Biological effects of Ionising Radiation

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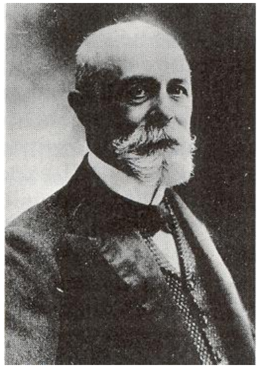
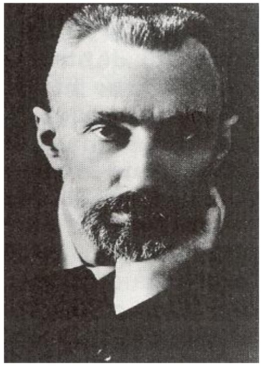
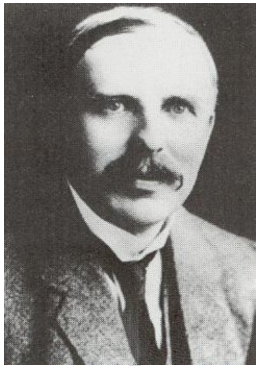
Biological effects of radiation

- Ionizing radiations have many beneficial applications, but they also may have detrimental consequences for human health and for environment

- Since X-rays were discovered in 1895, it was quickly realized that they may be harmful

- To protect people and the environment it is essential to understand how radiation-induced effects occur



BIOLOGICAL EFFECTS DEPEND ON

Radiation type (LET)

Acute or Chronic Exposure

Somatic Cells or Germ Cells

Type of tissue involved

Whole body or localized

Sensitivity of individual

Types of Ionising Radiation

INDIRECTLY IONIZING RADIATIONS

- X- and Gamma rays –electromagnetic radiations

X-rays are produced by a machine and gamma rays are produced when radioactive materials decay. Neither one has any mass.

- Neutrons-uncharged particles

DIRECTLY IONIZING RADIATIONS

- Electrons, protons, a- particles

they have mass and travel at high speeds

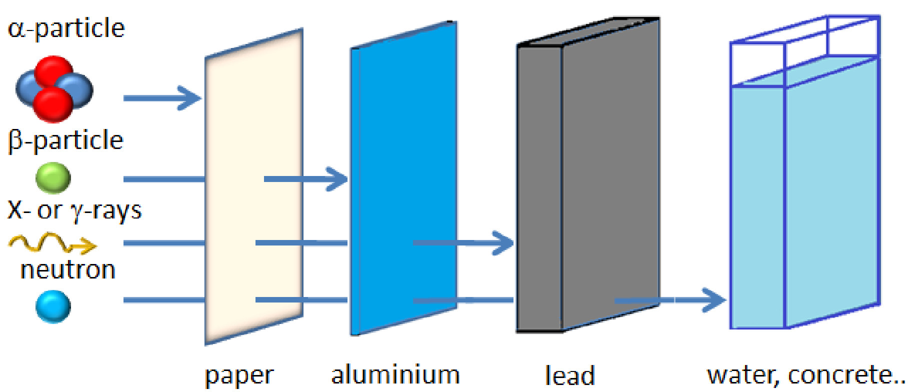
Both types of radiation transfer part of all of their energy when they interact with matter.

Ionising Radiation

A radiation can be considered as ionizing if deposited energy is high enough to ionize the traversed material

electromagnetic (X and γ- rays)
corpuscular (α- and β-particles and neutrons)

Each type interacts in its own way with material



Absorbed Dose, D

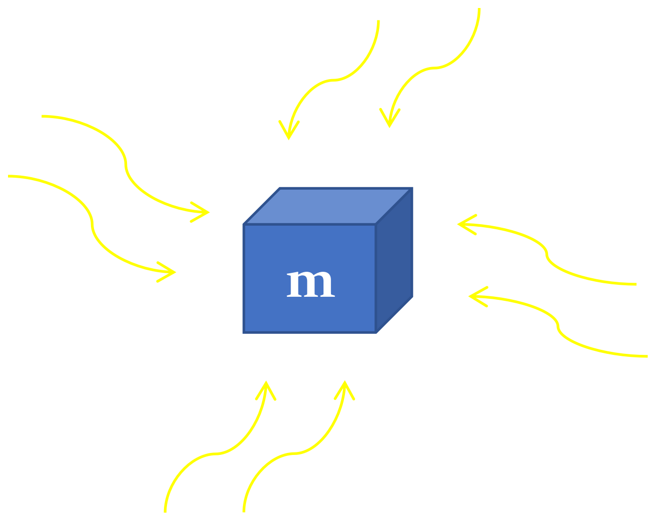
The effects of radiation depend not only on the energy transferred to the medium but also on the energy absorbed by it.

<u>Absorbed dose</u> is defined as the amount of energy absorbed per unit mass of the medium at the point of ineterest

D = dE/dm

D = J/kg

SI unit of dose is Gray (Gy) = 1J/Kg



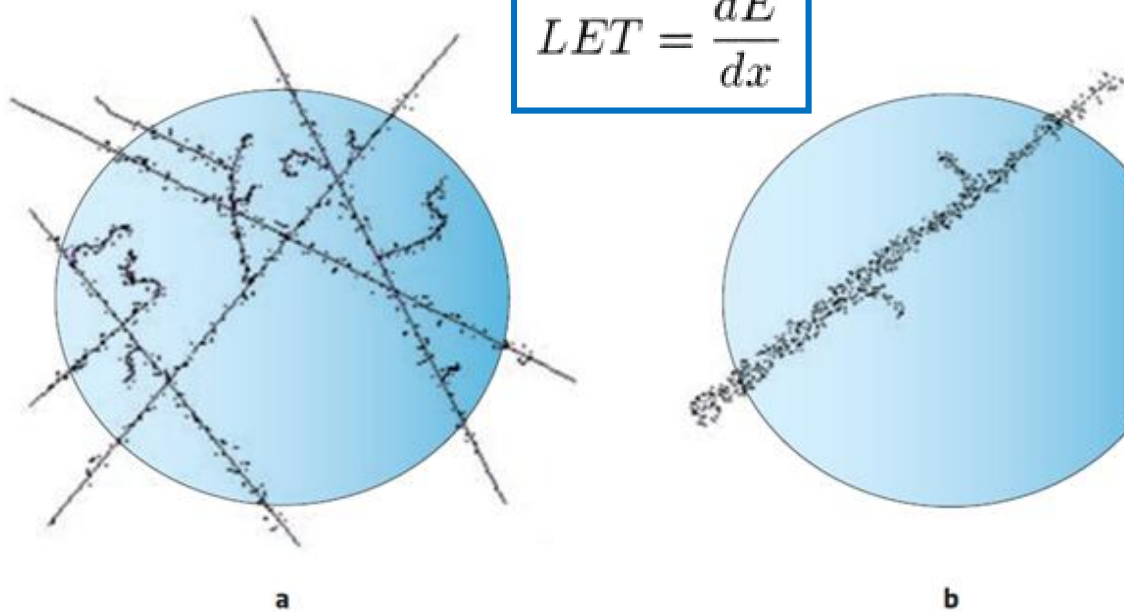
1 cGy (=1/100 Gy)

