**Nuclear Medicine**

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**ABSTRACT**

The examination of the rapid advancement of ultrasonography, CT, and MR is currently underway, as nuclear medicine's potential for diagnostic and therapeutic procedures is being assessed. Conversations often neglect to mention that nuclear medicine is a dynamic and continuously evolving diagnostic tool. The study illustrates the progression of nuclear medicine, which has advanced from basic in vitro testing to complex techniques for visualizing organ function, thanks to the improvements in radiopharmaceuticals and equipment. Furthermore, it offers a contemporary means to enhance cancer treatment for individual patients and explore cancer biology in vivo. Radionuclides connected with drugs, proteins, or peptides are among the other tracers that are workable. Iodine-131 or 18F-FDG, a radiolabel in a carrier molecule, are examples of tracers, which are radioactive substances that accumulate in the target tissue after injection into the body. Unlike the typical anatomical imaging methods like ultrasound, computed tomography or magnetic resonance imaging, nuclear medicine imaging techniques, such as single photon emission computer tomography and positron-emission tomography, have the potential to provide essential quantitative and functional insights into the health of tissues or disease states. Cancerous growths can be exposed to lethal radiation during therapy by means of tumor-targeting medications and therapeutic radionuclides. This overview offers a comprehensive analysis of nuclear medicine, covering its historical evolution, contemporary applications in cancer care, practical considerations, and function in medical imaging.

**Keywords-:** Radionuclide, tracers, Nuclear medicine, Radiopharmacology, Radiotherapy, Nuclear imaging, Cancer.

1. **INTRODUCTION**

Radioactive tracers (radiopharmaceuticals) are deployed in nuclear medicine to diagnose, cure, and appraise bodily function[1]. The evaluation of cellular physiology and function in nuclear diagnostic medicine is heavily reliant on imaging techniques. Medical practitioners can observe the path of these radioactive markers through cameras that are specifically engineered for this purpose. Within nuclear medicine, the two most widely used imaging modalities are: single-photon emission computed tomography (SPECT) and PET imaging using positron emission tomography[2].

1. **What are Radioactive tracers?**

Chemical reactions or physical processes often use tracers as markers to illustrate the position or monitor the pathway of a substance. To ensure reliable results, the tracers being used for observation should have similar chemical and physical activity as the component being studied in the environment. By tracking the radioisotope's activity, researchers are able to closely monitor the ongoing process. In addition, the use of radioactive material as a marker can be restricted to the lowest possible level. Radiotracer usage is based on the belief that the radioactive element will effortlessly merge with the system under investigation, and that the released radiation will not impact any system components[3].



**Fig 1: Radioactive tracing in CT scan of mouse [1]**

In Fig 1.1, Researchers demonstrate that a mouse's combined PET/CT (right) provides a more detailed picture regarding the spine than CT (left) or PET (centre) alone.

1. **What is Single Photon Emission Computed Tomography (SPECT is a medical imaging technique.**

There has been a rise in the usage of single photon emission computed tomography (SPECT) in nuclear medicine. Additional therapeutic uses are possible due to enhanced contrast, edge definition, and target separation from the background, in contrast to planar imaging. Additionally, the method provides a much superior means of assessing source distributions, particularly in organs such as the heart and brain[4].

Mounted on a revolving gantry that encircles the patient, Gamma cameras, varying from one to four in number, are employed by SPECT machines. SPECT-CT is a hybrid imaging method that is commonly used to correct attenuation and identify anatomical locations, but it can also be produced by combining SPECT with another CT scanner. The gamma cameras swivel around the subject, generating spatial data that allows for accurate mapping of radioactive dispersion within tissues. Several gamma cameras are employed to enhance the detector performance and spatial resolution. The camera projection data is reassembled into 3D visuals using axial slices, creating a realistic representation of the object[5-7].



**Fig 2: Osteomyelitis using SPECT/CT[8].**

**C .** What is Positron Emission Tomography (PET)?

Radioactivity in vivo can be measured using positron emission tomography (PET), a very non-invasive imaging technique. It involvesinjecting an intravenously with a positron-emitting radiopharmaceutical firstly waiting for systemic distribution, then secondly scanning for detecting and measuring radiopharmaceutical accumulation patterns in the body.

The results of a PET scan can be reconstructed and shown as a (3D)three-dimensional picture, similar to SPECT imaging. Scintigraphy, on the other hand, generates planar data that can only be utilised to make a two-dimensional image.[9]

The evaluation of cardiac issues and the detection of cancer and cancer metastasis (spread) have both shown to be extremely useful applications of PET. Scientists have learned more about how drugs affect the brain and how learning, language usage, and specific brain disorders like Parkinson's disease, stroke, and depression work by using PET scans. Additionally, researchers are working to create techniques that will allow them to measure how well a patient's therapy has worked for them by determining the molecular causes of neurological and behavioural disorders the results of PET.[10]

 

**Fig 3: Images of the human body produced using positron emission tomography (PET)[11].**

1. **HISTORY**

 Scientists from several fields, including physics, medicine, chemistry, and engineering, have long

collaborated pertaining to nuclear medicinE..The history of nuclear medicine has been difficult to trace because of this wide range of interaction. Between 1934, the year artificial radioactivity was discovered, and 1946, the year Oak Ridge National Laboratory generated the first radionuclides for medicinal application, researchers theorise that this medical speciality was born. In 1946, Sam Seidlin's description of nuclear medicine in the Journal of the American Medical Association marked the beginning of acceptance of nuclear medicine as a prospective medical specialty.Sam Seidlin's 1946 Journal of the American Medical Association article highlighting nuclear medicine as a future medical specialty.[12][13]

