Basic Radiotherapy Physics and Biology

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Second Edition

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Preface

Many radiation oncology textbooks are written in a formal academic style. When studying these highly detailed books, many residents struggle to find a good balance between time and comprehension. *Basic Radiotherapy Physics and Biology* is a by-product of long hours spent in preparation for the American Board of Radiology (ABR) Radiation Therapy Physics and Biology examinations. It is written in a concise and humorous style so that information may be rapidly reviewed, whether for daily use or for exam preparation. Using mnemonics, rules of thumb, and simple figures, we have attempted to make our text as "digestible" as possible. The intended audience for this book includes radiation oncology residents, radiation therapists, dosimetrists, physicists, medical students, and other readers motivated to learn about the physics and biology of radiation therapy.

The topics contained in this book are directly based on the *ABR Radiation Oncology Study Guide* that is available on the ABR website. Whereas the *ABR Study Guides* are formatted as a long list of topics, *this book* is organized into two equal parts. The physics topics are covered in Chaps. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, and 18 and the biology topics are covered in Chaps. 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, and 35. Each chapter consists of a series of concepts explained with bullet points of text, together with figures, equations, and mnemonics where appropriate and concise. A few math-heavy chapters also include a section entitled "Rules of Thumb." These rules intend to summarize mathematical concepts in plain language, favoring ease-of-use over detail. The book also includes two appendices of reference information: a glossary of terms and physical constants and a list of radionuclides used in imaging and radiotherapy.

This book does not cite specific references, as it is a collection of basic rules and principles and not a rigorous scholastic work. Those who wish to delve into the primary literature should refer to one of the many comprehensive textbooks and research papers that already exist. Instead, our book is designed as a quick reference, helpful for exam preparation and daily clinical practice in the real world. It is our hope that this book will be of great value to all students and would-be students in every discipline of radiation oncology.

Preface to the Second Edition

The unanimous decision by all co-authors to prepare a second edition of *Basic Radiotherapy Physics and Biology* was motivated not by the expectation of huge royalties. Nope! Those contemplating writing a textbook are in for a rude awakening if “financial windfall” is the main reason for writing a textbook, especially with 5 co-authors! Instead, we were motivated after receiving consistent positive feedback regarding the utility of the first edition in preparing radiation oncology residents for their board exams in biology and physics, and also by the realization that several of the chapters required an update.

We have endeavored to keep the writing style concise and with sporadic and well-placed injections of humor, so as to preserve the spirit of the first edition. However, with the realization that individualized medicine is here to stay and that cancer therapy will more frequently be guided by molecular tests that reveal genes, proteins, and pathways that can be targeted (or at least potentially targeted) and that residents and students would be expected to know about, we feel we would be remiss if we did not include what we believe to be the relevant players in the relevant pathways, with what we perceive to be the required level of minutiae. Thus, especially in the biology section, if readers were to compare the first and second editions, they would note an enhanced “attention to details” in several of the chapters. For example, the chapter on DNA damage/repair has been extensively updated, and the chapter that covers cell death and survival assays now includes additional sections that highlight other modes of death that now appear to be triggered by ionizing radiation.

Several other chapters were significantly revised. The chapter on effects of acute total body irradiation now includes more information about radiation countermeasures. The chapter in which we cover stochastic versus deterministic effects now includes updated recommendations for annual lens dose limits and current views on classification of cataractogenesis as stochastic or deterministic effect. Also, new content has been added about the exciting areas of immunotherapy and immunomodulation of the radiotherapy response.

Those that use this book to prepare for radiation oncology board exams are still advised to consult the *ABR Radiation Oncology Study Guide,* because content and emphasis can and does change over time. Since the book continues to be a collection of basic rules, principles, and current thinking in the fields of biology and physics, we continue to eschew citation of specific references. It remains a quick (though now somewhat more comprehensive) reference guide for exam preparation and practitioners. We hope that this updated edition will be helpful.