1 mGy (=1/1.000 Gy)

Radiation Quality -LET

Linear Energy Tranfer (LET) is a measure of energy transferred by ionizing radiation to transversed material (keV/µm)

$$\boxed{LET = \frac{dE}{dx}}$$



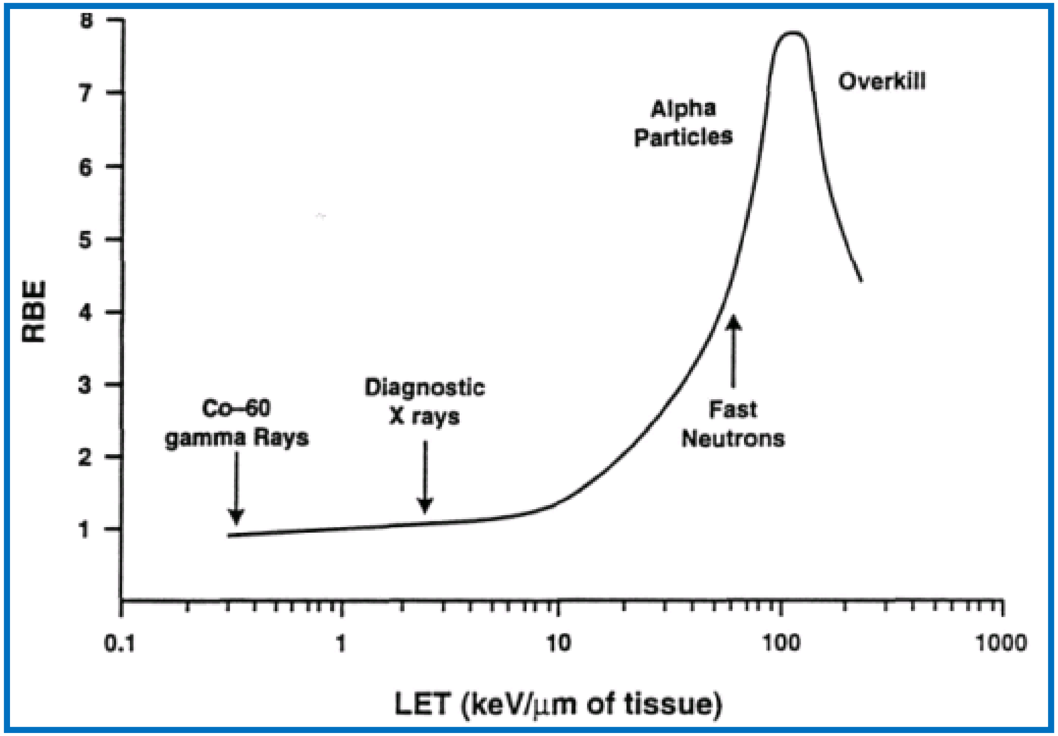
X and γ rays are sparsely ionizing radiations
Energy is distributed homogeneously

α, β particles and neutrons are densely ionizing radiations
The energy is distributed inhomogeneously

LOW LET

HIGH LET

Relationship between RBE and LET



$$\text{RBE} = \frac{\text{Dose of 250 kV}_p \text{ x-rays for a given level of a given biologic effect}}{\text{Dose of test radiation to produce the same isoeffect}}$$

Low LET Radiation

- i.e., MV photons or 250 kVp x-rays
- Inefficient cell killing

High LET Radiation

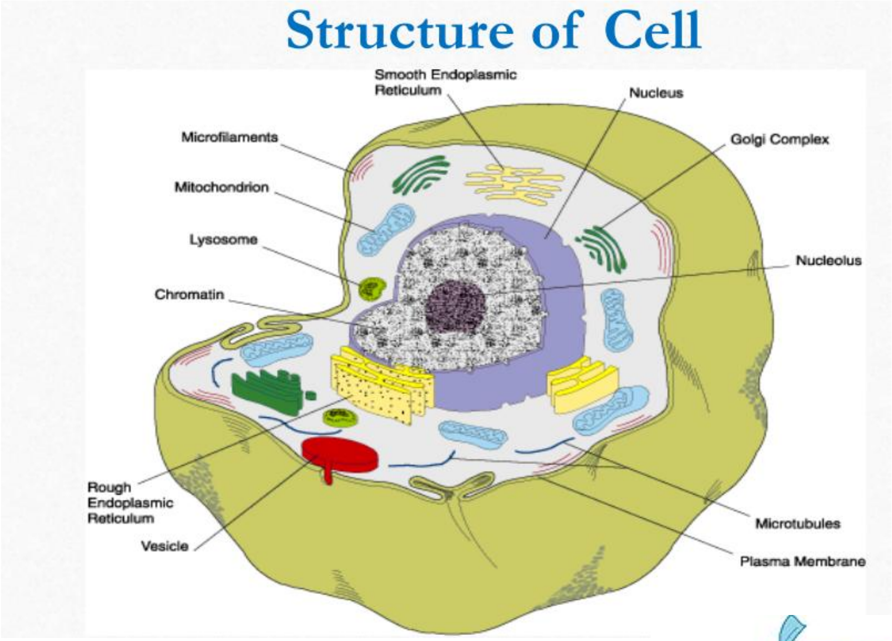
- i.e., 2 GeV Fe ions
- More dose is deposited than is needed to kill cells
- Also inefficient cell killing (per unit dose)

Optimal LET

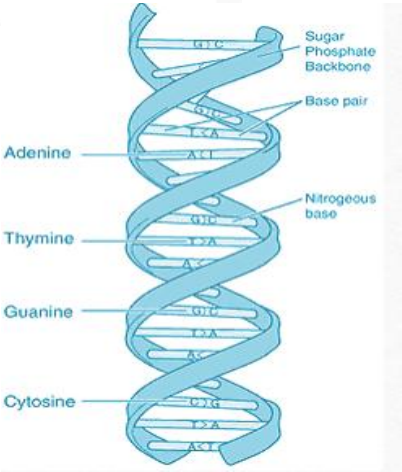
- i.e., 4 MeV α-particles
- Produces just enough DNA DSB to kill the cell

Human cell

- The smallest unit of body is called a cell.
- An adult person's body has about 10^{14} cells.
- Cells of different organs have different shapes & sizes.

