

BIOLOGICAL MOLECULAR AND CELLULAR EFFECTS OF IONIZING RADIATION

Abstract

The ionising radiation is a common tool in medicine as a diagnostic and therapeutic agent. The initial damage to DNA and chromosomes may result in either cell death, which can cause early tissue damage, or the conversion of cells into malignancy and, ultimately, cancer, increasing concerns about radiation protection in a number of exposure scenarios, including occupational and environmental exposure (such as radon). The scientific community must constantly refresh and enhance its understanding of the mechanisms behind the induction of radiation effects in biological targets in order to optimise the usage of ionising radiation and the accompanying radiation safeguarding techniques.

Keywords: Biological Molecular, Cellular, Ionizing Radiation.

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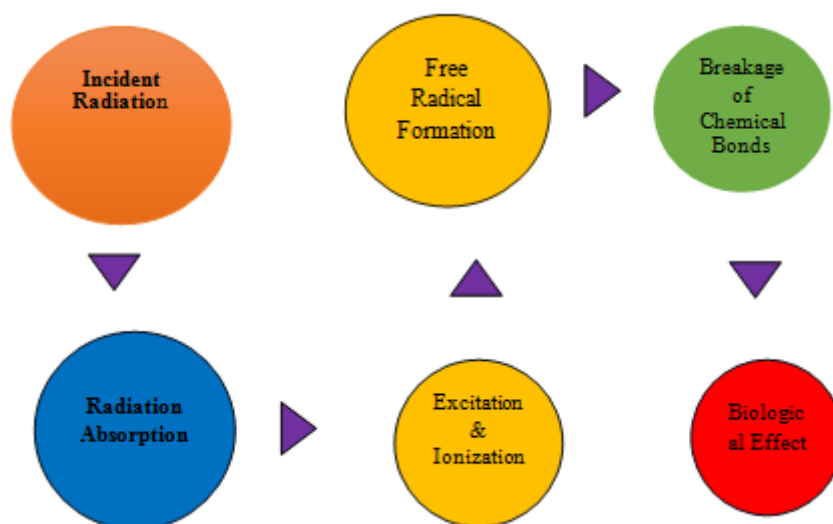
I. INTRODUCTION

Radiology = Radiobiology Biology is the study of ionizing radiation's effects on living things. Chemistry and Biology Ionizing radiation comes in a variety of forms. radiation that isn't ionized and that is: Electrons, protons, alpha particles, and heavy ions are among the charged particles that directly ionizing radiation deposits as dosage. Ionization (neutral particles) is caused by the indirect interaction of ionizing radiation with matter: neutrons and photons Atomic and molecular energy absorption causing biological harm The goal of radiotherapy's radiobiological principles is to treat cancer with the least amount of harm to healthy tissues.

II. BASIC CONCEPTS OF RADIATION BIOPHYSICS

Different radiation quality cause the same spectrum of DNA lesions, but the location of lesions within the target might vary greatly. The DNA Double Strand Break (DSB) is thought to be the form of lesion most directly connected to cell death. Radiation Effects on Cells at the Molecular Level.

Ionization or excitation occurs as a result of the energy that is deposited when radiation interacts with target atoms. Ionizing radiation's energy absorption damages molecules both directly and inadvertently. In the case of direct action, harm is brought about by the ionization of atoms on significant biological system molecules. The molecule is inactivated or undergoes functional modification as a result. The creation of reactive free radicals that cause the critical molecule toxic damage results in a biological reaction, which is referred to as indirect action.

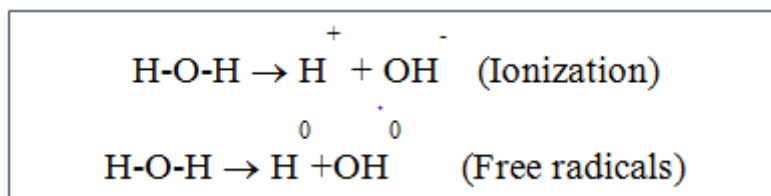


- Direct Effects:** The direct ionisation of atoms in molecules results from the energy absorbed via photoelectric and Compton interactions. Ionisation, the primary cause of damage in reactions involving high LET radiations, is the end outcome of all radiation properties. When enough energy is absorbed to remove an electron, bond breaking can take place.