 The origins of this medical notion may be traced back to the mid-1920s in Freiburg, Germany, when George de Hevesy conducted investigations using radionuclides administered to rats, exposing metabolic pathways and creating the tracer principle. When John Lawrence, dubbed "the father of nuclear medicine," walked out of his position as a professor at Yale Medical School in 1936 to visit his brother Ernest Lawrence at his brand-new radiation laboratory in Berkeley, California (now known as the Lawrence Berkeley National Laboratory), this medical specialty may have first emerged.John Lawrence used an artificial radionuclide for the first time ever in a patient when he used phosphorus-32 to treat leukaemia Later, he applied phosphorus-32 to treat leukaemia [14][15].

Many historians regard the 1934 discovery of artificially developed radionuclides by Frédéric Joliot-Curie and Irène Joliot-Curie to be the most significant turning point in nuclear medicine.

[14]. After learning about the radioactivity of aluminium foil irradiated with a polonium preparation, they published the first artificial generation of radioactive material in the journal Nature in February 1934. Their research took inspiration from Wilhelm Konrad Roentgen's work on X-rays, Henri Becquerel's work on radioactive uranium salts, and Marie Curie's work on radioactive thorium and polonium, which gave rise to the phrase "radioactivity." Taro Takemi conducted research on the application of nuclear physics in medicine in the 1930s. If these early pioneers were never addressed, the history of nuclear medicine would be lacking[16]..

On May 11, 1946, Dr. S.Hertz of Massachusetts General Hospital and Dr. Arthur Roberts of Massachusetts Institute of Technology posted an article in the Journal of the American Medical Association (JAMA) documenting the-: effective use of radioactive iodine (RAI) in the treatment of Graves' Disease.[17].

The discovery and development of Technetium-99m were more significant than any other radionuclides recognised for use in medicine. It was discovered in 1937 by C. Perrier and E. Segre as a synthesised element that fills atomic number 43 on the periodic table. In the 1960s, the development of a Technetium-99m generating system became a practical technology for use in medicine. The most often used element in nuclear medicine nowadays is technetium-99m, which is employed in a variety of nuclear medicine imaging tests. As knowledge of radionuclides, radioactivity detection, and the use of particular radionuclides to pinpoint biochemical processes increased in the early 1950s, nuclear medicine began to be widely used in clinical settings. Hal and Benedict Cassen's innovative achievement in creating the first rectilinear scanner .[16].

The earliest brain blood flow maps were created by Niels A. Lassen, David H. Ingvar, and Erik Skinhj in southern Scandinavia in the early 1960s using xenon-133 inhalation [18]. Later, an intra-arterial counterpart was developed that made it possible to assess the localization of brain activity in people with neuropsychiatric illnesses like schizophrenia[19]. Later versions would come with 254 scintillators, enabling the presentation of a two-dimensional picture in colour on a monitor. They were able to produce images that accurately depicted brain activity during voluntary movement, reading, speaking, and other cognitive tasks [20]. The method was also applied to research mental maths, imagined sequential motions, and mental navigation in space, among other things [21] [22].

By the 1970s, most bodily organs could be checked using nuclear medicine techniques. In 1971, the American Medical Association formally recognised nuclear medicine as a medical specialty [23].

1. **NUCLEAR MEDICINE’s HISTORICAL CHRONOLOGY**[24]

1896:- Henri Becquerel- Discovered enigmatic uranium “rays”

1897:- Marie Curie- Displayed the enigmatic beams the name “radioactivity”

1901:- Henri Alexandre Danlos and eugene Bloch - Applied radium for tuberculosis cutaneous lesion.

1903:- Alexander Graham Bell - Stated that “Radium’’ sources should be placed within or near tumours.

1913:-Frederick Proescher - Published the first study on the use of intravenous radium injection for treating various illness .

1914:- Seil - Investigated the presence of radon and radium in faeces following intravenous radium administration.

1924:- Georg de Hevesy , J.A. Christiansen , sven lomholt - Conducted the first Animal studies with radiotracers (lead-210 and bismuth - 2110)

1925:- Herman Blumgart and Otto Yens - Employed bismuth-214 (radium-C) to assess arm-to-arm circulation to patients.

1932:- Ernest O. Lawrence and M.satnley Livingston - First to publish a paper on the “the production of high speed light ions without the use of high voltages . “It was a significant turning point in the generation of radionuclides in acceptable amounts .

1935:- O.Chievitz and George de hevesy - Demonstrated bone mineral component regeneration in rats by giving phosphate labeled with phosphorus-32.

1935:- John H. Lawrence(Ernest Lawrence’s Brother) - Used thyroid physiology using iodine -128

1936:- Joseph Gilbert Hamilton - Conducted the first medical physiology investigation on the kinetics of sodium transport in the body.

1937:- John livinghood,Fred Fairbrother and Glenn seaborg - Discovered iron-59.

1937:- Joseph Gilbert hamilton - Conducted the first medical physiology investigation on the kinetics of sodium transport in the body.

1937:- Dr. Saul Hertzand Dr. Arthur Roberts and Robley Evans - Iodine-128 was used in thyroid physiology.

