Radiobiology Self-Assessment Guide

Jennifer S. Yu • Mohamed E. Abazeed
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To my dearest Yoon and Daniel, our parents, David and Min and their families, for their love, compassion, and inspiration.

–Jennifer S. Yu

Nanos gigantum humeris insidentes.

–Mohamed E. Abazeed
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We are pleased to introduce the inaugural edition of Radiobiology Self-Assessment Guide. This guide provides up-to-date comprehensive concepts in classical radiation biology and contemporary research on stem cell biology, tumor immunology and immunotherapy, and radiogenomics. It succinctly covers topics that are germane to the understanding of radiobiology and related disciplines in oncology. It uses more than 700 questions in a flash-card question-and-answer format to stimulate active learning and reinforce key concepts. Schematics and figures are used to clarify important ideas and references are included with each answer to facilitate independent in-depth learning.

This guide complements Radiation Oncology Self-Assessment Guide and Physics in Radiation Oncology Self-Assessment Guide. Together, these guides provide a thorough review of the clinical management of cancer, medical physics, and radiation biology.

We are indebted to the many experts from the Cleveland Clinic and Case Comprehensive Cancer Center who contributed to this book. We hope that this guide will prove an invaluable and high-yield resource for anyone interested in classical and contemporary radiation biology.

Jennifer S. Yu
Mohamed E. Abazeed
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INTERACTION OF RADIATION WITH MATTER

JOHN F. GRESKOVICH, JR., MIHIR NAIK, AND MARC APPLE
Question 1
What type of decay does Radium-226 undergo, and what particles are produced in the decay?

Question 2
What are the names of the types of photons within the electromagnetic spectrum from lowest and highest energy?

Question 3
What is the relationship between photon energy, wavelength, and frequency?

Question 4
What is a photon?
### Question 1
*What type of decay does Radium-226 undergo, and what particles are produced in the decay?*

**Answer 1**
Radium-226 decays by α-decay, creating radon gas (Rn-222) and an alpha particle plus 4.87 MeV of released energy. An alpha particle is a helium nucleus consisting of two protons and two neutrons. The emission of an alpha particle decreases the atomic number by two and the mass number by four.


### Question 2
*What are the names of the types of photons within the electromagnetic spectrum from lowest and highest energy?*

**Answer 2**
Photons travel as electromagnetic waves, described by the electromagnetic spectrum. This spectrum defines regions based on their energy (and hence wavelength or frequency). From lowest energy (and lowest frequency, highest wavelength) the spectrum starts with radio waves, then microwaves, infrared waves, visible waves, ultraviolet waves, x-rays, and gamma rays.


### Question 3
*What is the relationship between photon energy, wavelength, and frequency?*

**Answer 3**
The higher the photon energy, the higher the frequency and the smaller the wavelength. Therefore, photon energy is proportional to frequency and inversely proportional to wavelength. This is formalized in the relationship called Planck’s equation: \( E = hv \) where \( E \) is energy in Joules (J), \( h \) is Planck’s constant, \( 4.13 \times 10^{-18} \text{ keV-sec} \), and \( v \) is the frequency in Hertz (Hz, sec\(^{-1}\)). Using the electromagnetic wave equation, \( c = \lambda v \) we can arrive at the equation \( E = hc/\lambda \) where \( c \) is the speed of light, \( 3.0 \times 10^8 \text{ m/sec} \).

A useful equation is: Energy (keV) = 12.4/\( \lambda \)(angstroms) where angstrom = \( 10^{-10} \) m.


### Question 4
*What is a photon?*

**Answer 4**
A photon is the fundamental particle of electromagnetic radiation, typically described dually as “packets” of energy (Quantum Theory) and as waves of electrical and magnetic energy (Wave Theory). A photon has no mass or charge.

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<td>Describe the Compton scatter photon interaction.</td>
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**Question 5** What is the energy range for visible light? x-rays and γ-rays? Why doesn’t visible light cause ionization in tissue?

**Answer 5**
Using the equation Energy (keV) = 12.4/\(\lambda\) (angstroms), we can calculate the energy of visible light as 1 to 3 eV since the \(\lambda\) for visible light is 4,000 to 7,000 angstroms. The energy for x-rays and γ-rays are typically in the keV to MeV range since the \(\lambda\) for x-rays and γ-rays are in the 10^{-2} to 10^{-4} angstrom range. Visible light does not cause ionization in tissue since the average energy for an ionizing event is 34 eV, significantly higher than the 1 to 3 eV energy of visible light.

---

**Question 6** What is ionization? What is excitation? Which photons in the electromagnetic spectrum are ionizing and which are nonionizing?

**Answer 6**
Ionization is when enough energy is delivered to eject an electron from an atom or molecule, leading to an electron–ion pair. The average energy dissipated after an ionizing event is 34 eV, enough energy to break a carbon=carbon bond (C=C binding energy is 4.9 eV). Ionizing radiation consists of photons in the ultraviolet, x-ray, and γ-ray range. Nonionizing radiation consists of radio waves, microwaves, infrared (heat) radiation, and visible light. Excitation is the raising of an electron to a higher energy shell without ejection of the electron from the shell.

