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NUCLEAR MEDICINE: A COMPREHENSIVE REVIEW

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PET (Positron Emission Tomography), SPECT (Single Photon Emission Computed Tomography, PET/CT (Positron Emission Tomography/Computed Tomography), SPECT/CT (Single Photon Emission Computed Tomography/Computed Tomography), PET Agents, SPECT Agents

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ABSTRACT: Nuclear medicine is a branch of medicine that evaluates body functioning and diagnosis and treats the disease by using radiopharmaceuticals or radio tracers. 131-iodine was the first commercially used nuclear medicine for the diagnosis and treatment of thyroid disease. Nuclear medicine emits alpha, beta (β^- and β^+) and gamma rays, which are used for the diagnosis and treatment. Nuclear imaging studies can provide early and accurate diagnosis of cancer, many infections like diabetic foot osteomyelitis, vertebral osteomyelitis, endovascular graft infection, prosthetic joint infection and also for fever of unknown origin. PET and SPECT are techniques used for the diagnosis. Now a days hybrid technology PET/CT and SPECT/CT are used for the diagnosis. Different PET agents like Fluorine 18, Gallium 68, Carbon 11, Oxygen-15, Zirconium-89, Copper-64, Iodine-124 etc., are use for the diagnosis. SPECT agents like Technetium-99m, Thallium-201, Iodine-123 etc., are used for the diagnosis of the disease. Nuclear medicine used for the imaging of brain, myocardial perfusion, thyroid, parkinson's disease, alzheimer's disease, fever of unknown region, endovascular graft infection, etc. Alpha, beta minus and auger electron radiation used for the treatment of different disease. Nuclear medicine like Iodine-131 & 123, Strontium-89, Yttrium-90, Actinium-225, Phosphorus-32 & 33, Lutetium-177 etc., are used for therapeutic purpose. It is used in the treatment of thyroid cancer, prostate cancer, etc., with this paper precautions and dose, diagnosis and treatment can be very useful.

INTRODUCTION: Nuclear medicine: Nuclear medicine is a branch of medicine that evaluates body functioning and diagnoses and treats illnesses using radioactive tracers, or radiopharmaceuticals¹. Nuclear Medicine has established itself in clinical practice in a large variety of indications. Recent innovation in radiopharmaceuticals and equipment has led to a significant increase in diagnostic and therapeutic applications.

According to the World Nuclear Association more than 40 million nuclear medicine procedures are performed each year worldwide². Nuclear medicine is a vibrant and quickly developing field of medicine that has become a vital and effective tool for managing, diagnosing, and treating a wide range of illnesses.

Nuclear medicine uses the special qualities of radiopharmaceuticals to provide understanding of cellular physiological and molecular processes, which is crucial knowledge for both researchers and physicians³. Nuclear medicine can be delivered orally, intravenously, or by inhalation. In a therapeutic modality, a high dosage of radiation is administered using certain radiopharmaceuticals

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that target the sick organ in order to treat cancer or an over active thyroid gland and also used for the diagnosis of the such diseases condition ⁴.

Radiopharmaceuticals are employed in nuclear medicine for radiotherapy and diagnostic imaging, being crucial for the field of medicine as a whole to help with organ diagnosis and therapy diseases, including cancer, cardiovascular disease etc. Also use in detection of bone metastasis, to determine regional blood flow. Nuclear medicines are used in imaging techniques to visualize organs such as the kidneys, lungs, thyroid, heart, bone metabolism, and blood circulation. Nuclear medicine uses radioactive tracers generally called radiopharmaceuticals in the study of global and regional function, blood flow, metabolism and morphology of an organ ⁵.

Nuclear medicine emit or decay radiation like alpha particle, beta particle (β^- or β^+), gamma rays. Which are used in diagnostic as well as therapeutic purpose. The type of radiation emitted depends upon number of proton, number of neutron, atomic number, atomic weight, atomic number, position in periodic table *etc* ¹.

History: Diagnostic *in-vivo* imaging was born with the discovery of X-rays in 1895 by Wilhelm Conrad Roentgen, a German physics professor working in Wurzburg, on November 8, 1895 ⁶.

In 1896 Henri Becquerel applied uranium salts to photographic plates, the outcome was marked radiographs without light ⁶.

Marie and Pierre Curie were the first to propose using radium as a cancer treatment in 1905.

The first cyclotron, constructed in 1931 by Ernest Lawrence, was apparatus designed to accelerate alpha particles, such as protons, deuterons, or helium ions, with the goal of entering the nucleus and creating radioactive and stable isotopes. Ten years later, Lawrence's cyclotron had generated 223 radioactive isotopes, many of which are now highly valuable for research in the biological sciences and medicine ³.

The medical use of radionuclides began during World War II. The Atomic Energy Commission (AEC) was established in 1946 as a result of World

War II to further the peaceful applications of radiochemistry and nuclear chemistry. AEC promoting the use of nuclear medicine in imaging and therapy. Nuclear Medicine only had a diagnostic power when Paul Harper and his group introduced the ^{99m}Tc radionuclide as a marker ⁶. The first radiopharmaceuticals were commercialized in 1950 ¹³¹. I (Iodine-131) was the first commercially available isotope, with Abbott Laboratories being the first company to produce radiopharmaceuticals for medical uses ⁶.

Properties:

Nuclear Medicine Show Radioactivity: The nucleus of an atom consists of protons and neutrons held together by a strong nuclear force. Atoms are stable when this strong nuclear force can keep its constituent protons and neutrons within the nucleus. In stable nuclei ratio of neutron and proton have been found closely approximates a 1:1 in small molecular weight compound (i.e., $Z \leq 20$). That's narrow region called the "band of stability" As the atomic weight of an atom increases (i.e., $Z \geq 80$), this ratio skews towards a higher ratio of neutrons when compared to protons. That's make atom unstable, also called nuclear instability ¹.

Radioactivity is property of atomic nuclei and may be defined as the spontaneous transformation of a structurally unstable nucleus into structurally stable nucleus, with emission of energy in the form of ionizing radiation ⁷.

Modes of Radioactive Decay:

Alpha (α) Decay: Nuclei of element with (i.e., $Z \geq 80$) are unstable they become more stable by generating and emitting an alpha (α) particle. Alpha particle consist of two neutron and two proton is structurally identical to helium-4 nucleus. Alpha particles have a charge of +2 and alpha decay occurs in the nuclei of heavy elements, like radium, uranium, thorium, *etc* ^{7,8}.

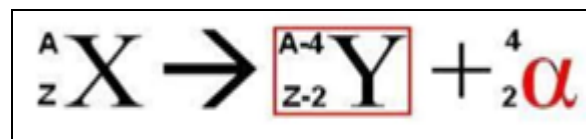
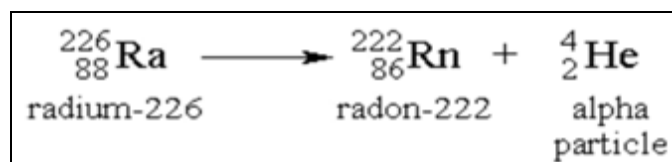


FIG. 1: GENERAL REACTION OF ALPHA DECAY

Here, A = atomic mass (proton + neutron), Z = atomic number (number of proton).

FIG. 2: EXAMPLE OF ALPHA DECAY (RADIUM)⁹

The Alpha particle's speed is ~20000 km/s and they interact with matter, causing much ionization over a very short distance. They usually pass short distances and can be stopped by a sheet of paper⁹.

Application of Alpha Particle in Nuclear Medicine: Historically, radium and radon were the principal alpha emitters of medical interest. Radium-223 dichloride is still used today in treating osseous metastases. Other alpha emitters are being researched for therapeutic approaches using radiopharmaceuticals that can target the delivery of short half-life alpha emitters into cancerous cells^{8,9}.

Beta (β) Decay: Beta decay represents radioactive decay in which a beta particles are emitted. Beta particles may be either electrons or positrons (β⁻ or β⁺), having negative or positive charge respectively^{7,8}.

Beta minus(β⁻) Decay: Nuclei ($Z \leq 80$) which show instability because they have an excess of neutron.

