**Nuclear Medicine**

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**ABSTRACT**

There are now a number of efficient routine procedures for diagnosis and treatment as a result of the development of nuclear medicine. The future of the activity is currently being discussed in light of how quickly ultrasonography, CT, and MR have developed. It is frequently forgotten in such conversations that nuclear medicine is also a dynamic diagnostic tool that is always evolving. This historical study shows how nuclear medicine has developed from relatively straightforward in vitro testing to extremely sophisticated ways to image organ function. The advancement of radiopharmaceuticals and equipment led to this.  Additionally, it provides a novel way to optimize cancer therapy for specific patients as well as investigate cancer biology in vivo. A tracer is a radionuclide that accumulates in the target tissue after being injected into the body, such as iodine-131 or a radiolabel in a carrier molecule like 18F in fluorodeoxyglucose (18F-FDG). Other viable tracers include radionuclides connected to drugs, proteins, or peptides. Contrary to traditional, anatomical imaging methods like ultrasound, computed tomography, or magnetic resonance imaging, nuclear medicine imaging, including single-photon emission computer tomography and positron emission tomography, can offer crucial quantitative and functional information about healthy tissues or disease conditions. Tumor-targeting medicines can be used with therapeutic radionuclides to deliver fatal radiation to tumor areas during treatment. This overview discusses nuclear medicine's history, applications in modern cancer treatment, practical issues, and function in medical imaging.

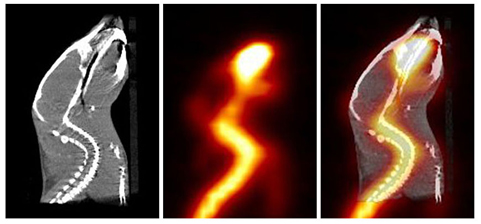
**Keywords-:** Radionuclide, tracers, Nuclear medicine, Radiopharmacology, Radiotherapy, Nuclear imaging, Cancer.

1. **INTRODUCTION**

A field of medicine that uses radioactive tracers (radiopharmaceuticals) to diagnose and cure diseases as well as assess how the body is functioning.[1] Nuclear diagnostic medicine makes extensive use of imaging techniques that assess cellular physiology and function. Doctors can track the passage of these radioactive markers using specially developed cameras. The two most prevalent imaging modalities in nuclear medicine are single-photon emission computed tomography (SPECT) and positron emission tomography (PET)[2].

1. **What is Radioactive tracers?**

Tracers are materials that act as markers in a chemical reaction or physical process to illustrate the position of a substance or to monitor the pathway of a substance. These tracers must exhibit the same physical and chemical activity in the milieu under observation as the component being examined.Because they exhibit the same chemical activity as the nonradioactive substance, radioactive isotopes are good tracers for a nonradioactive isotope that must be traced. The activity of the radioisotope is monitored in order to follow the process under research. Furthermore, the degree of radioactive material used as a marker can be limited to an utter minimal. The primary assumption in the use of radiotracers is that the radioactive component will blend in seamlessly with the system under investigation and that the emitted radiation will result in no impact on 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 (center) alone.

1. **What is SPECT?**

Single photon emission computed tomography (SPECT) has become more common in nuclear medicine. Better contrast, edge definition, and target separation from background leads to more therapeutic applications than planar imaging. The approach also provides a far greater possibility for quantifying source distributions, particularly in organs such as the brain and heart[4].

SPECT machines use an array of gamma cameras (from one to four) which rotate around the subject on a gantry. SPECT can also be paired with a separate CT machine in a hybrid imaging technique known as a single-photon emission computed tomography-computerized tomography (SPECT-CT), which is utilized mainly for attenuation correction and anatomical localization[5].

Gamma cameras move around the patient, delivering spatial information on radioactive distribution within tissues. Multiple gamma cameras are implemented to enhance detector efficiency and spatial resolution. The camera projection data is later rebuilt into three-dimensional visuals, often in axial slices[5][6][7].



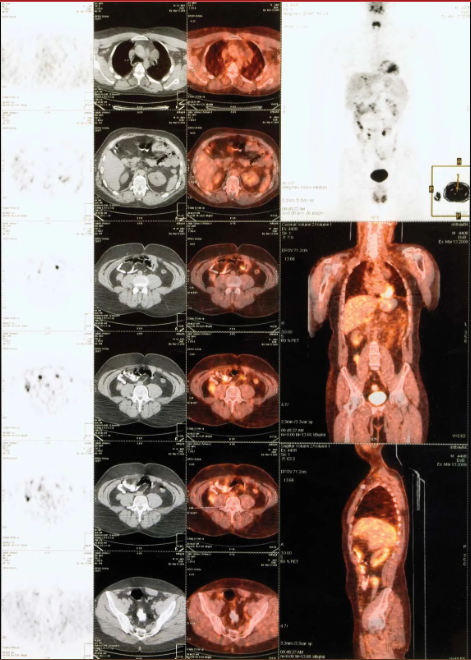
**Fig 2: Osteomyelitis using SPECT/CT[8].**

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

Positron emission tomography (PET) is a non-invasive imaging technology used to determine radioactivity in vivo. It entails injecting a positron-emitting radiopharmaceutical intravenously, waiting for systemic distribution, and then scanning for detecting and measurement of radiopharmaceutical accumulation patterns in the body.