1938:- Emilio Segre and Glenn Seaborg - Identified technetium - 99m

1939:- Joseph Gilbert Hamilton , mayo solely and robley evans - Published the first publication on the diagnostic application of iodine-131 in patients.

1939:- Charles Pecher - Detected strontium-89 uptake in bone metastases

1940:- The rockefeller Foundation - Funded the first biological radio-isotope generating cyclotron at Washington University in St.louis.

1941:- Saul Hertz - Administered in the first therapeutic dosage of iodine-130 to a patient.

1942:- Enrico Fermi and his colleagues - Performed the first controlled chain reaction beneath the stands at the university of chicago’s stagg field .

1946:- Allen Reid and albert keston - Developed iodine-125, which became crucial in the field of radioimmunoassay.

1946:- Samuel .M. Seidlin , Leo D. Marinelli , and Eleanor Oshry - Tapped an “atomic cocktail” of iodine-131 to treat a thyroid cancer patient.

1947:- Benedict Cssen - Executed radioiodine to determine if a thyroid nodule collected iodine, which assisted in distinguishing benign from malignant.

1948:- Abbott laboratoeies - Started distribution of radioisotopes .

1949:- B.Selverstone - Employed phosphorus-32 as a probe detector to identify brain tumours after surgery .

1950:- Abbott Laboratories - Released the first commercial radiopharmaceutical . iodine-131 human serum albumin

 1950:- The United States Food and Drug Administation ( FDA) - Approved sodium iodine 1-131 for use in thyroid patients . The FDA approoved it as the first radiopharmaceutical.

1951:- Benedict cassen , lawrence curtis , clifton reed and raymond libby - Used a scintillation detector to “scan” the thyroid gland for radioiodine distribution.

1953:- Gordon brownell and H.H.Sweet - Created a positron detector using coincidence counting to detect annhilation photons.

1954:- David kuhl - Invented a radionuclide scanning photo recording system. This advancement pushed nuclear medicine even closer to radiography.

1955:- Rex Huff - Used iodine-131 human serum albumin to calculate cardiac output in humans.

1957:- George V . Taplin - Imaged the liver with iodine-131 labelled rose bengal.

1958:- Hal anger - Developed the “scintillation camera” , and image technology that enabled dynamic analyses.

1959:- Solomon Berson and rosalyn yalow - Devised the radioimmunoassay to detect insulin antibodies in human serum .

1960:- John McAfee and Henry Wagner - Used radio mercury labelled chlormerodrin to scan the kidneys.

1961:- Allis - Chalmers - Built the first “medical centre’’ cyclotron in the united states at washington university

1962:- Nuclear Chicago's John Kuranz handed over the first commercial Anger camera to William Myers at Ohio State University.

1963:- The FDA exempted radiopharmaceuticals controlled by the Atomic Energy Commission from the "new drug" standards.

1963:- Henry Wagner - First to employ radiolabeled albumin aggregates to image lung perfusion in healthy people and pulmonary embolism patients.

1964:- The Food drug administration - Exempted radiopharmaceuticals controlled by the Atomic Energy Commission from the "new drug" standards.

1964:- Paul Harper and Katherine Lathrup - Created radiotracers labeled with Tc-99m for the investigation of the brain, thyroid, and liver.

1964:- Amersham - Offered the first commercial radioimmunoassay kit (iodine-125 insulin test).

1968:- Henry Wagner and colleagues - Employed xenon-133 breathing scans to detect pulmonary embolism

1969:- C.L. Edwards - Discovered gallium-67 buildup in cancer.

1970:- W. Eckelman and P. Richards - Created Tc-99m "instant kit" radiopharmaceuticals. Tc-99m-DTPA was the first.

1970:- The Food Drug Administration - Declared that it will progressively revoke radiopharmaceutical exemptions and begin regulating them like medications. The modification would be finished by January 20, 1977.

1971:- The American Medical Association - formally recognised nuclear medicine as a medical specialty

1971:- Gopal Subramanian and John McAfee - Developed Tc-99m labeled phosphates for bone imaging.

1971:- David Kuhl - First to undertake a quantitative measurement of cerebral blood volume in a living patient

1973:- H. William Strauss - Proposed the exercise stress-test myocardial scan

1973:- Elliot Lebowitz - Presented thallium-201 for myocardial perfusion imaging, first proposed by Kawana

1973:- David Goldenberg showed in animals the ability of radiolabeled antibodies against a human tumour antigen (CEA) to target and photograph human tumours

1976:- John Keyes - Invented the first single photon emission computed tomography (SPECT) camera and Ronald Jaszczak invented the first SPECT camera for the head

1976:- N. Firusian - Employed strontium-89 to alleviate discomfort associated with metastatic bone disease

1976:- Ronald Jaszczak - Invented the first SPECT camera for the head.

1977:- The Food Drug Administration - Approved New England Nuclear to distribute thallium-201 for myocardial perfusion as well as the diagnosis and localisation of myocardial infarction.

1978:- David Goldenberg - Experimented with radiolabeled antibodies to image tumors in humans.

1980:- J.P. Mach - Employed radiolabeled monoclonal antibodies to image tumors.

1981:- K.A. Krohn, D.R. Vera, and S.M. Steffen - Generated the first Tc-99m labelled receptor ligand.