---

**Question 7** What is the difference between x-rays and γ-rays?

**Answer 7**
X-rays and γ-rays are two forms of high-energy electromagnetic radiation. They are not different in their physical properties, but their designation reflects the different ways that they are produced. X-rays are produced extranuclearly and γ-rays are produced intranuclearly. For example, x-rays are produced in an electrical device that is used to accelerate electrons and stop them abruptly in a target made of a metal like tungsten or gold (i.e., linear accelerator). However, γ-rays are emitted by radioactive isotopes and represent excess energy that is given off as an unstable nucleus breaks up and decays to reach a more stable form.

---

**Question 8** Describe the Compton scatter photon interaction.

**Answer 8**
In a Compton scatter photon interaction, the incident x-ray photon interacts with a “free” outer shell electron, ejecting it from the nucleus as a fast electron, and continuing on as a scattered x-ray photon of lower energy. Part of the energy of the incident x-ray photon is imparted to the electron as kinetic energy, and the balance of energy is kept by the scattered x-ray photon. The initial photon may give 0% to 80% of its kinetic energy to the free electron, and this free electron causes ionization of other atoms and produces the chemical and biological effects seen.
Question 9
What tissue and energy factors drive the probability of Compton scatter?

Question 10
Why are high-energy x-rays (MeV) favored over low-energy x-rays (keV) for treatment of most tumors in the body?

Question 11
Describe the photoelectric effect photon interaction. For what energy x-rays does photoelectric effect occur? What tissue and energy factors drive the probability of photoelectric effect?
Question 9 What tissue and energy factors drive the probability of Compton scatter?

Answer 9
Compton scatter is the most common interaction for x-rays in the therapeutic radiation energy range, dominating for energies between 25 keV and 23 MeV. The probability of Compton scatter is directly proportional to the electron density (electrons/gram) of the material and inversely proportional to the photon energy, and is independent of the Z (atomic number) of the material. This is the most common type of interaction seen at energies used in radiotherapy treatment. The mass absorption coefficient for the Compton process is independent of the atomic number of the absorbing material, unlike the photoelectric effect where it varies based on the atomic number and is proportional to $Z^3$.


Question 10 Why are high-energy x-rays (MeV) favored over low-energy x-rays (keV) for treatment of most tumors in the body?

Answer 10
High-energy (MeV) x-rays are preferred for therapy since Compton scatter interactions predominate, leading to a nearly equal dose distribution in tissues of different Z (atomic numbers) such as bone, muscle, and soft tissue. Lower energy x-ray (keV) interactions in tissue are dominated by the photoelectric effect, which is dependent on the Z and is proportional to $Z^3$, leading to a higher energy deposition in high Z tissues such as bone.


Question 11 Describe the photoelectric effect photon interaction. For what energy x-rays does photoelectric effect occur? What tissue and energy factors drive the probability of photoelectric effect?

Answer 11
In a photoelectric effect photon interaction, the incident x-ray photon interacts with an “inner” shell electron, ejecting it from the nucleus as a fast electron, and losing all of its energy to the electron. As outer shell electrons (or outside electrons) fill in the inner shell electron vacancy, characteristic x-rays are released. The kinetic energy of the ejected inner shell electron equals the energy of the incident x-ray photon ($h\nu$) — $E_{\text{bind}}$, where $E_{\text{bind}}$ is binding energy of the inner shell electron.

The photoelectric effect is the most common interaction for x-rays in the diagnostic x-ray energy range, dominating for energies below 25 keV. The probability of the photoelectric effect is directly proportional to $Z^2$ (atomic number$^2$) and inversely proportional to $E^3$.

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<td>What are the names in the sequence of events along with the time it takes for each event to occur going from low linear energy transfer (LET) radiation exposure to biological effect?</td>
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Question 12 X-rays interact with tissue to produce fast electrons through Compton scatter. By what two mechanisms do fast electrons damage DNA?

Answer 12
Fast electrons produce DNA damage in two general ways: (a) direct action where the fast electron itself directly damages the DNA, and (b) indirect action where the fast electron interacts with water molecules to produce free radicals which cause the damage to the DNA. It is estimated that 2/3 of the DNA damage from x-ray therapy is via indirect action.


Question 13 What predominant form of DNA damage is caused by x-rays and low linear energy transfer (LET) radiation versus high LET radiation?

Answer 13
It is estimated that free radicals produced through indirect action cause approximately 2/3 of the DNA damage in low LET radiation and that direct action is the dominant form of DNA damage in high LET radiation.


Question 14 What is the theoretical maximum dose reduction factor for free radical scavengers when administered to decrease the biological effectiveness of low linear energy transfer (LET) radiation?

Answer 14
Since 2/3 of the DNA damage from x-ray therapy is via indirect action, that is, formation of free radicals such as the hydroxyl radical, the theoretical maximum dose reduction factor for free radical scavengers is 3.


Question 15 What are the names in the sequence of events along with the time it takes for each event to occur going from low linear energy transfer (LET) radiation exposure to biological effect?