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Part I

Radiation Therapy Physics

Check for updates

Atomic and Nuclear Structure

1

Introduction

The nucleus is the core of the atom and is made up of several nucleons called protons and neutrons that are held together by strong force but also have tension to fall apart by coulombic forces exerted by the protons. The individual nucleons are made up of quarks that are held together by the weak force. Mass and energy are interchangeable by $E = mc^2$, and this can be demonstrated by the nuclear binding energy that causes a mass deficit caused by the nuclear binding energy. Several factors go into determining the stability of a nucleus, including neutron-to-proton ratio, nucleon pairing, and binding energy per nucleon. For the purposes of this book, the Bohr model will be used to describe electron behavior and interactions. This model uses finite energy shells with fixed binding energies. Any transition of an electron into a higher energy shell requires energy absorption (often in the form of a photon), and any transition of an electron into a lower energy shell will result in energy release, either in the form of a characteristic X-ray or in the form of an Auger electron.

Atomic and Nuclear Nomenclature

- The **atom** includes a **nucleus** and **electrons**.
  - Electrons determine the chemical properties of an atom.
  - **Nuclide** refers to the composition of the nucleus (number of protons and neutrons).
  - **Nucleons** include **protons** and **neutrons**.
- **The numbers:**
  - **A = Atomic mass number** (total protons + neutrons).
  - **Z = Atomic number** (total protons).

    Z determines the number of electrons, and therefore the chemical properties of the atom.

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  - **N = Neutrons = A – Z.**
- **The four "isos"**:
  - Isoto**p**e: same number of **protons**, different neutrons.
    Same chemical behavior, different mass, and different nuclear decay properties.
    Ex: ^{125}**I** and ^{131} **I,** both behave like iodine but have different half-lives.
  - Isoto**n**e: same number of **neutrons**, different protons.
    Rarely used.
  - Iso**bar**: same number of **nucleons**, different nuclide (more protons and less neutrons, or vice versa).
    "**bar**" = same mass—think barbell.
    Beta decay (see Chap. 2) and **electron capture** always result in an **isobar**.
    Ex: ^{131}**I** decays to ^{131}**Xe**, which has the same mass number but is a different nuclide and has different chemical properties.
  - Iso**mer**: same **nuclide**, different energy state (excited vs. non-excited)
    Isomers release their energy through **gamma decay** (see Chap. 2).
    Ex: ^{99m}**Tc** decays to ^{99}**Tc**, releasing its excess energy without changing the number of protons or neutrons.

The Four Fundamental Forces

- In order of descending strength, these are:
- **Strong Nuclear Force**:
  - The strongest force in nature; "glues" the nucleus together.
  - Holds the nucleus together, counters the repulsive effect of protons' positive charge.
- **Electromagnetic (Coulombic) Force**:
  - ~1/100 as strong as the strong force.
  - Opposites attract. Electrons are attracted by the positively charged nucleus and are more attracted as they get closer; valence electrons are not strongly attracted and their movements are responsible for nearly all chemical reactions.
  - Protons repel each other within the nucleus but are held in place by the strong force.
- **Weak Nuclear Force**:
  - ~1/1,000,000 as strong as the strong force.
  - Works inside particles (between quarks) and is responsible for radioactive decay.
  - Ex: ^{14}**C** decays into ^{14}**N** when a proton turns into a neutron and a β^-**.**
- **Gravity**:
  - ~1 × 10–^{39} as strong as the strong force.
  - Not important on the atomic scale.

On Mass

- **Mass** and **energy** are always interchangeable based on Einstein's $\mathbf{E = mc^2}$.
  - Energy can be converted to mass and mass can be converted to energy by multiplying by c^2 (speed of light squared).
  - As particles approach the speed of light, the velocity must remain constant so as the particle gains energy, it actually gains mass.
- There are two common ways to measure **mass**.
- **Atomic mass units (AMU)**:
  - Defined as 1/12 the mass of a Carbon-12 atom.
  - This is slightly less than the mass of the component particles, due to the **binding energy** of the carbon atom (see below).
  - **Proton mass = 1.0073 AMU**.
  - **Neutron mass = 1.0087 AMU** (slightly larger than a proton).
  - **Electron mass = 0.0005 AMU** (approx. 1/2000).
- **Energy equivalent (MeV/c** ^{2}, may be shortened to just "**MeV**"):
  - Defined as the equivalent amount of energy **(mc** ^{2}**)**, measured in mega electron volts.
  - **Proton mass = 938.3 MeV.**
  - **Neutron mass = 939.6 MeV.**
  - **Electron mass = 0.511 MeV** (or **511 keV**).
  - **1 AMU = 931.5 MeV.**

