# Nuclear Medicine in Clinical Practice

P.B. Schneider and S. Treves
Editors

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# NUCLEAR MEDICINE IN CLINICAL PRACTICE

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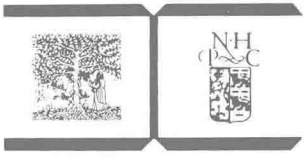

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# Preface

Although its roots extend from 1927 when naturally occurring "radium emanation" (Radon) was first used for the measurement of circulation times, Nuclear Medicine did not really begin its growth until the 1950's when man-made radionuclides became available. A period of rapid expansion followed in the 1960's and continues to the present when Nuclear Medicine is acknowledged as a coherent, important discipline most simply defined as the specialty devoted to the use of radionuclides for diagnosis and therapy. Because its development has been so recent, most physicians had already finished their training before courses in Nuclear Medicine were offered and even today, formal instruction in the field is not the rule in medical schools. However, since Nuclear Medicine has applications in almost all fields of clinical practice or investigation, it is important for physicians and surgeons to be aware of available radionuclide tests and procedures and to know under what circumstances they should be used.

This book has been designed as a guide to the appropriate utilization of Nuclear Medicine techniques. It is directed primarily at practising physicians and surgeons, whether specialists or not, but should also be of use to clinical investigators, house officers, and students. Though intended for those who are not specialists in Nuclear Medicine, we hope the book will also serve residents and physicians in Nuclear Medicine as a summary of the applicability of their field.

We have covered mainly in vivo procedures; that is, those tests in which radionuclides are administered to a patient usually for the purpose of obtaining an image. Select in vitro assays are included but an exhaustive discussion of radioimmunoassays is beyond the scope of this book. The book presents currently available radionuclide procedures in a format that covers their rationale and clinical applicability. Technical descriptions of instrumentation, radiopharmaceuticals, and procedural manipulations are given for background and to permit the physician to appreciate what the patient undergoes and which factors may influence the outcome of the tests. It is hoped that the presentation of the procedures and techniques is broad enough and provides enough background so that the physician might make ad hoc decisions about their use if a particular case does not fit an explicit description in this book. Although an attempt has been made to mention developing trends in Nuclear Medicine, it is quite probable, because of the rapid changes still occurring in this field, that when the book is read, some of the described applications may have been supplanted while others, not discussed, may have come into use. For that reason,

also, we have tried to provide enough general information to allow the reader to attain an insight into the principles of Nuclear Medicine so that even as the details change, he will retain the general picture and be better able to cope with progress.

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# Contents

*Nuclear Medicine in Clinical Practice, edited by P. B. Schneider and S. Treves*


# 1 Introductory Physics and Instrumentation

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## 1.1 INTRODUCTION

The imaging procedures described in subsequent chapters of this book have, for the most part, become available to clinical practice only in the past 10 years. The specialty of nuclear medicine has its roots in the last 5 years of the nineteenth century, when the phenomenon of radioactivity was discovered by Bequerel in 1896. This followed by less than one year the discovery of X-rays by Roentgen in 1895. Although the medical utility of X-rays was recognized and employed in diagnosis before the turn of the century, it was not until the 1940's that radioactive materials were used in the diagnosis of human disease.

The delay in the development of nuclear medicine (one of the few things that acquired a correct name in the "atomic" age – the *nucleus* of the atom is where things happen in atomic bombs and atomic reactors) had two causes. Until the 1930's only naturally-occurring radioactive elements were known, and none of these very heavy elements (bismuth, lead, radium, uranium, and thorium among others) had physical or physiological properties which would make them useful in medical diagnosis. The second cause of delay was the lack of instrumentation, which made it impossible to detect and localize small amounts of radioactive materials.

One of these barriers was overcome in the 1930's with the discovery of artificial radioactivity: almost every element could be converted to a radioactive form by changing its nuclear composition. The advent of nuclear reactors during World War II and their development thereafter resulted in the production of enormous quantities of radioactive materials, many of which were rapidly introduced into radiation therapy: $^{60}$Co and $^{137}$Cs quickly replaced $^{226}$Ra in many teletherapy applications. Other radioactive isotopes were soon recognized to have medical usefulness.

