Nuclear Medicine: Its Isotopes and Innovations

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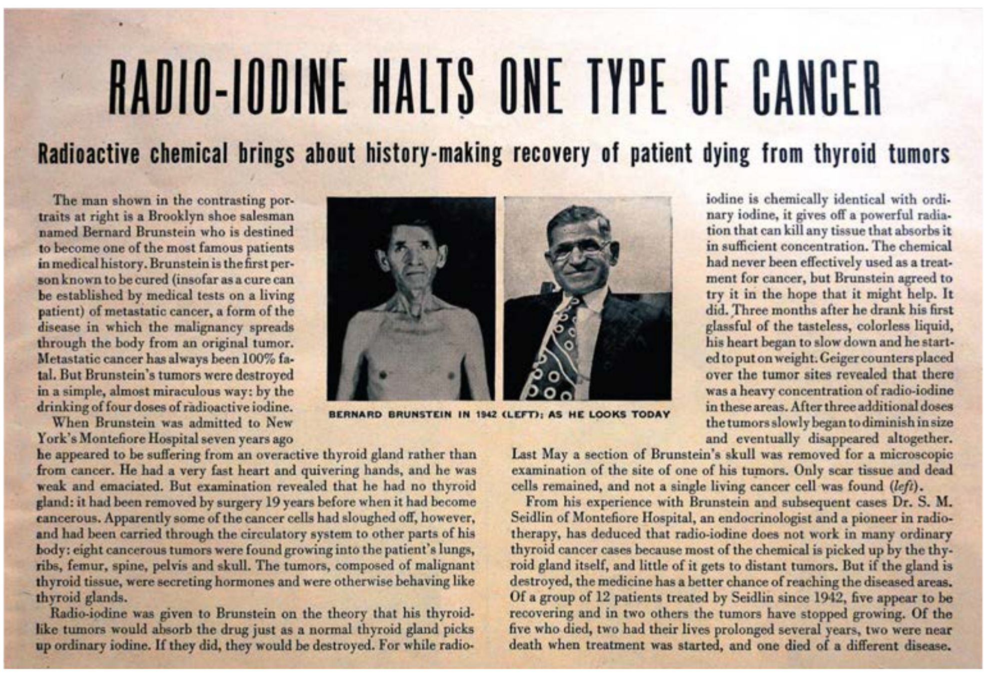
Introduction

Nuclear medicine, the use of radioisotopes for diagnosis and therapy, was first implemented in 1946 by Sam Seidlin, who successfully utilized radioactive iodine (I-131) in treating patients with advanced thyroid cancer.[1] Bernard Brunstein, featured in the news clipping below, became the first patient in clinical history to be cured of metastatic cancer. Before Seidlin's innovation, multiple doctors had always diagnosed Brunstein's condition as 100% fatal. However, through oral ingestion of iodine-131 solution, Brustein's recovery occurred almost miraculously. Since then, hundreds of innovations in nuclear medicine have improved the efficiency, convenience, and safety of patient care.



RADIO-IODINE HALTS ONE TYPE OF CANCER

Radioactive chemical brings about history-making recovery of patient dying from thyroid tumors

The man shown in the contrasting portraits at right is a Brooklyn shoe salesman named Bernard Brunstein who is destined to become one of the most famous patients in medical history. Brunstein is the first person known to be cured (insofar as a cure can be established by medical tests on a living patient) of metastatic cancer, a form of the disease in which the malignancy spreads through the body from an original tumor. Metastatic cancer has always been 100% fatal. But Brunstein's tumors were destroyed in a simple, almost miraculous way: by the drinking of four doses of radioactive iodine.

