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THE EVOLUTION OF NUCLEAR MEDICINE

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Abstract

Nuclear medicine is a rapidly evolving interdisciplinary field that integrates advances in physics, chemistry, and medicine for the diagnosis and treatment of diseases using radionuclides. This article provides a brief scientific overview of the historical development of nuclear medicine, from the discovery of X-rays and natural radioactivity to the introduction of key diagnostic technologies such as gamma cameras, technetium-99m–based radiopharmaceuticals, PET, and SPECT imaging. Modern therapeutic approaches, including radionuclide therapy, peptide receptor radionuclide therapy, targeted alpha therapy, and radioligand therapy, have significantly expanded treatment possibilities, particularly in oncology. Recent advances such as hybrid imaging technologies, theranostics, personalized medicine, and novel radiopharmaceuticals are expected to further enhance diagnostic accuracy and therapeutic effectiveness.

Keywords: *nuclear medicine, PET/CT, SPECT, radionuclide therapy, theranostics, personalized medicine.*

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Резюме

ЭВОЛЮЦИЯ ЯДЕРНОЙ МЕДИЦИНЫ

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Ядерная медицина является быстро развивающейся междисциплинарной областью, объединяющей достижения физики, химии и медицины для диагностики и лечения заболеваний с использованием радионуклидов. В статье представлен краткий научный обзор исторического развития ядерной медицины — от открытия рентгеновских лучей и природной радиоактивности до внедрения ключевых диагностических технологий, таких как гамма-камеры, радиофармацевтические препараты на основе технеция-99m, а также методы визуализации ПЭТ и ОФЭКТ. Современные терапевтические подходы, включая радионуклидную терапию, пептид-рецепторную радионуклидную терапию, таргетную альфа-терапию и радиолигандную терапию, значительно расширили возможности лечения, особенно в онкологии. Последние достижения, такие как гибридные технологии визуализации, тераностика, персонализированная медицина и новые радиофармацевтические препараты, как ожидается, будут и далее повышать точность диагностики и эффективность терапии.

Ключевые слова: *ядерная медицина, ПЭТ/КТ, ОФЭКТ, радионуклидная терапия, тераностика, персонализированная медицина.*

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Түйіндеме

ЯДРОЛЫҚ МЕДИЦИНА ЭВОЛЮЦИЯСЫ

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Ядролық медицина радионуклидтерді қолдану арқылы ауруларды диагностикалау және емдеу мақсатында физика, химия және медицина салаларындағы жетістіктерді біріктіретін қарқынды дамып келе жатқан пәнаралық ғылым саласы. Бұл мақалада ядролық медицинаның тарихи дамуына қысқаша ғылыми шолу ұсынылған: рентген сәулелері мен табиғи радиоактивтіліктің ашылуынан бастап, гамма-камералар, технеций-99m негізіндегі радиофармацевтикалық препараттар, сондай-ақ ПЭТ және ОФЭКТ бейнелеу әдістері сияқты негізгі диагностикалық технологиялардың енгізілуіне дейінгі кезең қарастырылады. Қазіргі терапиялық тәсілдер, соның ішінде радионуклидтік терапия, пептидті рецепторлық радионуклидтік терапия, нысаналы альфа-терапия және радиолигандтық терапия, әсіресе онкология саласында емдеу мүмкіндіктерін айтарлықтай кеңейтті. Гибридті бейнелеу технологиялары, тераностика, дербестендірілген медицина және жаңа радиофармацевтикалық препараттар сияқты соңғы жетістіктер диагностиканың дәлдігін арттырып, терапияның тиімділігін одан әрі күшейтеді деп күтілуде.

