INTERNSHIP PROGRAM
COIMBRA LISBOA MINHO

Dosimetry

Linking biological effects with physical quantities

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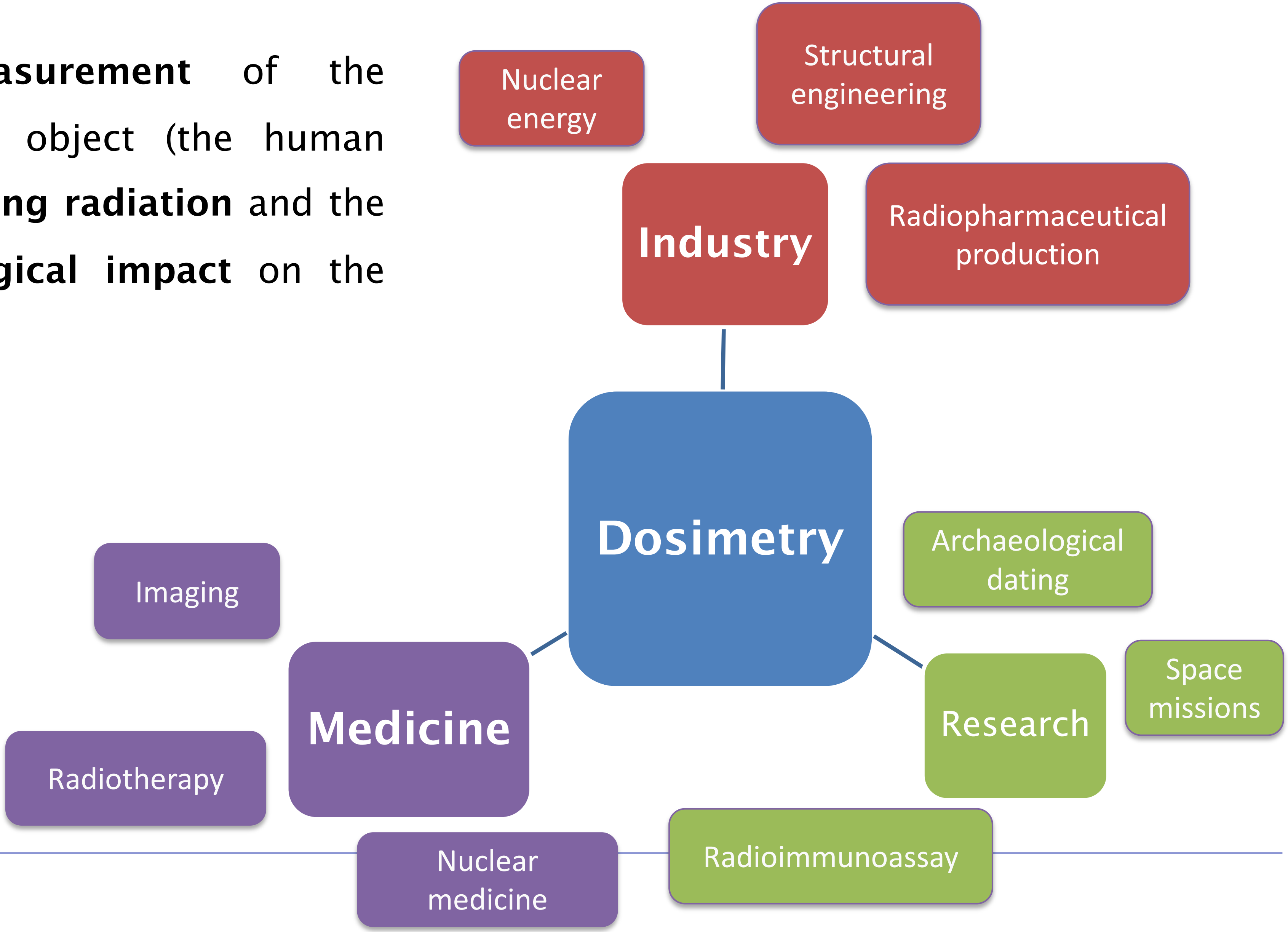
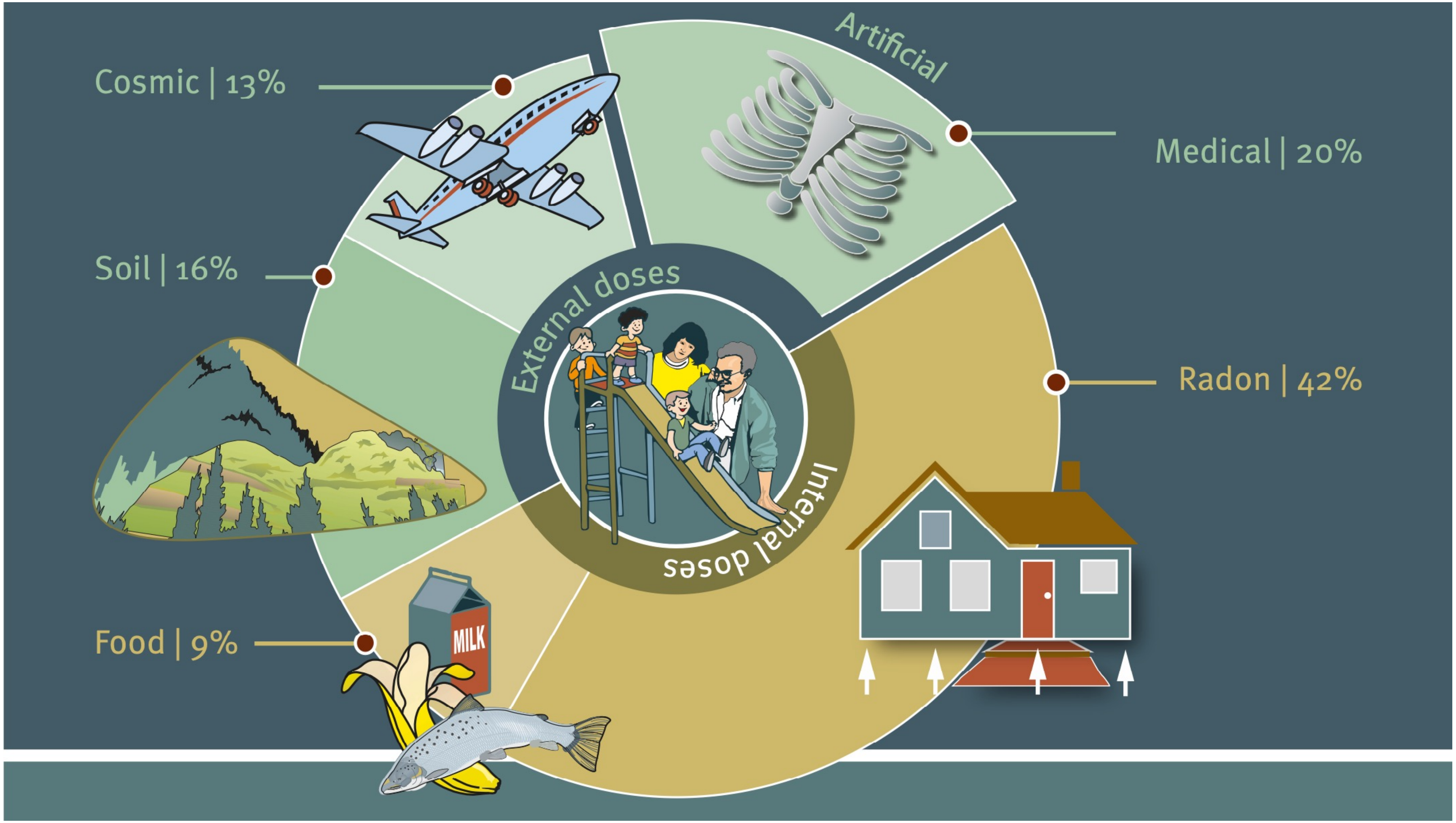
LIP
Ciências ULisboa

What is Dosimetry?

Calculation and **measurement** of the **absorbed dose** by an object (the human body!) exposed to **ionising radiation** and the evaluation of its **biological impact** on the organ and tissues.

