Cell Survival Curves

Faculty of Applied Science- Department of Radiology

Course Name: Radiobiology Course Code: MTR 211

Second Grade/ Fall Semester 2025-2026

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Outlines

- What is a Cell Survival Curve?
- Why Survival Curves Matter?
- Clonogenic Assay Overview.
- Basic Shape of Cell Survival Curve.
- Low-LET Vs High-LET Curves.
- Surviving Fraction.
- Key Cell Survival Curve Parameters.
- Low-LET Survival Curve Equation, Linear-Quadratic (LQ) Model, α/β Ratio.
- High-LET Radiation Effects.
- Relative Biological Effectiveness (RBE).
- Factors Influencing Survival Curves.

Learning Outcomes

By the end of the lecture, students should be able to:

- Define cell survival curve.
- Explain D_0, Dq, SF_2, and α/β ratio.
- Understand LQ Model (Linear-Quadratic).
- Compare survival curves for different cell types.
- Interpret clinical relevance in radiotherapy.

What Is a Cell Survival Curve?

- **Graph showing fraction of cells surviving vs radiation dose**

A survival curve plots the number of cells remaining alive after different radiation doses, illustrating the decline in survival as the dose increases.

- **Reflects cellular radiosensitivity**

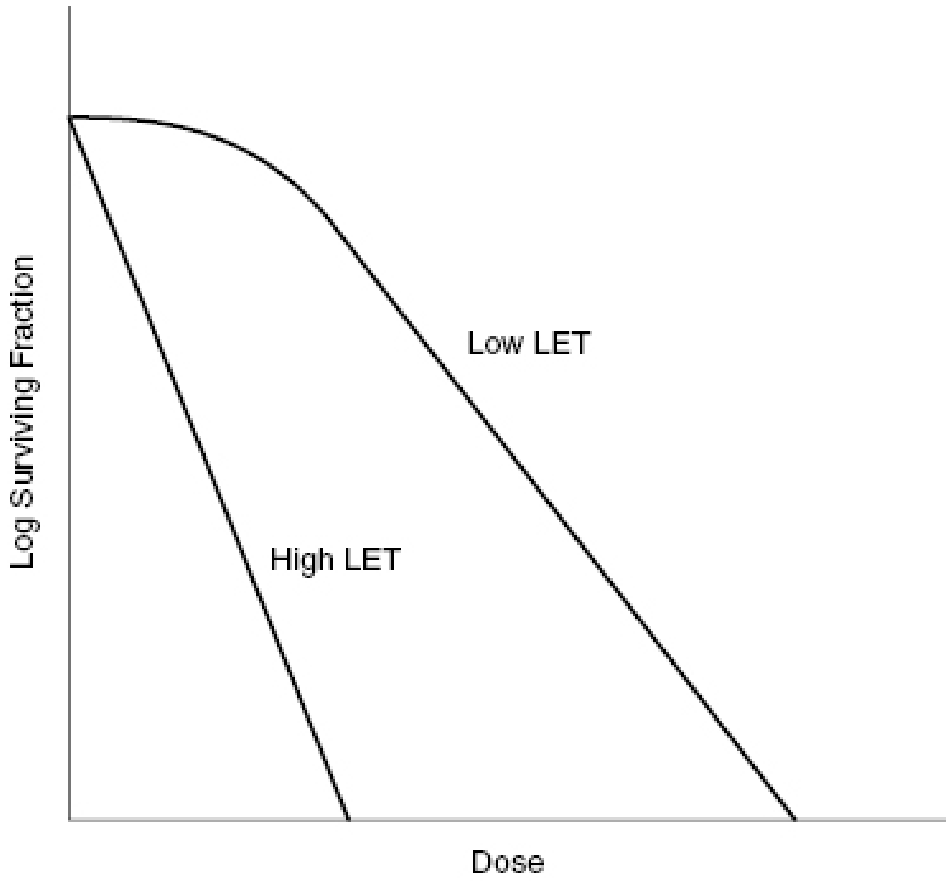
The curve's steepness indicates how sensitive the cells are to radiation; steeper curves mean greater sensitivity.

- **Based on colony-forming assays**

Survival is measured using clonogenic assays, where only cells that can still form colonies after radiation are counted as "**surviving**."

- **Shows how cells respond to increasing dose**

The curve illustrates the cell's dose-response pattern, showing how well it can repair damage at low doses and how rapidly it dies at higher doses.



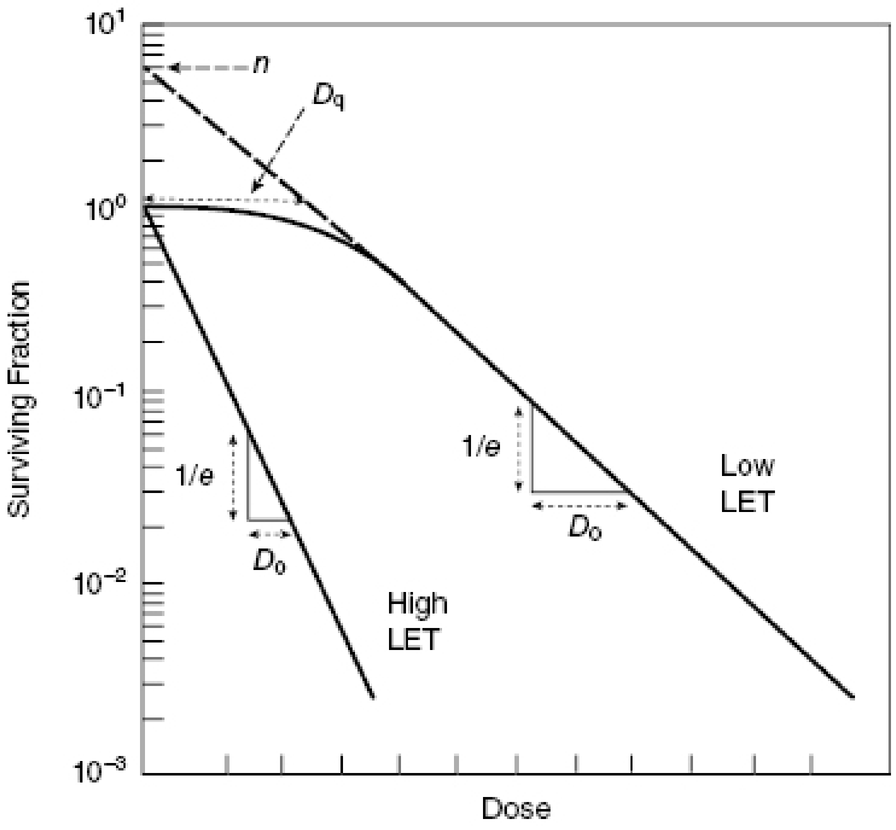
Why Survival Curves Matter?