Түйін сөздер: *ядролық медицина, ПЭТ/КТ, ОФЭКТ, радионуклидтік терапия, тераностика, дербестендірілген медицина.*

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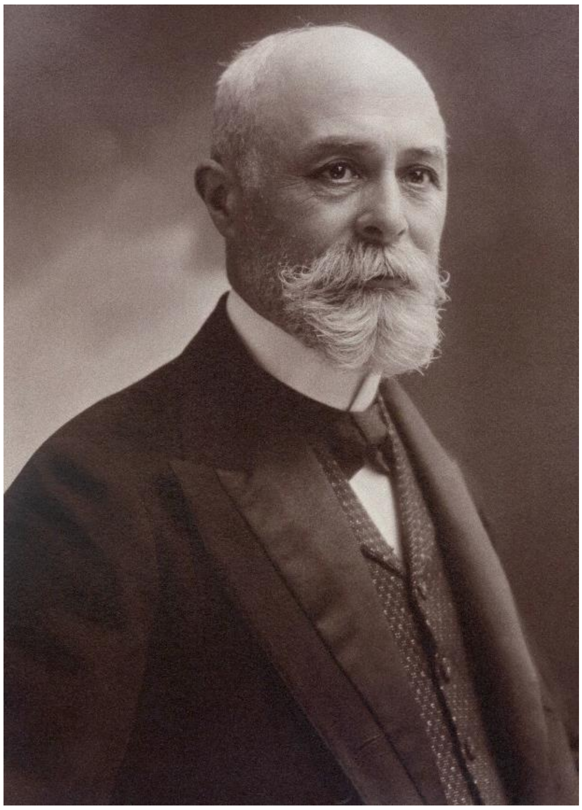
Nuclear medicine has evolved over a century, profoundly enhancing diagnostics and treatments in healthcare [1]. It is a fascinating and an evolving field that intertwines advanced technology, chemistry, physics, and medicine to diagnose and treat diseases [1].

In 1895, X-rays were discovered by Röentgen, followed soon by the discovery of natural radioactivity in 1896 by Henri Becquerel which was a landmark moment in the evolution of Nuclear Medicine [2].

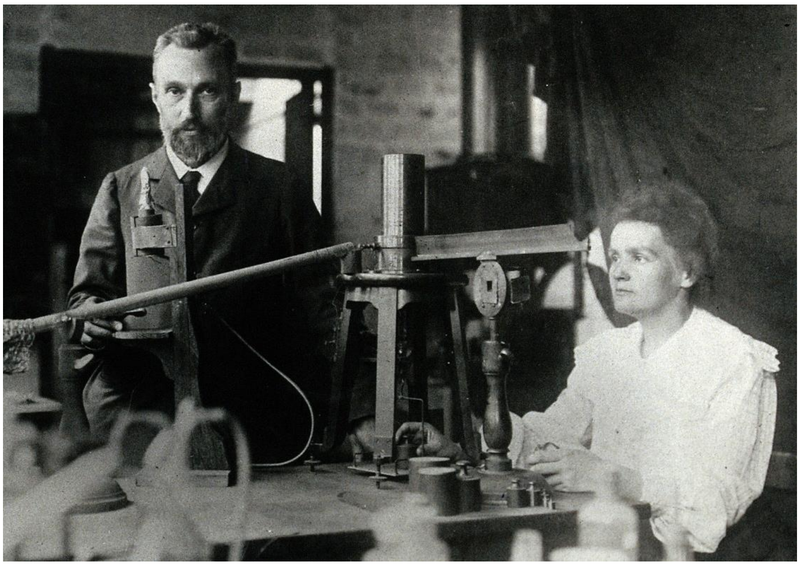
In 1896, Marie Curie, along with her husband Pierre Curie, extended Becquerel's work, discovering new radioactive elements – radium and polonium in 1898. The first recorded use of radionuclides in medicine was in 1913 by Georg de Hevesy also known as the Father of Nuclear Medicine [3].

The cyclotron, invented by physicist, Ernest O. Lawrence in the 1930s, was groundbreaking as this device accelerated charged particles to high energies, enabling the bombardment of materials to produce artificial radionuclides. Before the advent of the cyclotron, researchers relied on naturally occurring radionuclides, which were scarce and limited in variety [1].

Dmitri Ivanovich Mendeleev, Russian chemist known or formulating the periodic law and creating a version of the periodic table of elements. nominated for the Nobel Prize in Chemistry in 1906.