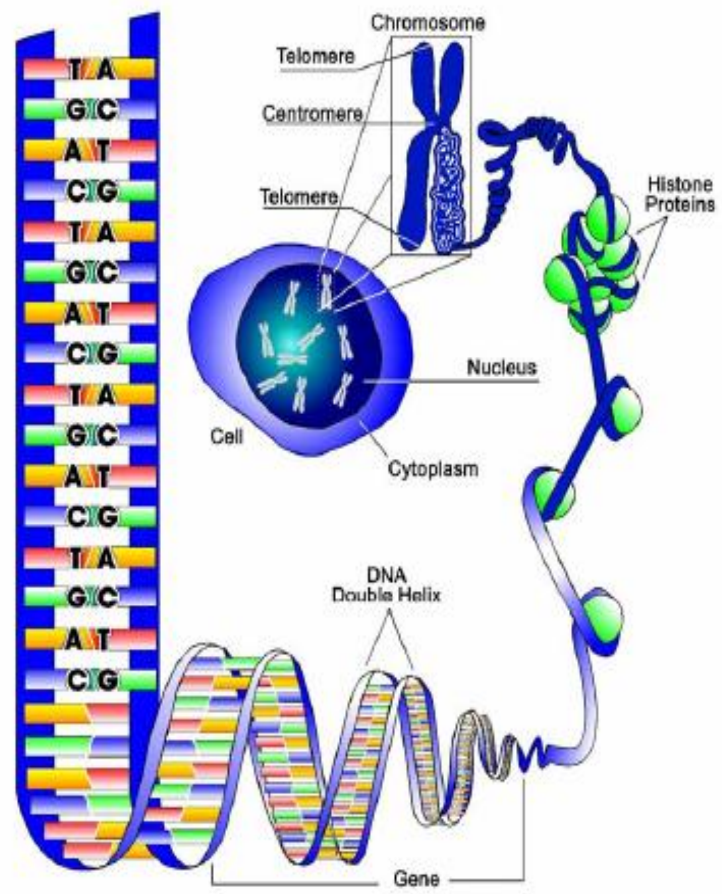


- The most sensitive organelle of the cell is the NUCLEUS
- Nucleus contains 46 thread like structures which are called CHROMOSOMES
- Each chromosome contains one very complex sensitive molecule called DNA (deoxyribonucleic acid).

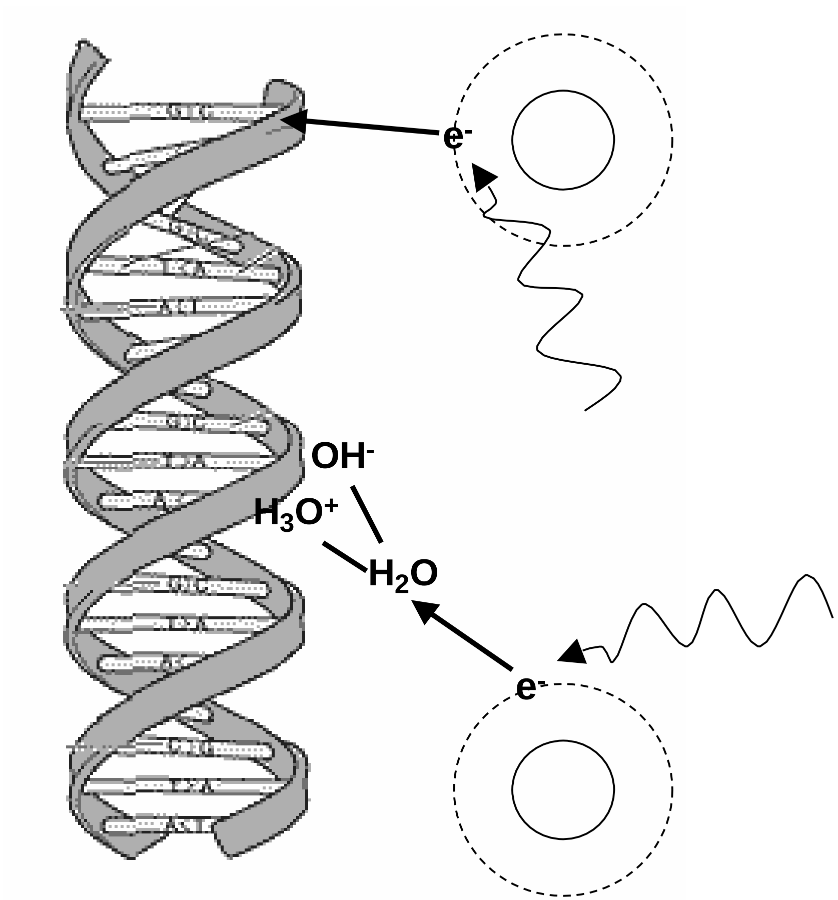


DNA (Target in cell)

- ❑ DNA contains very specialized code language made up of 4 molecules: A,T,G and C which are arranged in very specific order
- ❑ DNA is the ultimate sensitive target molecule
- ❑ When DNA is damaged by radiation, its coded language is also damaged resulting in death of cell or abnormal modification of cell



Indirect and Direct induction of radiation damage



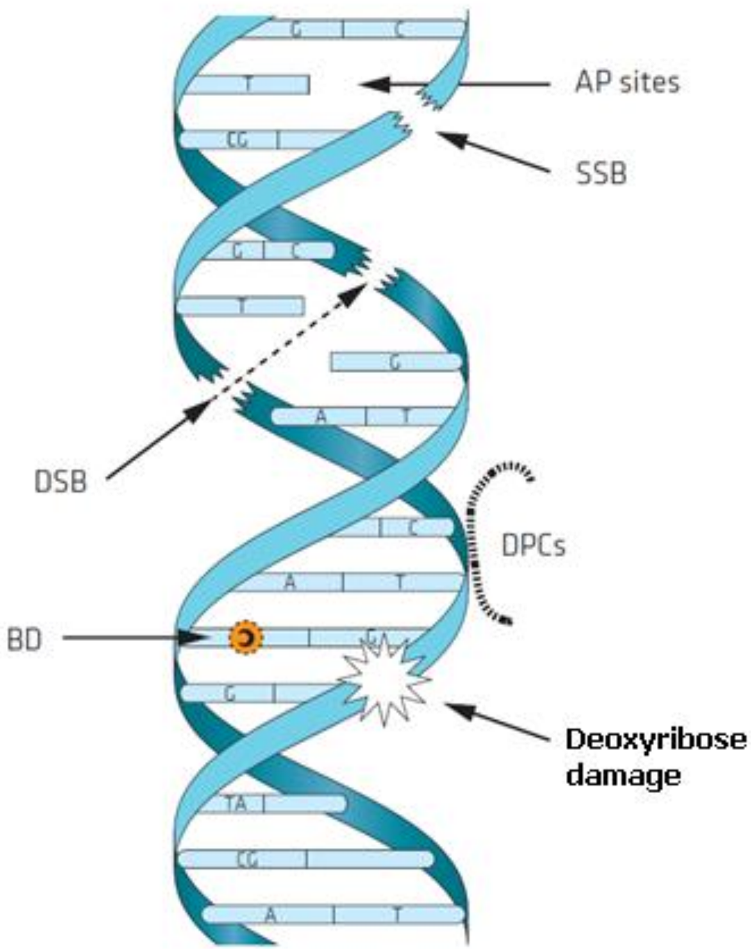
DIRECT EFFECT – Due to direct deposition of energy in the target molecule-DNA

