Basic Radiation Oncology

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Springer

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ISBN: 978-3-642-11665-0 e-ISBN: 978-3-642-11666-7

DOI: 10.1007/978-3-642-11666-7

Springer Heidelberg Dordrecht London New York

Library of Congress Control Number: 2010925732

Cover design: eStudio Calamar, Figueres/Berlin

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Dedication

Dedicated to the memory of Professor Ibtisam Lale Atahan, MD (1945–2007)

Foreword

Revolutionary advances have been taking place in radiation oncology as our world has entered a new millennium. Developments in radiological and functional imaging techniques over the last two decades have enabled us to delineate tumors more accurately in the three spatial and the fourth (temporal) dimensions. More powerful computerized planning systems are facilitating accurate three-dimensional dose calculations as well as inverse planning processes. We have even started to use robotic technology to track our targets in real time for more precise delivery of radiotherapy.

All of those high-tech machines sometimes cause us to spend many hours in front of detailed displays of serial computerized tomography (CT) slices. However, we are still treating our patients with the same types of ionizing radiation discovered more than a century ago. Therefore, every member of a radiation oncology team should know the interactions of ionizing radiation with matter at the atomic level, and be familiar with its effects in biological systems. In addition, every radiation oncologist should have an essential knowledge of evidence-based clinical oncology in relation to the indications and technical aspects of radiotherapy at major cancer sites.

Basic Radiation Oncology is an up-to-date, bedside-oriented textbook that integrates radiation physics, radiobiology and clinical radiation oncology. The book includes the essentials of all aspects of radiation oncology, with more than 300 practical illustrations and color figures. The layout and presentation is very practical and enriched with many eye-catching conceptual highlights. The first three chapters review crucial ideas in radiation physics and radiobiology as well as the terminology of clinical radiation oncology. Basic descriptions of all high-tech radiotherapy machines are also given. The remaining eleven clinical chapters describe anatomy, pathology, general presentation, treatment algorithms and the technical aspects of radiotherapy for major cancer sites. The 2010 (seventh) edition of the AJCC Staging System is provided for each tumor type. Practical details about key studies, particularly randomized ones, and available RTOG consensus guidelines for the determination and delineation of targets are also included at the end of each clinical chapter.

Basic Radiation Oncology meets the need for a practical and bedside-oriented radiation oncology textbook for residents, fellows, and clinicians of radiation, medical and surgical oncology, as well as for medical students, physicians and medical physicists interested in clinical radiation oncology.

K.S. Clifford Chao, MD

Preface

The aim of writing *Basic Radiation Oncology* was to provide a structured overview of the theory and practice of radiation oncology, including the principles of radiation physics, radiation biology and clinical radiation oncology. We have encompassed the fundamental aspects of radiation physics, radiobiology, and clinical radiation oncology. In the last two decades, there have been many technical and conceptual advances in both treatment planning systems and radiation delivery systems. However, there are no changes in the basic interactions of radiation with atoms or cells. Therefore, basic concepts that are crucial to understanding radiation physics and radiobiology are reviewed in depth in the first two sections. The third section describes radiation treatment regimens appropriate for the main cancer sites and tumor types according to the seventh edition of the American Joint Committee on Cancer Staging System. Many ‘pearl boxes’ are used to summarize important information, and there are more than 350 helpful illustrations. *Basic Radiation Oncology* meets the need for a practical radiation oncology book. It will be extremely useful for residents, fellows, and clinicians in the fields of radiation, medical, and surgical oncology, as well as for medical students, physicians, and medical physicists with an interest in clinical oncology.

Evidence-based data are also available at the end of the section on each clinical subsite. However, every clinician should be aware of the fact that there is a very fine line between evidence-based and probability-based medicine. Cancer is a highly complex subject, and it is impossible to fit it into a simple mathematical formula or “p” value. Therefore, we must not throw away experience-based data during our clinical decision-making procedures. We extend our most sincere gratitude to Zeki Bayraktar, the Dean of Gulhane Military Medical School, as well as to our families for their understanding as we worked to meet our publication deadlines.

Ankara, Turkey — Dr. M. Beyzadeoglu
Ankara, Turkey — Dr. Gokhan Ozyigit
Kocaeli, Turkey — Dr. Cuneyt Ebruli

Acknowledgments

The editors are indebted to Nel van der Werf, Ute Heilmann, Stefanie Schafer, Meike Stoeck, Wilma McHugh from Springer and Dakshinamoorthy Mahalakshmi from SPi for their assistance in preparing Basic Radiation Oncology. Special thanks are extended to Professor K.S. Clifford Chao, who is chairman of the radiation oncology departments at Columbia University, New York Presbyterian Hospital and Weill Cornell Medical College, for honoring us with his foreword. We extend our most sincere gratitude to our colleagues and friends at Gulhane Military Medical School and the Faculty of Medicine at Hacettepe University.