The second development, instrumentation, took much longer. The detection of the decay of individual atoms by Geiger counters is so inefficient that they cannot be effectively used for nuclear medicine imaging. It was not until the 1950's that scintillation detectors were developed, first for use in nuclear physics, then transferred

to medicine. The scintillation detector is almost 100% efficient in detecting certain types of radiation, and has been the making of nuclear medicine.

In the sections which follow, the phenomenon of radioactivity will be described to provide an appreciation of the requirements of the detection systems used in nuclear medicine. The current state of the art in nuclear medicine will be discussed with a view toward providing the clinician with a reasonable expectation of what can and cannot be seen in imaging procedures. Finally, the radiation exposures produced by nuclear medicine procedures will be compared with those of other radiologic procedures.

## 1.2 RADIOACTIVITY AND THE NUCLEAR ATOM

### *1.2. General structure*

Radioactivity is the spontaneous disintegration (decay) of the nucleus of a radioactive atom. In the decay event, several kinds of radiation may be emitted from the nucleus. The nucleus is the central, heavy part of the atom. The relative sizes of the nucleus in an atom is indicated in Fig. 1.1, where it can be seen that there is a factor of about 10,000 difference between the atomic diameter and the nuclear diameter. If nuclei could be expanded to golf-ball size, the atom itself would have a diameter of a quarter of a mile.

The nucleus contains the protons and neutrons (collectively called nucleons) of the atom. In one of the models of the atom (no one has ever seen an atom, so models have been developed to explain physical observations and predict the outcome of future experiments) the nucleus is surrounded by electrons which whirl around the nucleus in a way analogous to the rotation of the planets around the sun. The physical properties of three atomic constituents are listed in Table 1.1, along with their

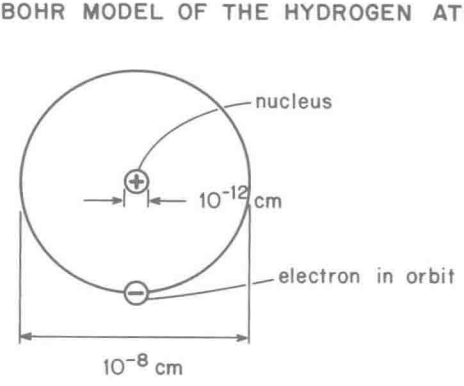


Fig. 1.1. The Bohr model of the hydrogen atom. The central nucleus contains essentially all the atom's mass, and is positively charged. The positive charge is balanced by the negative charge carried by the electron, which in this model circles the nucleus in a fixed orbit.

Table 1.1. PHYSICAL PROPERTIES OF SUB-ATOMIC PARTICLES

| Particle | Electric Charge | Weight | | Location |
|---|---|---|---|---|
| | | Grams | a.m.u. | |
| Proton | +1 | $1.66 \times 10^{-24}$ | 1.0 | Nucleus |
| Neutron | neutral | $1.66 \times 10^{-24}$ | 1.0* | Nucleus |
| Electron | −1 | $9.1 \times 10^{-28}$ | 0.00054 | Around nucleus |

*The neutron is actually 0.08% heavier than the proton.

location in the atom. Because the individual components of atoms weigh so little (the proton weighs 0.000 000 000 000 000 000 000 00166 gram), a new scale has been adopted: The atomic mass unit (a.m.u.): one a.m.u. is the wieght of one proton.

The number of protons in an atom's nucleus establishes the atom's elemental identity. For instance, atoms with one proton are called hydrogen, those with two are helium atoms, and three protons are in the nuclei of lithium atoms. The number of protons in the nucleus cannot be increased indefinitely: in nature, the atoms with the largest number of protons are those of uranium, with 92 protons. Man-made elements, which are all radioactive, have been produced with up to 106 protons.

Neutrons, the other nuclear component, also weigh one atomic mass unit. The number of neutrons plus the number of protons is the mass number (very close to the atomic weight) of an atom. Thus, in $^{131}I$, the 131 is the mass number, and refers to the number of nucleons, 53 protons and 78 neutrons. Atoms with the same number of protons but differing numbers of neutrons are called isotopes of that element. Only certain combinations of protons and neutrons are stable; the others are radioactive. For iodine, the only stable combination is 53 protons and 74 neutrons ($^{127}I$). Some elements have no stable isotopes: technetium, with 43 protons has only radioactive isotopes.