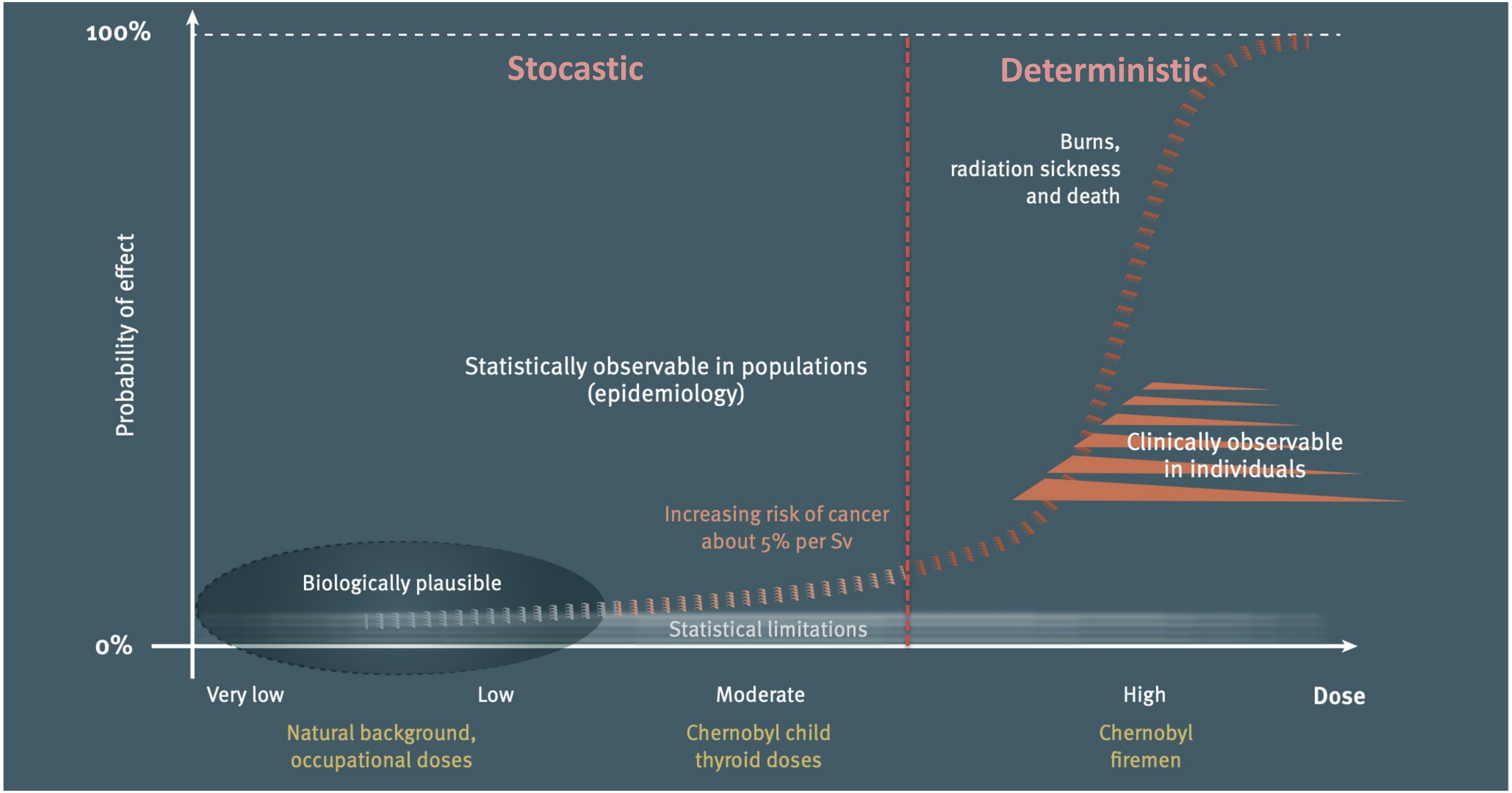


Radiation Sources



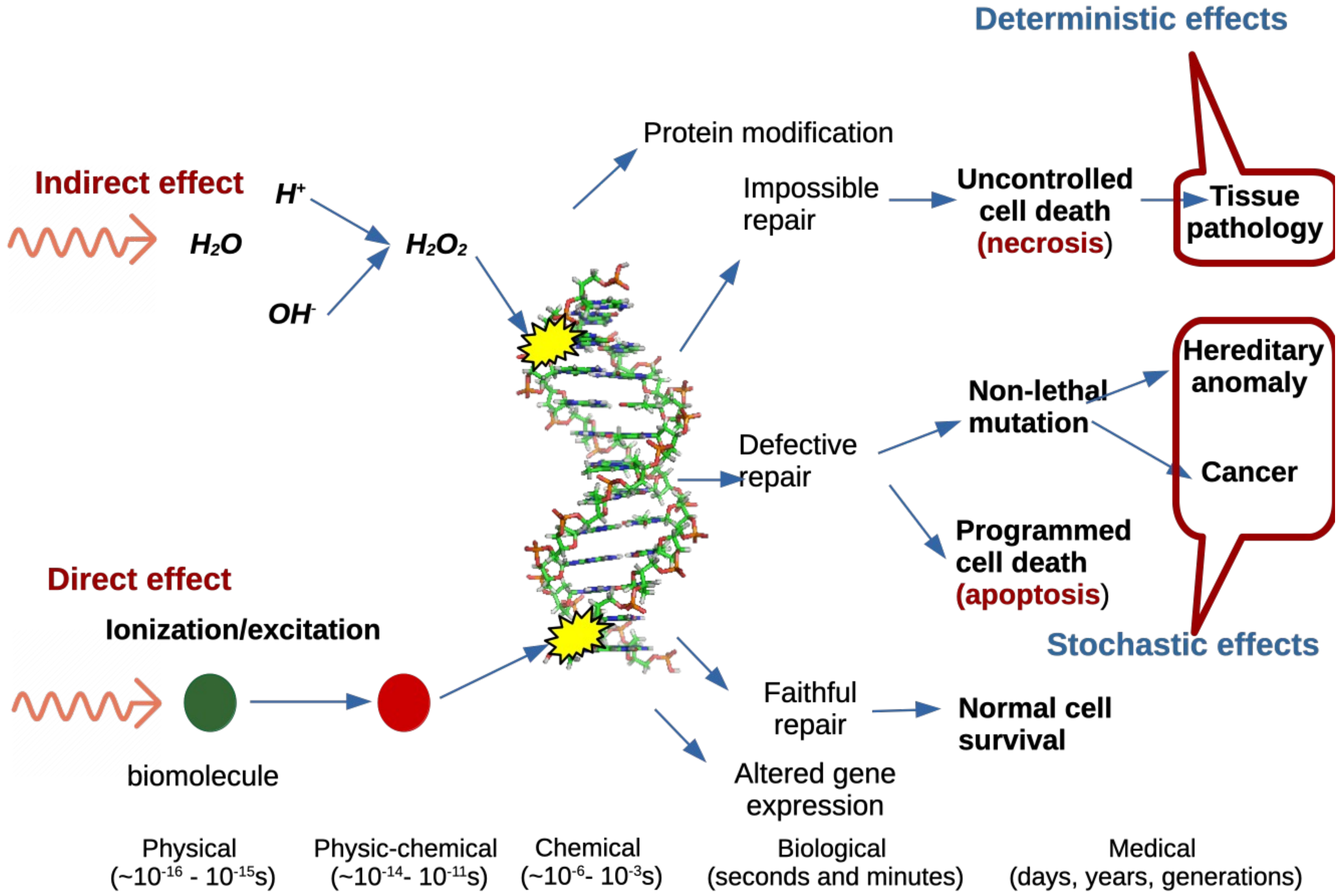
UNEP Booklet, Radiation effects and Sources (2016)

Radiation effects on us



UNEP Booklet, Radiation effects and Sources (2016)

Cellular damage mechanisms



Factors that influence cellular radiosensitivity

Physical

- Dose
- Dose rate
- Fractioning (time and space)
- LET
- Track structure
- Temperature

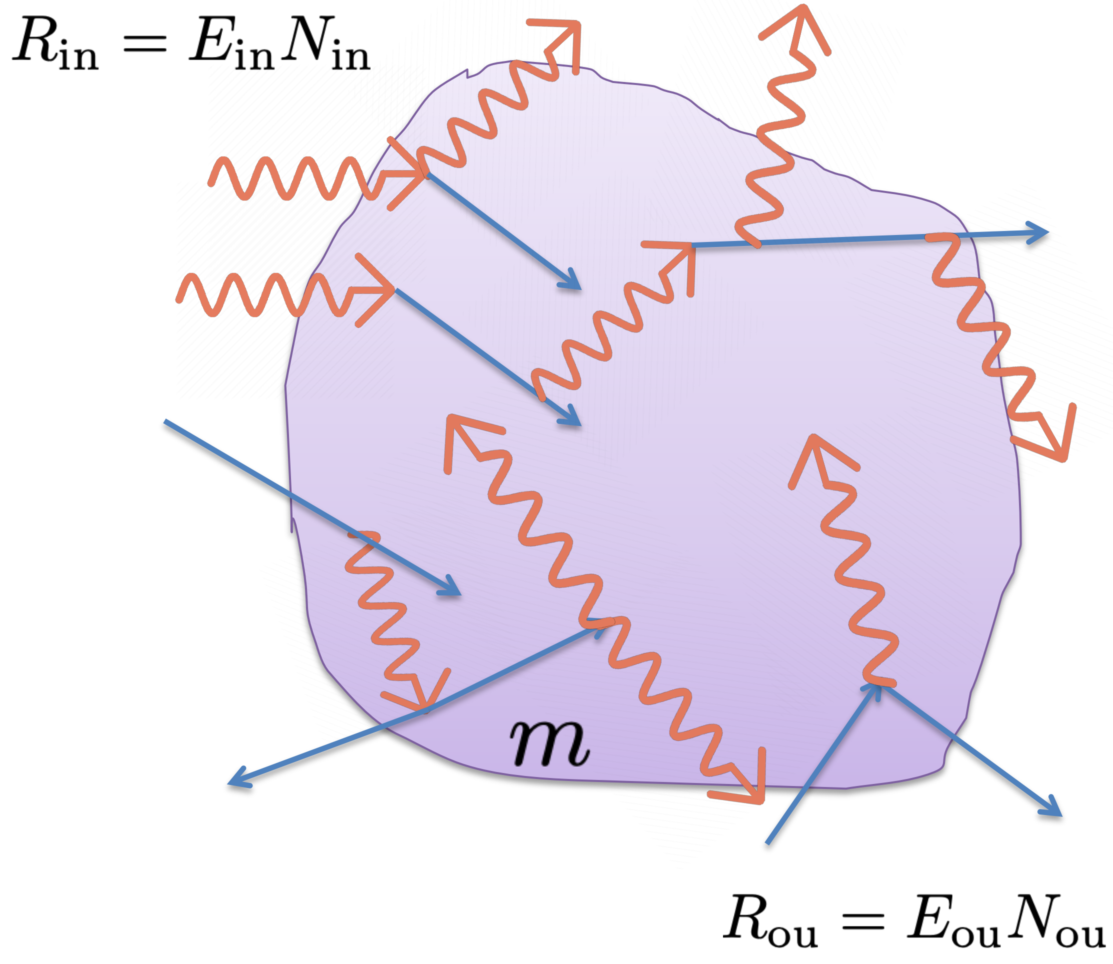
Chemical

- Oxygen content
- ROS production
- Presence of antioxidants

Biological

- Cell line
- Cell cycle
- Cellular end point
- Bystander effects
- Immune system response

Absorbed dose



Energy imparted

Related to the fraction of energy kinetic energy that is **imparted** in the volume

$$\bar{\epsilon} = R_{\rm in} - R_{\rm ou}$$

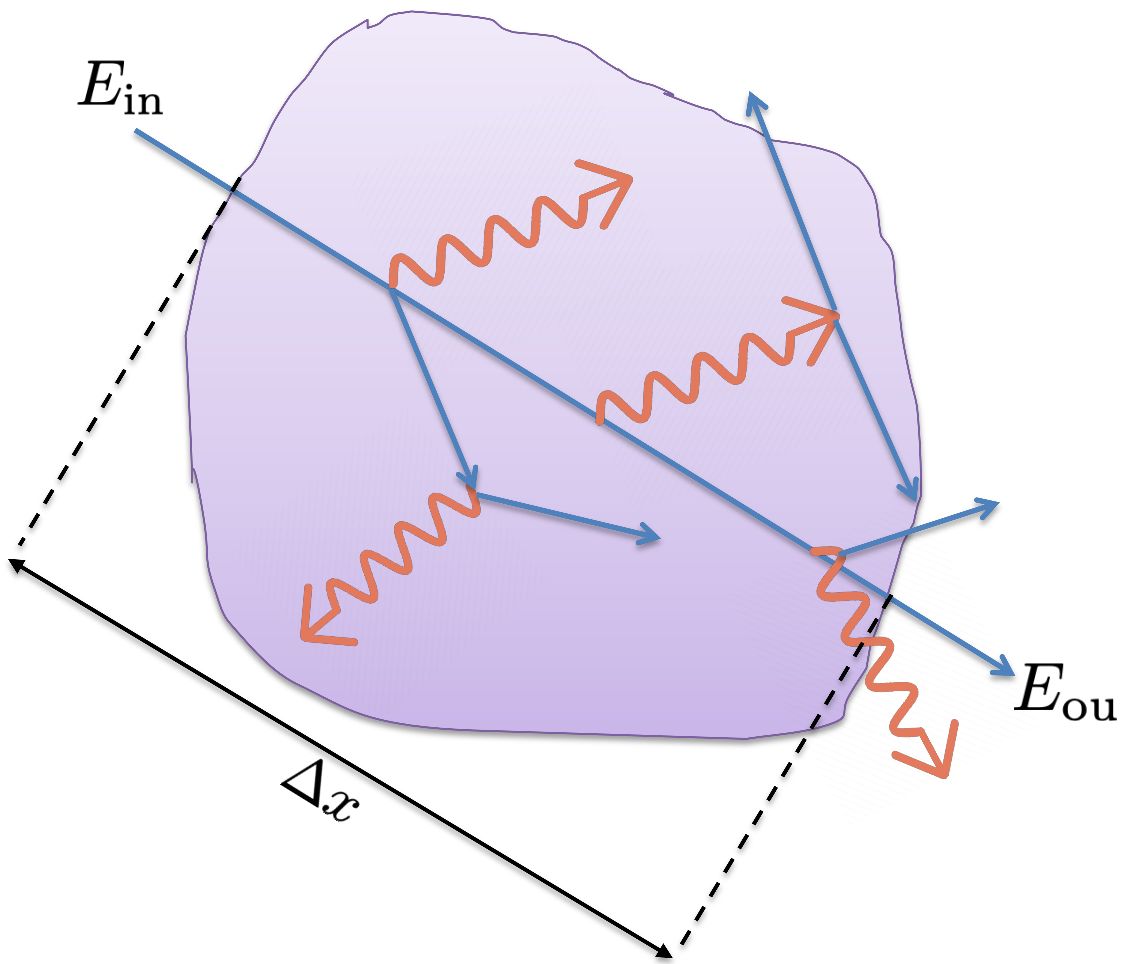
Absorbed dose

$$\boxed{D = \lim_{m \to 0} \left(\frac{\bar{\epsilon}}{m} \right) = \frac{d\bar{\epsilon}}{dm}}$$

