Nuclear Physics and Nuclear Medicine

17

Each atom contains a nucleus about 100,000 times smaller than the atom. The nuclear charge determines the number of electrons in the neutral atom and hence its chemical properties. The nuclear mass determines the mass of the atom. For a given nuclear charge there can be a number of nuclei with different masses or *isotopes*. If an isotope is unstable, it transforms into another nucleus through *radioactive decay*.

In this chapter we will consider some of the properties of radioactive nuclei and their use for medical imaging and for treatment, primarily of cancer (Ruth 2009; Williams 2008).

Four kinds of radioactivity measurements have proven useful in medicine. The first involves no administration of a radioactive substance to the patient. Rather, a sample from the patient (usually blood) is mixed with a radioactive substance in the laboratory, and the resulting chemical compounds are separated and counted. This is the basis of various *competitive binding assays,* such as those for measuring thyroid hormone and the availability of iron-binding sites. The most common competitive binding technique is called *radioimmunoassay.* A wide range of proteins are measured in this manner.

In the second kind of measurement, radioactive tracers are administered to the patient in a way that allows the volume of a compartment within the body to be measured. Examples of such compartments are total body water, plasma volume, and exchangeable sodium. Time-dependent measurements include red-blood-cell survival and iron and calcium kinetics. One can measure radioactivity from the whole body or from blood or urine samples drawn at different times after administration of the isotope.

For the third class of measurements, a *gamma camera* generates an image of an organ from radioactive decay of a drug that has been administered and taken up by the organ. These images are often made as a function of time.

The fourth class is an extension of these in which tomographic reconstructions of body slices are made. These include *single-photon emission computed tomography* and *positron emission tomography.*

Radioactive isotopes are also used for therapy. The patient is given a radiopharmaceutical that is selectively absorbed by a particular organ (e.g., radioactive iodine for certain thyroid diseases). The isotope emits charged particles that lose their energy within a short distance, thereby giving a high dose to the target organ. Isotopes are also used in self-contained implants for *brachytherapy.*

The first five sections introduce some of the nuclear properties that are important: size, mass, the modes of radioactive decay, and the amount of energy released.

It is important to know the dose to the patient from a nuclear medicine procedure, and a standard technique for calculating it has been developed by the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine and Molecular Imaging. Section 17.6 shows the steps in making these calculations. Section 17.7 describes some of the pharmacological considerations in selecting a suitable isotope.

The next few sections describe various ways of forming images. Section 17.8 describes the gamma camera, and Sect. 17.9 extends this to single-photon emission tomography. Section 17.10 describes positron emission tomography.

Radiotherapy is described in Sect. 17.11, including both the relatively common brachytherapy and the less common injection of isotopes that target particular organs.

The final section describes the nuclear decay of radon and some of the considerations in calculating the dose and the risk to the general population. It supplements the material that was introduced in Sect. 16.12.

17.1 Nuclear Systematics

An atomic nucleus is composed of Z protons and $N = A - Z$ neutrons. We call Z the *atomic number* and A the *mass number.* Neutrons and protons have very similar properties,

R. K. Hobbie, B. J. Roth, *Intermediate Physics for Medicine and Biology*,
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Table 17.1 Properties of nucleons, the electron, and the neutral hydrogen atom

Property	Neutron	Proton	Electron	H atom
Mass[a]	1.008664916	1.00727647	0.0005485799	1.007825032
Charge[b]	0	$+e$	$-e$	0
Rest energy m_0c^2 (MeV)	939.565	938.272	0.5110	938.783
Half-life	$\approx$ 12 min	Stable	Stable	Stable
Spin	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	...

[a] 1 u is the mass unit. The mass of ^{12}C is 12.0000000 u by definition. 1 u= 1.660539×10^{-27} kg
[b] $e = 1.602177 \times 10^{-19}$ C

as can be seen from Table 17.1. Therefore, they are classed as two different charge states of one particle, the *nucleon*.

Table 17.1 lists the *rest mass* m_0 and the *rest energy*, the rest mass times the square of the speed of light, m_0c^2. One can show using special relativity that the total energy E of an object with rest mass m_0 is related to its speed v and kinetic energy T by

$$E = \frac{m_0c^2}{(1 - v^2/c^2)^{1/2}} = m_0c^2 + T. \qquad (17.1)$$

The energy and mass of both the proton and neutral hydrogen atom are given; the distinction will be important later.

It is customary to specify a nucleus by a symbol such as the following for carbon ($Z = 6$, $N = 6$, $A = 12$):

$$^{A}_{Z}\mathrm{C} \quad \text{or} \quad ^{12}_{6}\mathrm{C}.$$

The mass number used to be written as a superscript on the right; however, this becomes confusing if the ionization state of the atom must also be specified. It is now customary to leave the right side of the symbol for atomic properties. Since the element symbol corresponds to a specific atomic number, Z is often omitted.

Different nuclei of the same element with different numbers of neutrons are called *isotopes*. Other isotopes of carbon are ^{11}C, which has five neutrons, and ^{13}C, which has seven.

The sizes of atoms are roughly constant as one goes through the periodic table, with exceptions as electron shells are filled. On the other hand, the size of nuclei grows steadily through the periodic table (Fig. 17.1). The nuclear radius R and atomic mass number are related by

$$R = R_0A^{1/3}. \qquad (17.2)$$

The precise value for R_0 depends on how the nuclear radius is measured. If it is measured from the charge distribution, then

$$R_0 = 1.07 \times 10^{-15}\,\mathrm{m}. \qquad (17.3)$$

The constancy of atomic size results from two competing effects: as Z increases the outer electrons have a larger value of the principal quantum number n. On the other hand, the greater charge means that Coulomb attraction makes the orbit radius smaller for a given n.

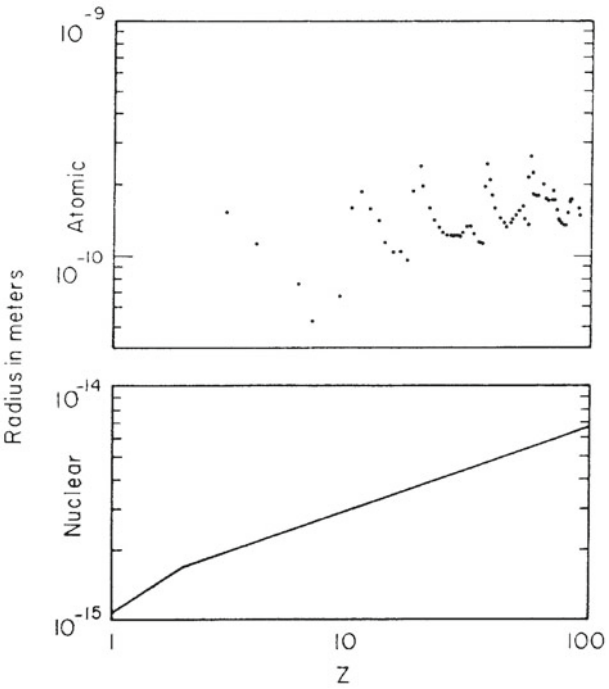


Fig. 17.1 Atomic radius and nuclear radius vs atomic number, showing the relative constancy of the atomic radius and the systematic increase of nuclear radius. Shell effects in atomic radii are quite pronounced; slight shell effects in the nuclear radius are not shown. Atomic data are from Table 7b–3 of *The American Institute of Physics Handbook*. New York, McGraw-Hill, 1957. Nuclear radii are from Eq. 17.2, using the average atomic mass to estimate A from Z

The $A^{1/3}$ dependence in the nuclear case means that the nuclear density is independent of A. To see this, note that the volume of a spherical nucleus is $4\pi R^3/3 = 4\pi R_0^3 A/3$. Since the mass and volume are both proportional to A, the density is constant. This implies that nucleons can get only so close to one another, and that as more are added, the nuclear volume increases. This constant density is the same effect we see in the aggregation of atoms in a crystal or a drop of water.

Scattering experiments measure the force between two nucleons. At large distances, there is no force between two

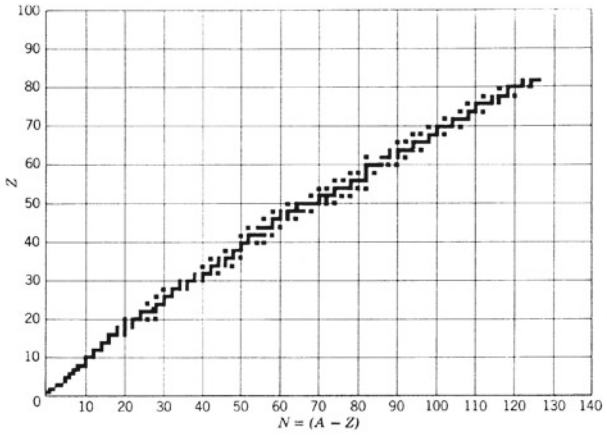


Fig. 17.2 Stable nuclei. Solid squares represent nuclei which are stable and are found in nature. (From Eisberg and Resnick 1985, p. 524. Reprinted with permission of John Wiley & Sons)

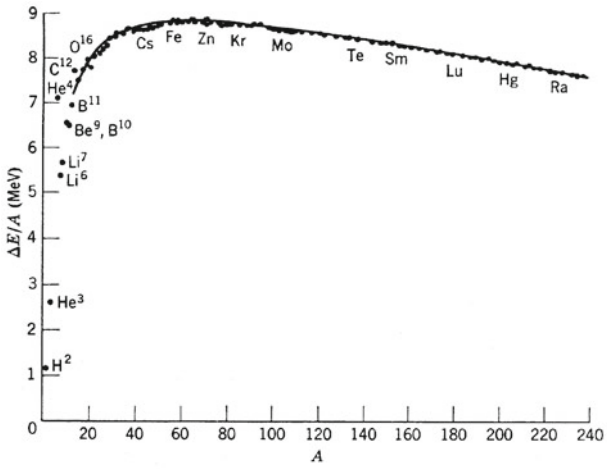


Fig. 17.3 The average binding energy per nucleon for stable nuclei. (From Eisberg and Resnick 1985, p. 524. Reprinted with permission of John Wiley & Sons)

neutrons or between a neutron and a proton. (Between two protons, of course, there is Coulomb repulsion.) As two nucleons are brought close together, a strong attractive force becomes important; at still closer distances, the nuclear force becomes repulsive.

If we look at the nuclei that are stable against radioactive decay and are therefore found in nature, we find that for light elements, $Z = N$. As Z increases, the number of neutrons becomes greater than Z; this can be seen in Fig. 17.2.

Equation 17.1 shows that when an object is at rest, its total energy (which is its internal energy) is related to its rest mass by

$$E = m_0 c^2. \tag{17.4}$$

The measurement of nuclear masses has provided one way to determine nuclear energies. It is necessary to supply energy to a stable nucleus to break it up into its constituent nucleons (or else it would not be stable). The *binding energy* (BE) of the nucleus is the total energy of the constituent nucleons minus the energy of the nucleus:

$$\text{BE} = Zm_p c^2 + (A - Z)m_n c^2 - m_{\text{nucl}} c^2. \tag{17.5}$$

It represents the amount of energy that must be added to the nucleus to separate it into its constituent neutrons and protons.

Suppose we add $Zm_e c^2$ to the first term. Then we have the energy of Z protons plus the energy of Z electrons. Except for the BE of each electron, this is the same as the mass of Z neutral hydrogen atoms, which we call $M_p c^2$. Similarly, we can add the mass of Z electrons to $m_{\text{nucl}} c^2$ and neglect the electron BE to obtain $M_{\text{atom}} c^2$. Capital M represents the mass of a neutral atom, while m stands for the mass of a bare nucleus. For the neutron, $m = M$. In Eq. 17.5, we can add $Zm_e c^2$ to the first term and add $Zm_e c^2$ to the last term, to obtain the BE in terms of the masses of the corresponding neutral particles:

$$\text{BE} = ZM_{\text{p}} c^2 + (A - Z)M_{\text{n}} c^2 - M_{\text{atom}} c^2. \tag{17.6}$$

This is fortunate, because neutral masses (or those for ions carrying one or two charges) are the quantities actually measured in mass spectroscopy.

Masses are measured in *unified mass units* u, defined so that the mass of neutral ^{12}C is exactly 12 u. Carbon is used for the standard because hydrocarbons can be made in combinations to give masses close to any desired mass. The carbon standard replaced one based on the naturally occurring mixture of oxygen isotopes in the early 1960s. (One of the troubles with the earlier standard was that the relative abundance of the various oxygen isotopes varies with time and with location on the earth.) The earlier unit was called the atomic mass unit, amu. One still finds confusion in the literature about which standard is being used, and the carbon standard is sometimes called an amu.

One unified mass unit is related to the kilogram, the joule, and the electron volt by

$$\begin{aligned} 1\,\text{u} &= 1.66054 \times 10^{-27}\ \text{kg}, \\ (1\,\text{u})(c^2) &= \begin{cases} 1.49242 \times 10^{-10}\ \text{J} \\ 931.49\ \text{MeV}. \end{cases} \end{aligned} \tag{17.7}$$

A plot of the BE per nucleon versus mass number, as in Fig. 17.3, shows that the BE per nucleon has a maximum near $A = 60$, and that the average BE (except for light elements) is about 8 MeV per nucleon. For less stable nuclei on either side of the stable line plotted in Fig. 17.2, the BE is less than that for the nuclei shown here.

The maximum near $A = 60$ is what makes both *fission* and *fusion* possible sources of energy. A heavy nucleus with A near 240 can split roughly in half, giving two fission products. Since the nucleons in each of the products are more tightly bound on the average than in the original nucleus, energy is released. This energy difference comes almost entirely from the Z^2 dependence of the Coulomb repulsion of the protons in the nuclei. In fusion, two nuclei of very low A combine to give a nucleus of higher A, for which the BE per nucleon is greater.

17.2 Nuclear Decay: Decay Rate and Half-Life

If a nucleus has more energy than it would if it were in its ground state, it can decay. If the nucleus has sufficient energy, it can emit a proton, neutron, or cluster of nucleons [α particle ($^4_2$He), deuteron ($^2_1$H), etc.]. When a nucleus has enough excitation energy to decay by nuclear emission it usually does so in such an extremely short time that the nuclei could never be introduced in the body after they were produced. An exception is the α decay of a few elements near the upper (high-Z) end of the periodic table. They are found in nature, either because their lifetimes are very long or because they are formed as the result of some other decay process that has a long lifetime.

If a nucleus has just a small amount of excess energy, it emits a γ *ray*, a photon analogous to the x-ray or visible photons emitted by an excited atom. Another process that can occur is the emission of a positive or negative electron, with the conversion of a proton to a neutron, or vice versa. This is called β *decay*. γ and β decay will be described in detail in the next two sections.

Each excited nucleus will decay or undergo a *nuclear transformation*. There can be several *transitions* associated with each transformation. For example, there might be a cascade of two or more successive gamma rays (γ_1 and γ_2 of Fig. 17.4), or competing pathways (branching) (γ_1, γ_3, β_2^-, γ_1 of Fig. 17.4).

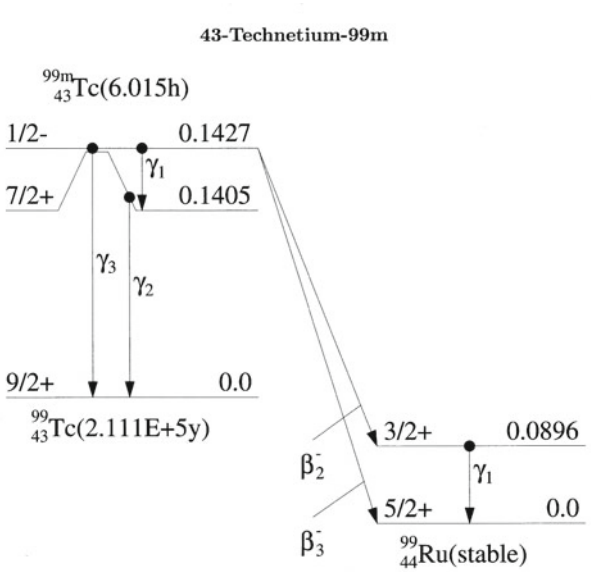
An excited nucleus has a probability λdt of transforming in time dt. When there are N nuclei present, the average number decaying in time dt is[1]

$$-dN = N\lambda\, dt.$$

This leads to the familiar exponential decay of Chap. 2:

$$N = N_0 e^{-\lambda t}.$$

[1] The decay constant is called λ in this chapter to conform to the usage in nuclear medicine.



$T_{1/2} = 6.015$ h — Decay Modes: β^- IT

Radiation	$Y(i)$ (Bq s)$^{-1}$	$E(i)$ MeV	$\Delta(i)$ Gy kg (Bq s)$^{-1}$
ce-M, γ-ray 1	8.62E−01	1.748E−03†	2.42E−16
ce-N$^+$, γ-ray 1	1.30E−01	2.173E−03†	4.52E−17
γ-ray 2	8.91E−01	1.405E−01	2.00E−14
ce-K, γ-ray 2	8.92E−02	1.195E−01	1.71E−15
ce-L$_1$, γ-ray 2	9.89E−03	1.375E−01	2.18E−16
ce-L$_2$, γ-ray 2	6.46E−04	1.377E−01	1.42E−17
ce-L$_3$, γ-ray 2	3.37E−04	1.378E−01	7.45E−18
ce-M, γ-ray 2	1.99E−03	1.401E−01†	4.47E−17
ce-N$^+$, γ-ray 2	3.80E−04	1.405E−01†	8.56E−18
ce-K, γ-ray 3	5.50E−03	1.216E−01	1.07E−16
ce-L$_1$, γ-ray 3	9.48E−04	1.396E−01	2.11E−17
ce-L$_2$, γ-ray 3	1.98E−04	1.398E−01	4.44E−18
ce-L$_3$, γ-ray 3	6.08E−04	1.400E−01	1.36E−17
ce-M, γ-ray 3	3.48E−04	1.422E−01†	7.93E−18
K - L$_2$ x-ray	2.14E−02	1.821E−02	6.23E−17
K - L$_3$ x-ray	4.06E−02	1.833E−02	1.19E−16
K - M$_3$ x-ray	6.53E−03	2.059E−02	2.16E−17
Auger KLL	1.48E−02	1.542E−02†	3.65E−17
Auger KLX	5.59E−03	1.782E−02†	1.60E−17
Auger LMM	9.03E−02	2.054E−03†	2.98E−17
Auger LMX	1.41E−02	2.333E−03†	5.26E−18
CK MMX	7.09E−01	1.142E−04†	1.30E−17
Auger MNN	1.08E+00	2.061E−04†	3.57E−17
CK NNX	2.47E+00	2.961E−05†	1.17E−17

Fig. 17.4 Energy levels and decay data for the isotope ^{99m}Tc. The various features are discussed in the text. (These results were originally published in Eckerman and Endo 2008, p. 232. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.)