### *1.2.2 Units of measurement*

The activity of a radioactive element is usually given in disintegrations per second (dps). The standard activity is the Curie (Ci), which is equal to 37 billion (37,000,000,000) dps. In nuclear medicine, the amounts of radioactivity administered vary from microcuries ($\mu$Ci, 37,000 dps) to millicuries (mCi). It should be emphasized that "dps" is an absolute measurement which differs from "cps" or "cpm" (counts per sec or min) which is the measure of activity recorded by the detecting device. The difference between the two stems from the fact that one disintegration may release varying numbers of particles and, more important, that the efficiency with which the detectors can record the particles varies from one machine to another.

The other important aspect of radioactive decay is the half-life ($t\frac{1}{2}$), which is defined as the time required for one-half of the atoms in a group of radioactive atoms to decay. Obviously, then, the recorded activity of a given amount of isotope will fall by half in one half-life. The half-life is a unique physical property of a radioactive isotope and is a constant for any given isotope. The half-life cannot be modified by temperature, pressure, or chemical form: the physical half-life of technetium-$^{99}$m

($^{99m}$Tc) is 6.0 h whether the technetium is in a vial in the laboratory or circulating in a patient's bloodstream or deposited in his liver (cf. effective half-life, Sec. 1.2.3).

The unit used to describe the energy of radioactive decay and of atomic radiation is the electron volt, usually expressed in multiples of a thousand (kiloelectron volts, keV) or millions (megaelectron volts, MeV). One electron volt is an extremely small amount of energy equivalent to $1.6 - 10^{12}$ ergs. The complete absorption of $26 \times 10^{12}$ one-MeV electrons for instance, is equivalent to the absorption of one calorie of heat energy (enough to raise the temperature of one gram of water one degree Celsius). One of the great achievements of nuclear instrumentation is the ability to detect the individual decay events as radioactive nuclei disintegrate.

### *1.2.3 Radioactive decay and emissions*

The process of radioactive decay produces radiations which can be of several types. There are three basic kinds of radiations, which were named for the first three letters of the Greek alphabet: alpha, beta, and gamma radiation. Alpha ($\alpha$) decay is the emission of a helium nucleus ($\alpha$-particles) by a radioactive atom. Although the $\alpha$-particles are emitted with considerable energy, their range in tissue is of the order of a few micrometers, which means that internally-deposited $\alpha$-emitters cannot be detected outside the patient. This short range also means that $\alpha$-particles produce considerable biological damage when decay occurs in tissues: all of the $\alpha$-decay energy is locally deposited.

Beta ($\beta$) particles are really high-speed electrons emitted by certain radioactive isotopes, such as iodine-131 ($^{131}$I). These electrons are emitted with energies ranging from a few keV to several MeV. Each different $\beta$-radioactive nuclide emits a characteristic spectrum of electrons with energies from close to zero up to a specific maximum. $^{131}$I, for example, emits most of its $\beta$-particles with a range of energies up to 608 keV. Electrons emitted by $\beta$-radioactive isotopes travel at speeds close to the speed of light (186,000 miles per sec). However, the range of $\beta$-particles in tissue is only a few millimeters, so external detection of internally-deposited $\beta$-particle emitters is almost impossible. The biological damage to tissues is also high, as indicated by the efficacy of thyroid ablation with $^{131}$I.

A unique kind of $\beta$-decay occurs in certain man-made radioisotopes: instead of emitting an electron, these radioisotopes ($^{18}$F is a typical example) produce a positively-charged $\beta$-particle (positron) in the decay process. The positron is physically identical to the electron except for its charge, the positron is an antiparticle, and when it slows down, it combines with a normal electron in a process called annihilation, which destroys both the electron and the positron and produces two energetic photons, each with 511 keV. These photons are similar to $\gamma$-rays (see below), and their energy is so unique that it is called annihiliation radiation. It is these photons that are used in nuclear medicine to produce bone scans with $^{18}$F.

Gamma ($\gamma$) rays are really electromagnetic radiation, radiation with properties similar to light-rays, radio waves, and X-rays. In fact, gamma radiation is physically indistinguishable from X-rays once the radiation has left the source. Like X-rays, $\gamma$-rays are very penetrating, and easily pass through tissue. In nuclear medicine,

radioisotopes which emit $\gamma$-rays are administered to the patient. The radioisotope is incorporated in a radiopharmaceutical designed to produce localization in a particular organ. The $\gamma$-rays emitted by the decaying radioisotopes in the organ are detected externally with extremely sensitive detectors, which detect individual gamma rays (photons). Although most nuclear medicine images are produced with up to one million detected $\gamma$-rays, as few as 50,000 $\gamma$-rays detected could produce an adequate image in nuclear medicine. This is in sharp contrast to the billions of X-rays which pass through a patient and produce a radiograph when the X-rays interact with X-ray film.