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Introduction and History

Roentgen was working on Crook's Vacuum tube on November 8th 1895. He suddenly realized that shadows of his wife's finger bones and ring in her finger appeared on the palette. This was the discovery of X-rays and the beginning of radiation history (Fig. 1).

Fig. 1 The first X-ray (X-ray of the hand of Anna Bertha Roentgen)

Henri Becquerel opened his drawer in his laboratory on March 1896. He was greatly surprised when he saw blackened photo glasses despite their being kept in a totally dark medium. This was the discovery of natural radioactivity (Fig. 2).

It has been more than a century since the discovery of X-rays by Roentgen and that of natural radioactivity by Becquerel, and in that time the field of radiation oncology has seen enormous changes due to the now-standard use of extraordinarily complex systems and

Fig. 2 The blurred photo glasses of Becquerel

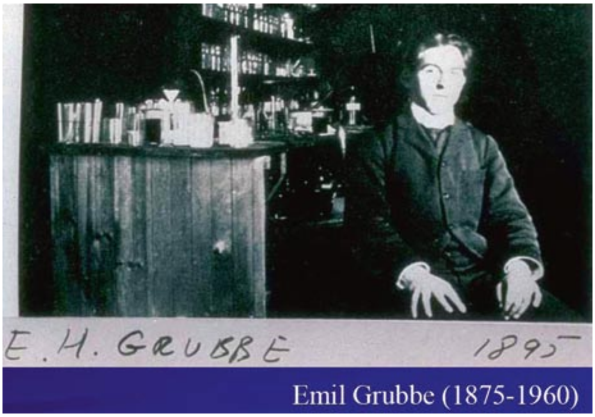


Fig. 3 The first radiation oncologist, Emil Grubbe

high-technology products to treat cancers. Indeed, just two months after the discovery of X-rays (i.e., on 1 Jan 1896), a medical student named Emil Grubbe (Fig. 3) used X-rays to treat a 65 year old female patient named Rosa Lee with recurrent breast carcinoma at a lamp factory in Chicago.

We can summarize the most important developmental steps in the field of radiation oncology chronologically as follows:

1895: Discovery of X-rays by Wilhelm Conrad Roentgen (Germany)
1895: Use of X-rays in breast cancer by Emil Grubbe (Chicago, USA)
1896: Use of X-rays in nasopharyngeal cancer and in pain palliation by Voigt J. Ärztlicher Verein (Germany)
1896: Discovery of natural radioactivity by Henri Becquerel (Paris, France)
1896: Use of X-rays in the treatment of gastric cancer by Despeignes (France)
1896: Use of X-rays in the treatment of skin cancer by Léopold Freund (Austria)
1897: Discovery of electrons (Thompson)
1898: Discovery of radium by Pierre and Marie Curie (France)
1899: Definition of the alpha particle (E. Rutherford)

1901: The first use of radium in skin brachytherapy (Dr. Danlos, France)
1903: Publications showing the efficacy of radiotherapy in lymphoma (Senn & Pusey)
1905: Discovery of the sensitivity of seminoma to radiation (A. Béclère, France)
1905: Discovery of the photoelectric effect by A. Einstein (Germany)
1906: Discovery of characteristic X-rays (G. Barkla)
1922: Demonstration of the Compton effect (Arthur H. Compton)
1931: First cyclotron (Ernest O. Lawrence, USA)
1932: Discovery of neutrons (Sir James Chadwick, UK)
1934: Discovery of artificial radioelements (Irène and Frédéric Joliot-Curie, France)
1934: 23% cure rate in head and neck cancer (Henri Coutard)
1934: Death of Mrs. Marie Curie due to pernicious anemia (myelodysplasia)
1940: The first betatron (Donald W. Kerst)
1951: The first cobalt-60 teletherapy machine (Harold E. Johns, Canada)
1952: The first linear accelerator (linac) machine (Henry S. Kaplan, USA)
1968: Discovery of the gamma knife (Lars Leksell)
1971: The first computerized tomography (CT) (G.N. Hounsfield, UK)
1973: The first MRI machine (Paul C. Lauterbur, Peter Mansfield)
1990: The first use of computers and CT in radiotherapy (USA)
1994: The first clinical IMRT treatment (USA)
1996: FDA approval of the first IMRT software
2001: FDA approval of robotic radiosurgery
2002: FDA clearance of spiral (helical) tomotherapy
2003: The first use of image-guided radiation therapy (IGRT) technology

Radiation Physics

1

Murat Beyzadeoglu, Gokhan Ozyigit, and Cuneyt Ebruli

1.1

Atom

The word “atom” derives from the Greek word “atomos,” which means indivisible; an atom was the smallest indivisible component of matter according to some philosophers in Ancient Greece [1]. However, we now know that atoms are actually composed of subatomic particles: protons and neutrons in the nucleus of the atom, and electrons orbiting that nucleus (Fig. 1.1).