PET scan data, like SPECT imaging, can be rebuilt and shown as an image with three dimensions. In contrast, scintigraphy produces planar data that can only be used to create a two-dimensional image.[9]

PET has shown to be an invaluable tool in the identification of cancer and cancer metastasis (spread), as well as in the assessment of heart problems. PET research have helped scientists discover more about how medications influence the brain and what happens during learning, language use, and specific brain illnesses like stroke, depression, and Parkinson's disease. Furthermore, scientists are striving to develop methods to use PET to identify the molecular origins of neurological and behavioral illnesses, as well as to assess how effectively therapy has been effective in patients. PET has revealed significant changes in the depressed brain, and understanding where these changes are located assists researchers understand the causes of depression and to assess the efficacy of a number of treatments[10].



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

1. **HISTORY**

Nuclear medicine has a lengthy history, with scientists from diverse domains such as physics, medicine, chemistry, and engineering collaborating over the years.Because of this diverse engagement,historians have had a difficult time determining the roots of nuclear medicine. Researchers believe the birth of this medical specialty occurred between 1934, when artificial radioactivity was discovered, and 1946, when radionuclides were first produced for medical use by the Oak Ridge National Laboratory. Nuclear medicine was first recognized as a potential medical specialty in 1946, when it was described by Sam Seidlin in the Journal of the American Medical Association. Nuclear medicine was initially recognized as a prospective medical specialty in 1946, when Sam Seidlin described it in the Journal of the American Medical Association which described the use of radioactive iodine (I-131) in the treatment of a patient who had advanced thyroid cancer. Later, I-131 was extended to applications such as thyroid gland imaging, hyperthyroidism therapy, and thyroid function quantification[12][13].

The beginnings of this medicinal concept could be traced back to the mid-1920s in Freiburg, Germany, when George de Hevesy conducted studies with radionuclides delivered to rats, revealing metabolic pathways and developing the tracer principle. The genesis of this medical field possibly occurred in 1936, when John Lawrence, known as "the father of nuclear medicine," took a leave of absence from his faculty position at Yale Medical School to visit his brother Ernest Lawrence at his new radiation laboratory in Berkeley, California (now known as the Lawrence Berkeley National Laboratory). Later, when he utilized phosphorus-32 to treat leukemia, John Lawrence made the first use of an artificial radionuclide in patients[14].

The beginnings of this medicinal concept can be traced back to the mid-1920s in Freiburg, Germany, when George de Hevesy conducted research on rats with radionuclides, demonstrating the metabolic pathways of these chemicals and establishing the tracer principle. The genesis of this medical field may have occurred in 1936, when John Lawrence, known as "the father of nuclear medicine," took a leave of absence from his faculty position at Yale Medical School to visit his brother Ernest Lawrence at his new radiation laboratory in Berkeley, California (now known as the Lawrence Berkeley National Laboratory). Later, when he applied phosphorus-32 to treat leukemia, John Lawrence made the first application of an engineered radioisotope to human beings[15].

Many historians regard Frédéric Joliot-Curie and Irène Joliot-Curie's 1934 discovery of artificially created radionuclides to be the most significant turning point in nuclear medicine[14], they published the first artificial generation of radioactive material in the journal Nature in February 1934, after knowing about the radioactivity of aluminum foil irradiated with a polonium preparation. Their discoveries drew on those of Wilhelm Konrad Roentgen for X-rays, Henri Becquerel for radioactive uranium salts, and Marie Curie (mother of Irène Curie) for radioactive thorium and polonium, coining the word "radioactivity." In the 1930s, Taro Takemi researched the use of nuclear physics in medicine. The journey of nuclear medicine would be incomplete if these early pioneers had never been mentioned[16].

On May 11, 1946, an article in the Journal of the American Medical Association (JAMA) by Massachusetts General Hospital's Dr. Saul Hertz and Massachusetts Institute of Technology's Dr. Arthur Roberts described the successful use of radioactive iodine (RAI) in treating Graves' Disease[17].