1. **Predict cell killing:** Survival curves help estimate how many cells will die at specific radiation doses, guiding dose selection.

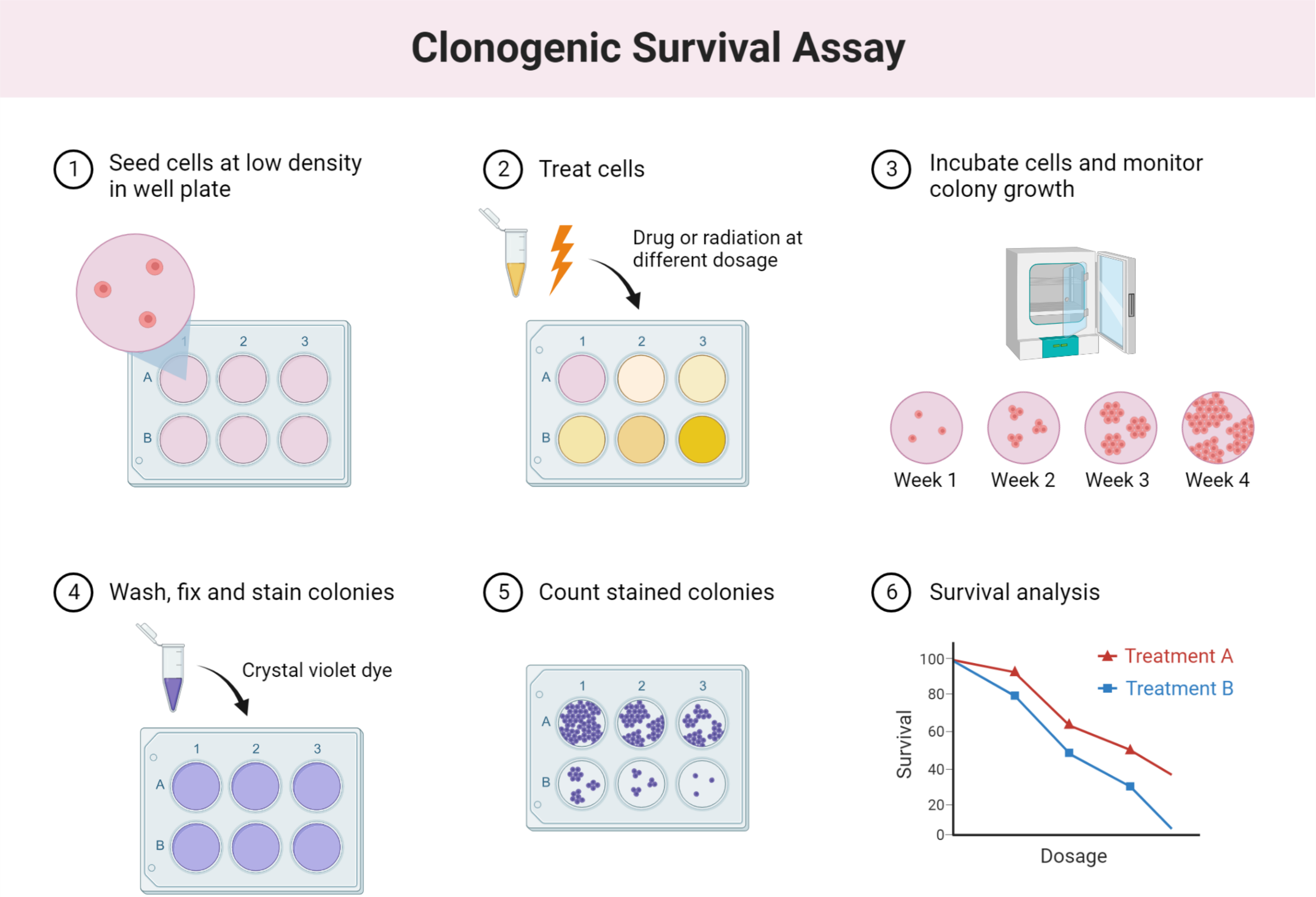
2. **Guide fractionation schedules:** They show how cells repair damage between doses, helping design effective fractionation plans in radiotherapy.

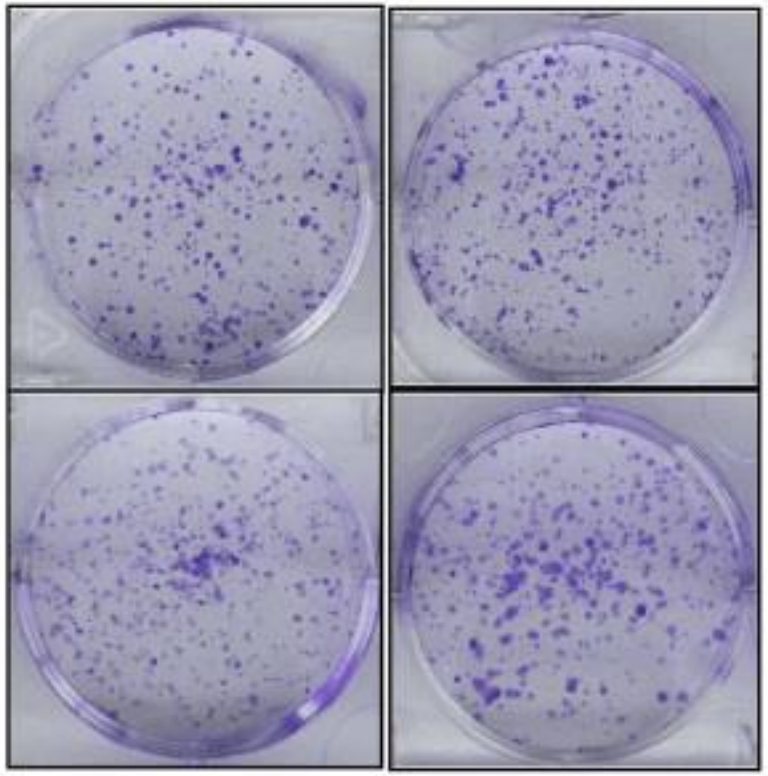
3. **Compare normal tissue vs tumor response:** Different tissues have different curve shapes, allowing comparison of how sensitive tumors are compared to surrounding normal tissues.

