“The 5 Rs in Radiotherapy”

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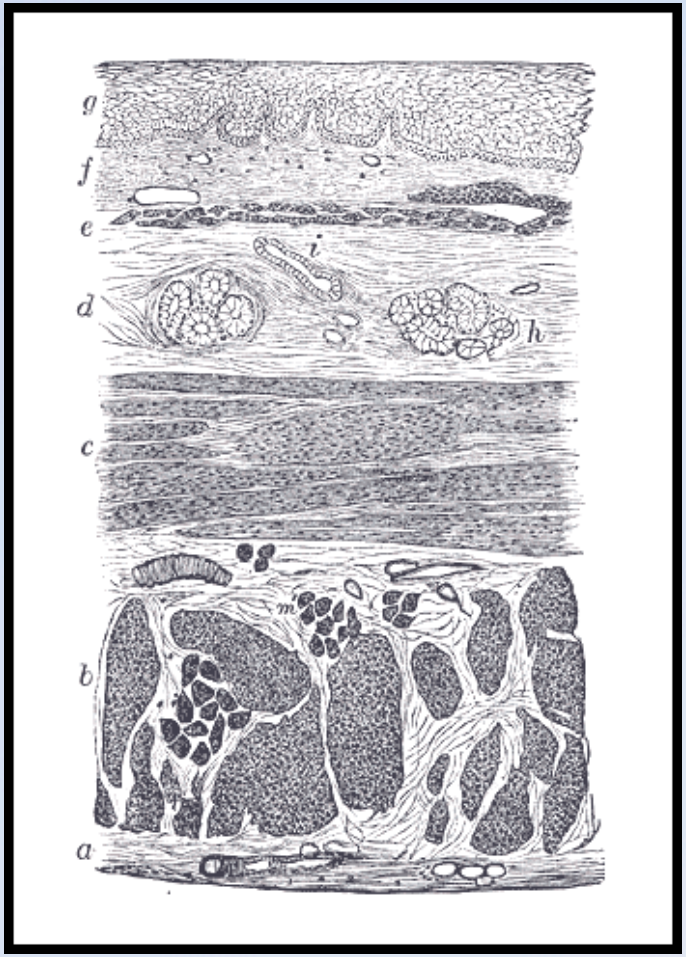
4º Grado Medicina

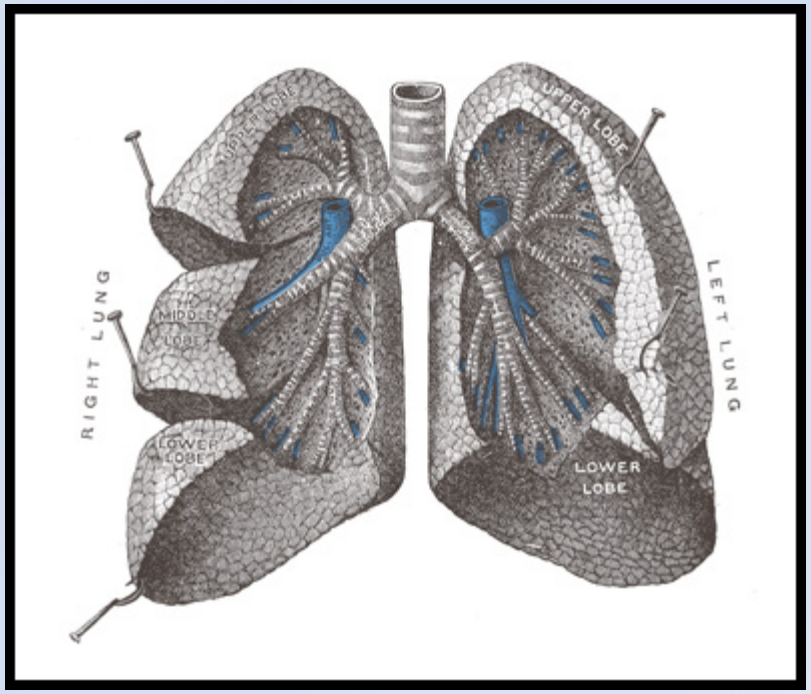
1-Radiation Effects on tissues (I)

- **-Proliferating tissues and tumor tissues:**
  - they respond similarly to radiation
  - the role of proliferative tissues is lost by alteration of stem cells
  - it results in acute effects and is governed by the alpha component.