DIRECT (low LET~30%)

INDIRECT EFFECT – Due to deposition of energy in the surrounding water and reaction of free radical formed in the water with the target molecule-DNA

INDIRECT (low LET ~70%)

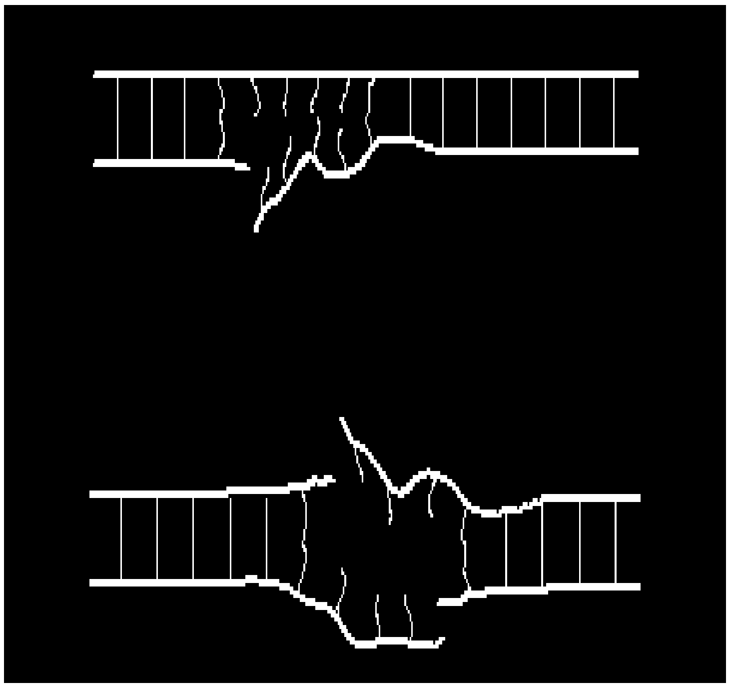
Types of DNA lesions



Damage type	Amount of damage
Base Damage (BD)	1000 - 2000
Deoxyribose damage	1200
SSBs	1000
AP sites	250
DSBs	40
DPCs	150

Estimation of numbers of radiation - induced different types of DNA lesions after 1 Gy irradiation with low-LET radiation

DNA strand breaks



- **Single strand break**

  repairable from mirror half of DNA

- **Double strand break**

  less repairable

  chromosome aberration

  distant breaks repaired as if 2 single breaks

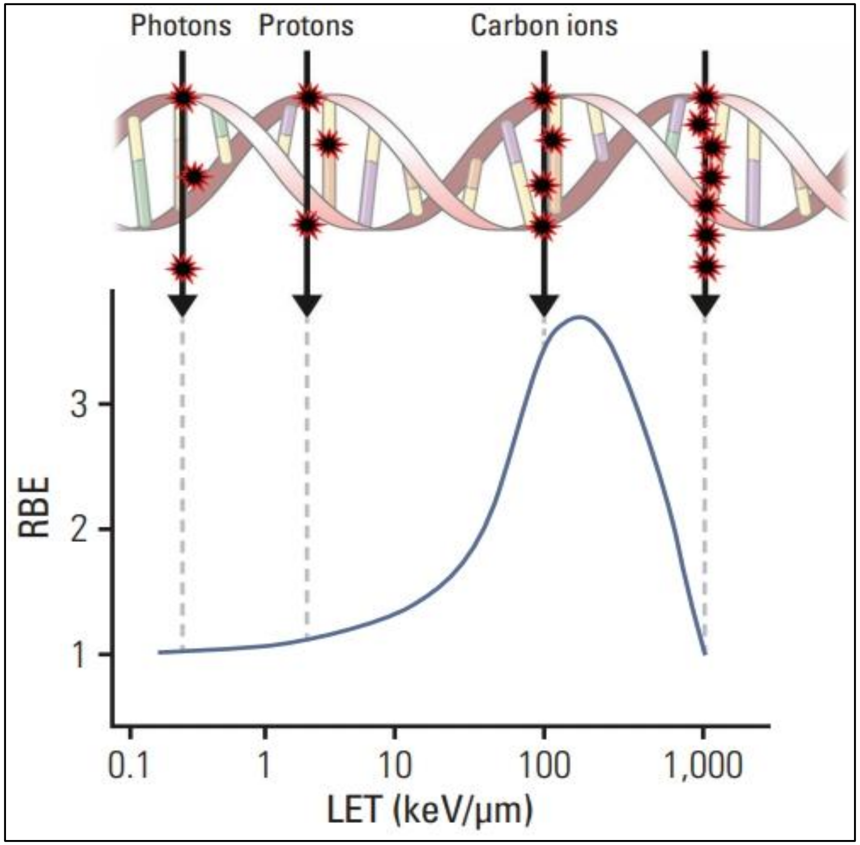
Why does RBE Peak at 100keV/µm

Diameter of DNA double helix ~ 2nm

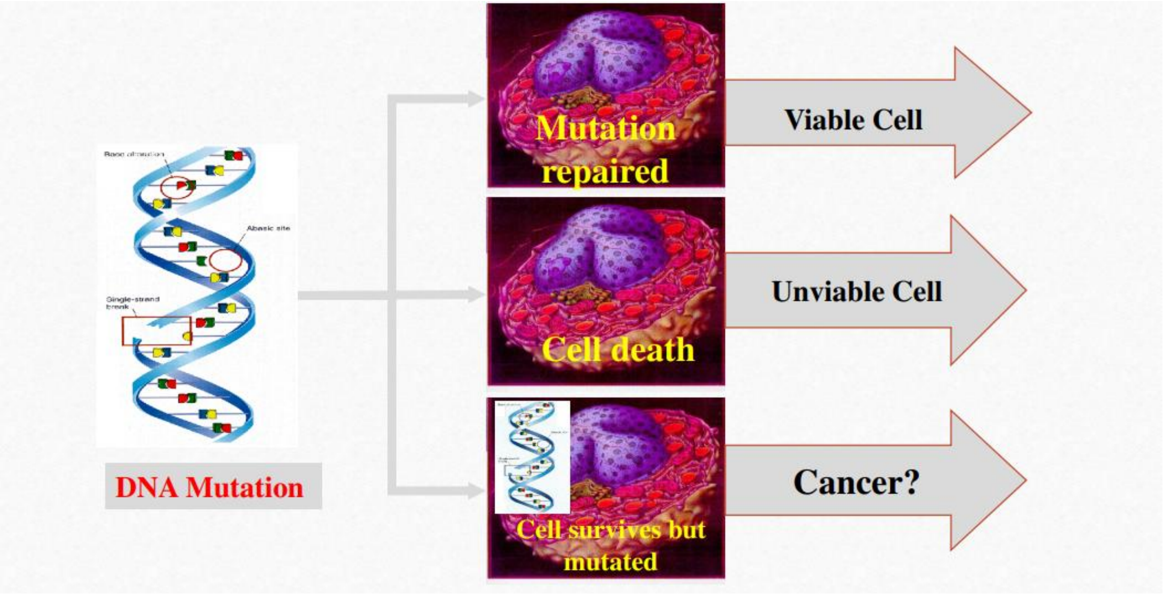
At ionisation density of 100keV/µm, average separation between ionization events is ~ 2nm

