history for the FDG examination
3. Instructions to perform FDG examinations on patients with diabetes and those without diabetes
4. Determination of the appropriate dosage for FDG examination
5. Imaging protocol for FDG examination
6. Interventions to be considered during FDG examination and sources of error:
    - Iodine-131 pre-examination specifications and precautions, including the use of sodium iodide ^{131}I during pregnancy and breastfeeding and the risks associated with radioiodine therapy.
    - Radium-223 dichloride therapy prerequisites (required) data, alter a medication's dose (dose modification is done) to maximize its therapeutic effects while minimizing potential adverse events.
    - The administration of Lutetium-177 PSMA, as well as its contraindications.
    - Following medical interventions, it is critical to provide patients with detailed instructions for discharge from the healthcare facility. Incorporating the **Patient Instruction Card** and other pertinent instructional information.

7. Comparison between Radiography (X-Rays) Vs Nuclear Medicine Vs Radiotherapy

7. Comparison between Radiography (X-Rays) Vs Nuclear Medicine Vs Radiotherapy

Medical applications of radiation are critical for diagnosing and treating a wide range of diseases, but people are frequently confused about their meanings due to their overlapping names. Despite their common origins, the various branches of medicine use vastly different technologies and techniques to achieve entirely different goals. The following are the main differences between the three medical specialties:

Table 5: Comparison between X-rays, nuclear medicine, and radiotherapy

X-rays or radiography	Nuclear Medicine	Radiation Oncology (Radiotherapy)
The medical specialty that provides images of the body's internal structures using a small dose of ionizing radiation. X-rays are the most widely used and oldest type of medical imaging.	The medical specialty that uses **unsealed** radiation sources for **diagnosis** and **therapy**.	The medical specialty that uses **sealed** radiation sources to **treat** a variety of cancers and other diseases.
Radiation **beams** pass through the body but do not originate from it. Radiographic procedures may be done using contrast agents. Contrast media are non-radioactive agents.	**Unsealed** sources of radiation, administration of powders, liquids, or gases, and injection all cause radiation exposure. These unsealed sources are known as radiopharmaceuticals or radiation-emitting drugs.	**Sealed** sources, radioactive material in capsules or solid form. In most cases, sealed sources are housed within radiation devices designed to regulate the dose of powerful radiation from outside the body to treat various conditions.
External energy waves are used in **diagnostic** radiology to generate images and assess organ **anatomy**.	Nuclear medicine scans detect radiation emitted by a radioactive substance **within a patient's body** to observe how organs or tissue **function** (for diagnosis) or to target and destroy diseased or **damaged organs** or tissue (for treatment). Nuclear medicine is also distinguished from other imaging techniques in detecting disease based on biological function rather than anatomical tissue changes.	Malignancy radiotherapy employs **high doses** of targeted energy to **kill cancer** cells and shrink tumors.

X-rays or radiography	Nuclear Medicine	Radiation Oncology (Radiotherapy)
Creating images of the structure of the body for **diagnostic purposes**. Display structure (**anatomy**)	**Used in diagnostic and therapeutic procedures.** Images of the human body depict the location and mode of tracer absorption. Clearly shows **functionality**.	Used in **treatment**.
Examples: • Conventional X-ray • Dental X-rays, etc • Computed tomography (CT) • Fluoroscopy • Mammography	**Examples:** A Single-Photon Emission Computed Tomography (SPECT) scan is used in diagnostic nuclear medicine to examine the body's organs, tissue, and bones. A SPECT scan is a nuclear imaging test that produces 3D images using a specialized camera. Positron Emission Tomography (PET) is a nuclear medicine imaging technique that provides metabolic and functional data. The radiotracers used in SPECT and PET scans are the primary difference.	**Examples:** External beam radiation therapy is a machine-assisted treatment. It does not come into contact with the patient but can move around him and emit radiation in multiple directions (**Teletherapy**). Internal radiation therapy is a treatment that involves implanting a radiation source within the body. **Brachytherapy** is a type of internal radiation therapy that uses a solid source. Seeds, ribbons, or capsules containing a radiation source are implanted in or around the tumor in this type of therapy.

8. Links and Resources

8. Links and Resources

Pharmacists can access these links and resources for the nuclear pharmacy practice:

- The International Atomic Energy Agency(IAEA) https://www.iaea.org/
- The U.S. Nuclear Regulatory Commission (NRC) https://www.nrc.gov/
- The University of Pittsburgh Radiation Safety Office http://www.pitt.edu/
- European Association of Nuclear Medicine https://www.eanm.org/
- The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) https://www.arpansa.gov.au/
- The British Nuclear Medicine Societyhttps://www.bnms.org.uk/
- The Journal of Nuclear Medicine (JNM) https://jnm.snmjournals.org/
- The Egyptian Journal of Nuclear Medicine (EJNM) https://egyjnm.journals.ekb.eg/
- Egyptian Nuclear and Radiological Regulatory Authority (**ENRRA)** https://enrra.org/
- To get a nuclear pharmacist licensed in Egypt, the pharmacist should fulfill all requirements issued by the Egyptian nuclear and radiological regulatory authority.

9. References

9. References

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