SI unit: Gy (gray)

Dose is defined in a **point** as an average value of **stochastic** processes e a (small) volume

Stopping power



Energy lost

Accounts for all energy **lost** by a single particle inside de volume

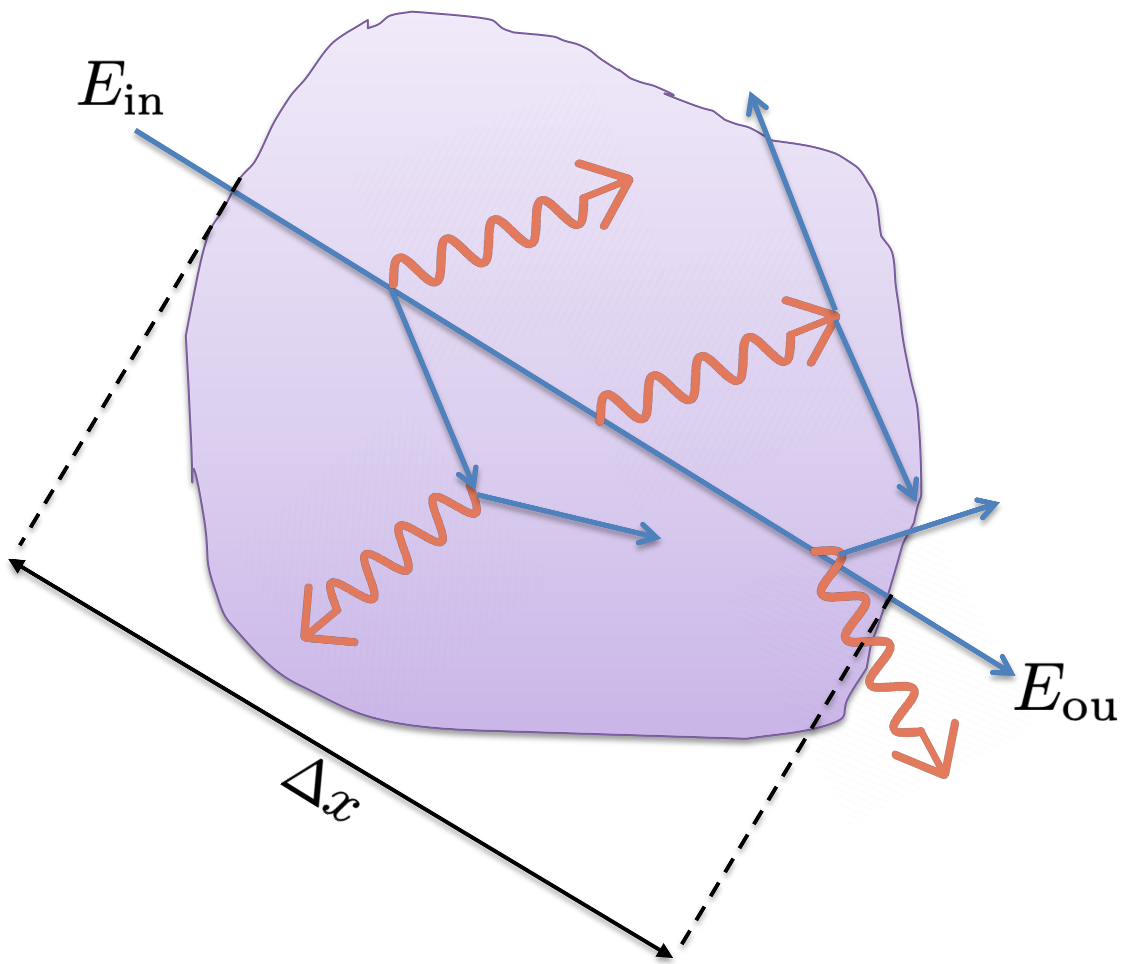
$$\Delta E = E_{\text{ou}} - E_{in}$$

Stopping power

$$S = \lim_{\Delta x \to 0} - \left(\frac{\Delta E}{\Delta x}\right) = -\frac{dE}{dx}$$

Unit: keV/µm or MeV/cm

Linear energy transfer



Energy transferred

Accounts for all energy **transferred** by a single particle inside de volume

$$\Delta E_{tr} = (E_{\text{ou}} - \Delta) - E_{in}$$

Energy that is deposited outside the volume

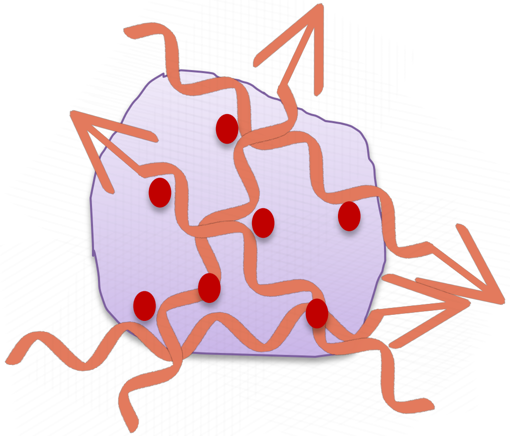
LET

$$L = \lim_{\Delta x \to 0} -\left(\frac{\Delta E_{tr}}{\Delta x}\right) = -\frac{dE_{tr}}{dx}$$

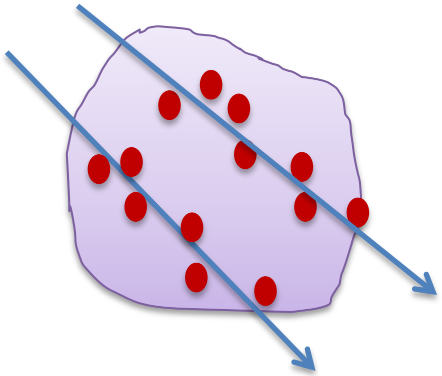
Unit: keV/µm or MeV/cm

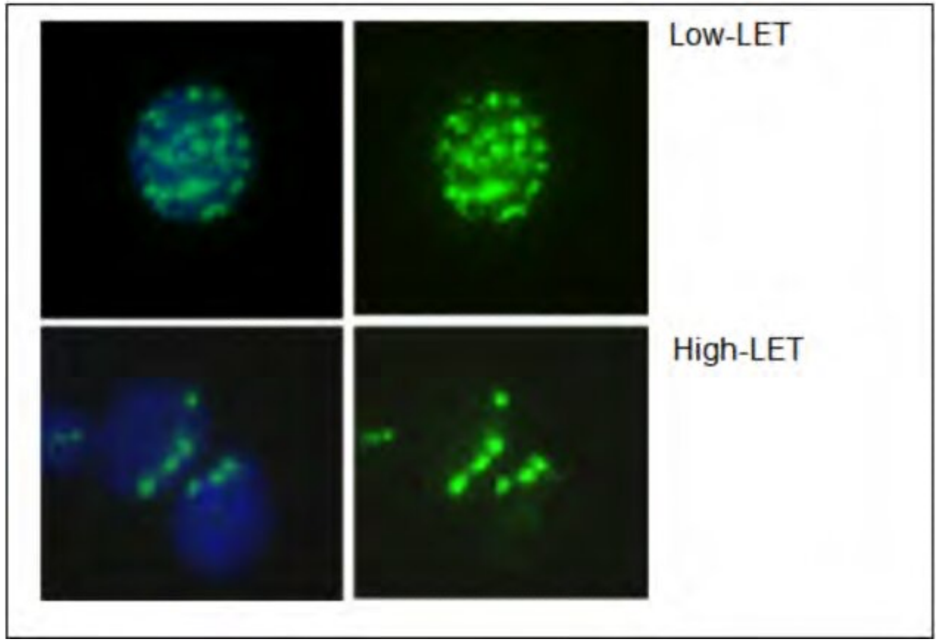
LET and the cell damage

Low-LET: Low density of ionisations and scattered



High-LET: High ionisation density and very localised





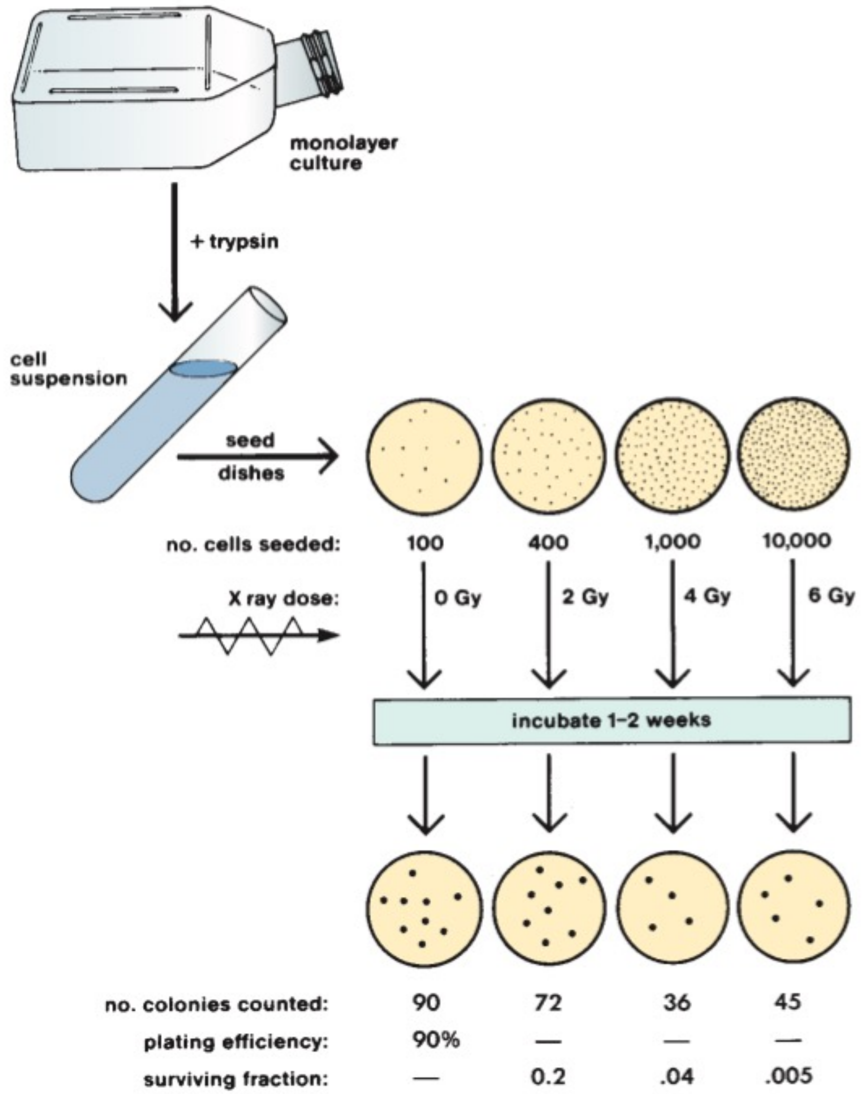
Immunofluorescence image of γ-H2AX foci on human lymphocytes cell nucleus

Low-LET: γ-rays

High-LET: 0.88 MeV protons (28 keV/μm)