Henri Becquerel: Got the Nobel Prize in physics in 1903 for his discovery of spontaneous radioactivity. Becquerel was awarded half of the Nobel Prize for Physics in 1903, the other half being given to Pierre and Marie Curie for their study of the Becquerel radiation.

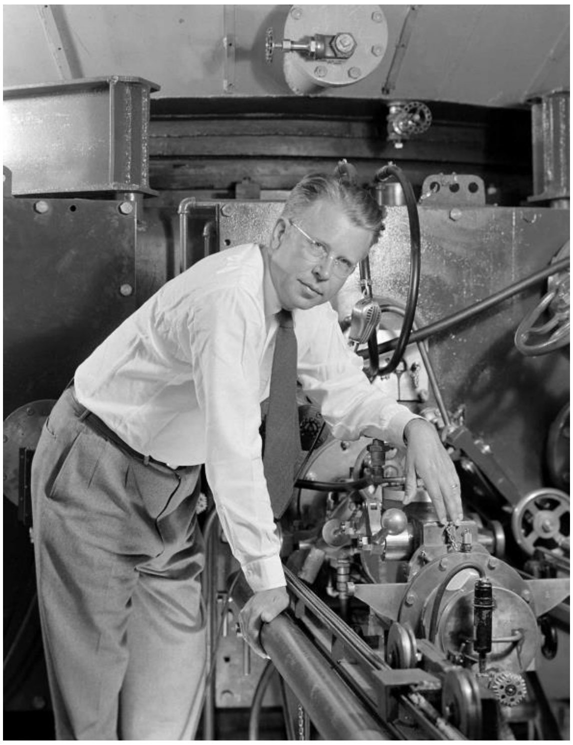


Marie Curie & Pierre Curie:

In 1903, Curie won the Nobel Prize in Physics for her research of radiation phenomena, she shared it with her husband Pierre Curie.

She was also the first woman in France to attain a PhD in Physics, and the first woman to teach at the Sorbonne. In 1911, she won a second Nobel Prize in chemistry for the discovery of polonium and radium.

George de Hevesy – The father of Nuclear Medicine. Got the Nobel Prize in Chemistry 1943 for his work on the use of isotopes as tracers in the study of chemical processes



The Nobel Prize in Physics in 1939 was awarded to Ernest Orlando Lawrence for the invention and development of the cyclotron and for results obtained with it, especially with regard to artificial radioactive elements.

On March 31, 1941, Elizabeth D., a patient referred to Dr. Saul Hertz at the Massachusetts General Hospital, USA for management of hyperthyroidism, was administered 2.1 mCi of a $^{130}I/^{131}I$ mixture. Thus, she became the first patient with thyroid disease to be treated with radioiodine. She received a second administration of 1.3 mCi on April 16, 1941. I-131 still used to treat Thyroid diseases including thyroid cancer. Dr.Saul Hertz is the pioneer to use Radioiodine [I-131] in patients in Thyroid diseases.

In the late 1930s, Dr. Saul Hertz, along with his colleagues, conducted pioneering research using radioactive iodine [I-131]. By the early 1940's, radioactive iodine was being used to treat hyperthyroidism and, later, thyroid cancer & is used till date [4].

In the 1950s, the first diagnostic scans using radionuclides were performed, marking a pivotal moment in medical imaging. The gamma camera, developed by Hal Anger in 1957, was a revolutionary invention in the field of nuclear medicine [1].

The 1960s witnessed the introduction of Technetium-99m (Tc-99m) which quickly became a cornerstone in diagnostic imaging due to its ideal physical and chemical properties & till date it remains the same. The metastable isotope technetium-99m (Tc-99m) was extracted for the first time by Emilio Segrè in collaboration with Glenn T. Seaborg in 1938, who together isolated it after bombarding natural molybdenum [Mo] with 08Mev deuterons in the 37-inch cyclotron of Ernest Orlando Lawrence's radiation laboratory [5].

