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Education Article

Biological Effects of Ionizing Radiation

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SUMMARY

Introduction: Living in the 21st century, we are surrounded by countless forms of radiation, a byproduct of our dependence on cutting-edge technology. Whether these advancements are essential or merely convenient, we often adopt them without hesitation, only later pausing to consider their implications through the lens of science and reason. Medically, our concerns tend to arise after the damage is done, when prevention is no longer possible. The authors present the effects of ionizing radiation on humans, with the goal of achieving urbanization through knowledge and at least a rational approach to health.

Methodology: An online search on ionizing radiation and its effects on the human body was conducted using PubMed, Cochrane, Embase, and Scopus databases. The search was performed using the following keywords: ionizing radiation, natural radiation sources, therapeutic radiation sources, adverse effects, biological effects, radiosensitivity, ALARA, radiation effects, radiation protection. The literature was searched in both English and Serbian equally, which may be a limiting factor in the search results.

Topic: The electromagnetic spectrum represents the entire range of electromagnetic radiation, classified by wavelength, frequency, and energy. It encompasses all known electromagnetic waves, from the longest-wavelength, lowest-energy radio waves to the shortest-wavelength, highest-energy gamma rays. This spectrum plays a fundamental role in numerous scientific, technological, and medical applications, ranging from communication systems and imaging technologies to quantum physics and astrophysical observations. Ionizing radiation interacts with biological tissues at the molecular, cellular, and systemic levels, leading to a range of effects that depend on radiation dose, energy, type, duration of exposure, and tissue radiosensitivity. The impact of ionizing radiation on the human body is influenced by multiple factors, including the intensity of the radiation dose, the total absorbed dose, the energy and type of radiation, the surface area of the exposed body region, and the radiosensitivity of different tissues. Individual radiosensitivity varies among populations and is influenced by genetic factors, age, and overall health status. Different organs and tissues exhibit varying levels of sensitivity to radiation. The impact of ionizing radiation on the human body is influenced by multiple factors, including the intensity of the radiation dose, the total absorbed dose, the energy and type of radiation, the surface area of the exposed body region, and the radiosensitivity of different tissues. Individual radiosensitivity varies among populations and is influenced by genetic factors, age, and overall health status. Different organs and tissues exhibit varying levels of sensitivity to radiation.

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Conclusion: Future advancements in radiation biology, DNA repair research, radioprotective agents, and personalized risk assessments will be essential in mitigating radiation-induced damage ćand enhancing the safety and efficacy of medical, industrial, and space-related radiation applications. By integrating scientific knowledge, technological innovation, and ethical responsibility, the field of radiation science will continue to improve human health, medical diagnostics, and cancer treatment, ensuring a balanced approach between radiation benefits and safety in the modern world.

Keywords: Biological Effects, Ionizing Radiation, Free Radicals

INTRODUCTION

Living in the 21st century, we are surrounded by countless forms of radiation, a byproduct of our dependence on cutting-edge technology. Whether these advancements are essential or merely convenient, we often adopt them without hesitation, only later pausing to consider their implications through the lens of science and reason. Medically, our concerns tend to arise after the damage is done, when prevention is no longer possible [1]. The 20th and 21st centuries have been characterized by extensive multidisciplinary collaborations among researchers across various scientific fields. This trend is particularly evident in biomedical research, where the combined efforts of physicians, biologists, geneticists, and biochemists intersect with those of biophysicists and engineers. The primary objective of these collaborations is to advance the understanding of fundamental biological processes related to life, health, and disease, while simultaneously translating this knowledge into biomedical applications that significantly impact daily medical practice and public well-being.

METHODOLOGY

The authors present the effects of ionizing radiation on humans, with the goal of achieving urbanization through knowledge and at least a rational approach to health.

An online search on ionizing radiation and its effects on the human body was conducted using PubMed, Cochrane, Embase, and Scopus databases. The search was performed using the following keywords: ionizing radiation, natural radiation sources, therapeutic radiation sources, adverse effects, biological effects, radiosensitivity, ALARA, radiation effects, radiation protection. The literature was searched in both English and Serbian equally, which may be a limiting factor in the search results.

TOPIC

The electromagnetic spectrum represents the entire range of electromagnetic radiation, classified by wavelength, frequency, and energy. It encompasses all known electromagnetic waves, from the longest-wavelength, lowest-energy radio waves to the shortest-wavelength, highest-energy gamma rays. This spectrum plays a fundamental role in numerous scientific, technological, and medical applications, ranging from communication systems and imaging technologies to quantum physics and astrophysical observations. Electromagnetic waves propagate at the speed of light in a vacuum (~299792458 m/s) and exhibit wave-particle duality, meaning they can behave as both waves and discrete particles called photons. The relationship between their fundamental properties - wavelength (λ, measured in meters), frequency (ν, measured in Hertz), and the speed of light (c) - is expressed by the equation:

$$c = \lambda \nu$$

where the frequency of the wave is inversely proportional to its wavelength. The energy (E) of a photon is further defined by Planck's equation:

$$E = h \nu$$

where h is Planck's constant (6.626×10^{-34} Js). These relationships illustrate the increasing energy of electromagnetic waves as their frequency rises and wavelength shortens.

The electromagnetic spectrum is conventionally divided into seven major regions, arranged in order of increasing frequency (or

decreasing wavelength):
1. Radio waves – characterized by the longest wavelengths and lowest frequencies, used in wireless communication, broadcasting, and radar technology.
2. Microwaves – employed in satellite transmissions, Wi-Fi, radar systems, and microwave ovens.
3. Infrared radiation – associated with heat transfer, used in thermal imaging, remote sensing, and fiber-optic communication.
4. Visible light – the only segment detectable by the human eye, crucial for vision and optical technologies.
5. Ultraviolet (UV) radiation – emitted by the Sun, utilized in sterilization, photolithography, and medical treatments but also linked to biological hazards.
6. X-rays – high-energy radiation penetrating soft tissues, widely applied in medical imaging, security screening, and astrophysical studies.
7. Gamma rays – the most energetic form of electromagnetic radiation, originating from nuclear reactions, radioactive decay, and cosmic phenomena, with applications in oncology, high-energy physics, and space exploration.

Each region of the electromagnetic spectrum interacts uniquely with matter, defining its applications across various scientific and technological domains. Understanding these interactions is crucial for advancements in spectroscopy, quantum mechanics, medicine, and space science [2].

Ionizing radiation refers to radiation with sufficient energy to remove electrons from atoms, leading to ionization. It is classified into electromagnetic ionizing radiation (X-rays and gamma rays) and particle radiation (alpha particles, beta particles, and neutrons). X-rays and gamma rays, both forms of high-energy electromagnetic radiation, penetrate deeply into matter and are widely used in medical imaging, radiotherapy, and industrial applications. Alpha particles (helium nuclei) and beta particles (high-energy electrons or positrons) result from radioactive decay and interact strongly with matter, making them hazardous when ingested or inhaled. Neutron radiation, primarily encountered in nuclear reactions, can penetrate deeply and induce secondary ionization, posing risks in nuclear energy and research environments.

Due to its ability to break chemical bonds, ionizing radiation can damage biological tissues, cause DNA mutations, and increase cancer risk. While potentially harmful, it is extensively applied in medicine (X-rays, CT scans, radiotherapy), sterilization, nuclear energy, and industrial processes. Despite its crucial applications, the biological effects of ionizing radiation are a major concern for public health, medical safety, and environmental protection. Understanding its interaction with biological systems is essential for risk assessment, optimizing therapeutic uses, and implementing protective measures to minimize exposure risks. Ongoing research enhances safety regulations, improves diagnostic and therapeutic technologies, and mitigates environmental contamination, ensuring a balance between radiation's benefits and its potential hazards [3]. This review examines the impact of ionizing radiation on human health, emphasizing the need for scientific awareness and evidence-based safety protocols in medicine, industry, and environmental protection.