None of the radionuclides identified for medical application were as significant as the discovery and development of Technetium-99m. C. Perrier and E. Segre found it in 1937 as a synthesized element that occupies the gap 43 in the Periodic Table. The creation of a generator system to produce Technetium-99m became a realistic technology for usage in medicine in the 1960s. Technetium-99m is now the most often used element in nuclear medicine, and it is used in a wide range of nuclear medicine imaging examinations. The early 1950s saw the widespread clinical implementation of nuclear medicine as understanding about radionuclides, radioactivity detection, and the use of specific radionuclides to locate biochemical processes evolved. Pioneering work by Benedict Cassen in constructing the first rectilinear scanner and Hal O. Anger's scintillation camera (the Anger camera) transformed nuclear medicine from a fledgling discipline into a full-blown medical imaging specialization. [16].

By the early 1960s, Niels A. Lassen, David H. Ingvar, and Erik Skinhj in southern Scandinavia had developed methods that offered the first blood flow maps of the brain, which first utilized xenon-133 inhalation [18]. Much later, an intra-arterial equivalent was created, allowing for the evaluation of the local distribution of brain activity in individuals suffering from neuropsychiatric diseases such as schizophrenia[19]. Later versions would include 254 scintillators, allowing a two-dimensional image to be displayed on a color monitor. It helped them to create visuals that reflected brain activity during speaking, reading, visual or auditory perception, and voluntary movement [20]. The technique was also used to study imagined sequential movements, mental calculation, and mental spatial navigation, among other things [21] [22].

Most organs of the body were capable of being examined deploying nuclear medicine procedures by the 1970s. Nuclear medicine was officially recognized as a medical speciality by the American Medical Association in 1971 [23].

1. **HISTORICAL TIMELINE OF NUCLEAR MEDICINE** [24]

