BASIC PRINCIPLES OF RADIATION THERAPY

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TOPICS COVERED

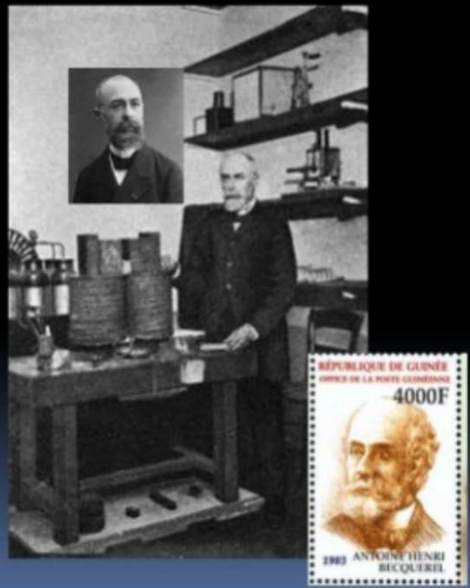
- Introduction
- History
- Basic physics
- Basics of Radiation Physics
- Basics of Radiation biology

History

The study and use of ionizing radiation in medicine started with three important discoveries

1. X rays by Wilhelm Roentgen in 1895
2. Natural radioactivity by Henry Becquerel in 1896
3. Radium-226 by Pierre and Marie Curie in 1898

Wilhelm Conrad Röntgen: Discovery of X-ray (November 8 ,1895)



The Nobel Prize in Physics 1903.......awarded to Antoine Henri Becquerel "in recognition of the extraordinary services he has rendered by his discovery of spontaneous radioactivity"

Courtesy
Dr Ritam Joarder

1898: Discovery of Radium And Polonium

Marie and Pierre Curie shared 1903 Nobel prize in physics with Becquerel

1896 : Controversial claims of Emil Grubbe

"First, that I was the first person exposed to x-rays who received sufficient cumulative effects to develop x-ray dermatitis.

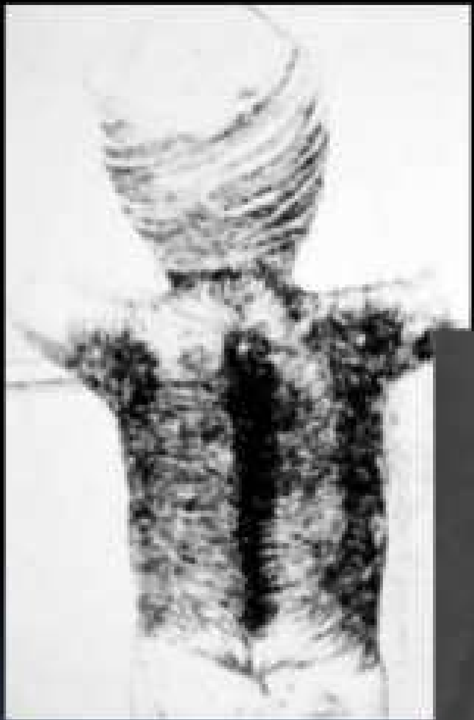
Second, that I was the first person to apply x-rays to pathologic lesions on living human subjects for therapeutic purposes."

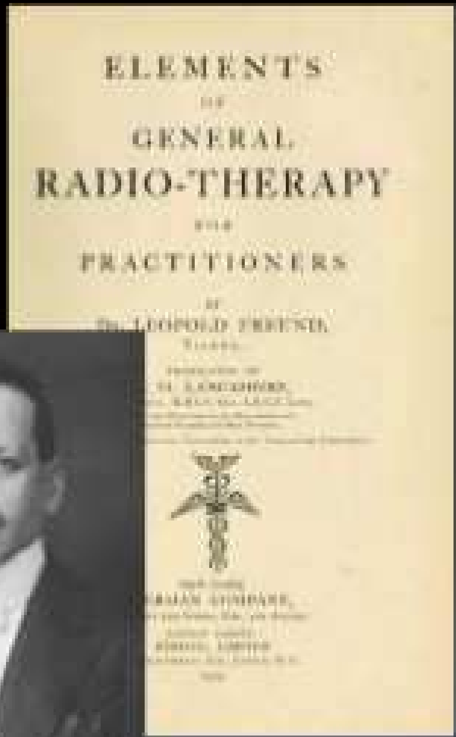
Treated a woman with breast cancer in 1896

1896 : Victor Despeignes

Treated a case of gastric carcinoma with 80 sessions lasting between 15 and 30 min daily

1896 : Therapeutic use of X-rays
1903 : Authored first textbook of radiotherapy





Leopold Freund

A five yr old girl with pigmented hairy naevus all over her back treated and cured , then lived upto 75 yrs.

1899 : Cure of Skin Cancer

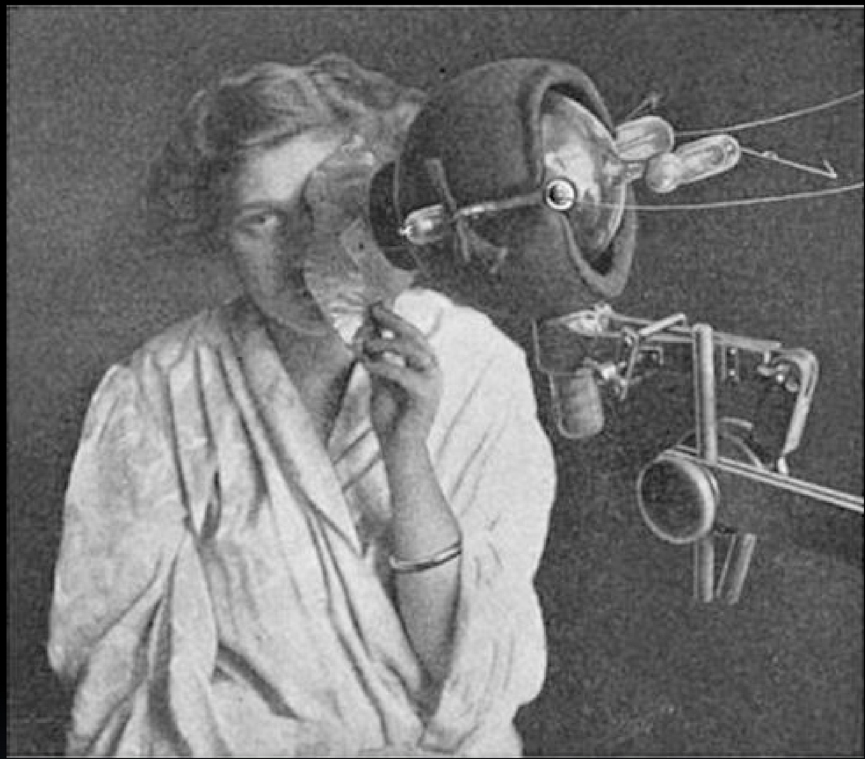
Thor Stenbeck cured BCC of Nose with 100 treatments over 9 months in Stockholm

Tage Sjoegren treated sq. cell epithelioma with 50 treatments over 30 months

1900 : Discovery of γ-rays

Paul Ulrich Villard discovered gamma radiation in 1900, while studying radiation emitted from radium. Villard's radiation was named "gamma rays" by Ernest Rutherford in 1903

Roentgen therapy



X-ray apparatus used for treatment of epithelioma of the face, 1915. The tube is in a localizing shield, and a perforated sheet of metal is securely fashioned to the surface by adhesive plaster.

Radium therapy

Small tubes containing radium salts are strapped to a woman's face to treat what was either lupus or rodent ulcer, 1905.