The *activity*, $A(t)$, is the number of decays per second:

$$A(t) = \left|\frac{dN}{dt}\right| = \lambda N.$$

The activity is measured in nuclear transformations per second or becquerel (Bq). The total number of transformations or *cumulated activity* is measured in bequerel seconds (Bq s).

The half-life $T_{1/2}$ is related to λ by Eq. 2.10:

$$T_{1/2} = \frac{0.693}{\lambda}. \tag{17.8}$$

17.3 Gamma Decay and Internal Conversion

When a nucleus is in an excited state, it can lose energy by photon emission. The energy levels of the nucleus are characterized by certain quantum numbers, and γ emission is subject to selection rules analogous to those for x-ray emission by atoms. Half-lives for γ emission range from 10^{-20} to 10^{+8} s.

Figure 17.4 shows an energy level diagram for $^{99}_{43}$Tc (technetium), an isotope widely used in nuclear medicine, along with some tabular material that we will need as we progress through this chapter. First, look at the energy level diagram. There are two important levels to consider in $^{99}_{43}$Tc. The ground state is not stable but decays by β^- decay, considered in Sect. 17.5. However, its decay rate is so small (half-life of 2.111×10^5 years) that we can ignore its decay. There is a level at an excitation of 0.1427 MeV above the ground state that has a half-life of 6.015 h for γ decay. This is an unusually long half-life; we call it a *metastable state* and denote it by ^{99m}Tc. We see that there are two modes of gamma decay from this state. The first is the emission of a 0.0022-MeV γ ray (γ_1) followed immediately by a 0.1405-MeV γ_2. The other, less common possibility, is the emission of γ_3 of energy 0.1427 MeV. The ^{99m}Tc can also undergo beta decay, considered in Sect. 17.5.

Whenever a nucleus loses energy by γ decay, there is a competing process called *internal conversion*. The energy to be lost in the transition, E_γ, is transferred directly to a bound electron, which is then ejected with a kinetic energy

$$T = E_\gamma - B, \tag{17.9}$$

where B is the binding energy of the electron.

We now turn to the tabular part of Fig. 17.4. Each line describes a unique transition associated with the nuclear transformation of the ^{99m}Tc.

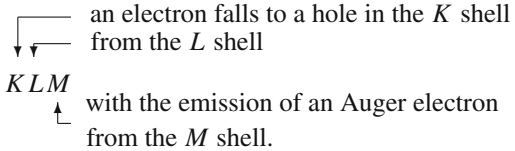
The *mean number per disintegration* $Y(i)$ in the table is the mean number of times that the indicated transition between energy levels takes place per nuclear transformation. (Think Y for yield.)

The first two lines in the table show that the only transitions associated with γ_1 are internal conversion of either an M-shell or N-shell electron (*ce* stands for conversion electron). Gamma-ray 2 is emitted 0.891 times per nuclear transformation, with internal conversion occurring 0.102 times per transformation.

17.4 Atomic Deexcitation

Once internal conversion has created a hole in the electronic structure of the atom, characteristic x rays and Auger and Coster-Kronig (CK) electrons are emitted as described in Sect. 15.9.

Characteristic x ray transitions have labels like K-L_2 x ray. The labels for Auger and CK electrons show this information:



The Auger cascade means that several of these electrons are emitted per transition. If a radionuclide is in a compound that is bound to DNA, the effect of several electrons released in the same place is to cause as much damage per unit dose as high-LET radiation. Linear energy transfer was defined in Chap. 15. A series of reports on this effect have been released by the American Association of Physicists in Medicine (AAPM) (Sastry 1992; Howell 1992; Humm et al. 1994).

Many electrons (up to 25) can be emitted for one nuclear transformation, depending on the decay scheme (Howell 1992). The electron energies vary from a few eV to a few tens of keV. Corresponding electron ranges are from less than 1 nm to 15 μm. The diameter of the DNA double helix is about 2 nm. A number of experiments (reviewed in the AAPM reports, and also in Kassis (2011)) show that when the radioactive substance is in the cytoplasm the cell damage is like that for low-LET radiation in Fig. 15.32 with relative biological effectiveness (RBE) = 1. When it is bound to the DNA, survival curves are much steeper, as with the α particles in Fig. 15.32 (RBE $\approx$ 8). When it is in the nucleus but not bound to DNA the RBE is about 4. The fraction of the Auger emitter that binds to the DNA depends on the chemical agent to which the nuclide is attached. There is also a significant bystander effect (Kassis 2011).

17.5 Beta Decay and Electron Capture

Nuclei that are not on the line of stability in Fig. 17.2 have greater internal energy and are susceptible to some kind of decay. They can lose energy by γ emission. In addition, nuclei above the line of stability have too many protons relative to the number of neutrons; nuclei below the line have relatively too many neutrons.

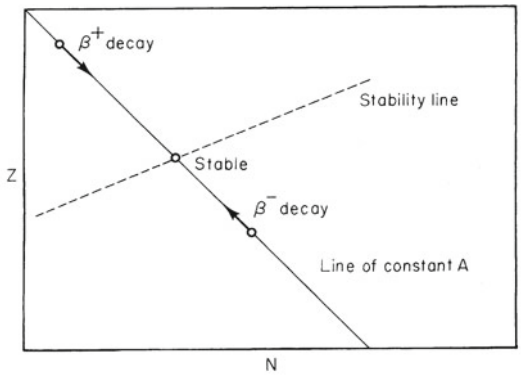


Fig. 17.5 β^- decay and β^+ decay do not change A. They do change N and Z to bring the nucleus closer to the stability line

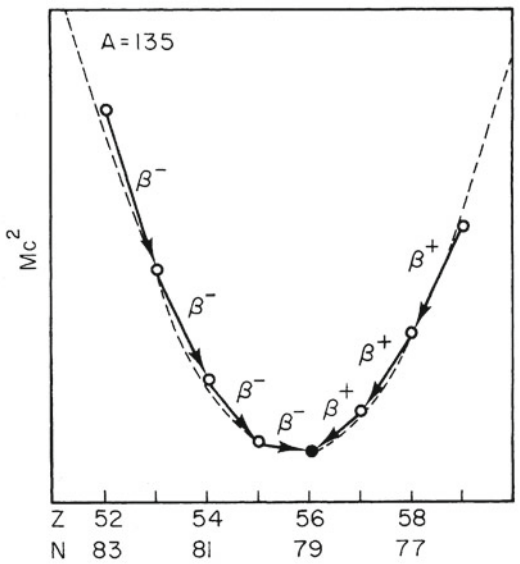


Fig. 17.6 Energy of nuclei as a function of Z for an odd value of A ($A = 135$). The only stable nucleus is $^{135}_{56}$Ba; nuclei of lower Z undergo β^- emission; those of higher Z undergo β^+ emission or electron capture

Two modes of decay allow a nucleus to approach the stable line. In *beta* (β^- or electron) *decay*, a neutron is converted into a proton. This keeps A constant, lowering N by one and raising Z by one. In *positron* (β^+) *decay*, a proton is converted into a neutron. Again A remains unchanged, Z decreases and N increases by 1. We find β^+ decay for nuclei above the line of stability and β^- decay for nuclei below the line. Figure 17.5 shows a portion of the line of stability, a line of constant A ($Z = A - N$), and the regions for β^+ and β^- decay.

We can plot the energy of the neutral atom for different nuclei along the line of constant A. Since there are one or two stable nuclei, there is some value of Z and N for which the

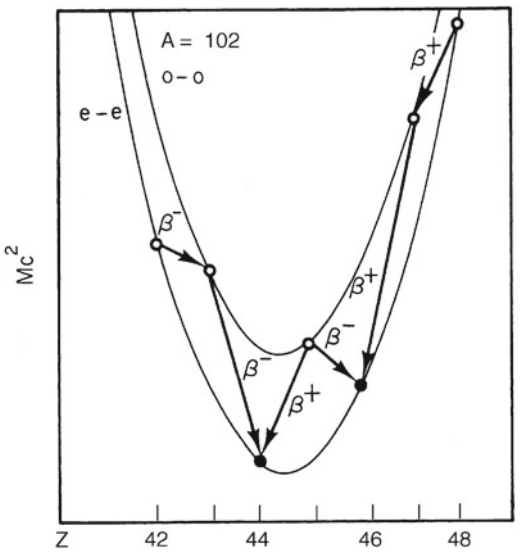


Fig. 17.7 Energy of even-A nuclei ($A = 102$) as a function of Z. Nuclei with an odd number of protons and neutrons have higher energies than those with an even number of each. This makes it possible for the same nucleus to decay by either β^- or β^+ emission

energy is a minimum. The energy increases in either direction from this minimum. The first approximation to a curve with a minimum is a parabola, as shown in Fig. 17.6 for a nucleus of odd A.[2] When Z is too small, a neutron is converted to a proton by β^- decay. If Z is too large, a proton changes to a neutron by β^+ decay or electron capture (to be described below).

When A is odd, there are an even number of protons and an odd number of neutrons (even–odd) or vice versa (odd–even). When we plot the energies of even-A nuclei, we find that the masses lie on two different parabolas (Fig. 17.7). The one for which both Z and N are odd (odd–odd) has greater energy than the parabola for which both are even. The reason is that nucleons have lower energy when they are paired with one another in such a way that their spins are antiparallel. In the even–even case, the neutrons and the protons are all paired off and have this lower energy; in the odd–odd case there are both an unpaired proton and an unpaired neutron, and the energy is higher. As we change Z by one, we jump back and forth between the odd–odd and the even–even parabolas. For odd-A nuclei, either the neutrons are paired and one proton is not, or vice versa. There is always one unpaired nucleon as Z changes, so there is only one parabola.

[2] This parabola and the general behavior of the BE with Z and A can be explained remarkably well by the semiempirical mass formula (Evans 1955, Chap. 11; Eisberg and Resnick 1985, p. 528).

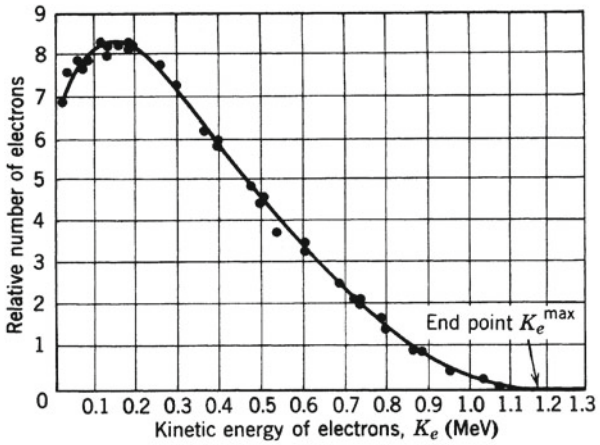


Fig. 17.8 A typical spectrum of β particles. In this case it is for the β decay of $^{210}_{83}$Bi. (From Eisberg and Resnick 1985, p. 566. Copyright ©1985 John Wiley & Sons. Reproduced by permission of John Wiley & Sons)

The existence of the two parabolas means that there are usually (but not always) two stable nuclei with an odd–odd nucleus between them that can decay by either β^- or β^+ emission.

The emission of a β^- particle is accompanied by the emission of a *neutrino* (strictly speaking, an antineutrino):

$$^A_Z X \rightarrow {}^A_{Z+1}Y + \beta^- + \overline{\nu}. \tag{17.10}$$

The neutrino has no charge and no rest mass,[3] so that like a photon, it travels with velocity c and its energy and momentum are related by $E = pc$. Neutrinos hardly interact with matter at all, so they are quite difficult to detect. Nevertheless they have been detected through certain specific nuclear reactions that take place on the rare occasions when a neutrino does interact with a nucleus. A particle that seemed originally to be an invention to conserve energy and angular momentum now has a strong experimental basis.

Suppose that β decay consisted of the ejection of only a β particle. If the original nucleus was at rest,[4] then the final nucleus would recoil in the direction opposite the β particle to conserve momentum; the ratio of its velocity to that of the β particle would be given by their mass ratio. The recoil nucleus and the β particle would each have a definite fraction of the total energy available from the decay, and the β particles would all have the same energy. However, the observed β-particle energy spectrum is not a line spectrum but a continuum ranging from zero to the expected energy, as shown in Fig. 17.8. The missing energy is carried by the neutrino. The different energies correspond to different angles of emission of the neutrino relative to the direction of the β particle. This kind of spectrum is characteristic of three bodies emerging from the reaction.

The total kinetic energy for the three emerging particles is

$$E_{\text{decay}} = m_{Z,A}c^2 - m_{Z+1,A}c^2 - m_e c^2.$$

If we add and subtract $Zm_e c^2$, the result is unchanged:

$$\begin{aligned} E_{\text{decay}} &= (m_{Z,A}c^2 + Zm_e c^2) - (m_{Z+1,A}c^2 \\ &\quad + Zm_e c^2 + m_e c^2) \\ &= M_{Z,A}c^2 - M_{Z+1,A}c^2. \end{aligned} \tag{17.11}$$

The energy released in the decay is given by the difference in rest energies of the initial and final neutral atoms. This energy is shared in different amounts by the three particles; it is shared mainly by the neutrino and electron, since the nucleus is so massive and its kinetic energy is $p^2/2m$. The maximum or end-point energy of the β spectrum in Fig. 17.8 corresponds to E_{decay}.

Figure 17.9 shows data for the decay of ^{24}Na, an isotope that has been used in nuclear medicine. The transition labeled β_3^- is overwhelmingly more common than β_4^-. The β_3^- emission is followed by two γ rays. The average energy of the β_3^- particle is 0.554 MeV, about 40 % of the end-point energy, 1.392 MeV.

Emission of a positron converts a proton into a neutron, and Z decreases by one. A neutrino is also emitted:

$$^A_Z X \rightarrow {}^A_{Z-1}\, Y + \beta^+ + \nu. \tag{17.12}$$

The decay energy is again given by

$$E_{\text{decay}} = m_{Z,A}c^2 - m_{Z-1,A}c^2 - m_e c^2.$$

However, this time, when we add $Zm_e c^2$ to the first term and subtract $(Z-1)m_e c^2$ from the second term to convert these to atomic masses, the electron masses do not cancel. Instead, we get

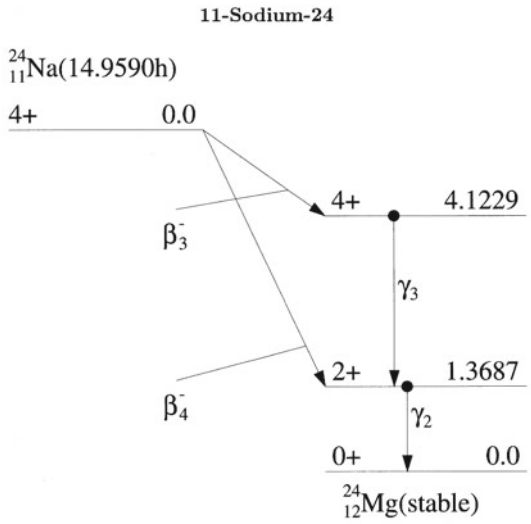
$$E_{\text{decay}} = M_{Z,A}c^2 - M_{Z-1,A}c^2 - 2m_e c^2. \tag{17.13}$$

Positron emission will not occur unless the initial neutral atomic mass exceeds the final neutral atomic mass by at least $2m_e c^2$.

Figure 17.10 shows the decay scheme for ^{18}F, which decays primarily by positron emission, with an average positron energy of 0.2498 MeV. The decay line in the energy level diagram is labelled EC$_1$, β_1^+. EC stands for *electron capture*, a process that competes with beta decay. Some of the inner electrons of the atom are close enough to the nucleus (quantum mechanically, the electron wave functions overlap the nucleus enough) so that the electron is captured by the nucleus, and a neutrino is emitted. In terms of nuclear

[3] Recent measurements indicate that the neutrino does have a rest mass, but it is too small to affect our argument.

[4] Its thermal energy of about $\frac{1}{40}$ eV is negligible compared to the energy released in decay.

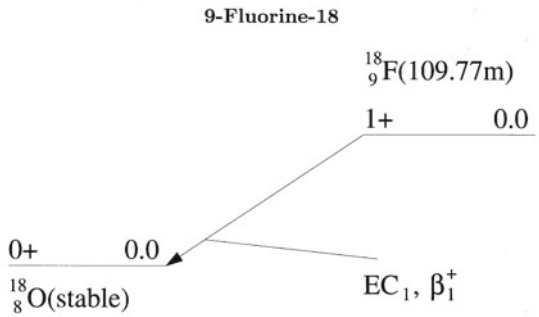


$T_{1/2}$ = 14.959 h — Decay Mode: β^-

Radiation	$Y(i)$ (Bq s)$^{-1}$	$E(i)$ MeV	$\Delta(i)$ Gy kg (Bq s)$^{-1}$
β^- 3	9.99E−01	5.540E−01†	8.88E−14
γ-ray 2	1.00E+00	1.369E+00	2.20E−13
γ-ray 3	9.99E−01	2.754E+00	4.41E−13
Listed X, γ and $\gamma\pm$ radiation			6.60E−13
Neglected X, γ and $\gamma\pm$ radiation‡			3.33E−16
Listed β and ce			8.88E−14
Neglected β and ce‡			2.11E−17
Listed radiations			7.48E−13
Neglected radiations‡			3.54E−16

†Average energy.
‡Each omitted transition contributes < 0.10% to $\Sigma\Delta(i)$.
Magnesium-24 daughter, yield of 1.0, is stable.

Fig. 17.9 Energy levels and data for the β decay of ^{24}Na. (These results were originally published in Eckerman and Endo 2008, p. 56. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.)



$T_{1/2}$ = 109.77 m — Decay Modes: EC β^+

Radiation	$Y(i)$ (Bq s)$^{-1}$	$E(i)$ MeV	$\Delta(i)$ Gy kg (Bq s)$^{-1}$
β^+ 1	9.67E−01	2.498E−01†	3.88E−14
$\gamma\pm$	1.93E+00	5.110E−01	1.58E−13
Listed X, γ and $\gamma\pm$ radiation			1.58E−13
Listed β and ce			3.88E−14
Listed radiations			1.97E−13

†Average energy.
Oxygen-18 daughter, yield of 1.0, is stable.