|  |  |
| --- | --- |
| 1896 | Henri Becquerel discovered mysterious "rays" from uranium. |
| 1897 | Marie Curie named the mysterious rays "radioactivity." |
| 1901 | Henri Alexandre Danlos and Eugene Bloch placed radium in contact with a tuberculous skin lesion. |
| 1903 | Alexander Graham Bell suggested placing sources containing radium in or near tumors. |
| 1913 | Frederick Proescher published the first study on the intravenous injection of radium for therapy of various diseases. |
| 1914 | Seil studied the appearance of radon and radium in excreta after an intravenous injection of radium. |
| 1924 | Georg de Hevesy, J.A. Christiansen and Sven Lomholt performed the first radiotracer (lead-210 and bismuth-210) studies in animals. |
| 1925 | Herrman Blumgart and Otto Yens used bismuth-214 (radium-C) to determine the arm-to-arm circulation time in patients. |
| 1932 | Ernest O. Lawrence and M. Stanley Livingston published the first article on "the production of high speed light ions without the use of high voltages." It was a milestone in the production of usable quantities of radionuclides. |
| 1935 | O. Chieivitz and Georg de Hevesy administered phosphate labeled with phosphorus-32 to rats and demonstrated the renewal of the mineral constituents of bone. |
| 1936 | John H. Lawrence, the brother of Ernest, made the first clinical therapeutic application of an artificial radionuclide when he used phosphorus-32 to treat leukemia. |
| 1936 | Joseph Gilbert Hamilton and Robert Spencer Stone administered sodium-24 to a leukemia patient. |
| 1937 | John Livingood, Fred Fairbrother and Glenn Seaborg discovered iron-59. |
| 1937 | Joseph Gilbert Hamilton performed the first medical physiology studies of the dynamics of sodium transport in the body. |
| 1937 | Saul Hertz, Arthur Roberts and Robley Evans studied thyroid physiology using iodine-128 |
| 1938 | John Livingood and Glenn Seaborg discovered iodine-131 and cobalt-60. |
| 1938 | Emilio Segre and Glenn Seaborg discovered technetium-99m. |
| 1939 | Joseph Gilbert Hamilton, Mayo Soley and Robley Evans published the first paper on the diagnostic uses of iodine-131 in patients |
| 1939 | Charles Pecher observed uptake of strontium-89 in bone metastases |
| 1939 | Martin Kamen and Sam Ruben discovered how to make carbon-14, a radioactive tracer widely used in medical and drug research. |
| 1940 | The Rockefeller Foundation funded the first cyclotron dedicated for biomedical radioisotope production at Washington University in St. Louis. |
| 1941 | Saul Hertz gave a patient the first therapeutic dose of iodine-130. |
| 1942 | Enrico Fermi and his associates demonstrated the first controlled chain reaction under the bleachers at Stagg Field at the University of Chicago. |
| 1946 | Allen Reid and Albert Keston discovered iodine-125, which became important in the field of radioimmunoassay. |
| 1946 | Samuel M. Seidlin, Leo D. Marinelli and Eleanor Oshry treated a patient with thyroid cancer with iodine-131, an "atomic cocktail." |
| 1947 | Benedict Cassen used radioiodine to determine whether a thyroid nodule accumulates iodine, helping to differentiate benign from malignant nodules. |
| 1947 | George Moore used iodine-131 labeled diiodofluorescein to "probe" the brain for tumors at surgery. |
| 1948 | Abbott Laboratories began distribution of radioistopes. |
| 1949 | B. Selverstone used phosphorus-32 to detect brain tumors at surgery with a probe detector. |
| 1950 | K.R. Crispell and John P. Storaasli used iodine-131 labeled human serum albumin (RISA) for imaging the blood pool within the heart. |
| 1950 | Abbott Laboratories sold the first commercial radiopharmaceutical, iodine-131 human serum albumin (RISA). |
| 1951 | The U.S. Food and Drug Administration (FDA) approved sodium iodide 1-131 for use with thyroid patients. It was the first FDA-approved radiopharmaceutical. |
| 1951 | Benedict Cassen, Lawrence Curtis, Clifton Reed and Raymond Libby automated a scintillation detector to "scan" the distribution of radioiodine within the thyroid gland. |
| 1953 | Gordon Brownell and H.H. Sweet built a positron detector based on the detection of annihilation photons by means of coincidence counting. |
| 1953 | Robert F. Schilling invented a test of vitamin B-12 absorption, which plays a key role in nuclear hematology. |
| 1954 | David Kuhl invented a photorecording system for radionuclide scanning. This development moved nuclear medicine further in the direction of radiology. |
| 1955 | Rex Huff measured the cardiac output in man using iodine-131 human serum albumin. |
| 1955 | George V. Taplin used iodine-131 labeled rose bengal to image the liver. He also used radioiodinated hippuran to measure kidney function with scintillation detectors. |
| 1957 | W.D. Tucker's group at the Brookhaven National Laboratory invented the iodine-132 and technetium-99m generator, making these short-lived radionuclides available at distant sites from the production of the parent radionuclides. |
| 1957 | H. Knipping used xenon-133 to measure lung ventilation. |
| 1958 | Hal Anger invented the "scintillation camera," an imaging device that made it possible to conduct dynamic studies. |
| 1959 | Solomon Berson and Rosalyn Yalow invented the technique of radioimmunoassay to detect insulin antibodies in human serum. |
| 1959 | Picker X-Ray Company delivered the first 3-inch rectilinear scanner. |
| 1960 | Louis G. Stang, Jr., and Powell (Jim) Richards advertised technetium-99m and other generators for sale by Brookhaven National Laboratory. Technetium-99m had not yet been used in nuclear medicine. |
| 1960 | John McAfee and Henry Wagner imaged the kidneys with radiomercury labeled chlormerodrin. |
| 1961 | Allis-Chalmers installed the first U.S. "medical center" cyclotron at Washington University Medical School. The cyclotron was designed by M.M. Ter-Pogossian. |
| 1962 | David Kuhl introduced emission reconstruction tomography. This method later became known as SPECT and PET. It was extended in radiology to transmission X-ray scanning, known as CT. |
| 1962 | John Kuranz, Nuclear Chicago, delivered the first commercial Anger camera to William Myers at Ohio State University. |
| 1963 | The FDA exempted the "new drug" requirements for radiopharmaceuticals regulated by the Atomic Energy Commission. |