Telecurietherapy (Radium bomb)

Sluys-Kessler Radium bomb

Failla's Radium bombs

Giaocchino Failla

- Rapid technology advances began in the early 1950s with Cobalt units followed by a linear accelerator few years later

1958 : Computerized treatment planning introduced :J. Laughlin, T. D. Sterling, K. C. Tsien, R. Wood

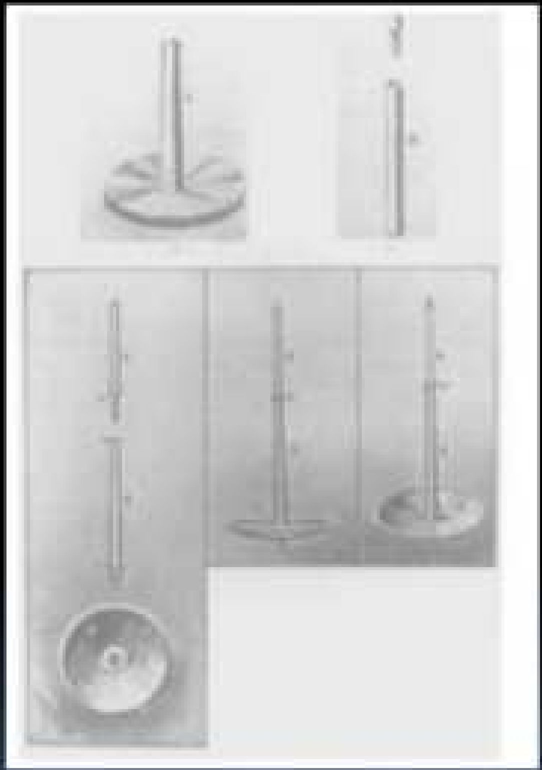
1962 : Electronic portal imaging introduced: S. Benner

1965: Conformal radiation therapy with multileaf collimation introduced : S. Takahashi

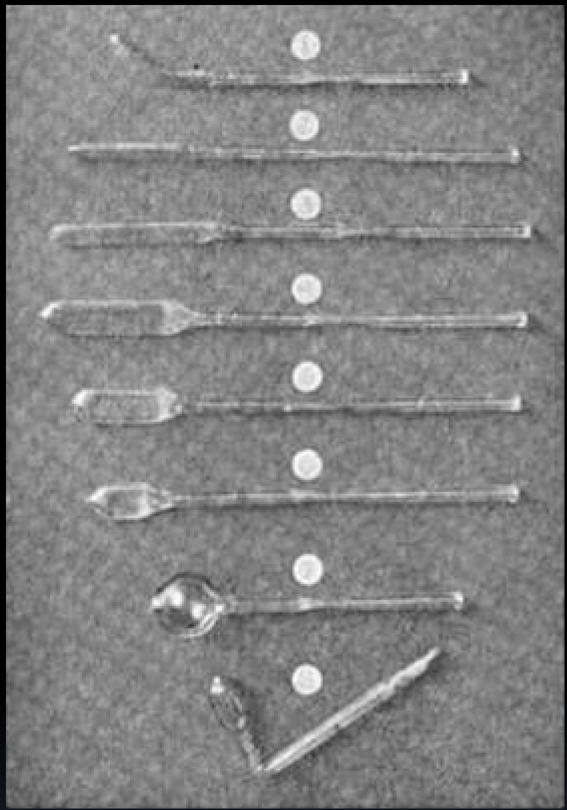
1968: Gamma Knife introduced :Leksell

1969: First commercial treatment planning systems :R. Bentley, J. Cox, W. Powers

1904 : Earliest intracavitary applicator



Used by Wickham and Degrais in Paris from 1904.



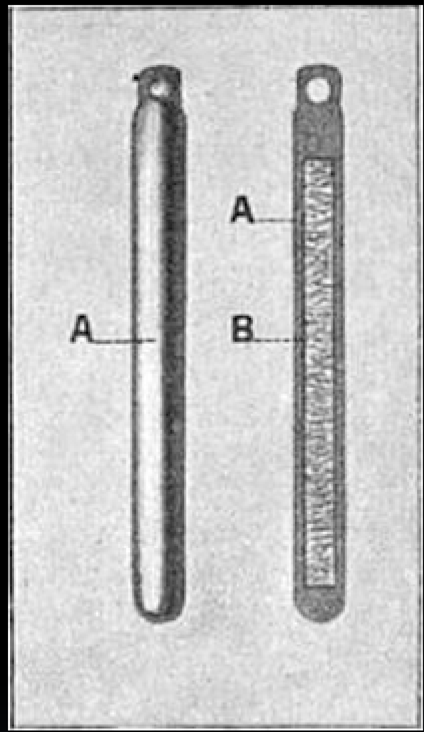


Illustration showing a tube for applying radium salts, 1918

Glass applicators for radium emanation, 1918

1920s : Radium Surface therapy

Radium surface brachytherapy treatment of skin cancer at the Institut Curie, Paris, 1922

1910-24 : Stockholm technique

Dr.Gosta Forssell : Started radium treatment in Ca Cervix in 1912

James Heyman : Published "Stockholm method in radiotherapy of uterine cencer " in 1924

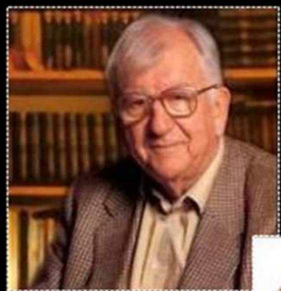
'Intensive, intermittent and intracavitary radium treatment method

1934 : Manchester Dosage System

Ralston Paterson And Herbert M Parker developed Manchester Dosage system for surface applicators of radium in 1934

Later revised by Margaret C Tod and W J Meredith as *Dosage System for Cancer of the Cervix* in 1938

1978 : Paris System



B Pierquin ; A Deutreix et al published Paris system for Interstitial brachytherapy in 1978

Issues

- Lack of rigorous quantitative dosimetry
- Disregard for radiation safety procedures
- Initially, naturally radioactive radium was applied in every situation
- Physicians , non physicians treated

Later the fields of the diagnostic use and the therapeutic use of radiation were separated and a branch of radiation oncology was established

- Radiate is defined as “to spread from the common center” or “to diverge or spread from the common point”
- Radiation is the emission or transmission of energy in the form of waves or particles through space or through a material medium.

- RADIATION ONCOLOGY is that discipline of human medicine concerned with the generation, conservation, and dissemination of knowledge concerning the causes, prevention, and treatment of cancer and other diseases involving special expertise in the therapeutic application of ionizing radiation.
- Radiation therapy is the clinical modality dealing with the use of ionizing radiations in the treatment of patients' with malignant neoplasias (and occasionally benign diseases).

Essential knowledge of

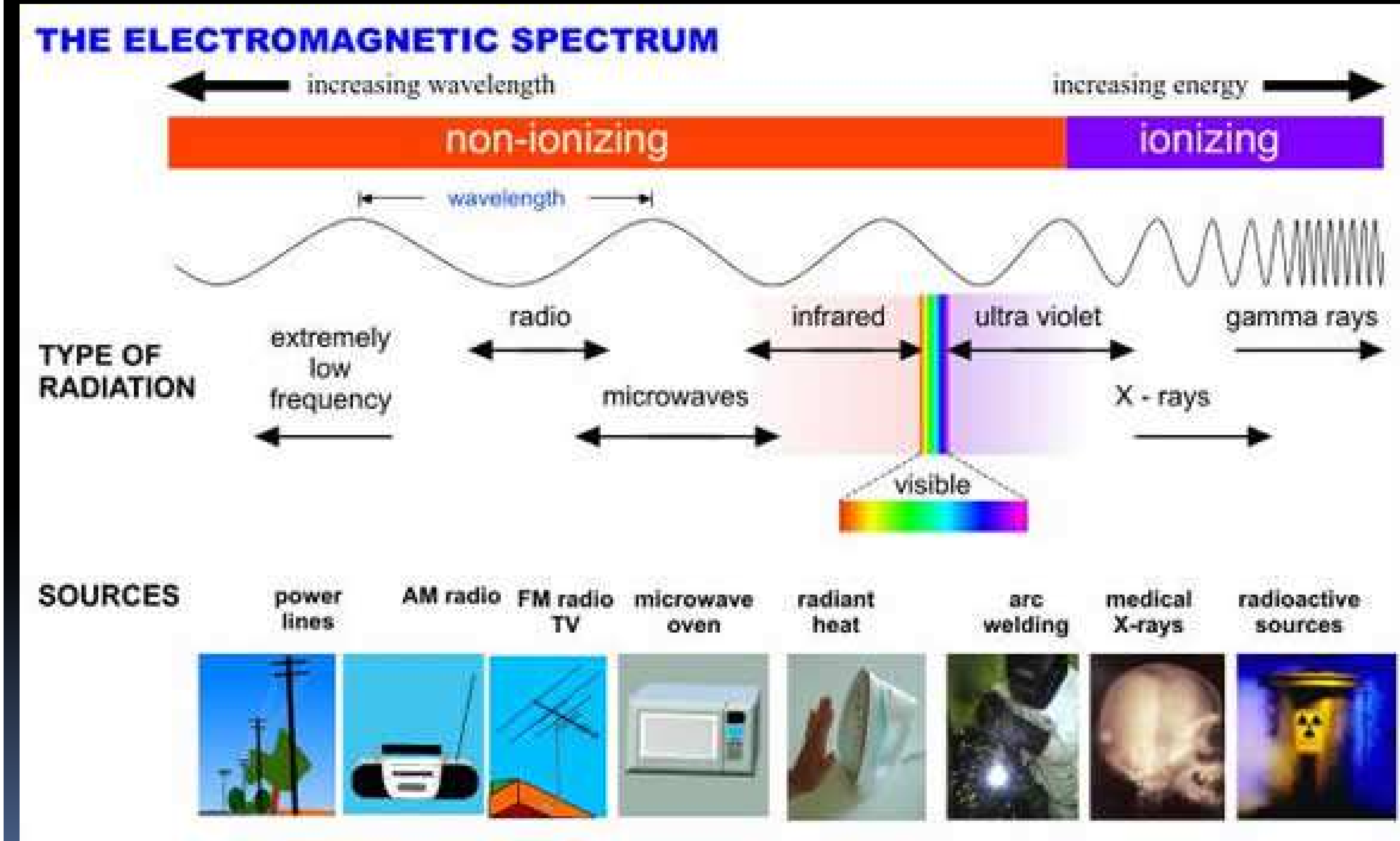
- Radiation physics - physical basis of therapeutic radiation
- Radiation Biology -biologic interaction of radiation with normal and malignant tissue
- Clinical oncology
- Radiation Oncology
- Molecular/cancer biology - fundamental principles

Radiation oncology is concerned with clinical care, scientific research, and the education of professionals within the discipline

Radiation is classified into two main categories depending on its ability to ionize matter.