When Brunstein was admitted to New York's Montefiore Hospital seven years ago he appeared to be suffering from an overactive thyroid gland rather than from cancer. He had a very fast heart and quivering hands, and he was weak and emaciated. But examination revealed that he had no thyroid gland: it had been removed by surgery 19 years before when it had become cancerous. Apparently some of the cancer cells had sloughed off, however, and had been carried through the circulatory system to other parts of his body: eight cancerous tumors were found growing into the patient's lungs, ribs, femur, spine, pelvis and skull. The tumors, composed of malignant thyroid tissue, were secreting hormones and were otherwise behaving like thyroid glands.

Radio-iodine was given to Brunstein on the theory that his thyroid-like tumors would absorb the drug just as a normal thyroid gland picks up ordinary iodine. If they did, they would be destroyed. For while radio-iodine is chemically identical with ordinary iodine, it gives off a powerful radiation that can kill any tissue that absorbs it in sufficient concentration. The chemical had never been effectively used as a treatment for cancer, but Brunstein agreed to try it in the hope that it might help. It did. Three months after he drank his first glassful of the tasteless, colorless liquid, his heart began to slow down and he started to put on weight. Geiger counters placed over the tumor sites revealed that there was a heavy concentration of radio-iodine in these areas. After three additional doses the tumors slowly began to diminish in size and eventually disappeared altogether. Last May a section of Brunstein's skull was removed for a microscopic examination of the site of one of his tumors. Only scar tissue and dead cells remained, and not a single living cancer cell was found (*left*).

From his experience with Brunstein and subsequent cases Dr. S. M. Seidlin of Montefiore Hospital, an endocrinologist and a pioneer in radio-therapy, has deduced that radio-iodine does not work in many ordinary thyroid cancer cases because most of the chemical is picked up by the thyroid gland itself, and little of it gets to distant tumors. But if the gland is destroyed, the medicine has a better chance of reaching the diseased areas. Of a group of 12 patients treated by Seidlin since 1942, five appear to be recovering and in two others the tumors have stopped growing. Of the five who died, two had their lives prolonged several years, two were near death when treatment was started, and one died of a different disease.

BERNARD BRUNSTEIN IN 1942 (LEFT); AS HE LOOKS TODAY

Figure 1.[2] Newspaper article highlighting Seidlin's famous patient, Brunstein, who was the first patient cured of a metastatic cancer by radiation therapy

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[1] Ehrhardt Jr, John Dennis, and Seza Güleç. "A Review of the History of Radioactive Iodine Theranostics: The Origin of Nuclear Ontology." Molecular Imaging and Radionuclide Therapy, vol. 29, no. 3, 1 Oct. 2020, pp. 88

[2] Ibid.