| 1963 | Henry Wagner first used radiolabeled albumin aggregates for imaging lung perfusion in normal persons and patients with pulmonary embolism. |
| 1963 | George V. Taplin developed albumin aggregates for study of phagocytosis by the reticuloendothelial system. |
| 1963 | B. Ansell and B.M. Cook used radiolabeled colloids for radiation synovectomy. |
| 1964 | The FDA exempted the "new drug" requirements for radiopharmaceuticals regulated by the Atomic Energy Commission. |
| 1964 | Paul Harper and Katherine Lathrup developed radiotracers labeled with Tc-99m for the study of brain, thyroid and liver. |
| 1964 | Amersham marketed the first commercial radioimmunoassay kit (iodine-125 insulin kit). |
| 1968 | Henry Wagner and colleagues used xenon-133 ventilation scans to diagnose pulmonary embolism. |
| 1969 | C.L. Edwards reported the accumulation of gallium-67 in cancer. |
| 1970 | W. Eckelman and P. Richards developed Tc-99m "instant kit" radiopharmaceuticals. The first one was Tc-99m-DTPA. |
| 1970 | The FDA announced that it would gradually withdraw the exemption granted to radiopharmaceuticals and start regulating them as drugs. The change would be completed by January 20, 1977. |
| 1971 | The American Medical Association officially recognized nuclear medicine as a medical speciality. |
| 1971 | Gopal Subramanian and John McAfee introduced Tc-99m labeled phosphates for bone imaging. |
| 1972 | David Kuhl performed the first quantitative measurement of cerebral blood volume in living patients. |
| 1973 | H. William Strauss introduced the exercise stress-test myocardial scan. |
| 1973 | Elliot Lebowitz introduced thallium-201 for myocardial perfusion imaging, first proposed by Kawana. |
| 1973 | David Goldenberg demonstrated that radiolabeled antibodies against a human tumor antigen (CEA) could target and image human tumors in animals. |
| 1976 | John Keyes developed the first general purpose single photo emission computed tomography (SPECT) camera. Ronald Jaszczak developed the first dedicated head SPECT camera. |
| 1976 | N. Firusian used strontium-89 to reduce pain from metastatic bone disease. |
| 1976 | Ronald Jaszczak developed the first dedicated head SPECT camera. |
| 1977 | The FDA required manufacturers to obtain an approved new drug application for new and existing radiopharmaceuticals. The requirements are essentially the same as those for other prescription drugs. |
| 1977 | New England Nuclear received FDA approval to distribute thallium-201 for myocardial perfusion and the diagnosis and location of myocardial infarction. |
| 1978 | David Goldenberg used radiolabeled antibodies to image tumors in humans. |
| 1981 | J.P. Mach used radiolabeled monoclonal antibodies for tumor imaging. |
| 1981 | K.A. Krohn, D.R. Vera and S.M. Steffen developed the first Tc-99m labeled receptor ligand. |
| 1982 | Steve Larson and Jeff Carrasquillo treated cancer patients with malignant melanoma using iodine-131 labeled monoclonal antibodies. |
| 1983 | William Eckelman and Richard Reba carried out the first successful SPECT imaging of a neuroreceptor in humans. |
| 1983 | Henry Wagner carried out the first successful PET imaging of a neuroreceptor using himself as the experimental subject. |
| 1987 | Medi-Physics received FDA approval to market the first brain perfusion imaging radiopharmaceutical, iodine-123 IMP. |
| 1988 | The first Tc-99m brain perfusion radiopharmaceutical, introduced by Amersham, was approved by the FDA for the diagnosis of stroke. |
| 1989 | The FDA approved the first positron radiopharmaceutical (rubidium-82) for myocardial perfusion imaging. |
| 1990 | Steve Lamberts and Eric Krenning imaged endocrine tumors with somatostatin receptor-binding radiotracers. |
| 1990 | Loyola University Nuclear Information System (LUNIS), the first educational worldwide interactive computer network for nuclear medicine, went on line. |
| 1990 | Alan Fischman used indium-111 labeled chemotactic peptides to detect foci of infection. |
| 1991 | The first Tc99m myocardial agent approved by FDA. |
| 1992 | The FDA approved the first monoclonal antibody radiopharmaceutical for tumor imaging. |
| 1993 | Medi-Physics/Amersham received FDA approval to market strontium-89 chloride for relief of bone pain. |
| 1994 | Mallinckrodt received FDA approval to market the first peptide radiopharmaceutical that binds somatostatin receptors for imaging granulomatous and autoimmune diseases. |
| 1995 | ADAC Laboratories shipped the first SPECT camera to offer coincidence detection capable of FDG/PET imaging. |
| 1996 | "Legitimacy" of brain PET |
| 1997 | Validation of 123I-beta-CIT in assessing dopamine transporters in the diagnosis of Parkinson's disease. |
| 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 | Sentinel node studies approved by HCFA for improved diagnosis and management of cancers. |
| 2000 | Time Magazine recognizes Siemens Biograph as the invention of the year. |
| 2001 | 16.9 million nuclear medicine procedures were performed in the United States. |
| 2002 | Formation of the National Institute for Biomedical Imaging and Bioengineering in the National Institutes of Health. |
| 2003 | FDA gives approval to IDEC Pharmaceuticals for clinical use of Zevalin™, a radioimmunotherapy agent. |
| 2004 | The Society of Nuclear Medicine celebrates its 50th anniversary. |
| 2004 | SNM inaugurates the PET Center of Excellence to advance the practice of nuclear medicine procedures, which are safe and effective ways to identify disease. |
| 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 society changes its name from the "Society of Nuclear Medicine" to "SNM: Advancing Molecular Imaging and Therapy" to reflect the widening scope of the society. |
| 2007 | SNM founds the Molecular Imaging Center of Excellence and expands the society's mission to focus on the fields of molecular imaging and nuclear medicine and applications for detecting, diagnosing and treating many types of disease. |
| 2007 | RT-Image names SNM "most influential" in radiology. |
| 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. |
| 2008 | Molecular imaging sees increasingly widespread fusion of images with PET/CT scans, which permit a functional understanding of the underlying causes of disease in the body by joining functional and anatomical information in the same image. |
| 2008 | SNM holds its 55th Annual Meeting in New Orleans and prepares to mark its 55th anniversary in 2009. |

