



THE PHYSICAL BASIS OF THE EFFECTS OF IONIZING RADIATION (X-RAY AND GAMMA RAYS) ON THE ORGANISM

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1. Introduction: The Nature of X-rays and Gamma Rays

X-rays and gamma rays are forms of high-energy electromagnetic radiation. They belong to the category of indirectly ionizing radiation because the photons themselves carry no electric charge and do not produce ionization directly as they traverse matter. Instead, they transfer energy to atomic electrons, setting them in motion. These secondary charged particles, primarily electrons, are responsible for the vast majority of ionizations and excitations that occur in biological tissues. This fundamental two-step process—photon interaction followed by electron-mediated energy deposition—determines the entire chain of events that leads to radiation-induced biological effects.

The energies of X-rays and gamma rays used in medicine and encountered in the environment span from around 10 keV to several MeV. This range governs the relative importance of the three principal interaction mechanisms: the photoelectric effect, Compton scattering, and pair production. The physics of these interactions forms the foundation for understanding how radiation dose is distributed in the body and why different tissues may respond differently.

2. Primary Photon Interactions with Tissue

When an X-ray or gamma photon enters biological material, it may interact with whole atoms, with tightly bound inner-shell electrons, or with loosely bound or free electrons. The three key processes are:

Photoelectric effect: The photon transfers all of its energy to a bound atomic electron, typically from an inner shell, which is then ejected. This



process dominates at photon energies below about 50 keV in soft tissue and is strongly dependent on the atomic number of the absorbing material (approximately proportional to Z^4). In tissues with elevated atomic number, such as bone, the photoelectric effect increases local energy absorption significantly, which is why bone receives a substantially higher dose than soft tissue in low-energy diagnostic X-ray examinations.

Compton scattering: At intermediate energies, from around 100 keV up to several MeV, Compton scattering becomes the predominant interaction. The photon collides with an outer-shell electron, which is ejected, while the photon itself is scattered with reduced energy and a change in direction. Because this process depends almost entirely on electron density rather than atomic number, it produces a much more uniform dose distribution across different tissue types. In medical linear accelerator beams (6 MV and above) and in many nuclear medicine procedures, Compton scattering is the main mechanism of energy deposition.

Pair production: For photon energies above 1.022 MeV, the photon can interact with the electromagnetic field of the atomic nucleus and materialize as an electron-positron pair. The positron subsequently annihilates, producing two 511 keV photons that may further interact or escape. Pair production gains importance at energies above several MeV and becomes significant in high-energy radiotherapy and some industrial radiation exposures.

The relative importance of these three processes determines not only the absorbed dose at a macroscopic level but also the microscopic pattern of energy deposition, which strongly influences the biological outcome.

3. Energy Deposition and Linear Energy Transfer (LET)

After a photon interacts, the kinetic energy of the released secondary electrons is deposited along their tracks through a series of ionizations and excitations of atoms. The spatial density of these events is described by the linear energy transfer (LET), defined as the average energy deposited per unit



path length. X-rays and gamma rays are classified as low-LET radiations because the secondary electrons are relatively sparsely ionizing, with LET values typically around 0.2–2 keV/μm in water.

This sparse ionization pattern means that energy is deposited in discrete, widely spaced clusters along the electron track. Biological molecules such as DNA are therefore hit in a non-uniform manner; one cell may receive multiple ionizations while a neighboring cell receives very few. This contrasts markedly with high-LET radiations (such as alpha particles or neutrons) that produce dense columns of ionizations, causing complex clusters of damage that are far more difficult for the cell to repair. The low-LET nature of X-rays and gamma rays explains why their biological effectiveness per unit absorbed dose is lower than that of high-LET radiations.

4. Physico-chemical Phase and Water Radiolysis

Because the human body consists of approximately 70–80% water, the interaction of secondary electrons with water molecules dominates the initial chemical changes. Within 10^{-15} to 10^{-12} seconds after energy deposition, water molecules are ionized and excited, leading to the formation of highly reactive free radicals and molecular products. The overall reaction can be summarized as:



Among these species, the hydroxyl radical ($\cdot\text{OH}$) is the most damaging to biological molecules. It is a strong oxidizing agent that can abstract hydrogen atoms from organic molecules, add to double bonds, or initiate chain reactions. It has a very short diffusion distance, on the order of a few nanometers, and therefore reacts only with molecules in its immediate vicinity to the site of its generation.

The hydrated electron (e^-_{aq}) and hydrogen atom ($\text{H}\cdot$) are reducing species that also participate in chemical reactions with cellular components, although their contribution to lethal damage is generally considered less



significant than that of the hydroxyl radical. Hydrogen peroxide (H_2O_2), a more stable molecule, can diffuse over longer distances and act as a source of oxidative stress.

5. Direct and Indirect Action of Radiation

Damage to critical biological target molecules occurs via two distinct pathways:

Direct action: In this case, the secondary electron directly ionizes or excites the target molecule itself, for example the DNA double helix or a key protein. The ionization may occur within the macromolecule or in its tightly bound water of hydration. For low-LET radiation like X-rays and gamma rays, direct action accounts for about one-third of the total biological effect. The ionized target molecule may undergo immediate bond breakage or subsequent chemical rearrangements that result in functional loss.

Indirect action: The majority of damage, approximately two-thirds of the total effect, is indirect. Here, radiation deposits energy in the water surrounding the target, generating hydroxyl radicals and other reactive species that diffuse to and react with the target molecule. In the case of DNA, the hydroxyl radical is responsible for about 60–70% of the indirect damage in living cells. The radical may attack the deoxyribose sugar moiety, causing strand breakage, or modify the DNA bases, producing lesions that can be mutagenic if not repaired.

