Chapter 1

Basic Nuclear Physics and Instrumentation

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1.1. Basic Nuclear Physics

1.1.1. Atom

The atom is the basic unit of matter and consists of a nucleus surrounded by negatively charged electrons (Fig. 1.1). The atomic nucleus comprises positively charged protons and electrically neutral neutrons. The protons and neutrons are much more massive than electrons. Atomic number ($Z$) refers to the number of protons in the nucleus, and mass number ($A$) is the total number of protons and neutrons ($N$). The chemical properties of an atom are determined by the number of orbital electrons, which is the same as the atomic number in the electrically neutral atom.

Notation

The notation to summarize the atomic and nuclear composition is:

$$\frac{A}{Z}X_N,$$

where $X$ is the atomic or chemical symbol. Because $X$ is determined by $Z$ and $N$ can be obtained by $A-Z$, the following shortened notation is also frequently used:

$$^AX$$

Nuclear families

The nuclide is a species of atoms characterized by the number of protons, neutrons, and the energy status of the atomic nucleus. The nuclear species
can be grouped into families having certain common properties, as summarized in Table 1.1.

### 1.1.2. Radiation and radionuclide

**Radiation**

In general, radiation refers to the energy that travels through a medium or space. Radiation can be categorized into two distinct types (ionizing and non-ionizing radiation). The term *radiation* is commonly used in reference to the ionizing radiation that has sufficient energy to ionize an atom.

Radiation can also be categorized into particulate and electromagnetic radiation. Particulate radiation is composed of atomic or subatomic particles and carries energy in the form of kinetic energy of mass in motion; this category includes alpha, proton, electron (β⁻), positron (β⁺), and neutron particles. Electromagnetic (EM) radiation carries energy in the form of oscillating electrical and magnetic fields. EM radiation has no mass, is not affected by electrical or magnetic fields, and has a constant speed in a given
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medium. The EM radiation commonly used in nuclear medicine imaging includes gamma (\(\gamma\)) and X-rays. The \(\gamma\)-rays are emitted from the nuclei of radioactive atoms and X-rays are produced in the electron shells.

There are two methods to describe EM radiation (waves and photons [particle-like discrete packets of energy]). The energy \((E)\) of electromagnetic radiation is inversely proportional to the wavelength \((\lambda)\), as shown in following equation:

\[
E = \frac{hc}{\lambda},
\]

where \(h\) is Planck’s constant and \(c\) is the velocity of light.

Radionuclide

A radionuclide (also often referred to as a radioisotope) is an atom with an unstable nucleus which is characterized by excess energy. The radionuclide undergoes radioactive decay to be a more stable atom. In radioactive decay, the unstable radionuclide is called the parent and the more stable product is the daughter.

1.1.3. Radioactive decay

Radioactive decay is a process in which an unstable radionuclide transforms into a more stable radionuclide by spontaneously emitting particles and/or photons. Several types of radioactive decay exist.

Alpha decay

An alpha (\(\alpha\)) particle is emitted from the nucleus in this decay mode, which occurs primarily among very heavy elements. The \(\alpha\) particles are helium nuclei \((A = 4, Z = 2)\). Alpha particles deposit large amounts of energy \((4 \sim 8\) MeV\) within a very short range in body tissues due to the large mass involved. The atomic mass of nuclei is decreased by a factor of four after decay, as shown in the following general equation of \(\alpha\) decay:

\[
\frac{A}{Z}X \rightarrow \frac{A-4}{Z-2}Y + \frac{4}{2}\alpha + \text{Energy}
\]
Beta minus decay

Beta particles ($\beta^-$) are negatively charged electrons emitted from radionuclides that have an excess number of neutrons (neutron rich) compared to the number of protons. In this decay mode, a neutron is converted into a proton with the simultaneous ejection of a $\beta^-$ and an anti-neutrino ($\bar{\nu}$). Consequently, the number of protons is increased by one and the atom is transformed into a different element, as shown by the following equation:

$$\frac{A}{Z}X \rightarrow \frac{A}{Z+1}Y + \beta^- + \bar{\nu} + \text{Energy}$$

The emitted $\beta^-$ particles have a continuous kinetic energy spectrum, ranging from 0 to the maximum energy ($E_{\text{max}}$). The average energy of $\beta^-$ is approximately $1/3 E_{\text{max}}$.