Electromagnetic (EM) Ionizing Radiation

Electromagnetic ionizing radiation includes X-rays and γ-rays (gamma rays), both of which share similar properties but differ in their origin and energy levels. The distinction between X-rays and gamma rays is based on photon energy, with X-rays typically ranging from 100 eV to 100 keV, while gamma rays generally have energies exceeding 100 keV.

X-rays are further classified based on their penetration ability. Soft X-rays, with wavelengths between 0.1 nm and 10 nm (corresponding to 0.12 to 12 keV), have lower penetration power, whereas hard X-rays, with wavelengths between 0.01 nm and 0.1 nm (12 to 100 keV), exhibit greater penetration ability. Gamma rays, on the other hand, typically have energies above 100 keV, extending up to several MeV, and correspond to wavelengths ranging from 10^{-9} cm to 10^{-12} cm.

The primary difference between X-rays and gamma rays lies in their origin. X-rays are generated in the electron shells of atoms, typically through Bremsstrahlung (braking radiation) or characteristic emission in X-ray tubes. In contrast, gamma rays originate from nuclear transitions and are emitted when an unstable atomic nucleus undergoes radioactive decay to reach a more stable state. These high-energy photons are commonly emitted by radioactive isotopes, nuclear reactions, and

astrophysical phenomena such as supernovae and neutron star mergers.

The intensity of electromagnetic ionizing radiation, such as X-rays and gamma rays, decreases exponentially as it passes through a material, following the Beer-Lambert law:

$$I=I_0e^{-\mu x}$$

where I is the transmitted intensity, I_0 is the initial intensity, μ is the linear attenuation coefficient, and x is the material thickness. The rate of attenuation depends on the photon energy, material density, and atomic number, with higher-density materials causing more rapid intensity reduction through photoelectric absorption, Compton scattering, and pair production [4].

Particle Ionizing Radiation

Particle ionizing radiation consists of charged and uncharged subatomic particles that possess sufficient energy to ionize atoms and molecules. Unlike electromagnetic ionizing radiation (X-rays and gamma rays), which consists of photons, particle radiation involves electrons, protons, neutrons, and particles emitted in radioactive decay processes [5].

Electrons are fundamental subatomic particles with a negative charge of -1.602 × 10^{-19} C and a rest mass of 9.109 × 10^{-31} kg (0.511 MeV/c^2). Electrons can originate from either atomic shells or nuclear beta decay, with key differences in their source and energy. Electrons from atomic shells are bound to atoms in discrete energy levels and play a crucial role in chemical bonding and electromagnetic interactions. When high-energy radiation, such as X-rays or gamma rays, interacts with an atom, these electrons can be ejected, leading to ionization. This process is fundamental in photoelectric absorption, Compton scattering, and Auger electron emission, which govern many radiation-matter interactions. Beta particles (β^-) from the nucleus are high-energy electrons emitted during beta decay, a process in which a neutron inside an unstable nucleus transforms into a proton, releasing an electron (β^-) and an antineutrino.

$$n \rightarrow p + e^- + \bar{\nu}$$

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

Unlike atomic electrons, beta particles are not part of the electron cloud but are newly created inside the nucleus. They have higher kinetic energies, often up to several MeV, allowing them to penetrate several millimeters of biological tissue before being absorbed. Due to their low mass and high velocity, beta particles lose energy through ionization, excitation, and Bremsstrahlung (braking radiation) when interacting with matter. Although both atomic and nuclear electrons contribute to ionization, beta particles travel further and require shielding materials like plastic or aluminum, whereas atomic electrons primarily participate in low-energy interactions within matter.

Positrons (β^+) are the antiparticles of electrons, possessing the same mass (9.109×10^{-31} kg or 0.511 MeV/c^2) but an opposite charge of +1.602 × 10^{-19} C. Like electrons, positrons are leptons, meaning they do not experience strong nuclear forces but interact through electromagnetic and weak nuclear interactions [6]. Positrons primarily originate from beta-plus (β^+) decay, a nuclear process in which a proton transforms into a neutron, emitting a positron and a neutrino.

$$p \rightarrow n + e^+ + \nu$$

$$^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \beta^+ + \nu$$

Unlike beta-minus (β^-) particles, which ionize matter directly by electron repulsion, positrons travel a short distance before undergoing annihilation upon encountering an electron. This annihilation process converts their entire mass into energy, producing two 511 keV gamma photons that are emitted in opposite directions, a principle crucial to positron emission tomography (PET) in medical imaging.

Protons are positively charged subatomic particles with the same magnitude of charge as electrons but with the opposite sign (+1.602 × 10^{-19} C). Their mass is approximately 1860 times greater than that of an electron, measuring 938 MeV/c2 (1.6726231 × 10^{-27} kg). As nucleons, they are a fundamental component of atomic nuclei, contributing to the structure and stability of atoms. Protons play a crucial role in cosmic radiation, radiation therapy, and particle physics. High-energy protons can ionize matter directly through Coulomb interactions, where they transfer energy to atomic electrons, leading to excitation

and ionization. Due to their large mass and charge, protons follow a distinct interaction pattern in matter, characterized by the Bragg peak—a sharp increase in energy deposition at a specific depth before a rapid decline. This property is exploited in proton beam therapy (PBT) for targeted cancer treatment, where protons deliver maximum energy to tumors while minimizing damage to surrounding healthy tissues. Protons occur naturally as part of cosmic radiation, particularly in solar wind emitted by the Sun. Although the Earth's magnetic field and atmosphere shield the planet from most of this radiation, high-energy protons pose a significant risk in space travel, as they can penetrate spacecraft and biological tissue, increasing radiation exposure for astronauts. This is a major concern for long-duration space missions, such as those to Mars. The proton was first identified in 1918. by Ernest Rutherford, who demonstrated that hydrogen nuclei are fundamental building blocks of all atomic nuclei. Protons, like other elementary particles, possess intrinsic spin (1/2), a quantum mechanical property that underlies nuclear magnetic resonance (NMR) spectroscopy, an essential technique in medical imaging (MRI) and chemical analysis.

Neutrons are electrically neutral subatomic particles with a mass nearly equal to that of protons (939.57 MeV/c^2 or 1.675 × 10^{-27} kg). They are fundamental components of atomic nuclei, except in hydrogen, which consists of only a single proton [7]. Since they carry no electric charge, neutrons do not interact with matter via Coulomb forces, maki ng their behavior in radiation processes significantly different from that of charged particles like electrons and protons. This lack of charge allows neutrons to penetrate deeply into matter, making them a crucial factor in radiation protection, nuclear reactions, and cosmic radiation exposure. Unlike charged particles, neutrons cannot be accelerated in electric or magnetic fields. However, they can be artificially produced through nuclear reactions, particularly when a charged particle, such as a deuteron (the nucleus of deuterium, consisting of one proton and one neutron), is accelerated to high energy and collides with a target material. Neutrons are also produced in nuclear fission, where heavy radioactive isotopes, such as uranium-235 or plutonium-239, split into smaller nuclei while releasing free neutrons. These secondary neutrons sustain the chain reactions in nuclear reactors and nuclear weapons. Additionally, some synthetic heavy radionuclides emit neutrons through spontaneous fission or (α, n) reactions, where alpha particles induce neutron emission in certain elements. Neutrons are also an essential component of cosmic radiation, particularly in secondary cosmic rays that result from high-energy particles interacting with the Earth's atmosphere. These neutrons significantly contribute to radiation exposure in aviation, affecting both passengers and crew on high-altitude flights. The biological impact of neutron radiation is particularly severe, as neutrons interact via nuclear collisions, producing highly ionizing secondary charged particles (protons, alpha particles, and heavy nuclear fragments), which can cause extensive cellular damage. A free neutron has a half-life of approximately 880 seconds (14.7 minutes), after which it undergoes beta decay, transforming into a proton, an electron (β^- particle), and an antineutrino [8]. This process occurs because the neutron is composed of one „up" quark (u) and two „down" quarks (d), giving it a net charge of zero. In contrast, the proton consists of two up quarks and one down quark, making it positively charged. Neutrons remain stable within atomic nuclei, where the strong nuclear force overcomes the natural tendency of free neutrons to decay. However, in nuclei with an excess of neutrons, beta decay occurs, leading to the emission of ionizing radiation in beta-emitting isotopes. Unlike charged ionizing radiation (e.g., alpha, beta, and proton radiation), neutron radiation primarily interacts through elastic and inelastic scattering with atomic nuclei, transferring energy and potentially making the nucleus unstable. Neutrons contribute to ionization indirectly by causing nuclear reactions that emit secondary charged particles, which subsequently ionize surrounding atoms. This makes neutron radiation particularly challenging to shield, as it requires materials rich in hydrogen (such as water, polyethylene, or concrete) to slow and absorb neutrons efficiently. Neutron radiation is of great significance in nuclear reactors, medical applications (such as boron neutron capture therapy), industrial neutron radiography, and fusion research. However, due to their deep penetration ability and high biological effectiveness, neutrons pose a significant radiation hazard, requiring specialized protection strategies.