Fig. 17.10 Energy levels and data for the β^+ decay of ^{18}F. (These results were originally published in Eckerman and Endo 2008, p. 52. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.)

masses, an electron rest energy is added to the parent nucleus (we ignore its kinetic energy):

$$E_{\text{e.c.}} = m_e c^2 + m_{Z,A}c^2 - m_{Z-1,A}c^2.$$

If we add and subtract $(Z-1)m_e c^2$, we have

$$E_{\text{e.c.}} = M_{Z,A}c^2 - M_{Z-1,A}c^2. \tag{17.14}$$

A K electron is usually captured. The energy from the nuclear transition is given to a neutrino. No electron or positron emerges from the nucleus, but there are K x rays and Auger electrons, as there are any time a vacancy in the K shell occurs, and these contribute to the radiation dose. Electron capture and positron emission can both occur in proton-rich isotopes. In the case of ^{18}F (and many other low-atomic-number isotopes) the decay is mainly by positron emission, with relatively little electron capture. In many heavier nuclei, electron capture dominates over positron emission. For instance, ^{125}I decays by electron capture, and the resulting cascade of Auger electrons makes a significant contribution to the dose.

The second entry, labeled $\gamma_\pm$, stands for *annihilation radiation*. Once a positron has been emitted, it slows down like any other charged particle. At some point it combines with an electron (since the positron and electron constitute a particle–antiparticle pair), and all of the rest energy of both particles goes into two photons.[5] The energy conservation equation is

$$2m_e c^2 = 2h\nu. \tag{17.15}$$

For each original positron emitted, two photons are produced, each of energy $m_e c^2 = 0.511$ MeV. Note that Y_i for the annihilation gamma rays is twice the value for positron emission.

17.6 Calculating the Absorbed Dose from Radioactive Nuclei within the Body: the MIRD Method

When a radiopharmaceutical is given to a patient for either diagnosis or therapy, the nuclei end up in different organs in varying amounts; for example, ^{99m}Tc-labeled albumin

[5] Three photons are occasionally emitted.

microspheres injected intravenously lodge in the lungs. The problem is to calculate the whole-body absorbed dose, the dose to the lungs, and the dose to other organs.

The dose calculation in this chapter follows the technique and notation recommended by the MIRD Committee of the Society of Nuclear Medicine and Molecular Imaging (Loevinger et al. 1988; ICRU 2002; Stabin et al. 2005; Stabin 2008; Bolch et al. 2009). It is carried out in the following way:

1. Calculate the total number of nuclear transformations or disintegrations in organ h. It is called the *cumulated activity* $\tilde{A}_h$ or N_h.
2. Calculate the mean energy emitted per unit cumulated activity for each type of photon or particle emitted.
   a) If the radioactive nucleus can emit several types of particles or photons per transformation, call Y_i the mean number of particles or photons of type i (transitions) emitted per transformation. These include γ rays, electrons, x rays and Auger electrons. The data are also available in electronic form (Eckerman et al. 1994; Stabin and da Luz 2002; RADAR (the Radiation Group Assessment Resource), www.doseinfo-radar.com; and the National Nuclear Data Center, www.nndc.bnl.gov/mird/).
   b) For each transition i determine E_i, the *mean energy per transition*.
   c) Calculate or look up $\Delta_i = Y_i E_i$, *the mean energy emitted per unit cumulated activity*, for each type of particle or photon emitted. (In earlier MIRD literature, this was called the *equilibrium absorbed dose constant*.)
3. Calculate $\phi_i(r_k \leftarrow r_h)$, the fraction of the radiation of type i emitted in source region r_h that is absorbed in target region r_k, and divide by the mass of the target region to get the *specific absorbed fraction*

$$\Phi_i(r_k \leftarrow r_h) = \frac{\phi_i(r_k \leftarrow r_h)}{m_k}.$$

   (Φ has the units of inverse mass.)
4. The *mean absorbed dose* in organ k due to activity in organ h, $\overline{D}$ (in J kg^{-1} or Gy) is

$$\overline{D}(r_k \leftarrow r_h) = \tilde{A}_h \sum_i \Delta_i \Phi_i(r_k \leftarrow r_h). \tag{17.16}$$

5. If several organs are radioactive, a sum must be taken over each organ:

$$\overline{D}(r_k) = \sum_h \tilde{A}_h \sum_i \Delta_i \Phi_i(r_k \leftarrow r_h). \tag{17.17}$$

Some tables (Snyder et al. 1976, 1978) give values of Φ_i for photons of various energies. It is necessary to multiply by Δ_i and sum for the isotope of interest. The sum is called the *mean absorbed dose per unit cumulated activity*:

$$S(r_k \leftarrow r_h) = \sum_i \Delta_i \Phi_i(r_k \leftarrow r_h), \tag{17.18}$$

$$\overline{D}(r_k \leftarrow r_h) = \tilde{A}_h S(r_k \leftarrow r_h), \tag{17.19}$$

$$\overline{D}(r_k) = \sum_h \tilde{A}_h S(r_k \leftarrow r_h). \tag{17.20}$$

These sums must be repeated over and over again for common radionuclides. A table of S for many common radionuclides is available (Snyder et al. 1976). The tables cannot be summed over h because the values of $\tilde{A}_h$ depend on how the isotope is administered. A computer program OLINDA/EXM is most commonly used for these calculations (Stabin et al. 2005). These authors call S the *dose factor*.

To discuss units, imagine there is only one type of radiation. In SI units the dose is simply

$$D\ (\text{Gy}) = \left[\tilde{A}\ (\text{dimensionless})\right][\Delta_i\ (\text{J})]\left[\Phi_i\ (\text{kg}^{-1})\right]. \tag{17.21a}$$

In day-to-day calculations, it is often easier to use mixed units and write

$$D\ (\text{Gy}) = k\left(\frac{\text{Gy kg}}{\text{MBq s MeV}}\right)\left[\tilde{A}\ (\text{MBq s})\right] \times [\Delta_i\ (\text{MeV})]\left[\Phi_i\ (\text{kg}^{-1})\right]. \tag{17.21b}$$

The numerical value of k in these units is 1.6×10^{-7}. In an older system of units, where the dose is in rad and the total number of transitions is in microcurie-hour (see below), the equation is

$$D\ (\text{rad}) = \left[\tilde{A}\ (\mu\text{Ci h})\right]\left[\Delta_i\ (\text{g rad}\ \mu\text{Ci}^{-1}\ \text{h}^{-1})\right]\left[\Phi_i\ (\text{g}^{-1})\right]. \tag{17.21c}$$

The next three subsections discuss cumulated activity, the mean energy emitted, and the absorbed fraction of the energy. Then all of these concepts are combined with examples of absorbed dose calculations.

17.6.1 Activity and Cumulated Activity

The activity $A(t)$ is the number of radioactive transitions (or transformations or disintegrations) per second. The SI unit of activity is the *becquerel* (Bq):

$$1\ \text{Bq} = 1\ \text{transition}\ \text{s}^{-1}. \tag{17.22}$$

The earlier unit of activity, which is still used occasionally, is the *curie* (Ci):

$$\begin{aligned} 1\,\text{Ci} &= 3.7 \times 10^{10}\,\text{Bq}, \\ 1\,\mu\text{Ci} &= 3.7 \times 10^{4}\,\text{Bq}. \end{aligned} \tag{17.23}$$

The cumulated activity $\tilde{A}$ is the total number of transitions that take place. The SI unit of cumulated activity is the transition or the Bq s. Both are dimensionless. The old unit of cumulated activity is the μCi h:

$$1\,\mu\text{Ci}\,\text{h} = 1.332 \times 10^{8}\ \text{Bq s}. \tag{17.24}$$

Consider a sample of N_0 radioactive nuclei at time $t = 0$. The total number of nuclei remaining at time t is $N(t) = N_0 e^{-\lambda t}$, and the total activity is $A(t) = \lambda N(t) = A_0 e^{-\lambda t}$. The cumulated activity between times t_1 and t_2 is

$$\begin{aligned} \tilde{A}(t_1, t_2) &= \int_{t_1}^{t_2} A(t)\,dt = \frac{A_0}{\lambda}\left(e^{-\lambda t_1} - e^{-\lambda t_2}\right) \\ &= N(t_1) - N(t_2). \end{aligned} \tag{17.25}$$

If all times are considered, $t_1 = 0$ and $t_2 = \infty$,

$$\tilde{A} = \tilde{A}(0, \infty) = \frac{A_0}{\lambda} = \frac{A_0 T_{1/2}}{0.693} = 1.443 A_0 T_{1/2}. \tag{17.26}$$

This is, as we would expect, N_0.

17.6.1.1 The General Distribution Problem: Residence Time

Suppose that a radioactive substance is introduced in the body by breathing, ingestion, or injection. It may move into and out of many organs before decaying, and it may even leave the body. The details of how it moves depend on the pharmaceutical to which it is attached.

The cumulated activity in organ h is the total number of disintegrations in that organ:

$$N_h = \tilde{A}_h = \int_0^{\infty} A_h(t)\,dt. \tag{17.27}$$

The dose to organ k is then

$$D_k = \textstyle\sum_h N_h S(r_k \leftarrow r_h). \tag{17.28}$$

The units of N_h are disintegrations (dimensionless) or Bq s. If initial activity A_0 (Bq) is administered to the patient, the ratio N_h/A_0 is called the *residence time*[6]

$$\tau_h = \frac{N_h}{A_0} = \frac{\tilde{A}_h}{A_0} = \frac{\tilde{A}_h(0, \infty)}{A_0}. \tag{17.29}$$

[6] Stabin (2008) says that residence time is confusing. He recommends that the ratio $\tilde{A}_h/A_0$ should be called the *normalized cumulative activity* which has units of Bq s per Bq administered.

The residence time is the length of time that activity at a constant rate A_0 would have to reside in the organ to give that cumulated activity. The residence time for a given substance and organ must be determined by measurement, guided by the use of appropriate models. Many residence times have been determined and published. The presence of an abnormality in some organ can drastically alter the residence time.

We now calculate the cumulated activity and residence time for some simple situations.

17.6.1.2 Immediate Uptake with No Biological Excretion

This is the simplest example. A certain fraction of the radiopharmaceutical is taken up very rapidly in some organ, and it stays there. This is a good model for $^{99\text{m}}$Tc–sulfur colloid, which is used for liver imaging. About 85 % is trapped in the liver; the remainder goes to the spleen and elsewhere (Loevinger et al. 1988, p. 23). The activity in the organ is $A_h(t) = A_h e^{-\lambda t}$. [Note the difference between the activity in organ h as a function of time, $A_h(t)$, the initial activity in organ h, A_h, and the cumulated activity in organ h, $N_h = \tilde{A}_h$.] Let the fraction of the activity in the organ be F_h. The cumulated activity is

$$\tilde{A}_h = A_h \int_0^{\infty} e^{-\lambda t}\,dt = \frac{A_h}{\lambda} = \frac{F_h A_0}{\lambda}.$$

The residence time is

$$\tau_h = \frac{\tilde{A}_h}{A_0} = \frac{F_h}{\lambda} = 1.443 F_h T_{1/2}. \tag{17.30}$$

17.6.1.3 Immediate Uptake with Exponential Biological Excretion

Suppose that in addition to physical decay with decay constant λ, the pharmaceutical moves to another organ while it is still radioactive. Such a process can be complicated, perhaps involving storage in the gut or bladder. In other cases, the disappearance from a particular organ may be close to exponential with a biological disappearance constant λ_j. (Assume for now that all the radioactive nuclei can disappear biologically. If some are bound in different chemical forms, this might not be true.) If N is the number of radioactive nuclei in the organ (not the total number originally administered), then the rate of change of N is

$$\frac{dN}{dt} = -(\lambda + \lambda_j)N,$$

the solution to which is $N(t) = N_0 e^{-(\lambda+\lambda_j)t}$. The activity is λN, not $|dN/dt|$. Since it is proportional to N, we can again write

$$A_h(t) = A_h e^{-(\lambda+\lambda_j)t} = \lambda N_0 e^{-(\lambda+\lambda_j)t}. \tag{17.31}$$

Again, $N_0 = A_h/\lambda$. The decay constant $\lambda + \lambda_j$ is larger than the physical decay constant. The effective half-life is

$$(T_j)_{\text{eff}} = \frac{0.693}{\lambda + \lambda_j}. \tag{17.32}$$

In terms of the physical and biological half-lives T and T_j, this is

$$\frac{1}{(T_j)_{\text{eff}}} = \frac{1}{T} + \frac{1}{T_j} \tag{17.33}$$

or

$$(T_j)_{\text{eff}} = \frac{TT_j}{T + T_j}. \tag{17.34}$$

The cumulated activity is

$$\begin{aligned} \tilde{A}_h(t_1, t_2) &= A_h \int_{t_1}^{t_2} e^{-(\lambda+\lambda_j)t}\, dt \\ &= \frac{A_h}{\lambda + \lambda_j} \left(e^{-(\lambda+\lambda_j)t_1} - e^{-(\lambda+\lambda_j)t_2}\right). \end{aligned} \tag{17.35}$$

The cumulated activity for all time is

$$\tilde{A}_h = \frac{A_h}{\lambda + \lambda_j} = 1.443\,(T_j)_{\text{eff}}\, A_h. \tag{17.36}$$

17.6.1.4 Immediate Uptake Moving through Two Compartments

Consider the simplest two-compartment model. A total of N_0 nuclei are administered that move immediately to the first compartment. They then move exponentially from the first compartment to the second but do not move back. The number in the first compartment is given by

$$\frac{dN_1}{dt} = -(\lambda_1 + \lambda)N_1. \tag{17.37}$$

The radioactive decay constant is λ and the biological disappearance rate is λ_1. In compartment 2, the substance enters from compartment 1 and is biologically removed with constant λ_2:

$$\frac{dN_2}{dt} = +\lambda_1 N_1 - (\lambda + \lambda_2)N_2. \tag{17.38}$$

Suppose we start with no nuclei in either compartment and inject N_0 nuclei in compartment 1 at $t = 0$. Then one can show (see Problem 13) that

$$N_1(t) = N_0 e^{-(\lambda+\lambda_1)t} \tag{17.39}$$

so

$$\frac{dN_2}{dt} = \lambda_1 N_0 e^{-(\lambda+\lambda_1)t} - (\lambda + \lambda_2)N_2, \tag{17.40}$$

the solution to which is

$$N_2(t) = N_0 \frac{\lambda_1}{\lambda_1 - \lambda_2} \left(e^{-(\lambda+\lambda_2)t} - e^{-(\lambda+\lambda_1)t}\right). \tag{17.41}$$

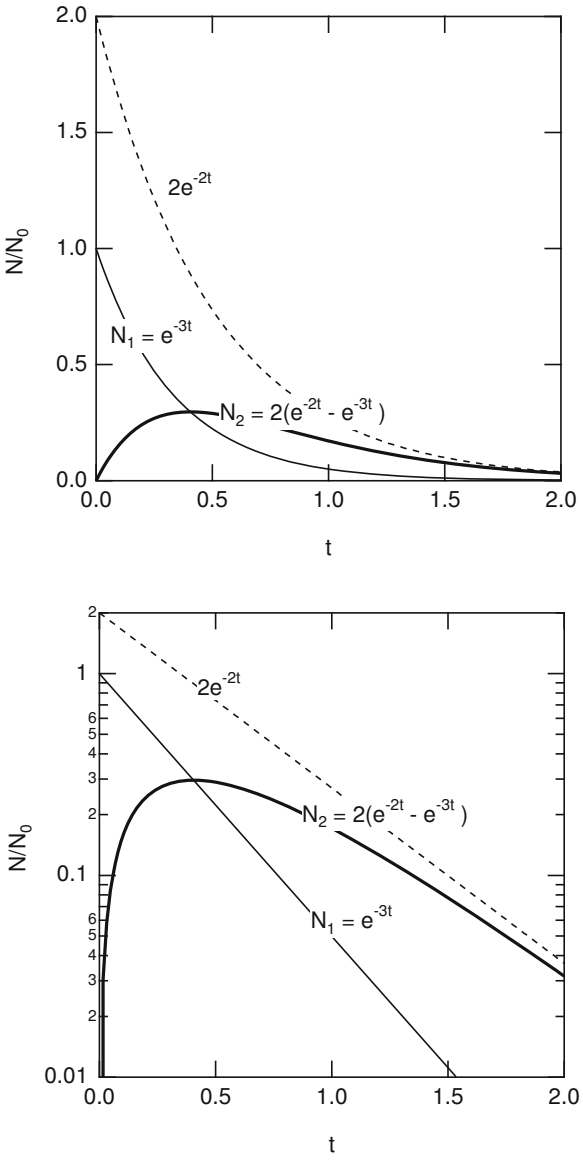


Fig. 17.11 An example of two-compartment transfer when $\lambda = 1$, $\lambda_1 = 2$, and $\lambda_2 = 1$

These solutions are worth examining. They are plotted in Fig. 17.11 for $\lambda = 1$, $\lambda_1 = 2$, and $\lambda_2 = 1$. The number of nuclei in compartment 1 is $N_0 e^{-3t}$. At first, many of the particles leaving compartment 1 enter compartment 2, and N_2 rises. When there is no more of the substance entering the second compartment from the first, N_2 decays at a rate $\lambda + \lambda_2 = 2$. This corresponds to the vanishing of the second term in Eq. 17.41. The larger the value of λ_1, the faster the second term vanishes. For very large values of λ_1, the second term vanishes quickly, the factor $\lambda_1/(\lambda_1 - \lambda_2)$ approaches unity, and the decay is nearly $N_2(t) = N_0 e^{-(\lambda+\lambda_2)t}$. The case

$\lambda_1 = \lambda_2$ is discussed in Problem 15. The activities are

$$A_1(t) = \lambda N_1(t), \qquad A_2(t) = \lambda N_2(t)$$

and the cumulated activities are obtained by integration:

$$\begin{aligned} \tilde{A}_1 &= \frac{A_0}{\lambda + \lambda_1}, \\ \tilde{A}_2 &= \frac{A_0 \lambda_1}{(\lambda + \lambda_1)(\lambda + \lambda_2)}. \end{aligned} \tag{17.42}$$

The residence times are

$$\begin{aligned} \tau_1 &= \frac{1}{\lambda + \lambda_1}, \\ \tau_2 &= \frac{\lambda_1}{(\lambda + \lambda_1)(\lambda + \lambda_2)}. \end{aligned} \tag{17.43}$$

17.6.1.5 More Complicated Situations

A number of more complicated situations are solved by Loevinger et al. (1988). These include situations where substances move between compartments in both directions, the experimental data for the activity have been fit with a series of exponentials, and convolution techniques are used. All of these cases are for isotopes and pharmaceuticals used in clinical practice.