Positron decay

Positron decay occurs with neutron poor radionuclides. A proton in a nuclide is converted into a neutron with the simultaneous ejection of a positron ($\beta^+$) and a neutrino ($\nu$). The positron is the anti-matter conjugate of the electron emitted in $\beta^-$ decay ($\beta^+$ and $\beta^-$ have the same physical characteristics, with the exception of electric polarity). The number of protons is decreased as the consequence of the positron decay, as follows:

$$\frac{A}{Z}X \rightarrow \frac{A}{Z+1}Y + \beta^+ + \nu + \text{Energy}$$

After ejection from the nucleus, a positron loses its kinetic energy in collisions with atoms of the surrounding matter and comes to rest within approximately $10^{-9}$ sec. The positron then combines with an ordinary electron in an annihilation reaction, in which the entire rest mass of both particles is instantaneously converted to energy and emitted as two oppositely directed 511 keV $\gamma$-ray photons. Positron emission tomography (PET) is a nuclear medicine imaging technique which produce the images of positron-emitting radionuclides by measuring the annihilated $\gamma$-rays.

Electron capture

Electron capture is an alternative way for positron decay involving neutron poor radionuclides. In this mode, an unstable nucleus captures an orbital
electron, with the conversion of a proton into a neutron and the simultaneous ejection of a neutrino as described by the following equation:

\[ {A\atop Z}X + \beta^- \rightarrow {A\atop Z+1}Y + \nu + \text{Energy} \]

Additional characteristic X-rays are generated when the vacancy in the electron shell created by electron capture is filled by an electron from a higher-energy shell. \(^{201}\text{Tl}\) is a well-known radionuclide undergoing electron capture and emitting characteristic X-rays. The electron capture decay frequently results in a daughter nucleus that is in an excited or metastable state. Thus, \(\gamma\)-rays (or conversion electrons) may also be emitted.

**Isomeric transition**

Often, during radioactive decay, a daughter is formed in an excited (unstable) state. Most excited states transit nearly instantaneously to lower energy states with emission of \(\gamma\)-rays. However, some excited states persist for longer periods, with half-lives ranging from approximately \(10^{-12}\) sec to more than 600 years. These excited states are called metastable or isomeric states and are denoted by the letter \(m\) after the mass number. \(^{99m}\text{Tc}\), which is the most commonly used radionuclide in nuclear medicine imaging, undergoes this isomeric transition. In the \(^{99}\text{Mo}/^{99m}\text{Tc}\) generator, \(^{99}\text{Mo}\) decays to \(^{99m}\text{Tc}\) that remains in the metastable states before decaying to stable \(^{99}\text{Tc}\) with a half-life of 6.02 h, as shown in the following equations:

\[ ^{99}\text{Mo} \rightarrow ^{99m}\text{Tc} + \beta^- + 1.37\text{ MeV} \]
\[ ^{99m}\text{Tc} \rightarrow ^{99}\text{Tc} + \gamma(0.14\text{ MeV}) \]

**1.1.4. Radioactivity and Half-life**

**Radioactivity**

The activity (\(A\)) is the quantity of radioactive material and is defined as the number of radioactive atoms undergoing radioactive decay per unit time (\(t\)). Therefore, the activity is equal to the change (\(dN\)) in the total number of radioactive atoms (\(N\)) in a given period (\(dt\)):

\[ A = -\frac{dN}{dt} \]
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The SI unit of activity is the becquerel (Bq), which is named after Henri Becquerel, who discovered radioactivity in 1896. One Bq is defined as one disintegration per second (dps). Because a Bq is a very tiny amount of activity, the curie (Ci; the historical unit of activity) is more frequently used in nuclear medicine. One curie is the activity of 1 g of pure $^{226}$Ra. Ci and Bq have the following relationship:

$$1 \text{ Ci} = 3.7 \times 10^{10} \text{ Bq}$$
$$1 \text{ mCi} = 37 \text{ MBq}$$

Decay constant and half-life

The radioactivity ($A_t$) of a radioactive atom after a time $t$ is given by

$$A_t = A_0 e^{-\lambda t},$$

where $A_0$ is the initial activity and $\lambda$ is the decay constant. The decay constant is the unique characteristic of each radionuclide and has the following relationship with the physical half-life ($T_{1/2}$), which is the time required for the activity to decrease by one-half, as follows:

$$T_{1/2} = \frac{\ln(2)}{\lambda} = \frac{0.693}{\lambda}$$

For example, after 10 half-lives, the radioactivity of a sample is reduced by approximately $10^{-3}$. The half-lives of typical radionuclides used in nuclear medicine are given in Table 1.2.

Table 1.2. The half-lives of typical radionuclides.