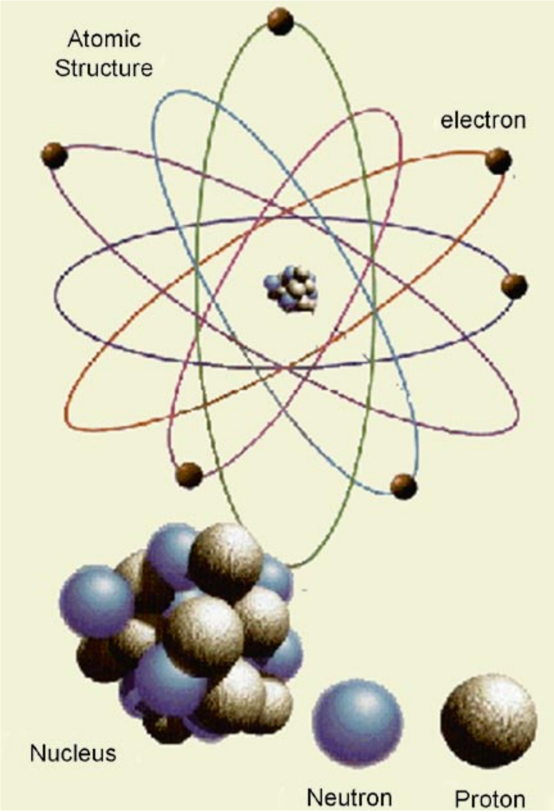


Fig. 1.1 The structure of an atom

M. Beyzadeoglu et al. *Basic Radiation Oncology*,
DOI: 10.1007/978-3-642-11666-7_1, © Springer-Verlag Berlin Heidelberg 2010

Electrons are negatively charged particles.

Protons are positively charged particles. The mass of a proton is about 1,839 times greater than that of an electron.

Neutrons are uncharged (neutral) particles. The mass of a neutron is very slightly larger than that of a proton.

Protons and neutrons form the nucleus of an atom, and so these particles are also called nucleons.

The diameter of an atom is about 10^{-8} cm, whereas the diameter of the atomic nucleus is 10^{-13} cm.

The total number of protons and neutrons in a nucleus (p + n) (i.e., the total number of "nucleons") is termed the mass number of that atom, symbolized by A [1]. The total number of protons is called the atomic number and is symbolized by Z. The atomic number and the mass number of an element X are usually presented in the form ${}^{A}_{Z}\mathrm{X}$ (Fig. 1.2).

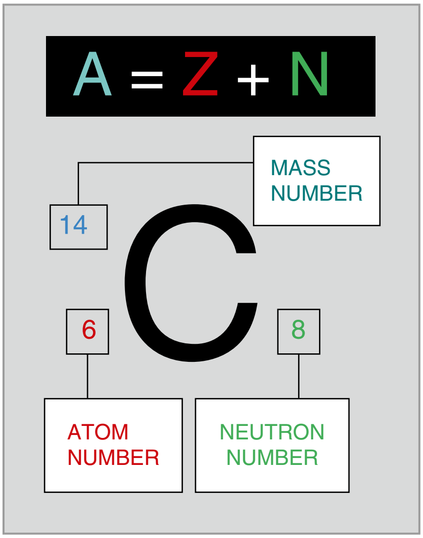


Fig. 1.2 Writing a element in nuclide format (carbon-14 is used as an example)

Nuclide → if an atom is expressed in the form ${}^{A}_{Z}X$, it is called a nuclide (e.g., ${}^{4}_{2}\mathrm{He}$).

Radionuclide → if the atom is expressed in the form ${}^{A}_{Z}\mathrm{X}$ and is radioactive, it is called a radionuclide.

1.2
Radiation

The propagation of energy from a radiative source to another medium is termed radiation. This transmission of energy can take the form of particulate radiation or electromagnetic radiation (i.e., electromagnetic waves). The various forms of radiation originating from atoms, which include (among others) visible light, X-rays and γ-rays, are grouped together under the terms "electromagnetic radiation" [1] or "the electromagnetic spectrum" [1, 2]. Radio waves, which have the longest wavelengths and thus the lowest frequencies and energies of the various types of electromagnetic radiation, are located at tone end of the electromagnetic spectrum, whereas X-rays and γ-rays, which have the highest frequencies and energies, are situated at the other end of this spectrum.

Photon

- If the smallest unit of an element is considered to be its atoms, the photon is the smallest unit of electromagnetic radiation [3].
- Photons have no mass.