1. **INTERVENTIONAL NUCLEAR MEDICINE**

A radionuclide (also known as a radioactive nuclide, radioisotope, or radioactive isotope) is an unstable nuclide that has an excess of nuclear energy. The extra energy can be released from the nucleus in one of three ways: as gamma radiation; by being transferred to one of its electrons and then released as a conversion electron; or by being created and released from the nucleus as a new particle (alpha particle or beta particle). The radionuclide is considered to experience radioactive decay during such processes[25]. Due to their high energy, these emissions qualify as ionizing radiation since they can cause an atom to lose an electron. A stable nuclide can be created via radioactive decay, but it can also occasionally create a brand-new unstable radionuclide that could go through more decay. At the level of individual atoms, radioactive decay is a random process; it is impossible to anticipate when a specific atom will decay[26][27][28][29]. However, the decay rate and hence the half-life (t1/2) for a group of atoms belonging to a single nuclide can be determined from the measured values of their decay constants. There are approximately 55 orders of magnitude in time between the half-lives of radioactive atoms, which have no known boundaries.

In nuclear reactors, cyclotrons, particle accelerators, or radionuclide generators, radionuclides can be generated artificially or naturally. About 730 radionuclides (see list of nuclides) 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 very short half-lives and are only created artificially. There are roughly 251 stable nuclides in comparison.

1. **Diagnostic medical imaging:**

In nuclear medicine imaging, radiopharmaceuticals are administered intravenously, orally, or through inhalation. The radiation that the radiopharmaceuticals release is then captured and converted into images by external detectors. This procedure is distinct from a diagnostic X-ray, which creates an image by exposing the body to external 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 (PET) to image functional activities.

Contrary to conventional anatomical imaging techniques like CT or MRI, nuclear medicine diagnostic tests typically depict the physiological function of the system being studied. This makes them different from most other imaging modalities. Compared to traditional radiology imaging, which 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 white blood cell scans, MIBG, octreotide scans, whole-body PET scans, and PET/CT scans are a few examples.

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

All human radiation exposures 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 on their characteristics and mode of delivery, 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 sort of targeted therapy employs the radiopharmaceutical's physical, chemical, and biological features to target specific body parts for radiation treatment [32]. Nuclear medicine, a related diagnostic technique, follows the same concepts but utilizes various types or doses of radiopharmaceuticals to image or 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 (human or animal) 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. While the majority of the gamma radiation is removed from the patient's body, the beta radiation affects both healthy thyroid tissue and any thyroid cancer that acts like healthy thyroid tissue by absorbing iodine, producing the 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:

Beta emitting phosphorus-32 (32P), 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

|  |  |  |
| --- | --- | --- |
| **Sr. No.** | **Substance** | **Condition** |
| 1. | Iodine-131-sodium iodide | hyperthyroidism and thyroid cancer |
| 2. | Yttrium-90-ibritumomab tiuxetan (Zevalin) and Iodine-131-tositumomab (Bexxar) | refractory lymphoma |
| 3. | 131I-MIBG (metaiodobenzylguanidine) | neuroendocrine tumors |
| 4. | Samarium-153 or Strontium-89 | palliative bone pain treatment |
| 5. | Rhenium-188 | squamous cell carcinoma or basal cell carcinoma of the skin |

**Table 1: Common nuclear medicine (unsealed source) therapies**[16]

1. Brachytherapy:

A sealed radiation source is positioned inside or close to 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 of the skin, breast, esophagus, prostate, cervix, and other organs. It can also be used 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:

Both temporary HDR brachytherapy and permanent LDR seed implantation are options for brachytherapy in the treatment of prostate cancer.

Permanent seed implantation has been proven to be a highly effective treatment to stop the cancer from coming back and is ideal for patients with a localized tumor and a good prognosis. The survival rate is comparable to that of surgery (radical prostatectomy) or EBRT, but with less unpleasant side effects including impotence and incontinence. The operation can be finished quickly, and patients can typically go home the same day as their treatment and resume their regular activities one to two days later. Compared to prostate surgery, permanent seed implantation is frequently a less invasive therapy option [50].

Breast cancer:

Radiation therapy is a crucial part of breast-conserving therapy and is the standard of care for women who have had mastectomy or lumpectomy surgery [44]. After surgery, before chemotherapy, or as a palliative treatment for advanced disease, brachytherapy is an option. The most common form of brachytherapy used to treat breast cancer is HDR temporary brachytherapy. Breast brachytherapy can be used as a boost after surgery in place of whole breast irradiation using EBRT. In more recent times, only the local area surrounding the original tumor has been exposed to radiation via Accelerated partial breast irradiation [51][52].