17.6.1.6 Activity per Unit Mass

It is sometimes convenient to use the *mean initial activity per unit mass*

$$C_h = \frac{A_h}{m_h} \,\mathrm{Bq\,kg^{-1}} \tag{17.44}$$

and the *cumulated mean activity per unit mass*

$$\tilde{C}_h = \frac{\tilde{A}_h}{m_h} = \frac{\tau_h A_0}{m_h} \,\mathrm{kg^{-1}}. \tag{17.45}$$

Earlier units for these were $\mu\mathrm{Ci\,g^{-1}}$ and $\mu\mathrm{Ci\,h\,g^{-1}}$.

17.6.2 Mean Energy Emitted Per Unit Cumulated Activity

The mean energy emitted per unit cumulated activity Δ_i is determined by knowing Y_i and E_i for each particle or photon that is emitted. For a given nuclear transformation, the Y_i and E_i must include all photons (whether γ rays or x rays) and all electrons (betas, internal conversion electrons, and Auger electrons). In SI units,

$$\Delta_i \text{ (in J)} = Y_i E_i \text{ (in J)}. \tag{17.46a}$$

If E_i is expressed in MeV, we must use the conversion factor $1\ \mathrm{MeV} = 1.6 \times 10^{-13}$ J. In the old system of units, there is the conversion factor:

$$\begin{aligned} \Delta_i \ (\mathrm{g\,rad\,\mu Ci^{-1}\,h^{-1}}) &= Y_i E_i \ (\mathrm{MeV}) \\ &\times (3.7 \times 10^4 \,\mathrm{s^{-1}\,\mu Ci^{-1}})(1.6 \times 10^{-13} \,\mathrm{J\,MeV^{-1}}) \\ &\times (10^7 \,\mathrm{erg\,J^{-1}})(3.6 \times 10^3 \,\mathrm{s\,h^{-1}})(10^{-2} \,\mathrm{rad\,g\,erg^{-1}}) \\ \Delta_i &= 2.13 Y_i E_i. \end{aligned} \tag{17.46b}$$

17.6.3 Calculation of the Absorbed Fraction

The remaining part of the dose determination problem is the most difficult: the calculation of $\phi(r_k \leftarrow r_h)$, the fraction of the radiation of a certain type emitted in region r_h that is absorbed in region r_k. A lot has been published on this problem; this section provides only an introduction.

17.6.3.1 Nonpenetrating Radiation

The simplest case is for charged particles or photons of very low energy that lose all their energy after traveling a short distance. If the source volume is much larger than this distance, we can say that the target volume is the same as the source volume:

$$\phi(r_k \leftarrow r_h) = \begin{cases} 0, & r_k \neq r_h \\ 1, & r_k = r_h. \end{cases} \tag{17.47}$$

17.6.3.2 Infinite Source in an Infinite Medium

Suppose that a radioactive source is distributed uniformly throughout a region that is so large that edge effects can be neglected. The activity per unit mass is C, so the total activity is $\tilde{A} = M\tilde{C}$, where M is the mass of the material. The energy released is $\tilde{A}\Delta$. This is absorbed in mass M, so the fractional absorbed energy is 1, as in case 1. The dose is

$$D = \frac{M\tilde{C}\Delta}{M} = \tilde{C}\Delta. \tag{17.48}$$

(This is why Δ used to be called the *equilibrium absorbed dose constant*.)

17.6.3.3 Point Source of Monoenergetic Photons in Empty Space

Another simple case is a point source of monoenergetic photons in empty space. The total amount of energy released by the source is $\tilde{A}\Delta_i$. If the energy of the radiation is E_i, the number of photons is $\tilde{A}\Delta_i/E_i$. At distance r the number per unit area is $\tilde{A}\Delta_i/4\pi r^2 E_i$. If a small amount of substance of

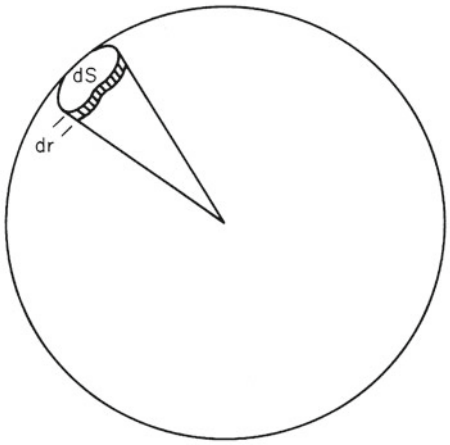


Fig. 17.12 A small volume of absorbing material is introduced at distance r from a point source of γ rays

area dS, density ρ, thickness dr, and energy absorption coefficient μ_{en} is introduced as in Fig. 17.12, the amount of energy absorbed in it is E_i times the number of photons absorbed: $\delta E = \tilde{A}\Delta_i dS\,\mu_{\text{en}} dr/4\pi r^2$. Therefore, the absorbed fraction is

$$\phi = \frac{\delta E}{\tilde{A}\Delta_i} = \frac{\mu_{\text{en}}\, dr\, dS}{4\pi r^2}. \tag{17.49}$$

This is exactly what we expect from the definition of ϕ. If the source radiates its energy isotropically, the fraction passing through dS is $dS/(4\pi r^2)$. The fraction of that energy absorbed in dr is $\mu_{\text{en}}\, dr$. The specific absorbed fraction is

$$\Phi = \frac{\phi}{M} = \frac{\phi}{\rho dS dr} = \frac{\mu_{\text{en}}}{4\pi r^2 \rho}. \tag{17.50}$$

17.6.3.4 Point Source of Monoenergetic Photons in an Infinite Isotropic Absorber

If the source is not in empty space but in an infinite, homogeneous, isotropic absorbing medium, the number of photons at distance r from the source is modified by the factor $e^{-\mu_{\text{atten}} r} B(r)$, where the *buildup factor* $B(r)$ accounts for secondary photons. Therefore,

$$\phi = \frac{\mu_{\text{en}}\, dr\, dS\, e^{-\mu_{\text{atten}} r}}{4\pi r^2} B(r) \tag{17.51}$$

and

$$\Phi = \frac{\mu_{\text{en}}}{\rho} \frac{e^{-\mu_{\text{atten}} r}}{4\pi r^2} B(r). \tag{17.52}$$

See also Sect. 15.17. The buildup factor has been tabulated for photons of various energies in water (Berger 1968).

17.6.3.5 More Complicated Cases—the MIRD Tables

For more realistic geometries, the calculation of ϕ is quite complicated. Tables for humans of average build have been prepared by the MIRD Committee (Snyder et al. 1975, 1976, 1978) . A *Monte Carlo* computer calculation was used. The description below shows how it works in principle; the actual calculations, though equivalent, are different in detail to save computer time. The radioactive nuclei are assumed to be distributed uniformly throughout the source organ. A point within the source organ is picked. The model emits a photon of energy E in some direction, picked at random from all possible directions. This photon is followed along its path; for every element ds of its path, the probability of its interacting, $\mu_{\text{atten}} ds$, is calculated. The computer program then "flips a coin" with this probability of having heads. If a head occurs, the photon is considered to interact at that point. If the interaction is Compton scattering, the angle is picked at random with a relative probability given by the differential cross section. The energy of a recoil electron for that scattering angle is calculated and deposited at the interaction site. Similar procedures are followed for the photoelectric effect and pair production. The scattered photon is then followed in the same way. If a tail occurred on the first flip, the photon is allowed to travel another distance ds and the probability of interaction is again calculated. This procedure is repeated until all the energy has been absorbed.

To determine what kind of material the photons are traveling through, a model of the body called a *phantom* is used. An example of a phantom is shown in Fig. 17.13.

This entire procedure is repeated many times for each organ, until one has a map of the radiation deposited in all organs by γ rays leaving that point in the source organ. The procedure is described in much greater detail by Snyder et al. (1976). Table 17.2 shows a portion of a table for ϕ. A computer code (OLINDA/EXM) is usually used to make the calculations (Stabin et al. 2005). Recently 3-d imaging has made it possible to make patient-specific dose calculations (Dewaraja et al. 2012).

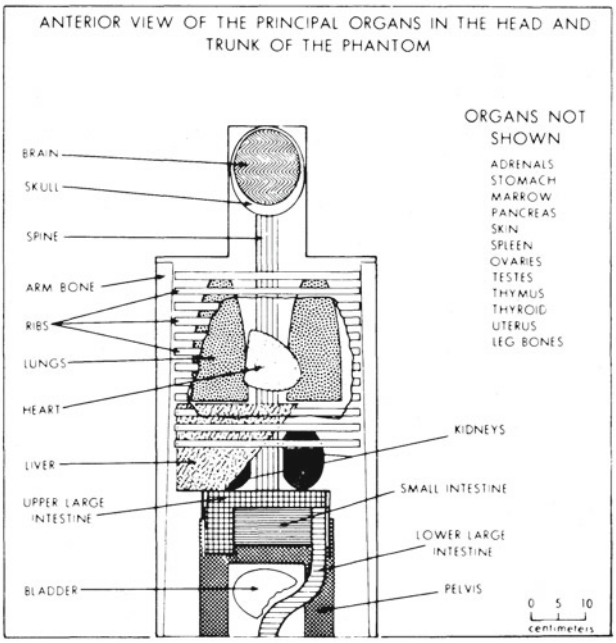
Arqueros and Montesinos (2003) provide a pedagogical discussion of Monte Carlo simulation of γ-ray transport. A pedagogical program for whole-body Monte Carlo calculations has been developed by Hunt et al. (2004). It is available through the RADAR (Radiation Dose Assessment Resource) web site: www.doseinfo-radar.com.

Often most of the isotope is taken up in one or two organs, and the rest of it distributes fairly uniformly through the rest of the body. Using the subscript h for the organs with the greatest activity, TB to mean total body, and RB to mean the rest of the body,

$$\tilde{A}_{\text{RB}} = \tilde{A}_{\text{TB}} - \textstyle\sum_h \tilde{A}_h. \tag{17.53}$$

The dose is then

$$D_k = \textstyle\sum_h \tilde{A}_h S(r_k \leftarrow r_h) + \tilde{A}_{\text{RB}} S(r_k \leftarrow \text{RB}). \tag{17.54}$$



(a)

HEART

The heart is half an ellipsoid capped by a hemisphere which is cut by a plane. A rotation and translation are then effected. The heart (Fig. 4) is represented by

$$x_1 = 0.6943\,(x + 1) - 0.3237\,(y + 3) - 0.6428\,(z - 51),$$

$$y_1 = 0.4226\,(x + 1) + 0.9063\,(y + 3),$$

$$z_1 = 0.5826\,(x + 1) - 0.2717\,(y + 3) + 0.7660\,(z - 51),$$

$$\left(\frac{x_1}{8}\right)^2 + \left(\frac{y_1}{5}\right)^2 + \left(\frac{z_1}{5}\right)^2 \leqq 1,$$

$$x_1^2 + y_1^2 + z_1^2 \leqq (5)^2 \quad \text{if} \quad x_1 < 0,$$

$$\frac{x_1}{3} + \frac{z_1}{5} \geqq -1 \quad \text{if} \quad x_1 < 0$$

and has a volume of 603.1 cm^3.

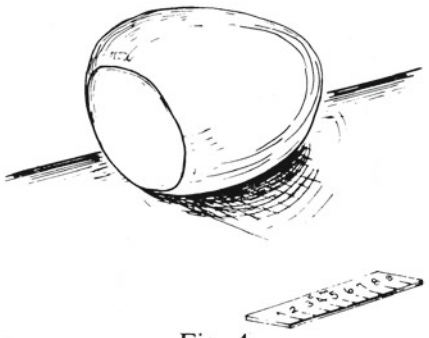


Fig. 4

(b)

Fig. 17.13 An early phantom used by the MIRD Committee for calculations of the absorbed fraction. **a** A view of the whole body. **b** Details of the heart boundaries. (Reprinted by permission of the Society of Nuclear Medicine and Molecular Imaging from W. S. Snyder, M. R. Ford, G. G. Warner, and H. L. Fisher. MIRD Pamphlet No. 5. Estimates of Absorbed Fractions for Monoenergetic Photon Sources Uniformly Distributed in Various Organs of a Heterogeneous Phantom. *J Nucl Med* 1969; **10** (Suppl. 3): 5–52, Figs. 4 and 5)

The quantity $S(r_k \leftarrow \mathrm{RB})$ cannot easily be tabulated, since it depends on what organs are included in the sum over h. Substituting the tabulated quantity $S(r_k \leftarrow \mathrm{TB})$ introduces errors because the "hot" organs that have significant activity are included a second time. One solution to this problem is to modify the cumulated activities (Coffey and Watson 1979). First, define a uniform total body cumulated activity that has the same cumulated activity per unit mass as the rest of the body:

$$\tilde{A}_u = \frac{m_{\mathrm{TB}}}{m_{\mathrm{RB}}} \tilde{A}_{\mathrm{RB}}. \tag{17.55}$$

This activity in the total body would give a dose

$$D_k = \tilde{A}_u S(r_k \leftarrow \mathrm{TB}).$$

Table 17.2 Absorbed fractions for a uniform source of ^{99m}Tc in the lungs, calculated using the tables in Snyder et al. (1976)

Target organ	ϕ
Adrenals	1.39×10^{-4}
Bladder	8.83×10^{-5}
GI(stomach)	2.58×10^{-3}
GI(SI)	1.46×10^{-3}
GI(ULI)	4.49×10^{-4}
GI(LLI)	7.02×10^{-5}
Heart	1.35×10^{-2}
Kidneys	9.14×10^{-4}
Liver	1.66×10^{-2}
Lungs	4.95×10^{-2}
Marrow	2.16×10^{-2}
Pancreas	5.35×10^{-4}
Skeleton (rib)	2.03×10^{-2}
Skeleton (pelvis)	4.21×10^{-4}
Skeleton (spine)	7.59×10^{-3}
Skeleton(skull)	1.11×10^{-3}
Skeleton (total)	5.21×10^{-2}
Skin	5.43×10^{-3}
Spleen	1.46×10^{-3}
Thyroid	4.14×10^{-5}
Uterus	1.55×10^{-5}
Trunk	3.71×10^{-1}
Legs	4.05×10^{-4}
Head	7.70×10^{-3}
Total body	3.79×10^{-1}

Then define for each organ of interest the quantity $\tilde{A}_h^*$, which is the difference between the actual activity in organ h and that assuming the substance is uniformly distributed in the total body:

$$\tilde{A}_h^* = \tilde{A}_h - \frac{m_h}{m_{\text{RB}}}\tilde{A}_{\text{RB}}. \tag{17.56}$$

Then the dose to organ k is

$$D_k = \sum_h \tilde{A}_h^* S(r_k \leftarrow r_h) + \tilde{A}_u S(r_k \leftarrow \text{TB}). \tag{17.57}$$

Problem 31 shows that Eqs. 17.55–17.57 are consistent with Eqs. 17.53 and 17.54 if

$$\frac{m_{\text{RB}}}{m_{\text{TB}}} S(r_k \leftarrow \text{RB}) + \sum_h \frac{m_h}{m_{\text{TB}}} S(r_k \leftarrow r_h) = S(r_k \leftarrow \text{TB}), \tag{17.58}$$

which is consistent with a uniform source $\tilde{A}_u$ distributed throughout the body. The dose can be determined either by calculating the modified activities and using the total body S in Eq. 17.57, or by calculating S for the rest of the body from Eq. 17.58 and using the unmodified activities. Problem 32 shows how these reformulations work in a simple case.

17.6.4 Sample Dose Calculation

We pull this discussion together by making a simplified calculation of the dose to various organs from ^{99m}Tc-labeled microspheres used in a lung scan. We assume that 37 MBq of ^{99m}Tc is injected, that it all lodges in the capillaries of the lung, and that it remains there long enough so that the half-life is the physical half-life.[7] The residence time is then $\tau_h = 1.443 T_{1/2} = (1.443)(6) = 8.658$ h, so the cumulated activity is $\tilde{A}_{\text{lung}} = (3.7 \times 10^7)(8.658 \times 60 \times 60) = 1.153 \times 10^{12}$ Bq s (Table 17.3).

The dose to the lungs is considerably greater than in a chest x ray; however, a chest x ray is almost useless for diagnosing a pulmonary embolus. The whole body dose is not unreasonable.

Table 17.4 shows some typical doses from various nuclear medicine procedures. The effective dose is defined on page 491.

17.7 Radiopharmaceuticals and Tracers

A radioactive nucleus by itself is not very useful. It must usually be attached to some substance that will give it the desired biological properties, for example, to be preferentially absorbed in the region of interest. It must also be prepared in a sterile form, free of toxins that produce a fever (*pyrogens*) so that it can be injected in the patient. This section surveys some of the properties of *radiopharmaceuticals*. Much more detail can be found in Cherry et al. (2012) and Kowalsky and Falen (2011).

The radioactive nuclei used in nuclear medicine are not found in nature. They are produced by bombarding a stable isotope with neutrons (from a nuclear reactor) or protons (from a cyclotron). The bombardment may yield fission fragments or an isotope that is useful as produced. In other cases the isotope produced has a half life that is long enough to ship it to a hospital. Its decay product has a shorter half life and is the isotope used in the pharmaceutical. See Cherry et al. (2012), Chap. 5.

17.7.1 Physical Properties

The half-life must be short enough so that a reasonable fraction of the radioactive decays take place during the diagnostic procedure; any decays taking place later gives the patient a dose that has no benefit. (This requirement can be relaxed if

[7] The last is not a good assumption. The ^{99m}Tc leaches from the microspheres into the general circulation. A more accurate calculation requires measurements and the use of a convolution integral, as described in Loevinger et al. (1988, pp. 79–81). The principal residence times are 4.3 h in the lung, 1.8 h in the extravascular space, 0.83 h in the urine, 0.7 h in the kidney, and 0.6 h in the blood.