Common features of electromagnetic radiation [4, 5]:

- It propagates in a straight line.
- It travels at the speed of light (nearly 300,000 km/s).
- It transfers energy to the medium through which it passes, and the amount of energy transferred correlates positively with the frequency and negatively with the wavelength of the radiation.
- The energy of the radiation decreases as it passes through a material, due to absorption and scattering, and this decrease in energy is negatively correlated with the square of the distance traveled through the material.

Electromagnetic radiation can also be subdivided into ionizing and nonionizing radiations. Nonionizing radiations have wavelengths of $\geq 10^{-7}$ m. Nonionizing radiations have energies of <12 electron volts (eV); 12 eV is considered to be the lowest energy that an ionizing radiation can possess [4].

Types of nonionizing electromagnetic radiation [5]:

- Radio waves
- Microwaves
- Infrared light
- Visible light
- Ultraviolet light

1.3 Ionizing Radiation

Ionizing (high-energy) radiation has the ability to remove electrons from atoms; i.e., to ionize the atoms. Ionizing radiation can be electromagnetic or particulate radiation (Fig. 1.3). Clinical radiation oncology uses photons (electromagnetic) and electrons or (rarely) protons or neutrons (all three of which are particulate) as radiation in the treatment of malignancies and some benign conditions [6].

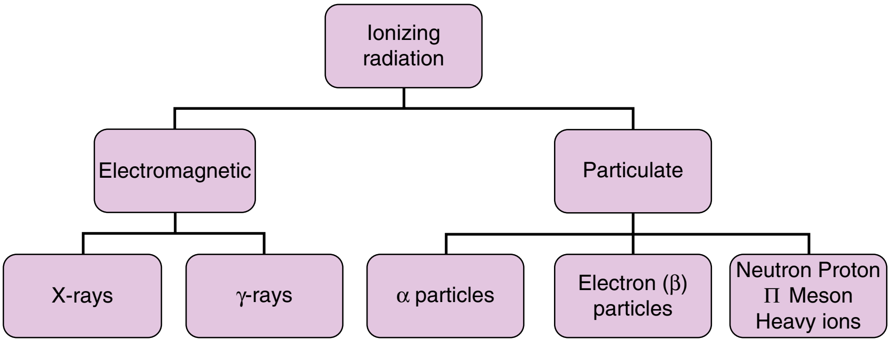


Fig. 1.3 Ionizing radiations

1.3.1 Ionizing Electromagnetic Radiation

The electromagnetic spectrum comprises all types of electromagnetic radiation, ranging from radio waves (low energy, long wavelength, low frequency) to ionizing radiations (high energy, short wavelength, high frequency) (Fig. 1.4) [7].

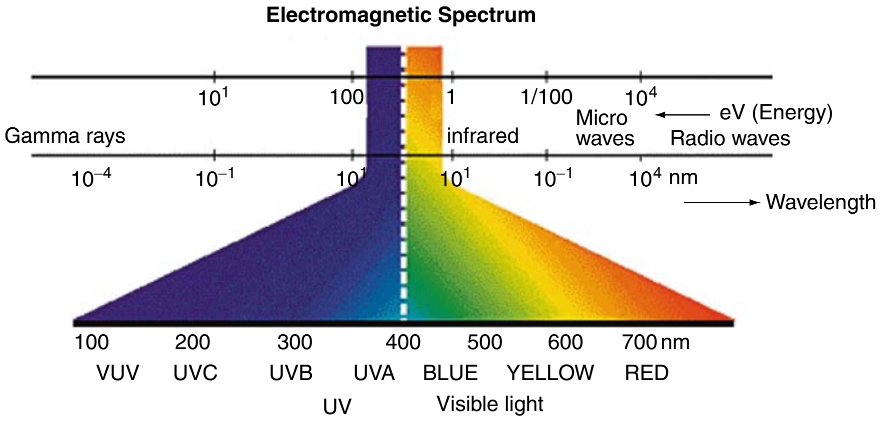


Fig. 1.4 Electromagnetic spectrum

Electrons are knocked out of their atomic and molecular orbits (a process known as ionization) when high-energy radiation interacts with matter [8]. Those electrons produce secondary electrons during their passage through the material. A mean of energy of 33.85 eV is transferred during the ionization process, which in atomic and molecular terms is a highly significant amount of energy. When high-energy photons are used clinically, the resulting secondary electrons, which have an average energy of 60 eV per destructive event, are transferred to cellular molecules.

1.3.1.1
X-Rays

X-rays were discovered by the German physicist Wilhelm Conrad Roentgen in \95 [9]. The hot cathode Roentgen tube, which was developed by William David Coolidge in 1913, is a pressured (to 10^{-3} mmHg) glass tube consisting of anode and cathode layers between which a high-energy (10^6 –10^8 V) potential is applied (Fig. 1.5a, b). Electrons produced by thermionic emission in the cathode are accelerated towards the anode by the potential. They thus hit the anode, which is a metal with high melting temperature. X-rays are produced by the sudden deceleration of these electrons due to Coulomb interactions with nuclei in the anode (this sudden deceleration of fast-moving electrons is known as bremsstrahlung; Fig. 1.6). The energy and the wavelength of the X-rays depend on the atomic number of the target (anode) metal, as well as the velocity and the kinetic energy of the electrons. This process is used to produce medical radiation in diagnostic X-ray units, linear accelerators (linacs), and betatrons.