1982:- Steve Larson and Jeff Carrasquillo - Used iodine-131 labeled monoclonal antibodies to treat cancer patients with malignant melanoma.

1983:- William Eckelman and Richard Reba - Performed the first effective SPECT imaging of a neuroreceptor in humans

1987:- Medi-Physics - Created the first FDA-approved brain perfusion imaging radiopharmaceutical, iodine-123 IMP.

1988:- The Food Drug Adminisstartion - Authorized Amersham's first Tc-99m brain perfusion radiopharmaceutical for the diagnosis of stroke.

1989:- The Food Drug Administartion - Authorized the first positron radiopharmaceutical (rubidium-82) for myocardial perfusion imaging.

1990:- Steve Lamberts and Eric Krenning - Used somatostatin receptor-binding radiotracers to scan endocrine tumors

1990:- The Loyola University Nuclear Information System (LUNIS) - World's first and most important educational worldwide interactive computer network for nuclear medicine.

1991:- The Food drug administration - Authorised the first Tc99m myocardial agent

1992:- The Food drug administartion - Approved the first monoclonal antibody radiopharmaceutical for tumor imaging

1993:- The Food drug administartion - Approved Medi-Physics/Amersham to commercialise strontium-89 chloride for the management of bone pain

1994:- Mallinckrodt - Gained FDA permission to commercialise the first peptide radiopharmaceutical that binds to somatostatin receptors and may be used to image granulomatous and autoimmune disorders

1995:- ADAC Laboratories - Manufactures the first SPECT camera with FDG/PET imaging capability.

1996:- "Legitimacy" of brain PET.

1997:- Validation of 123I-beta-CIT -: Evaluated dopamine transporters in Parkinson's disease diagnosis

1998:- FDG PET studies were used to assess the response of an initial dose of chemotherapy to predict the response to subsequent high-dose chemotherapy.

1999:- HCFA -: Authorised sentinel node research for improved cancer detection and management

2000:- Siemens Biograph - Named the year's best invention by Time Magazine.

2001:- In the United States, 16.9 million nuclear medicine operations were conducted.

2003:- IDEC Pharmaceuticals receives FDA approval for clinical use of ZevalinTM, a radioimmunotherapy drug.

2004:- The Society of Nuclear Medicine celebrates its 50th anniversary

2004:- SNM - Establishes the PET Centre of Excellence to enhance the practise of nuclear medicine procedures, which are both safe and effective methods of illness detection

2004:- FDA - Approves the use of Bexxar™ for use in lymphoma.

2006:- SNM's Education & Research Foundation - Received $6 million from the Hal Anger Estate, the largest gift ever received for advancing the field of nuclear medicine

2007:- The name of the society is changed from "Society of Nuclear Medicine" to "SNM: Advancing Molecular Imaging and Therapy" to reflect the society's expanding scope

2008:- 40th anniversary of the publication of Dr. Henry Wagner's seminal text, Principles of Nuclear Medicine.

2008:- The first hybrid PET/MRI system for humans, created by Siemens, was installed

1. **INTERVENTIONAL NUCLEAR MEDICINE**

A radionuclide is an unstable nuclide with an excess of nuclear energy. It is sometimes referred to as a radioactive nuclide-isotope. One of the nucleus' electrons can receive the extra energy and released as a conversion electron, gamma radiation, or an entirely new particle that is formed and discharged from the nucleus. During such operations, radionuclide is thought to undergo decay[25]. These emissions are ionizing radiation due to their high energy, which might result in an atom losing an electron. Radioactive decay can produce a stable nuclide, but it can also occasionally produce a brand-new unstable radionuclide that may undergo decay. It is a random process at the level of individual atoms, it is difficult to predict when a particular atom will start decaying[26][27][28][29]. However, the measured values of a set of atoms' decay constants can be used to calculate the half-life (t1/2) and, consequently, the decay rate for that nuclide. The distance between the half-lives of radioactive atoms, which have no limits, is about 55 orders of magnitude.

In nuclear reactors, particle accelerators, cyclotrons or radionuclide generator, radionuclides can be generated artificially or naturally. About 730 radionuclides have half-lives that are greater than 60 minutes. Of those, 32 are primordial radionuclides, which were produced prior to the formation of the earth[27]. There are at least 60 more radionuclides that can be found in nature, either as offspring of the original radionuclides or as radionuclides created naturally on Earth by cosmic radiation. Half-lives of more than 2400 radionuclides are shorter than 60 minutes. The majority of them have short half lives and are only created artificially. There are roughly 251 stable nuclides in comparison.

1. **Diagnostic medical imaging:**

Radiopharmaceuticals are administered intravenously in nuclear medicine imaging, orally, or through inhalation. The radiation that the radiopharmaceutical release is then captured and converted into images by external detectors as this procedure is distinct from a diagnostic X-ray. This creates an image by exposing the body to outer radiation. Nuclear medicine diagnostic methods come in a variety.

2D: Scintigraphy is the process of producing two-dimensional images using internal radionuclides.

3D: Gamma camera data from numerous projections are used in the 3D tomographic technique known as SPECT, which can reconstruct images in various planes. Coincidence detection is used in Positron Emission Tomography to image related activities.