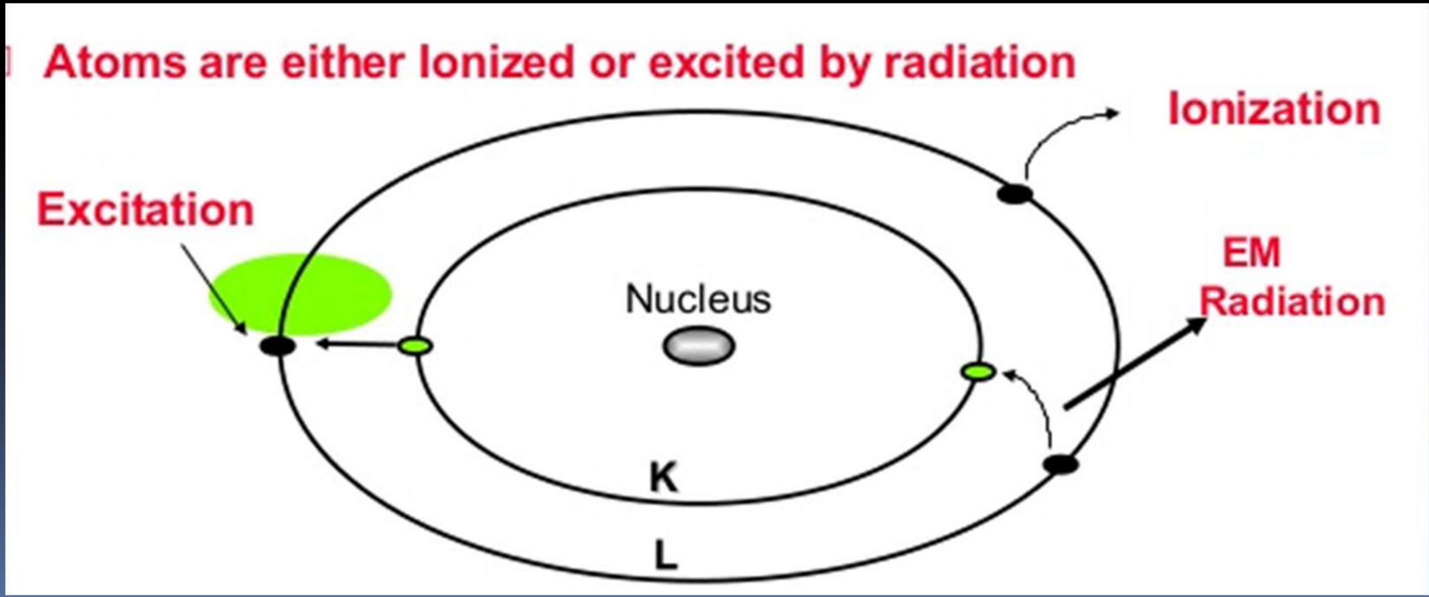
- Nonionizing
- ionizing

Types of Radiation



The absorption of energy from radiation in biologic material may lead to excitation or to ionization.

- Excitation: The raising of an electron in an atom or molecule to a higher energy level without actual ejection of the electron
- Ionization: If the radiation has sufficient energy to eject one or more orbital electrons from the atom or molecule



Types of Ionizing radiation

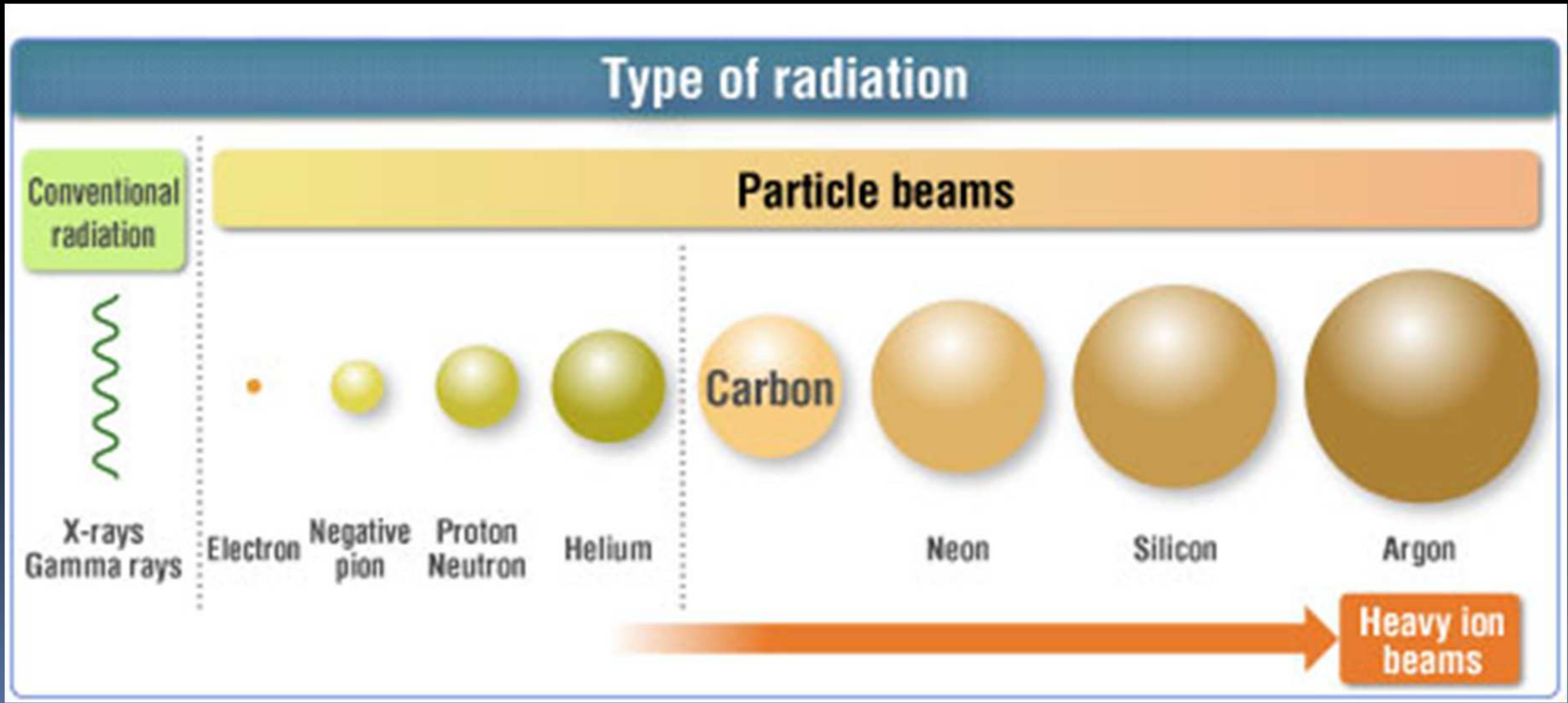
1. Electromagnetic:

X-rays- produced extranuclealry

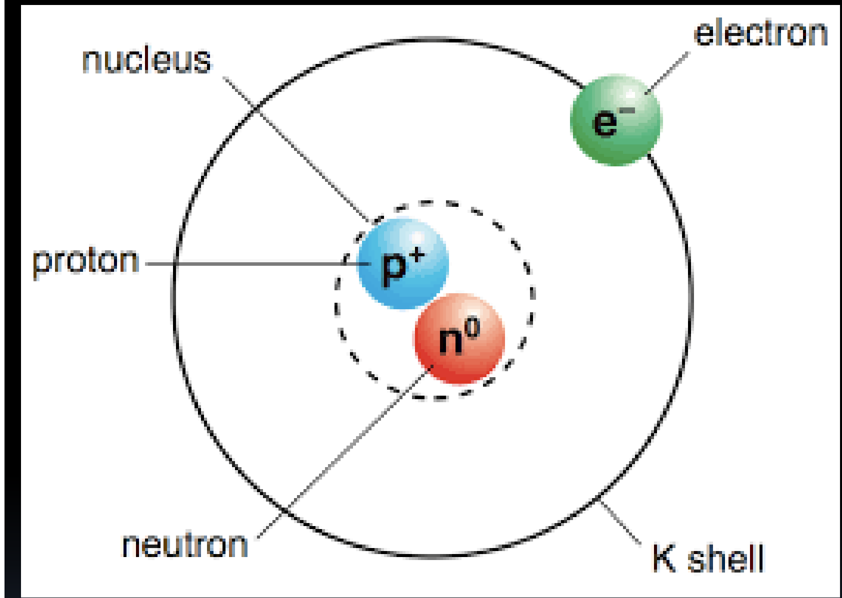
Gamma rays- produced intranuclearly

2. Particulate_- Light charged particles: Electrons

Heavy charged particles.