4. **Basis of radiation treatment planning:** Understanding these curves supports decisions about total dose, dose per fraction, and balancing tumor control with normal tissue protection.



Clonogenic Assay Overview





Clonogenic Assay Overview

- **Gold standard to measure cell survival**

The clonogenic assay is the most reliable method to assess whether cells can keep dividing after radiation.

- **Cells irradiated at different doses**

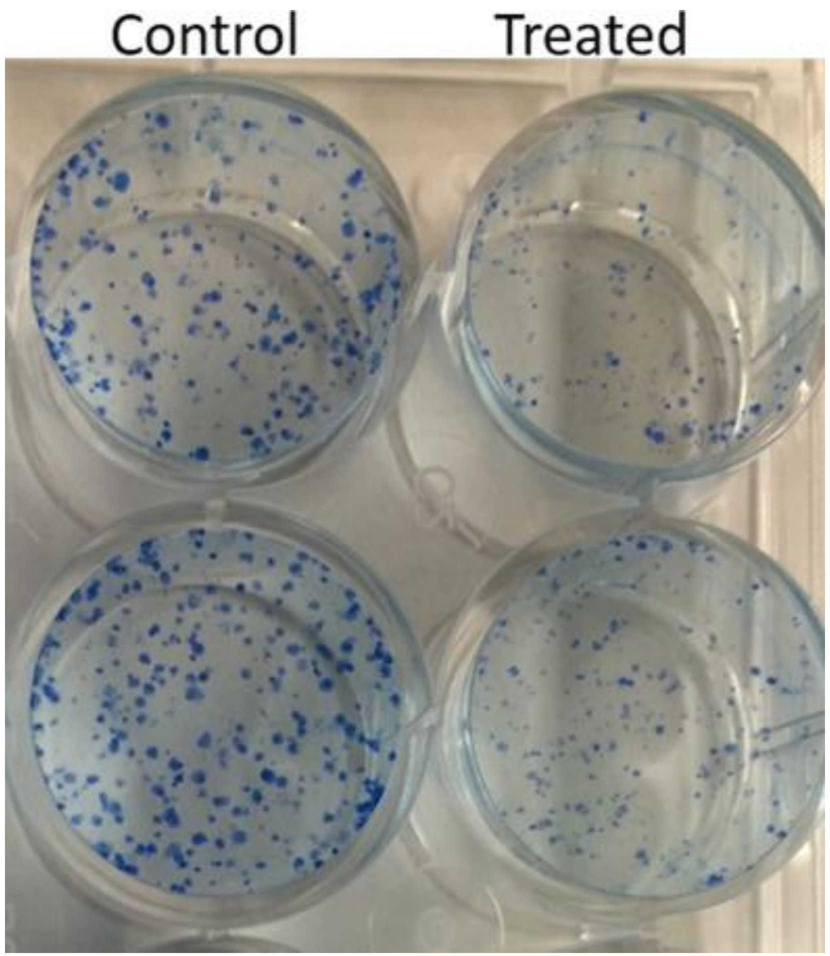
Cells are exposed to several radiation doses to observe how survival changes with increasing dose.

- **Allowed to form colonies (10–14 days)**

After irradiation, cells are left to grow; only those that remain reproductively intact will form visible colonies.

- **Surviving Fraction (SF) = colonies counted / cells plated × plating efficiency**

SF calculates the proportion of cells that survive radiation, correcting for how well cells normally attach and grow.