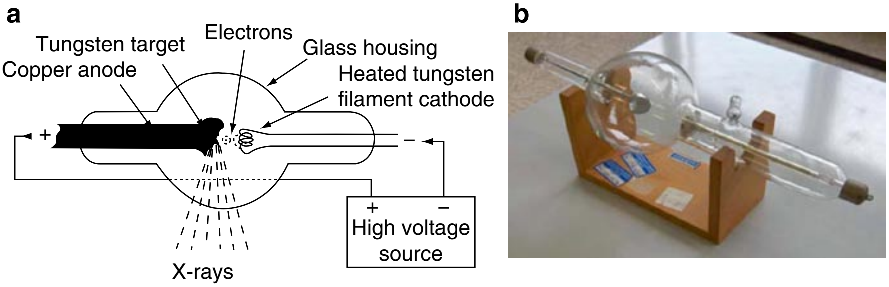


Fig. 1.5 (**a**) Schematic representation of an X-ray tube; (**b**) photograph of an X-ray tube

X-rays are produced by extranuclear procedures. Two kinds of X-rays are created by X-ray tubes [10, 11]. The first type corresponds to the bremsstrahlung X-rays mentioned above. The second type occurs because an electron in an inner atomic orbital is knocked out by an incoming electron, and the resulting space in the orbital is filled by other electron that moves from an outer atomic orbital (Fig. 1.7). This electron must shed energy to move in this manner, and the energy released is radiated as characteristic X-rays [12]. They are characteristic due to the fact that their energy depends on the target metal onto which the electrons are accelerated.

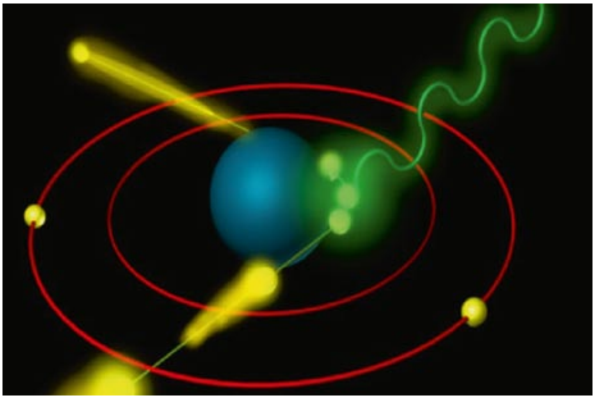


Fig. 1.6 Bremsstrahlung process

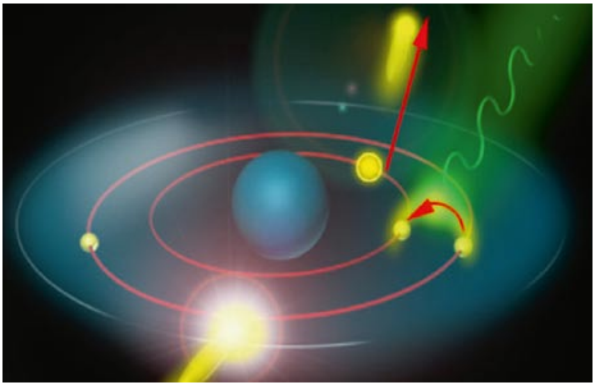


Fig. 1.7 Characteristic X-ray generation

X-rays produced by bremsstrahlung have a broad energy spectrum (→ heterogeneous), while characteristic X-rays are monoenergetic beams.

1.3.1.2
Gamma (γ) Rays

Gamma rays are physically identical to X-rays, but they are emitted from atomic nuclei (intranuclearly). An unstable atomic nucleus sheds its excess energy in the form of either an intranuclear electron (e^-) (beta particle) or a helium nucleus (an "alpha particle") (Fig. 1.8). If it still possesses excess energy after that, gamma rays are emitted in order to reach its steady state (Fig. 1.9).