MATTER



- Matter is made up of atomic and nuclear particles that have interaction and binding energies from 1 to 10 million electron volts (MeV).

The atom has a nucleus consisting of protons and neutrons and a surrounding cloud of orbiting electrons.

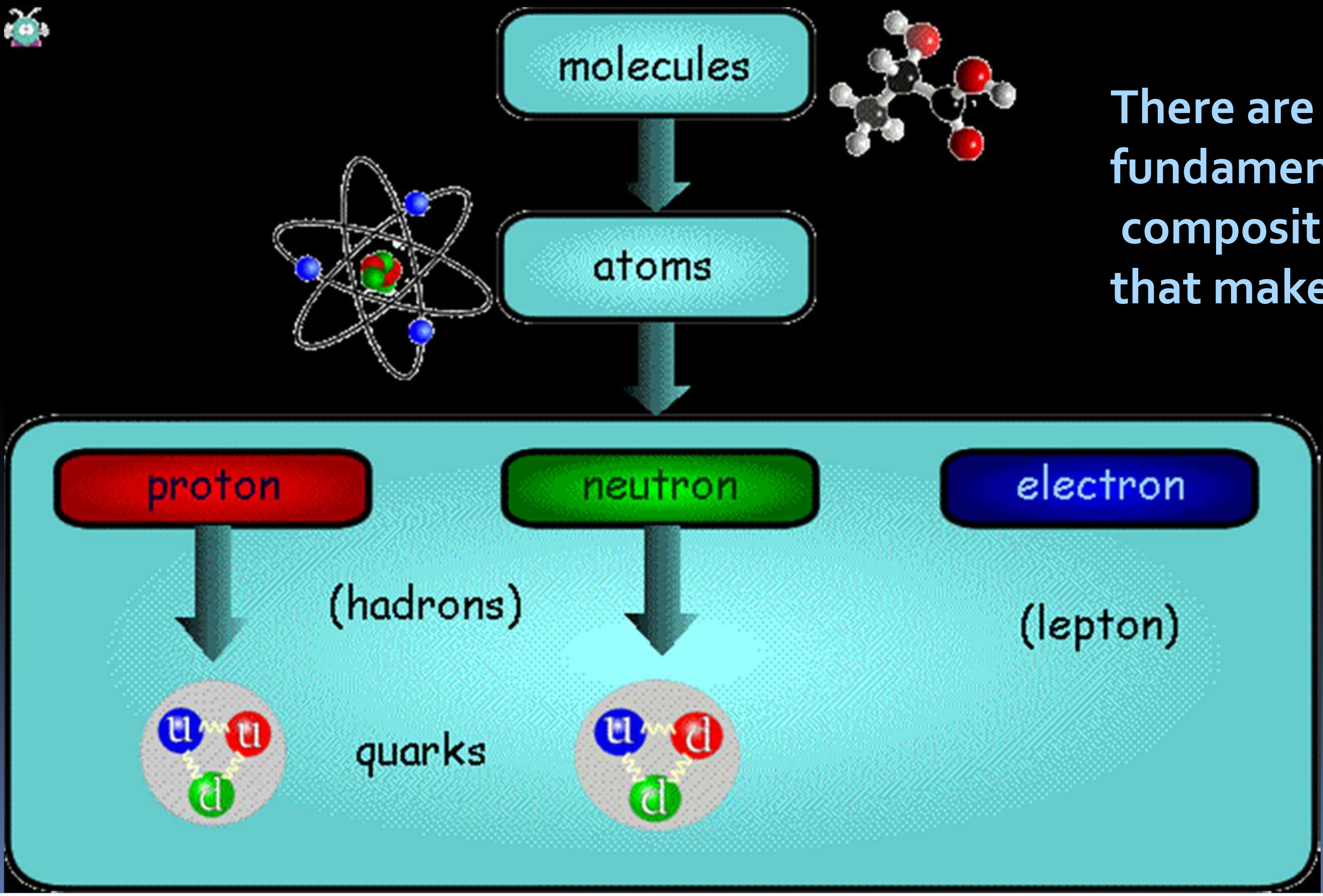
Main characteristics of the atom constituents.

Particle	Symbol	Mass [kg]	Energy [MeV]	Charge
Proton	p	1.672×10^{-27}	938.2	+
Neutron	n	1.675×10^{-27}	939.2	0
Electron	e	0.911×10^{-30}	0.511	–

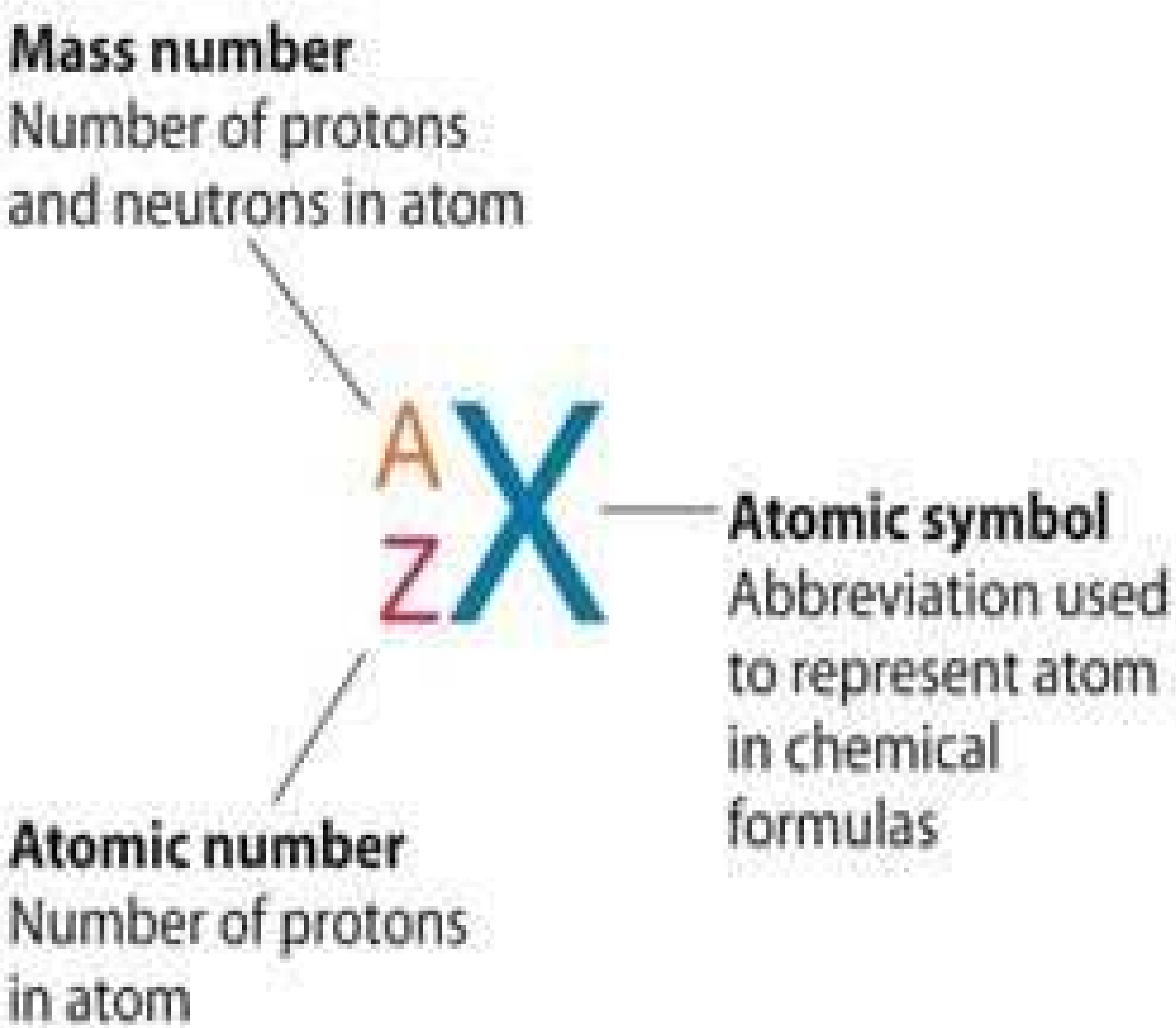
- Besides, other particles which exist include neutrinos, pions, muons and others