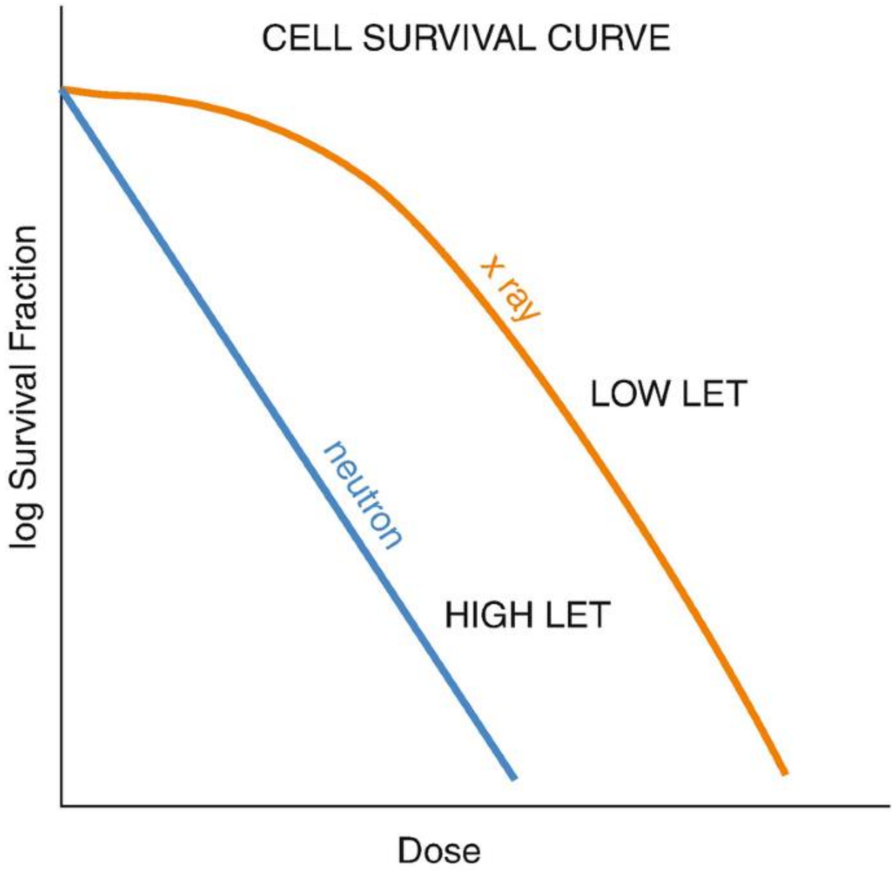


Basic Shape of Survival Curves

- **Initial shoulder = sublethal damage repair:** The shoulder region represents the cell's ability to repair some radiation damage before it becomes lethal.

- **Exponential region = direct lethal damage dominates:** At higher doses, repair mechanisms are overwhelmed, and cell killing increases steadily in an exponential pattern.

- **Characteristic for low-LET radiation (X-rays, γ rays):** This shoulder-plus-slope shape is typical of low-LET radiation because it produces more repairable DNA damage.



Low-LET vs High-LET Curves

- **Low-LET (X-rays, γ-rays): curved with a shoulder**

Low-LET radiation produces damage that cells can often repair, creating a shoulder before the steep killing phase.

- **High-LET (α-particles, neutrons): straight line**

High-LET radiation causes dense, complex damage that is harder to repair, resulting in a straight-line survival curve with little or no shoulder.

- **More lethal per unit dose**

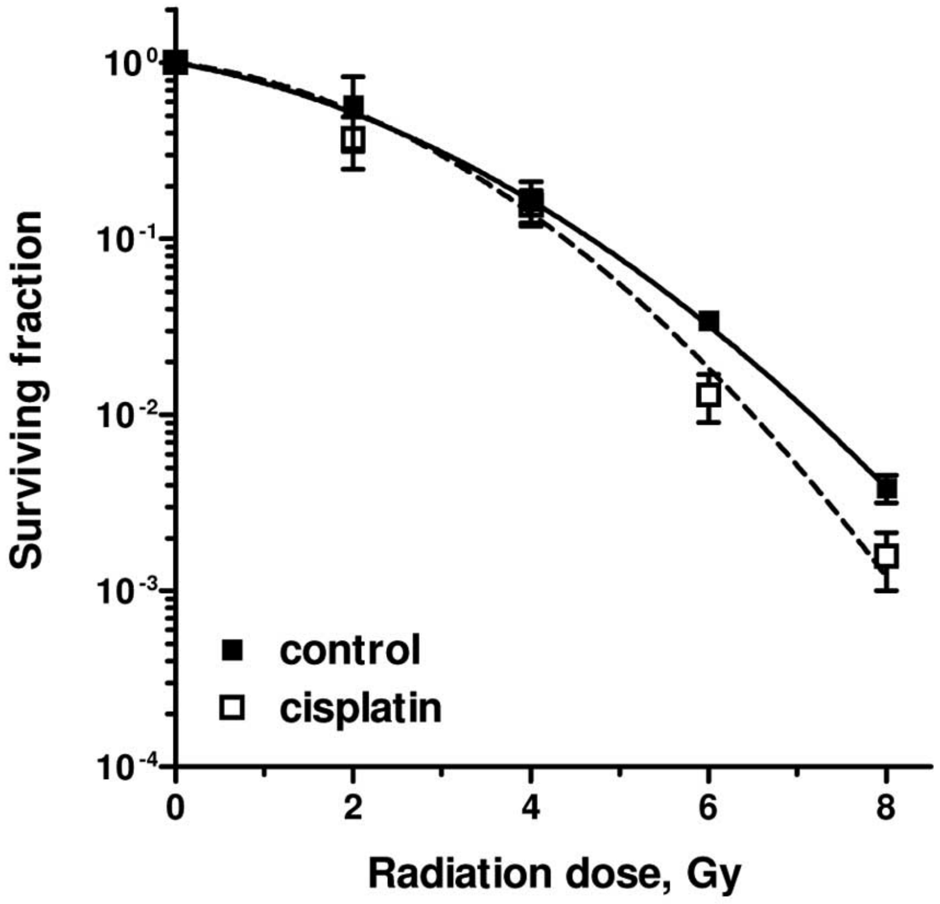
High-LET radiation delivers more biological damage for the same dose, making cells die more efficiently.

Surviving Fraction (SF)

- **Probability a cell retains reproductive integrity:** SF reflects the chance that a cell can still divide and form colonies after radiation exposure.

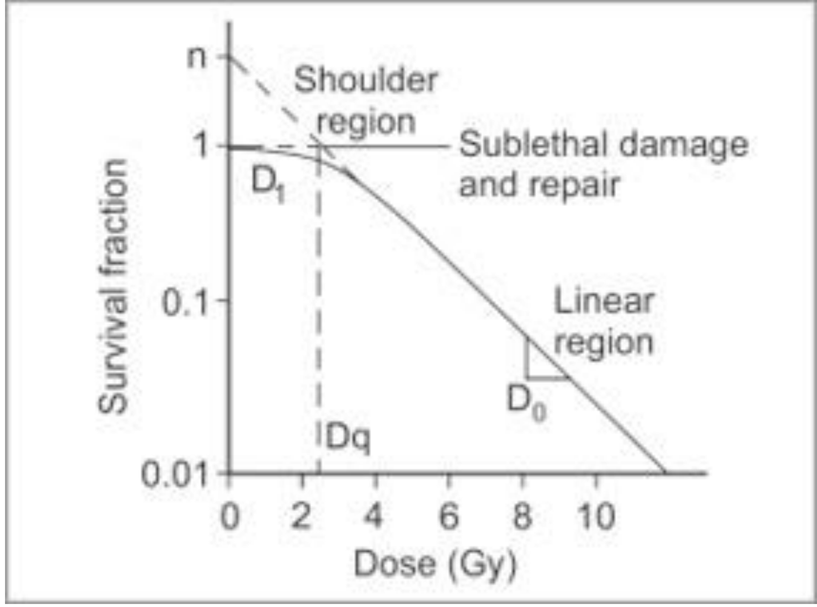
- **SF decreases with increasing dose:** As radiation dose rises, fewer cells survive, causing the SF value to drop.