Nuclear Binding Energy

- When particles are bound to each other, they give off energy.
  - Stars shine as they perform fusion (atoms combining) and synthesize nuclei!
  - **Nuclear binding energy** is the energy from binding neutrons and protons into a nucleus.
- This energy is "paid for" in mass, according to $\mathbf{E = mc^2}$.
  - This "**mass deficit**" is equal to the **binding energy**.
  - **Ex: Carbon-12** (^{12}**C**) contains 6 protons and 6 neutrons.
    The sum of masses should be **12.09565 AMU**, but ^{12}**C** has a mass of **12.00000 AMU**.
  - The mass deficit is 0**.09565 AMU**, or **89.1 MeV**, and this is the binding energy that holds the nucleus together.
- In order to unbind something, you need to spend at least as much energy as the binding energy.
  - You cannot split a carbon nucleus with 18 MeV photons from an average linac, but you could with a cyclotron throwing 200+ MeV protons.

On Nuclear Stability

- **Neutron-to-proton (n/p) ratio**:
  - Protons generally hate each other due to their charge; they need neutrons to keep the peace.
  - Too many neutrons and the nucleus just becomes uncomfortable.
  - Unstable nuclei will decay toward more stable products. The mode of decay depends on the n/p ratio.

    See Chap. 2 for more detail on nuclear decay.
- For elements up to **Z = 20 (Calcium)**, the magic n/p ratio is **1:1**.
  - **Ex**: Stable carbon (**^{12} C**) has n = 6, p = 6.
- For elements heavier than **Z = 20**, the magic n/p ratio is **>1:1**.
  - **Ex:** Stable gold **(^{197}Au)** has n = 118, p = 79 (Fig. 1.1**).**

Binding Energy per Nucleon

- As atomic number increases, strong force increases and therefore total binding energy increases.
- At the same time, after a certain threshold (**iron, Z = 26**), the repulsive electrostatic force of protons begins to take over (since they hate each other).
  - Even though the total binding energy continues to increase, the binding energy per nucleon starts to decrease.
  - Binding energy must be at least 8.6 MeV per nucleon to remain stable.

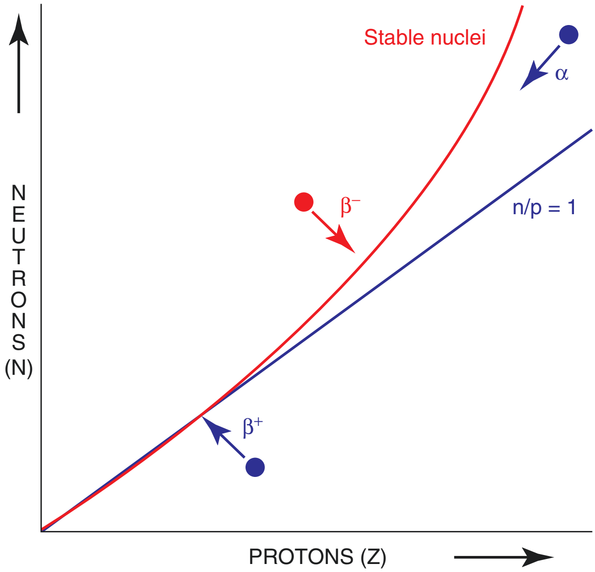

Fig. 1.1 Stable nuclei (*red line*) initially follows a 1:1 ratio of neutrons to protons but gradually requires more nexutrons to keep the nucleus stable

  - When atoms are unstable, weak forces allow nucleon transformations (example: a proton may turn into a neutron).
  - Unstable atoms larger than Tellurium (Z = 52) may break off in large chunks (usually in even numbers such as alpha particles).
  - **Bismuth (Z = 83)** is the heaviest stable nucleus, after which total binding energy decreases and all nuclei become unstable.

Pairing of Nucleons

- Paired nucleons are generally more stable than odd-numbered ones.
  - Most stable nuclei are "even-even," with an even number of protons and an even number of neutrons.
  - A few stable nuclei are "odd-even" or "even-odd."
  - Only four stable "odd-odd" nuclei exist: **H-2** (1n, 1p), **Li-6** (3n, 3p), **B-10** (5n, 5p), and **N-14** (7n, 7p).
- For this reason, it is much easier to emit an alpha particle (2n, 2p) than a lone neutron or proton in heavier nuclei.

