TUMOR TISSUE RESPONSE TO RADIATION

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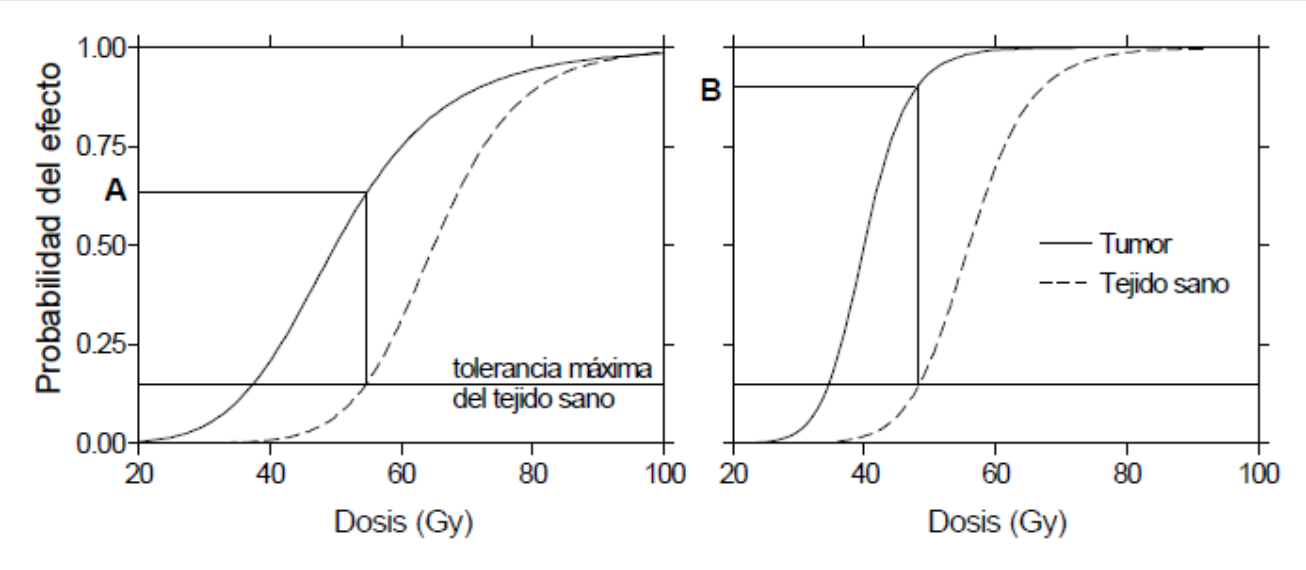
PURPOSE OF RADIOTHERAPY

- Destroy by means of radiation the maximum amount of tumour cells without harming nearby healthy tissue



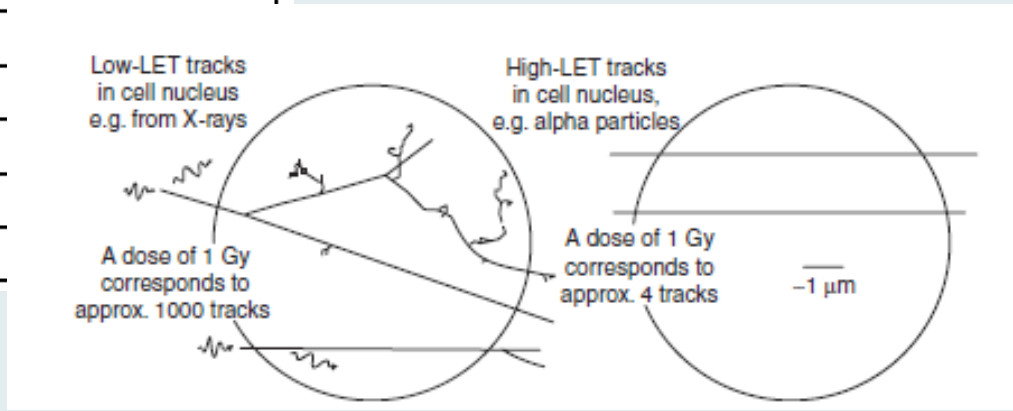
- Índice terapéutico y ventana terapéutica. (Radiobiología Clínica. "SEFM." Juan Ciudad Platero, Damián Guirado Llorente, Alberto Sánchez-Reyes Fernández, Waldo Sanjuanbenito Ruiz de Alda, Santiago Velázquez Miranda)