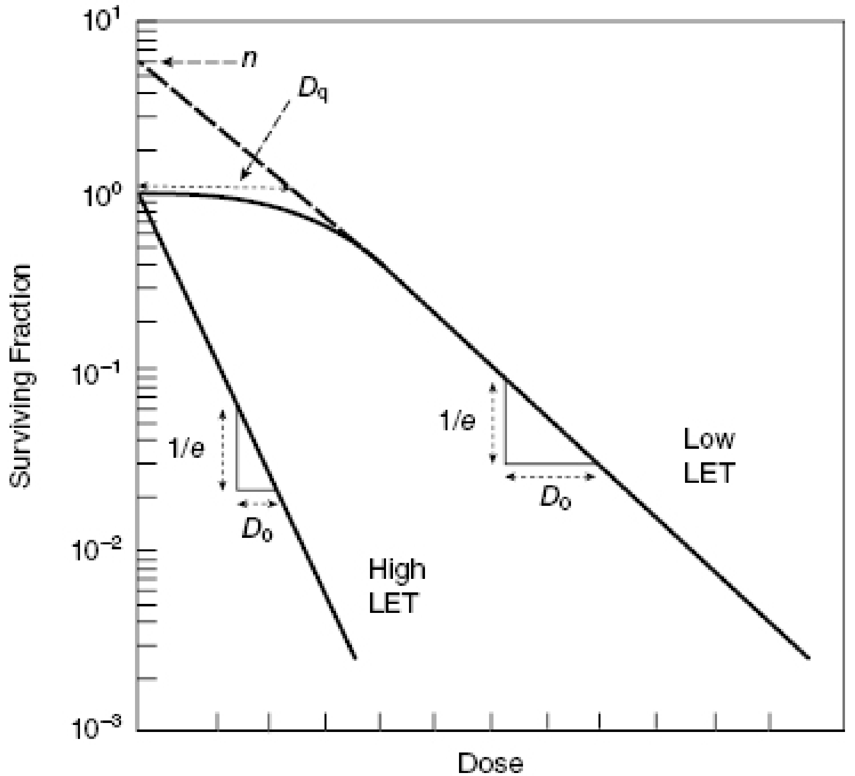
- **SF at 2 Gy (SF_2) is clinically important:** SF_2 is widely used to compare the radiosensitivity of tumors, since 2 Gy is a standard daily fraction in radiotherapy.



Key Survival Curve Parameters

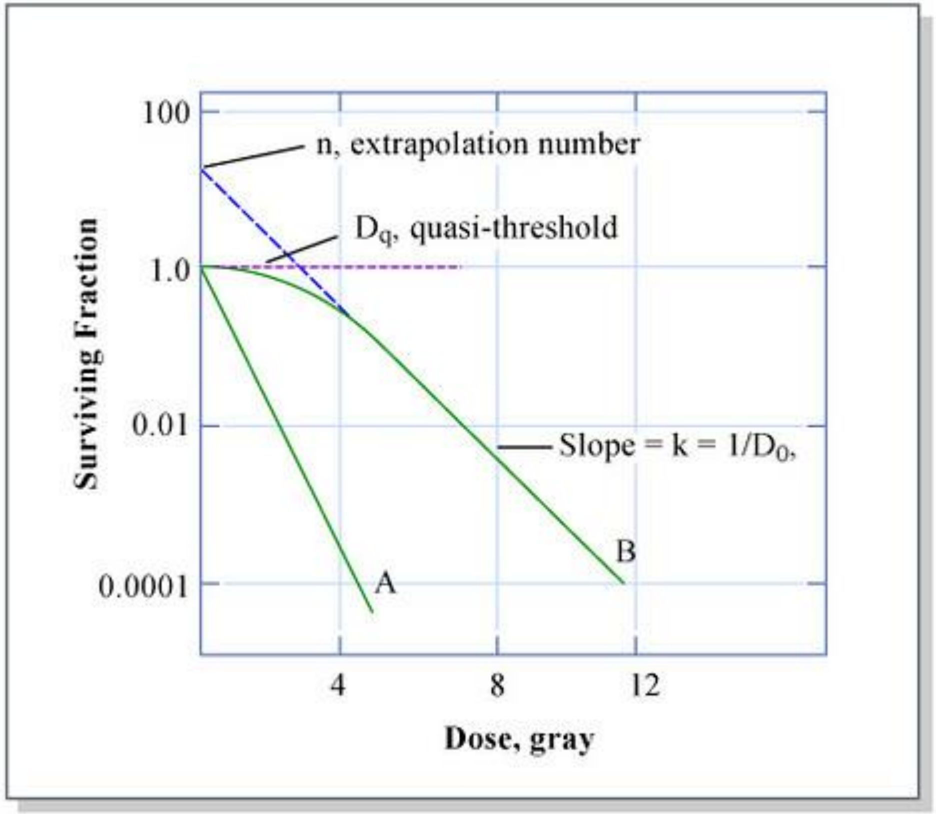
- **D_0 (Mean lethal dose):** Shows how much dose is needed to reduce survival on the exponential part of the curve; indicates radiosensitivity.
- **Dq (Quasi-threshold dose):** Represents the width of the shoulder and reflects how well cells repair sublethal damage.
- **n (Extrapolation number):** Indicates the "size" of the shoulder and how many hits a cell can tolerate before dying.
- **α and β components:** α represents single-event killing; β reflects damage from two-event interactions.
- **α/β ratio:** Describes tissue response to fraction size and distinguishes early- vs late-responding tissues.