Some radioisotopes produce both $\beta$- and $\gamma$-radiation when they decay. $^{131}$I is a good example: $^{131}$I emits $\beta$-particles with an average energy of about 200 kiloelectron volts (keV), and several $\gamma$-rays, the most important of which for nuclear medicine imaging is the $\gamma$-ray of 364 keV.

Another kind of radioactive decay process is called electron capture. This type of decay does not occur in nature ($\alpha$- and $\beta$-emitters are numerous in naturally-occurring materials). Radioisotopes which decay by electron capture are produced in atom-smashing machines such as cyclotrons and linear accelerators. An important isotope for thyroid studies, $^{123}$I decays by electron capture. There is no particle emission when electron capture decay occurs, but there usually is one or more $\gamma$-ray emitted, as well as an X-ray or two. The absence of particle emission (except the usually small number of electrons produced by internal conversion which competes with $\gamma$-ray emission) makes radioisotopes which decay by electron capture very attractive from a biologic hazard point of view.

The most widely used radioisotope in nuclear medicine is technetium-99m ($^{99m}$Tc). The "m" in "99m" refers to a metastable state of the nucleus which decays with a very short half-life (6 h) to the more stable $^{99}$Tc by emitting a $\gamma$-ray of 140 keV. However, not all of the atoms of $^{99m}$Tc decay by emitting a $\gamma$-ray. About 10% of the $^{99m}$Tc atoms give up their decay energy to an atomic electron, which then leaves the atom. This mode of decay, called internal conversion, produces high energy electrons within the patient. Thus, $^{99m}$Tc is not a "pure" $\gamma$-emitter. The electrons produce the same type of biologic damage that $\beta$-particles do. The process of internal conversion, producing energetic electrons, can have important biologic consequences: For example more than half the radiation dose delivered to the liver by $^{99m}$Tc-labeled sulfur colloid is produced by the internal conversion electrons of $^{99m}$Tc. Most of the $\gamma$-rays leave the liver, because their range in tissue is so large, while the range of the internal conversion electrons is less than one millimeter. Thus, all of their energy is deposited in the liver.

The physical properties of several radioisotopes which are currently used in nuclear medicine are summarized in Table 1.2. These are important to the nuclear medicine specialist, who chooses a particular radioisotope for its physical properties first: Obviously, the isotope must emit $\gamma$-rays to make it detectable outside the patient, and its physical half-life should be short to minimize radiation exposure to the patient. The former characteristic is necessary, but the latter can be modified by biologic removal. The real measure of radiation exposure is related to the effective half-life $[(t_{1/2})_{\text{eff}}]$ of a radioisotope in the body.

Table 1.2. PHYSICAL PROPERTIES OF SOME RADIOISOTOPES USED IN NUCLEAR MEDICINE

| Isotope | Half-life | Radiation | Energy | Used for |
|---|---|---|---|---|
| $^{99m}Tc$ | 6.0 h | Gamma | 140 keV | Brain, bone, liver, lung |
| $^{131}I$ | 8.0 days | Beta, | 180 keV | Thyroid, liver |
| | | Gamma | 364 keV | |
| $^{75}Se$ | 120 days | E.C.*, gamma | 136,260 keV | Pancreas |
| $^{51}Cr$ | 28 days | E.C., gamma | 320 keV | Red-cell studies |
| $^{133}Xe$ | 5.3 days | Beta, gamma | 80 keV | Lung |
| $^{111}In$ | 2.84 days | E.C., gamma | 172,247 keV | Cisternograms, bone marrow |

*E.C. = electron capture.

The $(t_{1/2})_{eff}$ is given by the formula

$$(t_{1/2})_{eff} = \frac{(t_{1/2})p \times (t_{1/2})b}{(t_{1/2})p + (t_{1/2})b}$$

where
$(t_{1/2})p$ is the physical half-life, and
$(t_{1/2})b$ is the biological half-life.