They becoming stable by converting a neutron to proton with emission of beta minus particle (electron) and an antineutrino. The antineutrino has no rest mass nor electric charge and does not interact readily with the matter¹⁰. The isotopes that undergo β⁻ decay, each nucleus emits an electron and an antineutrino. The mass number remains the same but the atomic number increases by one.

Example: cobalt-60, iodine-131¹⁰

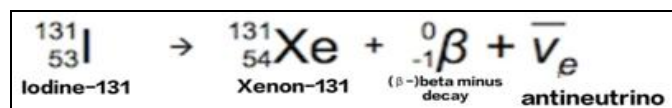


FIG. 3: EXAMPLE OF BETA MINUS DECAY (IODINE-131)

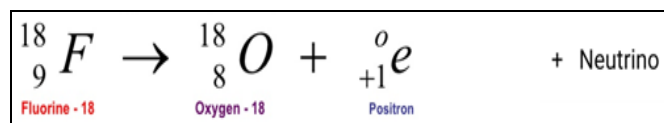
Example: Iodine-131 which undergoes beta minus decay and convert into xenon-131 by increasing atomic number by 1 while keeping the same mass number¹⁰.

Beta plus decay (β⁺) or Positron Decay: Nuclei ($Z \leq 80$) shows beta plus (β⁺) decay. Their N to Z ratio is unstably low⁸.

They have deficiency of neutron, they become more stable by converting proton to neutron and emission of beta plus (β⁺) particle or positron and a neutrino. Similar to an antineutrino, a neutrino has no electric charge nor rest mass¹⁰.

In the case of the β⁺ decay, each decaying nucleus emits a positron and a neutrino, reducing its atomic number by one while the mass number stays the same. A positron does not exist for a long period of time in the presence of matter. There are no positron emitters in nature they are produce in nuclear reaction¹⁰.

The most important positron emitters in medicine are ¹¹C, ¹⁵O, ¹⁸F, ³⁰P etc¹⁰.

FIG. 4: EXAMPLE OF BETA PLUS DECAY (FLUORINE)¹⁰

This emission is basis of PET (Positron imaging technique). Positron mainly used in diagnostic purpose¹⁰. E.g. 18-FDG (Fluoro- deoxy glucose)¹⁰.

Gamma (γ) Rays: Gamma decay is a mode of radioactive decay¹¹.

It differs from alpha and beta decay in that it does not involve a change to a different daughter nuclide. A gamma photon is produced as the nucleus transitions from this excited state to a lower energy state. Gamma rays have energies far greater than that of similar atomic process and therefore have high penetration depths¹¹.

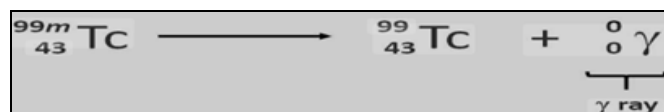


FIG. 5: EXAMPLE OF GAMMA DECAY (TECHNETIUM-99M)

Example: Technetium-99m agents like ¹¹ technetium-99m sulfur colloid, technetium-99m pertechnetate, technetium-99m labelled RBCs

Nuclear Medicine for Diagnosis: Nuclear imaging studies can provide early and accurate diagnoses of

many infectious disease syndromes, particularly in complex cases where the differential remains broad. Nuclear medicine imaging can be an excellent resource in trying to diagnose complicated infections^{5, 12}.

Nuclear medicine is useful for diagnosis of cancer, infections like diabetic foot osteomyelitis, vertebral

osteomyelitis, endovascular graft infection, prosthetic joint infection and also diagnosis origin of unknown fever¹². From last decade many new nuclear medicine are discover and used as diagnosis of many disease. Brief information about discovery of nuclear medicine for the diagnosis purpose are listed in the **Table 1**.

TABLE 1: DISCOVERY OF NUCLEAR MEDICINE (FOR DIAGNOSTIC PURPOSE)¹³

Year	Discovery of nuclear medicine (for diagnostic purpose)
1930s	E.O. Lawrence developed the cyclotron, later on produced the first medically including iodine-131, thallium-201, technetium-99 m, carbon-14, and gallium-67.
1940s	The first reactor-produced radionuclides for medical research were made at Oak Ridge National Laboratory (ORNL) including phosphorous-32, iron-52 & chromium-51.
1950s	Benedict Cassen invented the first automated scanner at the University of California at Los Angeles to image the thyroid gland after administering radioiodine to patients.
1960s	Scientists at ORNL discovered the affinity of gallium-67 for soft-tissue tumors. This radionuclide had been used to image lymphomas, lung cancer, and brain tumor.
1970s	PET scanners were developed by Michael Phelps, Edward Hoffman, and Michel Ter-Pogossian at Washington University based on earlier work by Gordon Brownell at the Massachusetts Institute of Technology (MIT) and James Robertson at BNL. 18F-FDG, a positron-emitting compound, was synthesized by chemists at BNL They use 18F-FDG to image glucose metabolism in the human brain.
1980s	A new radiopharmaceutical, iodine-131-m-iodine-benzyl-guanidine, was developed by Donald Wieland for the diagnosis and treatment of rare childhood cancers.
1990s	A high-resolution PET scanner designed to image small laboratory animals.

Radionuclide Characteristics Required for Diagnosis: Diagnostic nuclear medicine primarily uses medium energy photons (gamma and X-rays). The specific energy of gamma photons is ideal for detection. Radiations emitted as a result of radioactive decay, such as X, γ and β^+ rays, are ionizing radiations. X and γ rays are far more penetrating than rays β . The high-energy photons of x-rays, γ -rays, and annihilation radiation associated with radiotracers in nuclear medicine¹⁴.

Annihilation Radiation: A positron (β^+), after expending its kinetic energy in an inelastic collisions, combines with an electron (β^-) of the absorbing medium. Both the particles are annihilated, and their mass appears as electromagnetic radiation (usually two 511-keV photons), known as annihilation radiation¹⁴.

It's also depends upon the protein binding or metabolic uptake and the ratio of the radiopharmaceutical's concentration⁴. Other biochemical characteristics that need to be considered include low toxicity, the specific gravity for optimal flow and distribution during administration, the appropriate pH, and the optimal clearance rate (except for permanent tracer).⁴

Basic Principle of Nuclear Medicine For Dignosis: Nuclear medicine uses a small amount of radioactive material combined with a carrier molecule. This compound is called a radiotracer.

In nuclear medicine we use radioactive compound which are administered almost always systemically and usually intravenously. The radiation that comes from the decay of radioactive substances can be detected, measured and imaged using tools like single-photon emission computed tomography (SPECT), positron emission tomography (PET), PET/CT and SPECT/CT. This imaging allows viewing of kidneys, lungs, thyroid, heart, bone metabolism and blood circulation, among other organs³. Radiations emitted as a result of radioactive decay, such as X, γ and β^+ rays, are ionizing radiations. X and γ rays are far more penetrating than rays β^+ ¹⁴.

Positrons then undergo mutual annihilation with an ordinary electron, or negatron, in the medium, with positrons and negatron representing antiparticles of one another. As a result of the positron-negatron annihilation, their rest mass energies (511 keV each) are converted to two 511-keV gamma rays emitted in opposite directions or 180° apart^{14, 15}.

Annihilation: The conversion of matter into energy, especially the mutual conversation of a particle and antiparticle into electro-magnetic radiation (gamma rays) $e^{-} + e^{+} \rightarrow \gamma + \gamma$.

PET (Positron Emission Tomography): PET is the most precise (specific) and sensitive approach to image molecular interactions and routes inside the human body. This imaging probably offers more translational possibilities than any other modality due to its combination of sensitivity and quantitative accuracy. PET is a non-invasive imaging modality that provides physiological information through the injection of radioactive compounds (radiotracers) ¹⁶.

When radiotracer are taken up by the particular organ, they release the positron. That positron undergoes the annihilation process, and emits two

511 keV gamma photons at nearly opposite directions or 180° apart. These photons can be detected by PET detectors and instrument, utilizes this information to reconstruct an image ^{16, 17}.

Example: Use of radioactive fluorine as 18F-FDG ¹⁶.

Annihilation Process: In this process. The neutron-deficient 18F isotope (radioactive fluorine) convert to the stable isotope oxygen-18 (18O) by converting a proton to a neutron and thus emitting a positron. The positron encounters its antiparticle, the electron (The electron and positron come into contact with each other). The resulting annihilation of both particles generates two 511 keV annihilation photons traveling in opposite directions ¹⁶.