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>$T_{1/2}$</th>
<th>Radionuclide</th>
<th>$T_{1/2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>6.02 h</td>
<td>$^{11}$C</td>
<td>20.4 min</td>
</tr>
<tr>
<td>$^{123}$I</td>
<td>13 h</td>
<td>$^{13}$N</td>
<td>9.96 min</td>
</tr>
<tr>
<td>$^{99}$Mo</td>
<td>2.79 d</td>
<td>$^{15}$O</td>
<td>2.03 min</td>
</tr>
<tr>
<td>$^{111}$In</td>
<td>2.82 d</td>
<td>$^{18}$F</td>
<td>109.8 min</td>
</tr>
<tr>
<td>$^{201}$Tl</td>
<td>3.08 d</td>
<td>$^{68}$Ga</td>
<td>68.3 min</td>
</tr>
<tr>
<td>$^{67}$Ga</td>
<td>3.25 d</td>
<td>$^{82}$Rb</td>
<td>1.25 min</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>8.05 d</td>
<td>$^{124}$I</td>
<td>4.18 d</td>
</tr>
<tr>
<td>$^{125}$I</td>
<td>60.2 d</td>
<td>$^{64}$Cu</td>
<td>12.7 h</td>
</tr>
</tbody>
</table>
1.1.5. Interaction of radiation with matter

Particle interactions

High-energy charged particles, such as $\alpha$ and $\beta$ particles, interact with matter by electrical forces and lead to the excitation and ionization of atoms. The particles predominantly interact with orbital electrons of an atom. The ejected electrons sometimes have sufficient energy to yield secondary interactions with neighboring atoms. These electrons are called delta ($\delta$) rays. The charged particles deposit a large amount of energy in a short distance of travel relative to the photons.

Photon interactions

High-energy photons interact with matter through several different mechanisms, depending on the energy, and include Rayleigh (coherent) scattering, Compton scattering, photoelectric effect, and pair production. The dominant mechanisms in nuclear medicine imaging are photoelectric effect and Compton scattering (Fig. 1.2).

In photoelectric effect, all of the energy in incident photons is transferred into an orbital electron in an atom, and some of the energy is used to overcome binding energy of the electron to be ejected from the atom. The photoelectric effect dominates in human tissues at photon energies $\lesssim 100$ keV. In contrast, Compton scattering is a dominant interaction mechanism for photons with $> \sim 100$ keV energy and $< \sim 2$ MeV. In this interaction, loosely

![Fig. 1.2. Interaction of photons with matter: (a) Photoelectric effect and (b) Compton scattering.](image-url)
bound orbital electrons are ejected by absorbing part of the energy of the incident photons. After the interaction, the photon with the reduced energy changes its direction. Attenuation of photons is the removal of photons from a beam of X- or $\gamma$-rays as the photons pass through matter. The attenuation is mostly caused by absorption and scattering of the primary photons in nuclear medicine.

1.2. Instrumentation

1.2.1. Imaging procedures

The most important role of nuclear medicine imaging modalities is the quantitative measurement of physiologic and biochemical characteristics by the *in vivo* imaging of radioactive substances to investigate biochemical and pathologic phenomena, diagnosis of diseases, and determination of prognosis after treatment. In the typical nuclear imaging procedure, we first inject the radiotracer that tracks a particular biochemical process in our body, and using a gamma ($\gamma$) camera or PET scanner, we measure the radiation emitted from the tracer to produce a picture of the body showing where the tracer has accumulated.

*Types of nuclear imaging methods*

There are two types of nuclear imaging methods (single-photon imaging and PET). The distinction between these two imaging modalities is based on the physical properties of the radioisotopes used for imaging. In single-photon imaging, single-photon emitters are used. These radioisotopes emit single $\gamma$-ray photons with each radioactive decay. The most widely used single-photon emitters include $^{99m}$Tc, $^{201}$Tl, and $^{123}$I. In contrast to single-photon imaging, PET uses the radioisotopes that finally emit two $\gamma$-ray photons simultaneously.

1.2.2. Gamma camera

A $\gamma$-camera is a single-photon imaging device, also called a scintillation camera or Anger camera, and comprises a collimator, a scintillation (or semiconductor) detector, and readout electronics (Fig. 1.3).
Collimator

In γ-cameras, the most unique component is a mechanical collimator. This mechanical collimator is made of heavy materials, such as lead or tungsten, to select only the γ-rays traveling in a specific direction. Because these heavy materials absorb radiation energy easily, γ-rays with an oblique direction to the collimator septa are blocked, and only the γ-rays traveling parallel with the collimator septa (except for the pinhole collimator) can be detected by the scintillation detector. Without the collimation, the γ-rays will be detected by the camera in all possible random directions without any information about the incident direction, thus leading to severe blurring of the projection images.