The relative contributions of direct and indirect action depend on the spatial distribution of radicals, the presence of radical scavengers such as glutathione, and the level of intracellular oxygen, which can fix radical lesions and make them permanent.

6. DNA as the Principal Target

While radiation induces damage in many cellular components, including membranes and proteins, the DNA molecule in the cell nucleus is widely regarded as the principal target for the lethal, mutagenic, and carcinogenic effects of radiation. The evidence for this includes the observation that



irradiating the nucleus is far more lethal than irradiating the cytoplasm, that DNA repair-deficient cells are hypersensitive to radiation, and that cells can be killed by the incorporation of radioactive isotopes into their DNA.

Radiation produces a variety of DNA lesions. The most numerous are single-strand breaks (SSBs), which are efficiently repaired by base excision repair pathways and have little biological consequence in normal cells. Far more important are the double-strand breaks (DSBs), which are produced at a rate of about 20–40 DSBs per cell per gray for low-LET radiation. A single unrepaired DSB can be lethal, and misrepaired DSBs can lead to chromosomal aberrations such as dicentrics, translocations, and deletions, which are hallmarks of radiation exposure and are causally linked to cancer induction.

In addition to strand breaks, radiation causes a spectrum of base damages, abasic sites, and DNA-protein crosslinks. The complexity of the damage, known as “clustered damage” or “locally multiply damaged sites,” is an important concept. Even low-LET radiation can produce sites where several lesions are formed within one or two helical turns of the DNA, making repair more difficult and error-prone.

7. Determinants of the Biological Response

The effectiveness of a given absorbed dose of X-rays or gamma rays is modulated by several physical, chemical, and biological factors.

Oxygen effect: Molecular oxygen is a potent radiosensitizer for low-LET radiations. In the presence of oxygen, the radicals produced in the target molecule (through direct action) or on DNA from indirect action can react with oxygen to form organic peroxy radicals. This effectively “fixes” the chemical damage, making it permanent and preventing chemical repair by hydrogen donation from thiol compounds. The ratio of doses required to produce the same biological effect under hypoxic and fully oxygenated conditions is called the oxygen enhancement ratio (OER). For X-rays and gamma rays, the OER is



typically between 2.5 and 3. This has profound implications for radiotherapy, where tumor hypoxia can be a cause of treatment resistance.

Dose rate and fractionation: The effect of a given total dose is strongly influenced by the rate at which it is delivered. At low dose rates or when the dose is divided into multiple fractions separated in time, cells have the opportunity to repair sublethal damage between exposures. For low-LET radiation, the dose-rate effect is substantial; lowering the dose rate can reduce the biological effect by a factor of two or more. This is the basis of fractionation in radiotherapy, which spares late-responding normal tissues more than tumors.

Cell cycle dependency: Cells exhibit varying radiosensitivity depending on their position in the cell cycle. In general, cells are most sensitive in the G₂ and mitosis (M) phases and most resistant in the late S phase. The molecular basis of this variation lies in the availability of homologous recombination repair templates (sister chromatids are present in S and G₂) and in differences in chromatin compaction.

LET and relative biological effectiveness (RBE): The biological effectiveness per unit dose increases with LET up to a maximum around 100 keV/μm, after which it declines because of “overkill” effects where energy is wasted on already lethally damaged cells. For X-rays and gamma rays as the reference low-LET radiation, the RBE is defined as 1. The RBE of higher-LET radiations is therefore obtained by comparing them against X-rays or gamma rays.

8. Biological Consequences: Deterministic and Stochastic Effects

The clinical and biological consequences of radiation exposure are grouped into two major categories.

Deterministic effects (tissue reactions): These are caused by the killing of a large number of cells within a tissue or organ, leading to functional impairment. They have a threshold dose below which the effect is not clinically detectable, and the severity increases with dose above that threshold. Examples



include skin erythema and desquamation, cataract formation, bone marrow depletion resulting in haematological syndrome, and gastrointestinal damage following whole-body irradiation. The threshold for most deterministic effects is in the range of several hundred milligray to several gray.

Stochastic effects: These arise from the mutation of a single surviving cell that goes on to proliferate into a clone of altered cells. They are assumed to have no threshold, and their probability—but not severity—increases with dose. The principal stochastic effects of concern are radiation-induced cancer and heritable genetic effects. While heritable effects have not been demonstrated convincingly in human populations, the risk of cancer following low-dose exposure is supported by epidemiological evidence from atomic bomb survivors and medically exposed cohorts. The current risk models used by international bodies estimate a lifetime cancer mortality risk of approximately 5% per sievert for acute, whole-body exposure to low-LET radiation in a population of all ages.

9. Summary

The effects of X-rays and gamma rays on living organisms are initiated by a sequence of physical interactions that occur within the first femtoseconds after exposure. Photons set electrons in motion through the photoelectric effect, Compton scattering, or pair production, and these charged particles deposit energy along their tracks in a sparse, low-LET pattern. The vast majority of this energy is absorbed by water, leading to the production of hydroxyl radicals and other reactive species that attack critical cellular targets, especially DNA. The resulting lesions, particularly double-strand breaks and multiply damaged sites, can be repaired, misrepaired, or left unrepaired. The interplay of dose, dose rate, cellular oxygen concentration, and cell cycle status determines the ultimate biological outcome. Deterministic effects reflect mass cell killing above threshold doses, while stochastic effects represent rare mutational events that can lead to malignancy. A thorough understanding of these physical and



chemical processes is essential for radiation protection, dosimetry, and the clinical use of radiation in diagnosis and therapy.

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