Diagnostic Medicine and Nuclear Imaging

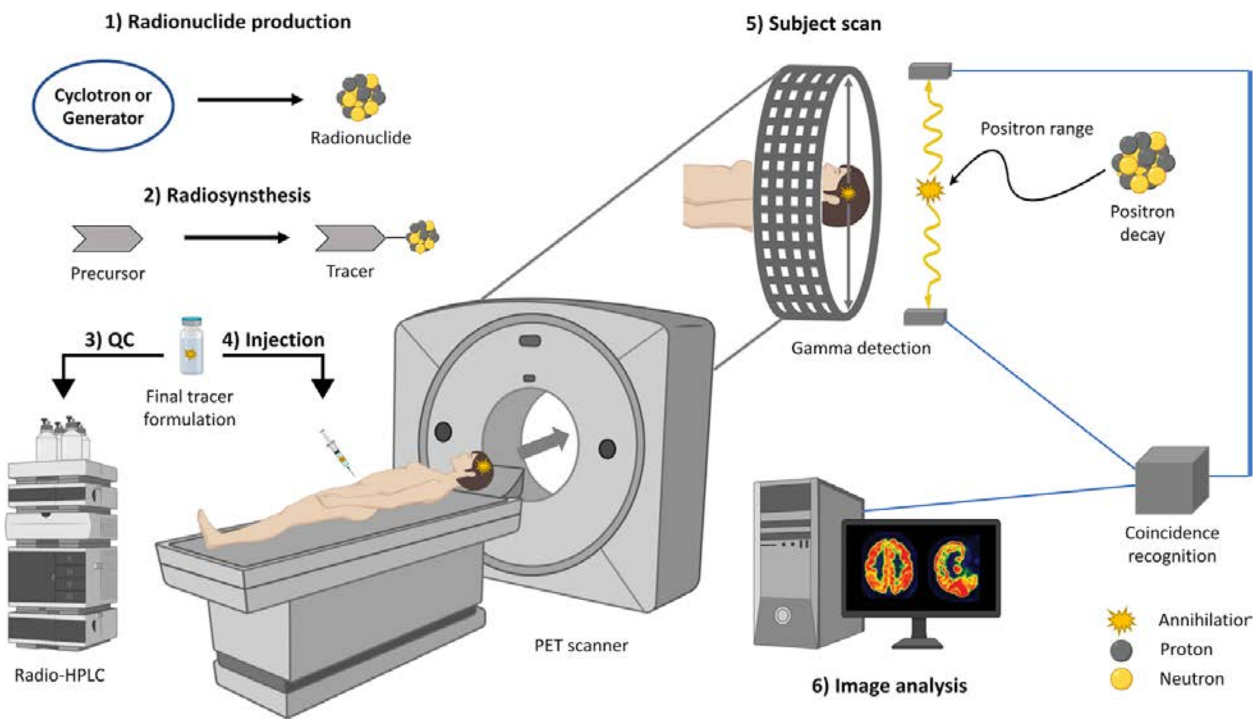

Figure 1.[3] Nuclear Imaging Schematic

One notable area revolutionized by nuclear medicine is the field of diagnostic medicine and imaging. Due to nuclear imaging's ability to provide information on both organ function and visualization, it surpasses traditional X-rays.[4] X-rays largely pass through soft tissues, such as intestines, muscles, and blood vessels, making visualization of these tissues challenging.[5] Referencing the figure below, the lungs appear as vague shadows. Only the hard tissue, or bones, are detailed. X-Rays also cannot detect tissue functionality and metabolism, making the diagnosis of tumors and other metabolic irregularities unlikely.

[3] John Hopkins Medicine. "Nuclear Medicine." John Hopkins Medicine, 2019, www.hopkinsmedicine.org/health/treatment-tests-and-therapies/nuclear-medicine.
[4] "Nuclear Imaging." stanfordhealthcare.org/medical-tests/n/nuclear-imaging.html. Accessed 20 Feb. 2024.
[5] Cherry, S. R., & Sorenson, J. A. (2012). Physics in nuclear medicine (4th ed.). Elsevier Health Sciences.