Tc-99m has a half-life [T/2] of 06 hrs, & emits 140 kev of monoenergetic gamma rays, which is most suitable for imaging by gamma camera, and can be incorporated into various compounds to target different organs and systems [5].

These developments fundamentally changed the landscape of medical imaging and diagnosis. In the 1970s and 1980s, two major imaging technologies emerged in nuclear medicine: Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) [1]. Positron Emission Tomography (PET) was invented by Michael E. Phelps and Edward J. Hoffman. They developed the first human PET scanner in 1973.[6]

Hal Oscar Anger was the inventor of the scintillation camera and one of the pioneers in the field of instrumentation used in nuclear medicine , In 1952, Dr. Anger integrated a pinhole collimator and a wide NaI(Tl) scintillator crystal with a photographic plate into a gamma camera that could directly convert the fluorescence created by gamma rays into visible images.

The Nobel Prize in Physics 1959 was awarded jointly to Emilio Gino Segrè and Owen Chamberlain for their discovery of the antiproton.

Eric Krenning and his team, made significant contributions to the field of nuclear medicine in the late 1990s, particularly in pioneering Peptide Receptor Radionuclide Therapy (PRRT) [7].

TheraSphere, involving Y-90 [Yttrium -90] microspheres, is another noteworthy advancement, & is used for radioembolisation, a process where radioactive beads are delivered directly to liver tumours [8].

These developments underscore nuclear medicine's continuous evolution and impact in cancer therapy, blending innovative scientific research with practical, clinically effective solutions.

Maurits Geerlings and other pioneers in radioligand therapies, like Richard Baum, Rod Hicks, Mike Sathekge have made monumental contributions to the field of theranostics, a blend of therapy and diagnostics. Their work, particularly in the development and application of Actinium-225 (Ac-225), has paved the way for significant breakthroughs in the treatment of various diseases, notably cancer [1].

Ac-225, an alpha-emitting radionuclide, has shown great potential in targeted alpha therapy (TAT), a form of radioligand therapy (RLT) [9].

PET/CT is a non-invasive study & does the biochemical imaging of the body. Most commonly used in oncology to detect and evaluate tumors, staging & restaging of cancers & is also useful in cardiology to assess myocardial viability. It is also used in neurology & psychiatry [10].

PET radionuclides are short lived. Most commonly used is ^{18}F ($t_{1/2}$= 110 min) due to its longer half-life. Is more commonly used worldwide. Other agents are - ^{15}O ($t_{1/2}$= 2 min), ^{13}N ($t_{1/2}$= 10 min), ^{11}C ($t_{1/2}$= 20 min), but due to their very short half-lives we need onsite cyclotron for production & injecting fast in the patient after its preparation [11].

Therapeutic nuclear medicine has also evolved from the use of Iodine-131 since the 1940s for the treatment of Graves' disease, solitary thyroid nodule [STN], autonomously functioning thyroid nodule [AFTN] & Thyroid Cancer to further new radionuclide therapeutic agents like Samarium -153 [Sm-153] /Phosphorus -32 [P-32] /Strontium -89[Sr-89] for bony pain palliation in osteoblastic metastatic disease in breast cancer, prostate cancer [12].

Radiation synovectomy is done using Er [erbium]-169, Y [Yttrium]-90 and many other radionuclides are being used for treatment of rheumatoid arthritis & hemophilic arthropathy [13].

The newly evolved therapy using Lu-177 [Lutetium -177] labelled with DOTANOC / DOTATATE is vastly used for the treatment of metastatic neuroendocrine tumours [NET's] [14].

The magic bullet is a scientific concept developed by the German Nobel laureate Paul Ehrlich in 1907. While working at the Institute of Experimental Therapy he formed an idea that it could be possible to kill specific microbes (such as bacteria), which cause diseases in the body, without harming the body itself [15].