Radiation with LET=100 keV/µm is most likely to cause a double strand break by the passage of particle (low energy neutrons, a particles, carbon ions)

Beyond the point at which RBE reaches a peak, energy is wasted because the ionization events are closer than the diameter of the DNA helix



Outcomes after cell exposure



- Human body has a very good self repair mechanism for damaged cells
- 999 out of 1000 lesions are repaired
- 999 out of 1000 damaged cells die (not a major problem as millions of cells die every day in every person)
- Many cell may live with damage (but could be mutated)

Radiation damage may lead to…

- Inhibition of cell division

Delay or inhibit the process of cell division, which may impair the functions of tissues/organs

- Chromosome aberrations

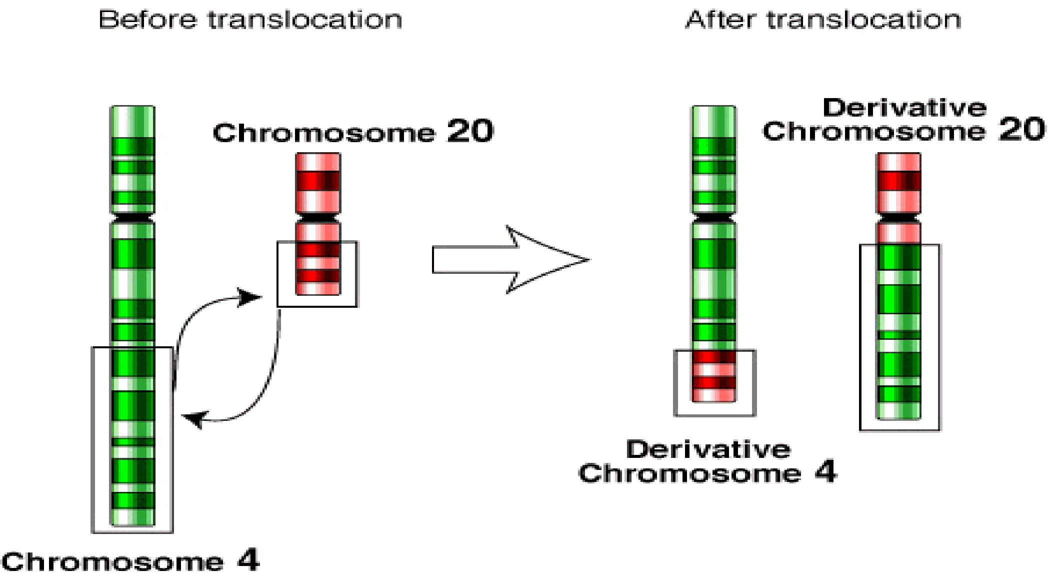
Lead to rearrangement of genetic information. Serve as biological dosimeter (above 100mSv)

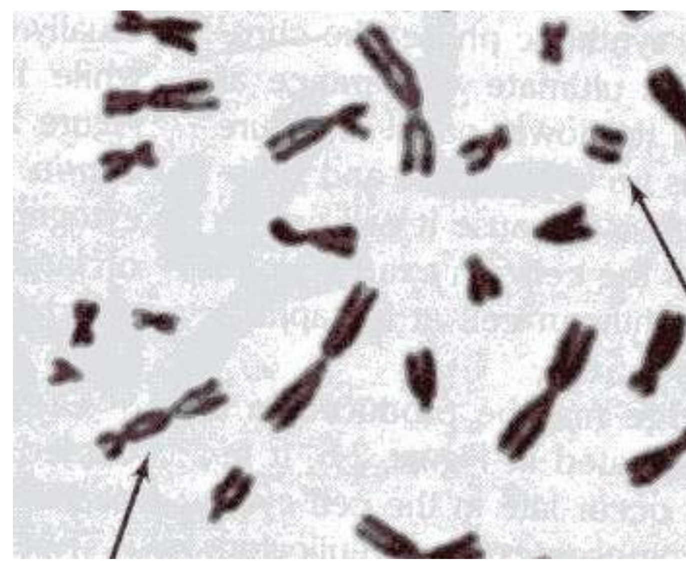
- Gene mutation

Alteration in the information content of genes

- Cell death

Potential Chromosome Damage





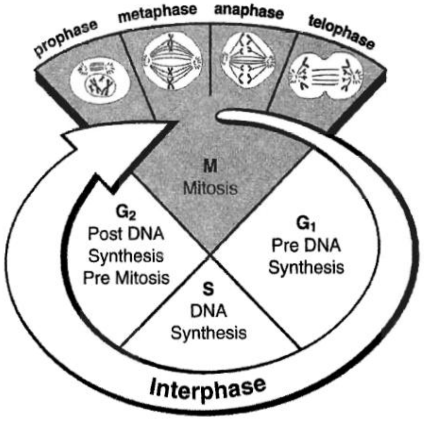
Factors Affecting Cellular Radiosensitivity

Conditional factors - physical or chemicals factors that exist previous to and/or at irradiation