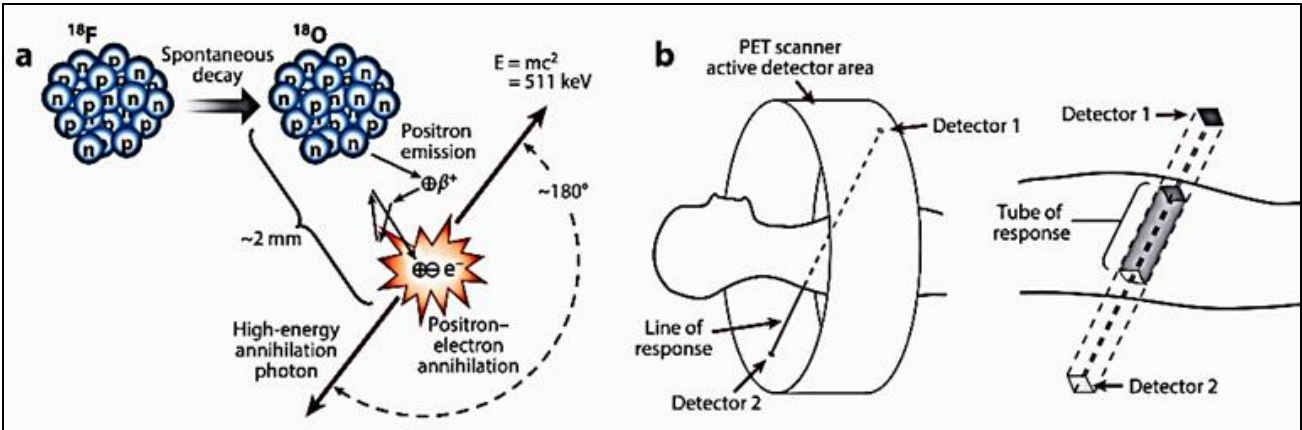


FIG. 6: WORKING PRINCIPLE OF PET BY USING 18F-FDG

Schematic of PET Imaging Process: The patient is placed inside the gantry and surrounded by a ring of detectors that define the scanner’s active sensor area. When two annihilation photons are detected within a few nanoseconds of each other, the two points of interaction define a line of response.

Because the detector’s elements have finite dimensions, the line of response schematically represents the ensemble of coincidences that fall inside the tube of response, which is defined by the size of the detector’s elements ¹⁶.

TABLE 2: RADIOPHARMACEUTICALS USED IN CLINICAL PRACTICE IN DIFFERENT MEDICAL FIELDS AND THEIR PROPERTIES ^{2, 13}

Radionuclide	Half life	Radiopharmaceuticals	Medical field
Fluorine 18	1.83h	18-FDG	Oncology (cancer application) Musculoskeletal (epilepsy & dementia Application Cardiology
		18-FLT (Fluorothymidine)	Oncology
		18-FDOPA	Oncology (brain tumor)
		Dihydroxyphenylalanine)	Oncology (brain tumor)
		18-FET	
		O-(2-[18F]-Fluoroethyl)-L-tyrosine	
Gallium 68	1.14h	18F-Fluciclovine	Oncology
		68Ga-DOTA-conjugated Peptides (DOTA-NOC,	Oncology (brain tumor)

		DOTA-TOC and DOTA-TATE)	
		68Ga-PSMA (prostate specific membrane antigen)	Oncology (prostate cancer)
		68Ga-FAPI (Fibroblast activation protein inhibitors)	Oncology
Carbon 11	20.4min	11C-MET (Methionine)	Neurology& Psychiatry
Oxygen-15	2.05min	15O-Water	Neurology& Psychiatry
Zirconium-89	78.4h	89Zr-trastuzumab	Oncology
Copper-64	12.7h	Cu-ATSM (Diacetyl-bis-methylthiosemicarbazone)	Oncology
Iodine-124	4.18days	Iodine-124	Oncology(thyroid cancer)

SPECT (Single Photon Emission Computed Tomography): Gamma rays released by radionuclides are distributed in three dimensions (3D) using photon emission computed tomography (SPECT) ¹⁸. A tracer (gamma photon emitting radiopharmaceutical) is injected intravenously into the bloodstream of the patient and participates in the body’s metabolism and distributes accordingly. ¹⁹ After administration of a gamma photon emitting radiopharmaceutical (like Thallium-201, Technetium-99, etc.) SPECT imaging may be

performed. The most common technique for SPECT imaging is to rotate the detector head 360 degrees around the subject to gather count data. This greatly enhances localization and contrast resolution over planar imaging and permits reconstruction of data in all required planes, including axial, sagittal, and coronal ¹⁸. These images offer functional details about the tissues and organs, making it possible to identify functional abnormalities earlier to the occurrence of morphological changes ¹⁸.

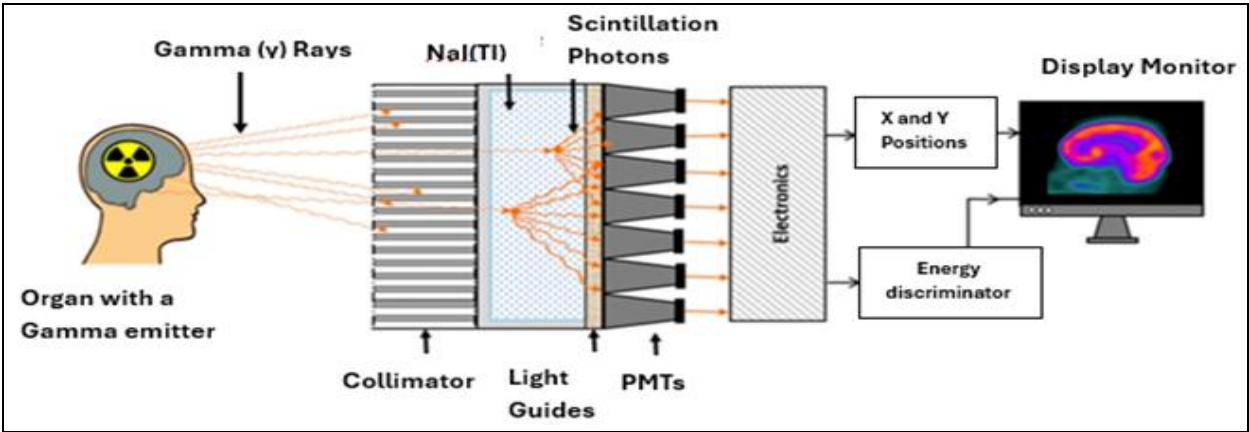


FIG. 7: THE WORKING PRINCIPLE OF SPECT

TABLE 3: PHYSICAL PROPERTY OF RADIONUCLIDES USED IN SPECT ^{18, 19}

Radionuclides	Half life	Energy	Example of Radiotracer
Technetium-99m (^{99m} Tc)	6.05h	140KeV	^{99m} Tc –HMPAO (Hexamethyl propylene amine oxime) ^{99m} Tc-ECD (Ethyl cysteinat dimer) ^{99m} Tc-RGD
Thallium-201	73h	65-32KeV	
Iodine - 123	13.2h	159KeV	I-123 Ioflupane

Hybrid Technology: PET and SPECT imaging are valuable tools for understanding the functional aspects of neuropathology, but they have certain drawbacks.

PET/CT: PET offers useful data based on the biodistribution of a certain radiopharmaceutical ²⁰. One of the main limitations of PET imaging alone is the very limited spatial resolution and unclear anatomical reference frame ²¹.

Because of the relatively limited spatial resolution, it is difficult to precisely localize functional information with anatomical reference. Also, it is possible for the uptake of PET radiopharmaceuticals to be non-specific ^{20, 21}. Commercial availability of the first hybrid PET/CT system for clinical use took place in 2001 ²¹.

Why do we need PET/CT: Attenuation is the term used to describe the loss of real coincident photon

detection in PET imaging caused by the photons' absorption and subsequent energy loss in the body. This results in degraded images because there are fewer photons detected than there are real coincidence events occurring within the body. Body parts in closer proximity to the detectors experience less attenuation, leading to improved detection. Because of photon attenuation, the deeper parts of the body, including the periaortic area, might not be as clearly visible²¹.