Table 17.3 Values of Δ_i, E_i, and ϕ_i for ^{99m}Tc in the lung

i, Line in Fig. 17.4	Δ_i (J)	E_i (keV) (e denotes an electron)	ϕ_i				
			Lung	Heart	Liver	Head	Whole body
1	2.42×10^{-16}	e	1	0	0	0	1
2	4.52×10^{-17}	e	1	0	0	0	1
3	2.00×10^{-14}	140.5	0.0495	0.0135	0.0166	0.0077	0.3785
4	1.71×10^{-15}	e	1	0	0	0	1
5	2.18×10^{-16}	e	1	0	0	0	1
6	1.42×10^{-17}	e	1	0	0	0	1
7	7.45×10^{-18}	e	1	0	0	0	1
8	4.47×10^{-17}	e	1	0	0	0	1
9	8.56×10^{-18}	e	1	0	0	0	1
10	1.07×10^{-16}	e	1	0	0	0	1
11	2.11×10^{-17}	e	1	0	0	0	1
12	4.44×10^{-18}	e	1	0	0	0	1
13	1.36×10^{-17}	e	1	0	0	0	1
14	7.93×10^{-18}	e	1	0	0	0	1
15	6.23×10^{-17}	18.21	1	0	0	0	1
16	1.19×10^{-16}	18.33	1	0	0	0	1
17	2.16×10^{-17}	20.59	1	0	0	0	1
18	3.65×10^{-17}	e	1	0	0	0	1
19	1.60×10^{-17}	e	1	0	0	0	1
20	2.98×10^{-17}	e	1	0	0	0	1
21	5.26×10^{-18}	e	1	0	0	0	1
22	1.30×10^{-17}	0.11	1	0	0	0	1
23	3.57×10^{-17}	e	1	0	0	0	1
24	1.17×10^{-17}	0.029	1	0	0	0	1
$\sum \Delta_i \phi_i$			3.79×10^{-15}	2.70×10^{-16}	3.32×10^{-16}	1.54×10^{-16}	1.04×10^{-14}
m (kg)			0.999	0.603	1.833	5.278	70.036
$S = \sum \Delta_i \phi_i / m$			3.79×10^{-15}	4.48×10^{-16}	1.81×10^{-16}	2.92×10^{-17}	1.48×10^{-16}
Dose (Gy) $A_0 = 37$ MBq			4.37×10^{-3}	5.16×10^{-4}	2.09×10^{-4}	3.36×10^{-5}	1.71×10^{-4}

Table 17.4 Some typical doses for nuclear medicine procedures. (Adapted from Table 9-3 in Zanzonico et al. 1995)

Study and agent	A_0 (MBq)	Organ and highest dose (mSv)		Total body dose (mSv)	Effective dose (mSv)
Bone ^{99m}Tc–pyrophosphate	555	Bladder wall	51	2.0	4.4
Heart ^{201}Tl–chloride	55	Kidneys	20	3.6	13
Liver ^{99m}Tc–sulfur colloid	185	Bladder wall	17	0.9	2.6

the biological excretion is rapid.) On the other hand, the lifetime must be long enough so that the radiopharmaceutical can be prepared and delivered to the patient.

For diagnostic work, the decay scheme should minimize the amount of nonpenetrating radiation. Such radiation provides a dose to the patient but never reaches the detector. This means that there should be as few charged particles (β particles) as possible. The ideal source then is a γ source, which means that the nucleus is in an excited state (an isomer). Such states are usually very short-lived. Not only should the nucleus be a γ emitter, but the internal conversion coefficient should be small, since internal conversion produces nonpenetrating electrons. Positron emitters are more desirable than are β^- emitters because the positrons produce 0.5-MeV radiation that can reach an external detector. For therapy, on the other hand, nonpenetrating radiation is ideal.

It is also necessary that the decay product have no undesirable radiations. If the decay is a β^- or β^+ decay, the product has different chemical properties from the parent and may be taken up selectively by a different organ. If it is also radioactive, this can confuse a diagnosis and give an undesirable dose to the other organ.

Ease of chemical separation of the radioactive substance from whatever carrier it is produced with is also important. It is necessary to remove the radioactive isotope from stable isotopes of the same element, because the chemicals are

usually toxic. This toxicity is avoided by giving the chemical in minute amounts, which can only be done if the specific activity is high.

17.7.2 Biological Properties

For diagnostic work, a pharmaceutical is needed that is taken up more by the diseased tissue to give a *hot spot* or taken up less to give a *cold spot*. The former is easier to see with small amounts of radioactivity, but both techniques are used. For therapy one wishes to have selective absorption of the pharmaceutical so that the radiations will destroy the target organ but not the rest of the body. There are several mechanisms by which a pharmaceutical may be localized.

1. *Active transport.* The drug is concentrated by a specific organ against a concentration gradient. Examples are the selective concentration of iodine in the thyroid, salivary, and gastric glands. (It is rapidly excreted from the last two but is retained in the thyroid). This technique is also effective for certain drugs in the kidney.
2. *Phagocytosis*. Particles in the size range 1–1000 nm may be phagocytized—taken up by specialized cells of the reticuloendothelial system. This can take place in liver, bone marrow, and spleen. Particles of size 1 nm go to the Kupfer cells of the liver and to the marrow, while larger particles (100–1000 nm) are gathered by phagocytes in the liver and spleen.
3. *Sequestration*. Still larger particles, such as red blood cells that have been denatured by heat, are gathered in the spleen or liver by the process called sequestration. The particles are trapped as the blood percolates through the pulp of the spleen and are later phagocytized.
4. *Capillary blockade*. The capillaries have a diameter of 7-10 μm. Particles from 20 to 40 μm diameter injected into a vein will find progressively larger vessels as they work their way through the right heart and will be stopped in the capillaries of the lung.
5. *Diffusion*. It is also possible for a pharmaceutical to move through a membrane to a region of lower concentration. There is a blood–brain barrier between the blood and the central nervous system that is relatively impermeable even to small ions. In a brain scan the chemical is not concentrated in normal brain tissue but leaks into tissue where the blood–brain barrier is compromised by a lesion.
6. *Compartmental localization*. A suitable pharmaceutical injected in the blood may remain there a long time, mixing well and allowing the blood volume to be determined.

The most widely used isotope is ^{99m}Tc. As its name suggests, it does not occur naturally on earth, since it has no stable isotopes. We consider it in some detail to show how an isotope is actually used. Its decay scheme has been discussed above.

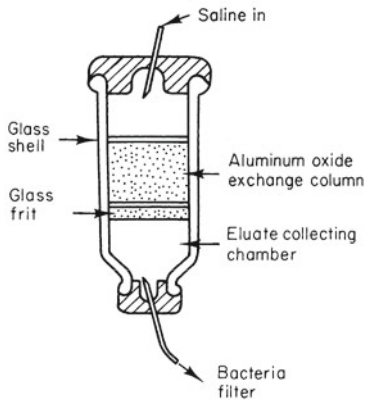


Fig. 17.14 A ^{99}Mo–^{99m}Tc generator system. Molybdenum is trapped in the aluminum oxide layer. Eluant introduced at the top flows through and is collected at the bottom

There is a nearly monoenergetic 140-keV γ ray. Only about 10 % of the energy is in the form of nonpenetrating radiation. The isotope is produced in the hospital from the decay of its parent, ^{99}Mo, which is a fission product of ^{235}U and can be separated from about 75 other fission products. The ^{99}Mo decays to ^{99m}Tc.

Technetium is made available to hospitals through a *generator* that was developed at Brookhaven National Laboratories in 1957 and is easily shipped. Isotope ^{99}Mo, which has a half-life of 67 h, is adsorbed on an alumina substrate in the form of molybdate (MoO_4^{2-}). From 8 to 100 GBq of ^{99}Mo can be provided. The heart of such a generator (without the lead shielding) is shown in Fig. 17.14. As the ^{99}Mo decays, it becomes pertechnetate (TcO_4^-). Sterile isotonic eluting solution is introduced under pressure above the alumina and passes through after filtration into an evacuated eluate container. After removal of the technetium, the continued decay of ^{99}Mo causes the ^{99m}Tc concentration to build up again. A generator lasts about a week.

Several steps must be taken to prepare the pertechnetate as a radiopharmaceutical. First, it must be checked for breakthrough of the ^{99}Mo. The Nuclear Regulatory Commission allows 1.5×10^{-4} Bq of ^{99}Mo per Bq of ^{99m}Tc. The purity is checked by placing the eluate in a lead sleeve that attenuates the ^{99m}Tc γ ray much more than the $\approx$ 750-keV γ rays from ^{99}Mo and measuring the activity. It is also checked with a colorimetric test for the presence of aluminum ion.

The eluate can be used directly for imaging brain, thyroid, salivary gland, urinary bladder, and blood pool, or it can be combined with phosphate, albumin or aggregated albumin, colloidal sulfur, or $FeCl_3$. Commercial kits are available for making these preparations.

For example, kits for labeling aggregated human albumin are commercially available. A vial containing 10 ml of saline solution is enough for ten doses. The aggregated albumin

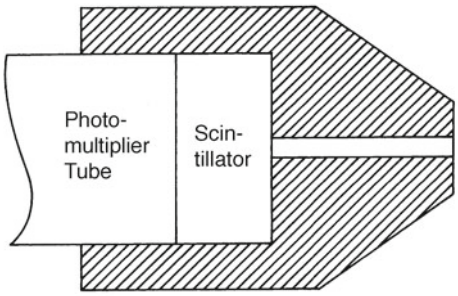


Fig. 17.15 A scintillator with a lead collimator to give directional sensitivity

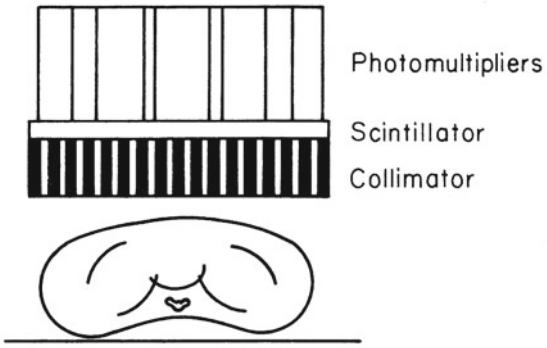


Fig. 17.16 Side view of a scintillation camera. A collimator allows photons from the patient to strike the scintillator directly above the source. An array of photomultiplier tubes records the position and energy of the detected photon

particles are 10–70 μm in diameter. Each milliliter of solution contains $(4 - 8) \times 10^5$ particles. Tin is attached to the microspheres and serves to bind technetium. Up to 10^9 Bq of technetium pertechnetate is added to the vial by the user. A typical adult dose is 10–40 MBq (3.51×10^5 albumin particles). The problems consider attaching Tc to the microspheres and what fraction of the capillaries are blocked by this kind of study.

Other common isotopes are ^{201}Tl, ^{67}Ga, and ^{123}I. Thallium, produced in a cyclotron (see Sect. 8.1), is chemically similar to potassium and is used in heart studies, though it is being replaced by ^{99m}Tc–sestamibi and ^{99m}Tc–tetrofosmin. Gallium is used to image infections and tumors. Iodine is also produced in a cyclotron and is used for thyroid studies. For many more details see Cherry et al. (2012) or Kowalsky and Falen (2011).

17.8 Detectors; The Gamma Camera

Nuclear medicine images do not have the inherent spatial resolution of diagnostic x-ray images; however, they provide functional information: the increase and decrease of activity as the radiopharmaceutical passes through the organ being imaged (Zanzonico 2012).

Early measurements were done with single detectors such as the scintillation detector[8] shown in Fig. 17.15. Directional sensitivity is provided by a collimator, which can be cylindrical or tapered. Single detectors are still used for in vitro measurements and for thyroid uptake studies.

Two-dimensional images can be taken with the *scintillation camera* or *gamma camera* shown in Figs. 17.16 and 17.17. The scintillator is 6–12 mm thick and about 60 cm

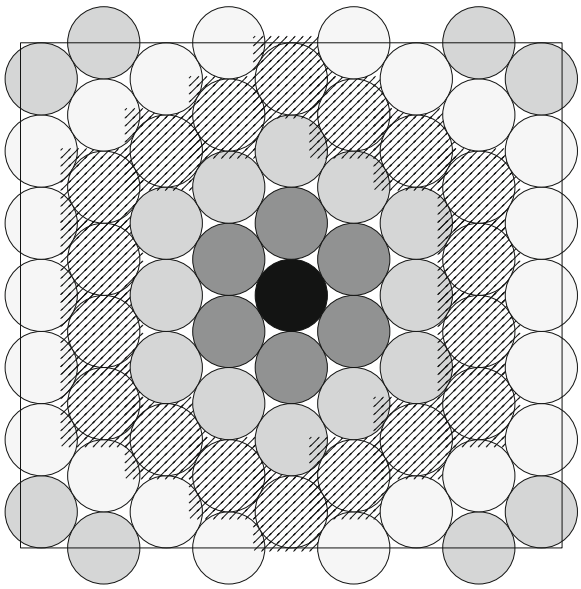


Fig. 17.17 A square scintillator viewed by an array of 67 photomultiplier tubes. The hexagonal arrangement of the tubes above the scintillator gives the closest spacing between tubes

across. Modern scintillators are rectangular. The scintillator is viewed by an array of 50–100 photomultiplier tubes arranged in a hexagonal array. The tube nearest where the photon interacts receives the greatest signal. Signals from each tube are combined to give the total energy signal and x and y position signals.

The collimator is a critical component of the gamma camera. The channels are usually hexagonal, with walls just thick enough to stop most of the photons which do not pass down the collimator opening. The collimator usually has parallel channels. Single pinholes, diverging, and converging channels are sometimes used and can lead to geometric distortions of the image (Cherry et al. 2012). The spatial resolution depends on the distance from the source to the collimator, as

[8] Scintillation detectors were discussed in Sect. 16.3.

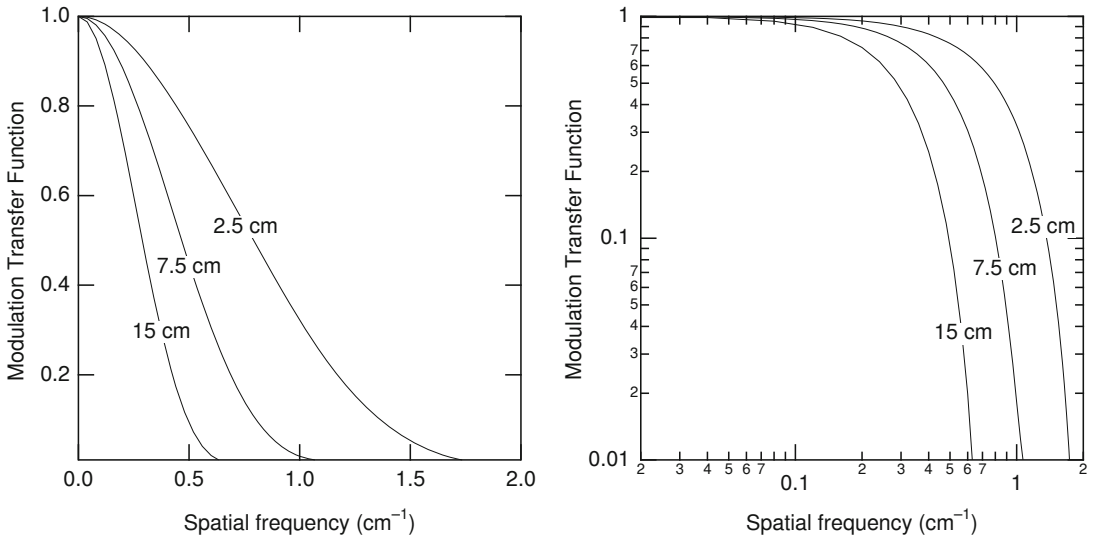


Fig. 17.18 Modulation transfer function curves for a typical parallel-hole collimator for different source-to-collimator distances. Both linear and log-log plots are shown. The source-to-collimator distances are 2.5, 7.5, and 15 cm. (Data are from Erhardt et al. 1978, p. 39)

shown for one collimator in Fig. 17.18. There are trade-offs between sensitivity and resolution (Links and Engdahl 1995). Some of the aspects of collimator design are discussed in Problems 49–51.

Figure 17.19 shows a bone scan of a child taken with a gamma camera. The ^{99m}Tc–diphosphonate is taken up in areas of rapid bone growth. Bone growth at the epiphyses at the end of each bone can be seen. There are also hot spots at the injection site, in one kidney, and in the bladder.

Nuclear medicine can show physiologic function. For example, if the isotope is uniformly distributed in the blood, viewing the heart and synchronizing the data accumulation with the electrocardiogram (gating) allows one to measure blood volume in the heart when it is full and contracted, and to calculate the *ejection fraction*, the fraction of blood in the full left ventricle that is pumped out. Fig. 17.20, shows pictures and contours of the heart at end-systole and end-diastole. The imaging agent was ^{99m}Tc-labeled human red blood cells.

Figure 17.21 shows a series of images taken at six different angles around a patient who has had a lung transplant. The left lung is new and shows considerably more activity than the diseased right lung.