Bohr Model of the Atom

- This is the "classical" description of electrons orbiting the nucleus such as planets around the sun (Fig. 1.2).

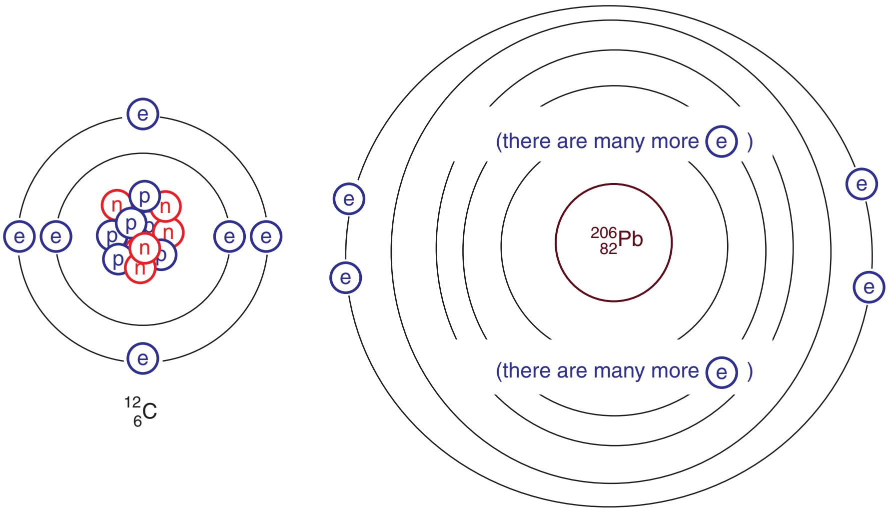

Fig. 1.2 Bohr model of the atom has a nucleus (like the sun) with electrons revolving around it (like planets). As electrons are added, they fill higher energy orbitals (further away from the nucleus) in fixed paths

  - Within an atom, electrons may only travel in discrete orbits (energy shells) with discrete energies.
  - Electrons may only gain or lose energy by changing orbits or by exiting the atom.
  - This model works great for a hydrogen atom (and for the ABR exam), but it is a gross oversimplification of the more accurate quantum mechanical model.
- **Electron binding energy**:
  - Electrons are bound to the nucleus by the attraction between negative and positive charges.
  - This attraction means that it takes energy from outside to separate the nucleus from the electron.
    - Electron binding energy (the energy required to knock an electron loose) increases with proximity to the nucleus by radius squared (r^2).
    - Electron binding energy increases with increasing charge of the nucleus (Z).
  - Inner shell electrons have a large binding energy because they are very close to the nucleus.
    - Even though they have a higher "binding energy," these electrons are said to be at a "lower energy level."
  - Valence (outer) electrons have little binding energy because they are further away and are easily removed.
- Any change in orbit is associated with a change in energy (see section "Electron Transitions").
  - Pushing energy into an atom can knock an electron loose from its valence shell (or raise the shell to a higher shell).
  - When an electron moves from a higher shell to a lower shell, it actually gives off energy, either in the form of a photon or by kinetic energy and knocking another electron to a higher shell.

Electron Orbits (Energy Levels)

- Each electron fits into energy levels in an orderly fashion with a particular address.
- **Principle quantum number** (n) = 1, 2, 3, etc. or K, L, M, N, etc.
- **Orbital quantum number** (l)—can have (n − 1) values.
  - Named s, p, d, f for sphere, peanut, dumbbell, fan.
  - Ex: if n = 3, then there are l orbitals 0,1,2.
- **Magnetic quantum number** (m_l)—can have $2l+1$ values.
  - Numbered negative (n − 1) through positive (n − 1).
  - Ex: n = 3, l = 2, therefore m_l can be −2,−1,0,+1,+2.
- **Spin quantum number**—for our purposes, either +1/2 or − 1/2.
- **Outer (valence) shell** can have up to eight electrons.
  - These are generally s^2 and p^6.