- 2. Indirect Action:** These effects are brought on by free radicals. Free radicals are electrically neutral atoms with an unshared electron in the orbital position. The radical is very electrophilic and reactive. Water frequently functions as an intermediary in the production and spread of radicals since it is the most prevalent molecule in biological systems.

- **Indirect Action- Radiolysis of Water**



Free radicals are easily converted back into neutral electrical and orbital states. However, in situations when there are lots of them, such as under high radiation fluence, orbital neutrality can be attained by

- Dimerization of hydrogen radicals (H₂)
 - The generation of hazardous hydrogen peroxide (H₂O₂).
 - An organic molecule in the cell can also get the radical.
- **Indirect Action - The Lifetimes of Free Radicals:** Simple free radicals (H⁰ or OH⁰) have extremely brief lives, on the order of 10⁻¹⁰ seconds. Even though they are often quite reactive, they do not last long enough to go from the place of production to the cell nucleus. Hydroperoxy free radical, for example, is an oxygen-derived species that does not readily interact with neutral forms. These more durable versions have a lifespan that allows them to get to the nucleus, where significant harm can happen.
 - **Indirect Action- Free Radicals:** A biological molecule may sustain enough harm from a free radical transfer to result in bond breaking or the deactivation of crucial processes. When an organic peroxy free radical comes into contact with another molecule, it might spread and destroy that molecule. Thus, rather of a single ionization or broken bond, a cumulative impact may take place.

III. BIOCHEMICAL REACTIONS WITH IONIZING RADIATION

DNA, the most important part of the chromosomes, serves as the main structural blueprint for the cell. It regulates the types of RNA that are produced, which in turn regulates the types of proteins produced. The DNA molecule resembles a ladder or double helix. The phosphate and sugar group strands that make up the ladder's sides are alternated. Each sugar group branches into one of the four nitrogenous bases: cytosine, thymine, adenine, and guanine.

IV. BIOCHEMICAL REACTIONS WITH IONIZING RADIATION-DNA DAMAGE

Strong evidence suggests that DNA is the primary target of cell damage brought on by ionising radiation. Cell death, mutagenesis, and malignant transformation appear to be toxic

effects at low to moderate concentrations that are caused by cellular DNA damage. As a result, ionising radiation is a well-known genotoxic agent.

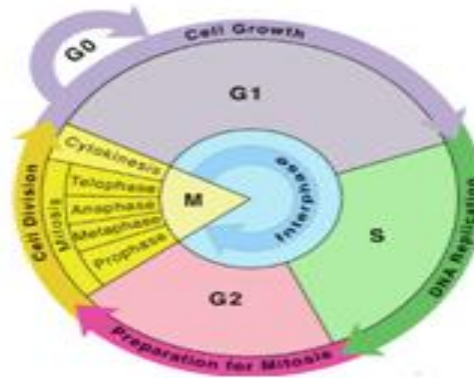
- 1. DNA Damage and Biochemical Reactions with Ionising Radiation:** Active enzymatic activity can repair DNA base damage and DNA strand breaks. Double-strand DNA breaks may commonly be repaired by the enzymes DNA polymerase and DNA ligase. Repairing double strand fractures can be challenging and include recombination mechanisms depending on the type of initial break.
- 2. Radiation Induced Chromosome Damage:** Active enzymatic activity can repair DNA base damage and DNA strand breaks. Two enzymes that could commonly fix double-strand DNA breaks are DNA polymerase and DNA ligase. The treatment of double-strand fractures is a challenging procedure that necessitates recombination mechanisms, depending on the nature of the initial break.
- 3. Radiation Induced Chromosome Damage:** After irradiation, chromosomes may appear "sticky" because transient or permanent intrachromosomal bridges prevent normal chromosome separation during mitosis and the transcription of genetic material. Additionally, radiation can change the chromosomes' structure, causing damaged pieces to take on unnatural shapes. Uneven nuclear chromatin material division can result in the production of nonviable, abnormal nuclei in daughter cells.
- 4. Damage to Membrane Induced by Radiation:** The highly trained mediators between the environment and the cell (or its organelles) are biological membranes. Changes in the structure of the proteins that make up a membrane can affect the permeability it is to various substances, including electrolytes. The ability of nerve cells to transmit electrical impulses would be impacted by this. Life-threatening consequences could occur if the catabolic enzymes in lysosomes escape into the cell unchecked. The ionising radiation has been shown to lead to plasma membrane degradation, which may play a key role in cell death (interphase death). Cell Cycle.