Scintillation detector

The scintillation detector, another component of a γ-camera, is located behind the γ-camera. Most γ-camera systems are based on a scintillation detector that consists of a scintillation crystal (mostly NaI(Tl) in γ-cameras) and photosensors. The scintillation crystal emits visible light following interaction with radiation. Thus, the energy of the γ-ray is absorbed by the scintillation crystal and part of this energy is converted into visible light.
photons. Therefore, photosensors are required to measure these visible photons. The most common photosensor used in a \(\gamma\)-camera is the photomultiplier tube (PMT), in which the visible light photons are converted into an electrical signal at the photocathode that is amplified by the strong electric potential between the cascading dynodes arranged in this device.

**Semiconductor radiation detector**

There are increasing attempts to use semiconductor detectors for direct radiation measurement (i.e., Cd-Zn-Te [CZT]) in \(\gamma\)-cameras. The semiconductor detectors provide much better energy resolution than scintillation detectors. The better energy resolution provides improved performance in the rejection of cross-talk photons in dual or multiple isotopes imaging (i.e., simultaneous scans of \(^{99}\text{Tc}\) and \(^{123}\text{I}\)). In addition, because the CZT can also be operated in a magnetic field, the SPECT/MRI system based on this device holds promise for simultaneous SPECT/MRI acquisition.

### 1.2.3. SPECT

**Principles and types**

Similar to X-ray computed tomography (CT), tomographic imaging is also possible with \(\gamma\)-cameras. This imaging technology is called single-photon emission computed tomography (SPECT). During SPECT, the \(\gamma\)-camera collects projection data by means of rotating around the objects. A dual-head \(\gamma\)-camera is most commonly used for SPECT imaging. A triple-head \(\gamma\)-camera is also available (Fig. 1.4). Currently, the use of SPECT/CT, which is a hybrid imaging system to acquire functional and anatomic information altogether, is on the increase. The major SPECT applications include perfusion imaging in the heart and brain.

**Pinhole SPECT**

For small animal imaging, pinhole collimators are usually used to achieve high spatial resolution. In the pinhole collimation system, with the smaller aperture diameter, we can obtain images with higher spatial resolution. The cost to obtain high spatial resolution is the loss of sensitivity because the sensitivity of the pinhole collimator is inversely proportional to the diameter.
of the aperture. Therefore, to compensate for this sensitivity loss with the smaller aperture, most small animal SPECT systems now use multi-pinhole collimators in which the multiple pinhole apertures collect the projection data simultaneously (Fig. 1.5).

Multi-pinhole collimator technology has been translated into the clinical SPECT systems as well. A stationary multi-pinhole collimator is used in a cardiac-specific SPECT, in which the each pinhole aperture is focused on the myocardium and provides angular data sufficient for the stationary data acquisition without camera rotation.
1.2.4. **PET**

**Basic principles**

The radioisotopes used in PET have a fewer number of neutrons than stable isotopes (e.g., $^{11}$C has only five neutrons, although the stable isotope, $^{12}$C, has six neutrons) and undergo positron decay. As previously described, one of the protons in this unstable isotope is changed into a neutron by emitting the positron to become a stable atom. When the positron is emitted from the nucleus, the positron travels a short distance (the so-called positron range), and finally meets an electron. The positron and electrons that meet each other lose their mass, which is changed into the energy in the form of $\gamma$-rays.

In this conversion of particles into the $\gamma$-rays, three physical quantities (energy, momentum, and electrical charge) should be preserved. Therefore, 2 $\gamma$-rays with 511-keV energy are annihilated in opposite direction, as shown in Fig. 1.6.

**PET scanner**

The PET scanner detects these two $\gamma$-rays to determine the line of response (LOR), which gives us the information about the location where the $\gamma$-rays were emitted and the direction of the $\gamma$-ray flight. Because LOR provides

![PET principle: mutual annihilation.](image-url)
the information regarding both the position and direction of the incident photons, PET scanners do not require the mechanical collimator in contrast to the $\gamma$-camera. This is the reason why PET has a better sensitivity than a $\gamma$-camera in which most of the $\gamma$-rays are absorbed by the collimator. To generate the sinogram (raw data for image reconstruction) from the LOR data, the $\gamma$-rays are sorted according to the direction of incidence and distance from the center during or after the PET scan. Iterative reconstruction algorithms, such as the OSEM algorithm, are commonly used to obtain the reconstructed PET data.