Alpha (α) particles are highly ioniz-

ing, positively charged particles that consist of two protons and two neutrons, making them identical to helium-4 nuclei. Due to their +2 charge and relatively large mass (4.0015 atomic mass units or approximately 6.644×10^{-27} kg), alpha particles exhibit unique properties in particle ionizing radiation. Their high charge and mass result in strong interactions with matter, leading to rapid energy loss and limited penetration depth. Alpha particles are primarily emitted during alpha decay, a type of radioactive decay that occurs in heavy, unstable radionuclides such as uranium-238, thorium-232, radium-226, and polonium-210. In this process, the parent nucleus loses two protons and two neutrons, forming a new element with an atomic number reduced by two and a mass number reduced by four. The emitted alpha particle typically has an energy in the range of 4 to 9 MeV, which is relatively high compared to other ionizing particles.

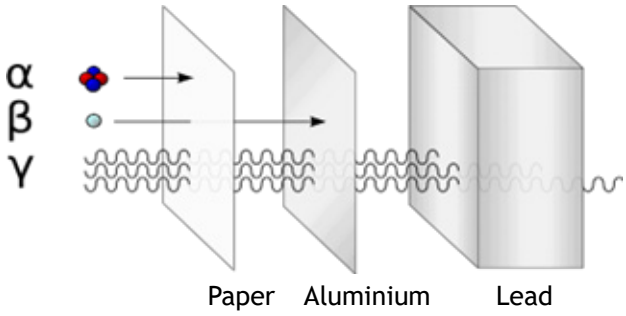
$$ {}^{A}_{Z}X \rightarrow {}^{A-4}_{Z-2}Y + {}^{4}_{2}He $$

$$ {}^{238}_{92}U \rightarrow {}^{234}_{90}Th + {}^{4}_{2}He $$

Alpha particles are highly effective ionizers due to their double positive charge and large mass, which result in intense Coulomb interactions with electrons in matter. This strong interaction leads to dense ionization tracks, where energy is deposited over a short distance, causing significant biological and material damage. Unlike beta particles or gamma rays, which can travel deeper into materials, alpha particles have a very short range, typically only a few centimeters in air and a few micrometers in biological tissue. They can be completely stopped by a sheet of paper, human skin, or even a few centimeters of air. However, despite their low penetration ability, alpha particles are extremely hazardous when inhaled, ingested, or introduced into the body. When an alpha-emitting substance (such as radon gas or plutonium dust) is internalized, the localized ionization causes severe cellular damage, increasing the risk of mutations and cancer. This is particularly concerning in radon exposure, where inhaled radon decay products emit alpha particles directly inside the lungs, posing a significant health risk. Due to their positive charge, alpha particles can be accelerated in large machines such as cyclotrons and linear accelerators, similar to protons. Accelerated alpha particles are used in nuclear research, radiation therapy, and isotope production. In medicine, alpha-emitting radionuclides such as actinium-225 and radium-223 are utilized in targeted alpha therapy (TAT) for cancer treatment, where their short range ensures that energy is delivered precisely to cancerous cells with minimal damage to surrounding tissues. Shielding against alpha particles is relatively simple, as even low-density materials like paper, plastic, or a few centimeters of air can block them. However, respiratory protection and contamination control are crucial in environments where alpha-emitting substances are present, such as uranium mining, nuclear reactors, and handling of radioactive materials.

Penetration of Ionizing Radiation

To summarize, the penetration ability of ionizing radiation varies based on whether it consists of electromagnetic (EM) waves or charged and uncharged particles, with factors such as mass, charge, and interaction mechanisms determining how deeply radiation can travel through matter [9]. Alpha particles, due to their large mass and +2 charge, have very low penetration, being stopped by a sheet of paper or a few centimeters of air. Beta particles (electrons, β^-), being much lighter and carrying a single negative charge, can penetrate several millimeters into biological tissue but are effectively shielded by plastic or aluminum. Positrons (β^+), the antimatter counterpart of electrons, behave similarly but undergo annihilation upon encountering an electron, producing two 511 keV gamma photons that contribute to secondary radiation. Protons, being much heavier and positively charged, penetrate deeper than beta particles, traveling several centimeters in soft tissue, with their energy deposition following a Bragg peak, making them useful in proton therapy. Neutrons, being uncharged, do not ionize directly but interact through elastic and inelastic nuclear scattering, allowing them to penetrate deeply into matter, requiring hydrogen-rich shielding like polyethylene or water. In contrast, X-rays and gamma rays, as uncharged electromagnetic radiation, have no mass and can travel deep into materials, with higher-energy photons penetrating even lead or thick concrete.



Biological Effects of Ionizing Radiation

Ionizing radiation interacts with biological tissues at the molecular, cellular, and systemic levels, leading to a range of effects that depend on radiation dose, energy, type, duration of exposure, and tissue radiosensitivity [10]. The biological effects of radiation are classified as either stochastic or deterministic, based on their dose dependence and manifestation.

Stochastic effects occur without a well-defined dose threshold, meaning even low doses of radiation carry some probability of causing harm. The severity of these effects does not increase with dose, but their likelihood does. These effects often manifest years or decades after exposure and include radiation-induced cancers and genetic mutations.

Deterministic effects occur only when a specific dose threshold is exceeded, and their severity increases with dose. These effects result from direct cellular damage and tissue destruction, leading to conditions such as radiation burns, cataracts, sterility, and acute radiation syndrome (ARS). At very high doses, exposure can lead to multi-organ failure and death due to extensive biological damage.

The impact of ionizing radiation on the human body is influenced by multiple factors, including the intensity of the radiation dose, the total absorbed dose, the energy and type of radiation, the surface area of the exposed body region, and the radiosensitivity of different tissues. Individual radiosensitivity varies among populations and is influenced by genetic factors, age, and overall health status. Different organs and tissues exhibit varying levels of sensitivity to radiation. The most radiosensitive tissues include the gonads and the hematopoietic system (bone marrow and lymphoid tissues), as they contain rapidly dividing cells that are more susceptible to radiation-induced damage. Organs such as the thyroid gland, liver, kidneys, and the eye lens exhibit moderate sensitivity, while skin, bones, and extremities are considered more resistant due to their lower cellular turnover rates. The degree of tissue damage depends on the radia-

Table 1. Tissue Weighting Factors according to ICRP Publications No. 60 and 26 [11]

Main Organs	Tissue weighting factors			
	ICRP 60 (1991)	ICRP 26 (1977)		ICRP103 (2007)
Gonads	0.20	0.25		0.08
Bone marrow	0.12		0.12	
Large intestine	0.12		-	
Lungs	0.12	-		0.04
Stomach	0.12		-	
Bladder	0.05	0.15		0.12
Chest	0.05	-		0.04
Esophagus	0.05	-		0.04
Liver	0.05			0.04
Thyroid gland	0.05	0.03		
Skin	0.01		-	
Bone surface	0.01		0.03	
Remainder (brain, kidneys, adrenal glands, spleen, pancreas, muscles, small intestine, thymus, uterus)	0.05		0.30	

tion dose and the ability of cells to repair DNA damage. In cases of repeated or high-dose exposure, damage accumulation may exceed the body's repair capacity, leading to permanent functional impairments or malignancies.