Nuclear medicine diagnostic tests typically depict the physiological function of the system being studied and this phenomenon makes them different from most other imaging modalities. In Comparison with traditional radiology imaging that focuses on a specific area of the body, nuclear medicine imaging tests are typically more organ, tissue, or disease-specific. Additionally, nuclear medicine studies enable whole-body imaging based on certain cellular receptors or functions. Gallium scans, indium WBC scans, MIBG, octreotide-scans, whole-body PET scans, and PET/CT scans are a few examples.

1. **Practical concerns in nuclear medicine:**

All radiation exposure in humans should be maintained as low as reasonably practicable, or "ALARP," despite the fact that the effects of low-level radiation exposures are poorly understood [29].

In accordance with the ALARP principle, it is necessary to determine the benefits of a nuclear medicine examination before exposing a patient to them. When necessary, this must take into account the patient in question's unique circumstances. It would be unwise to proceed with injecting the patient with the radioactive tracer, for example, if it is uncertain that they will be able to tolerate the treatment in sufficient amounts to make a diagnosis.

The radiation exposure (amount of radiation provided to the patient) should be maintained as low as is practically possible when the benefit does justify the procedure. This means that nuclear medicine images should never be higher quality than what is necessary for a certain diagnosis. Larger radiation exposures can make images less noisy and more appealing to the eye, but if the clinical query can be resolved without this level of specificity, then this is unsuitable.

As a result, depending on the type of investigation, the radiation dose from nuclear medicine imaging varies substantially. The effective radiation dosage may be significantly greater than the annual background radiation dose from the environment as a whole, lower, comparable, or neither.

1. **Nuclear medicine in therapy:**
2. Unsealed source radio therapy:

Radiopharmaceuticals are radioactive chemicals that are used in radionuclide treatment to treat diseases, primarily cancer. These enter the body by a variety of methods (injection and ingestion are the two most frequent) and, depending upon characteristics and delivery mode, localize to particular sites, organs, or tissues. This ranges from straightforward biopharmaceuticals like sodium iodide, which binds to the iodide ion in the thyroid to sophisticated biopharmaceuticals like recombinant antibodies, which are bound to radionuclides and look for specific antigens on cell surfaces [30][31]. This targeted therapy includes the radiopharmaceuticals physical, chemical, and biological features to target specific body parts for radiation treatment [32]. Nuclear medicine, a diagnostic technique, follows the same concepts but utilizes different types or doses of radiopharmaceuticals to analyze the patient's functional systems [33].

1. Clinical uses:
2. Thyroid conditions:

The most widely used RNT in the world, iodine-131 (131I), combines a radioactive isotope of : iodine with the chemical sodium iodide. The patient may consume a solid or liquid dose orally, or they may have an intravenous injection of the chemical solution. The thyroid gland specifically absorbs the iodide ion[34]. The radiation produced by radioiodine can be used to treat both benign illnesses like thyrotoxicosis and some malignant conditions like papillary thyroid carcinoma. Radiation from iodine-131 emits beta and gamma rays. The majority of the Gamma radiation is removed from the patients body, the beta radiation affects both healthy thyroid tissue and any thyroid cancer that acts like healthy thyroid tissue by absorbing iodine, producing a therapeutic effect [35]. The kidneys excrete most of the iodine that is not absorbed by thyroid tissue into the urine. Following radioiodine therapy, the patients' urine will be radioactive or "hot," and they will also emit gamma radiation [36].

1. Bone metastasis:

Treatment options for secondary malignancy in the bones include samarium-153 EDTMP, strontium-89 chloride, and radium-223 chloride, Strontium and radium act similarly to calcium in the body [37][38]. Samarium is linked to the tetraphosphate EDTMP, and osteoblastic repairs that take place close to some metastatic lesions absorb phosphates from the environment [39].

1. Bone marrow conditions:

In this a Beta emitting phosphorus-32 as sodium phosphate, is used to treat overactive bone marrow, in which it is otherwise naturally metabolised [40][41][42].

Common nuclear medicine (unsealed source) therapies

|  |  |
| --- | --- |
| Substance | Condition |
| Iodine-131-salt iodide | Thyroid cancer and hyperthyroidism |
| Yttrium-90-ibritumomab tiuxetan (Zevalin) and Iodine-131-tositumomab (Bexxar) | Refractory lymphoma |
| 131I-MIBG (metaiodobenzylguanidine) | Tumours of the neuroendocrine system |
| Samarium-153 or Strontium-89 | Palliative bone pain treatment |
| Rhenium-188 | Skin squamous cell cancer or basal cell carcinoma |

**Table 1: Common nuclear medicine (open source) treatments**[16]

1. Brachytherapy:

A radiation source which is covered is positioned near the area that has to be treated in brachytherapy, a type of radiation therapy. Greek for short is Bracy. Brachytherapy is frequently used as a successful treatment for cancers like: skin, breast, esophagus, prostate, cervix, and other organs. It is required to treat tumors in many other parts of the body [39]. Brachytherapy has been shown to have cancer-cure rates that are either on par with surgery and external beam radiation (EBRT) or even higher when combined with these treatments, according to treatment outcomes. Surgery, EBRT, and chemotherapy are just a few examples of various treatments that can be used with brachytherapy [43][44][45].