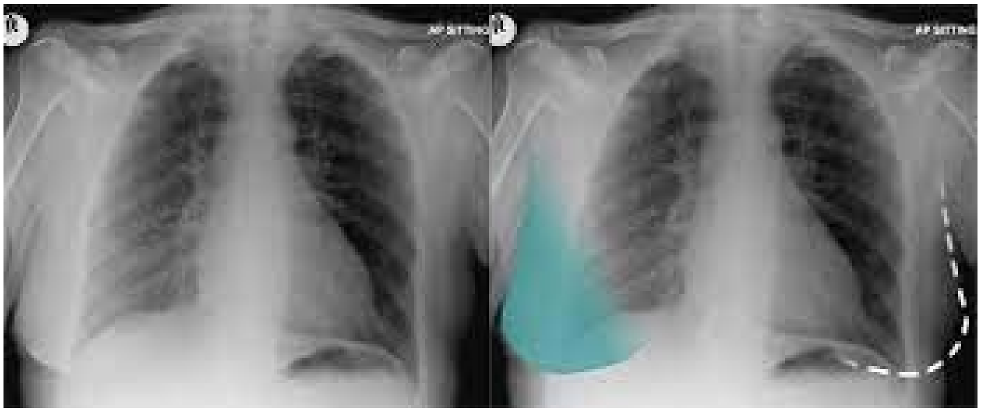

Figure 2.[6] Chest X-Rays

Nuclear imaging addresses these issues effectively. PET and SPECT scans, two of the most common nuclear imaging techniques, offer functional information about tissues and organs through calculations of half-life and measurements of radiation emissions. In addition to imaging both soft and hard tissue, these scans provide invaluable data about blood flow, receptor binding, and metabolism. Thus, PET and SPECT scans can detect abnormalities at an earlier stage than X-ray scans, as changes in cellular metabolism can be detected before structural changes are even visible on X-Rays. Nuclear imaging's versatility allows physicians to target and image all tissues more effectively, bypassing otherwise necessary invasive procedures.

Usage of Technetium-99, the ideal medical isotope

Before delving into other uses of radioisotopes in medicine, we must first understand the process of sourcing and selecting specific radioisotopes. Technetium-99 is the most common sourced radionuclide in nuclear medicine, utilized in over 80% of all procedures (both diagnostic and therapeutic). Technetium-99 (Tc-99) is not a naturally occurring isotope due to the instability caused by an excess of neutrons and can only be produced artificially. Because Tc-99 is unstable and constantly decaying, technetium generators filled with molybdenum-99 (Mo-99) are

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[6] Townsend, D. W., Beyer, T., & Blodgett, T. M. (2008). PET/CT scanners: A hardware approach to image fusion. Seminars in Nuclear Medicine, 38(3), 152-166.

supplied to hospitals to ensure a running supply for diagnostic treatments.[7] On the right of the figure is a schematic of a Tc-99 generator, in which the Tc-99 is supplied in saline as Mo-99 continuously undergoes nuclear decay. This occurs through a process known as beta decay, where a neutron decays into a proton and electron facilitated by the weak nuclear force.[8]

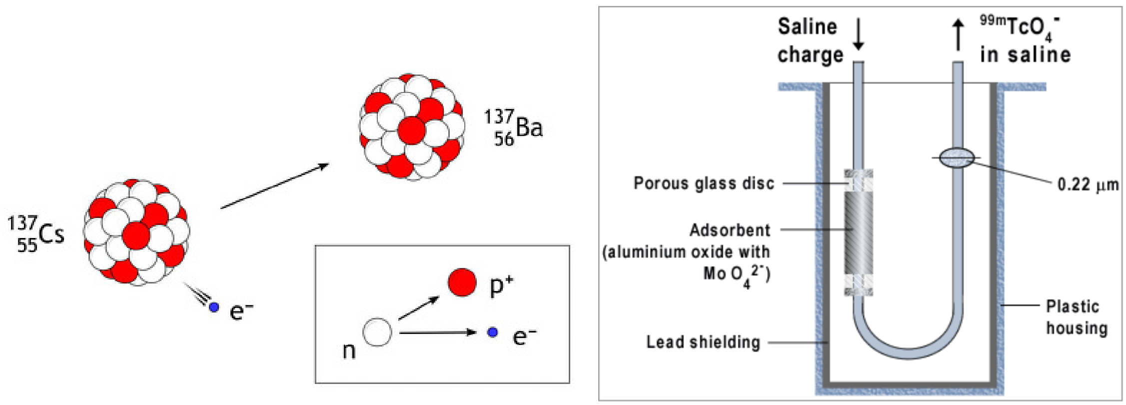

Figure 3.[9] Beta Decay and Technetium Generators

Tc-99 is predominantly used because it possesses ideal characteristics for scanning procedures, *maximizing* both patient safety and diagnostic return. A Tc-99 tracer administers a very low radiation dosage, and thus is very safe, due to its short half-life of six hours. A half-life of 6 hours is just long enough to examine functionality and metabolic processes, but short enough to minimize radiation dosage.[10] In addition, the decay only emits low-energy gamma rays and electrons, minimizing the majority of the ionizing radiation the patient is opposed to, in contrast to other more harmful beta-decay processes.