- Dose rate
- LET
- Fractionation
- Presence of oxygen

Inherent factors - biologic factors characteristic of the cell

- Mitotic rate
- Degree of differentiation
- Cell cycle phase



Mechanism of Causing Effects on Human Body

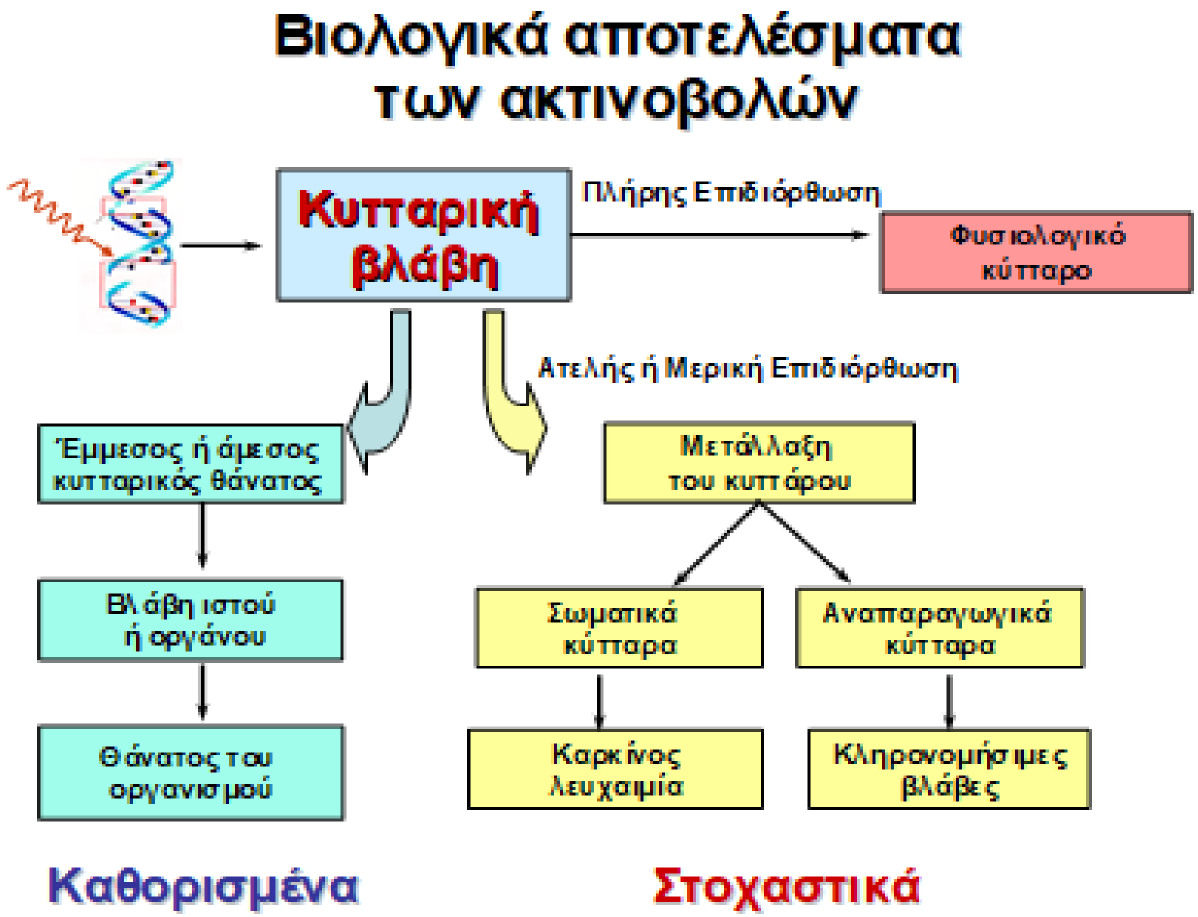
Radiosensitivity of Organs and Tissues

Active cell division **High sensitivity**

- **Hematopoietic system**: Bone marrow and lymphatic tissues (spleen, thymus gland, lymph node)
- **Reproductive system**: Testis and ovary
- **Gastrointestinal system**: Mucous membrane and small-intestinal villus
- **Epidermis and eyes**: Hair follicle, sweat gland, skin and lens
- **Other**: Lung, kidney, liver and thyroid gland
- **Support system**: Blood vessel, muscle and bone
- **Transmission system**: Nerve

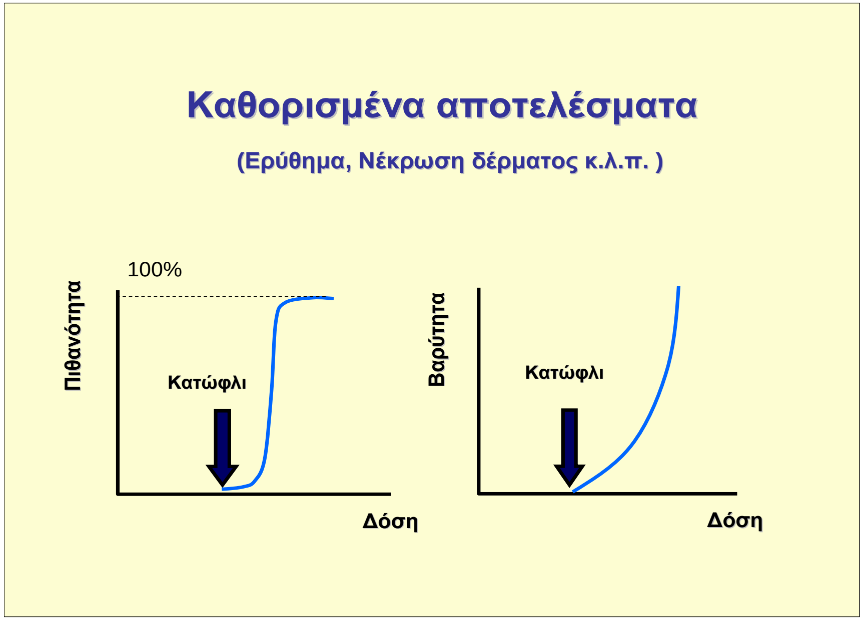
No cell division **Low sensitivity**

Κατηγοριοποίηση βιολογικών αποτελεσμάτων



Deterministic Effects

- Significant number of cells are injured or killed causing organ or tissue dysfunction
- Also called early or acute effects
- Dose threshold
- Severity of harm proportional to dose



Ραδιολογικά και πυρηνικά ατυχήματα (ολόσωμη έκθεση)

LD 50 /60 =   3-5Gy

Βλάβη	Συμπτώματα	Δόση κατωφλίου	Χρόνος εκδήλωσης
Σύνδρομο αιμοποιητικού συστήματος	Λεμφοπενία, αιμορραγία, αναιμία	2 Gy	24 ώρες
Σύνδρομο γαστρεντερικού συστήματος	Ναυτία, εμετός, διάρροια, έλκη, εντερική αιμορραγία	7 Gy	3-10 ημέρες
Σύνδρομο κεντρικού νευρικού συστήματος	Εγκεφαλικό οίδημα, μείωση του ενδοαγγειακού όγκου αίματος	50 Gy	Θάνατος σε 1-4 ημέρες

Ιατρικές εφαρμογές

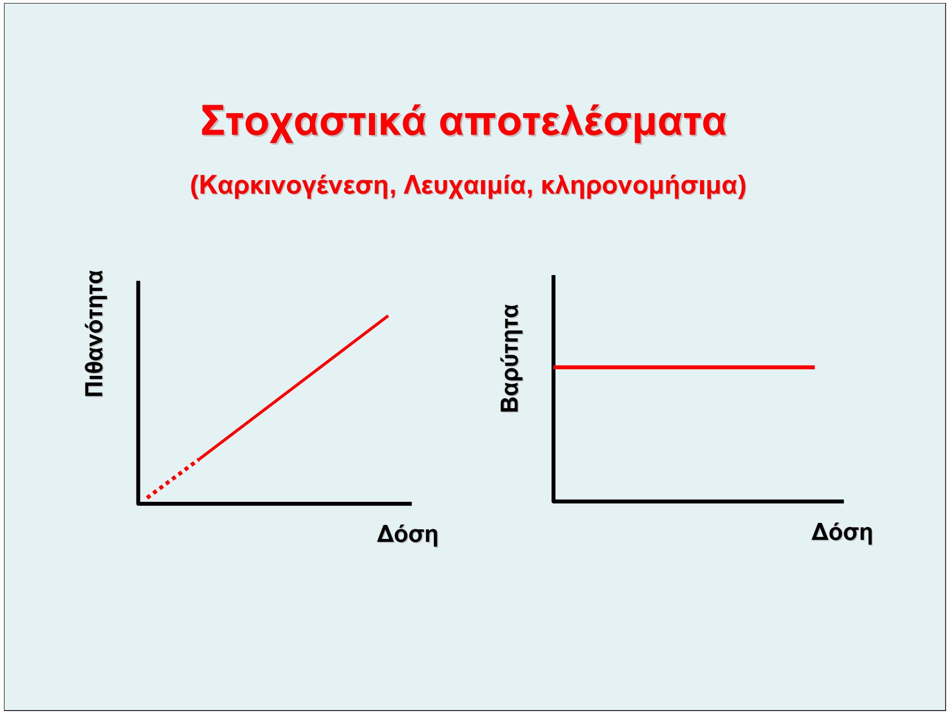
Καταρράκτης (5Gy) ,
ερύθημα (2Gy) , οίδημα, εξέλκωση