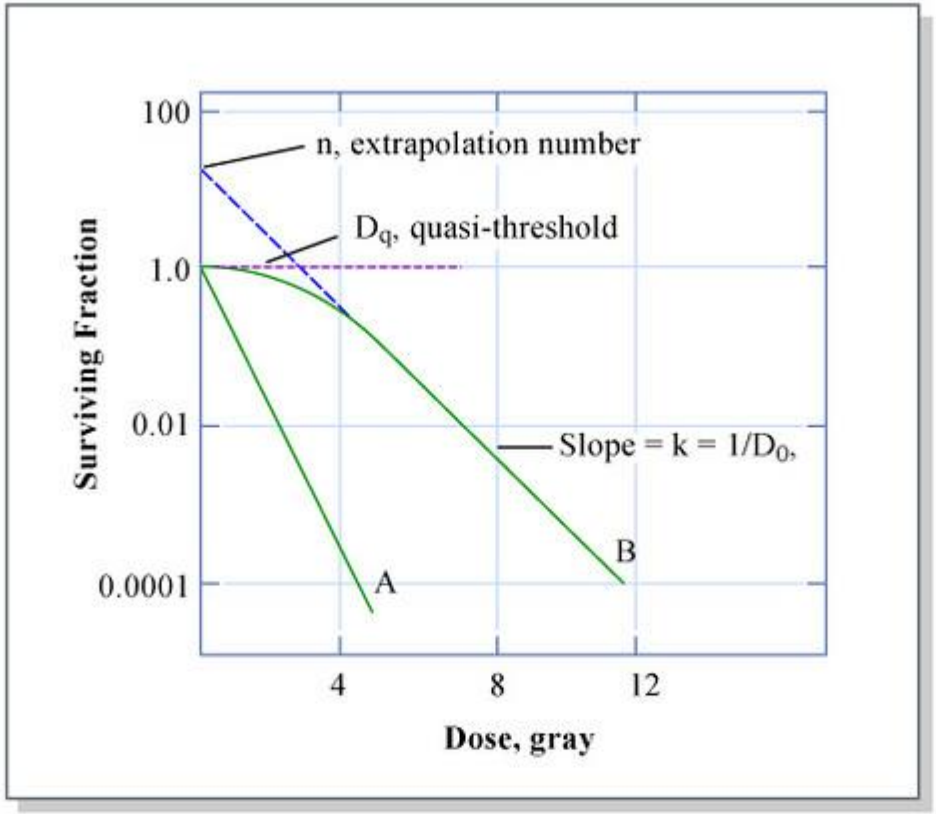
D_0 (Mean Lethal Dose)

- **D_0** is the dose that reduces cell survival to 37% on the exponential portion of the curve.
- **Indicates radiosensitivity:** Smaller D_0 values mean cells are more sensitive to radiation, while larger D_0 values indicate resistance.
- **Exponential region relevance:** D_0 applies to the straight-line portion of the survival curve, where repair is minimal, and killing is mostly direct.



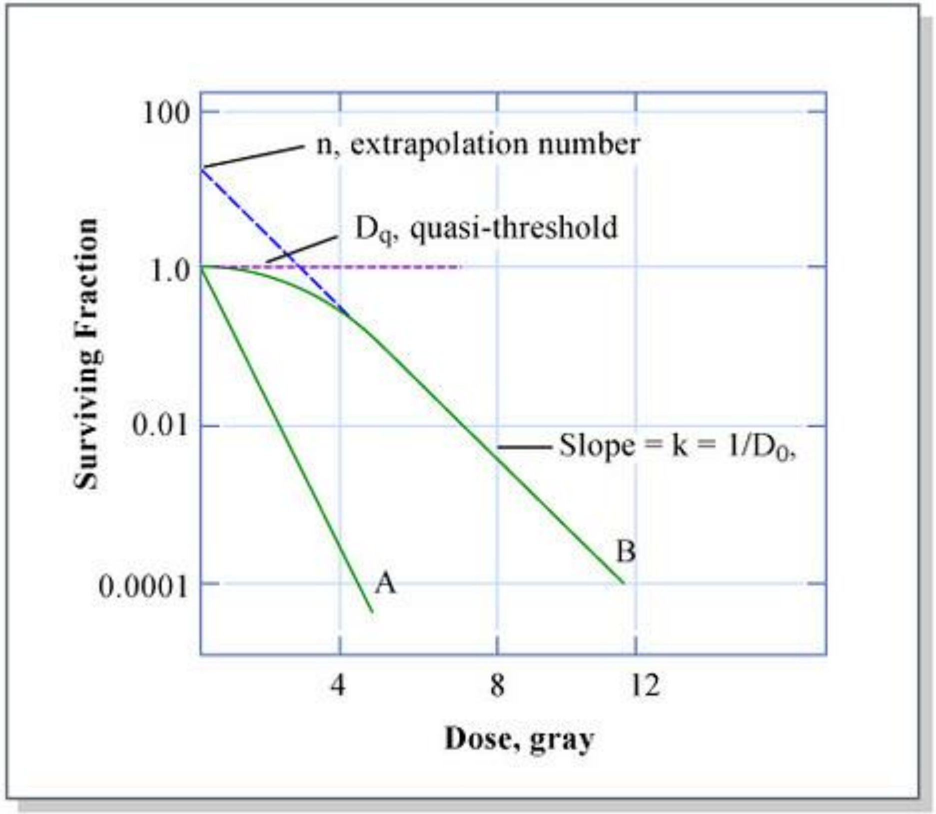
Dq (Quasi-Threshold Dose)

- **Dq** is the dose that represents the width of the shoulder on the survival curve.
- **Reflects repair capacity:** A larger Dq means cells can repair more sublethal damage before death.
- **Clinical relevance:** Cells with a broad shoulder (high Dq) are more resistant at low doses, affecting fractionation strategies in radiotherapy.