The Regulation on Exposure Limits to Ionizing Radiation and Measurements for Assessing Exposure Levels (Regulation 86/2011) establishes dose limits for occupationally exposed individuals and the general population, as well as risk classification and assessment methodologies. These limits are determined based on the concept of effective dose, measured in millisieverts (mSv), which accounts for both the absorbed dose and the biological impact on different organs. The International Commission on Radiological Protection (ICRP) and national regulatory bodies set dose constraints to minimize health risks associated with radiation exposure. For radiation workers, exposure risks are categorized based on annual effective dose estimates. A high-risk classification applies to individuals receiving more than 20 mSv per year, while an increased risk is associated with doses exceeding 6 mSv per year. Moderate-risk exposure falls within the range of 1 to 6 mSv per year, while negligible risk is considered at doses below 1 mSv per year. For professionally exposed individuals, an annual effective dose exceeding 50 mSv is considered very high, while doses above 20 mSv are classified as high. Exposure levels ranging from 6 to 20 mSv per year are considered increased, while levels below 6 mSv are classified as low, and those under 2 mSv per year are considered very low. The general population is subject to stricter limits, with increased exposure considered above 1 mSv per year, low exposure above 0.3 mSv per year, and negligible exposure below 0.01 mSv per year. These limits aim to prevent deterministic effects and reduce the risk of stochastic effects, particularly radiation-induced malignancies.

Since no level of radiation exposure is entirely risk-free, the primary principle in radiation protection is ALARA (As Low As Reasonably Achievable), which emphasizes minimizing radiation exposure through appropriate time management, distance from sources, and effective shielding materials [12]. Protective barriers such as lead for X-rays and gamma radiation, polyethylene or water for neutron radiation, and plastic or aluminum for beta radiation help limit exposure. Strict regulatory oversight, monitoring of occupational doses, and public awareness are crucial in mitigating long-term health risks associated with ionizing radiation.

Cellular Effects of Ionizing Radiation

The impact of ionizing radiation at the cellular level serves as the foundation for understanding its broader effects on the human body [13]. However, accurately assessing the damaging potential of ionizing radiation, as well as its therapeutic applications, remains challenging due to individual variations in radiation sensitivity, DNA repair capacity, and overall biological resilience. Each person possesses a unique ability to recover from radiation-induced damage, influenced by the regulatory mechanisms of tissues, organs, and physiological systems, which work synergistically to enhance survival. Ionizing radiation interacts with cells through two primary mechanisms: direct and indirect effects.

Direct effects occur when ionizing irradiation, whether in the form of photons, neutrons, or charged particles, directly interact with DNA or other critical biomolecules, leading to ionization or excitation. This initiates a cascade of biochemical events that may result in mutations, cellular dysfunction, or cell death. Direct interaction is the dominant mechanism for high linear energy transfer (LET) radiation, such as alpha particles and neutrons, which deposit their energy densely along their path, causing significant molecular disruption.

Indirect effects occur when ionizing radiation interacts with water molecules in the cell's protoplasm, generating reactive oxygen species (ROS) and free radicals, such as hydroxyl radicals (•OH) and hydrogen peroxide (H_2O_2). These highly reactive species can cause secondary damage to DNA, proteins, and cellular membranes, amplifying radiation-induced harm beyond the initial interaction. The indirect effect is particularly relevant for low-LET radiation, such as X-rays and gamma rays, where secondary free radical formation contributes significantly to biological damage.

Free Radicals and Their Role in Ionizing Radiation-Induced Damage

Free radicals are highly reactive molecular species characterized by the presence of unpaired electrons, making them highly unstable

and prone to rapid chemical interactions. Free radical's formation plays a significant role in cellular damage, particularly through the indirect effect of radiation. When ionizing radiation interacts with biological tissues, it primarily affects water molecules (which make up approximately 70% of the human body), triggering the radiolysis of water and generating a cascade of reactive oxygen species (ROS) and other free radicals [14]. These radicals, in turn, induce oxidative stress, leading to damage in DNA, proteins, and cell membranes, which can result in mutations, apoptosis, or carcinogenesis.

Biologically Relevant Free Radicals in Radiation Damage

Several free radicals and reactive oxygen/nitrogen species (ROS/RNS) are involved in the cellular response to ionizing radiation:

- Superoxide radical ($^{\bullet}O_2^-$): A primary ROS formed from molecular oxygen, contributing to oxidative stress and secondary free radical generation.
- Hydroxyl radical ($^{\bullet}OH$): One of the most reactive and damaging radicals, capable of breaking DNA strands, modifying nucleotides, and disrupting lipid membranes.
- Hydroperoxyl radical ($^{\bullet}HO_2$): A protonated form of superoxide, capable of damaging lipids and proteins, leading to membrane instability.
- Singlet oxygen ($^1O_2$): A highly reactive excited-state form of oxygen involved in oxidative modifications of biomolecules.
- Nitric oxide ($NO^{\bullet}$): A signaling molecule that modulates vascular function and immune response, but in excess, it contributes to nitrosative stress and inflammation.
- Hydrogen radical ($H^{\bullet}$): Involved in redox reactions that influence the cellular oxidative environment.
- Peroxyl radical ($^{\bullet}RO_2$) and alkoxyl radical ($^{\bullet}RO$): Organic radicals that propagate lipid peroxidation, leading to cell membrane breakdown.
- Nitrogen dioxide ($^{\bullet}NO_2$) and nitrate radical ($^{\bullet}NO_3$): Reactive nitrogen species involved in inflammatory responses and DNA damage.

Free Radical-Induced Cellular Damage in Ionizing Radiation Exposure

When ionizing radiation directly interacts with DNA, it induces base modifications, strand breaks, and chromosomal aberrations, leading to genetic instability. However, the majority of radiation-induced biological damage arises from indirect effects, where free radicals, particularly hydroxyl radicals ($^{\bullet}OH$), react with lipids, proteins, and nucleic acids, triggering oxidative stress [15]. This stress can lead to apoptosis or necrosis through mitochondrial dysfunction, disrupt cellular signaling pathways, alter gene expression and inflammatory responses, and contribute to long-term genomic instability, increasing the risk of cancer and degenerative diseases. Since free radical formation is a key mediator of radiation-induced damage, various radioprotective strategies have been explored to mitigate oxidative stress. The use of antioxidants, such as vitamin C, vitamin E, glutathione, and superoxide dismutase, helps neutralize reactive oxygen species (ROS) and reduce cellular injury. Additionally, targeted radiation therapy is employed to limit exposure to healthy tissues while maximizing the therapeutic effect on cancer cells. Post-exposure treatments, including free radical scavengers and anti-inflammatory agents, may further help reduce delayed radiation effects, offering potential protective benefits in radiation-exposed individuals.