Interstitial breast brachytherapy:

Interstitial breast brachytherapy involves the temporary placement of several flexible plastic catheters in the breast tissue [53]. These are carefully positioned to allow optimal targeting of radiation to the treatment area while sparing the surrounding breast tissue. The catheters are connected to an after-loader, which delivers the planned radiation dose to the treatment area. Interstitial breast brachytherapy can be used as boost after EBRT, or as APBI [54].

Brain tumors:

A specific kind of brachytherapy implant called Surgically Targeted Radiation Therapy (STaRT), also known as GammaTile Therapy, is made to be used inside the brain. Meningiomas, metastases, high-grade gliomas, and glioblastomas are among the operable malignant intracranial neoplasms and operable recurrent intracranial neoplasms that can be treated with GammaTile, according to the FDA. In a clinical trial, GammaTile Therapy reduced the likelihood of side effects while enhancing local tumor control in comparison to earlier same-site therapies.

Esophageal cancer:

Brachytherapy is one option for effective radiation therapy for esophageal cancer and involves palliative or definitive radiotherapy (boost).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:

For non-melanomatous skin cancers including basal cell carcinoma and squamous cell carcinoma, HDR brachytherapy offers an alternative to surgery. This is particularly pertinent in cases of cancer on the lips, eyelids, nose, or ears, when surgery may result in deformity or necessitate substantial reconstruction. Different applicators that fit to the curvature of the skin and help ensure precise delivery of the ideal irradiation dosage can be employed to ensure close contact between the radiation source(s) and the skin. The Rhenium-SCT (Skin Cancer Therapy) is a different form of brachytherapy offered, and it offers benefits similar to those of the HDR. To cure basal cell or squamous cell carcinomas,

Rhenium-188&#39;s beta ray emissions are used.

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 brachytherapy (ICBT) is the treatment of in-stent restenosis (ISR). Vascular brachytherapy, 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].

Commonly used radiation sources (radionuclides) for brachytherapy

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Sr. No.** | **Radionuclide** | **Type** | **Half-life** | **Energy** |
| 1. | Caesium-137 (137Cs) | γ-ray | 30.17 years | 0.662 MeV |
| 2. | Cobalt-60 (60Co) | γ-ray | 5.26 years | 1.17, 1.33 MeV |
| 3. | Iridium-192 (192Ir) | β−-particles | 73.8 days | 0.38 MeV (mean) |
| 4. | Iodine-125 (125I) | γ-rays | 59.6 days | 27.4, 31.4 and 35.5 keV |
| 5. | Palladium-103 (103Pd) | γ-ray | 17.0 days | 21 keV (mean) |
| 6. | Ruthenium-106 (106Ru) | β—particles | 1.02 years | 3.54 MeV |

**Table 2: Commonly used radiation sources (radionuclides) for brachytherapy**[55]

1. **SOURCES OF RADIONUCLIDES:**

Molybdenum-99 (99Mo), which is commonly produced as a fission product of 235U in nuclear reactors, is the parent radionuclide of 99mTc, which is typically delivered to hospitals by a radionuclide generator. However, worldwide supply constraints have prompted the investigation of alternative production techniques. The Petten nuclear reactor in the Netherlands produces about one-third of the medical isotopes used in the globe and the majority of Europe. Up to its final closure in 2018, the Chalk River Laboratories in Chalk River, Ontario, Canada, generated a further third of the global supply and the majority of that of North America. The most common radioisotope used in PET, 18F, is created in a cyclotron, a circular accelerator instead of a nuclear reactor. The stable heavy oxygen isotope 18O is bombarded with protons that have been accelerated in a cyclotron. The extracted 18O makes up around 0.20% of the regular oxygen, which is primarily oxygen-16. Usually, the 18F is utilized to create FDG after that [56]. Technetium-99m, iodine-123, iodine-131, thallium-201, gallium-67, fluorine-18 fluorodeoxyglucose, and indium-111 tagged leukocytes are the most frequently utilized intravenous radionuclides.  The most commonly used gaseous/aerosol radionuclides are xenon-133, krypton-81m, (aerosolised) technetium-99m [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" \o "Fluorine-18) | 18F | 9 | 109.77 m | β+ | 511 (193%) | 634 (97%) |
| [gallium-67](https://en.wikipedia.org/wiki/Gallium-67" \o "Gallium-67) | 67Ga | 31 | 3.26 d | Ec | 93 (39%), | - |
| 185 (21%), |
| 300 (17%) |
| [krypton-81m](https://en.wikipedia.org/wiki/Krypton-81m" \o "Krypton-81m) | 81mKr | 36 | 13.1 s | IT | 190 (68%) | - |
| [rubidium-82](https://en.wikipedia.org/wiki/Rubidium-82" \o "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" \o "Nitrogen-13) | 13N | 7 | 9.97 m | β+ | 511 (200%) | 1198 (99.8%) |
| [technetium-99m](https://en.wikipedia.org/wiki/Technetium-99m" \o "Technetium-99m) | 99mTc | 43 | 6.01 h | IT | 140 (89%) | - |
| [indium-111](https://en.wikipedia.org/wiki/Indium-111" \o "Indium-111) | 111In | 49 | 2.80 d | Ec | 171 (90%), | - |
| 245 (94%) |
| [iodine-123](https://en.wikipedia.org/wiki/Iodine-123" \o "Iodine-123) | 123I | 53 | 13.3 h | Ec | 159 (83%) | - |
| [xenon-133](https://en.wikipedia.org/wiki/Xenon-133" \o "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" \o "Thallium-201) | 201Tl | 81 | 3.04 d | Ec | 69–83\* (94%), | - |
| 167 (10%) |
| Therapy: | | | | | | |
| [yttrium-90](https://en.wikipedia.org/wiki/Yttrium-90" \o "Yttrium-90) | 90Y | 39 | 2.67 d | β− | - | 2279 (99.98%) |
| [iodine-131](https://en.wikipedia.org/wiki/Iodine-131" \o "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" \o "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 | Polycythemia vera, cystic craniopharyngioma, PVNS |
| 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 | Painful 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 | Painful bone metastasis, 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 | Painful bone metastasis, rheumatoid arthritis, RIT for various cancer treatments |
| 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