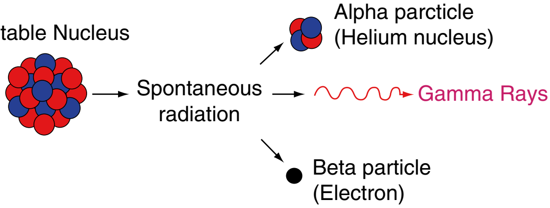


Fig. 1.8 Alpha particle generation

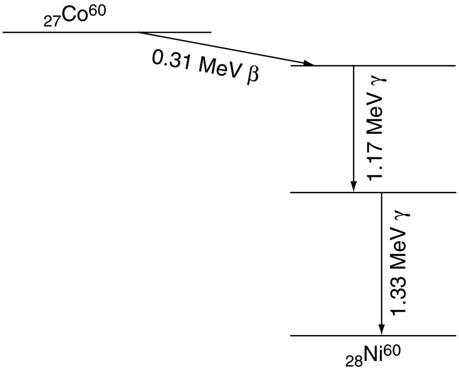


Fig. 1.9 Co-60 decay

Gamma rays have well-defined energies. For instance, two monoenergetic gamma rays with a mean energy of 1.25 MV (1.17 and 1.33 MV) are emitted after beta rays of 0.31 MV energy have been emitted during the decay of ^{60}Co (cobalt-60; Co-60). Through this process, ^{60}Co transforms into a final, stable decay product, ^{60}Ni (nickel-60; Ni-60). There is actually a stable naturally occurring form of cobalt: ^{59}Co. ^{60}Co is created through neutron bombardment in nuclear reactors, and has a half-life of 5.26 years. One gram of ^{60}Co has an activity of 50 Ci (1.85 terabecquerels) [13, 14].

The half-life of a radioisotope is the time required for its activity to half [15].

The activity of a radioisotope is the number of decays per second, and is defined in becquerels or curies.

- Becquerel (Bq): the standard unit of (radio)activity; it is defined as one disintegration (decay) per second.
- Curie (Ci): an older unit of (radio)activity, corresponding to 3.7×10^{10} disintegrations per second.

The decay of a radioactive nucleus is a spontaneous process. There are three forms of radioactive decay. Alpha or beta particles are emitted during the alpha and beta decays of an unstable nucleus in order to reach a stable nucleus. A gamma decay occurs without any change in the form of the nucleus.

Alpha Decay [16]. An alpha particle consisting of two protons and two neutrons is emitted if a nucleus is unstable because it has an excessive number of both protons and neutrons (Fig. 1.10).

After alpha decay, the alpha particle possesses most of the energy, due to the conservation of momentum and the fact that the alpha particle is much less massive than the residual nucleus. Although the $^{4}_{2}\mathrm{He}$ nucleus is very energetic, does not travel very far compared to most forms of radiation, due to its relatively heavy mass. Alpha decay is usually observed in nuclei with mass numbers of more than 190. The energy spectrum of alpha decay is not continuous, and varies between 4 and 10 MeV. Alpha particles strongly interact with the electrons of the matter through which they pass, since they are charged particles.

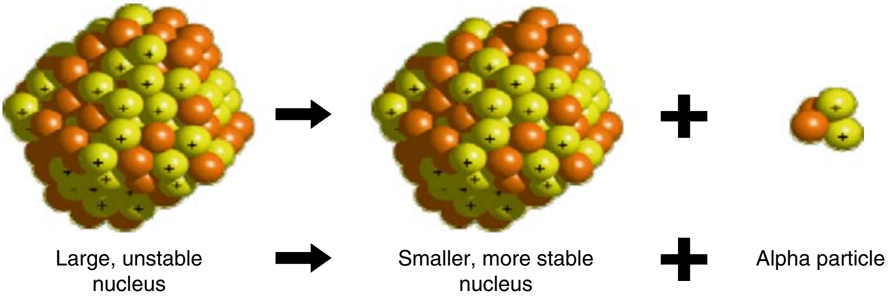


Fig. 1.10 Alpha decay

Beta Decay [17]. There are three types of beta decay.

If a radionuclide is unstable because it has an excess number of neutrons in its nucleus, it transforms one of the neutrons into a proton and an electron in order to reduce the amount of energy in its nucleus (Fig. 1.11). The electron is rapidly propelled out of the nucleus, while the proton remains. This high-speed electron called a β^- particle or negatron, and the process is termed *β^- decay*. The atomic number of the radionuclide increases by one, and thus it changes into the next element in the periodic table. Note that the mass number does not change (it is an "isobaric" decay) [16, 17].

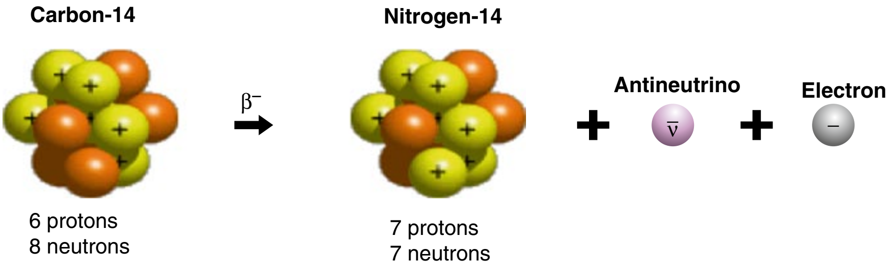


Fig. 1.11 β^- decay

If a radionuclide is unstable due to an excess amount of protons or a lack of neutrons, one of the protons transforms into a neutron and a small positively charged particle called a positron in a process termed *β^+ decay* [17]. The neutron stays in the nucleus while the positron is propelled out of it (Fig. 1.12). The atomic number of the radionuclide that emits the positron decreases by one, and thus it changes into the preceding element in the periodic table. Again, note that the mass number does not change.