- Different **RADIOSENSITIVITY** of both tissues, that depends on:

1. Radiation Quality

- "LET, it expresses the quantity of average energy transferred by a particle in the distance of a micron " (Biocáncer 1,2004. Generalidades en Oncología Radioterápica (I). Radiobiología. Betatriz Pinar Sedeño , Pedro C. Lara Jiménez)

Radiaciones	LET (KeV/micra)
Rayos X Co 60	0.2
Rayos X 250 KV	2.0
Protones 10 MeV	4.7
Protones 150 MeV	0.5
Neutrones 14 MeV	100
Partículas alfa 2.5 MeV	166
Iones Fe 2 GeV	1000



- (Biocáncer 1,2004. Generalidades en Oncología Radioterápica (I). Radiobiología. Betatriz Pinar Sedeño, Pedro C. Lara Jiménez)
- (Basical Clinical Radiobiology. Michael Jonier, Albert van der Kogel)

conclusion: **the ↑LET, the more deleterious effects**

2. Dose fractionation/Dose rate

- **Hyperfractionation** : "Use of reduced size fractions given twice or more per day such that a greater total dose is delivered by increasing the number of treatments in the same total treatment time" (Biologic Basis of Radiation Therapy. Arno J. Mundt, MD, John C. Roeske, PhD, Theodore D. Chung, MD, PhD, and Ralph R. Weichselbaum, MD)

- **Hypofractionation**: "Use of larger than standard daily fractions" (Biologic Basis of Radiation Therapy. Arno J. Mundt, MD, John C. Roeske, PhD, Theodore D. Chung, MD, PhD, and Ralph R. Weichselbaum, MD)

More dose fractionation/dose rate (cGy/min):
mortality increases, cell survival decreases

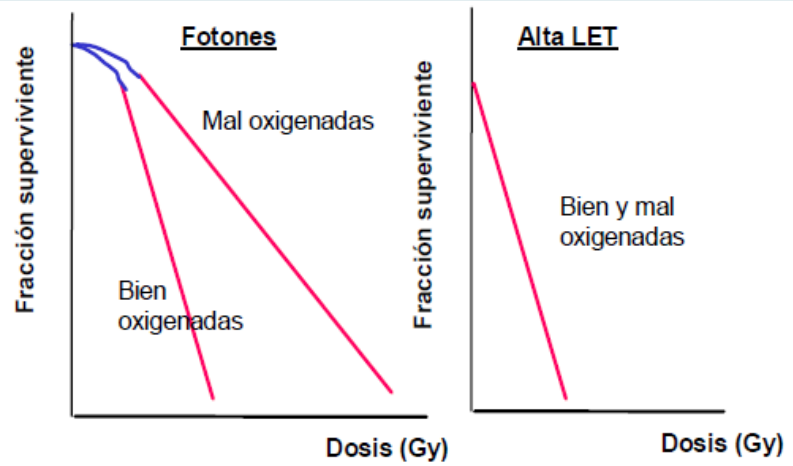
3. Presence of radiosensitizers/radioprotectors

- Radiosensitizers
  - O2 (OER). Tumours in anaerobic atmospheres need 2’5 more radiation

More LET, O2 radiosensitizers effect decreases

The best thing is to give:

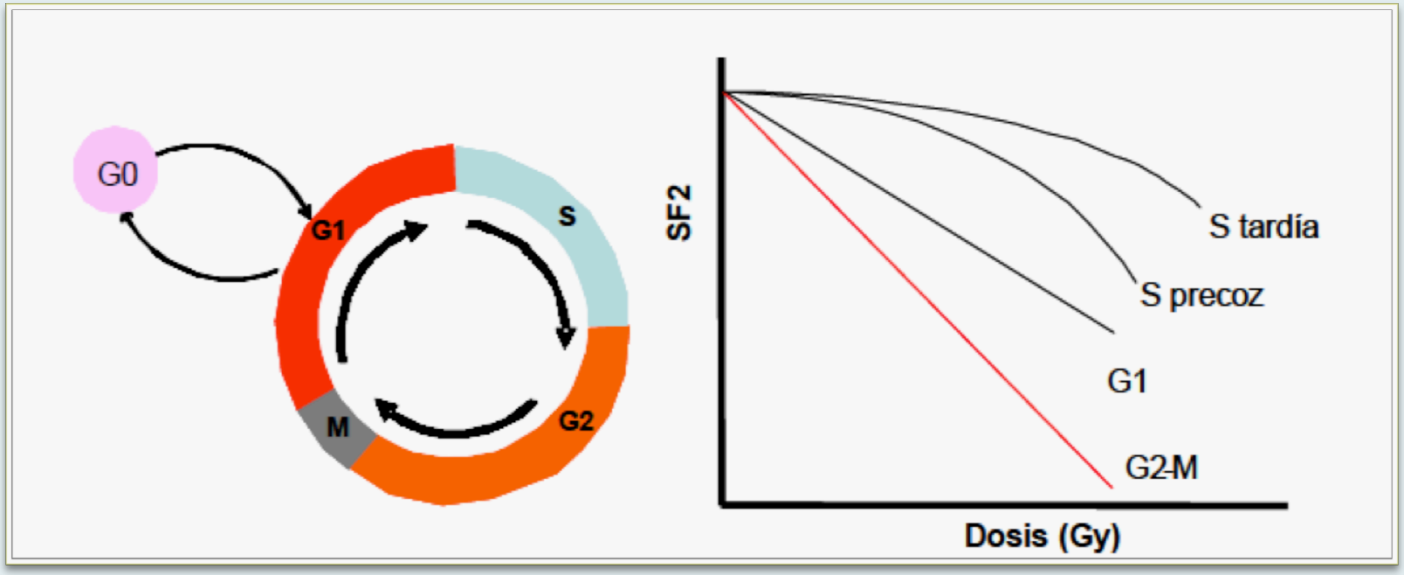
Low LET radiation + O2 al 2-3%



(Biocáncer 1,2004. Generalidades en Oncología Radioterápica (I). Radiobiología. Betatriz Pinar Sedeño , Pedro C. Lara Jiménez)

- Radioprotectors
  - Cyclic nucleotides (AMPc, GMPc)
  - Vitaminas(A, C y E)
  - Group –SH compounds (Cysteine, Cysteamine, Glutathione)

4. Cell Cycle Phase



- (Biocáncer 1,2004. Generalidades en Oncología Radioterápica (I). Radiobiología. Betatriz Pinar Sedeño, Pedro C. Lara Jiménez

- More radiosensitivity in the late G2 phase
- Increased radioresistance in the S phase

5. Tissue Damage and Repair

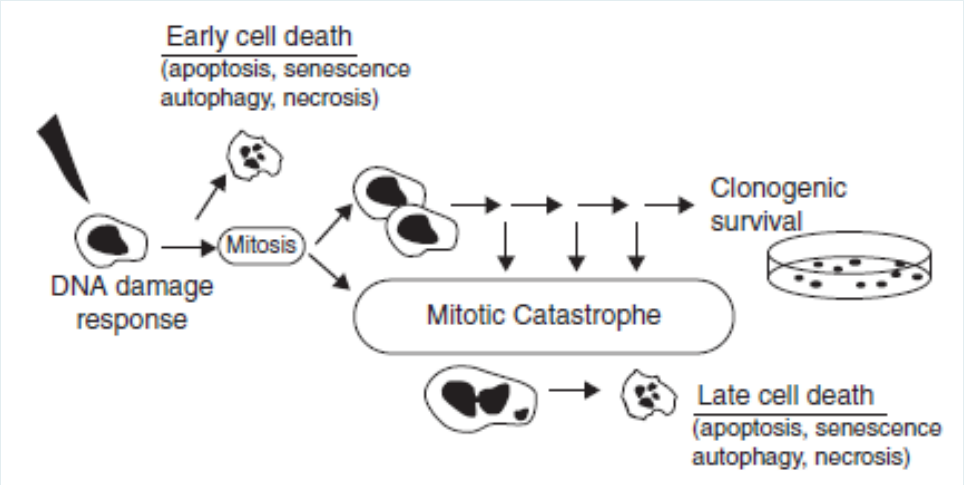
- Linear relation between the average time of repair and cell survival fraction