1-Radiation Effects on tissues (II)

- **-Non-proliferative tissues:**
  - their function is lost when causing damage to the differentiated cells
  - they show late effects
  - they are governed by the beta component.



2-Reparation

- It restores the original DNA sequence prior to the appearance of the lesion through enzymatic mechanisms state [1].

- **-Repair mechanisms:**
  - Injuries nucleobases à NER, Mismatch.
  - Single strand breaks à VER.
  - Double strand breaks à RH, NHEJ.

- **-Influence on tumor control:**
  - **Normal tissues**: It is necessary to let them rest in between fractions of radiation for them to repair the potential radiation-induced damage.
  - **Tumor tissue**: It partially counteracts cell death due to radiation.

3-Cellular Redistribution influenced by the cell cycle (I)

- **-Fractionation of radiation:** It gets to destroy more tumor cells than those of normal tissues of slow response.

- -Mechanism:

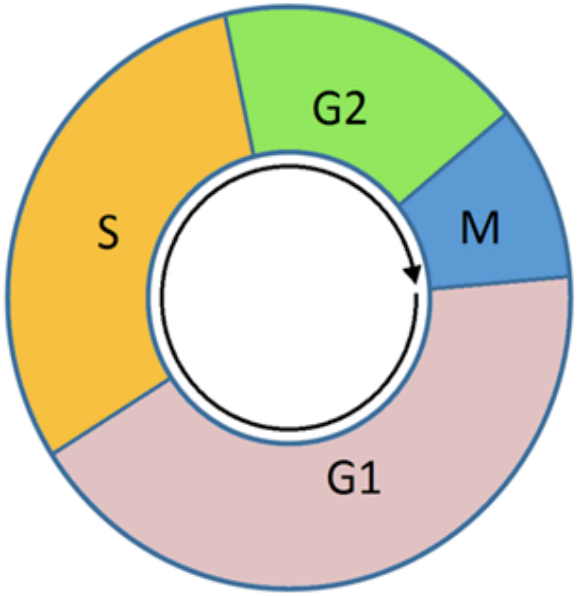
tumor cells are not equally radiosensitive in the different phases of the cell cycle (radiosensitivity: G2 and M> G1> S)

radiation dose eliminates the most radiosensitive cells

Survivors: distributed in the different phases of the cell cycle

some cells are located in the most radiosensitive phases

3-Cellular Redistribution influenced by the cell cycle (II)



G1 - Growth — Medium radiosensivity

S - DNA synthesis — Low radiosensivity

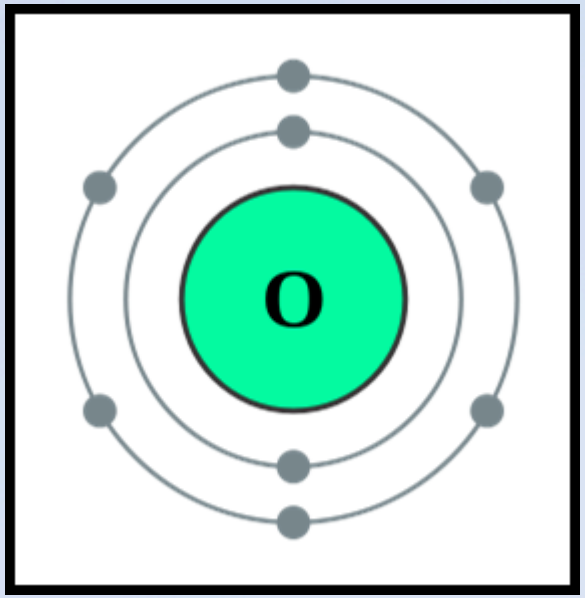
G2 - Growth and preparation for mitosis

M - Mitosis (cell division)

High radiosensivity

4-Reoxygenation (I)

- -Radiation can cause damage to the cells in two ways:
  - a) **Direct** (ionization of the DNA).
  - b) **Indirect**: through the formation of free radicals of cellular molecules, mainly of H2O.



- -The **O2** interacts with free radicals to form more stable and harmful compounds → →They react with the DNA.

4-Reoxygenation (II)

-Hypoxia: It influences/ has an impact on the treatment of cancer in two ways:

- 1st - Report: It prevents the arrival of O2 to the cells → less radiation sensitization → worse tumor control by radiotherapy.