Undifferentiated cells that are growing will eventually divide. A number of variables, including species, tissue type, age, and environmental conditions, have an impact on the cell cycle, or the time interval between cell divisions. Mitosis follows cell division. The cell cycle is divided into four distinct stages: G₁ (gap), S (synthesis), G₂ (gap), and M (mitosis). Dormant cells reside in the fifth phase, G₀. A cell in G₀ can frequently be stimulated by the environment to enter the active cycle.

Cells in the G₀, G₁, S, and G₂ phases of the cell cycle spend time in the interphase interval. During mitosis (M phase), chromosomes condense (prophase) and align (metaphase) on the equatorial plane. Pairs split (anaphase) and condense (telophase) at the poles of dividing cells, and each cell produces a new nucleus as a result.

Cells are particularly vulnerable to cell death during late interphase (G₂), just before M phase, and throughout M phase. Cells in S phase, late G₁ phase, and all cells in G₀ phase exhibit higher resistance. The presence of synthetic enzymes capable of speedy DNA break repair may be the cause of resistance in the S phase. However, cells that are in or about to enter the S phase have a higher mutation frequency.

Due to the cell's incapacity to divide, radiation causes cell death during mitosis. Protein and RNA production continue in the sterilised cell after mitotic death. As a result, the gigantic cell is created, whose uncontrolled development ultimately proves fatal to the cell.



Bergonié-Tribondeau Law: These pioneering radiobiologists postulated in 1906 that the radiation reaction in tissue was a function of

- a high percentage of undifferentiated cells in the tissue, and
- a high percentage of cells that are actively mitotic.
- How long the cells continue to proliferate actively.

V. RADIOSENSITIVITY

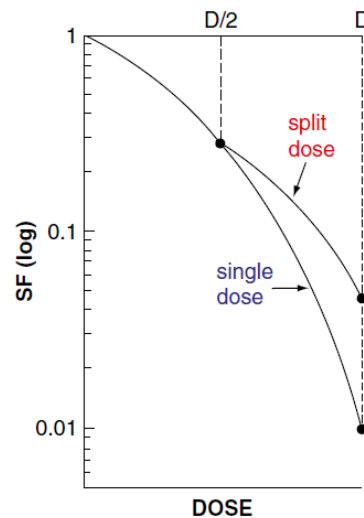
- The cornerstone of fractionation is anchored in five fundamental biological elements that influence the responses of normal and tumour tissues in fractionated radiotherapy, known as the five Rs of radiotherapy.
- High-dose radiotherapy is ineffective for tumour management and has substantial side effects.

1. Repopulation

- Radiation exposure does not stop tumour or healthy normal cells from proliferating.
- Because of this repopulation, tumour cells are able to partially withstand the deadly effects of radiotherapy. The "tumour doubling time," T_p , which can also be referred to as the repopulation time, is the amount of time needed for the tumour cell count to double.
- After the initial radiation doses, repopulation picks up speed. Repopulation is initially slow during radiotherapy. This rise in the pace of repopulation is known as "accelerated repopulation," and the period of time it takes to start is known as the "kick-off time" (T_k).
- 4. Repopulation must be considered while delaying radiation, for example, because of planned (or unplanned) pauses like holidays.
- During radiotherapy, normal tissue also replenishes, which is an important mechanism to reduce acute side effects. e.g. the irradiation of skin or mucosa.