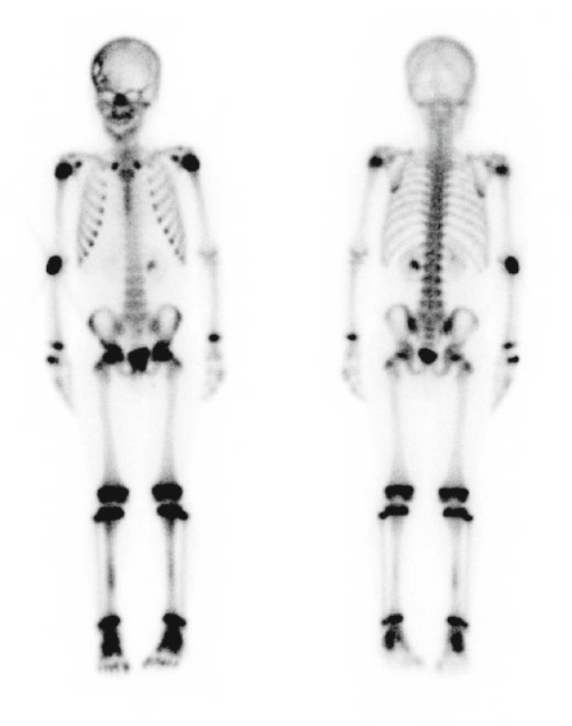


Fig. 17.19 A scintillation camera *bone scan* of a 7-year-old male who received a ^{99m}Tc–diphosphonate injection. An anterior view is on the left, and a posterior view is on the right. The scan shows an area of decreased uptake surrounded by a dark ring in the right anterior skull, consistent with an *eosinophilic granuloma*. Identifiable hot regions are the injection site in the right elbow, an attempted injection site in the right hand, the bladder, and the left kidney, which is probably not remarkable on this exam, along with the ends of the long bones. (Photograph courtesy of B. Hasselquist, Ph.D., Department of Diagnostic Radiology, University of Minnesota)

17.9 Single-Photon Emission Computed Tomography

Still another detection scheme, *single-photon emission computed tomography* (SPECT), is analogous to computed tomography (CT). The detector is sensitive to all radioactivity

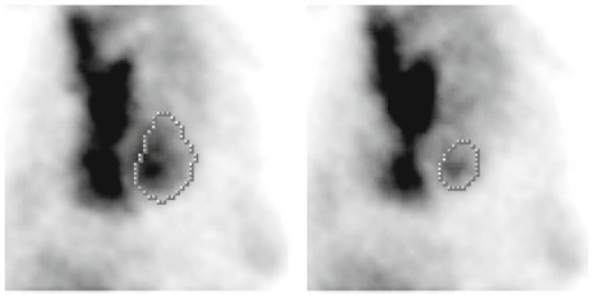


Fig. 17.20 Two gated-scintillation camera views of the heart, imaged with ^{99m}Tc-labeled red blood cells. The dots outline the left ventricle. On the left is end diastole (left ventricle filled with blood). On the right is end systole (left ventricle at smallest volume). The ejection fraction is 66 %. (Photograph courtesy of B. Hasselquist, Ph.D., Department of Diagnostic Radiology, University of Minnesota)

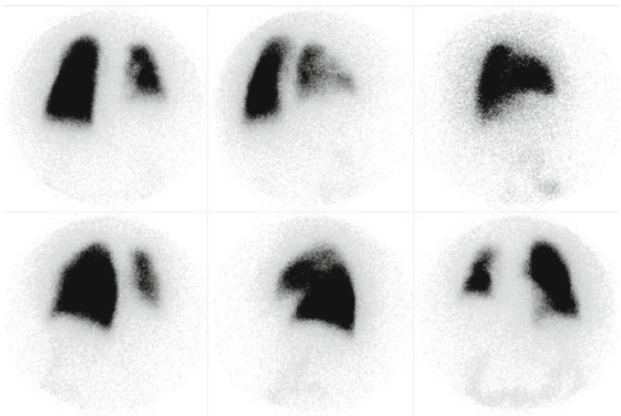


Fig. 17.21 Lung scans of a patient who has received a lung transplant. The upper left is a posterior view; each successive view is rotated about the patient, ending with an anterior view on the lower right. The left lung is the transplant. It has much more activity than the diseased right lung. (Photograph courtesy of B. Hasselquist, Ph.D., Department of Diagnostic Radiology, University of Minnesota)

Fig. 17.22 Single photon emission computed tomographic (SPECT) slices of the heart. The patient was injected with ^{99m}Tc–tetrofosmin, an agent that is taken up by myocardium. The images have been reconstructed in planes parallel to the axis of the heart. The dark myocardium surrounds the blood in the left ventricle. (Photograph courtesy of B. Hasselquist, Ph.D., Department of Diagnostic Radiology, University of Minnesota)

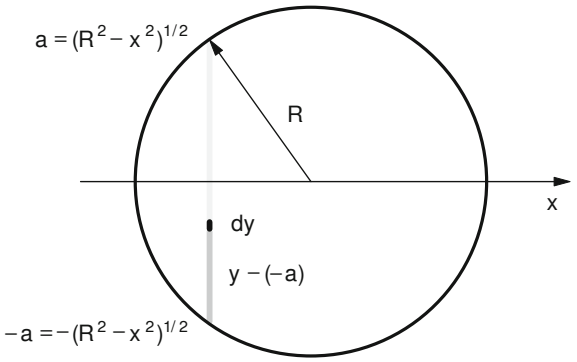


Fig. 17.23 Projection perpendicular to the x axis for a radioactive source of uniform concentration, including the effect of photon attenuation

along a line passing through the patient. The counting rate is thus proportional to a projection through the patient, and a cross-sectional slice can be reconstructed from a series of projections, just as was done with x-ray CT using the techniques in Chap. 12. A series of images like those in Fig. 17.21, but at more angles, are used to reconstruct a three-dimensional image that can then be viewed from any direction, with slices at any desired depth. A SPECT scan is shown in Fig. 17.22. There are five reconstructed slices in planes parallel to the long axis of the heart. The left ventricle is prominent, and the right ventricle can be seen faintly in the last few slices.

One of the problems with SPECT is photon attenuation along the projection line. This is shown in Fig. 17.23 for a cylindrical source with uniform activity throughout. Let A_V be the activity per unit volume, and ignore variations in $1/r^2$. The projection $F(x)$ is

$$F(x) = \int_{-a}^{a} A_V(x, y)\, \Delta x\, \Delta z\, e^{-\mu(y+a)}\, dy, \qquad (17.59)$$

where $dy\, \Delta x\, \Delta z$ is the volume detected. When $A_V(x, y)$ is constant (a uniform activity distribution), this can be integrated to give

$$F = \frac{A_V \Delta x \Delta z}{\mu} \left(1 - e^{-2\mu(R^2 - x^2)^{1/2}}\right). \qquad (17.60)$$

This is plotted in Fig. 17.24 for $\mu = 0$, $\mu = 10\ \mathrm{m}^{-1}$ (511-keV annihilation radiation) and $\mu = 15\ \mathrm{m}^{-1}$ (140-keV ^{99m}Tc). When $\mu = 0$, $F(x) = A_V(2a\Delta x \Delta z)$, where $2a$ is the thickness of the source along the projection. Corrections for attenuation are made in a number of ways.[9] Other nuclides used besides ^{99m}Tc are ^{81m}Kr, ^{133}Xe, ^{131}I, ^{67}Ga, ^{123}I, and ^{201}Tl.

[9] See Cherry et al. (2012), pp. 288–303.

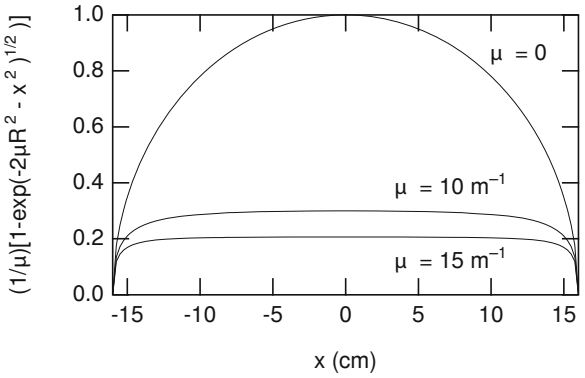


Fig. 17.24 Plot of the projection including attenuation, Eq. 17.60, for $\mu = 0$, $\mu = 10\ \mathrm{m}^{-1}$ (corresponding to 511-keV annihilation radiation) and $\mu = 15\ \mathrm{m}^{-1}$ (corresponding to the photons from ^{99m}Tc). The radius of the circle is 16 cm

More details can be found in Cherry et al. (2012) and Zanzonico (2012).

17.10 Positron Emission Tomography

If a positron emitter is used as the radionuclide, the positron comes to rest and annihilates an electron, emitting two annihilation photons back to back. In *positron emission tomography* (PET) these are detected in coincidence. This simplifies the attenuation correction, because the total attenuation for both photons is the same for all points of emission along each γ ray through the body (see Problem 55); also the photons have a higher energy (511 keV) and lower attenuation coefficient than those used in SPECT. Positron emitters are short-lived, and it is necessary to have a cyclotron for producing them in or near the hospital. This is proving to be less of a problem than initially imagined. Commercial cyclotron facilities deliver isotopes to a number of nearby hospitals. Patterson and Mosley (2005) found that 97 % of the people in the United States live within 75 miles of a clinical PET facility. Muehllehner and Karp (2006) review the history and uses of PET. See also Zanzonico (2004).

We have mentioned that nuclear medicine procedures have the potential to measure function, as the molecules to which the isotopes are bound move from organ to organ in the body. This is particularly true for some of the lighter positron emitters, which have the advantage of being natural constituents of molecules in the body or similar to them (Table 17.5). PET can provide a *functional image* with information about metabolic activity. A very common positron agent is ^{18}F fluorodeoxyglucose—glucose in which a hydroxyl group has been replaced with ^{18}F. The PET signal is largest in those cells that have taken up the ^{18}F because they are actively metabolizing glucose. PET has become particularly important in studies of brain function, where active neurons are detected by an increase in their metabolism, and in locating metastatic cancer. The number of installed PET scanners is growing very rapidly. Most of them have built-in CT scanners to provide accurate fused PET/CT images (Christian and Waterstram-Rich 2012).

Table 17.5 Positron emitters used in nuclear medicine

Nuclide	Half-life
$^{11}_{6}$C	20.3 min
$^{13}_{7}$N	10.0 min
$^{15}_{8}$O	2.1 min
$^{18}_{9}$F	109.7 min

There is great interest in using ^{11}C, in spite of its short (20-min) half life, because it can be incorporated in molecules of biological interest.

A PET scan overlaid on a magnetic resonance (MRI) image is shown in Fig. 17.25 The positron emitter is ^{15}O-labeled water (2.1-min half life). The views are described in the caption. The subject is sequentially touching each finger of the left hand with the thumb. Activity can be seen in the right cerebral sensorimotor cortex (slice, upper right) and in the left cerebellum (slice, lower left). The technique is described by Rehm et al. (1994) and Strother et al. (1995).

17.11 Brachytherapy and Internal Radiotherapy

Brachytherapy (*brachy* means short) involves implanting directly in a tumor sources for which the radiation falls off rapidly with distance because of attenuation, short range, or $1/r^2$. Originally the radioactive sources (seeds) were implanted surgically, resulting in high doses to the operating room personnel. In the *afterloading* technique, developed in the 1960s, hollow catheters are implanted surgically and the sources inserted after the surgery. Remote afterloading, developed in the 1980s, places the sources by remote control, so that only the patient receives a radiation dose.

We saw in Chap. 16 that fractionation of the dose results in better sparing of normal tissue for a given probability of killing the tumor. Afterloading allows the sources to be placed and removed, but it is often difficult for the patient to tolerate the catheters for long periods of time. This has led to the development of *high-dose-rate brachytherapy* (HDR), in which the dose is given in one or a few fractions over the course of a day or two (Nag 1994). Though this is much easier for the patient, tissue sparing is not as great as with

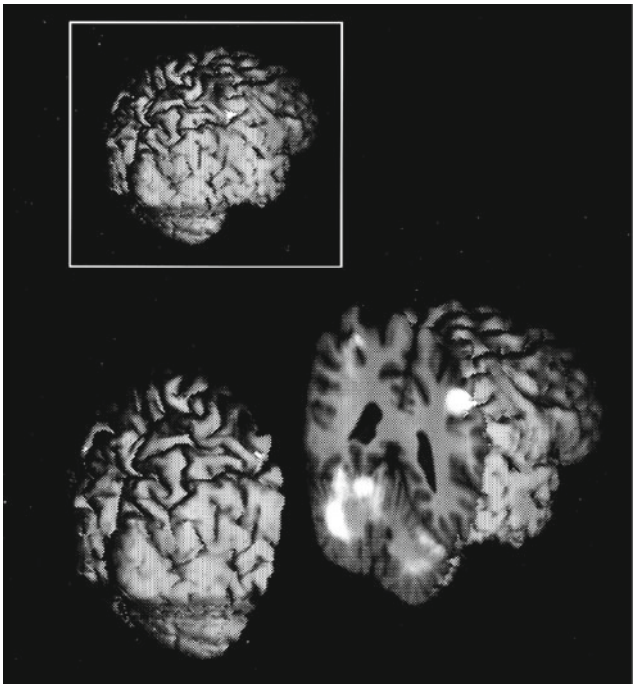


Fig. 17.25 A positron emission tomography (*PET*) scan is overlayed on an MR image. At the upper left is a three dimensional MRI of the brain viewed from above and to the right. At the bottom the image has been sliced through the motor strip and cerebellum, and the two pieces are separated. The PET image has been overlaid on the slice. The positron emitter is ^{15}O-labeled water. The subject is sequentially touching each finger of the left hand with the thumb. Activity can be seen in the right cerebral sensorimotor cortex (slice, upper right) and in the left cerebellum (slice, lower left). (Image courtesy of Prof. Kelly Rehm, University of Minnesota and the PET Imaging Service, Veterans Administration Medical Center, Minneapolis)

a longer treatment. Current practice seeks to compensate for this by meticulous treatment planning based on an extended version of the linear-quadratic model, and by making sure that the tumor receives much higher doses than the surrounding normal tissue.

Radium was the first brachytherapy source, but it has been replaced by a number of nuclei that decay by β^- emission or electron capture. One common source is ^{137}Cs. It undergoes β^- decay to a metastable state of ^{137}Ba, which then emits a 662-keV gamma ray. The β particles are absorbed in the stainless steel tube enclosing the cesium, so the dose is due to the gamma rays (Khan 2010, Chap. 15). Conventional low-dose-rate brachytherapy is delivered at 0.4–1.0 Gy hr^{-1}. High dose rates are about 1 Gy min^{-1}.

Patients with coronary artery disease are often treated with *balloon angioplasty*, in which a coronary artery is dilated by inserting a balloon on the end of a catheter into the femoral artery in the leg and from there through the aorta and into the coronary artery. One problem is *restenosis* or reclosure of the artery. Restenosis can be reduced by placing a *stent*—a helical coil of wire—in the artery at the time of the angioplasty. Restenosis sometimes occurs within a stent, though the rate of recurrence is reduced by using a stent which elutes (gives off) a restenosis-inhibiting drug. If restenosis does occur, it can be treated by placing a string of radioactive seeds in the stent. Treatments may use either a gamma emitter, ^{192}Ir, for 20 min, or a beta emitter (^{90}Sr/^{90}Y) for 3 min (Kaluza and Raizner 2004; Fox 2002).

Internal radiotherapy treats the patient with a radionuclide in a chemical that is selectively taken up by the tumor. The classic example is the administration by mouth of capsules containing ^{131}I for treatment of hyperthyroidism and thyroid cancer. Other nuclides are being used for breast cancer, neuroendocrine tumors, and melanoma (Fritzberg and Wessels 1995). A radionuclide for this purpose should emit primarily nonpenetrating radiation, have a physical half-life long compared to the biological half-life, have a large activity per unit mass, and exhibit a high degree of specificity for the tumor. If the nuclide can be delivered within the cell, then Auger electrons can be exploited. One way to achieve high concentrations in the tumor is *radioimmunotherapy*: monoclonal antibodies are tagged with the radionuclide such as ^{125}I (see the special issue of *Medical Physics* edited by Buchsbaum and Wessels 1993). It turns out that double-strand DNA breaks from Auger cascades occur more often than had been expected, and that the bystander effect is important. The use of Auger electrons from nuclides attached to the appropriate antibodies for cancer therapy is under active development; see Kassis (2011). The MIRD formulation can be adapted to the dose calculations (Watson et al. 1993). Radionuclide therapy is described for a general audience by Coursey and Nath (2000).

17.12 Radon

The naturally occurring radioactive nuclei are either produced continuously by cosmic γ ray bombardment, or they are the products in a decay chain from a nucleus whose half-life is comparable to the age of the earth. Otherwise they would have already decayed. There are three naturally-occurring radioactive decay chains near the high-Z end of the periodic table. One of these is the decay products from $^{238}_{92}$U, shown in Fig. 17.26. The half-life of ^{238}U is 4.5×10^9 yr, which is about the same as the age of the earth. A series of α and β decays lead to radium, ^{226}Ra, which undergoes α decay with a half-life of 1620 yr to radon, ^{222}Rn.

Uranium, and therefore radium and radon, are present in most rocks and soil. Radon, a noble gas, percolates through grainy rocks and soil and enters the air and water in different concentrations. Although radon is a noble gas, its decay

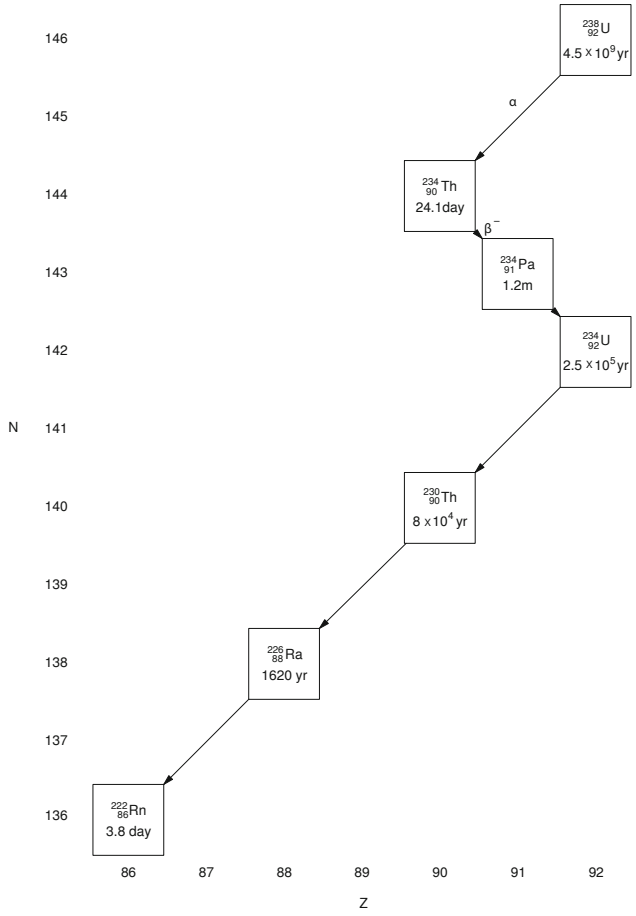


Fig. 17.26 Decay of ^{238}U to radon

products have different chemical properties and attach to dust or aerosol droplets which can collect in the lungs. High levels of radon products in the lungs have been shown by both epidemiological studies of uranium miners and by animal studies to cause lung cancer (Committee on the Biological Effects of Ionizing Radiations, BEIR IV 1988; BEIR VI 1999). The deposition process is quite complicated. A certain fraction of the decay products attach to aerosol droplets. That fraction is an important parameter in estimating the dose, because the unattached particles are deposited in the airways; those that have attached to aerosols are also deposited in the airways, the site depending on the droplet size. The rate at which natural mucus clearing from the lungs removes them is also variable.