- Biphasic Response
  - Fast tissue repair → NHEF
  - Slow tissue repair → RH

6. Activation of cell death routes

- Cell death in Radiotherapy = Loss of cell reproductive capacity

- Types of cell death
  - Apoptosis
  - Autophagy
  - Necrosis
  - Senescence
  - Mitotic Catastrophe

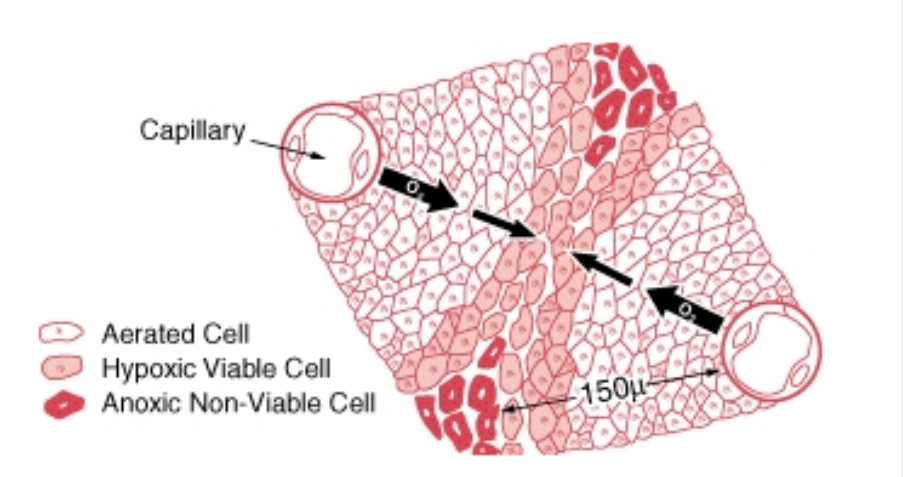


- (Basical Clinical Radiobiology. Michael Jonier, Albert van der Kogel)

- In most cases, cells die after trying mitosis (late cell death)

TUMOUR STRUCTURE

- Furthest part from blood vessel→ Necrosis
- Intermediate part→ Hypoxic cells
- Closer part to blood vessel→ Proliferative cells → **more radiosensitivity** (remember O2 effect)

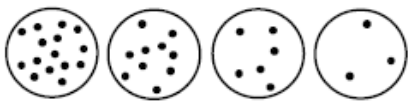


(Biologic Basis of Radiation Therapy. Arno J. Mundt, MD, John C. Roeske, PhD, Theodore D. Chung, MD, PhD, and Ralph R. Weichselbaum, MD)

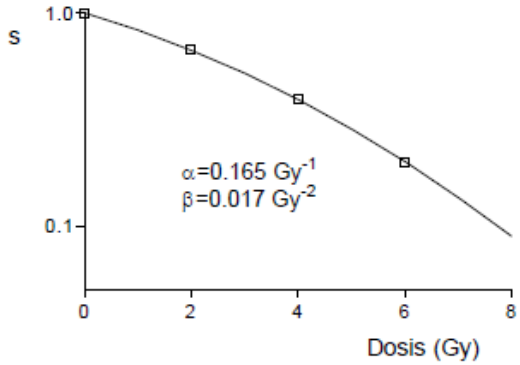
TUMOUR STRUCTURE

- Tumour heterogeneity
  - **Undifferentiated cells more radiosensitive than differentiated cells**
- **STEM CELL** → Undifferentiated
  - They can't be identified *in vivo*
  - The are identified *in vitro* by means of clonogenic test (**CLONOGENIC CELL**) → **COLONY**: Group of 50 or more cell elements derived from the same mother cell