Deterministic effects

- ***Examples:***
- Skin erythema (threshold dose: 2 Gy)
- Cataract of the lens of the eye (threshold dose: 5 Gy)
- Permanent sterility (threshold dose 3-6 Gy)
- Temporary sterility (threshold dose 0,1-0,5 Gy)

Stochastic effects

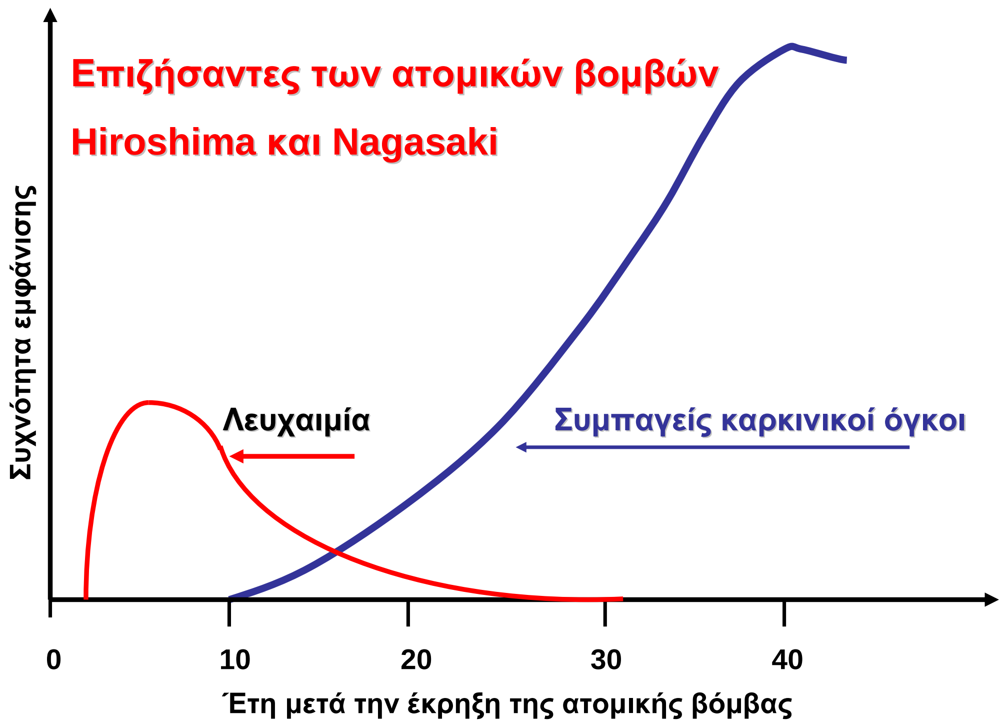
- The probability of a stochastic effect increases with dose
- The severity of the effect is not dose related
- Applied for low dose, low dose-rate irradiations



Πηγές πληροφορίας

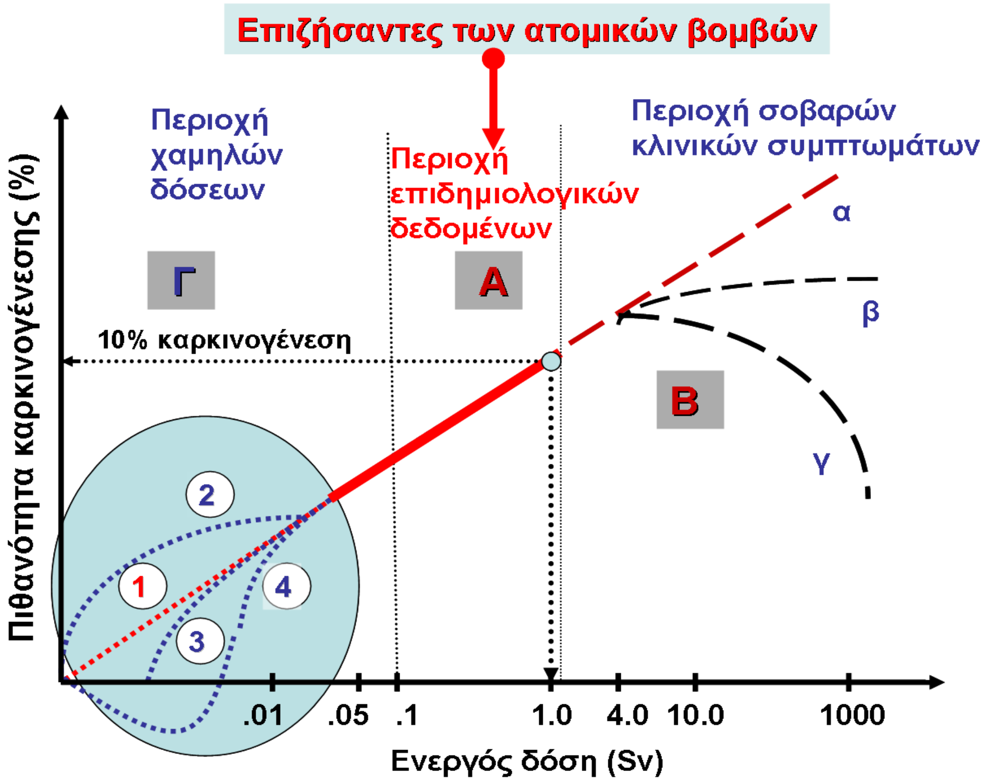
- Επιδημιολογία
- Πειραματική ραδιοβιολογία
- Κυτταρική και μοριακή βιολογία

Χρονική εμφάνιση στοχαστικών αποτελεσμάτων



Καρκινικοί όγκοι μετά από ακτινοβολία:

- Λευχαιμία
- Πολλαπλούν μυέλωμα
- Καρκίνος μαστού, θυρεοειδή, πνεύμονα, ουρ κύστης, οισοφάγου, στομάχου, ΚΝΣ



Περιοχή Α >200mSv
Περιοχή Β >1-2Sv (>κατώφλι)
Περιοχή Γ <100mSv

Στοχαστικό αποτέλεσμα	**Μέση πιθανότητα εμφάνισης* (% ανά Sv)**
Λευχαιμία	~0.9
Θανατηφόροι συμπαγείς καρκινικοί όγκοι	~11.00 **