Extrapolation Number (n)

- **The extrapolation number** "n" estimates the size of the shoulder on a survival curve.
- **Represents cell tolerance:** It indicates the number of "hits" a cell can endure before being killed.
- **Interpretation:** Higher n → broader shoulder → cells are more resistant to low doses; lower n → narrow shoulder → more sensitive cells.



Low-LET Survival Curve Equation

- **Equation**

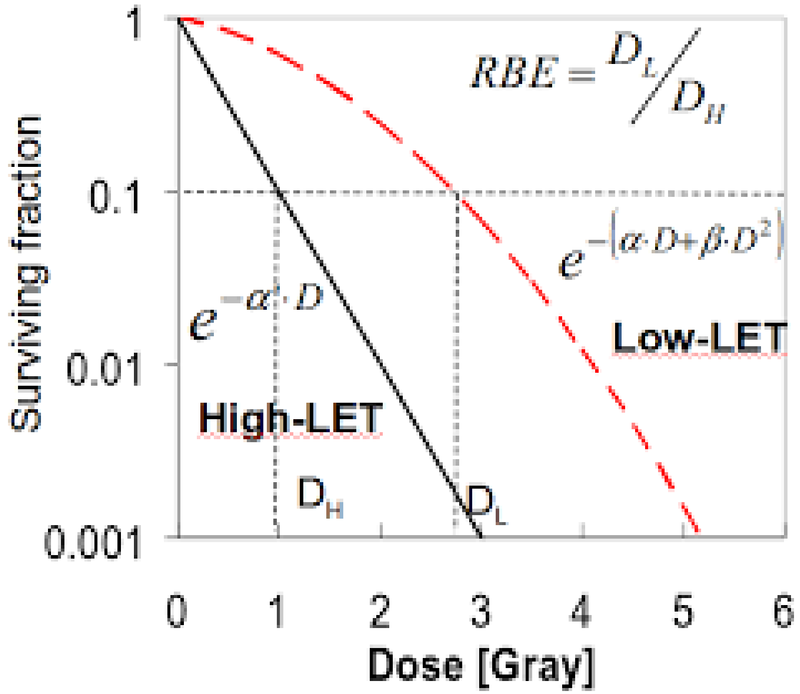
$SF = 1 - (1 - e^{(-D/D_0)})^n$

- **Meaning**

Describes survival based on dose (D), mean lethal dose (D_0), and extrapolation number (n).

- **Usage**

Works well for high doses and low-LET radiation but is less accurate at low doses.



Linear-Quadratic (LQ) Model

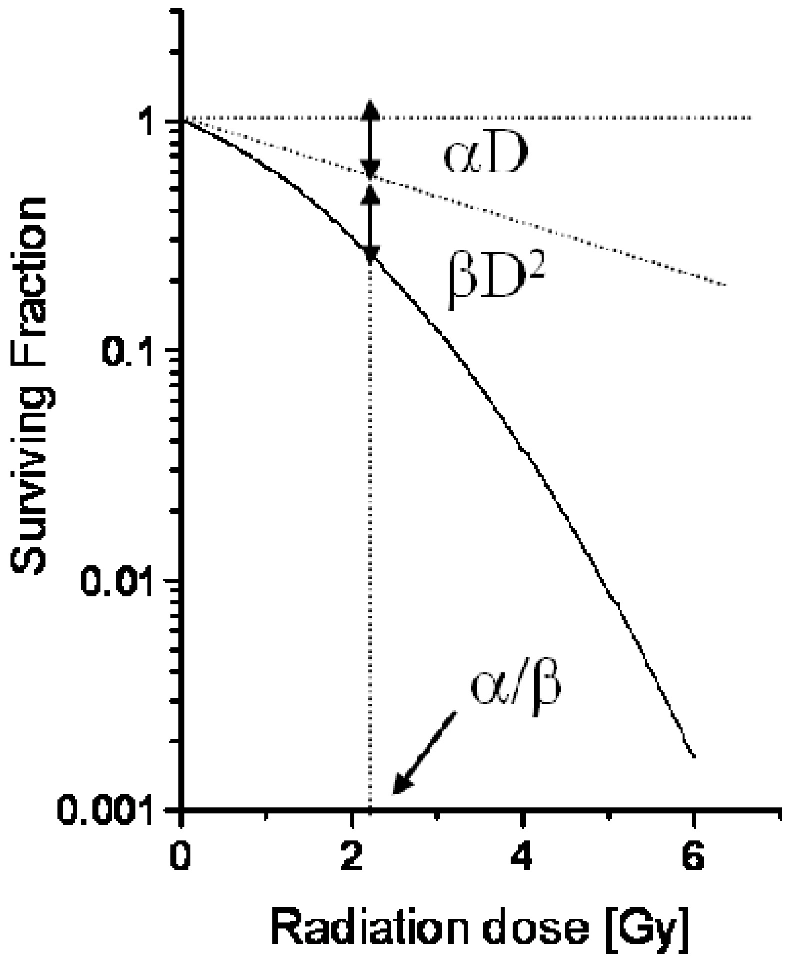
- **Equation**

SF = e^(–(αD + βD²))