Particles are classified by their mass as leptons or hadrons

- Leptons: are fundamental or elementary particles which include electrons and neutrino and can not be divided
- Hadrons: Protons, neutrons and other hadrons are made up of fundamental particles called quarks

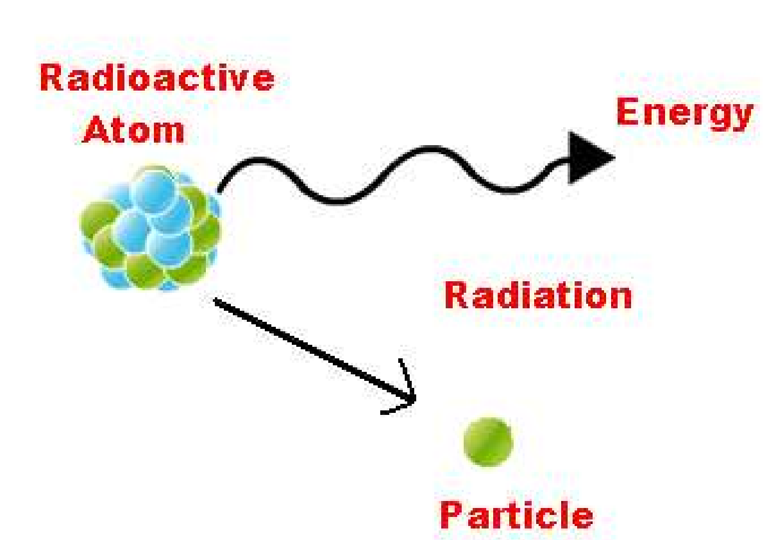


There are about 170 fundamental and composite particles that make up matter.


Mass number
Number of protons
and neutrons in atom
A
Z
X
Atomic symbol
Abbreviation used
to represent atom
in chemical
formulas
Atomic number
Number of protons
in atom

RADIOACTIVITY

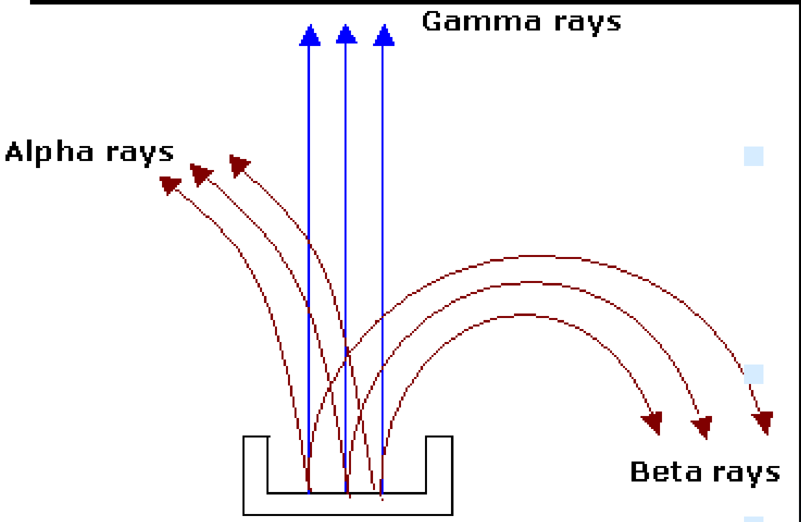
- The numerical combination of protons and neutrons in most nuclides is such that the nucleus is quantum mechanically stable and the atom is said to be stable, i.e., not radioactive
- If there are too few or too many neutrons, the nucleus is unstable and the atom is said to be radioactive.



The property of emission of radioactive rays from radioactive elements is termed as radioactivity

- Unstable nuclides undergo radioactive transformation, a process in which a neutron or proton converts into the other and a beta particle is emitted, or else an alpha particle is emitted.

  Each type of decay is typically accompanied by the emission of gamma rays.
- These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity.



- If the radiations given out by a radioactive substance are subjected to an electric field perpendicular to their path, they separate into three constituents.
- Those which turn towards the negative plate are the positively charged alpha particles.
- Those, which turn towards the positive plate, are the negatively charged beta particles.
- Those, which pass un deviated, are the uncharged gamma radiations.
- Further investigation has shown that an alpha ray is a stream of helium nuclei, a beta ray is a stream of electrons and a gamma ray is an electromagnetic radiation whose frequency is higher than that of X-rays.

- Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide.
- The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products

RADIOACTIVE DECAY MODES

The most important radioactive decay modes are:

- alpha (α) decay,
- β+ decay, β– decay,
- electron capture (ε),
- and isomeric transition (IT) which is also called internal conversion (IC),
- spontaneous fission (sf),
- proton (p) decay,
- neutron (n)decay and special mixed beta-decay processes.

Most of the decay processes are followed by gamma emissions.

In general there are two classifications of radioactivity and radionuclides:

Natural:

- Naturally occurring radioactive material (NORM) exists in nature
- No additional energy is necessary to place them in an unstable state.
- Property of some naturally occurring, usually heavy elements, that are heavier than lead.
- Radium -226

Artificial (man-made).

- Artificial radioactive atoms are produced either as a by-product of fission of uranium or plutonium atoms in a nuclear reactor or by bombarding atoms with particles (such as neutrons, protons, or heavy nuclei) at high velocity via a particle accelerator.
- Cobalt-60, Phosphorus-32

1934 : Artificial Radioactivity

Irène and Frédéric Joliot Curie shared Noble prize in Chemistry 1935

Half-Life and Activity

- For any given radionuclide, the rate of decay is a first-order process that is constant, regardless of the radioactive atoms present and is characteristic for each radionuclide.

- The process of decay is a series of random events; temperature, pressure, or chemical combinations do not affect the rate of decay.

- For any pure radioactive substance, the rate of decay is usually described by its radiological half-life, $t_{1/2}$, i.e., the time it takes for a specified source material to decay to half its initial activity.
- The specific activity is an indirect measure of the rate of decay, and is defined as the activity per unit mass or per unit volume. The higher the specific activity of a radioisotope, the faster it is decaying.

- The mean or average life is the average lifetime for the decay of radioactive atoms.

$$A = A_0 e^{-\lambda t}$$

$$T_{1/2} = \frac{0.693}{\lambda}$$

$$T_a = 1.44\ T_{1/2}$$

Units of radioactivity

- **Curie:** corresponds to activity of 1 gram of Radium 226
- Original unit
- 1 Curie = 3.7×10^{10} radioactive decay per second
- SI unit is Becquerel
- 1 Bq = 1 radioactive decay per second

  = 2.703×10^{-11} Ci
- Also as a measure of quantity of radioactive material

  i.e. the no. of atoms that will produce 1 Ci of radiation is

$$N = \frac{3.7 \times 10^{10}}{\lambda}$$

- 1 gram of Cobalt 60 prod 44 TBq of radioactivity

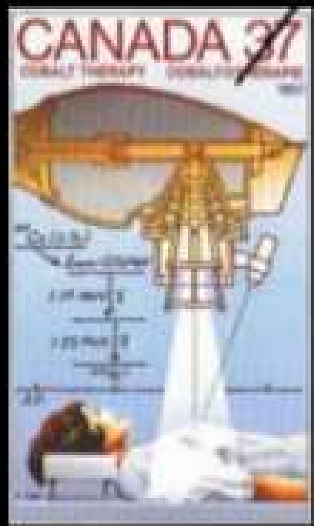
  883μg of ^{60}Co produces 1 Ci of radiation

1938 : Discovery of Co^{60} isotope

Glenn T Seaborg

Glenn T Seaborg shared Noble prize in Chemistry 1951 with Edwin M McMillan for discovery of transuranium elements

1951 : Cobalt Bomb (H.E.Johns)



First Cobalt 60 machine

in Saskatoon ,Canada

The first cobalt machine in Italy, installed in Borgo Valsugana in 1953.