The elementary module in most PET scanners is a block detector. In the block detector, the scintillation crystal array is coupled with the array of photosensors. Sharing of visible light by multiple photosensors to determine the position of $\gamma$-ray interaction is a common method used in the PET block detector. However, the direct coupling of each crystal element with each photosensor is also a possible way. The block detectors compose a PET detector ring, and axial field-of-view of PET scanners can be extended by the combination of multiple rings of detector blocks. General-purpose human PET scanner has a ring diameter between 80 and 90 cm and the axial field-of-view between 15 and 20 cm. Currently, combined PET/CT scanners, in which a PET gantry is in tandem with a CT gantry, are predominantly used (Fig. 1.7).
Time of flight–PET

If we measure the difference in arrival times of two $\gamma$-rays (time-of-flight [TOF] information) exactly, we can pinpoint the annihilation position. In this ideal situation, we no longer need the image reconstruction algorithm based on the back-projection technique. However, in the practical situation, there is always uncertainty in the timing measurement. Although the timing resolution of the current PET systems equates to a positional uncertainty of $\sim 9$ cm, TOF information is still useful for the back-projection–based image reconstruction to reduce the background noise.

In conventional non–TOF-PET, the probability of annihilation position is equally distributed to all voxels along the LOR for image reconstruction. However, in TOF-PET, the probability can be limited within the segment of response using TOF information (Fig. 1.8). Therefore, TOF information is useful for localizing the source position and reducing the propagation of noise along the LOR.

Small animal PET

Small animal–dedicated PET scanners basically have the same configuration as the clinical PET scanners for human or large animal studies. However, smaller scintillation crystals are employed to achieve better spatial resolution. In addition, a 10- to 20-cm diameter is common in small animal

![Fig. 1.8. Principle of TOF-PET: (a) Non–TOF-PET; (b) TOF-PET. (Reproduced from Lee JS, Technical advances in current PET and hybrid imaging systems, Open Nucl Med J 2:192–208, 2010.)](image)

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PET scanners and the relatively long axial field-of-view and scintillation crystal elements compared to ring diameter ensures better sensitivity than human scanners (Fig. 1.9).

Many advanced detector technologies, such as depth-of-interaction (DOI) measurement, are used in small animal PET scanners for high spatial resolution and sensitivity. The relatively small diameter and long crystal elements in small animal PET cause a parallax error at the periphery of the transverse field-of-view, which is produced by the penetration of oblique $\gamma$-rays. If the DOI position in the PET detector is measured, the parallax error can be much reduced.

1.2.5. Hybrid systems

PET/CT and SPECT/CT

The combination of the nuclear medicine images with the anatomic imaging modalities, such as CT or MRI, can enhance the clinical information from both modalities and bring on the synergetic effects by merging the information. For example, the accurate anatomic localization, correlative studies, partial volume correction, and statistical reconstruction based on the anatomic prior are possible by the combination. Before the development of multimodal imaging devices, software co-registration and fusion technologies were available. However, these technologies were used for limited clinical purposes because it is time-consuming, non-user-friendly, and unsuccessful outside the brain.

PET/CT and SPECT/CT are the integrated hardware systems in which both modalities are combined in a single gantry. The PET/CT or SPECT/CT
images provide accurate anatomic localization of abnormal lesions in PET and SPECT. CT also provides information on photon attenuation. CT-based attenuation correction has several advantages as follows: CT-based attenuation reduces the whole-body PET scan time by up to 40% and provides essentially noiseless attenuation correction factors.

**PET/MRI**

Although there are many benefits of PET/CT over the stand-alone PET (*vide supra*), several limitations of PET/CT have also been identified. Physiologic or voluntary motion of body and organs between the CT and PET scans often cause artifacts in the fused images because they are not simultaneously acquired. In addition, radiation exposure during the PET/CT examination is twice that of the standalone PET or CT. Therefore, if the PET/MRI is available, it will be especially useful in pediatric studies and repeated scans for treatment monitoring. Another advantage of PET/MRI is the higher soft tissue contrast in MRI. Therefore, PET/MRI is expected to yield superior diagnostic accuracy, particularly in brain studies, to PET/CT. In addition, it would also be useful in local tumor assessment and whole-body staging in which higher soft tissue contrast of MRI is beneficial.

However, simultaneous PET/MR imaging is technically challenging because PMT, the working horse in conventional PET scanners, is very sensitive to the magnetic field. Among the many approaches to overcome this challenge, two approaches currently adopted by major vendors include separation of conventional PMT-based PET scanners away from the MRI.
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machine (tandem type) and use of semiconductor photosensors in PET that is not influenced by the magnetic field (integrated type) (Fig. 1.10).

Bibliography