The $^{222}_{86}$Rn decay scheme is shown in Fig. 17.27. (Alternate branches that occur very rarely are not shown.) The shaded nuclides are the greatest contributors to the dose. Radon is a noble gas; once it decays the other shaded nuclides decay shortly after. Radon dosimetry is described on pp. 137–158 of BEIR IV (1988) and in BEIR VI (1999). Typical uranium activities in soil are 20 Bq kg^{-1} (range 7–40), leading to radon concentrations in the air over average soil of about 4 Bq m^{-3}.

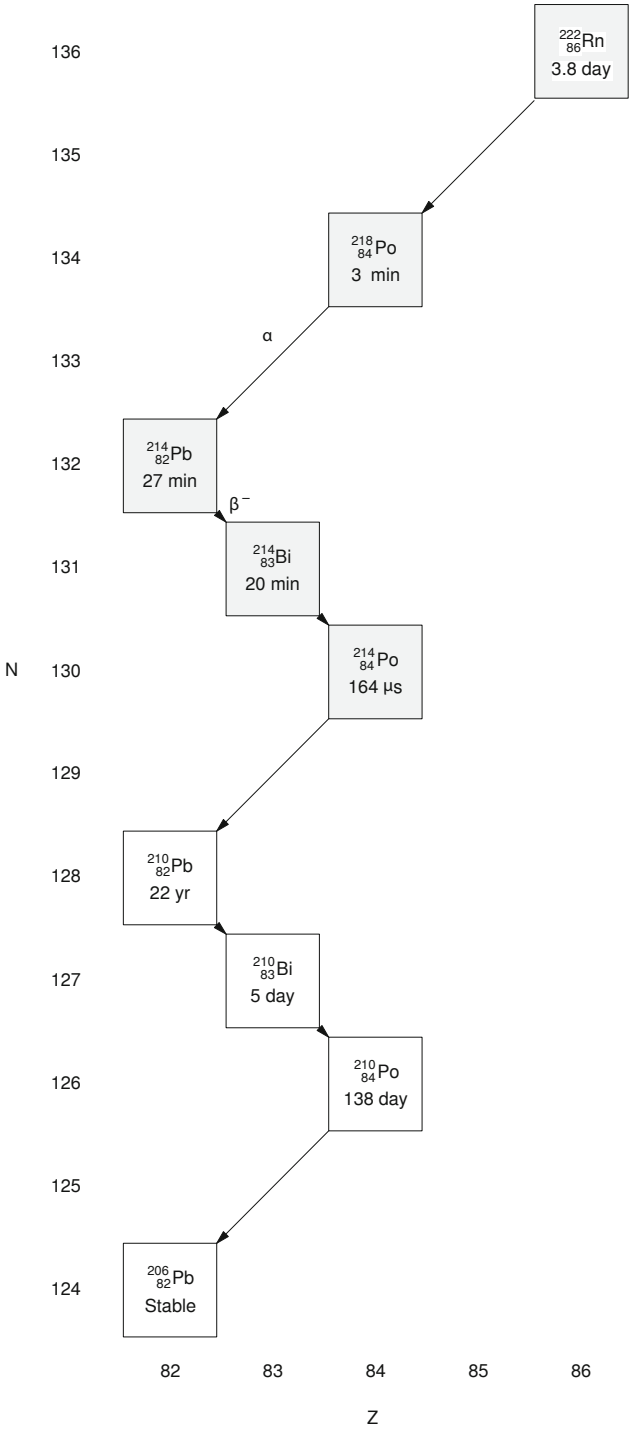


Fig. 17.27 Decay of radon. The decay of the shaded nuclides is most significant in determining dose

The *working level* (WL) has been defined to be any combination of the shaded isotopes in Fig. 17.27 in 1 l of air at ambient temperature and pressure that results in the ultimate emission of 1.3×10^5 MeV of α-particle energy. This is about the energy liberated by the decay products in equilibrium with 100 pCi (3.7 Bq) of radon. Thus 1 WL corresponds

to 3.7 Bq l^{-1} or 3700 Bq m^{-3}. More recently, the activity of radon and its decay products has been described by the *Potential Alpha Energy Concentration* (PAEC) (BEIR VI 1999, p. 179). Its units are J m^{-3}.

The *working-level month* (WLM) measures the total radon exposure and is 1 WL for 170 h (1 month of 40-h work weeks). Another unit is the PAEC multiplied by the number of hours exposure, measured in J h m^{-3}. There are 3.5×10^{-3} J h m^{-3} per WLM.

Dose estimates for the miners and for the general population require models of aerosol size, unattached fraction, target cells, exercise level, and occupancy factors that are described in BEIR IV (1988). Averaging over all of these variables shows a dose in the lungs of about 6 mGy per WLM, with a factor-of-2 uncertainty because of these variables.

The report uses a time-since-exposure model to estimate the risk of lung cancer on the basis of four studies of groups of miners. The model predicts a relative risk ratio that is unity for no exposure and increases linearly to 3.5 for a continuous exposure of 5 WLM per year over a lifetime.[10] The report uses the linear-no-threshold model to estimate risks to the general population at small exposures. The issue of applying the linear-no-threshold model was discussed in Sect. 16.12. See particularly the data from the Cohen study in Fig. 16.53. Typical radon concentrations in houses are usually less than $4r_0$ or 4 pCi l^{-1} (128 Bq m^{-3}) or 0.04 WL. (We saw in Sect. 16.12 that $r_0 = 37\,\mathrm{Bq\,m^{-3}} = 1\,\mathrm{pCi\ l^{-1}}$). Exposure to r_0 for 24 h per day for one year gives 0.5 WLM. The miners had exposures of 5–100 WLM per year, over periods of 3–20 years.

Symbols Used in Chapter 17

Symbol	Use	Units	First used page
a	Distance	m	522
b	Source to collimator distance	m	530
c	Speed of light	m s^{-1}	504
d	Width of collimator channel	m	530
e	Electron charge	C	504
g	Detector efficiency		530
h	Planck's constant	J s	510
h, k	Denote specific organs		511
l	Collimator thickness	m	530
m_0	Rest mass	kg	504
m_x	Rest mass of particle type x	kg	505
p	Momentum	kg m s^{-1}	509
r_h, r_k	Source and target regions		511
r	Distance	m	515
r_0	Radon concentration unit	Bq m^{-3}	526
s	Path length	m	515
t	Time	s	506
t	Collimator septum thickness	m	530
v	Speed	m s^{-1}	504
w	Distance across collimator wall in the direction of photon travel	m	530
x, y, z	Position	m	522
A	Mass number		503
A, A_0	Activity	Bq	507
$\tilde{A}_h$	Cumulated activity in organ h	Bq s	511
B	Buildup factor		515
B, B_K, B_L	Binding energy	eV	507
$C_h, \tilde{C}_h$	Activity and cumulated activity per unit mass in organ h	Bq kg^{-1}; kg^{-1}	514
D	Dose	J kg^{-1} (Gy)	511
E, E_γ	Energy	J, eV	504
F_h	Fraction of activity in organ h		512
F	Projection	Bq	522
K	Geometric factor		530
M, M_X	Mass	kg	509
N	Neutron number		503
N, N_0	Number of nuclei		506
R, R_0	Nuclear radius	m	504
R	Radius of disk	m	522
R_t, R_o	True and observed counting rates	s^{-1}	530
S	Mean absorbed dose per unit cumulated activity	J kg^{-1}	511
S	Area	m^2	515
T	Kinetic energy	J, eV	504
T	Time	s	527
$T_{1/2}$	Half-life	s	507
T_j	Half-life for jth biological disappearance process	s	513
Y_i	Mean number (fraction) of transitions of type i per transformation		511
Z	Atomic number (number of protons)		503
α_h	Fraction of total activity in organ h		528
β^-, β^+	Electron and positron (in β decay)		507
λ	Physical decay constant	s^{-1}	506
λ_j	Decay constant for jth biological process	s^{-1}	512
μ	Attenuation coefficient	m^{-1}	522
μ_{en}	Energy absorption coefficient	m^{-1}	515
$\nu, \overline{\nu}$	Neutrino, antineutrino		509
ν	Photon frequency	Hz	510
ρ	Density	kg m^{-3}	515
ϕ_i	Absorbed fraction		511
τ	Detector dead time	s	530
τ_h	Residence time in organ h	s	512
Δ_i	Mean energy emitted in radiation type i	J	511
Φ_j	Specific absorbed fraction	kg^{-1}	511

[10] BEIR IV (1988), Fig. 2.2. This is averaged by BEIR over smokers and nonsmokers and by us over sex.

Problems

Section 17.1

Problem 1. In the 1940s, a pressing question in biology was whether DNA or protein was responsible for the transmission of genetic information. A simple system to study this is a *bacteriophage*, a virus that injects a substance into *Escherichia coli*, thereby transforming the bacteria's genetic material. Design an experiment using radioactive tracers that could determine whether DNA or protein was the injected substance. Hint: DNA contains many phosphorus atoms but no sulfur, whereas protein has many sulfur atoms but no phosphorus. Alfred Hershey and Martha Chase performed such an experiment in 1952.

Problem 2. An alpha particle is fired directly at a stationary aluminum nucleus. Assume the only interaction is the electrostatic repulsion between the alpha particle and the nucleus, and the nucleus is so heavy that it is stationary. Calculate the distance of their closest approach as a function of the initial kinetic energy of the alpha particle. This calculation is consistent with Ernest Rutherford's famous alpha particle scattering formula for energies lower than 3 MeV, but deviates from his formula for energies higher than 3 MeV. If the alpha particle enters the nucleus, the nuclear force dominates and the formula no longer applies. Estimate the radius of the aluminum nucleus.

Problem 3. The best current (2010) value for the mass of the proton is 1.007276467 u. The mass of the electron is $5.485799095 \times 10^{-4}$ u. The BE of the electron in the hydrogen atom is 13.6 eV. Calculate the mass of the neutral hydrogen atom.

Problem 4. Solve Eq. 17.1 for the kinetic energy, T. Show that when $v \ll c$, it reduces to the familiar $T = m_0 v^2/2$.

Problem 5. The rest energy of the ${}^{184}_{74}\mathrm{W}$ nucleus is 171303 MeV. The average binding energies of the electrons in each shell are

Shell	Number of electrons	BE per electron (eV)
K	2	69,525
L	8	11,015
M	18	2125
N	32	213
O	12	49
P	2	≈ 6

Calculate the atomic rest energy of tungsten.

Section 17.5

Problem 6. Refer to Figs. 17.2 and 17.5. Uranium splits roughly in half when it undergoes nuclear fission. Will the fission fragments decay by β^+ or β^- emission?

Problem 7. The following nuclei of mass 15 are known: ${}^{15}_{6}\mathrm{C}$, ${}^{15}_{7}\mathrm{N}$, and ${}^{15}_{8}\mathrm{O}$. Of these, ${}^{15}\mathrm{N}$ is stable. How do the others decay?

Problem 8. Look up the decay schemes of the following isotopes (for example, in the *Handbook of Chemistry and Physics,* CRC Press or at www.nndc.bnl.gov/). Comment on their possible medical usefulness: ${}^{3}\mathrm{H}$, ${}^{15}\mathrm{O}$, ${}^{13}\mathrm{N}$, ${}^{18}\mathrm{F}$, ${}^{22}\mathrm{Na}$, ${}^{68}\mathrm{Ga}$, ${}^{64}\mathrm{Cu}$, ${}^{11}\mathrm{C}$, ${}^{123}\mathrm{I}$, and ${}^{56}\mathrm{Ni}$.

Problem 9. Look up the half lives of the isotopes in Fig. 17.6 (for instance in the Handbook of Chemistry and Physics. CRC Press or at www.nndc.bnl.gov/). Relate qualitatively the half life to the position of the isotope on the parabola.

Section 17.6

Problem 10. Calculate the conversion factor k of Eq. 17.21b.

Section 17.6.1

Problem 11. Show that 1 μCi h $= 1.332 \times 10^8$ disintegrations or Bq s.

Problem 12. Obtain a numerical value for the residence time for ${}^{99\mathrm{m}}\mathrm{Tc}$-sulfur colloid in the liver if 85 % of the drug injected is trapped in the liver and remains there until it decays.

Problem 13. Derive Eqs. 17.39–17.41.

Problem 14. Calculate numerical solutions of Eqs. 17.39 and 17.41 and plot them on semilog paper. Use $\lambda = 2$, $\lambda_1 = 0.5$, $\lambda_2 = 3$.

Problem 15. Eq. 17.41 is not valid if $\lambda_1 = \lambda_2$. In that case, try a solution of the form $N_2 = Bte^{-\alpha t}$ where α is to be determined, and obtain a solution.

Problem 16. Derive Eqs. 17.42 and 17.43.

Problem 17. The biological half-life of iodine in the thyroid is about 25 days. ${}^{125}\mathrm{I}$ has a half-life of 60 days. ${}^{132}\mathrm{I}$ has a half-life of 2.3 h. Find the effective half-life in each case.

Problem 18. For Sect. 17.6.1.4, with $\lambda = 0.05\ \mathrm{h}^{-1}$, $\lambda_1 = 1\ \mathrm{h}^{-1}$, and $\lambda_2 = 0.1\ \mathrm{h}^{-1}$, find $\tilde{A}_1$ and $\tilde{A}_2$ in terms of the initial activity A_0 and in terms of the initial number of nuclei N_0.

Problem 19. N_0 radioactive nuclei with physical decay constant λ are injected in a patient at $t = 0$. The nuclei move into the kidney at a rate λ_1, so that the number in the rest of the body falls exponentially: $N(t) = N_0 e^{-(\lambda+\lambda_1)t}$. Suppose that the nuclei remain in the kidney for a time T before moving out in the urine. (This is a crude model for the radioactive nuclei being filtered into the glomerulus and then passing through the tubules before going to the bladder.)

(a) Calculate the cumulated activity and the residence time in the kidney by finding the total number of nuclei entering the kidney and multiplying by the probability that a nucleus decays during the time T that it is in the kidney.
(b) Calculate the cumulated activity and residence time in the bladder, assuming that the patient does not void.

Problem 20. Suppose that at $t = 0$, ^{99m}Tc with an activity of 370 kBq enters a patient's bladder and stays there for 2 h, at which time the patient voids, eliminating all of it. What is the cumulated activity? What is the cumulated activity if the time is 4 h?

Problem 21. Suppose that the ^{99m}Tc of the previous problem does not enter the bladder abruptly at $t = 0$, but that it accumulates linearly with time. At the end of 2 h the activity is 370 kBq and the patient voids, eliminating all of it. What is the cumulated activity?

Problem 22. A radioactive substance has half-life $T_{1/2}$. It is excreted from the body with biological half-life T_1. N_0 radioactive nuclei are introduced in the body at $t = 0$. Find the total number that decay inside the body.

Problem 23. The *fractional distribution function* α_h is the fraction of the total activity that is in organ h: $\alpha_h(t) = A_h(t)/A(t) = A_h(t)/A_0 e^{-\lambda t}$.
(a) Show that $\tau_h = \int_0^\infty \alpha_h(t) e^{-\lambda t} dt$.
(b) Calculate $\alpha_1(t)$ and $\alpha_2(t)$ for Eqs. 17.39 and 17.41 and show that integration of these expressions leads to Eqs. 17.43.

Problem 24. Suppose that the fractional distribution function (defined in the previous problem) is $\alpha(t) = 1,\ t < T$; $\alpha(t) = b,\ t > T$; $(b < 1)$. Find the residence time. This is a simple model for the situation where a bolus (a fixed amount in a short time) of some substance passes through an organ once and is then distributed uniformly in the blood.

Problem 25. The *distribution function* $q_h(t)$ is defined to be the activity in organ h corrected for radioactive decay to a reference time. If the correction is from time t to time 0, find an expression for $q_h(t)$ in terms of $A_h(t)$.

Problem 26. The "official" definition of the fractional distribution function $\alpha_h(t)$ is the ratio of the distribution function $q_h(t)$ produced by a bolus administration to the patient, divided by the activity A_0 in the bolus. Show that this is equivalent to the definition in Problem 23.

Problem 27. Show that if the uptake in a compartment is not instantaneous but exponential, with subsequent exponential decay, the cumulated activity is $\tilde{A} = 1.443 A_0 (T_e T_{ue}/T_u)$, where T_e is the effective half-life for excretion, and $T_{ue} = T_u T_{1/2}/(T_u + T_{1/2})$. Hint: see Eq. 17.42.

Section 17.6.2

Problem 28. Rearrange the data of Fig. 17.4. Find the total Δ for emission of photons below 30 keV and charged particles. Rank the radiations in the order they contribute to the dose.

Problem 29. Nitrogen-13 has a half-life of 10 min. All of the disintegrations emit a positron with end point energy 1.0 MeV (average energy 0.488 MeV). There is no electron capture. Make a table of radiations that must be considered for calculating the absorbed dose and determine E_i and Δ_i for each one.

Problem 30. A patient swallows 3.5×10^9 Bq of ^{131}I. The half-life of the iodine is 8 days. Ten min later the patient vomits all of it. If none had yet left the stomach and all was vomited, determine the cumulated activity and residence time in the stomach.

Section 17.6.3

Problem 31. Derive Eq. 17.57 by substituting Eqs. 17.55 and 17.56 in Eq. 17.54. You will also have to justify and use Eq. 17.58.