1. Medical uses:
* Cervical cancer:

The standard of care in many nations for the treatment of early-stage or locally contained cervical cancer is brachytherapy. LDR, PDR, or HDR brachytherapy are three options for the treatment of cervical cancer [43]. Brachytherapy, when combined with EBRT, has the potential to produce superior results than EBRT alone. Brachytherapy's accuracy makes it possible to administer a high dosage of radiation to the cervix while minimizing radiation exposure to nearby tissues and organs.[47][48]. The chances of remaining healthy and alive are comparable for LDR, PDR, and HDR therapies. However, a major benefit of HDR treatment is that each dose can be administered outside of the hospital with little downtime, which makes it more convenient for many patients [49][50].

* Prostate cancer:

The two types of radiation therapy for the treatment of prostate cancer are transient HDR brachytherapy and long-term LDR seed implantation.Long term implantation is the best option for patients with a confined tumor and a good prognosis as it has been shown to be a highly successful treatment to prevent the cancer from returning, as there are less unpleasant side effects, such as impotence and incontinence, the survival rate is comparable to that of surgery or External beam radiation therapy. The procedure is very quick, and patients can return home after treatment the same day and resume their normal routines couple of days later. This is typically treatment option with less invasion than prostate surgery [50].

* Breast cancer:

An essential component of breast-conserving therapy is therapy with the help of radiation. This is the accepted standard of treatment for female patients who have undergone mastectomy or lumpectomies [44]. Brachytherapy is a possibility after surgery, prior to chemotherapy, or as a palliative treatment for advanced disease. HDR temporary brachytherapy is the most used type of brachytherapy used to treat breast cancer. Instead of irradiating the entire breast with EBRT following surgery, Interstitial brachytherapy of breast can be utilized as a boost. Through accelerated partial breast irradiation, only the immediate vicinity of the original tumor has recently been treated to radiation [52][53].

* Interstitial breast brachytherapy:

In interstitial breast brachytherapy, a number of temporary flexible plastic catheters are inserted into the breast tissue [54]. These are placed with care to allow for the best radiation targeting to the treatment area while sparing the breast tissue around it and the after loader, which is attached to the catheters, delivers the intended dose of radiation to the treatment area. Interstitial brachytherapy of breast can be utilized as an APBI or as a boost following EBRT [55].

* Brain tumors:

A Radiation Therapy using surgery, a specialized type of radiation therapy implant, is designed for usage in the brain. According to the FDA, operable malignant neoplasms in the cranium and operable recurrent neoplasms of cranium that can be treated with GammaTile Therapy include meningiomas, metastases, gliomas of high grade, and glioblastomas. As a result, these conditions are also referred to as GammaTile Therapy.

In comparison to earlier same-site therapies, GammaTile Therapy improved local tumor control while decreasing the incidence of side effects.

* Esophageal cancer:

The option effective here is brachytherapy, radiation therapy for esophageal cancer and involves palliative or definitive radiotherapy. Palliative therapies can be used to address dysphagia while definitive radiation (boost) can deliver the dose properly. The after loader is used in conjunction with large diameter applicators or a balloon-type catheter to widen the esophagus and make it easier to administer radiation doses to the tumor while sparing neighbouring healthy tissue. For patients with esophageal cancer, brachytherapy administered after EBRT or surgery has been demonstrated to increase local recurrence and survival rates compared to EBRT or surgery alone.

* Skin cancer:

HDR brachytherapy offers an alternative to surgery for non-melanomatous skin malignancies such carcinoma of the basal cell and carcinoma of the squamous cell. This is especially important when there is cancer in the lips, eyelids, nose, or ears because surgery may leave a deformity or require extensive repair. To establish intimate contact between the radiation source and the skin, several applicators can be used. These applicators can be tailored to the curvature of the skin and aid in the accurate delivery of the optimal radiation dosage.

A different type of radiation therapy that is available is called Rhenium- Skin Cancer Therapy, and it has advantages comparable to those of HDR. With the help of Rhenium-188's beta ray emissions, basal cell or squamous cell carcinomas can be cured.

* Blood vessels:

In order to insert and remove sources through a catheter that is put into blood arteries, brachytherapy can be utilized to treat coronary in-stent restenosis. Drug eluting stents (DES) have been reported to be more effective than intracoronary radiation therapy is the treatment of in-stent restenosis (ISR). Vascular radiation therapy, however, is still being researched for persistent restenosis in vein graft and stent failure. Additionally, the therapy has been looked into as a potential treatment for atrial fibrillation and peripheral vascular stenosis[16].

**Most Commonly used radionuclides for brachytherapy**

|  |  |  |  |
| --- | --- | --- | --- |
| **Radionuclide** | **Type** | **Half-life** | **Energy** |
| Caesium-137 (137Cs) | γ-ray | 30.17 years | 0.662 MeV |
| Cobalt-60 (60Co) | γ-ray | 5.26 years | 1.17, 1.33 MeV |
| Iridium-192 (192Ir) | β−-particles | 73.8 days | 0.38 MeV (mean) |
| Iodine-125 (125I) | γ-rays | 59.6 days | 27.4, 31.4 and 35.5 keV |
| Palladium-103 (103Pd) | γ-ray | 17.0 days | 21 keV (mean) |
| Ruthenium-106 (106Ru) | β—particles | 1.02 years | 3.54 MeV |