- 2nd - It induces a signaling cascade that promotes the expression of genes involved in processes such as angiogenesis.

- -Mediator: **Hypoxia Inducible Factor (HIF)** →overexpressed in many types of cancer → it is associated with a worse prognosis [2].

-OER: radiation dose for an effect in the absence of O2 / radiation dose for the same effect in the presence of O2.

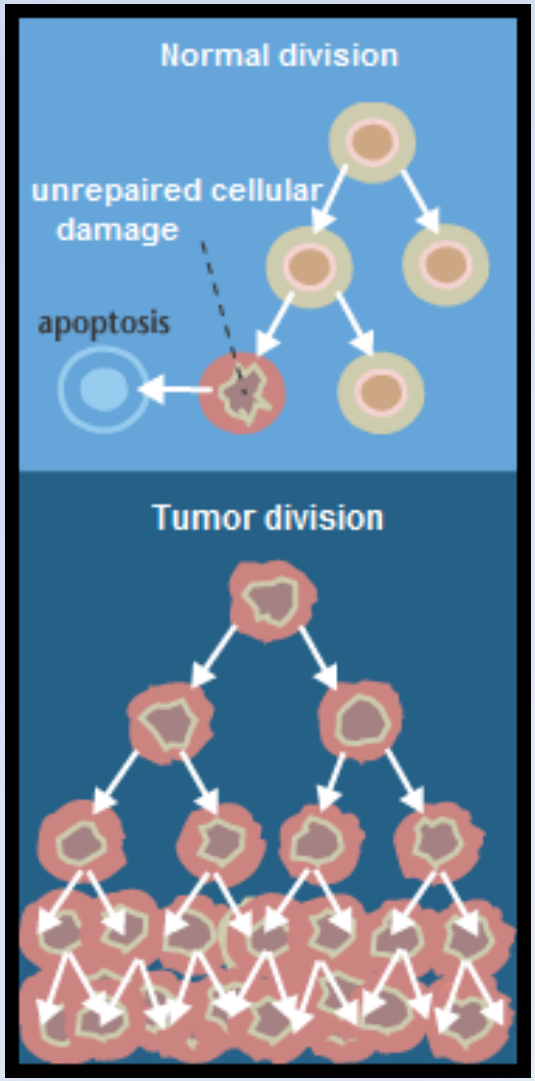
1- ↑ Dose of radiation →↑ Effect of O2.

2- OER in Low LET radiation > OER in High LET radiation.

3- G2 and S → ↑ Effect of O2.

5-Regeneration

- -After irradiation, surviving tumor cells increase their proliferative rate to compensate cell death caused by radiation.
- -The longer the time a tumor is irradiated, the less acute effects, the greater the tumor reoxygenation time, and the higher the proliferation of tumor cells.
- -This increase in tumor proliferation hinders the control of the tumor through radiotherapy.



6-Intrinsic tissue Radiosensitivity (I)

-The susceptibility (loss of reproductive capacity) of a cell or living tissue shows deterioration and modifications due to radiation, regardless the environmental factors.

- **-Molecular radiosensitivity:** inverse relationship between the double breaks of the DNA chain and the survival fraction at 2 Gy (SF2).
  - SF2: correlates with tumor response to radiation.

- **-Tumor radiosensitivity** → it is necessary to see the SF2 and the response of the tumor after being irradiated.
  - 5 Tumor categories: A, B, (radiosensitive); and C, D, E, (radioresistant).

6-Intrinsic tissue Radiosensitivity (II)

-Factors modifying the radiosensitivity:

1-Radiation characteristics

2 Environmental conditions

3-Cell growth properties [3]

7-“To Take Away”

	Influence on tumor control
Repair	Normal tissues: ☺ Tumor tissues: ☹
Redistribution	↑ tumor Radiosensitivity
Reoxygenation	↑ Dose of radiation → ↑ Effect of O2 OER Low LET radiation > OER in High LET radiation G2 and S → ↑ Effect of O2 Hypoxia: ☹
Regeneration	↑ Irradiation time → ↑ Regeneration à worse tumor control
Radiosensitivity	Increased Radiosensitivity → better tumor control SF2: correlates with tumor response to radiation

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