Water Radiolysis and Its Role in Ionizing Radiation Damage

When a water molecule (H_2O) is exposed to high-energy ionizing radiation, it undergoes decomposition, a process known as the radiolysis of water [16]. This occurs when incoming radiation, such as gamma photons or high-energy charged particles, transfers sufficient energy to excite or ionize water molecules, leading to their dissociation. Radiolysis plays a crucial role in biological radiation damage, as water constitutes approximately 75% of the human body, making it the primary medium through which radiation interacts with living tissues. Upon energy absorption (E), a water molecule transitions to an „excited state H_2O^*", which subsequently decomposes into a hydrogen atom ($H^{\bullet}$) and a hydroxyl radical ($^{\bullet}OH$). The process can be represented by the following reactions:

$$E + H_2O \rightarrow H_2O^*$$
$$H_2O^* \rightarrow {}^{\bullet}H + {}^{\bullet}OH$$

The hydroxyl radical ($^{\bullet}OH$), along

with other reactive oxygen species (ROS), is highly reactive and interacts rapidly with cellular molecules, inducing oxidative stress and cellular damage. ROS attack proteins, lipids, and nucleic acids, leading to enzyme inactivation, DNA strand breaks, and lipid peroxidation. During lipid peroxidation, lipid peroxyl radicals and lipid hydroperoxides are formed, which can disrupt biological membranes, compromising cellular integrity and function [17]. The radiolysis of water is a critical mechanism in radiation-induced damage, as the free radicals generated propagate oxidative reactions, amplifying the effects of ionizing radiation.

Lipid peroxidation (LP) is a chain reaction initiated by reactive oxygen species (ROS) and free radicals, leading to the oxidative degradation of polyunsaturated fatty acids (PUFAs) in biological membranes [18]. This process plays a crucial role in radiation-induced cellular damage, as it compromises membrane integrity, alters cellular signaling, and contributes to radiation-induced cytotoxicity. The initiation phase of lipid peroxidation begins when a radical species ($R^{\bullet}$), generated through ionizing radiation or other oxidative processes, abstracts a hydrogen atom from a polyunsaturated lipid molecule (LH), forming a lipid radical ($L^{\bullet}$). This unstable radical reacts with molecular oxygen (O_2), leading to the formation of a lipid peroxyl radical ($LOO^{\bullet}$) and subsequently an organic hydroperoxide (LOOH). The process is illustrated by the following reactions:

$$R^{\bullet} + LH \rightarrow RH + L^{\bullet}$$
$$L^{\bullet} + O_2 \rightarrow LOO^{\bullet}$$
$$LOO^{\bullet} + LH \rightarrow LOOH + L^{\bullet}, \text{ or}$$
$$LOO^{\bullet} + RH \rightarrow LOOH + R^{\bullet}$$

Once initiated, lipid peroxidation rapidly propagates, as newly formed peroxyl radicals continue to interact with adjacent lipid molecules, resulting in a self-sustaining cycle of membrane destruction. This chain reaction leads to the accumulation of lipid hydroperoxides and secondary oxidation products, such as malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE), which further exacerbate oxidative damage. The reaction eventually terminates either through radical recombination, forming non-reactive end-products, or via antioxidant intervention, where enzymatic and non-enzymatic defense mechanisms neutralize reactive species. Lipid peroxidation is particularly relevant in radiation-induced cellular damage, as the highly reactive peroxyl radicals and lipid hydroperoxides can interact with DNA, leading to mutations, strand breaks, and chromosomal aberrations. These interactions interfere with the normal transfer of genetic information and may contribute to radiation-induced carcinogenesis and genomic instability. The extent of free radical accumulation in tissues depends on the balance between radical formation and antioxidant defense mechanisms. Radical formation is influenced by the radiation dose, tissue oxygenation, and enzymatic activity that generates ROS, while antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, play a critical role in mitigating oxidative stress. However, under conditions of severe ionizing radiation exposure, where the direct irradiation of DNA in the cytoplasm occurs, damage is exacerbated by water radiolysis, producing an abundance of secondary ROS that further amplify lipid peroxidation and DNA damage.

Effect of Radiation on Proteins

It has long been recognized that exposure to ionizing radiation leads to decreased protein stability and an increased susceptibility to denaturation, a phenomenon first described in early radiobiological studies [19]. More recent research has largely focused on the effects of radiation on proteins within cellular environments, employing both *in vitro* models (cell cultures) and *in vivo* models (animal studies) to investigate molecular and structural changes. These studies have highlighted the necessity of distinguishing between the effects of acute and chronic radiation exposure, as their biological consequences can significantly differ in terms of cellular response and protein integrity. A critical aspect of understanding radiation-induced protein damage lies in differentiating the effects of continuous low-dose radiation from those of acute high-dose exposure. Investigations involving human primary cells, cultured directly from organ tissues, subjected to chronic gamma radiation at dose rates of 6–20 mGy/h have yielded intriguing findings. Although such low-dose radiation exposure is estimated to induce fewer than one double-strand DNA break per hour per cell, it has been observed to significantly impair cell proliferation and accelerate cellular

senescence. This suggests that even sub-lethal, chronic irradiation may trigger cellular stress responses that impact proteostasis, potentially through oxidative damage or dysregulation of protein homeostasis mechanisms. In contrast, acute exposure to high doses of ionizing radiation has been shown to induce extensive proteolytic degradation of histone proteins, a process closely associated with the generation of reactive oxygen species (ROS) and other free radicals [20]. This oxidative stress-mediated damage not only affects histones but also other nuclear and cytoplasmic proteins, leading to conformational changes, aggregation, and loss of function. The breakdown of histones is particularly significant, as it contributes to chromatin destabilization and genomic instability, which are key factors in radiation-induced cellular damage. Additionally, the oxidative modifications of proteins under high-dose radiation exposure can result in irreversible carbonylation and cross-linking, further compromising cellular integrity.

How Free Radicals Affect DNA

Free radicals are highly reactive molecular species that rapidly interact with biomolecules, including deoxyribonucleic acid (DNA), leading to structural damage, mutations, and breaks in both DNA strands and cellular membranes [21]. Such alterations contribute to accelerated aging and significantly elevate the risk of various diseases, particularly cancer and cardiovascular disorders. Among the most biologically relevant free radicals are hydroxyl radicals ($OH^{\bullet}$), superoxide anion radicals ($O_2^{\bullet -}$), and hydrogen peroxide (H_2O_2), which are primarily generated through radiolysis of water when cells are exposed to ionizing radiation. These radicals induce a cascade of molecular events that can compromise genomic stability and cellular function. A widely used technique for studying radiation-induced free radical interactions with DNA is electron paramagnetic resonance (EPR) spectroscopy, which enables the direct detection of unpaired electrons within radical species. Through EPR-based experiments, researchers have identified specific mechanisms by which hydroxyl radicals interact with DNA components. One such experiment involves irradiating an aqueous solution containing pyrimidine bases, critical components of DNA, with high-energy electron beams. For instance, in a 5 mmol (millimolar) aqueous solution of pyrimidine bases, exposure to a 3 MeV electron beam generates hydroxyl radicals that predominantly target specific molecular sites. Thymine, one of the four nucleobases in DNA, is particularly susceptible to hydroxyl radical attack at the C5=C6 double bond, where the radical preferentially attaches to the C6 atom, resulting in cleavage of the C6-N1 bond. This interaction leads to the irreversible fragmentation of the thymine ring, effectively altering the structural integrity of the pyrimidine base. Since pyrimidine bases play an essential role in maintaining the fidelity of genetic information, such modifications can have severe consequences, including point mutations, frame shifts, or even strand breaks in the DNA double helix. The thymine radical formed as a result of this interaction can be directly detected via EPR spectroscopy, where the unpaired electron in the radical state exhibits a unique resonance signature under an applied magnetic field. This method provides a powerful analytical tool for characterizing DNA damage at the molecular level and quantifying the extent of radiation-induced mutagenesis. Beyond individual molecular interactions, the broader implications of ionizing radiation on genetic integrity must be considered. DNA lesions caused by free radicals contribute to genomic instability, leading to mutations that, if left unrepaired, can be transmitted to daughter cells during replication. In reproductive cells, such mutations can accumulate over generations, a phenomenon summarized by the concept of hereditary radiation effect - the accumulated exposure to ionizing radiation that affects hereditary material. Notably, even extremely low doses of radiation received by the gonads (reproductive organs) are considered deleterious, as there is no known threshold dose below which genetic damage does not occur [22]. Furthermore, given that cells consist of 70–80% water, the majority of ionizing radiation energy deposited within a biological system is initially absorbed by water molecules. This results in the rapid radiolysis of water, generating a flux of free radicals that subsequently interact with nucleic acids, proteins, and cellular membranes. These interactions contribute to oxidative stress, apoptosis, and carcinogenesis, highlighting the critical role of radiation-induced radical formation in determining the biological effects of exposure.