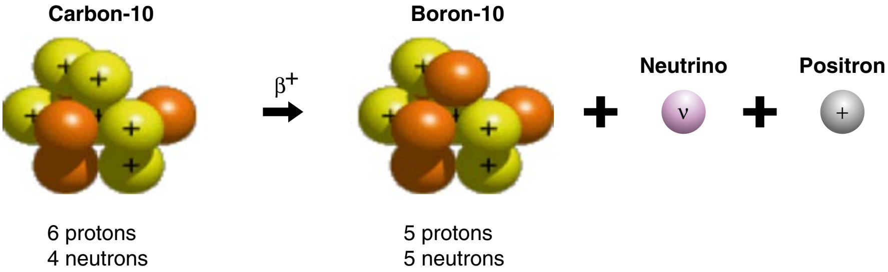


Fig. 1.12 β^+ decay

If the nucleus is unstable due an excess amount of protons, one of the electrons close to the atomic nucleus, such as an electron in a K and L orbital, is captured by the nucleus (Fig. 1.13). This electron then combines with a proton, yielding a neutron and a neutrino. This process is called *electron capture* [16]. Note that no particle is emitted from the nucleus, but the atomic number decreases by one, as in positron decay. Yet again, the mass number does not change. The space in the inner orbital is filled by an electron from an outer orbital, resulting in the emission of characteristic X-rays.

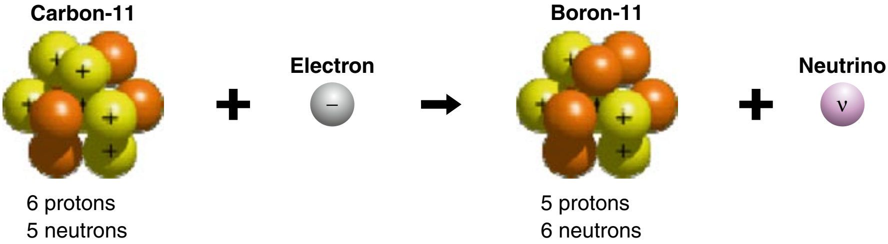


Fig. 1.13 Electron capture phenomenon

There are also three types of beta decay. In all of them, the mass number of the nucleus remains constant during the decay, while the numbers of protons and neutrons change by one unit. Furthermore, the emission of some massless, uncharged particles called neutrinos and antineutrinos is observed during each beta decay process. The existence of these particles was first suggested by Pauli in 1930, although it was Fermi that provided the name “neutrino” [16].

Gamma Emission [13, 14, 16]. A nucleus is not always fully stable (i.e., at its basal energy level) just after it decays; sometimes, the nucleus will be in a semi-stable state instead (Fig. 1.14). The excess energy carried by the nucleus is then emitted as gamma radiation. There is no change in the atomic or mass number of the nucleus after this decay, so it is termed an “isomeric” decay.

The half-lives of gamma radiation sources are much shorter than sources of other types of decay, and are generally less than 10^{-9} s. However, there are some gamma radiation sources with half-lives of hours or even years. Gamma energy spectra are not continuous.

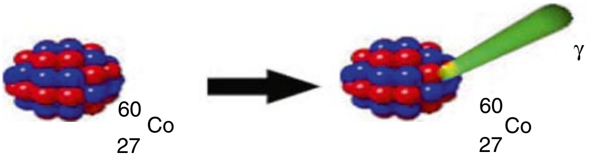


Fig. 1.14 Gamma emission

Isotope [18]. Atoms with the same atomic number but different mass numbers are called isotopes (e.g., ${}^{11}_{6}\mathrm{C}$, ${}^{12}_{6}\mathrm{C}$, ${}^{13}_{6}\mathrm{C}$).
Isotone. Atoms with the same number of neutrons, but different numbers of protons are called isotones (e.g., ${}^{9}_{3}\mathrm{Li}$, ${}^{10}_{4}\mathrm{Be}$, ${}^{11}_{5}B$, ${}^{12}_{6}\mathrm{C}$).
Isobar. Atoms with the same number of nucleons but different numbers of protons are called isobars (e.g., ${}^{12}_{5}\mathrm{B}$, ${}^{12}_{6}C$, ${}^{12}_{7}\mathrm{N}$).
Isomer. Atoms with the same atomic and mass numbers but which are in different energy states are called nuclear isomers ($\mathrm{Tc}^{99\mathrm{m}}$)

1.3.2
Ionizing Particulate Radiation

Electrons, protons, alpha particles, neutrons, pi mesons and heavy ions are all forms of ionizing particulate radiation [19]. Electrons are the particles that are generally used in routine clinics. Other particles are only used in specific clinics worldwide.