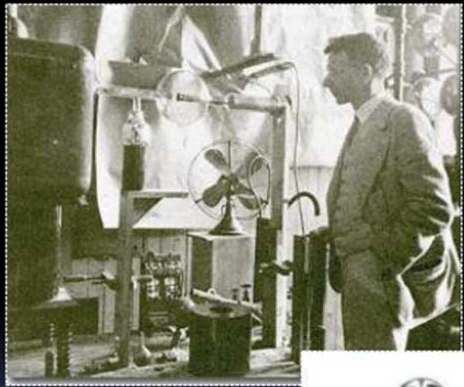
ELECTRICAL (ARTIFICIAL) RADIATION SOURCES

Although radioactive decay of naturally occurring radionuclides has a probabilistic character their applications are limited by

- The difficulties in maintaining radioactive sources
- Their lack of purity for chemical processing
- Low intensity
- Poor geometry
- sometimes uncontrolled broad range of energies.
- Radioactive sources can be expensive and require replenishment.

This makes electrical (artificial) sources, beams of accelerated particles, produced using different physical phenomena and techniques, very attractive. These particles may additionally produce beams of secondary particles.

1913: Hot Cathode tube ~ W D Coolidge



- Peak voltage of 140 Kv with 5 mAmp current
- Max. dose at skin with rapid dose fall-off with depth inside tissue

1923 : Grenz Ray therapy (Gustav Bucky)

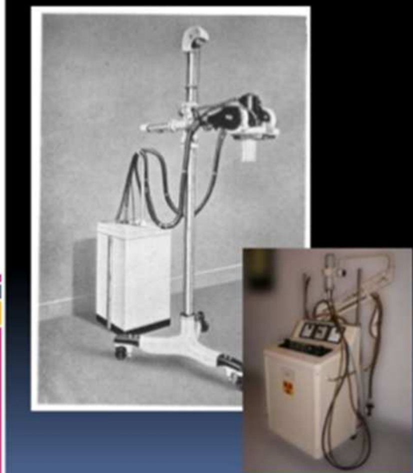
- < 20kV Voltage
- Filtration of 1.0 mm Al
- Used to treat skin lesions

Contact Therapy Or Chaoul Therapy

- 40-50 kV potential
- 2mA current
- SSD 2cm or less
- 0.5-1.0mm thickness Al filter
- Rapidly decreasing depth dose in tissue

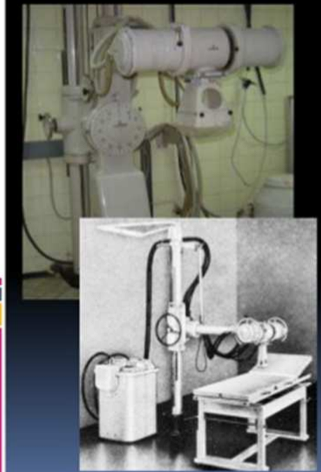
Papillon technique for Superficial Rectal Cancer

Superficial Therapy



- 50 – 150 Kv Voltage
- 1- 6mm Al filtration
- 1- 8 mm Al HVL
- 15- 20 cm SSD
- Operated at 5- 8 mA current

1930s: Orthovoltage therapy or Deep Therapy (Sieman's Stabilapan)



- ❑ 150-500 Kv voltage
- ❑ 10-20 mA current
- ❑ 50 cm SSD
- ❑ HVL 1-4mm Cu

❑ Disadvantage :
High skin dose
Increased absorbed dose in bone
Increased Scattering

1929 : Invention of Cyclotron

Ernest Lawrence received Noble prize in Physics 1939

1931 : Van de Graaff Generator (MIT)

40 feet high Electrostatic device capable of operating at 5,000,000 volts

Robert van de Graaff

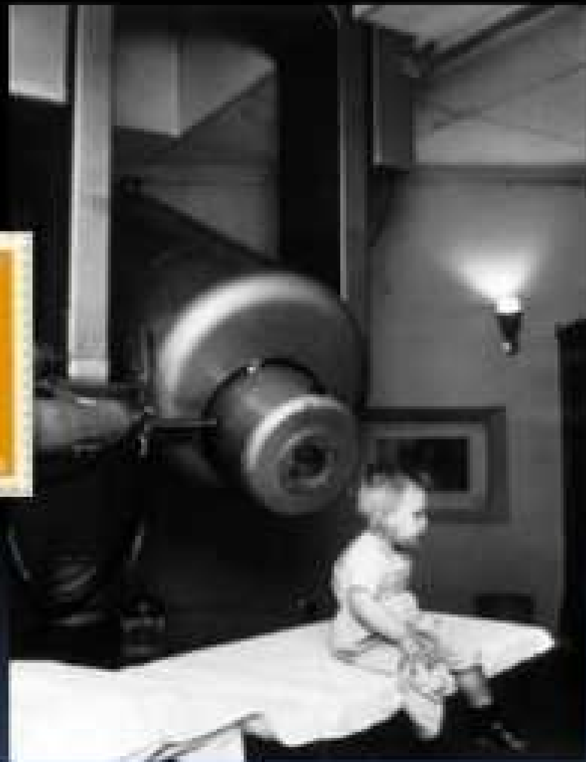
2 MeV Clinical Van de Graaff X-ray machine

1940 : Betatron (Donald W Krest)

20 MeV Betatron created by Krest in University of Ilionis , USA (originally planned by Achen Widroe)

1953: First Linear Accelerator
1956: First pt treated with LINAC

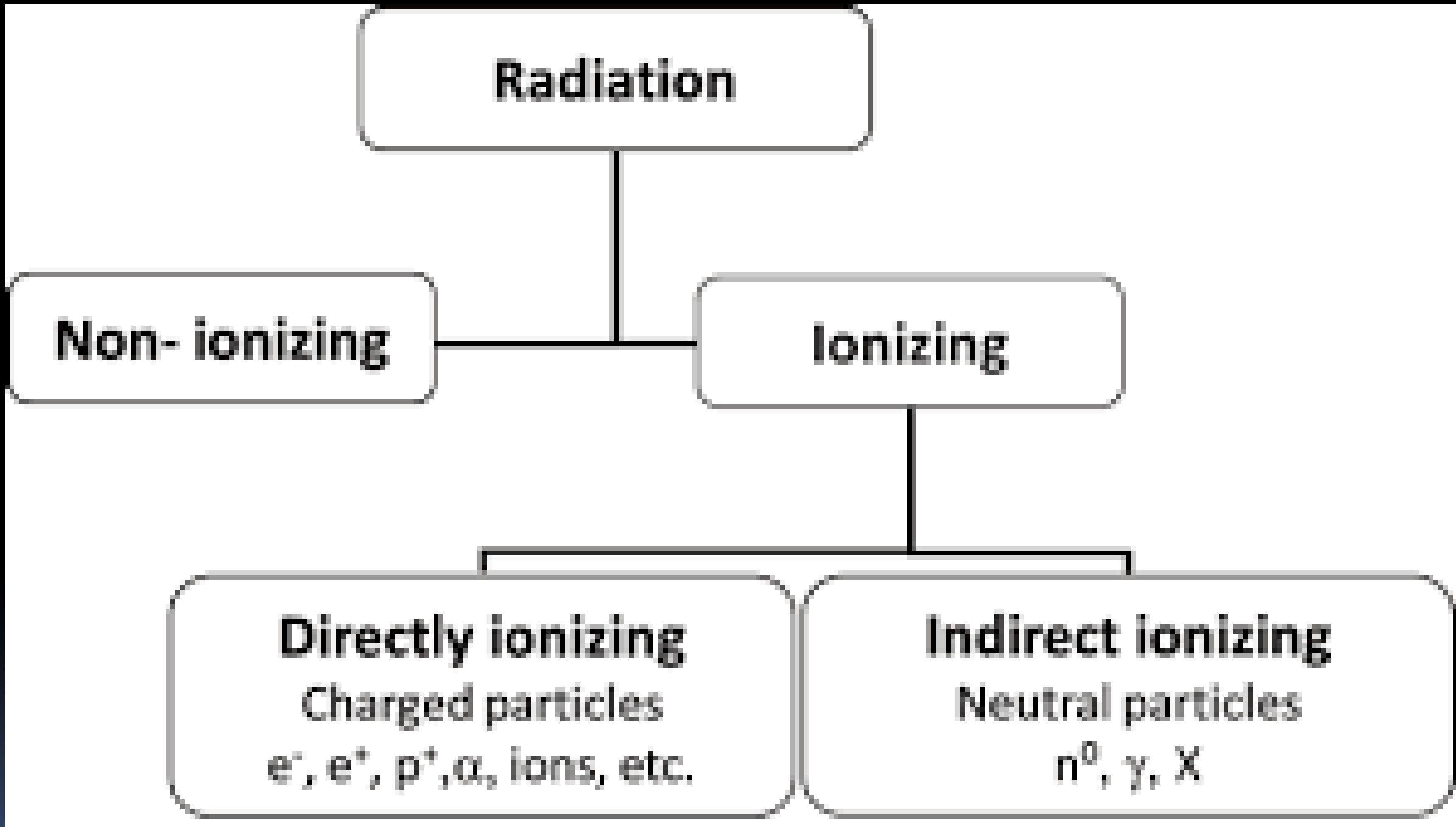
Henry Kaplan



Gordon Issac,2yr old pt
of B/I Retinoblastoma

Events took place after irradiation of matter

- Physical events: Result in ionizations and Radiation dose, is over in 10^{-15} second
- Chemical events: ionization result in broken atomic and molecular bonds or chemical changes- longer because the lifetime of the DNA radicals is about 10^{-5} second
- Biologic events- the biology takes hours, days, or months for cell killing, years for carcinogenesis, and generations for hereditary damage.
- Clinical events