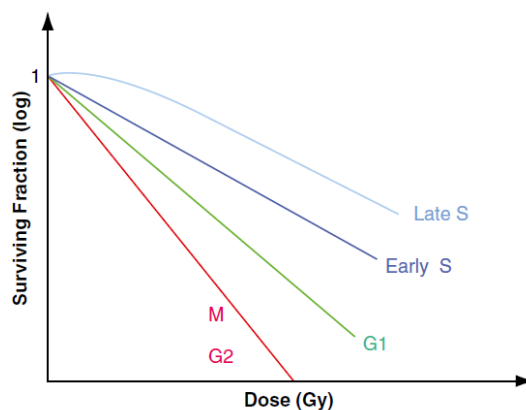
2. Repair

- Radiotherapy kills tumour cells and causes sublethal harm to healthy tissues. Normal tissues can heal sublethal damage when radiation is applied in fragmented doses.
- The parameter $2.t_{1/2}$, whose value ranges from minutes to hours, is utilised in this effect to determine that half the time needed for cell healing following radiation damage ($t_{1/2}$).
- As a result, interfraction gaps should be at least 6 hours long to give normal tissue cells time to recover from radiation damage before administering another radiation fraction.



3. Redistribution

- Redistribution is the selective eradication of cells during a certain cell cycle phase.
- Cellular radiosensitivity varies depending on the cell cycle stage.
- The S phase is the most resistant, whereas M and G2 are the most vulnerable phases. During the following dose fraction, cells in the resistant phase of the cell cycle could transition into the sensitive phase. As a result, there is a higher chance that tumour cells will be exposed to radiation when they are in a sensitive phase.

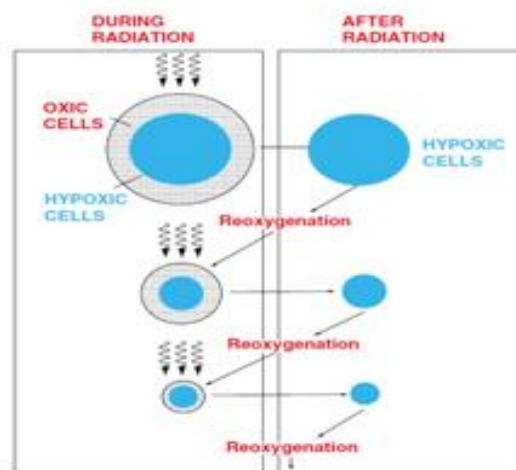


4. Re-Oxygenation

- Oxygen plays a key role in enhancing the effects of radiation.
- The tumour tissue's insufficient vascularity results in hypoxic zones inside the tumour cells as the tumour volume grows as a result of the proliferation of tumour cells. Thus, hypoxic cells are more radiation-resistant.
- 3.The hypoxic cells gradually improve their vascularity and oxygenation throughout the duration of fractionated radiation, and their radiosensitivity rises.

5. Radiosensitivity

- Bergonie and Tribendau proposed that radiosensitivity was directly related to mitosis and inversely proportional to differentiation when they initially introduced the term "radiosensitivity".
- The damage is determined by the following factors: i.) Type of cell irradiated, ii.) Volume of tissue irradiated, and iii.) Received dose.
- The environment may have an impact on radiosensitivity.
- The term "SF2" (SF2 stands for "surviving cell fraction after a radiation dose of 2 Gy") was first used. Radiosensitivity reduces as SF2 rises. To reduce SF2, radiosensitizers are employed.



REFERENCES

- [1] Radiation Physics for Medical Physicists (Biological and Medical Physics, Biomedical Engineering) - 2 Ed. Ervin B. Podgorsak
- [2] Technical Basis of Radiation Therapy: Practical Clinical Applications (4th Edition), by S. H. Levitt , € 219.00 Springer
- [3] Radiobiology for the Radiologist by Eric J. Hall, Lippincott
- [4] Introduction to Radiological Physics and Radiation Dosimetry by Frank H. Attix, 978-0471011460, Wiley-VCH
- [5] Physics in Biology and Medicine, Third Edition (Complementary Science) by Paul Davidovits (Sep 14, 2007) , 978-0123694119, Academic Press; 3 edition (September 14, 2007)
- [6] Introduction to Health Physics: Fourth Edition by Herman Cember and Thomas Johnson (Jul 25, 2008) , 978-0071423083, McGraw-Hill Medical
- [7] Radioactivity Radionuclides Radiation (with CD) by Joseph Magill
- [8] Treatment Planning in Radiation Oncology, 2Ed. by Faiz M.Khan, US.