Mutations

One of the most significant biological consequences of ionizing radiation exposure is the induction of mutations, which are permanent alterations in the genetic material of an organism. These mutations can affect single nucleotides (point mutations), cause insertions or deletions, or even lead to large chromosomal rearrangements such as translocations, inversions, and aneuploidy. Depending on the nature of the mutation and its location in the genome, such changes can have various consequences, ranging from silent mutations with no functional effect to severe genetic disorders, carcinogenesis, or hereditary diseases. External factors capable of inducing mutations are collectively referred to as mutagens. Mutagens can be categorized into three major groups: physical, chemical, and biological agents. Ionizing radiation is one of the most potent physical mutagens, as it directly interacts with DNA or induces the formation of free radicals, which in turn cause oxidative damage to nucleotides and disrupt the integrity of the DNA double helix. Ionizing radiation can have either a natural origin (e.g., cosmic radiation, radon gas, background terrestrial radiation) or an artificial origin (e.g., radiation from medical imaging procedures, nuclear power plants, radiation therapy, and nuclear accidents) [23,24]. In addition to ionizing radiation, non-ionizing radiation, such as ultraviolet (UV) light, can also induce genetic mutations, though through different mechanisms, primarily causing pyrimidine dimer formation. However, unlike ionizing radiation, non-ionizing radiation lacks the energy required to induce deep chromosomal breaks or major structural DNA damage. Chemical mutagens, such as alkylating agents (e.g., ethyl methanesulfonate), intercalating agents (e.g., ethidium bromide), and reactive oxygen species (ROS), can modify DNA bases, interfere with replication fidelity, or cause DNA strand breaks. These mutagens may act independently or in synergy with ionizing radiation, amplifying its mutagenic effects. Biological mutagens, including certain viruses (e.g., human papillomavirus HPV or Epstein-Barr virus EBV), can integrate their genetic material into the host genome, disrupting gene expression and promoting mutagenesis. Some bacterial infections, such as those caused by Helicobacter pylori, have also been linked to genetic instability through chronic inflammation and oxidative stress. Mutations induced by ionizing radiation and other mutagens play a central role in the development of radiation-induced carcinogenesis. This process is particularly concerning in radiation-exposed populations, including nuclear industry workers, astronauts, patients undergoing radiotherapy, and survivors of nuclear disasters. Furthermore, germline mutations, when occurring in reproductive cells, can be passed on to offspring, contributing to hereditary genetic disorders and increasing the overall mutational burden in future generations. Given the profound impact of radiation-induced mutations, extensive research has been dedicated to understanding DNA repair mechanisms, including base excision repair (BER), nucleotide excision repair (NER), homologous recombination (HR), and non-homologous end joining (NHEJ). These repair pathways determine the extent of mutagenesis and influence cellular survival after radiation exposure. Advances in radiation biology and genetics continue to improve our understanding of mutational processes, aiding in the development of protective measures and therapeutic interventions against radiation-induced genetic damage.

Genetic Effects of Ionizing Radiation

Extensive experimental studies on animals and plants have demonstrated that the frequency of mutations induced by ionizing radiation is directly proportional to the absorbed dose, meaning that the higher the dose, the greater the number of mutations observed. This relationship aligns with the linear no-threshold (LNT) model, which posits that even the smallest doses of ionizing radiation carry some risk of genetic damage, with no known threshold below which radiation has no effect. As a result, exposure to even low-dose radiation can induce genetic mutations, though the probability of occurrence is lower than at high doses. A critical characteristic of the genetic effects of ionizing radiation is its cumulative nature. Each exposure contributes to the total absorbed dose, meaning that radiation-induced genetic damage accumulates over time. This accumulation is of particular concern for germline mutations, which occur in reproductive cells (sperm or ova) and can be passed on to future generations. The total number of radiation-induced mutations is directly

proportional to the cumulative gonadal dose, reinforcing the importance of minimizing unnecessary radiation exposure, particularly for individuals with occupational or medical radiation exposure [23]. The biological consequences of genetic mutations induced by ionizing radiation depend on the type and extent of DNA damage. Point mutations or small deletions may lead to subtle genetic changes, some of which could be silent or neutral, while large chromosomal aberrations may result in severe genetic disorders, embryonic lethality, or hereditary diseases such as cancer predisposition syndromes. The effects of radiation-induced genetic mutations have been well-documented in epidemiological studies of atomic bomb survivors, populations exposed to nuclear accidents (e.g., Chernobyl and Fukushima), and patients undergoing radiotherapy, where high-dose exposure has been linked to an increased incidence of heritable genetic disorders and carcinogenesis. Special attention is given to protecting individuals in radiation-exposed professions (e.g., radiologists, nuclear industry workers, astronauts) and ensuring minimal exposure in medical imaging procedures, particularly for pregnant women and children. Advances in radiation biology continue to improve our understanding of DNA repair mechanisms, radiation-induced mutagenesis, and dose-response relationships, enabling the development of protective strategies and risk assessment models to mitigate the long-term genetic risks of ionizing radiation.

Cellular Antioxidant Protection

Cells are constantly exposed to oxidative stress due to the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) during normal cellular metabolism, particularly in the mitochondria. These reactive species can damage DNA, proteins, and lipids, leading to cellular dysfunction, aging, and disease. To counteract oxidative damage, cells have evolved a complex endogenous antioxidant defense system, composed of a network of enzymatic and non-enzymatic antioxidants that maintain redox homeostasis [25].

The primary enzymatic antioxidants include:

- Superoxide dismutase (SOD)
- Catalase (CAT)
- Glutathione peroxidase (GSH-Px)
- Glutathione reductase (GR)

These enzymes work in concert to neutralize harmful free radicals and their derivatives, preventing oxidative stress-induced cellular injury. The efficiency of this system depends on an individual's genetic profile, which determines the expression and activity of antioxidant enzymes. This genetic variability plays a crucial role in cell survival, tissue homeostasis, and overall resistance to oxidative damage [26].

Mitochondrial Role in Antioxidant Defense

The mitochondrion, a double-membrane organelle, is the central site of cellular respiration and the major source of ROS production due to electron leakage from the electron transport chain (ETC). To mitigate the harmful effects of mitochondrial ROS, the organelle possesses its own intrinsic antioxidant defense mechanisms. Key antioxidant enzymes are encoded by nuclear DNA, but their production and function are regulated within the mitochondrial environment.

Enzymatic Antioxidant Defense System

Superoxide dismutase (SOD) is the first line of defense against oxidative stress, catalyzing the dismutation of the superoxide anion ($O_2^{\bullet -}$) into hydrogen peroxide (H_2O_2) and molecular oxygen (O_2).

$$2\ O_2^{\bullet -} + 2H^+ \rightarrow H_2O_2 + O_2$$

SOD is one of the fastest biological catalysts ever discovered and exists in multiple isoforms in different cellular compartments:

- Cu/Zn SOD (SOD1) – Located in the cytosol and mitochondrial intermembrane space (encoded by a gene on chromosome 21).
- Mn SOD (SOD2) – Located in the mitochondrial matrix, where it protects mitochondrial components from oxidative stress (encoded by a gene on chromosome 6).
- EC SOD (SOD3) – Found in extracellular fluids, contributing to systemic antioxidant defense (encoded by a gene on chromosome 4).

Catalase (CAT) is primarily responsible for breaking down hydrogen peroxide (H_2O_2) into water (H_2O) and oxygen (O_2):

$$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$$

This enzyme is localized in peroxisomes, specialized organelles involved in lipid metabolism and detoxification. However, in certain cell types, such as erythrocytes, CAT is also found in the cytosol. The human catalase gene (CAT) is encoded on chromosome 11.