Radiation
Non- ionizing
Ionizing
Directly ionizing
Charged particles
e^-, e^+, p^+, α, ions, etc.
Indirect ionizing
Neutral particles
n^0, γ, X

- Directly ionizing radiation: deposits energy in the medium through direct Coulomb interactions between the directly ionizing charged particle and orbital electrons of atoms in the medium.
- Indirectly ionizing radiation (photons or neutrons): deposits energy in the medium through a two step process:
  - In the first step a charged particle is released in the medium (photons release electrons or positrons, neutrons release protons or heavier ions);
  - In the second step the released charged particles deposit energy to the medium through direct Coulomb interactions with orbital electrons of the atoms in the medium.

Types of photon interaction

Photons may undergo various possible interactions with the atoms of an attenuator; the probability or cross-section for each interaction depends on the

- Energy hn of the photon
- On the atomic number Z of the attenuator.

Types of targets

Photon orbital electron interaction

- With bound electron
    - Photoelectric effect
    - Rayleigh scattering
- With free electrons
    - Compton scattering
    - Thomson scattering
- With coulomb field of electron
    - Triplet production

Photon nucleus interaction

- With nucleus directly
  - Photodisintegration
- With coulomb field of nucleus
  - Pair production

During the interaction the photon may completely disappear or it may be scattered coherently

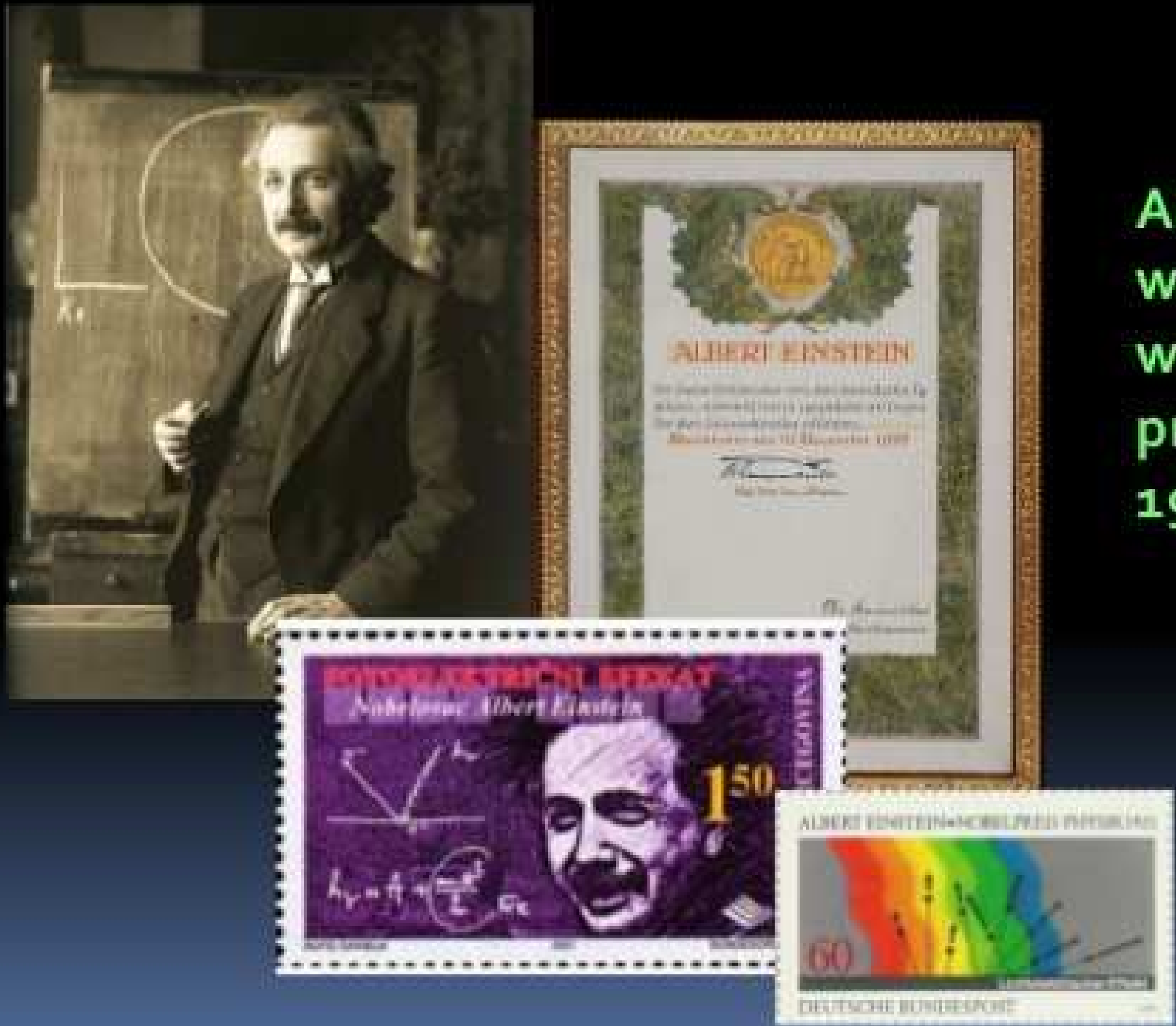
Complete absorption of photon

- Photoelectric effect
- Pair production
- Triplet production
- Photodisintegration

Photon scattering

- Thomson scattering
- Rayleigh scattering
- Compton scattering

1903 : Law of the Photo electric effect



Albert Einstein was awarded with Noble prize in Physics 1921

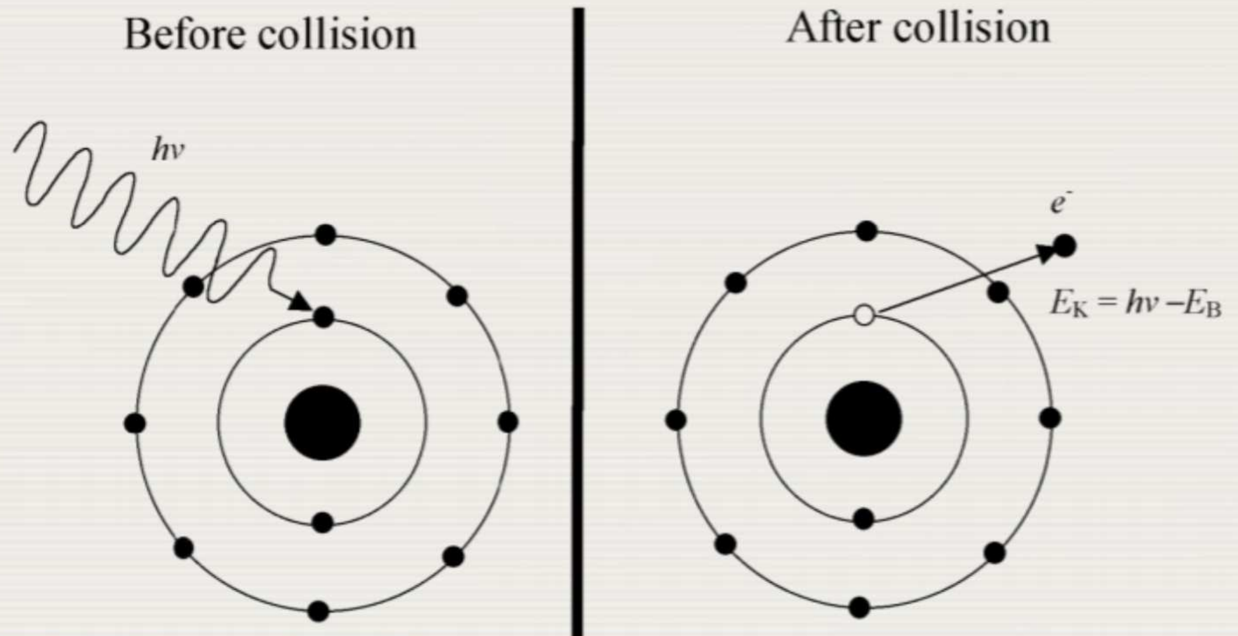
Photoelectric effect

- In this process, an incoming photon undergoes a collision with a tightly bound electron.
- The photon transfers practically all of its energy to the electron and ceases to exist.
- The electron departs with most of the energy from the photon and begins to ionize surrounding molecules.
- This interaction depends on the energy of the incoming photon, as well as the atomic number of the tissue; the lower the energy and the higher the atomic number, the more likely that a photoelectric effect will take place.