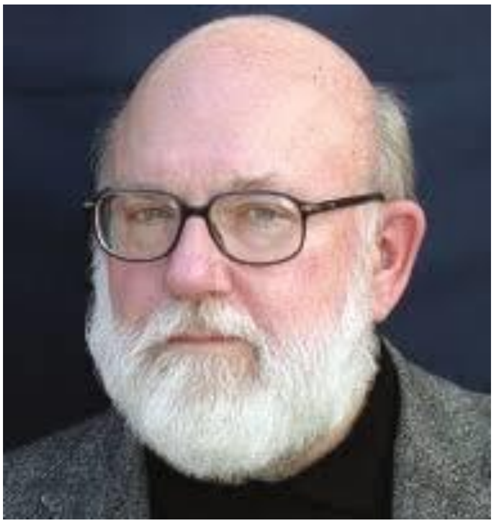
Based on his concept, it was not until the early 1950s that an Ab [antibody] was conjugated to a radionuclide. Leichner and co-workers studied the use of ^{111}In [Indium -11] / ^{90}Y [Yttrium -90] - labelled anti-ferritin for RIT [radioimmunotherapy] in patients with hepatoma [16].

For the first time the FDA - approved radiolabeled anti-CD20 mAbs [monoclonal antibody], ^{90}Y-labeled Zevalin® (ibritumomab tiuxetan) in 2002 and ^{131}I-labeled Bexxar® in 2003 for the treatment of non-Hodgkin's lymphoma (NHL) &

is considered a landmark event in the developmental history of therapeutic radiolabeled mAbs (RIT) [17].

Another remarkable development has been the use of alpha therapy which is done to ionize tumours using – Ra [Radium] - 223, At [Astatine] - 211 & many more alpha emitters [18].

More recently, the integration of nuclear medicine techniques with other imaging modalities like MRI (Magnetic Resonance Imaging) and CT (Computed Tomography) has led to the development of hybrid imaging technologies [19].



Michael E. Phelps[Lt.] & Edward J.Hoffmann[Rt.] invented the Positron Emission Tomography (PET). They developed the first human PET scanner in 1973 at Washington University in St. Louis.

Dr. Richard Baum is a pioneer in theranostics, a term he helped popularise. His work in the early 2000s, particularly with Lutetium-177 (Lu-177) based therapies, laid the groundwork for later advancements with Ac-225

Combining the functional imaging of PET or SPECT with the anatomical detail provided by MRI or CT has greatly improved diagnostic accuracy and treatment planning. This integration allows clinicians to simultaneously evaluate the structure and function of tissues and organs, leading to more precise diagnoses and personalised treatment strategies [19].

The future of nuclear medicine is being shaped by several exciting trends and advancements, particularly in the area of personalised medicine, advanced radiopharmaceuticals, and the integration of nanotechnology. These developments are poised to significantly enhance the precision and effectiveness of nuclear medicine in both diagnostics and therapy [20].

The concept of personalised medicine in nuclear medicine involves tailoring diagnostic procedures and therapies to the individual's specific biological characteristics. This approach aims to optimise the effectiveness of treatment by considering factors like genetic makeup, molecular/cellular analysis, and individual health history [20].

New radiopharmaceuticals could offer better localisation of diseases, more precise imaging, and targeted therapy with minimal impact on healthy tissues [21].

Integration of nanotechnology into nuclear medicine is an area of significant potential. Nanotechnology involves working with materials at the atomic or molecular level, which can be applied to design more effective radiopharmaceuticals and imaging agents. By leveraging nanotechnology, researchers aim to create agents that can target diseases at a cellular or even molecular level [21].

This precise targeting could lead to earlier detection of diseases and more effective treatments, especially in the case of cancer, where early detection and targeted therapy are crucial [21].

These advancements are expected to revolutionise the field of nuclear medicine and have a broader impact on healthcare. They promise to improve the accuracy of diagnoses and the effectiveness of treatments and ultimately lead to better patient outcomes [22].

The future of nuclear medicine is bright and dynamic, with personalised medicine, advanced radiopharmaceuticals, and the integration of nanotechnology leading the way. These advancements hold the promise of transforming the way diseases are diagnosed and treated, offering hope for more effective, efficient, and personalised healthcare solutions [22].

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