Glutathione peroxidase (GSH-Px) is a selenium-dependent enzyme that detoxifies hydrogen peroxide (H_2O_2) and organic peroxides by converting them into water and alcohols, using reduced glutathione (GSH) as a cofactor:

$$H_2O_2 + 2GSH \rightarrow 2H_2O + GSSG$$

GSH-Px is primarily located in the mitochondria, where it plays a vital role in protecting mitochondrial integrity against oxidative damage. The gene encoding glutathione peroxidase (GPX1) is found on chromosome 3.

Glutathione reductase (GR) is a flavin adenine dinucleotide (FAD)-dependent enzyme that regenerates reduced glutathione (GSH) from oxidized glutathione (GSSG) using NADPH as an electron donor:

$$GSSG + NADPH + H^+ \rightarrow 2GSH + NADP^+$$

This enzyme ensures a continuous supply of GSH, which is essential for maintaining cellular redox balance. Glutathione reductase is localized in the mitochondria and cytosol, and its gene (GSR) is located on chromosome 8.

Exogenous Antioxidants and Pharmacological Modulators

In addition to endogenous antioxidant enzymes, exogenous antioxidants play a critical role in neutralizing free radicals and enhancing cellular defense mechanisms [27,28]. These include:

1. Dietary Antioxidants

• Vitamin C (ascorbic acid) – A water-soluble antioxidant that scavenges ROS and regenerates vitamin E.

• Vitamin E (tocopherol) – A lipid-soluble antioxidant that protects membranes from lipid peroxidation.

• Selenium (Se) – A cofactor for glutathione peroxidase, essential for reducing peroxides.

• Magnesium (Mg) – Involved in stabilizing mitochondrial function and preventing oxidative stress.

• Zinc (Zn) – A key component in SOD and essential for DNA repair.

2. Pharmacological Antioxidants

Several drugs have demonstrated direct antioxidant activity, providing additional protection against oxidative stress:

• Carvedilol – A beta-blocker with potent antioxidant properties, reducing oxidative damage in cardiac tissues.

• Metformin (Glucophage) – A widely used antidiabetic drug with antioxidant effects, decreasing ROS production and improving mitochondrial efficiency.

The cellular antioxidant defense system is a finely tuned network of enzymes and molecular regulators that protect against oxidative stress. Genetic variability influences the expression and efficiency of these antioxidants, making antioxidant capacity highly individualized. Given the cumulative effects of oxidative stress, understanding the interplay between endogenous and exogenous antioxidants is crucial for disease prevention, aging research, and therapeutic interventions aimed at mitigating radiation-induced damage.

Application of Radiation in Diagnostics and Therapy

Positron Emission Tomography (PET) is a non-invasive nuclear imaging technique that provides functional imaging of organs and tissues by detecting gamma rays emitted from a radiopharmaceutical injected into the patient's bloodstream. Unlike anatomical imaging techniques such as Computed Tomography (CT) or Magnetic Resonance Imaging (MRI), which primarily visualize structural details, PET scans provide insights into the biochemical and metabolic activity of tissues, making them particularly valuable for early disease detection and monitoring [29]. A PET scan utilizes radiopharmaceuticals, such as fluorodeoxyglucose (FDG), which consists of a glucose molecule tagged with fluorine-18 (^{18}F), a positron-emitting radionuclide. Since glucose is a primary energy source for cells, FDG preferentially accumulates in highly metabolically active tissues, such as cancer cells, where glucose uptake is significantly increased. Upon positron decay, the emitted positron (β^+) interacts with an electron, resulting in annihilation and the simultaneous release of two 511 keV gamma photons in opposite directions.

These gamma rays are detected by scintillation detectors arranged in a ring around the patient, forming the PET scanner. Advanced computer algorithms reconstruct the data into a three-dimensional image, mapping metabolic activity throughout the body. The clinical applications of PET extend beyond oncology to neurology, cardiology, and psychiatry.

Oncology - PET is the most sensitive imaging modality for detecting cancer and its recurrence, with superior diagnostic capabilities compared to CT and MRI. It differentiates benign from malignant tumors, determines tumor grade, and detects distant metastases, which is crucial for staging and treatment planning. It also plays a role in monitoring treatment response, assessing the effectiveness of chemotherapy, radiation therapy, and immunotherapy.

Neurology - PET imaging is invaluable in neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and epilepsy. It enables early diagnosis, allowing visualization of glucose hypometabolism in affected brain regions before structural changes become apparent. PET can also assess dopamine receptor activity, aiding in the diagnosis of schizophrenia and other psychotic disorders.

Cardiology - PET evaluates myocardial perfusion and viability, distinguishing ischemic but viable myocardium from irreversibly damaged tissue following a heart attack. This differentiation helps in determining the need for revascularization procedures such as coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI).

Compared to CT and MRI, PET has the unique advantage of detecting early biochemical changes before structural abnormalities manifest, making it the gold standard for identifying early-stage malignancies, neurodegenerative diseases, and cardiac dysfunctions [30].

Radiotherapy

Radiotherapy (radiation therapy) is a cornerstone in cancer treatment, utilizing high-energy ionizing radiation to destroy malignant cells while minimizing damage to surrounding healthy tissue. It is one of the three main treatment modalities for cancer, alongside surgery and chemotherapy, and is used in curative, palliative, and adjuvant settings. An estimated 40% of cancer cures involve radiotherapy at some stage of treatment [31]. Radiotherapy works by damaging the DNA of cancer cells, leading to cell cycle arrest, apoptosis (programmed cell death), or mitotic catastrophe. It primarily acts through direct damage - high-energy X-rays, gamma rays (γ), or charged particles directly ionize DNA molecules, causing single-strand or double-strand breaks (DSBs), and indirect damage - ionizing radiation induces the radiolysis of water, generating reactive oxygen species (ROS) such as hydroxyl radicals (·OH), which in turn damage cellular components, including DNA, proteins, and lipids. The most commonly used radiation sources include: X-photons (X-rays), Gamma (γ) photons from radioactive isotopes such as Cobalt-60 (^{60}Co), High-energy electrons for superficial tumors, Protons and heavy ions (e.g., carbon ions), which offer superior precision and reduced damage to adjacent normal tissues. Radiotherapy can be classified into three major types based on the method of radiation delivery: External Beam Radiotherapy (EBRT), Brachytherapy, and Systemic Radiation Therapy. Each of these methods has distinct advantages depending on the location, type, and stage of cancer being treated.

External Beam Radiotherapy (EBRT) is the most commonly used form of radiotherapy, in which high-energy radiation is delivered from an external source to precisely target the tumor [32]. This method is highly effective for treating localized cancers and can be further refined using advanced techniques to optimize tumor targeting while minimizing damage to surrounding healthy tissues. One such technique is Intensity-Modulated Radiotherapy (IMRT), which allows precise modulation of radiation intensity to conform to the shape of the tumor, thereby reducing exposure to adjacent normal tissues. Another advanced form of EBRT is Stereotactic Body Radiotherapy (SBRT), which delivers highly focused radiation beams in a small number of fractions, making it particularly effective for treating tumors in the lungs, liver, and brain. A significant advancement in external radiotherapy is Proton Beam Therapy, which uses protons instead of conventional photons. Due to the unique physical properties of protons, radiation is deposited primarily within the tumor with minimal exit dose, significantly reducing radiation exposure to surrounding tissues. This makes proton therapy particular-

ly beneficial for pediatric cancers and tumors located near critical organs where radiation-induced damage must be minimized.

Brachytherapy is another effective radiotherapy technique, involving the placement of radioactive sources directly inside or near the tumor [33]. This approach delivers a high local radiation dose to the tumor while sparing surrounding healthy tissues. Brachytherapy is commonly used in the treatment of prostate, cervical, and breast cancers, where precise radiation delivery is essential to preserve normal tissue function. The close proximity of the radiation source to the tumor allows for highly concentrated radiation exposure, enhancing therapeutic effectiveness while reducing systemic side effects.