M. Moganato et al. The DNA-Damage Response to Ionizing Radiation in Human Lymphocytes (2011)

Clonogenic assay: the gold standard of radiobiology



Plating effciency

$$PE = \frac{\#\text{ of colonies formed @ } D = 0}{\#\text{ of cells plated}}$$

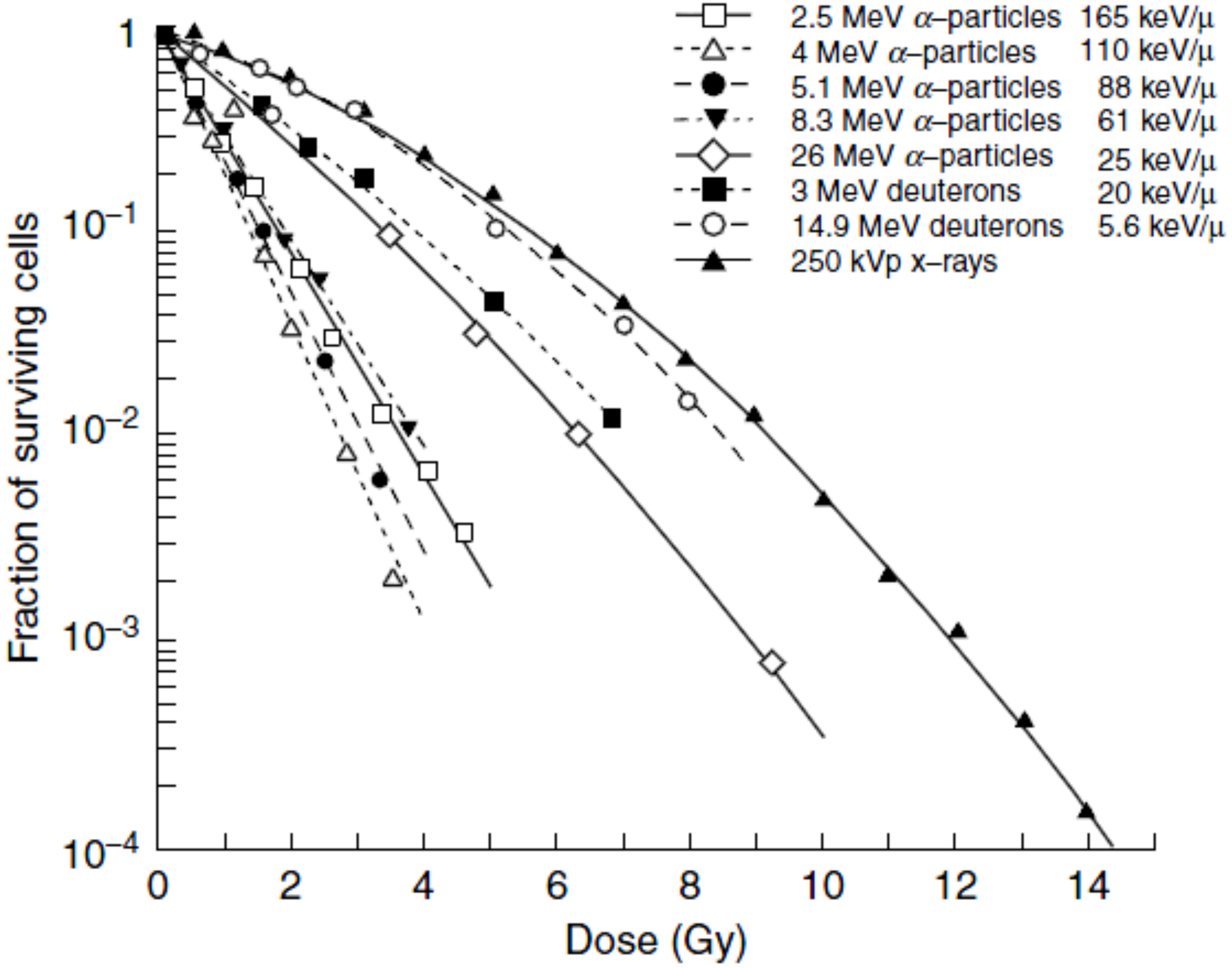
Survival fraction

$$SF = \frac{\#\text{ of colonies formed @ } D \neq 0}{\#\text{ of colonies formed @ } D = 0}$$

$$= \frac{\#\text{ of colonies formed @ } D \neq 0}{\#\text{ of cells plated} \times PE}$$

E. J. Hall and A. J. Giaccia, Radiobiology for the Radiologist (2012)

SF dose response: LET dependence



Low-LET: Linear Quadratic Model (LQM)

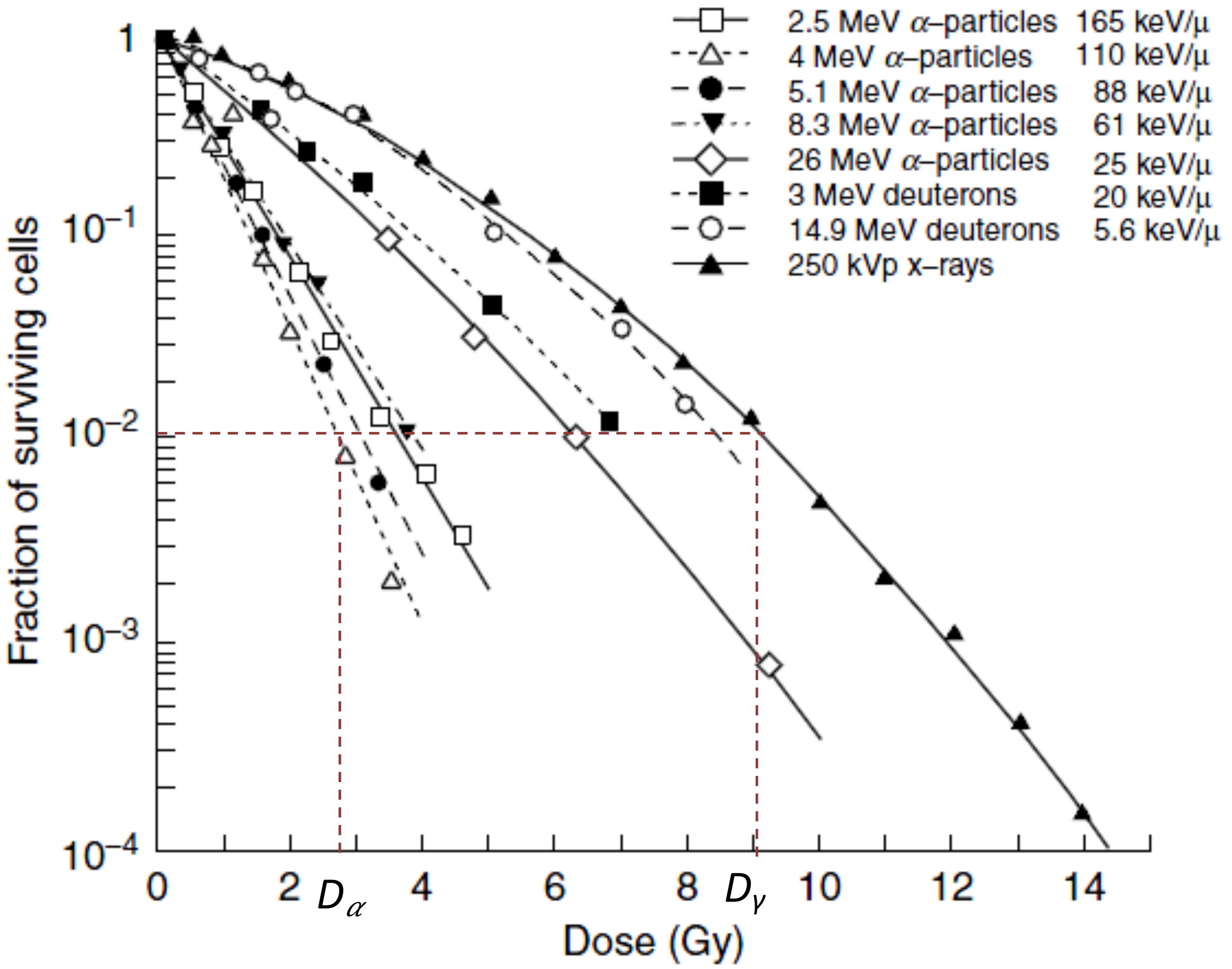
$$SF_{\mathrm{LQM}} = e^{-\alpha D - \beta D^2}$$

High-LET: Linear Model (LM)

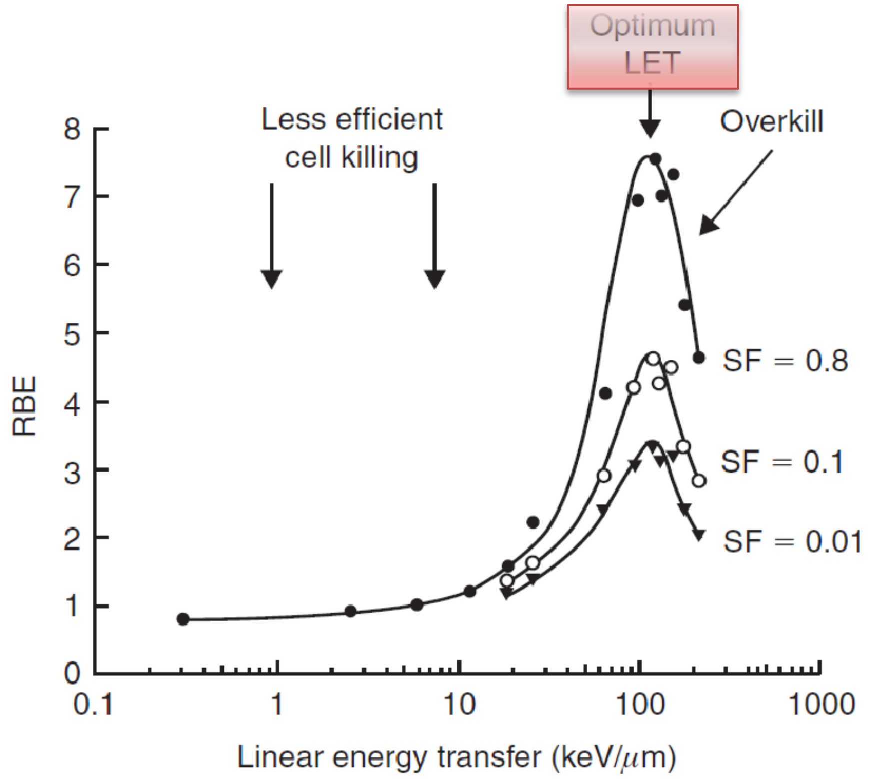
$$SF_{\mathrm{LM}} = e^{-\alpha D}$$

Radiosensitivity increases with LET

Relative Biological Effictiviness (RBE)