Attenuation correction is carried out by the use of X-rays from the CT scan component of PET/CT cameras. In an integrated PET/CT camera, the emission scan produced by the PET component of the camera is applied to an attenuation map of the body created using X-rays from the CT scan. The resulting image correctly shows the activity of the deeper structures of the body²¹.

SPECT/CT: Functional nuclear medicine imaging using single-photon emission computed tomography (SPECT) in conjunction with computed tomography (CT) has been commercially accessible since beginning of the century. The two modalities combined have improved many clinical applications' sensitivity and specificity, and when CT is used in conjunction with SPECT, it enables the spatial overlay of SPECT data on high-quality anatomy images. These days, SPECT and CT are frequently combined to provide SPECT/CT imaging, in which the CT data offers anatomical reference frames that enhance the diagnostic utility of the SPECT image data²².

Application of SPECT/CT²²:

- In bone imaging
- In thyroid
- Myocardial perfusion imaging

Scientists have discovered a wide range of substances that are absorbed by particular organs.

Example: iodine absorbed by thyroid, glucose absorb by brain. Blood flow to the brain, liver, lung, heart, and kidney can be monitored with diagnostic radiopharmaceuticals.

Nuclear Medicine Used For Diagnosis Different Disease Condition: Nuclear medicine that generates the radiation can be located in a certain

organ used for diagnostics and imaging of organ or tissue.

Radiopharmaceuticals used for diagnosis are ¹⁸F-FDG (Fludeoxyglucose),¹²³I-iodine, ^{99m}Tc-Technetium agents (technetium-99m sulfur colloid, technetium-99m pertechnetate, technetium-99m labeled RBCs),⁶⁸Ga-FAPI (68-Gallium-fibroblast activation protein inhibitors), ¹⁷⁷Lu-Lutetium (¹⁷⁷Lu), ⁵¹Cr(Cromium),⁵⁸Co(⁵⁸cobalt), *etc.* used for diagnostic and imaging purpose^{2,3}.

Use of nuclear medicine depends upon organ or tissue which undergoes diagnostic or imaging. Nuclear medicine are useful for the diagnosis of cancer, cardiovascular disease, inflammation reaction, complicated infections, fever of unknown region, *etc.*

Nuclear Medicine in Brain Imaging: SPECT and PET are methods used for nuclear imaging of the brain. PET utilizes radionuclides that produce positrons and detects the annihilation radiations from them. SPECT procedure uses radionuclides that releases gamma radiations. Different SPECT agents used for imaging are excluded by normal brain cells, but can enter into tumor cells because of altered BBB²³.

Five factors affecting differential uptake of radiopharmaceuticals by brain tumors are as follows²³:

- Increased vascularity of the abnormal lesion/tumor.
- In brain lesions, abnormal capillary permeability (due to damage in BBB) is produced by the absence of capillaries with a tight endothelial junction or damage in BBB.
- Pinocytosis caused by the lack of healthy astrocytes in abnormal brain tissue;
- Brain tumors and other lesions are linked to increased extracellular space and reactive edema.
- Increased metabolic activity in brain lesions.

Diagnosis in Brain Tumor: A brain tumor is an abnormal growth of cells within the brain or spinal canal. Tumors can be benign (non-cancerous) or

malignant (cancerous). They can arise from brain cells, the membranes surrounding the brain (meninges), nerves or glands within the brain ²⁴.

Currently, the most clinically beneficial application of nuclear medicine imaging is the use of FDG PET/CT to investigate or diagnosis possible recurrence in high grade initial brain tumor.

PET imaging is used with three main types of radiotracers ²⁵:

1. 18Ffluorodeoxyglucose (FDG), a radioactive glucose analogue used to evaluate tumour glucose metabolism (FDG uptake usually reflects tumour grade);
2. amino acid radiotracers, such as 18F-FDOPA, 18F-FET or 11C-methionine, usually used for suspicion of low-grade gliomas; and
3. 68Ga conjugated to SSTR ligands that targets somatostatin type 2 receptors.
4. Gliomas are the most frequent intrinsic tumours of the CNS.

Diagnosis by 18F-FDG PET: Primary braintumors typically exhibit elevated glucose metabolism and enhanced uptake of FDG, and

FDG is actively transported through the intact blood-brain barrier, similar to the majority of malignant tumor ²⁶. 18F-FDG PET dignosed by identification of high-grade gliomas based on evaluation of the ratio between the tumour uptake and the contralateral normal brain tissue uptake ²⁴.

Limitations of 18F-FDG PET ^{24, 26}: The typical brain's strong physiologic glucose intake results in a comparatively high background uptake of FDG, due to that limited specificity to distinguish gliomas from other nonneoplastic (normal cell) lesions.

A variety of nonmalignant intracerebral lesions also have various levels of increased FDG uptake due to infectious or inflammatory causes. Thus, these and other features may limit specificity and hamper differentiation between malignant and non-malignant causes.

PET imaging at one hour and three to eight hours after injection enhances visual and quantitative assessment, according to a number of more recent investigations. Due to increased FDG washout from benign cells or normal brain tissue in late images in comparison with malignant cells ^{24, 26}.

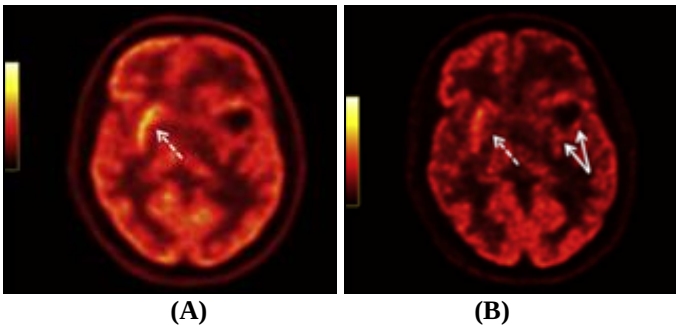


FIG. 8: EXAMPLE OF COMPARISON OF CONVENTIONAL AND PET IMAGING

(A) After1 hour and

(B) After 3-hour of PET imaging

The 3-hour shows an increase of tumor-to-background ratio (solid arrows) and a generally higher washout in the healthy brain parenchyma, for example, the basal ganglia (dashed arrows) ²⁶.

Diagnosis by Amino Acid Radiotracers: In this we use different type of amino acid tracer such as 18F-FDOPA, 18F-FET or 11C-Methionine Compared to FDG PET and MRI alone, amino acid PET has a superior diagnostic accuracy for distinguishing gliomas (high radiotracer uptake) from non-neoplastic lesions (low radiotracer uptake) ²⁴.

TABLE 4: DIAGNOSTIC VALUE OF DIFFERENT AMINO ACID TRACERS

Diagnostic Value of Different Amino Acid Tracers ²⁷			
	MET	FET	FDOPA
Value of amino acid PET for	BTV larger than contrast	BTV larger than	Preliminary studies

radiotherapy target delineation or for diagnosis	enhancement in WHO grade III/IV gliomas, validation of imaging findings by histology	contrast enhancement in WHO grade III/IV gliomas, validation of imaging findings by histology	suggest that BTV larger than contrast enhancement in WHO grade III/IV gliomas
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BTV - (Biological Tumor Volume), FDOPA - (3,4-Dihydroxy-6-[18F]-Fluoro-L-Phenylalanine), FET - [O-(2-[18F]-Fluoroethyl)-L-tyrosine; MET([11C-Methyl]- L-Methionine)

⁶⁸Ga Conjugated to SSTR ligands that Targets Somatostatin Type 2 Receptors: Meningiomas express somatostatin receptor (SST) subtype 2 (SST2) (meningiomas are the most common primary brain tumour in adults, they have been significantly understudied compared to other CNS tumor, as most of these tumours are benign) ²⁸. SSTR2A can be targeted with 68-Gallium

radiolabelled somatostatin analogues: DOTATOC, DOTATATE or DOTANOC ^{24, 28}. SSTR PET ligands may diagnose meningiomas with very high sensitivity and specificity, non-invasive, PET is useful when MRI does not show typical meningioma features and/or when biopsy is complicated, such as for optic nerve sheath meningiomas.