Inspection of the equation indicates that when there is a wide disparity between the physical and biological half-lives, the shorter half-life controls the effective half-life. For example, the biological half-life (in the liver) of $^{99m}Tc$ in labeled technetium sulfur colloid is very long. If the $(t_{1/2})b$ is assumed to be 1000 h, the equation reads

$$(t_{1/2})_{eff} = \frac{6.0 \times 1000}{6.0 + 1000} = \frac{6000}{1006} = 5.97\,h$$

*1.3. Interactions of radiation with matter.*

In order to understand the mechanism of image production in nuclear medicine, it is necessary to understand the process of detection of the radiations emitted by radioactive isotopes. The design of a radiation detector must depend on the interaction of the radiation with matter. The primary process responsible for energy loss by nuclear radiation is ionization – the removal of one or more electrons from an atom or molecule: radiation $\rightsquigarrow N_2 \rightarrow N_2^+ + e^-$. In Geiger counters, the phenomenon of ionization is used to produce an electronic pulse which is ultimately seen as a meter deflection or heard as a click of the meter. The phenomenon of ionization of interest to nuclear medicine is produced by two kinds of interactions of $\gamma$-rays with matter: the photoelectric effect and the Compton scattering effect. These interactions occur in all types of matter – tissue, air, and the detectors used to measure radiation.

The photoelectric effect involves the complete absorption of the $\gamma$-ray photon. The entire energy of the $\gamma$-ray is given up in a single collision with an electron in an atom of the absorber material. The $\gamma$-ray no longer exists. The energy imparted to

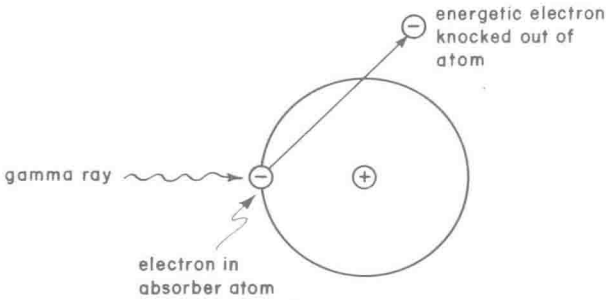


Fig. 1.2. The photoelectric interaction. The $\gamma$ -ray gives up all its energy to an atomic electron in a single collision. The electron is knocked out of the atom and goes on to produce ionization in nearby atoms or molecules.

the electron is usually sufficient to knock it completely out of the atom, ionizing the atom. The electron goes on to deposit its energy over a path length of a few millimeters or less; the energy loss is by further ionization of atoms and molecules along the path. The processes involved in the photoelectric effect are indicated in Fig. 1.2.

Compton scattering differs from the photoelectric process primarily in one way: in Compton scattering, the incoming $\gamma$-ray gives up only a part of its energy to an electron of an atom in the absorber material. The remaining energy leaves the scattering site in the form of a $\gamma$-ray of lower energy. The scattered $\gamma$-ray may go on to be completely absorbed in a photoelectric event, within the absorber, or undergo another Compton scattering in the absorber, or leave the absorber entirely. Again, energy is transferred from the $\gamma$-ray to electrons in the absorber. The energetic electrons leave the atoms to which they were attached, ionizing them, and produce additional ionization in nearby atoms and molecules. The Compton-scattering process is shown schematically in Fig. 1.3.

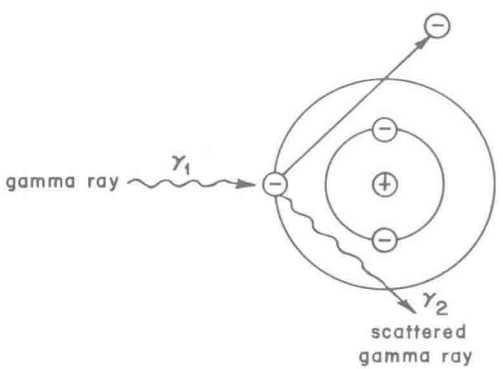


Fig. 1.3. The Compton-scattering interaction. The incoming $\gamma$-ray gives up part of its energy to an atomic electron in the absorber. The scattered $\gamma$-ray ($\gamma_2$) may undergo a photoelectric interaction (see Fig. 1.2), or additional Compton scattering in the absorber, or may leave the absorber entirely.