** σταθμισμένη ως προς το φύλλο και την ηλικία*

*** ~9% για τους άνδρες & ~13% για τις γυναίκες*

Βλάβη	Χρόνος	Μέση πιθανότητα εμφάνισης	Φυσιολογική πιθανότητα εμφάνισης
Λευχαιμία	8 χρόνια	0,5% ανά Sv	0,015%
Καρκινογένεση	40 χρόνια	5% ανά Sv	25%
Κληρονομήσιμες βλάβες		0,2% ανά Sv	3-6%

Περιοχή Γ επιδημιολογικών μελετών

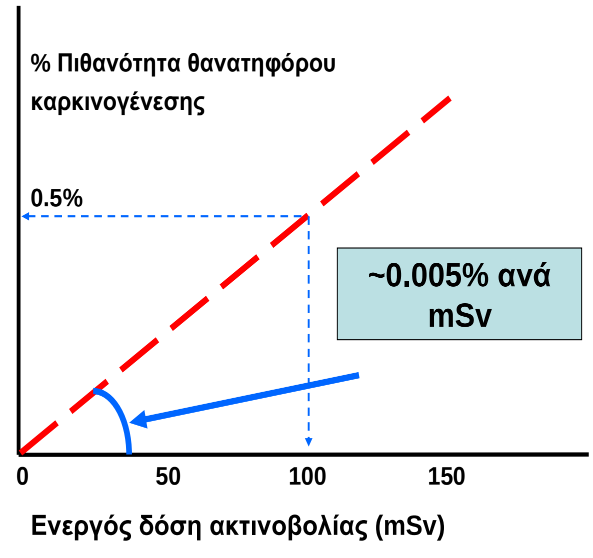
Γραμμικό πρότυπο πιθανότητας-δόσης (LNT) χωρίς κατώφλι

Συντελεστής μείωσης της πιθανότητας εμφάνισης ανά μονάδα δόσης – DDREF = 2

ICRP 103

Η υπόθεση LNT

Πιθανότητα εμφάνισης θανατηφόρου καρκίνου σε χαμηλές δόσεις και χαμηλούς ρυθμούς δόσης (DDREF=2)



Κυτταρικοί μηχανισμοί υπό διερεύνηση

- Genomic instability
- Bystander effects

ικανότητα ακτινοβοληθέντων κυττάρων να επάγουν ακτινικές βλάβες σε γειτονικά κύτταρα που δεν αποτελούν στόχο ακτινοβόλησης (μέσω μεταβίβασης σημάτων

- Adaptive Response

προσαρμοστικότητα, ευαισθητοποίηση και εγρήγορση κυτταρικών μηχανισμών επιδιόρθωσης σε χαμηλούς ρυθμούς δόσεων)

- Hormesis

η απόπτωση των μεταλλαγμένων κυττάρων προς όφελος νέων, υγιών κυττάρων με συμβολή στην αναζωογόνηση ιστού

Βιολογικά αποτελέσματα κατά την κύηση

Στοχαστικά

Πιθανότητα εμφάνισης =0,015% / mSv

(μετά την 3η εβδομάδα από τη σύλληψη)

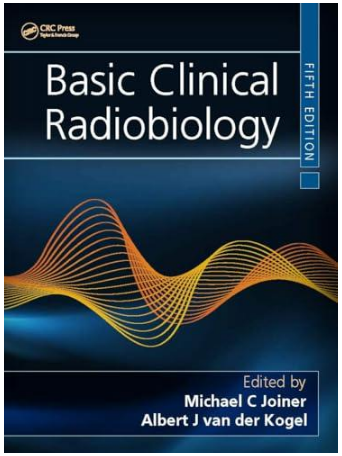
Καθορισμένα κατώφλι 100mSv

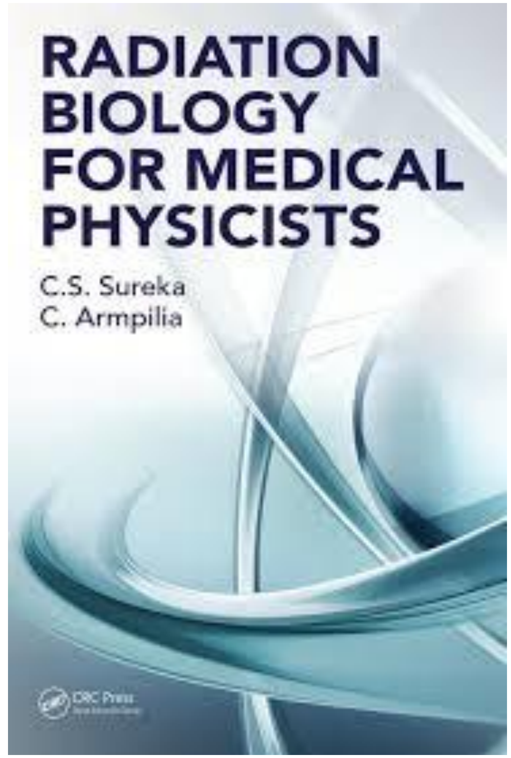
Αποτυχία εμφύτευσης ωαρίου (1-3 εβδομάδες μετά τη σύλληψη)

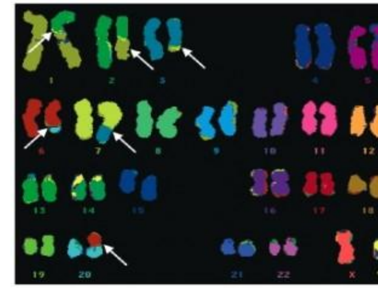
Δυσπλασία οργάνων (3η-8η εβδομάδα μετά τη σύλληψη)

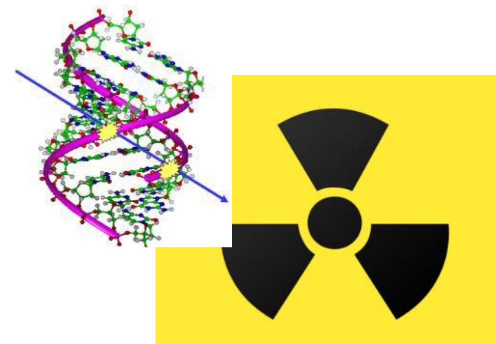
Νευρολογικά αποτελέσματα (8η –τοκετός)

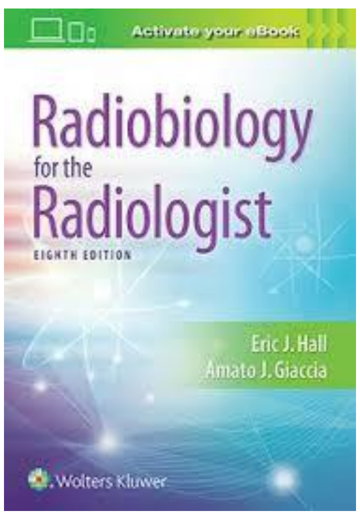
Thank you











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