Problem 32. The body consists of two regions. Region 1 has mass m_1 and cumulated activity $\tilde{A}_1$. It is completely surrounded by region 2 of mass m_2 and cumulated activity $\tilde{A}_2 = \tilde{A}_0 - \tilde{A}_1$. We can say that the mass of the total body is $m_{TB} = m_1 + m_2 = m_1 + m_{\mathrm{RB}}$. A single radiation is emitted with disintegration energy Δ. The radiation is nonpenetrating so that

$$\phi(1 \leftarrow 1) = \phi(2 \leftarrow 2) = 1,$$

$$\phi(1 \leftarrow 2) = \phi(2 \leftarrow 1) = 0.$$

(a) What are $\phi(\mathrm{TB} \leftarrow 1)$ and $\phi(\mathrm{TB} \leftarrow 2)$?
(b) What are the corresponding values of Φ and S?
(c) Show that directly from the definition, Eq. 17.54

$$D_1 = \tilde{A}_1 \Delta / m_1,$$

$$D_2 = D_{\mathrm{RB}} = \tilde{A}_2 \Delta / m_2,$$

$$D_{\mathrm{TB}} = \tilde{A}_0 \Delta / (m_1 + m_2)$$

(d) Calculate $\tilde{A}_u$ and $\tilde{A}_1^*$.
(e) What is $S(1 \leftarrow \mathrm{TB})$? Remember that ϕ is calculated for activity uniformly distributed within the source region.
(f) Calculate the dose to region 1 using Eq. 17.57 and show that it agrees with (c).
(g) Evaluate $S(1 \leftarrow \mathrm{RB})$ using Eq. 17.58 and show that it agrees with $S(1 \leftarrow 2)$.

Problem 33. The body consists of two regions. Region 1 has mass m_1 and cumulated activity $\tilde{A}_1$. It is completely surrounded by region 2 of mass m_2 and cumulated activity $\tilde{A}_2$. A single radiation is emitted with disintegration energy Δ. The characteristics of the radiation are such that

$$\phi(1 \leftarrow 1) + \phi(2 \leftarrow 1) = 1,$$

$$\phi(1 \leftarrow 2) + \phi(2 \leftarrow 2) + \phi(0 \leftarrow 2) = 1,$$

where $\phi(0 \leftarrow 2)$ represents energy from region 2 that has escaped from the body. Obtain expressions for the dose to each region and the whole body dose.

Problem 34. Consider the decay of a parent at rate λ_1 to an offspring that decays with rate λ_2.

(a) Write a differential equation for the amount of offspring present.
(b) Solve the equation.
(c) Discuss the solution when $\lambda_2 > \lambda_1$.
(d) Discuss the solution when $\lambda_2 < \lambda_1$.
(e) Plot the solution for a technetium generator that is eluted every 24 h.

Problem 35. N_0 nuclei of ^{99m}Tc are injected into the body. What is the maximum activity for the decay of the metastable state? When does the maximum activity for decay of the ground state occur if no Tc atoms are excreted? What is the ratio of the maximum metastable state activity to the maximum ground-state activity?

Problem 36. If 1 μCi of ^{99m}Tc is injected in the blood and stays there, relate the activity in a sample drawn time t later to the volume of the sample and the total blood volume. If the gamma rays are detected with 100 % efficiency, what will be the counting rate for a 10-ml sample of blood if the blood volume is 5 l? (Using non-SI units was intentional.)

Problem 37. Assume that aggregated human albumin is in the form of microspheres. A typical dose of albumin microspheres is 0.5 mg of microspheres containing 80 MBq of ^{99m}Tc and 15 μg of tin. There are 1.85×10^6 microspheres per mg.

(a) How many ^{99m}Tc atoms are there per microsphere?
(b) How many tin atoms per microsphere?
(c) How many technetium atoms per tin atom?
(d) What fraction of the surface of a microsphere is covered by tin? Assume the sphere has a density of 10^3 kg m^{-3}.

Problem 38. It is estimated that the total capillary surface area in the lung is 90 m^2. Assume each capillary has 50 segments, each 10 μm long, and a radius of 5 μm.

(a) How many capillaries are there in the lung?
(b) There are about 3×10^8 alveoli in both lungs. How many capillaries per alveolus are there?
(c) An alveolus is 150–300 μm in diameter. Are the above answers consistent?
(d) A typical dose of albumin microspheres is 0.5 mg with an average diameter of 25 μm. There are 1.85×10^6 spheres per mg. What fraction of the capillaries are blocked if there is good mixing?

Section 17.6.4

Problem 39. Look up the decay schemes and half-lives for ^{123}I and ^{131}I. Explain why ^{123}I is used to image the thyroid and ^{131}I is used to treat thyroid cancer.

Problem 40. Identify all the isotopes in Fig. 17.7 using the ^A_ZSymbol notation. What are the stable isotopes? What isotope can decay by both β^- and β^+ emission?

Problem 41. The half-life of ^{99m}Tc is 6.0 h. The half-life of ^{131}I is 8.07 day. Assume that the same initial activity of each is given to a patient and that all of the substance remains within the body.

(a) Find the ratio of the cumulated activity for the two isotopes.
(b) ^{99m}Tc emits 0.141-MeV photons. For each decay of ^{131}I the most important radiations are 0.89 β^- of average energy 0.192 MeV and 0.81 photons of 0.365 MeV. If all of the decay energy were absorbed in the body, what would be the ratio of doses for the same initial activity?

Problem 42. A patient is given an isotope that spreads uniformly through the lungs. It emits a single radiation: a γ ray of energy 50 keV. There are no internal-conversion electrons. The cumulated activity is 40 GBq s. Find the absorbed dose in the liver ($m = 1.83$ kg).

Problem 43. The decay of ^{99m}Tc can be approximated by lumping all of the decays into two categories:

Radiation	E_i (MeV)	Δ_i (J)
γ	0.14	2×10^{-14}
Electrons and soft x rays		2.76×10^{-15}

Sulfur colloid labeled with 100 MBq of ^{99m}Tc is given to a patient and is taken up immediately by the liver. Assume it stays there. Find the dose to the liver, spleen, and whole body. Use the following information:

Absorbed fraction for a source in the liver

Target organ	Mass (kg)	$E(\gamma) =$ 0.14 MeV
Liver	1.833	0.161
Spleen	0.176	0.000629
Whole body	70.0	0.431

Problem 44. An ionization type smoke detector contains 4.4 μCi of ^{241}Am. This isotope emits α particles (which we will ignore) and a 60-keV γ ray, for which $n = 0.36$. The half-life is 458 yr.

(a) How many moles of ^{241}Am are in the source?
(b) Ignoring attenuation, backscatter, and buildup in any surrounding material (such as the cover of the smoke detector), what is the absorbed dose in a small sample of muscle located 2 m away, if the muscle is under the detector for 8 h per day for 1 year?

Problem 45. One mCi of a radioactive substance lodges permanently in a patients lungs. The substance emits a single 80-keV γ ray. It has a half-life of 12 h. Find the cumulated activity and the dose to the liver (mass 1833 g).

Problem 46. The dose calculation for microspheres in the lung was an oversimplification because technetium leaches

off the spheres. The footnote in Sect. 17.6.4 lists some more realistic residence times. If none of the technetium is excreted from the body, the sum of all the residence times will still be 8.7 h. Assume that the residence time in the lungs is 4.3 h and the residence time in the rest of the body is 4.4 h.

(a) Show that $\tilde{A}_u = 4.46 \times 3600 \times A_0$ and $\tilde{A}^*_{\text{lung}} = 4.24 \times 3600 \times A_0$.

(b) For a source distributed uniformly throughout the total body, the absorbed fractions for 140-keV photons are $\phi(\text{lung} \leftarrow \text{TB}) = 0.0053$, $\phi(\text{TB} \leftarrow \text{TB}) = 0.3572$. Split the radiation into penetrating and nonpenetrating components:

$$S(\text{lung} \leftarrow \text{TB}) = (\phi_{\text{nonpen}} \Delta_{\text{nonpen}} + \phi_{\text{penetrating}} \Delta_{\text{penetrating}})/m_{\text{lung}}.$$

Remember that for activity uniformly distributed in the total body, $\phi(\text{lung} \leftarrow \text{TB}) = m_{\text{lung}}/m_{\text{TB}}$ and use some of the information in Table 17.3 to show that

$$S(\text{lung} \leftarrow \text{TB}) = 1.463 \times 10^{-16}\,\text{J kg}^{-1},$$

$$S(\text{TB} \leftarrow \text{TB}) = 1.414 \times 10^{-16}\,\text{J kg}^{-1}.$$

(c) Calculate the dose to the lungs and the total body dose for an initial activity of 37 MBq. Compare the values to those in Table 17.3.

Section 17.8

Problem 47. Nuclear counting follows Poisson statistics. Show that for a fixed average counting rate R (counts per second) the standard deviation of a sum of N measurements each of length T is the same as a single measurement of duration NT. (Hint: You will first have to consider the situation where one measures $y = x_1 + x_2 + \cdots$ and find the variance of y in terms of the variances of the x_i when there is no correlation between the x_i.)

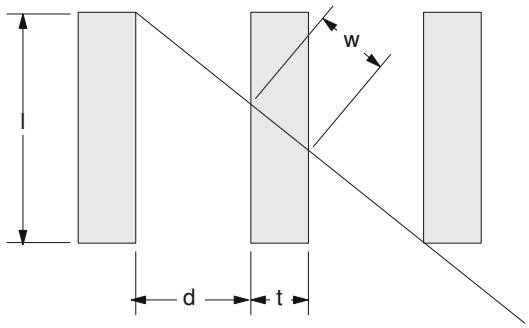
Problem 48. The interaction of a photon in a nuclear detector (an "event") initiates a process in the detector that lasts for a certain length of time. A second event occurring within a time τ of the first event is not recorded as a separate event. Suppose that the true counting rate is R_t. A counting rate R_o is observed.

(a) A nonparalyzable counting system is "dead" for a time τ after each recorded event. Additional events that occur during this dead time are not recorded but do not prolong the dead time. Show that $R_t = R_o(1 - R_o\tau)$ and $R_o = R_t/(1 + R_t\tau)$.

(b) A paralyzable counting system is unable to record a second event unless a time τ has passed since the last event. In other words, an event occurring during the dead time is not only not recorded, it prolongs the dead time. Show that in this case $R_o = R_t e^{-R_t\tau}$. (Hint: Use the Poisson distribution of Appendix J to find the fraction of events separated by a time greater than τ. The probability that the next event occurs between t and $t + dt$ is the probability of no event during time t multiplied by the probability of an event during dt.)

(c) Plot R_o vs R_t for the two cases when τ is fixed. The easiest way to do this is to plot $R_o\tau$ vs $R_t\tau$.

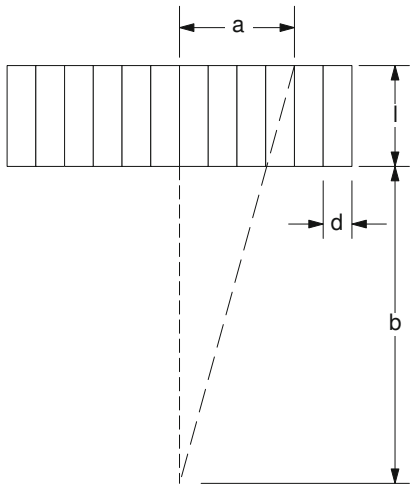
Problem 49. Two channels of a collimator for a gamma camera are shown in cross section, along with the path of a photon that encounters the minimum thickness of collimator septum (wall).



(a) Show that if $(d + t)/l \ll 1$, then $w/t = l/(2d + t)$.

(b) If transmission through the septum is to be less than 5 %, what is the relationship between t, d, l, and μ? Evaluate this for ^{99m}Tc and for a positron emitter.

Problem 50. Photons from a point source a distance b below a collimator pass through channels out to a distance a from the perpendicular to the collimator passing through the source.



(a) Find an expression for a in terms of b, d, and l.

(b) Assume that a is related to the spatial frequency k for which the modulation transfer function (MTF) = 0.5 in Fig. 17.18 by $a = K/k$, where K is a constant. Calculate the thickness l of the collimator.

Problem 51. The collimator efficiency of a gamma camera is defined to be the fraction of the γ rays emitted isotropically by a point source that pass through the collimator into the scintillator.

(a) Consider a circular channel of diameter d in the collimator directly over the source. Show that the fraction of the photons striking the scintillator after passing through that channel is $d^2/16(l+b)^2$. (Assume that any which strike the septum are lost).

(b) Use the result of the previous problem to estimate the number of channels through which at least some photons from the point source pass. Assume that the fraction of collimator area that is occupied by channels rather than lead is $\left[d/(d+t)\right]^2$.

(c) Calculate the geometric efficiency g assuming that all channels that pass any photons have the same efficiency as the one on the perpendicular from the source. Show that it is of the form

$$g = K^2 \left(\frac{d}{l}\right)^2 \left(\frac{d}{d+t}\right)^2$$

and evaluate K. More detailed calculations show that K is about 0.24 for a hexagonal array of round holes and 0.26 for hexagonal holes.[11]

(d) How does the detector efficiency relate to the collimator resolution?

Section 17.9

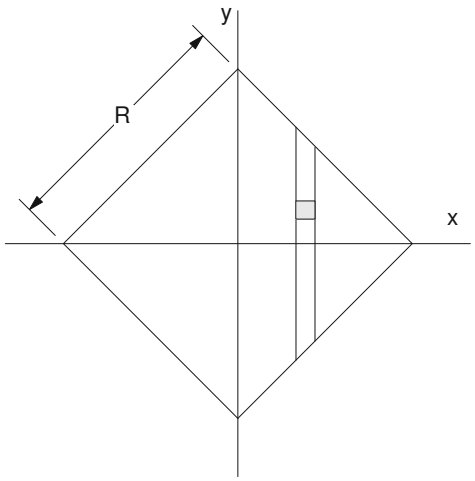
Problem 52.

(a) Derive Eq. 17.60 from Eq. 17.59.

(b) Calculate the limit of Eq. 17.60 when there is no attenuation.

Problem 53. The attenuation distortion for SPECT can be reduced by making measurements on opposite sides of the patient and taking the geometric mean. The geometric mean of variables x_1 and x_2 is $(x_1 x_2)^{1/2}$. Calculate the geometric mean of two SPECT measurements on opposite sides of the patient. Ignore possible $1/r^2$ effects.

Problem 54. Consider a radioactive source having a uniform activity per unit volume A_V and the square geometry shown below.

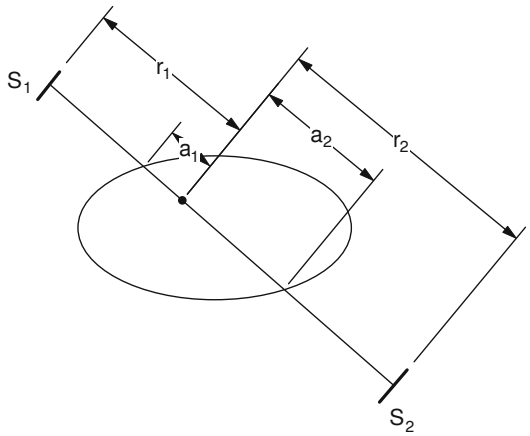


(a) Calculate the projection $F(x)$ including the effects of attenuation with coefficient μ.

(b) Plot $F(x)$ for $\mu = 0$ and for $\mu R = 3$.

Section 17.10

Problem 55. Suppose that A positrons are emitted from a point per second. They come to rest and annihilate within a short distance of their source. When a positron annihilates, two photons are emitted in opposite directions. Two photon detectors are set up on opposite sides of the source. The source is distance r_1 from the first detector, of area S_1, and r_2 from the second detector of area S_2. The area S_2 is large enough so that the second photon will definitely enter detector 2 if the first photon enters detector 1. Assume that both detectors count with 100 % efficiency.



(a) Show that the number of counts in the first detector would be $2AS_1/4\pi r_1^2$ if there were no attenuation between source and detector, and that it is $(2AS_1/4\pi r_1^2)e^{-\mu a_1}$ if attenuation in a thickness a_1 of the body is considered.

[11] Cherry et al. (2012, p. 222), Grenier et al. (1974).

(b) Detector 2 detects the second photon for every photon that strikes detector 1. Assuming a uniform attenuation coefficient and body thickness a_2, find an expression for the number of events in which both photons are detected.

Problem 56. Positron emission tomography relies on simultaneous detection of the back-to-back annihilation gamma rays (a *coincidence*). In addition to true coincidences, there can be "scatter coincidences" in which annihilation photons coming from a point that is not on the line between the two detectors enter both detectors. There can also be "random coincidences" which arise from photons from completely independent decays that occur nearly simultaneously. Consider a ring of detectors around a patient. Make three drawings showing true coincidences, scatter coincidences and random coincidences.

Section 17.12

Problem 57. The half-life of ^{235}U is 7×10^8 yr. The age of the earth is 4.5 billion years. What fraction of the ^{235}U that existed on the earth when it was first formed is present now?

Problem 58. There are three naturally-occurring decay series beginning with three long-lived isotopes: ^{238}U (Figs. 17.26 and 17.27), ^{235}U, and ^{232}Th. The ^{232}Th series begins with the α decay of ^{232}Th (half life $= 1.4 \times 10^{10}$ yr) to nucleus A which undergoes β^- decay to nucleus B which undergoes β^- decay to nucleus C which undergoes α decay to nucleus D which undergoes α decay to nucleus E, etc. Make a chart like Fig. 17.26 showing the first five steps in the series, and identify the five nuclei A–E.

Problem 59. One way to determine the age of biological remains is *carbon-14 dating*. The common isotope of carbon is stable ^{12}C. The rare isotope ^{14}C decays with a half-life of 5370 yr. ^{14}C is constantly created in the atmosphere by cosmic rays. The equilibrium between production and decay results in about 1 of every 10^{12} atoms of carbon in the atmosphere being ^{14}C, mostly as part of a CO_2 molecule. As long as the organism is alive, the ratio of ^{12}C to ^{14}C in the body is the same as in the atmosphere. Once the organism dies, it no longer incorporates ^{14}C from the atmosphere, and the number of ^{14}C nuclei begins to decrease. Suppose the remains of an organism have one ^{14}C for every 10^{13} ^{12}C nuclei. How long has it been since the organism died?

Problem 60. Consider a fictitious two-step decay series analogous to the more complex series shown in Fig. 17.26. The series starts with isotope A which decays at rate λ_1 to isotope B. Isotope B decays to isotope C with rate λ_2. Isotope C is stable.

(a) Derive the differential equation governing the number of nuclei N_A, N_B, and N_C. Where else in this chapter have you seen the same equations?

(b) Solve the differential equations using the initial conditions $N_A(0) = N$, $N_B(0) = N_C(0) = 0$. Make sure your solutions make sense for $t \to 0$ and $t \to \infty$.

(c) Find N_B/N_A in the limit $\lambda_2 \gg \lambda_1$. Ignore short times. Also find activities A_A and A_B. Explain physically how such a small number of nuclei N_B can contribute so much to the total activity.

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