CLONOGENIC TEST



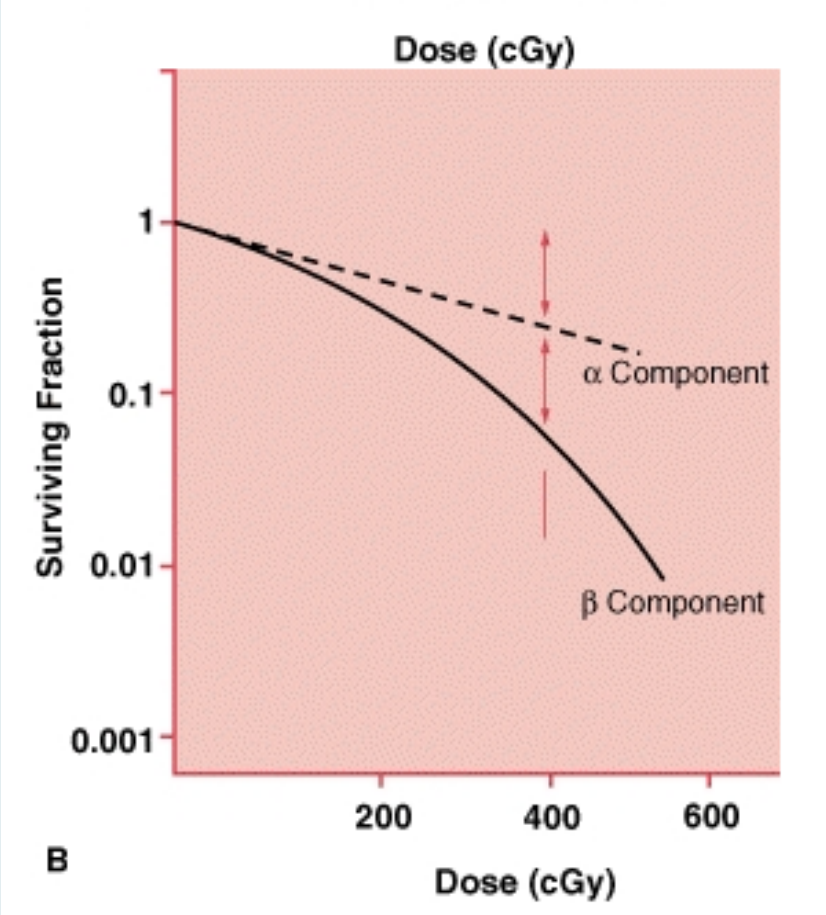
	Control	2 Gy	4 Gy	6 Gy
eficacia de siembra	0.03	0.02	0.012	0.006
s	1.00	0.67	0.40	0.20



- "Diagram of a clonogenic test. For a particular dose, survival fraction is calculated by divinding the sow efficiency for that dose by the sow efficiency for the control. Data fits the LQ model."
- (Radiobiología Clínica. "SEMF." Juan Ciudad Platero, Damián Guirado Llorente, Alberto Sánchez-Reyes Fernández, Waldo Sanjuanbenito Ruiz de Alda, Santiago Velázquez Miranda)

LINEAR QUADRATIC MODEL

$$FS\ global = e^{-(\alpha D+\beta D2)}$$



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LINEAR QUADRATIC MODEL

- **α** (High dose). Inmediate molecular alterations (lethal damage) → cell death (deterministic elements).
  - Linear component
- **β** (Low dose). Late molecular alterations with transmission to following cell lines (sublethal damage) → neoplasm (random effects).
  - Quadratic component

- 2 Gy is the limit. With a radiation dose below 2 Gy, the lethal effects prevail, whereas with a radiation dose above 2 Gy the sublethal injuries prevail.
- As the cell survival curve has a wider "shoulder", the more radioresistant the cell line is.

BIBLIOGRAPHY

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