Electrons, due to their negative charge and low mass, can be accelerated to high energies in linacs or betatrons.

The mass of an electron is $9.109\,3826(16)\times10^{-31}$ kg.
The electrical charge of an electron is $-1.602\,176\,53(14)\times10^{-19}$ C.

Electrons are normally bound to a (positively charged) nucleus. The number of electrons is equal to the number of protons in a neutral atom. However, an atom can contain more or less electrons than protons, in which case it is known as a negatively or positively charged ion, respectively. Electrons that are not bound to an atom are called free electrons; free electrons can be produced during nuclear decay processes, in which case they are called beta particles.

Electrons have much smaller ranges (i.e., they travel smaller distances) in matter than gamma and X-rays, and can be absorbed by plastics, glass or metal layers (Fig. 1.15).

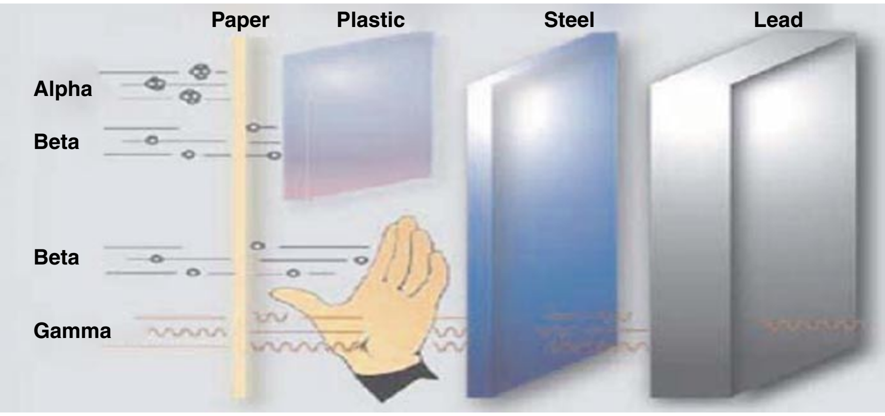


Fig. 1.15 Penetration ranges of various ionizing radiations

Neutrons are the neutrally charged particles that enable the formation of stable large atomic nuclei (Fig. 1.16) by decreasing the repulsion between the protons in the nucleus. However, neutrons, like protons, actually consist of particles called quarks; a neutron is one up quark and two down quarks, while a proton (Fig. 1.17) is two up quarks and one down quark.

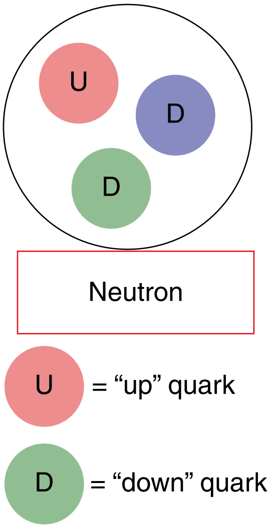
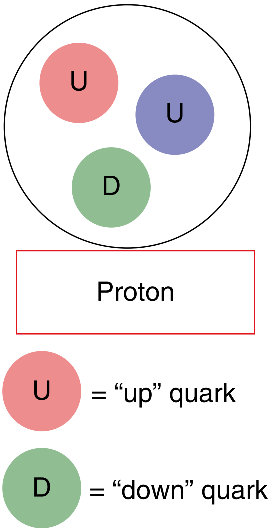


Fig. 1.16 Neutron

Fig. 1.17 Proton



1.4
The Interaction of Radiation with Matter

Radiation is scattered and absorbed when it passes through tissue [19, 20]. The intensities of monoenergetic X-rays or gamma rays attenuate exponentially within tissues. In other words, the intensity of radiation constantly decreases as it propagates within tissues. This decrease depends on the type of tissue and its thickness. If the wavelength stays constant, the intensity of the radiation passing through a tissue can be calculated by the following formula:

$$I = I_0 . e^{-\mu t} \tag{1.1}$$

I = intensity of outgoing radiation beam
I_0 = intensity of incoming radiation beam
μ = absorption coefficient (which is positively correlated with the fourth power of the atomic number of the penetrated tissue, and the third power of the wavelength of the radiation)
t = tissue thickness

As seen in the above formula, the intensity of the radiation decreases exponentially with the absorbent thickness, and the intensity of the outgoing radiation depends on the tissue absorption coefficient and its thickness.