**Table 2: Most commonly used radionuclides for brachytherapy**[55]

1. **SOURCES OF RADIONUCLIDES:**

Molybdenum-99 (99Mo), which is normally created in nuclear reactors as a fission product of 235U, is the parent radionuclide of 99mTc, which is typically given to hospitals via a radionuclide generator. However, global supply constraints have driven the exploration of alternate manufacturing techniques. The Petten nuclear reactor in the Netherlands provides almost one-third of the medical isotopes used throughout the world and most of Europe. Chalk River Laboratories at Chalk River, Ontario, Canada, generated another third of global production and the majority of North American supply until its closure in 2018. Instead of a nuclear reactor, the most common radioisotope used in PET is generated in a cyclotron, a circular accelerator. The stable heavy oxygen isotope 18O is attacked with cyclotron-accelerated protons. The extracted 18O accounts for around 0.20% of the regular oxygen, which is mostly oxygen-16. Typically, the 18F is then used to produce FDG [56]. Technetium- 99m, iodine- 123, iodine- 131, thallium- 201, gallium- 67, fluorine- 18 fluorodeoxyglucose, indium- 111 tagged leukocytes, Xenon -133, are the most commonly utilized gaseous/aerosol radionuclides are the most commonly used intravenous nucleotides[57].

**Common isotopes used in nuclear medicine**[58][59][60]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Isotope** | **Symbol** | **Z** | **T1/2** | **Decay** | **gamma (kev)** | **Maximum β** |
| **energy (keV)/ Abundance[61]** |
| **Imaging** |
| [fluorine-18](https://en.wikipedia.org/wiki/Fluorine-18) | 18F | 9 | 109.77 m | β+ | 511 (193%) | 634 (97%) |
| [gallium-67](https://en.wikipedia.org/wiki/Gallium-67) | 67Ga | 31 | 3.26 d | Ec | 93 (39%), | - |
| 185 (21%), |
| 300 (17%) |
| [krypton-81m](https://en.wikipedia.org/wiki/Krypton-81m) | 81mKr | 36 | 13.1 s | IT | 190 (68%) | - |
| [rubidium-82](https://en.wikipedia.org/wiki/Rubidium-82) | 82Rb | 37 | 1.27 m | β+ | 511 (191%) | 3381 (81.8%) |
| 2605 (13.1%) |
| 1906 (0.14%) |
| 1209 (0.32%) |
| [nitrogen-13](https://en.wikipedia.org/wiki/Nitrogen-13) | 13N | 7 | 9.97 m | β+ | 511 (200%) | 1198 (99.8%) |
| [technetium-99m](https://en.wikipedia.org/wiki/Technetium-99m) | 99mTc | 43 | 6.01 h | IT | 140 (89%) | - |
| [indium-111](https://en.wikipedia.org/wiki/Indium-111) | 111In | 49 | 2.80 d | Ec | 171 (90%), | - |
| 245 (94%) |
| [iodine-123](https://en.wikipedia.org/wiki/Iodine-123) | 123I | 53 | 13.3 h | Ec | 159 (83%) | - |
| [xenon-133](https://en.wikipedia.org/wiki/Xenon-133) | 133Xe | 54 | 5.24 d | β− | 81 (31%) | 346 (99.1%) |
| 267 (0.9%) |
| [thallium-201](https://en.wikipedia.org/wiki/Thallium-201) | 201Tl | 81 | 3.04 d | Ec | 69–83\* (94%), | - |
| 167 (10%) |
| **Therapy** |
| [yttrium-90](https://en.wikipedia.org/wiki/Yttrium-90) | 90Y | 39 | 2.67 d | β− | - | 2279 (99.98%) |
| [iodine-131](https://en.wikipedia.org/wiki/Iodine-131) | 131I | 53 | 8.02 d | β− | 364 (81%) | 807 (0.4%) |
| 606 (89.4%) |
| 334 (7.2%) |
| 248 (2.1%) |
| [lutetium-177](https://en.wikipedia.org/wiki/Isotopes_of_lutetium) | 177Lu | 71 | 6.65 d | β− | 113 (6.6%), | 498 (79.3%) |
| 208 (11%) | 385 (9.1%) |
|  | 177 (11.6%) |