In addition to safety, technetium is highly *versatile* and can be integrated *seamlessly* into a wide range of biologically-active substances to target specific tissues or organs of interest. Tc-99 can be used to label red blood cells to image hemangiomas (or clusters of large blood

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[7] "Nuclear Medicine." Www.nibib.nih.gov, www.nibib.nih.gov/science-education/science-topics/nuclear-medicine
[8] Ibid.
[9] Matis, Howard "Beta Decay." *Lbl.gov*, 2019,www2.lbl.gov/abc/wallchart/chapters/03/2.html.

[10] Ibid.

filled-sinuses), bleeding, or salivary glands of the gastrointestinal system.[11] Another technique known as perfusion scintigraphy utilizes the assertion of a colloid (homogeneous mixture of Tc-99 dispersed and diluted in another liquid) intravenously to examine the cardiovascular system, which is invaluable for determining heart function and eligibility for organ grafts.[12] Utilizing the help of a gamma-camera, physicians can visualize and measure the metabolic function of organs from almost all systems using Tc-99.

Targeted Alpha Therapy

In addition to visualization, radioisotopes can be used in therapeutic applications as well. One of the most recent breakthroughs in therapeutic nuclear medicine is Targeted Alpha Therapy (TAT). In contrast to conventional chemotherapy, TAT is able to precisely target cancer cells while sparing healthy tissues. Through the use of alpha-emitting radioisotopes coupled with tumor-specific targeting agents, such as antibodies or peptides, TAT can deliver highly localized radiation. Thus, collateral damage to surrounding healthy tissues is minimized, reducing side effects such as radiation sickness which overall improves patient experience and outcome.[13]

Targeted Alpha Therapy gets its name due to the use of alpha particles as the primary ionizing radiation. Unlike beta or gamma decay, alpha decay has a high linear energy transfer. This means that alpha decay is much more localized and short ranged, and thus can mitigate collateral damage to healthy cells. Additionally, this high linear energy transfer allows TAT to deeply into solid tumors, reaching regions that may be inaccessible to other treatment methodologies.[14] Thus, TAT is extremely effective in clinical trials against metastatic tumors and other larger tumor sites.

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[11] Moriguchi, Sonia Marta, et al. Clinical Applications of Nuclear Medicine. Www.intechopen.com, IntechOpen, 20 Feb. 2013, www.intechopen.com/chapters/43034.
[12] Ibid
[13] Tafreshi, Narges K., et al. “Development of Targeted Alpha Particle Therapy for Solid Tumors.” Molecules
[14] Ibid.

Sterilization and Epidemic Control

It is clear that radioisotopes have amazing potential and impact in bettering direct patient care in the clinic. In addition to bettering direct patient care, nuclear medicine has many equally beneficial auxiliary uses, two of which are epidemic control and sterilization of medical equipment.

Mosquito-borne illnesses have wreaked havoc globally in the past decades. According to the World Health Organization, dengue fever infects an estimated 390 million people annually worldwide, leading to 25,000 deaths among children.[15] The outbreak of Zika in 2015-2016 in North and South America was particularly deadly. Malaria continues to pose a substantial threat, particularly to vulnerable populations in sub-Saharan Africa, where it remains a leading cause of morbidity.[16] In fact, in 2019 alone, there were an estimated 229 million cases of malaria worldwide, resulting in approximately 409,000 deaths, predominantly among children under five years of age.[17] It is clear that something must be done to control the spread of such vector borne illnesses, and the use of radioisotopes may be key!