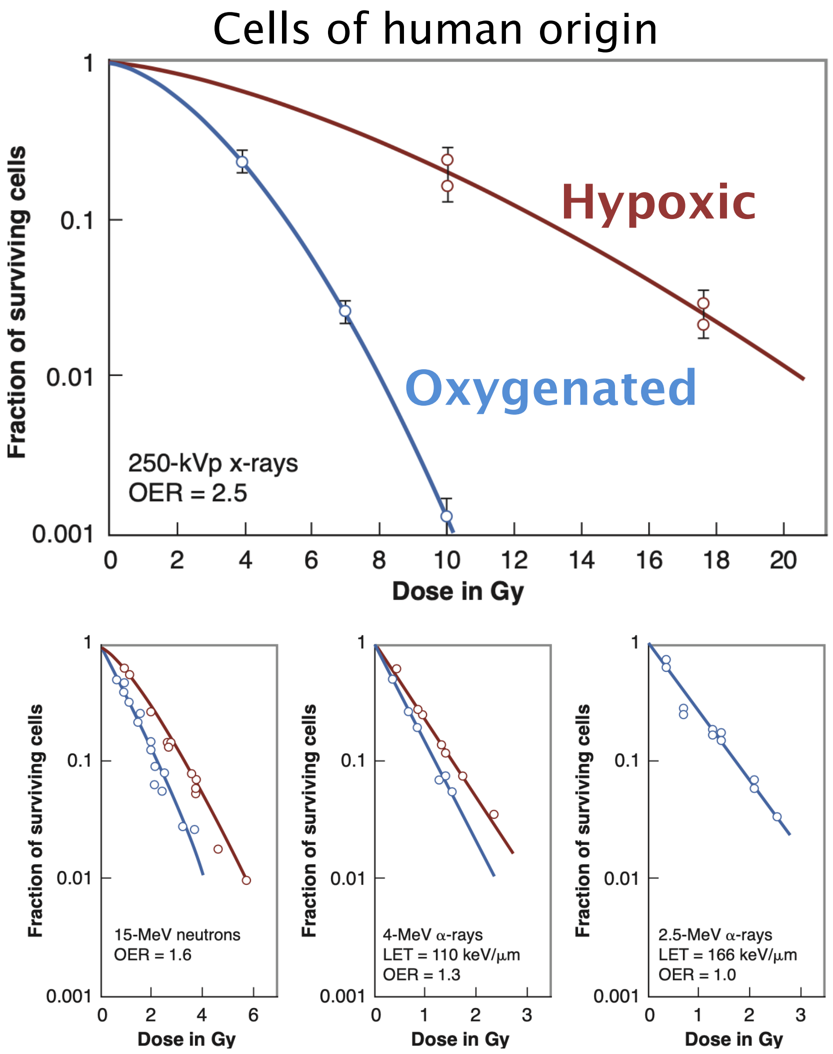


$$RBE = \left(\frac{D_\gamma}{D_\alpha}\right)_{\text{same effect}}$$



J. M. Søbstad, Monte Carlo based comparison of constant vs. variable RBE for proton therapy patients (2017).

SF dose response: Oxygen enhancement effect



Lower LET:

Hypoxic: lower biological effectiveness (tumour cells)

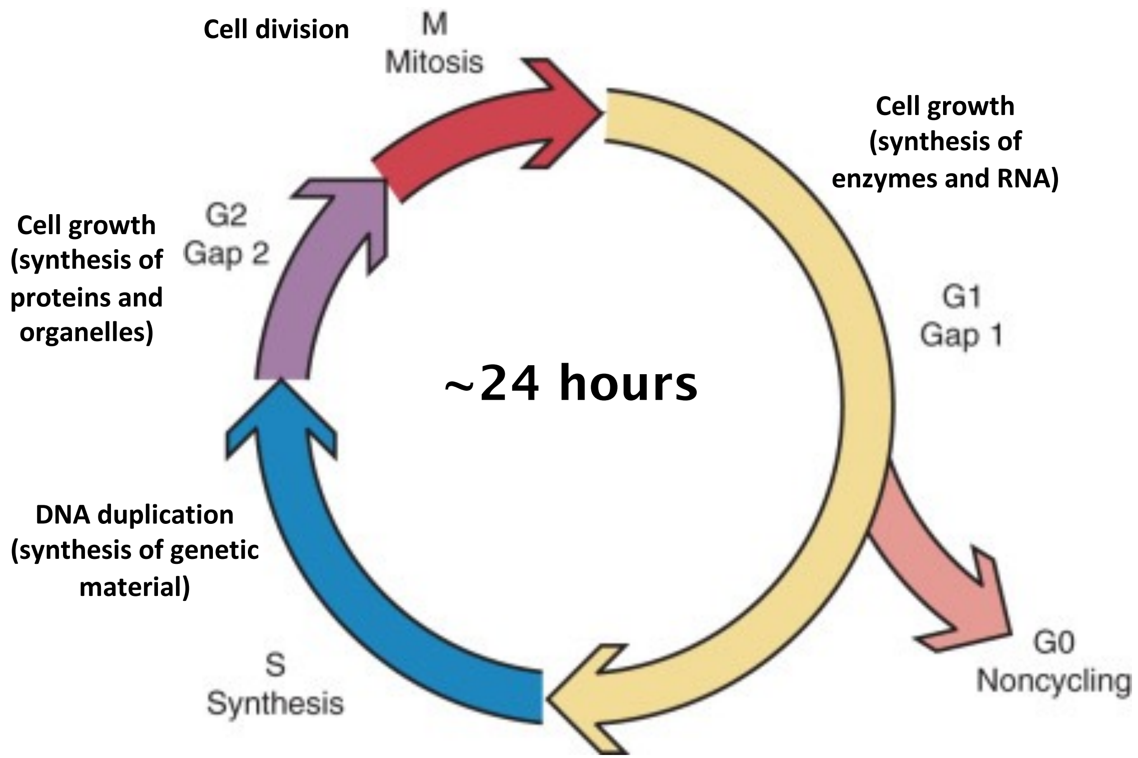
Oxygenated: higher biological effectiveness (normal cells)

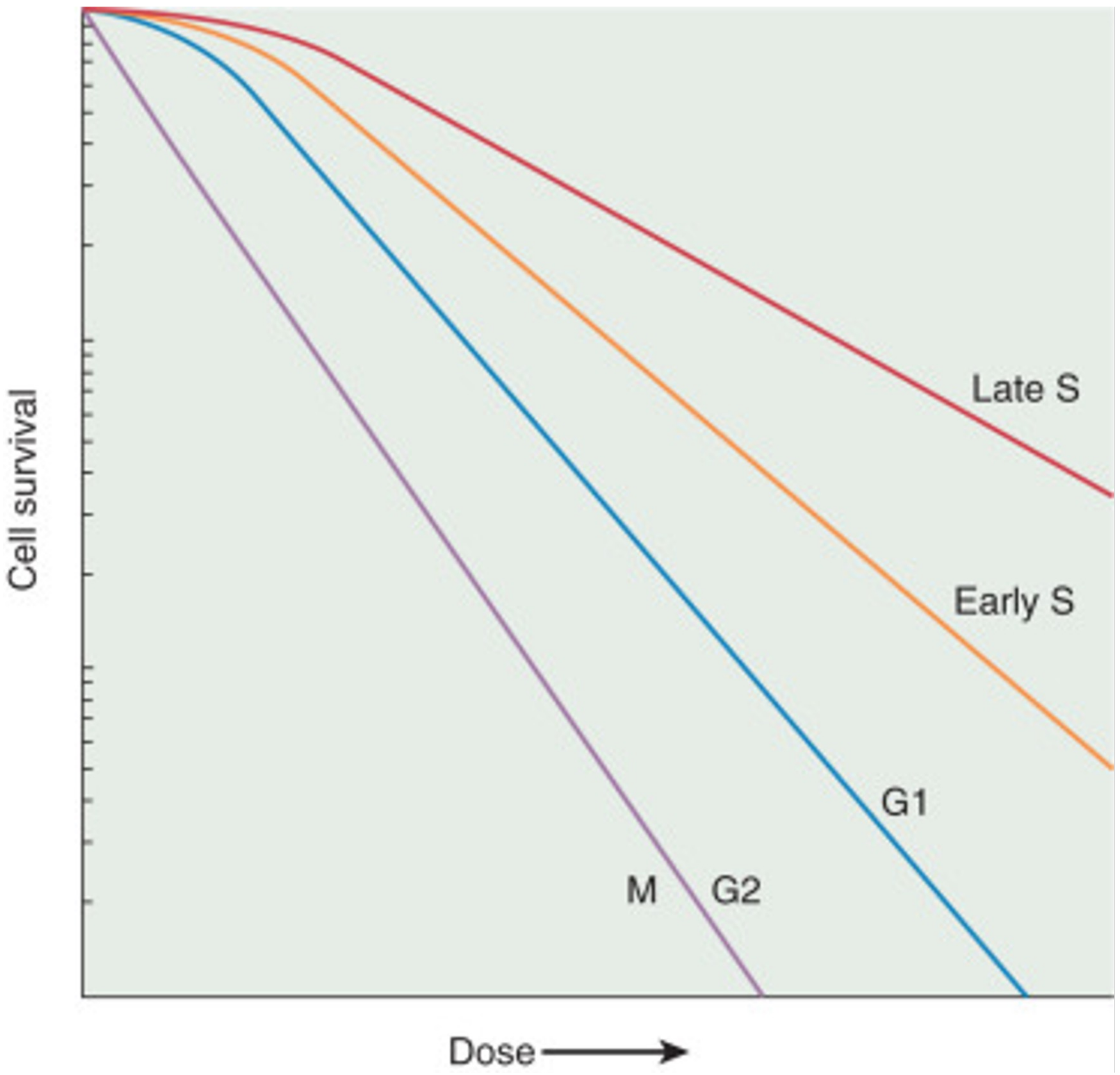
Higher LET: independent of oxygen conditions

Radiosensitivity increases with oxygen concentration

E. J. Hall and A. J. Giaccia, Radiobiology for the Radiologist (2012)

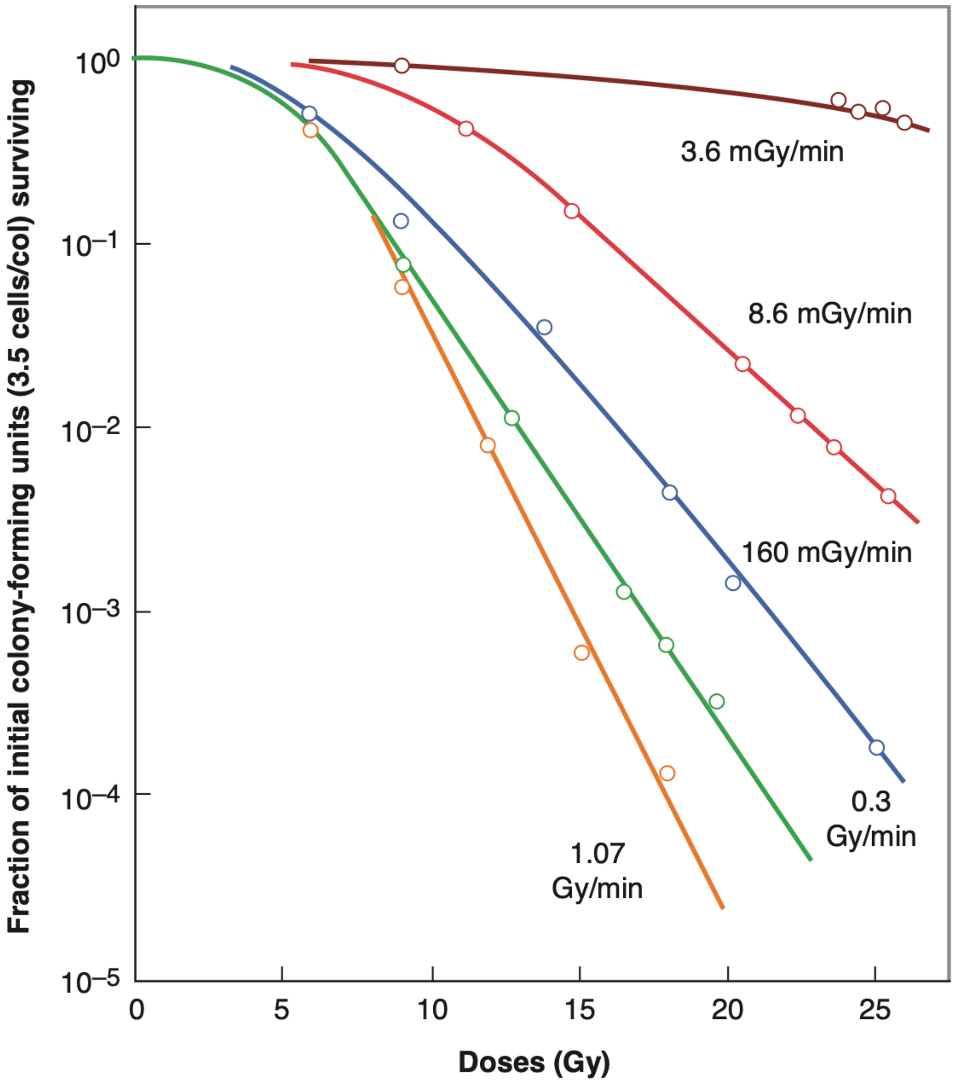
SF dose response: Cell cycle





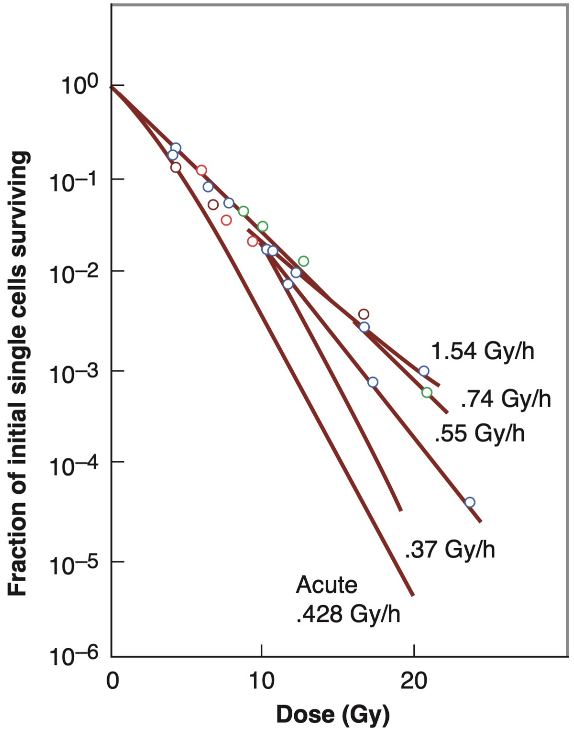
Radiosensitivity increases during the mitotic phase (G2–M–G1).