- **Components**

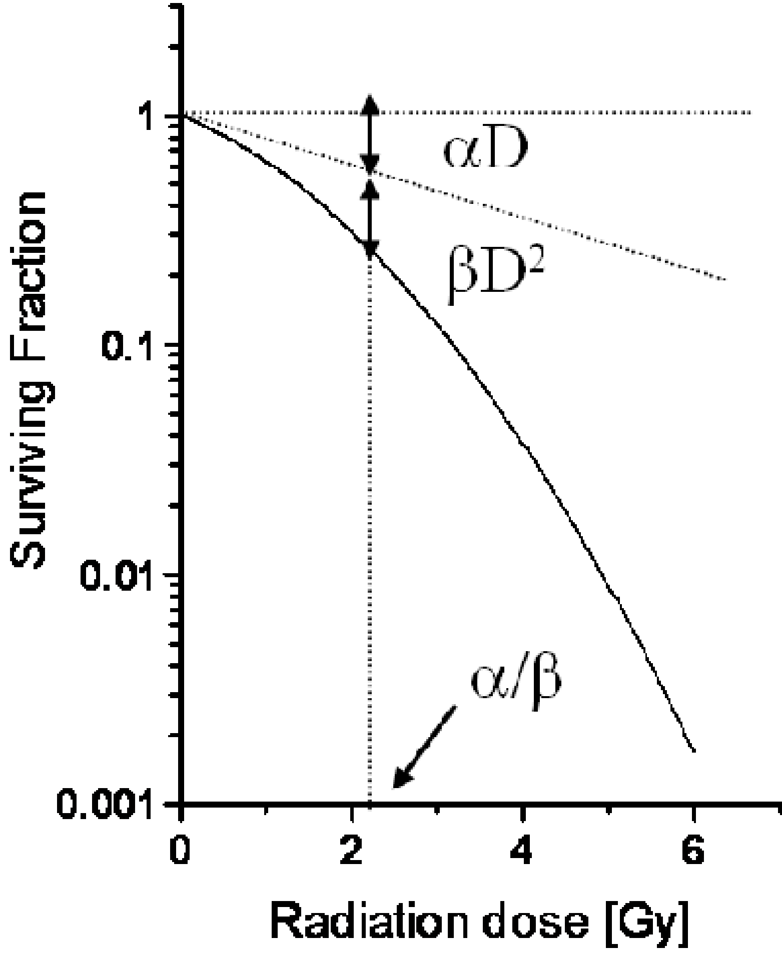
1. **α**: linear, single-track killing
2. **β**: quadratic, two-track interactions

- **Importance:** Accurately predicts cell survival for both low and high doses; widely used in radiotherapy planning.
- **α (Linear component):** Dominates at low doses; represents cell death from single-track events.
- **β (Quadratic component):** Dominates at higher doses; represents cell death from two-track interactions.
- **Clinical relevance:** Tumors with high α/β are more sensitive to small doses per fraction, influencing fractionation choices.



α/β Ratio

- **The α/β ratio** is the dose at which linear (α) and quadratic (β) components contribute equally to cell killing.
- **Low α/β (2–4 Gy):** Typical of late-responding tissues (e.g., spinal cord, kidney); more sensitive to fraction size changes.
- **High α/β (8–12 Gy):** Typical of early-responding tissues and many tumors (e.g., skin, mucosa); less sensitive to fraction size.



Clinical Importance of α/β

1. **Guides fractionation schedules:** Tissues with low α/β are more sensitive to larger fraction sizes, helping design hypofractionation.
2. **Tumor vs normal tissue response:** Understanding α/β allows balancing tumor control with minimizing normal tissue damage.
3. **Predicts treatment outcomes:** α/β ratio helps estimate how changes in dose per fraction affect both tumor killing and late complications.

High-LET Radiation Effects

- **Minimal shoulder**

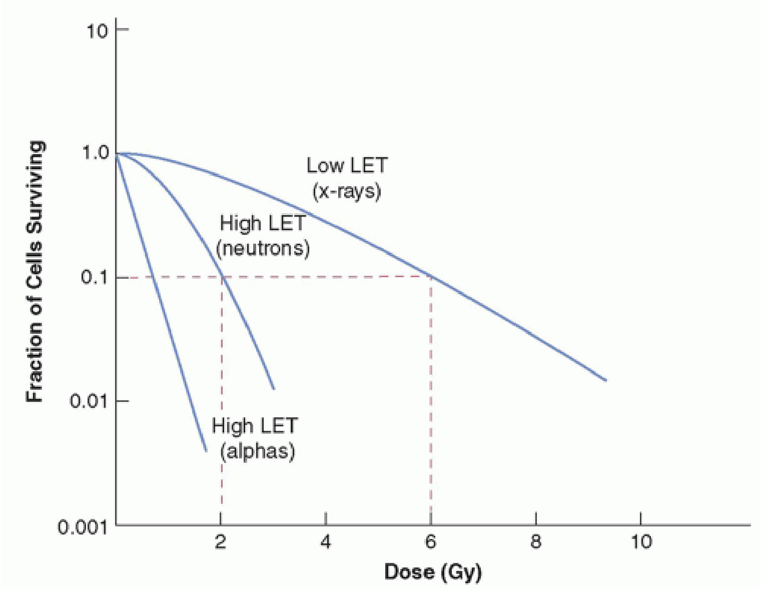
High-LET radiation causes complex damage that is difficult to repair, so the survival curve is almost straight.

- **Straight-line survival curve**

Cell killing increases directly with dose, without a significant shoulder.

- **More effective cell killing**

High-LET radiation delivers dense energy, making it more lethal per unit dose compared to low-LET radiation.



Relative Biological Effectiveness (RBE)

- **RBE** = Dose of reference radiation / Dose of test radiation to achieve the same biological effect.

- **High-LET → higher RBE**

Radiations with higher LET produce more complex damage, increasing their effectiveness.

- **Factors affecting RBE**

Depends on LET, dose, cell type, oxygenation, and the biological endpoint measured.

RBE(Relative Biological Effectiveness)

- RBE of a test radiation (r)

$$= \frac{D_{250}}{D_r}$$

- D_{250}: doses of 250 kv x rays
- D_r : doses of test radiation.

to produce same biological effect

Factors Influencing Survival Curves

- **Cell cycle phase:** Cells in G2/M are most sensitive; S phase cells are more resistant.
- **Hypoxia:** Low oxygen levels reduce radiosensitivity, flattening the survival curve.
- **DNA repair capacity:** Cells with strong repair mechanisms show broader shoulders and higher survival.
- **Dose rate & fractionation:** Lower dose rates allow repair, increasing survival; fractionation exploits this for normal tissue protection.
- **Radiosensitizers/radioprotectors:** Chemical agents can increase or decrease cell killing, modifying the curve shape.

Questions? Comments?

Thank you!