TABLE 5: NUCLEAR MEDICINES USED FOR THE IMAGING OF BRAIN ²⁴

Radiotracer	Main Indication	Advantage	Limitation
FDG	High-grade gliomas Lymphomas (brain and systemic evaluation)	Most use radiotracer (specially in brain tumor)	Nonspecific radiotracer, Low lesion/background ratio due to high brain cortical glucose uptake, Negative in low grade, Gliomas.
Amino acid radiotracer	All type gliomas	May be used in all type	Depends upon glycemia Less available than FDG
SSTR PET ligand	Differentiate tumours from non-neoplastic lesion Diagnose of meningioma Differentiate meningioma from other tumours	Gliomas High tumour/ background ratio High tumour/background Ratio Specific radiotracer Possible theranostic.	Possibility to negative tumor and nonspecific uptake Rare meningioma with no or low SSTR expression

Parkinson’s disease: Parkinson Disease is a progressive neurodegenerative condition. The clinical evaluation of parkinsonism can be extremely challenging, for experts or specialist. Treatment and prognosis are significantly affected by the difference made between Parkinson's disease (PD) ²⁹. PET, SPECT, and MRI neuroimaging biomarkers have been suggested as crucial instruments for the differential diagnosis and prognosis of Parkinson's disease (PD) cases ³⁰. SPECT and PET imaging of DAT (dopamine

transporter), dopamine receptors, brain glucose metabolism, and myocardial autonomic function are increasingly used to diagnosis the Parkinson’s disease ³⁰. Oppenheim's 1911 finding that "tremor is not always the first symptom" served as a basis for the idea of PD's prodromal or preclinical stages. This stage consisted of the following subsequent steps: idiopathic rapid eye movement sleep behaviour disorder (RBD or IRBD) → depression → constipation → anxiety → hyposmia → onset of motor symptoms ³⁰.

TABLE 6: NUCLEAR MEDICINE USED FOR THE DIAGNOSIS OF PARKINSON’S DISEASE ³⁰

Conditions	Radiotracer
IRBD (Idiopathic rapid eye movement sleep behavior disorder)	18F-DOPA PET, 18F-FDG PET, 11C-Dihydropyridabenazine PET, 11C-Donepezil PET, 123I-MIBG SPECT, 123I-FP-CIT SPECT
Depression	123I-FP-CIT SPECT, DAT PET
Constipation	18F-DOPA PET, 11C-Donepezil PET
Anxiety	123I-FP-CIT SPECT, DAT PET
Hyposmia	123I-FP-CIT DAT-SPEC, 18F-FDG-PET
Onset of motor symptoms	All of the above but mainly 18F-DOPA PET

¹⁸F-DOPA PET (3,4-Dihydroxy-6-[18F]fluoro-L-phenylalanine), ¹⁸F-FDG PET (Fluoro deoxy glucose), ¹²³I-MIBG SPECT (123I-Metaiodobenzylguanidine), ¹²³I-FP-CIT SPECT (123I-Ioflupane), DAT (Dopamine transporter).

It was determined in 2016 that 18F-DOPA PET (3,4-Dihydroxy-6-[18F]fluoro-L-phenylalanine)

exhibits remarkable accuracy, with a sensitivity of 95% and specificity of 100% ³⁰.

Alzheimer’s disease (AD) ³¹: It is a progressive neurodegenerative disorder and the most common cause of dementia. AD is characterized by the deposition of abnormal proteins which form senile or amyloid plaques that are located extracellularly and represent beta- amyloid deposits (A β), and intracellular neurofibrillary tangles (NFTs) consisting of hyperphosphorylated tau protein aggregates. Additional metabolic processes such as oxidative damage, lysosomal dysfunction, and inflammation coexist with the aberrant protein deposition. The clinical symptoms of AD progresses over time, frequently precede a phase of mild cognitive impairment (MCI). Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) may be more effective methods for AD diagnosis. In AD, the diagnosis is done by Beta-amyloid imaging, Tau imaging, Imaging of neuroinflammation, Imaging of brain perfusion and glucose metabolism.

TABLE 7: RADIOLIGANDS FOR IMAGING WITH PET AND SPECT³¹

Method	Radiotracer	Molecular Target
PET	[18F] FDDNP	beta- amyloid deposits (A β) and tau protein
	[11C]PiB, [18F]florbetapir, [18F]florbetaben, [18F]flutemetamol, [18F]THK523, [18F]THK5105, [18F]THK5117, [18F]THK5317, [18F]THK5351, [11C] THK951, [18F]AV-1451, [18F]T808, [11C]PBB3	beta- amyloid deposits (A β) Tau protein
	[11C]PK11195, [11C]DPA713, [11C]CLINME, [18F]DPA714, [18F]PBR111, [11] C-PBR28, [18F]GE-180, [11C]NE40, [11] C-DED, [11C]DHA	Neuroinflammation
	18F-FDG	Brain perfusion and glucose metabolism.
SPECT	[123/125I]DRM106, [125I]IMPY, [123I]ABC577 [123I]PK11195, [123I]CLINDE	beta- amyloid deposits (A β) Neuroinflammation

PET: Positron emission tomography, SPECT: Single photon emission computed tomography, [18F]FDDNP:2-(1-{6-[(2-[¹⁸F]Fluoroethyl)(methyl)amino]-2naphthyl}ethylidene) malononitrile, [11C] PiB: ¹¹C-labelled Pittsburgh Compound-B, [18F] THK: series of compound derived from initial research, [11C] PBB3: Pyridinyl-Butadienyl-Benzothiazole 3, [11C] DPA: Dipyrindamol molecule, [18F] PBR:Peripheral benzodiazepine receptor, [11C] DHA: Docosahexaenoic Acid, 18F-FDG: Fluorodeoxyglucose, 125I DRM: Dopamine receptor mapping.

Myocardial Perfusion Imaging (MPI): This method plays a crucial role in diagnostic and therapeutic action in cardiac disease. It is a set of non-invasive imaging procedures that physicians can use to evaluate blood flow to different parts of the myocardium. It provides information on perfusion and metabolite uptake of blood from myocardium which plays important role in determining the appropriate medical treatment or intervention for optimizing cardiac health ³². Over the past ten years, MPI has become a crucial part of the clinical routine procedure for cardiovascular risk assessment and the identification of hemodynamically severe obstructive coronary artery disease (CAD) ³³. MPI using SPECT and PET has demonstrated diagnostic and Predicted treatment for the patients with known or suspected coronary artery disease (CAD) ³³. MPI is carried out both at rest and under pharmacological or physical stress to investigate regional variations in MBF (myocardial blood flow). It offers a qualitative and quantitative evaluation of the left ventricle's relative, regional perfusion (both under stress and at rest) in order to detect ischemia and infarction. The mainly used MPI SPECT tracers are Thallium-201 (201Tl), Technetium-99 m Sestamibi (99 mTc-MIBI) and Technetium-99 m-Tetrofosmin ^{33, 34}. The main MPI PET tracers are 13 N-ammonia (13 N-NH₃), Oxygen-15-water (15O-H₂O), Rubidium- 82 (82Rb) and Fluorine-18 (18 F)-flurpiridaz ^{33, 34}.

TABLE 8: PET & SPECT AGENTS USED FOR MYOCARDIAL IMAGING ³⁵

Method	Radioactive isotopes	Tracer name	Marketing approval
PET	Rb-82, N-13, O-15	Rubidium chloride, Ammomia, Water	EMA, FDA, EMA, FDA, EMA
SPECT	TI-201, Tc-99m, Tc-99m	Thallous chloride, Sestamibi, Tetrofosmin	EMA, FDA, EMA, FDA, EMA, FDA

PET: Positron emission tomography, SPECT: Single photon emission computed tomography, EMA: European Medicines Agency, FDA: US Food and Drug Administration.

Cancer Diagnosis: Nuclear medicine imaging has emerged as a potent cancer diagnostic technique by directly or indirectly detecting gamma rays from radionuclides to create images with the advantageous properties of high sensitivity, limitless penetration depth, and quantitative capability. Nowadays the most common nuclear

medicine imaging methods are positron emission tomography (PET) and single-photon emission computed tomography (SPECT). Recently many radioactive tracers have been developed to enhance nuclear medicine imaging capabilities for the early and precise diagnosis of malignancies ³⁶.