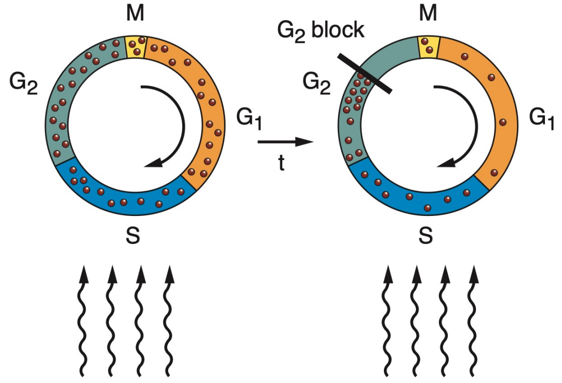
SF dose response: Dose rate effect



In general, radiosensitivity increases with dose rate, but…

Inverse dose rate effect

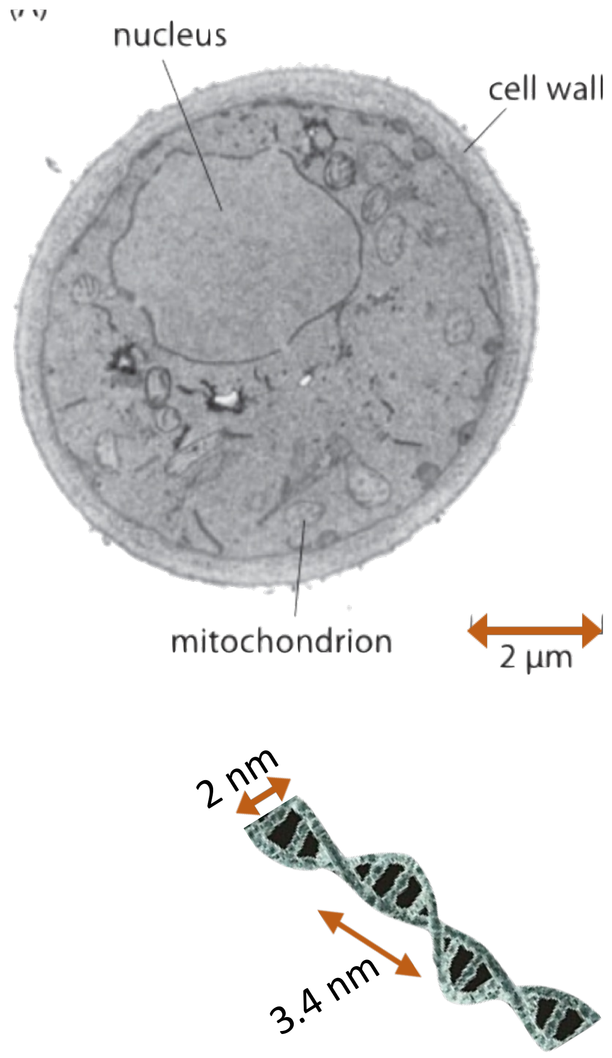


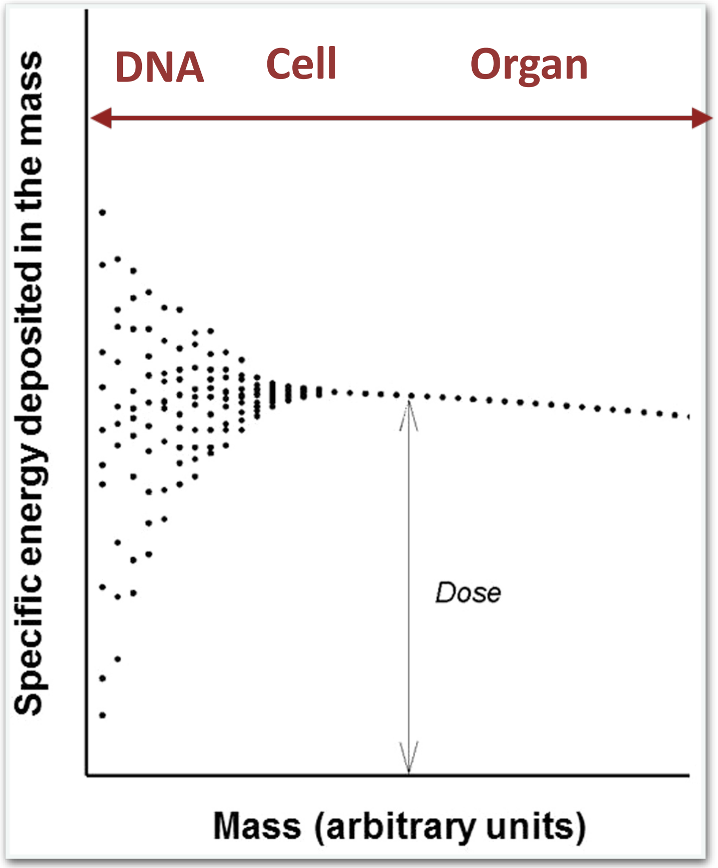


Some cells (HeLa) become blocked in the G2 phase at low dose rates→Higher radiosensitivity

E. J. Hall and A. J. Giaccia, Radiobiology for the Radiologist (2012)

The need for micro- and nanodosimetry





Stochastic quantities

Specific energy

$$z = \frac{\epsilon}{m}$$

$$\bar{z} = \int z f_z(z) dz \sim D$$

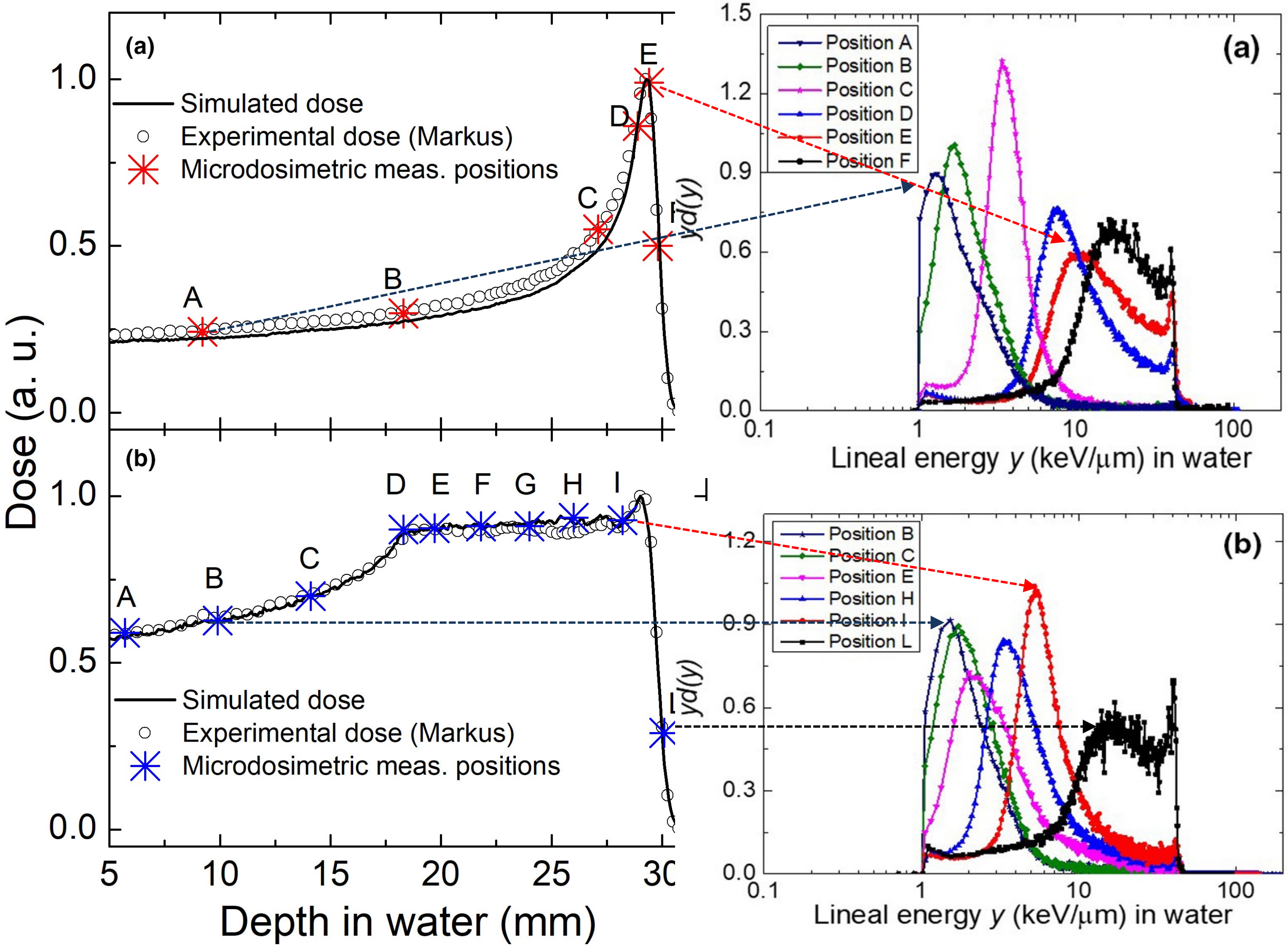
Lineal energy

$$y = \frac{\epsilon}{l}$$

$$\bar{y} = \int y f_y(y) dy \sim L$$

H. H. Rossi and M Zaider, Microdosimetry and Its Applications (1996)

Example: 62 MeV proton beam measurements



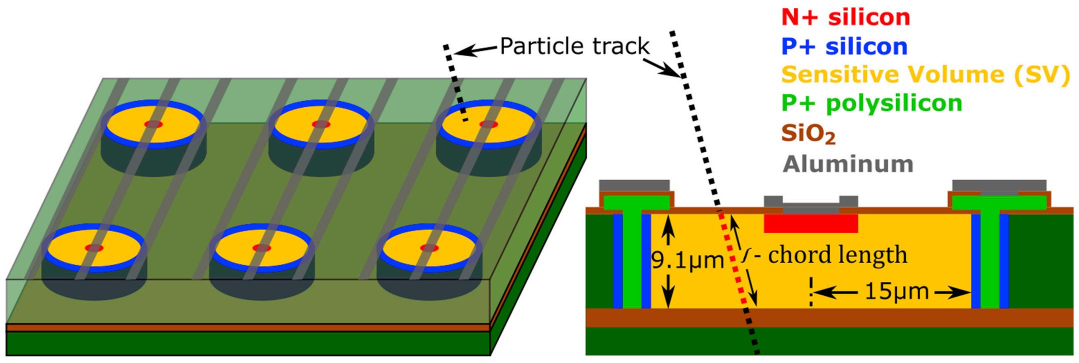
At each depth there is no well-defined LET, but rather a distribution around a mean value.