In the past year, research regarding the Sterile Insect Technique has emerged as a promising strategy for controlling such insect borne illnesses. This technique utilizes Cobalt-60 (Co-60), a waste byproduct commonly found in fission reactors, to irradiated male insects.[18] Co-60 is a gamma-emitter, highly ionizing radioisotope that causes damage to the DNA and reproductive structures of these mosquitoes. After irradiation, these mosquitoes are released into the wild. Subsequently, these sterile males mate with wild females, leading to non-viable

[15] "Mosquito Sterilization Offers New Opportunity to Control Chikungunya, Dengue, and Zika." Www.who.int
[16] Ibid.
[17] Ibid.
[18] Ibid.

offspring, thus reducing the target insect population dramatically. With a decreased density of disease carrying vectors, the spread of such illnesses is decreased rapidly, mitigating risk for outbreaks.

Cesium-137 (Cs-137), also a byproduct from fission waste, is another crucial isotope employed in medical sterilization procedures. In medical facilities, Cs-137 is utilized in the sterilization of equipment such as surgical instruments, syringes, and catheters.[19] The high-energy radiation emitted from gamma radiation disrupts the DNA of microorganisms such as bacteria, viruses and other pathogens, ensuring that medical instruments are free from infectious agents before use. The use of radioisotopes in sterilization is far superior to conventional autoclave methods. Autoclaves use steam under pressure to sterilize equipment, which may not effectively penetrate dense or complex instruments, leaving potential areas untouched by the sterilizing agent.[20] In contrast, nuclear radiation can penetrate materials deeply and evenly, reaching all surfaces of the equipment, ensuring thorough sterilization. Additionally, nuclear sterilization is a cold process, meaning it doesn't require high temperatures that can damage heat-sensitive materials, such as certain medicines, vaccines, or ointments. Finally, autoclave sterilization often leaves residual moisture on sterilized equipment, creating a potential breeding ground for bacteria and other pathogens. Nuclear sterilization, however, leaves no residual moisture, reducing the risk of post-sterilization contamination and ensuring a higher level of sterility. Thus, it is clear that radioisotopes have tremendous benefits both directly and indirectly with relation to patient care, whether in diagnosis, treatment, epidemic mitigation, or sterilization!

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[19] National Academies of Sciences, Engineering, et al. “Radioactive Sources and Alternative Technologies in Sterilization.” Www.ncbi.nlm.nih.gov, National Academies Press (US)
[20] Ibid.

Conclusion

Nuclear medicine advances in the last 70 or so years have been incredible. However, this field is still underutilized in both developed and developing countries. According to the World Nuclear Association, the utilization frequency of nuclear diagnostic medicine is under 1.9% yearly, and the frequency of nuclear therapy is 1/10th of this, even in developed countries.[21] This lack of utilization can be attributed to two main factors: stigma and cost. For many, nuclear medicine is unfortunately coupled with the negative stigma towards the destructive nature of nuclear weapons. As many as 80.4% of people surveyed in one study considered nuclear weapons destructive, and up to 68.7% of these people extended this sentiment to all things nuclear, including but not limited to nuclear medicine and power.[22]

In addition to overcoming the stigma, it is also important to continually innovate and lower the cost of nuclear medicine treatments. Due to inherent radioactive instability, funding for the constant restock of different radioisotopes and disposal of nuclear waste is very expensive. Additionally, there are only seven main suppliers of radioisotopes necessary in these procedures, and there exist problems in transport, waste management, and overall efficiency.[23] Limited by high cost and low availability, many with financial limitations are unable to experience the benefits of nuclear medicine, diminishing quality of patient care.[24] Thus, it is important that students, government workers, physicians, and patients alike need to join together in educating and spreading awareness of the innovations and limitations of nuclear medicine. With an united front, we can bring improved patient care to all!

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[21] "Radioisotopes in Medicine | Nuclear Medicine - World Nuclear Association"
[22] Baron, J., & Herzog, S. (2020). Public opinion on nuclear energy and nuclear weapons: The Attitudinal Nexus in the United States. Energy Research & Social Science, 68, 101567
[23] Ibid.
[24] "Radioisotopes in Medicine | Nuclear Medicine - World Nuclear Association"

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