TABLE 9: PET AND SPECT RADIOISOTOPES AND RADIOTRACER FOR CANCER DIAGNOSIS ³⁷

Imaging modality	Radioisoto-pes	Radiotracer	Application
PET	Fluorine-18 (18F)	[18F]-FDG	Widely used in oncology
		F-DOPA	
		[18F]-FET	
		[18F]-FSPG	Track glioblastoma(in brain tumor)
		[18F]-FACBC	
		([18F]-F-FES)	Breast cancer
		[18F]-NaF	Bone cancer
		[18F]-Fluciclovine	Prostate cancer
		[18F]-PSMA	
PET	Iodine-124	124I-MIBG	Diagnosis of thyroid cancer
		124I-IAZA	
		124I-IAZG	
PET	Copper-64	(Cu-ATSM)	Imaging of hypoxia and diagnosis of cervical cancer
		[64Cu]-DOTATATE	Neuroendocrine tumor imaging
PET	Gallium-68 (68Ga)	[68Ga]-Ga-DOTA-TOC	
		[68Ga]-Ga-DOTA-TATE	Imaging of neuroendocrine tumors.
		[68Ga]-Ga-DOTA-LAN,	
		[68Ga]-Ga-DOTA-NOC	
SPECT		[99mTc]-Tc-EDDA/HYNIC-TOC	Imaging of neuroendocrine tumors. by Somatostatin receptor imaging
		99mTc-TECANT-1	
		99mTc-TECANT-1	Imaging of prostate cancer
		[99mTc]-HYNIC/EDDA-ipsma	

[18F]-FDG-fluorodeoxy glucose, F-DOPA: (3,4-dihydroxy-6-[18F]fluoro-L-phenylalanine), [18F]-FET: O-(2-[18F]-fluoroethyl)-L-tyrosine, [18F]-FSPG: (S)-4-(3-[18F]-Fluoropropyl)-L-glutamate, [18F]-FACBC : Anti-1-amino-3-[18F]-fluorocyclobutane-1-carboxylic acid, [18F]-F-FES : [18F]-Fluoroestradiol, ([18F]-F-FES: -[18F]-Fluoroestradiol, [18F]-NaF: Sodium [18F]-Fluoride, [18F]-PSMA: [18F]-Prostate-Specific Membrane Antigen, 124I-MIBG: [124I]-Metaiodobenzylguanidine, 124I-IAZA: [124I]-Iodoazomycin Arabinoside, 124I-IAZG: [124I]-IodoazomycinGalactoside, (Cu-ATSM): Copper-diacetyl-bis(N4-methylthiosemicarbazone), [64Cu]-DOTATATE: [64Cu]-DOTA-[Tyr3]-Octreotate, [68Ga]-Ga-DOTA-TOC: [68Ga]-DOTA-[Tyr3]-Octreotide, [68Ga]-Ga-DOTA-TATE: [68Ga]-DOTA-[Tyr3]-Octreotate, [68Ga]-Ga-DOTA-LAN: [68Ga]-DOTA-Lanreotide, [68Ga]-Ga-DOTA-NOC: [68Ga]-DOTA-[1-Nal3]-Octreotide, [99mTc]-Tc-EDDA/HYNIC -TOC: [99mTc]-Technetium-Ethylenediamine-N,N'-diacetic Acid/Hydrazinonicotinamide-Tyr3-Octreotide, [99mTc]-HYNIC/EDDA-ipsma: [99mTc]-Hydrazinonicotinamide/Ethylenediamine-N,N'-diacetic Acid-imaging Prostate-Specific Membrane Antigen.

Fever of Unknown Origin ¹²: Nuclear medicine imaging can image the entire body at once. Nuclear medicine tests may be well suited for imaging of fever of unknown origin, because these tests also detect functional and metabolic changes. Most modalities are capable of detecting infections, malignancies and inflammatory conditions such big vessel vasculitides, which collectively contribute for most FUO etiologies. Mainly 18F-FDG-PET used for the detection of FUO because 18F-FDG-

PET has higher sensitivity, specificity and spatial resolution. When hybrid technology is used in conjunction of PET with CT (PET/CT), it may be more beneficial with improved anatomic localization.

Endovascular Graft Infection ¹²: It is diagnosed by using the PET with 18-FDG as a tracer. The level of FDG avidity can be used to predict infection.

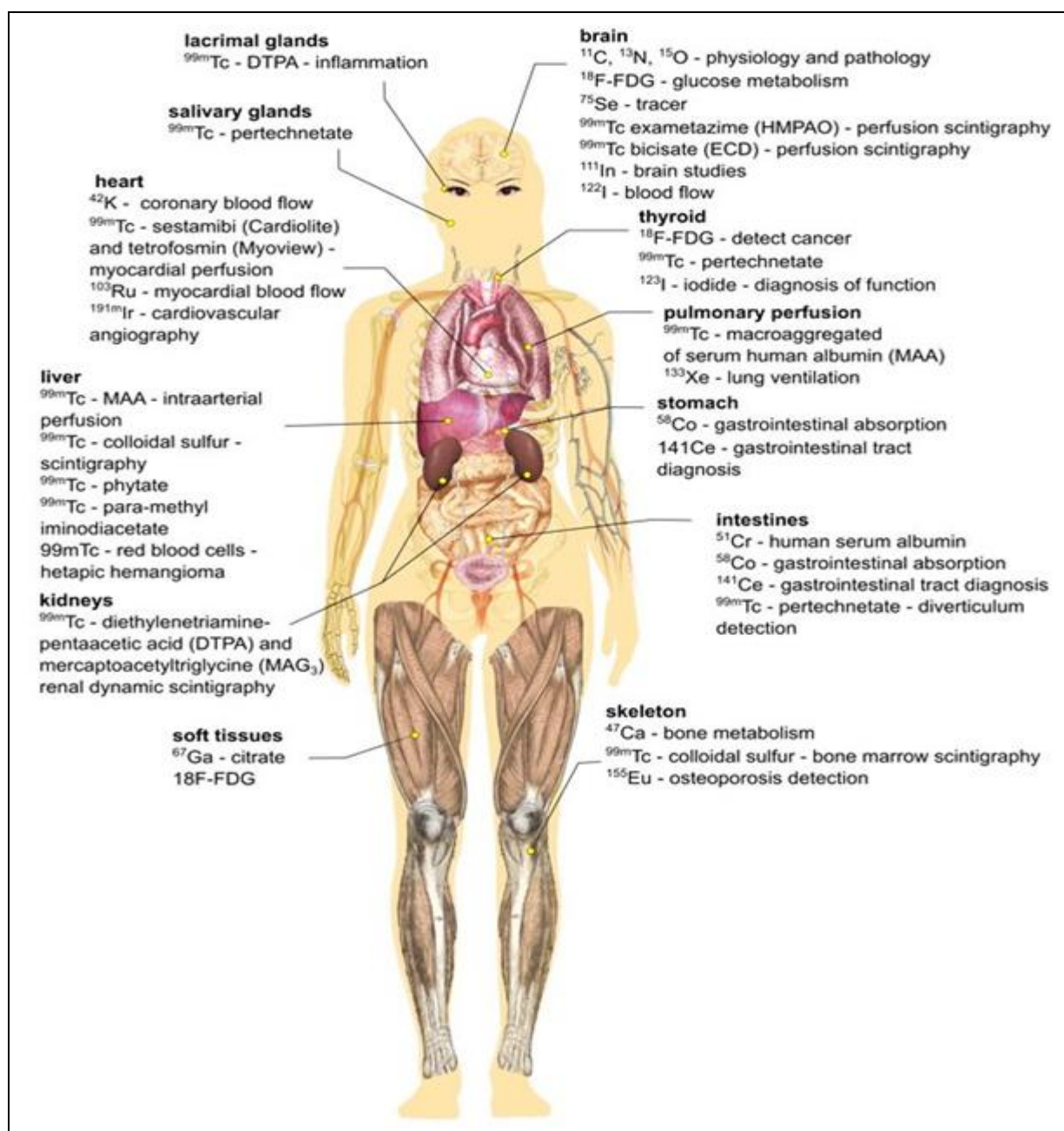


FIG. 9: DIFFERENT RADIOPHARMACEUTICALS (RADIOISOTOPES) AND TARGET ORGAN FOR IMAGING ³

Therapeutics: Nuclear medicine is also used as the therapeutic agent. Nuclear medicine therapy is designed to treat specific disease by using ionizing radiation. Radionuclide which are used as therapeutic agents, emit particulate radiations which have relatively short path lengths and are absorb by particular organ and shows their effect. Short pathlength protects nearby non targeting tissues. The ionizing radiation induces irreversible damage to nuclear DNA (faulty DNA) by breakdown of double strand DNA there by inhibiting further proliferation of these cells. Radionuclides decay alpha, beta, or Auger electron which can be used as therapeutics ³⁸.