|  |  |  |  |
| --- | --- | --- | --- |
| **Sr. No.** | **Radiopharmaceuticals** | **Targeting mechanism** | **Indication** |
| 1. | 131I-iodide | Thyroid hormone synthesis | Differentiated thyroid cancer, Graves’ disease, hyperfunctioning nodules |
| 2. | 90Y-microspheres | Intravascular trapping | Liver metastasis, hepatocellular carcinoma |
| 3. | 89Sr-chloride | Calcium analogue | Bone pain palliation |
| 4. | 153Sm-EDTMP | Chemo-adsorption | Bone pain palliation |
| 5. | 90Y-octreotide | Somatostatin receptor binding | Neuroendocrine tumours |
| 6. | 131I-MIBG | Active transport into neuroendocrine cells and intracellular storage | Neuroblastoma, pheochromacytoma, carcinoid, paraganglioma, medullary thyroid carcinoma |

**Table 5: Commonly used radiopharmaceuticals for radionuclide therapy**[72].

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

A patient undergoing a nuclear medicine operation will receive a radiation dosage, and it is thought that any radiation dose, no matter how tiny, poses a danger under current international criteria. Though unverified, the radiation dose administered to a patient during a nuclear medicine study is widely believed to pose a very low chance of causing cancer. In this regard, it is comparable to the danger associated with X-ray investigations, except that the dose is supplied internally rather than from an external source such as an X-ray machine, and dosage amounts are often far higher than those associated with X-rays.

A nuclear medicine investigation's radiation exposure is given as an effective dose in sieverts. The amount of radioactivity delivered in megabecquerels (MBq), the physical qualities of the radiopharmaceutical employed, its distribution in the body, and its rate of clearance from the body all influence the effective dose obtained from a study. The effective dose for a 3 MBq chromium-51 EDTA measurement of glomerular filtration rate can range from 6 mSv (0.006 mSv) to 11.2 mSv (11,200 mSv) for an 80 MBq thallium-201 cardiac imaging procedure. The typical bone scan with 600 MBq of technetium-99m MDP has an effective dosage of about 2.9 mSv (2,900 mSv).[73]

Previously, units of measurement were the curie (Ci), which was 3.7E10 Bq, as well as 1.0 gram of Radium (Ra-226); the rad (radiation absorbed dose), which has been replaced by the gray; and the rem (Röntgen equivalent man), which has been replaced by the sievert. For practically all nuclear medicine treatments, the rad and rem are essentially comparable, with only alpha radiation producing a greater Rem or Sv value due to its substantially higher Relative Biological Effectiveness (RBE). Alpha emitters are now infrequently employed in nuclear medicine, but they were widely used prior to the introduction of nuclear reactor and accelerator-produced radionuclides.[74]

1. **Regulatory framework and guidelines:**

The use of radionuclides in various medical settings is governed by regulatory frameworks that are upheld by various nations across the world. For instance, in the US, hospitals must abide by regulations set forth by the Food and Drug Administration (FDA) and the Nuclear Regulatory Commission (NRC) [75]. When it comes to the NRC, radioactive elements that aren't used, like X-rays, are governed by the individual states rather than the organization. International institutions like the International Atomic Energy Agency (IAEA) frequently release various articles and recommendations for best practices in nuclear medicine in addition to reporting on new developments in the field.[76][77]

Nuclear medicine also takes the patient's medical background and post-treatment management into account. Information on how to handle the discharge of patients from a hospital with unsealed radionuclides has been made available by organizations like the International Commission on Radiological Protection.[78]

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