Answer 15
There are six events which occur after low LET radiation exposure to tissue, leading to biological effects: (a) ionization ($10^{-15}$ sec), (b) ion radical ($10^{-10}$ sec), (c) free radical ($10^{-9}$ sec), (d) DNA radicals ($10^{-5}$ sec), (e) chemical reactions (minutes to days), and (f) biological effect (minutes to generations).

**Question 16**

Compare and contrast the following particulate radiation: electrons, positrons, protons, neutrons, and alpha particles. What is their mass ratio?

**Question 17**

How does radon gas cause lung cancer?

**Question 18**

What are neutrons?
**Question 16** Compare and contrast the following particulate radiation: electrons, positrons, protons, neutrons, and alpha particles. What is their mass ratio?

**Answer 16**

Electrons are small, negatively charged particles with a charge of $-1$ which are accelerated in a linear accelerator to near the speed of light and can be symbolized by either $e^-$ or $\beta^-$. Positrons have the same mass as an electron but are a positively charged particle with a charge of $+1$ and are symbolized by $\beta^+$. Positrons are antimatter and undergo an annihilation reaction when they encounter an electron, creating two 511 keV photons released “back-to-back” (i.e., 180° apart), forming the basis for positron emission tomography (PET) imaging. Protons are larger, positively charged particles with a charge of $+1$, are accelerated in a cyclotron to become useful energy for therapy, and are symbolized by $p^+$. Neutrons have approximately the same mass as a proton but are neutral particles having no charge, are created in a nuclear reactor through high-speed collisions of deuterons or protons with a beryllium target in a particle accelerator, or by decay of man-made Californium-242, and can be symbolized by $n$. Neutrons interact with nuclei of atoms of the absorbing material and set in motion “fast recoil protons,” alpha particles, and heavier nuclear fragments. Alpha particles are heavier, positively charged particles made up of two protons and two neutrons (i.e., Helium nucleus) with a charge of $+2$; they occur naturally during alpha decay of radioisotopes such as radium and uranium, and can be symbolized by $\alpha$ or He$^{2+}$. The mass ratio of these particles is $1:1:2000:2000:8000$ for $\beta^-:\beta^+:p^+:n:\alpha$.


**Question 17** How does radon gas cause lung cancer?

**Answer 17**

Radon gas (Radon-222) is created when naturally occurring Radium-226 decays via alpha decay, creating radon gas and an alpha particle. Once radon gas is inhaled it will decay with a half-life of 3.8 days into radon gas “daughters,” which are solids that become trapped in the lung. Once radon gas decays to Polonium-218 (Po-218) through alpha decay, then two additional alpha decays and two beta decays occur in less than 1 hour, resulting in Lead-2010 (Pb-210) which has a half-life of 22.3 years. High linear energy transfer (LET) alpha particle and low LET beta particle radiation to the lungs can lead to an estimated 10,000 to 20,000 cases of lung cancer each year in the United States.


**Question 18** What are neutrons?

**Answer 18**

Neutrons are particles with a mass similar to protons, but they do not carry an electrical charge. Because of their neutrality they are not able to be accelerated in an electrical device. Neutrons are created in two ways; first, if a charged particle accelerates to a high energy and hits an appropriate target material, and second, as a by-product of heavy radioactive atoms undergoing fission.

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Question 19 Since neutrons are uncharged particles, how do they damage DNA?

Answer 19
Neutrons are uncharged, neutral particles and thus can penetrate deeply into tissue. Neutrons damage cells by indirect ionization through inelastic and elastic collisions with nuclei, setting into motion recoil protons, alpha particles, and heavy nuclei. Most of the neutron interactions in tissue are by elastic collisions with hydrogen atoms since hydrogen is the most abundant atom in tissue. Once neutron energies reach over 6 MeV, inelastic collisions occur and spallation products (alpha particles) are formed when high-energy neutrons collide with carbon and oxygen nuclei. For neutrons that are heavily ionizing, high linear energy transfer (LET) particles, direct action dominates with only a small percent of DNA damage occurring from the indirect action (creation of free radicals).


Question 20 What is the difference between direct and indirect ionizing radiation?

Answer 20
Directly ionizing radiation particles are all charged particles that have sufficient energy to cause ionization. Examples of directly ionizing radiation are electrons, protons, alpha particles, and heavy nuclei. Indirectly ionizing radiation particles are uncharged and do not directly produce chemical and biological damage themselves but lead to the production of charged particles. Examples of indirectly ionizing radiation are x-rays, γ-rays, and neutrons.


Question 21 What are examples of low linear energy transfer (LET) and high LET radiation?

Answer 21
Examples of low LET radiation are x-rays, electrons, and protons (excluding the Bragg peak). Examples of high LET radiation are alpha particles, neutrons, heavy charged particles, and the proton Bragg peak.


Question 22 What are heavy charged particles, and how may they be used for radiation therapy?

Answer 22
Heavy charged particles are nuclei of elements such as carbon, neon, argon, or even iron that has a positive charge because some or all of the electrons are stripped from them. These particles must be accelerated to very high energies (thousands of millions of volts). Only a few heavy charged particle radiotherapy facilities exist around the world.