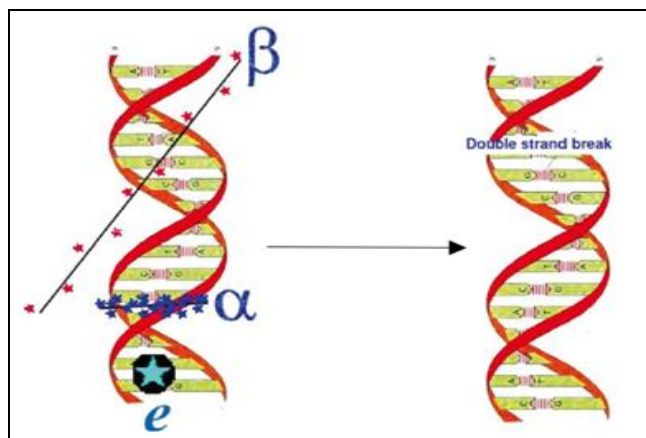


FIG. 10: EFFECT OF IONIZING RADIATION ON FAULTY DNA

TABLE 10: RADIONUCLIDES USED AS THERAPEUTICS³⁹

Type of radiation	Particles	Examples	Half life
Alpha (α)	2 proton and 2 neutron	²¹¹ At (Astatine-211)	7.2h
		²¹² Bi (Bismuth-212)	61min
		²¹³ Bi (Bismuth-213)	46min
		²²⁵ Ac (Actinium-225)	10 d
Beta minus (β^-)	Electrone	³² P (Phosphorus-32)	25.4d
		³³ P (Phosphorus-33)	14.3d
		¹⁷⁷ Lu (Lutetium-177)	6.7d
		⁶⁷ Cu (Copper-67)	61.9h
		¹³¹ I (Iodine-131)	8.0d
		⁸⁹ Sr (Strontium-89)	50.5d
		⁹⁰ Y (Yttrium-90)	64.1h
Auger electrone	Electrone	¹²⁵ I (Iodine-125)	60.5d
		¹²³ I (Iodine-123)	13.3h
		⁷⁷ Br (Bromine-77)	57h
		¹¹¹ In (Indium-111)	3d

Treatment of Thyroid Disease:

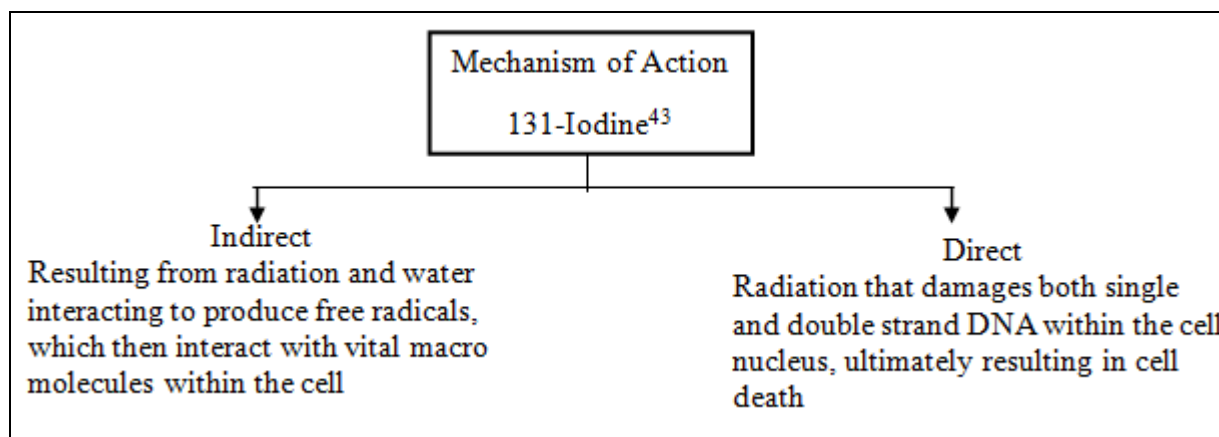
Treatment of Thyroid Cancer: Thyroid malignancies can originate from lymphoid tissue (primary thyroid lymphomas), the thyroid's follicular cells (papillary and follicular thyroid cancers), or the thyroid's parafollicular cells (medullary thyroid cancer). Radioactive iodine (¹³¹I) is used for the treatment of the thyroid cancer since more than 40 years^{40, 41}.

Radioactive iodine (I-131) is used in radioiodine therapy after surgery, to target any remaining thyroid tissue or malignant thyroid cells⁴¹. The I-131 beta particles are most effective in tiny areas they penetrate tissue only a few millimetres (within 2mm). Surgery is the first step in removing the majority of the thyroid gland and after surgery, treatment with I-131 helps in the destruction of any cancer cells that may remain after surgery⁴². Combination of both surgery and radioactive iodine treatment ensure greater survival rate than the surgery alone⁴².

Treatment of Hyperthyroidism (grave's disease)⁴³: There are mainly 3 options to treat hyperthyroidism:

1. Antithyroid drug
2. Thyroidectomy (surgery)
3. Therapy with ¹³¹I-iodide

In the case of antithyroid drugs there is a high risk of recurrence after tapering and also risk of minor to major adverse effects like rashes, agranulocytosis or hepatitis, etc. Surgery is often only performed on a limited number of individuals whose recurrent GD (grave's disease) or TMNG (toxic multinodular goiter) cannot be managed with medication⁴³. In the treatment of hyperthyroidism, ¹³¹I-iodine emitted beta minus particles, are responsible for the beneficial effects either direct or indirect⁴³.



Treatment of Neuroendocrine Tumor (NET): Neuroendocrine tumor is malignant growth originating from neuroendocrine cells. Neuroendocrine tumors are rare cancers categorized as NENs (Neuroendocrine neoplasms)⁴⁴. The majority of NETs have somatostatin receptors (SSTRs) on their cell surface, radiolabeled somatostatin analogues (SSAs) can be used with them (somatostatin regulate the cell growth and hormone secretion)⁴⁵.

¹¹¹In-pentetreotide which emit auger electeons was first used for the treatment of NET in the beginning of 90s.⁴⁶

Radiolabile somatostatin analogue like⁴⁶: SARTATE-Based Radiotracer like ⁶⁴Cu/⁶⁷Cu-SARTATE DOTA-TATE-Based Radiotracer like ¹⁵³Sm-DOTA-TATE Radiotracers Based on SSTR2 Antagonists like the ¹⁷⁷Lu-DOTA-LM3 can be used for the treatment⁴⁵.

TABLE 11: MOLECULES TARGETING SOMATOSTATIN RECEPTOR^{45, 46}

Radiotracer	Type of radiation	Type of molecule	Target
⁶⁴ Cu-SARTATE	Beta minus (β ⁻)	Agonist	Pancreatic tumor
⁶⁷ Cu-SARTATE	Beta minus (β ⁻)	Agonist	Pancreatic tumor, Neuroblastoma
²²⁵ Ac-DOTA-TATE	Alpha (α)	Agonist	Lung neuroendocrine
¹⁵³ Sm-DOTA-TATE	Beta minus (β ⁻)	Agonist	Pancreatic tumor
¹⁷⁷ Lu-DOTA-LM3	Beta minus (β ⁻)	Antagonist	Pancreatic tumor, Neuroendocrine tumors
¹⁶¹ Tb-DOTA-LM3	Beta minus (β ⁻)	Antagonist	Neuroendocrine tumor (Pancreatic tumor)

Intravenous injection of ⁹⁰Y-DOTATOC (Beta minus radiation) is also used for the treatment of NET⁴⁶.