Systemic Radiation Therapy involves the administration of radiopharmaceuticals - radioactive substances that circulate through the body to selectively target cancer cells. This approach is particularly useful for treating metastatic cancers and conditions that require systemic radiation delivery. For example, radioiodine (^{131}I) is widely used in the treatment of thyroid cancer, where the thyroid gland selectively absorbs the radioactive iodine, leading to targeted destruction of cancerous cells. Similarly, radium-223 is used for the treatment of metastatic bone tumors, where it preferentially targets bone tissue affected by cancer, helping to alleviate pain and slow disease progression. Radiotherapy is a powerful tool in cancer treatment. However, exposure to ionizing radiation carries potential somatic and genetic risks that must be carefully considered. Somatic effects refer to radiation-induced damage that affects normal tissues, both acutely and over the long term. Acute effects may include skin reactions, inflammation, and tissue swelling, whereas late effects, such as fibrosis and secondary malignancies, can develop years after treatment. Genetic risks, on the other hand, arise when radiation induces mutations in germ cells, leading to potential hereditary disorders that may be passed on to future generations. A fundamental principle in medical radiology and radiation oncology is the risk-benefit assessment, ensuring that the benefits of radiation exposure outweigh its potential harms. In medical imaging and radiotherapy, radiation dose must always be justified by the expected clinical benefit. The decision to use radiation-based diagnostics or treatments must take into account the patient's individual risk factors, as well as risk of professional staff, ensuring that unnecessary exposure is avoided whenever possible.

CONCLUSION

Ionizing radiation is an inescapable aspect of life, as humans are continuously exposed to natural background radiation from various sources, including cosmic rays, radionuclides present in the Earth's crust, and trace amounts of radioactive isotopes such as potassium-40 (^{40}K) and carbon-14 (^{14}C), which are absorbed through food, water, and air. While modern technology has expanded the use of ionizing radiation in medicine, industry, and research, it is important to recognize that humans have evolved multiple protective mechanisms against radiation-induced damage. These include antioxidant defense systems (superoxide dismutase, catalase, glutathione peroxidase), DNA repair pathways (base excision repair, homologous recombination, non-homologous end joining), and adaptive cellular responses that help mitigate radiation-induced mutations, oxidative stress, and cellular dysfunction.

A key aspect of radiation-induced damage is the formation of free radicals, particularly reactive oxygen species (ROS) generated through water radiolysis. These radicals play a dual role in biological systems: on one hand, excessive free radical production contributes to DNA damage, lipid peroxidation, protein denaturation, and increased cancer risk. On the other hand, controlled levels of ROS are involved in cell signaling, immune responses, and adaptive radioprotection, demonstrating the complexity of radiation biology. The balance between oxidative stress and antioxidant defense ultimately determines the extent of radiation-induced harm, with radioprotective enzymes and DNA repair mechanisms playing a critical role in maintaining genomic stability.

Despite its risks, ionizing radiation remains an indispensable tool in medicine, particularly in diagnostics (e.g., PET, CT) and therapeutics (e.g., radiotherapy, nuclear medicine). Advanced imaging technologies allow for early disease detection, while targeted radiotherapy techniques, such as proton beam therapy and brachytherapy, enable precise tumor destruction with minimal damage to healthy tissues. As medical and industrial applications of radiation continue to expand, it is

crucial to maximize the benefits while minimizing unnecessary exposure.

The ALARA (As Low As Reasonably Achievable) principle, along with strict dose monitoring, shielding strategies, and occupational safety protocols, must be rigorously enforced to protect both professionals working with radiation (e.g., healthcare workers, astronauts, nuclear industry personnel) and the general population. Additionally, the concept of hereditary radiation effects highlights the importance of long-term radiation safety regulations, as even low-dose exposure can have cumulative biological consequences over generations.

While high-dose radiation exposure is unequivocally harmful, ongoing research explores the biological effects of low-dose radiation, including the adaptive response and radiation hormesis hypothesis, which suggests that low doses may activate protective cellular mechanisms. However, the long-term effects of chronic low-dose radiation exposure remain a subject of scientific debate, warranting further investigation into its potential risks and benefits.

Future advancements in radiation biology, DNA repair research, radioprotective agents, and personalized risk assessments will be essential in mitigating radiation-induced damage and enhancing the safety and efficacy of medical, industrial, and space-related radiation applications. By integrating scientific knowledge, technological innovation, and ethical responsibility, the field of radiation science will continue to improve human health, medical diagnostics, and cancer treatment, ensuring a balanced approach between radiation benefits and safety in the modern world.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Biološki efekti jonizujućeg zračenja

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KRATAK SADRŽAJ

Uvod: Živimo u 21. veku, okruženi smo bezbrojnim oblicima zračenja, nusproizvodom naše zavisnosti od savremene tehnologije. Bilo da su ta unapređenja nužna ili samo korisna, često ih prihvatamo bez razmišljanja, a tek kasnije sagledavamo njihove posledice kroz prizmu nauke i zdravog razuma. Medicinski, naši problemi obično se javljaju nakon što je šteta već nanesena, kada prevencija više nije moguća.
Autori predstavljaju efekte jonizujućeg zračenja na ljude, sa ciljem postizanja urbanizacije kroz znanje i barem racionalan pristup zdravlju.
Metodologija: Online pretraga o jonizujućem zračenju i njegovim efektima na ljudsko telo sprovedena je korišćenjem PubMed, Cochrane, Embase i Scopus baza podataka. Pretraga je obavljena korišćenjem sledećih ključnih reči: jonizujuće zračenje, prirodni izvori zračenja, terapijski izvori zračenja, negativni efekti, biološki efekti, radiosenzitivnost, ALARA, efekti zračenja, zaštita od zračenja. Literatura je pretraživana na engleskom i srpskom jeziku ravnomerno, što može biti ograničavajući faktor u rezultatima pretrage.
Tema: Elektromagnetni spektar obuhvata celu paletu elektromagnetnog zračenja, klasifikovanu prema talasnoj dužini, frekvenciji i energiji. Obuhvata sve poznate elektromagnetne talase, od radio talasa sa najdužom talasnom dužinom i najnižom energijom do gama zraka sa najkraćom talasnom dužinom i najvišom energijom. Ovaj spektar igra ključnu ulogu u brojnim naučnim, tehnološkim i medicinskim primenama, od sistema komunikacije i tehnologija snimanja do kvantne fizike i astrofizičkih posmatranja. Jonizujuće zračenje stupa u interakciju sa biološkim tkivima na molekularnom, ćelijskom i sistemskom nivou, izazivajući niz efekata koji zavise od doze zračenja, energije, vrste, trajanja izlaganja i radiosenzitivnosti tkiva. Uticaj jonizujućeg zračenja na ljudsko telo zavisi od više faktora, uključujući intenzitet doze zračenja, ukupnu apsorbovanu dozu, energiju i vrstu zračenja, površinu izložene oblasti tela i radiosenzitivnost različitih tkiva. Radiosenzitivnost pojedinaca varira među populacijama i zavisi od genetskih faktora, starosti i opšteg zdravlja. Različiti organi i tkiva pokazuju različite nivoe osetljivosti na zračenje.
Zaključak: Budući napreci u biologiji zračenja, istraživanju popravke DNK, radioprotektivnim sredstvima i personalizovanim procenama rizika biće ključni za ublažavanje oštećenja izazvanih zračenjem i poboljšanje sigurnosti i efikasnosti medicinskih, industrijskih i svemirskih primena zračenja. Integracijom naučnog znanja, tehnoloških inovacija i etičke odgovornosti, oblast nauke o zračenju nastaviće da unapređuje ljudsko zdravlje, medicinsku dijagnostiku i lečenje raka, obezbeđujući uravnotežen pristup između koristi od zračenja i sigurnosti u savremenom svetu.

Ključne reči: biološki efekti, jonizujuće zračenje, slobodni radikali

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