C. Verona et al. Med. Phys. 47 (2020)

Microdosimeters

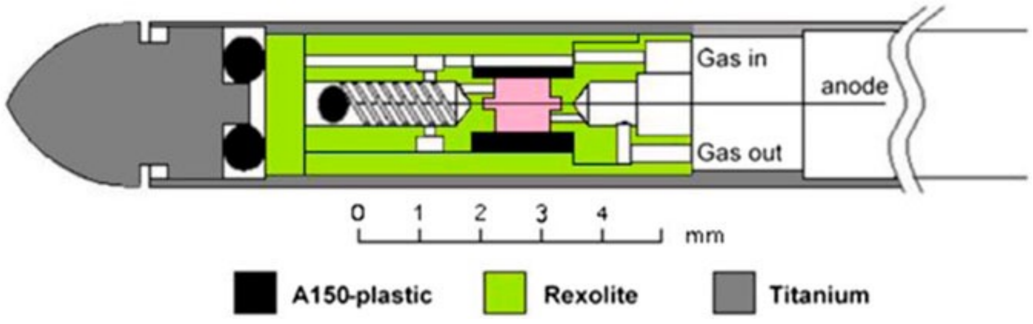
Rossi TEPC (1960)

3D SOI μD



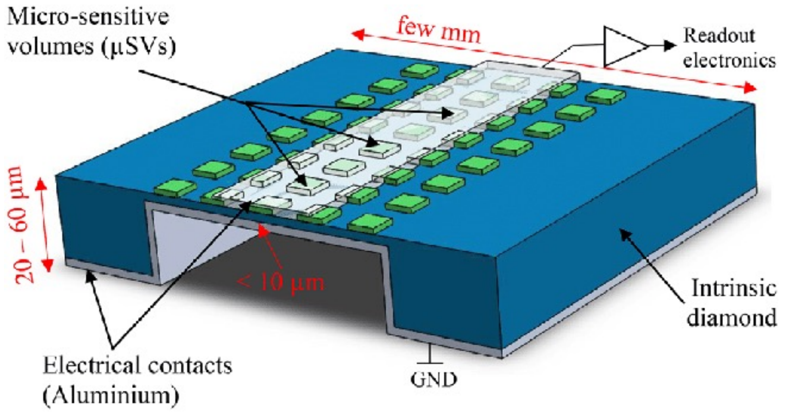
A. T. Samnøy et al. Rad. Phys. Chem. 176 (2020)

Mini-TEPC



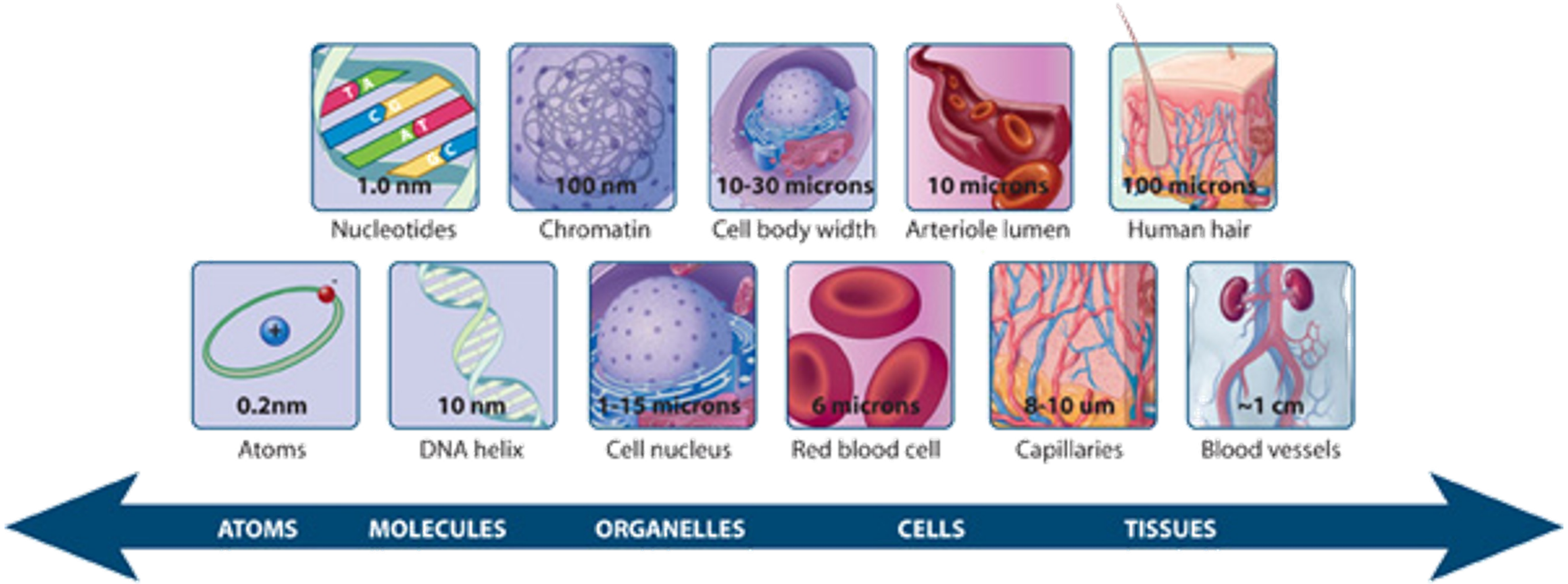
A. Bianchi et al. Rad. Phys. Chem. 202 (2023)

scCVD Diamond μD



I. A. Zahradnik et al. Phys. Status Solidi A,215 (2018)

Radiation Dosimetry to Advance RadioTherapy (RADART)



Group thematic lines

- Detectors and materials for high-res. dosimetry
- New modalities and applications in RT

Projects and collaborations

Detectors and materials for dosimetry

- Scintillating optical fibre array for high-res. dosimetry
- Development of materials for micro and nanodosimetry

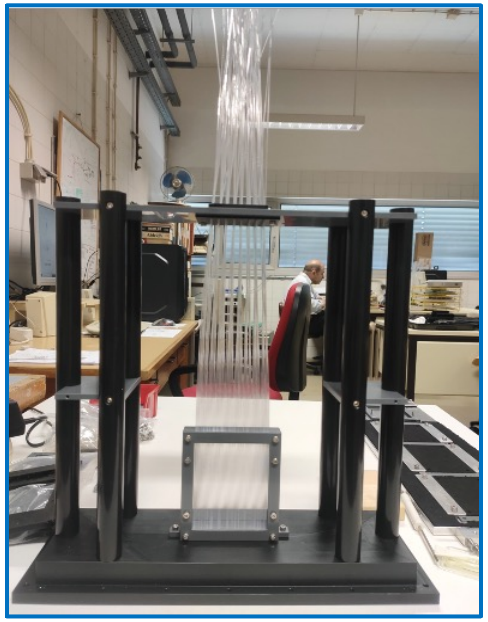
New modalities and applications in RT

- Modelling radiobiological effects of NPs
- Advance charged-particle MBRT
- Advance FLASH-RT
- Effects of PT in NDDs

RADART

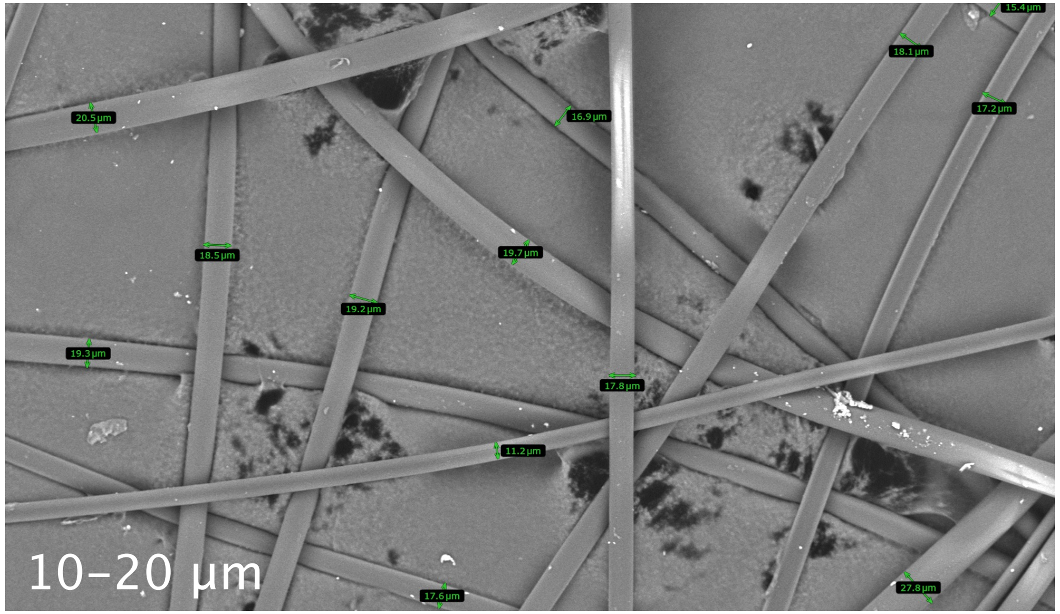
Detectors and materials for high-res. dosimetry

SPOF array for high-res. detector

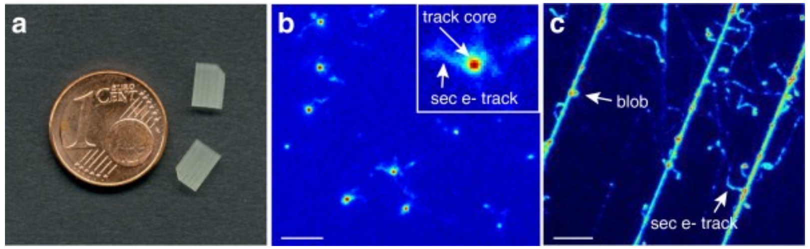


- Construction and testing
- Cell growth on the detector surface
- Radiobiology experiments