Treatment of Prostate Cancer (PC): PC is the most common epithelial neoplasia in men starting around age of 50. Particular prostate ligands that can carry by radioactive isotopes including β-/γ(¹⁷⁷Lu), and α (²²⁵Ac) emitters which have therapeutic activity. PSMA (prostate specific membrane antigen) is present on the prostate. Radioactive isotopes binds with PSMA and shows their action⁴⁷.

PSMA targeting radio tracer agents like ¹⁷⁷Lu (lutetium-177), ²²⁵Ac(actinium-225), ²¹¹At(astatine-211) and ²¹³Bi(bismuth-213) are mainly used for the treatment.

Therapeutics agents which target PSMA are.⁴⁵

- ¹⁷⁷Lu-PSMA-617 - suppress tumor- Beta minus(β⁻) emitter
- ²²⁵Ac-PSMA-617 -alpha emitter
- ¹⁷⁷Lu-L1
- ¹⁷⁷Lu-EB-PSMA-617
- ²¹¹At-PSMA1

Radioimmuno Therapy (RIT): It is a cell targeting therapy which uses monoclonal antibodies labelled with a radioactive nuclide against tumour-associated antigens⁴⁸. [Antibodies (Abs) are glycoproteins secreted from plasma B cell to identify and remove foreign pathogens such as bacteria and viruses, monoclonal antibodies are laboratory made antibodies which are used to bind particular receptor]⁴⁹.

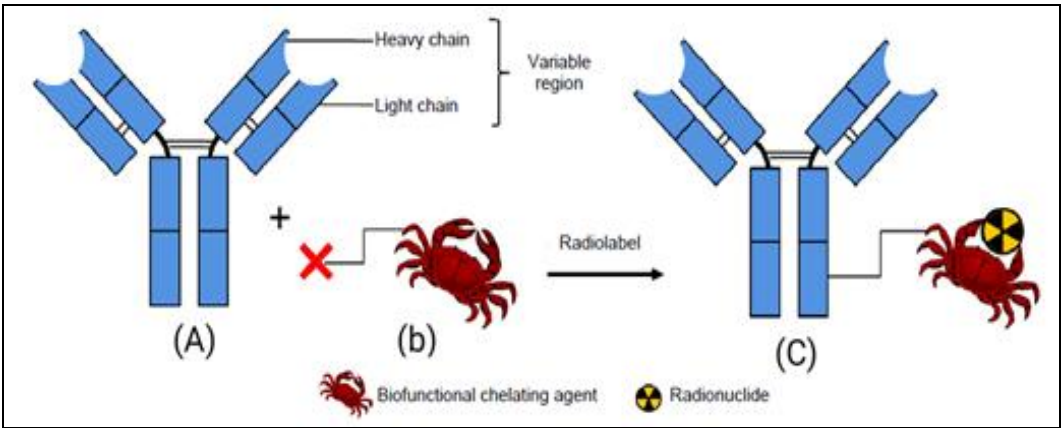


FIG. 11: MECHANISM OF ACTION OF RIT

- A. Antibody** Biofunctional chelating has two properties
- B. Biofunctional chelating agent**
- Binds with radionuclides
- C. Monoclonal antibodies labelled with radionuclide**
- Biofunctional has functional group X which binds with antibody^{48,49}

TABLE 12: RECENTLY DEVELOPED MONOCLONAL ANTIBODIES (MABS) FOR ADVANCED RADIOIMMUNOTHERAPY AND THE STATUS OF THE CLINICAL TRIALS^{48, 49}

Monoclonal antibodies	Radioisotopes	Antigen	Disease	Clinical trial Status
Ibritumomab tiuxetan	⁹⁰ Y	CD20	Non-Hodgkin's lymphoma	Approved by FDA
Tositumomab	¹³¹ I	CD20	Non-Hodgkin's lymphoma	Approved by FDA
Epratuzumab	⁹⁰ Y	CD22	Non-Hodgkin's lymphoma	Phase III
			Chronic lymphocytic leukemia	
			Immune diseases	
131I-chTNT-1/B	¹³¹ I	DNA	Glioblastoma multiforme, Anaplastic-astrocytoma	Phase III
cT84.66	⁹⁰ Y	Carcinoembryonic antigen (CEA)	Cororectal cancer	Mouse xenograft model
Labetuzumab	⁹⁰ Y & ¹³¹ I	Carcinoembryonic antigen (CEA)	Breast, lung, pancreatic, stomach, and colorectal carcinomas	Pending Phase III
131I-L19	¹³¹ I	Fibronectin	Hepatological malignancy, refractory Hodgkin's lymphoma, non-small cell, lung cancer, Melanoma, head and neck carcinoma	Phase II

Application of Nuclear Medicine⁵⁰: Providing information about the function and anatomy of the body

PET and SPECT imaging provide 3D image of the organ, compared to conventional imaging methods like X-rays, CT scans, and MRI scans, nuclear medicine offers a number of advantages, the most important one is its ability to provide information about the physiological and metabolic functions of the body.

1. Nuclear medicine detect the disease at the early stage, before they become symptomatic.
2. Nuclear medicine involves painless treatment.
3. It is non-invasive technique
4. Minimize the amount of radiation.

When using nuclear medicine, radiation exposure is reduced to that of a standard x-ray.

5. Nuclear medicine is important in therapy.

They are used to treat conditions like bone pain which is resistant to the usual medication regimen.

6. No accumulation in the body.

7. Helpful in cases of hyperthyroidism and thyroid cancer is nuclear medicine.

Limitations of Nuclear Medicines⁵¹: As the diagnosis and treatment is done using ionizing radiation, there is a small and measurable risk of the carcinogenicity. Radiation safety is a problem with nuclear medicine that can affects many different groups, including patients, the general public, friends, family, caregivers, and medical, technical, and nursing personnels. Local unavailability (less availability) of radioisotopes (radiopharmaceutical).

Example technetium-99m (^{99m}Tc) obtained from a molybdenum-99 (⁹⁹Mo)/^{99m}Tc generator. It's derived from nuclear fission reactions in nuclear reactors. Only developed nations, including the USA, Canada and certain European nations, have nuclear reactors.

1. Cost of the nuclear medicine

Nuclear medicine diagnosis and therapeutics are very costly, so some time it's challenging for the patient.

2. Nuclear medicine handling requires highly qualified specialists, skilled radiopharmacists, medical physicists, imaging scientists (nuclear medicine technologists), and nuclear medicine doctors.
3. Management of radioactive waste is a challenging task.
4. Inadequate facilities for nuclear medicine in developing countries.

Remedies: To avoid the risk of radiation, proper calculation of the cumulative effective dose for the patient is very important. Radiation emitted by patients undergoing nuclear medicine procedures are considerably lower than the limits recommended by ICRP and IAEA which are not as such harmful⁵².

Use of concept of the ALARA (as-low as-reasonably-achievable) is mandatory to avoid risk of radiation⁵³.

ALARA concept include mainly three principles time, distance & protective shield

1. **Time:** To reduce time spent close to nuclear installations
2. **Distance:** Being far away from a radioactive source (as the amount of radiation received decreases with increasing distance).
3. **Protective shield:** Using gloves and laboratory coats or other personal protective equipment (PPE) is designed to minimize or eliminate absorption of radiation through intact skin.

CONCLUSION: The nuclear medicines are used for diagnostic and therapeutics purpose. It is helpful to diagnose, number of disease at the early stage. Diagnosis done by the mainly two methods PET and SPECT. Nuclear diagnosis provides anatomical and functional 3D imaging and also provide good resolution image. Many of the radiotracer used for the diagnosis of the disease mostly uses 18-F-FDG. Diagnosis by nuclear medicine provides the better results than MRI and

CT scan. Nuclear medicine used as the therapeutics agents that emit the particular radiation which can be used to treat many types of cancer and other disease. Now a days many new radionuclides are discovered and many of them are approved by the USFDA and EMA. Some radionuclides are under the clinical trial [phase-2 and 3].

Nuclear medicine have many limitation like radiation hazards, high cost of therapy, unavailability of the radionuclides, etc. Radiation hazards can be control by giving the cumulative effective dose to the patients.

Nuclear medicine is very effective for theranostic purpose. Now a days further research is going on to discover new radionuclides for more effective diagnosis and treatment, with lesser limitations. So, "Nuclear medicine can be the ray of hope in future disease management".

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