Electron Transitions (Absorption and Emission of Energy)

- Whenever an electron absorbs energy, it becomes uncomfortable.
  - The electron may move to a higher shell, or it may be ejected from the atom.
  - If an electron moves to a lower energy shell, excess energy may be carried away as the electron's kinetic energy, or it may be emitted as a photon (Fig. 1.3).
- When a vacancy exists in a lower shell, an electron will "fall" into a more comfortable position.
  - The electron loses energy, so this energy must be transferred to some other particle.
  - When energy is transferred to a photon, it is known as a **characteristic X-ray**. This is known as "characteristic" because the energy levels are unique to a given nuclide and orbital.
  - When energy is transferred to another electron, it becomes an **Auger electron**. The energy of the **Auger electron** is equal to the energy transferred minus the binding energy that had to be overcome in order to eject an electron (Fig. 1.4).

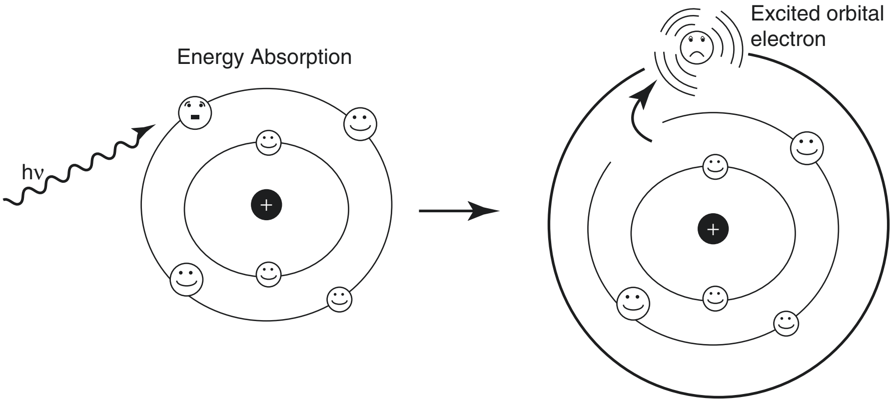

Fig. 1.3 Energy absorption: There is a relatively content orbital electron (it is not as happy as the inner circle electrons). There is an unpleasant orbital above his head that is empty and has a lower binding energy. The orbital electron is hit square in the jaw with a photon containing an intermediate amount of energy, and it absorbs the entire amount and therefore is knocked into a higher orbital. Had he absorbed energy higher than his binding energy, it might have been knocked completely out of the atom (ionization)

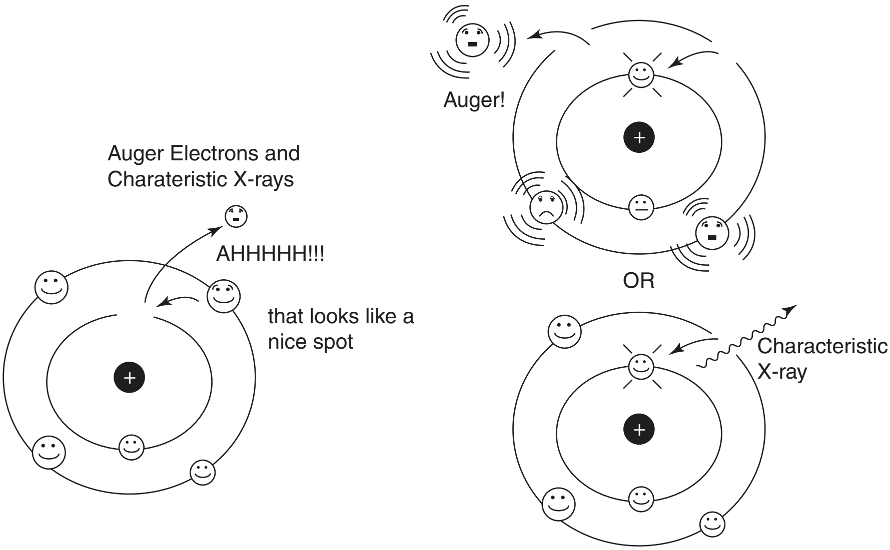

Fig. 1.4 Energy emission consequences: Somehow, a very happy electron was kicked out of the inner orbital and completely disappeared (many things can cause this). An ambitious electron in a higher energy orbital decided to move closer to the nucleus which had a lower energy level (higher binding energy). Since it moved to a lower energy level, it had to give up some of that energy. There are two ways that an electron can give off energy when it drops to a lower energy level. It can emit a **characteristic X-ray** (basically the opposite of Fig. 1.3), or it can transfer that energy to the entire orbital, which makes everyone in the orbital angry until they actually kick out another electron (called an **Auger electron**)