Micrometer fibres

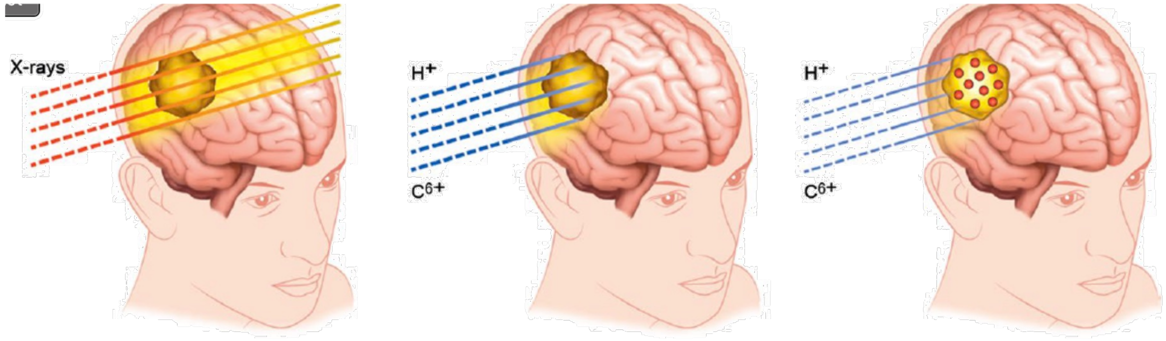


FNTD for nanodosimetry



M. Niklas et al. Radiat. Oncol 8 (2013)

New modalities and applications in RT



S. Lacombe at al. Cancer Nanotechnol. 8(1) (2017)

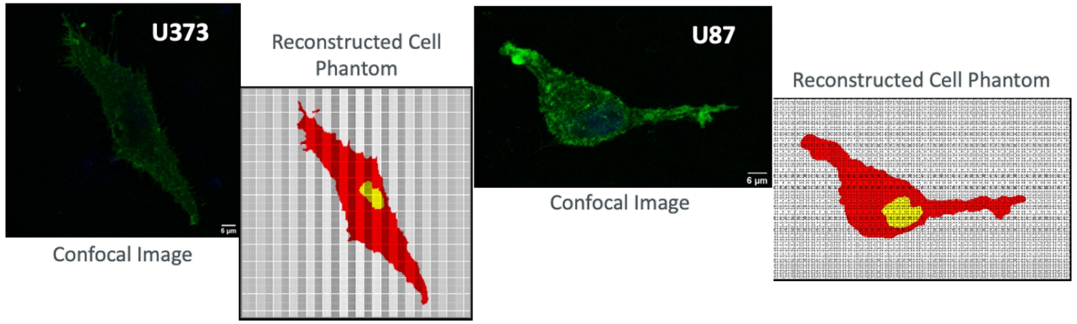
- Increase production of secondary particles
- Increase production of ROS

↓

Enhnancement of the therapeutic effect

Modelling radiobiological effects of NPs

Confocal Image → Segmented image → Binary File → Import to TOPAS



- Monte Carlo simulations (TOPAS nBio)
- Radiobiological models
- Compare with experimental data

New modalities and applications in RT

Effects of low-dose (< 0.1 Gy) in neurodegenerative disorders (NDDs)

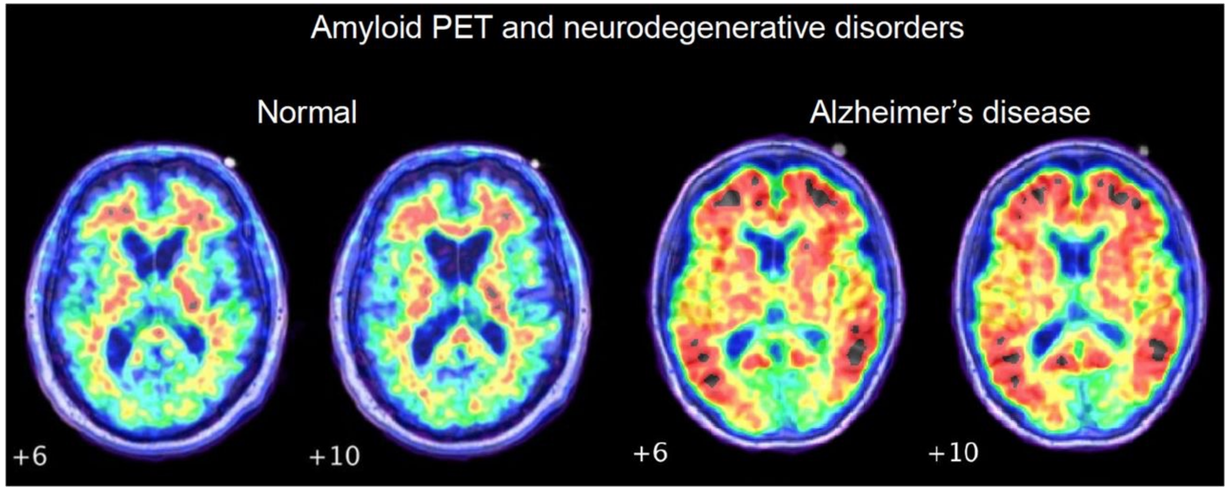
- Irradiation of brain cells with different types of radiation
- Assess the production of ROS
- Effects on the destruction of protein aggregates (amyloid
- Model based on Monte Carlo simulations (TOPAS nBio)

International Journal of
Molecular Sciences
MDPI

Review

Radiation as a Tool against Neurodegeneration—A Potential Treatment for Amyloidosis in the Central Nervous System

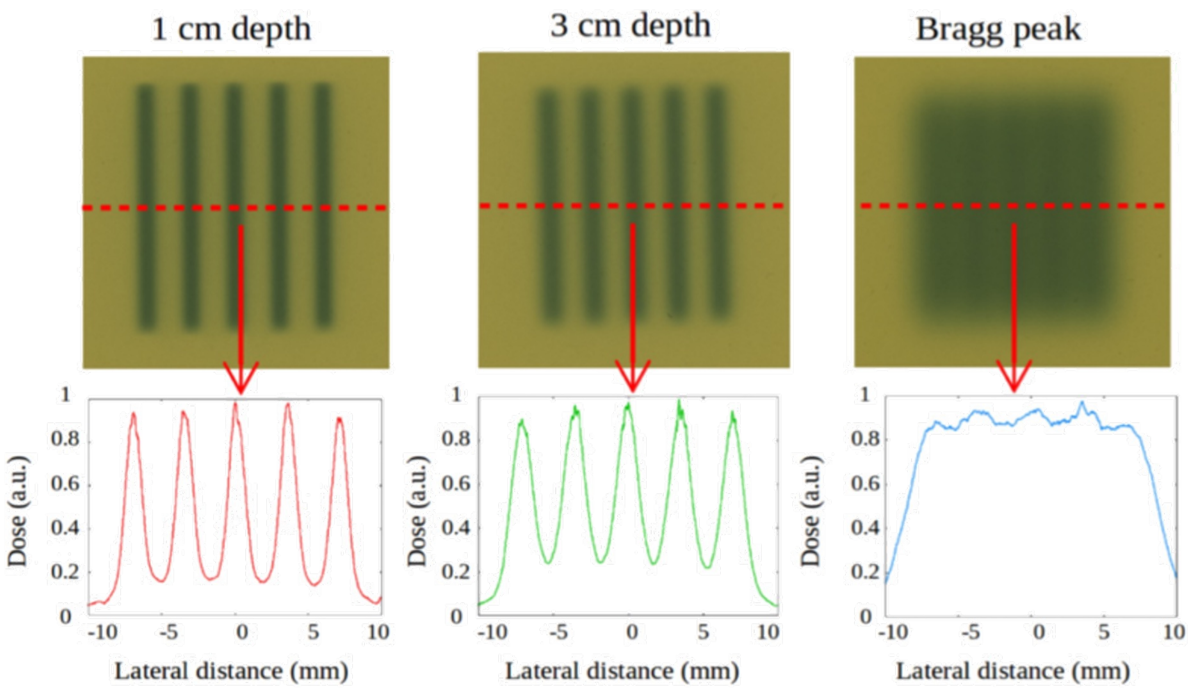
Carina Marques Coelho [1,2,†], Lia Pereira [1,2,†], Pamela Teubig [1], Pedro Santos [3], Filipa Mendes [3,4], Sílvia Viñals [5], Daniel Galaviz [1,6] and Federico Herrera [2,7,*]



NDD are associated with increased protein aggregations (amyloidosis)

M. Chapleau et al. J. Nuc. Med. 63 (2022)

New modalities and applications in RT



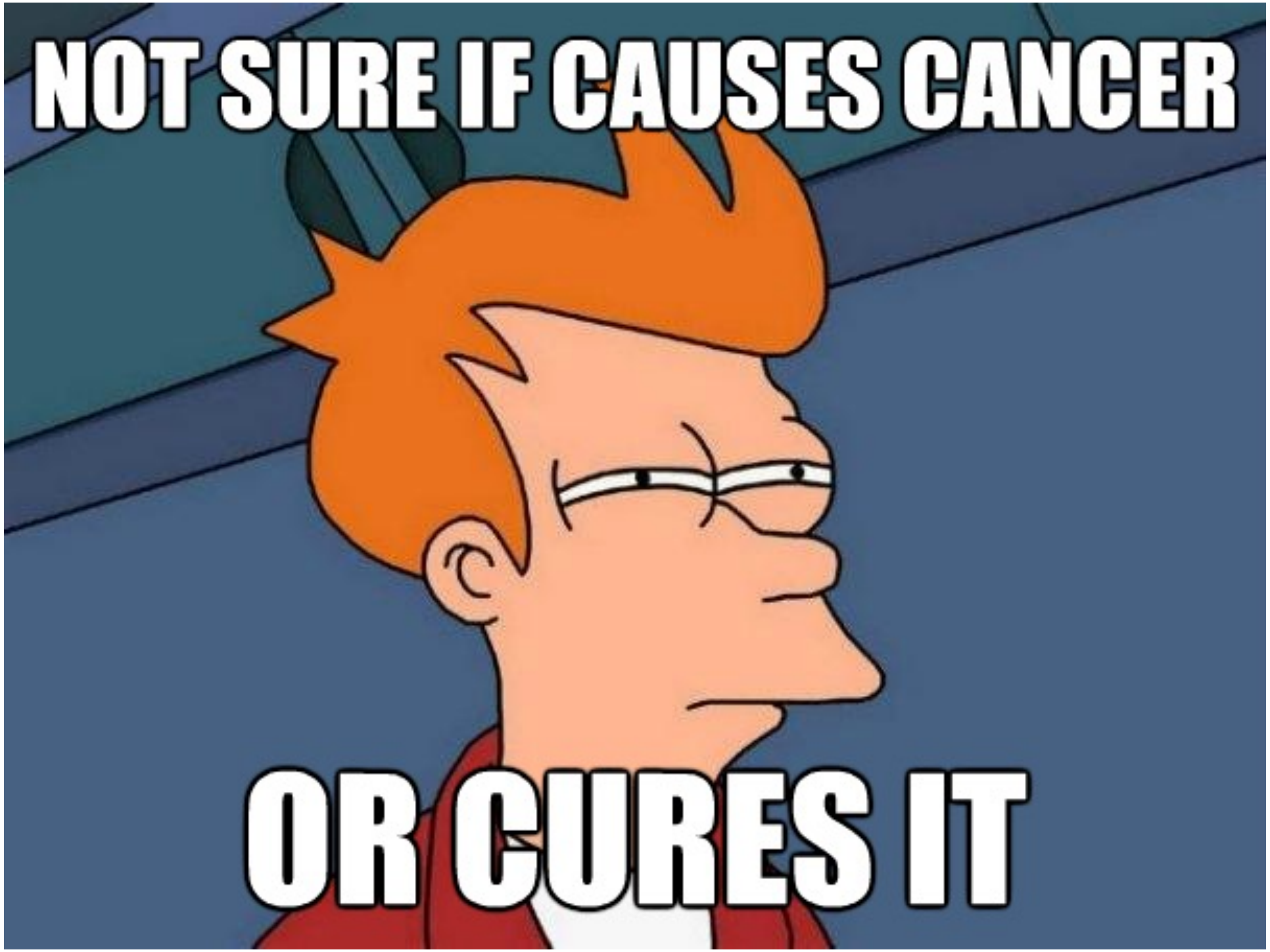
Advance charged particle MRT

- Obtain calibration factors for MBRT dosimetry (TOPAS)
- Simulation of MBRT treatment plans from CT images (TOPAS)
- Fast GPU-based MC simulation (MOQUI)

- High peak-to-dose ratio (PVDR) in healthy tissues
- Homogeneous distribution at the Bragg peak

→ **Sparing effect on healthy tissues**

Y. Prezado et al. Sci .Rep. 8 (2018)



Thanks
for your
attention!