**Table 3: Common isotopes used in nuclear medicine**

1. **SOME COMMON RADIONUCLIDES AND THERE APPLICATION:**

Physical characteristics of commonly available therapeutic radionuclides

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Radionuclide** | **Physical half-life** | **Mode of decay** | **Principal *E* γ (keV) [% intensity]** | **Max. *E* β− (keV) [% intensity]** | **β− range in soft tissue (mm)** | **Method of production** | **Daughter nuclide** | **Clinical indication** |
|  |  |  |  |  | **Mean** | **Max** |  |  |  |
| 32P[62][63][67][69][70][71] | 14.26 d | β− |  | 1710 | 2.6 | 7.9 | 31P (n, γ) 32P, 32S (n, p) 32P | 32S | PVNS, polycythemia vera, cystic craniopharyngioma |
| 89Sr[62][63][65][66][67][70][71] | 50.53 d | β− | 910 [0.01] | 1496 [100.0] | 2.4 | 8 | 88Sr (n, γ) 89Sr, 89Y (n, p) 89Sr | 89Y | Severe bone metastasis |
| 90Y[62][65][66][70][71] | 64.10 h | β− |  | 2280.1 [100.0] | 3.6 | 11 | 89Y (n, γ) 90Y, 90Sr/90Y generator | 90Zr | Hepatic metastasis, PVNS, RIT for NHL |
| 117mSn[65][70][71] | 13.60 d | IT | 158.6 [86] | 130\*, 150\* | 0.22, 0.29 | 0.27 | 116Sn (n, γ) 117mSn, 117Sn (n, n’, γ) 117mSn | 117Sn | Bone tumour treatment |
| 131I[65][70][71] | 8.02 d | β− | 364.5 [81.7] | 606 [89.3] | 0.4 | 2.4 | 130Te (n, γ) 131m,gTe→131I | 131Xe | Hyperthyroidism, thyroid cancer, RIT for NHL and neuroblastoma |
| 153Sm[62][63][64][65][66][67][70][71] | 46.50 h | β− | 103.2 [29.8] | 808.2 [100.0] | 0.7 | 3.1 | 152Sm (n, γ) 153Sm | 153Eu | Painful bone metastasis, synovitis |
| 169Er[62][66][70] | 9.40 d | β− | 84 [0.16] | 350 | 0.3 | 1 | 165Ho (p, n) 165Er | 169Tm | Synovitis |
| 177Lu[62][70][71] | 6.73 d | β− | 208 [11.0] | 497.8 [100.0] | 0.28 | 1.7 | 176Yb (n, γ, β−) 177Lu, 176Lu (n, γ) 177Lu | 177Hf | Synovitis, RIT for various cancer treatments |
| 186Re[62][63][65][66][67][71] | 3.72 d | EC, β− | 137 [9.4] | 1069.5 [92.5] | 1.2 | 3.6 | 185Re (n, γ) 186Re | 186Os (unstable), 186W | A severe bone metastasis, as well as a painful arthritis |
| 188Re[62][64][65][70][71] | 17.00 h | β− | 155 [15.1] | 2120.4 [100.0] | 2.1 | 11 | 188W/188Re generator | 188Os | Rheumatoid arthritis, painful bone metastases, and RIT for multiple cancer therapies |
| 223Ra[68][70] | 11.44 d | Α | 154 [5.59] | 5979.2α |  | <10 μmα | 227Ac/227Th/223Ra generator | 219Rn (unstable) | Bone metastasis |

**Table 4: Physical characteristics of commonly available therapeutic radionuclides**

Commonly used radiopharmaceuticals for radionuclide therapy

|  |  |  |
| --- | --- | --- |
| **Radiopharmaceutical** | **Targeting mechanism** | **Indication** |
|  131I-iodide | Thyroid hormone production | Differentiated thyroid cancer, Graves’ disease, hyperfunctioning nodules |
|  90Y-microspheres | Intravascular trapping | Hepatocellular carcinoma, metastases of the liver |
|  89Sr-chloride | Calcium substitute | Palliation of bone pain |
|  153Sm-EDTMP | Chemo-adsorption | palliation of bone pain |
|  90Y-octreotide | Somatostatin receptor binding | Neuroendocrine tumours |
|  131I-MIBG | Intracellular storage and active transfer into neuroendocrine cells | Neuroblastoma, pheochromocytoma, carcinoid, paraganglioma, and medullary thyroid carcinoma are all types of cancer. |

**Table 5:Radiopharmaceuticals that are often used in radionuclide treatment** [72].

1. **POLICIES AND PROCEDURES**
2. **Radiation dose:**

Any dose of radiation administered on a patient undergoing a nuclear medicine procedure is deemed to be dangerous under current international standards, regardless of how small the dose may be even. Though it is unproven, it is generally accepted that the radiation dose given to a patient during a nuclear medicine research poses a very minimal risk of producing cancer. This danger is comparable to that of X-ray examinations, with the exception that the dose is delivered inside rather than externally, like from an X-ray machine, and the dosage amounts are frequently much higher. The effective dose of radiation used in nuclear medicine studies is reported in sieverts. The physical characteristics of the radiopharmaceutical used, its distribution in the body are all factors that affect the effective dose discovered during a study. The effective dose for an 80 megabecquerel thallium-201 cardiac imaging technique can be as low as 0.006 megabecquerels and as high as 11,200 megabecquerels for a 3 megabecquerel chromium-51 EDTA measurement of gfr. The effective dose for a standard bone scan using 600 megabecquerels of technetium-99m is around 2,900 mSv.[73]

The Röntgen equivalent man and the sievert have replaced the formerly used measuring units, the radiation absorbed dosage and the Röntgen equivalent curie, which were both equal to 3. 7E10 Bq and 1.0 gram of radium (Ra-226), respectively.The rad and rem are nearly identical for almost every nuclear medicine procedures, with only alpha radiation having a higher Röntgen equivalent man or Sievert value because of its significantly higher Relative Biological Effectiveness . Although they were regularly utilized before nuclear reactor and accelerator-produced radionuclides were introduced, alpha emitters are now only occasionally used in nuclear medicine.[74]

1. **Regulatory framework and guidelines:**

 An Internationally recognized regulatory systems govern the use of radionuclides in a variety of medicinal situations. The Nuclear Regulatory Commission and the Food and Drug Administration in US both have requirements that hospitals in the US must follow [75]. Radioactive substances that aren’t used, like X-rays, are regulated by the states individually rather than by the Nuclear Regulatory Commission. In addition to reporting on new advancements in the field, international organizations like the International Atomic Energy Agency routinely publish a variety of articles and recommendations for best practices in nuclear medicine.[76][77]

 The patient’s medical history and post-treatment management are also taken into consideration in nuclear medicine. Organizations like the International Commission on Radiological (ICR) Protection have made information available on handling a patient on radiation therapy while discharging.[78]

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