- An example of this interaction in practice can be seen on a diagnostic x-ray film. Since the atomic number of bone is 60% higher than that of soft tissue, bone is seen with much more contrast and detail than is soft tissue.

- The energy range in which the photoelectric effect predominates in tissue is about 10–25 keV.

- A photon with energy $h\nu$ interacts with a K-shell orbital electron.
- Orbital electron is emitted from the atom as a photoelectron.



1922: Discovery of Compton Scattering

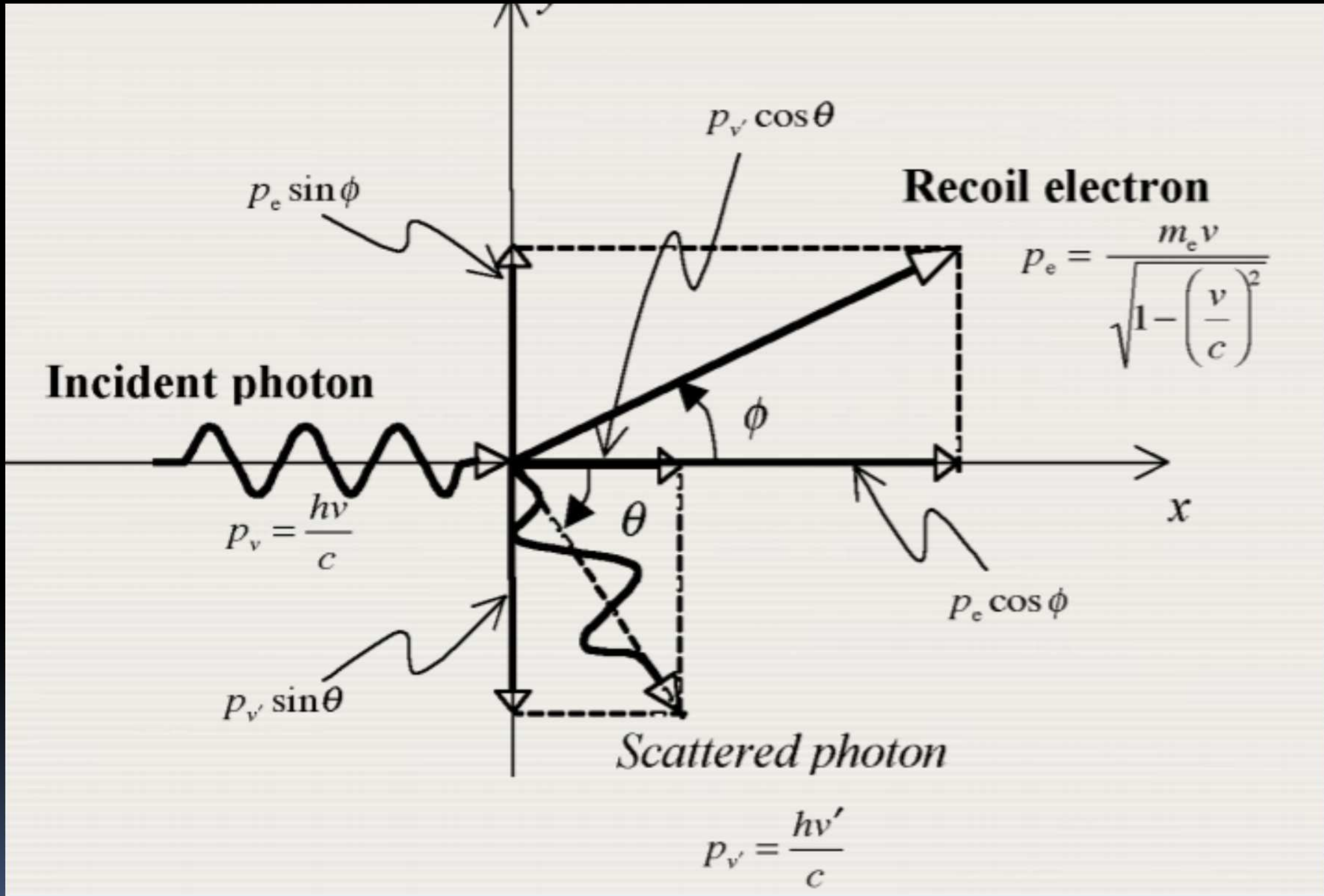
Received Noble Prize

in Physics 1927

Compton effect

- The Compton effect is the most important photon-tissue interaction for the treatment of cancer.
- In this case, a photon collides with a "free electron," ie, one that is not tightly bound to the atom.
- Unlike the photoelectric effect, in the Compton interaction both the photon and electron are scattered. The photon can then continue to undergo additional interactions, albeit with a lower energy. The electron begins to ionize with the energy given to it by the photon.
- The probability of a Compton interaction is inversely proportional to the energy of the incoming photon and is independent of the atomic number of the material.

- When one takes an image of tissue using photons in the energy range in which the Compton effect dominates (~25 keV–25 MeV), bone and soft-tissue interfaces are barely distinguishable. This is a result of the atomic number independence.
- The Compton effect is the most common interaction occurring clinically, as most radiation treatments are performed at energy levels of about 6–20 MeV.

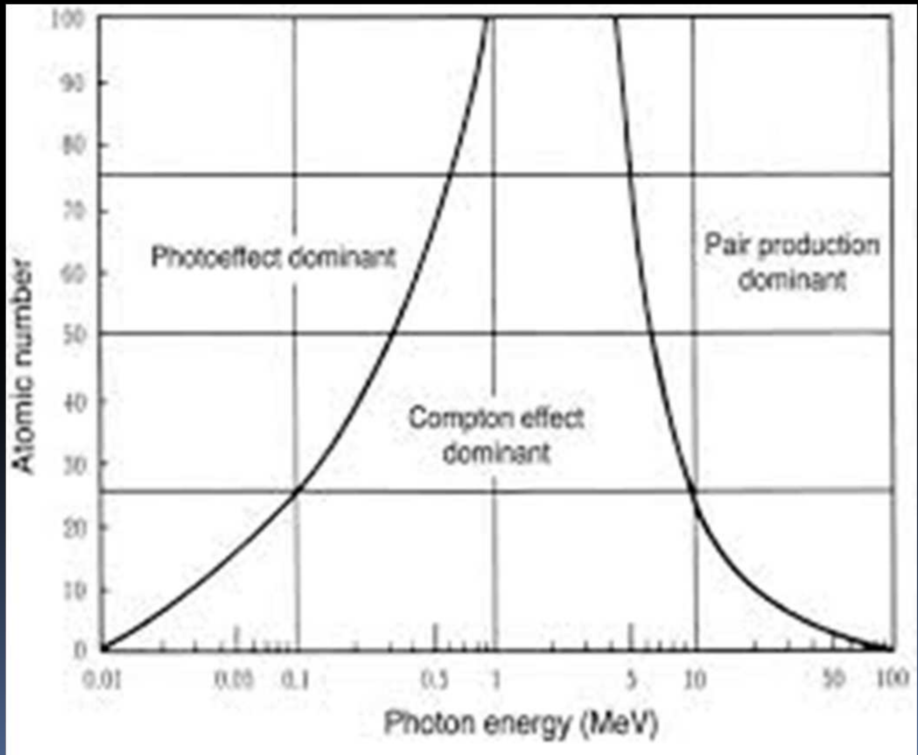


$p_{v'} \cos\theta$
Recoil electron
$p_e \sin\phi$
$p_e = \frac{m_e v}{\sqrt{1-\left(\frac{v}{c}\right)^2}}$
Incident photon
ϕ
$p_v = \frac{hv}{c}$
θ
x
$p_e \cos\phi$
$p_{v'} \sin\theta$
Scattered photon
$p_{v'} = \frac{hv'}{c}$

Pair production

- In pair production the photon disappears and an electron–positron pair with a combined kinetic energy is produced in the nuclear Coulomb field.
- Since mass is produced out of photon energy in the form of an electron–positron pair, pair production has an energy threshold (minimum photon energy required for the effect to happen) = 1.02 MeV.
- The probability for pair production is zero for photon energies below the threshold energy and increases rapidly with photon energy above the threshold.

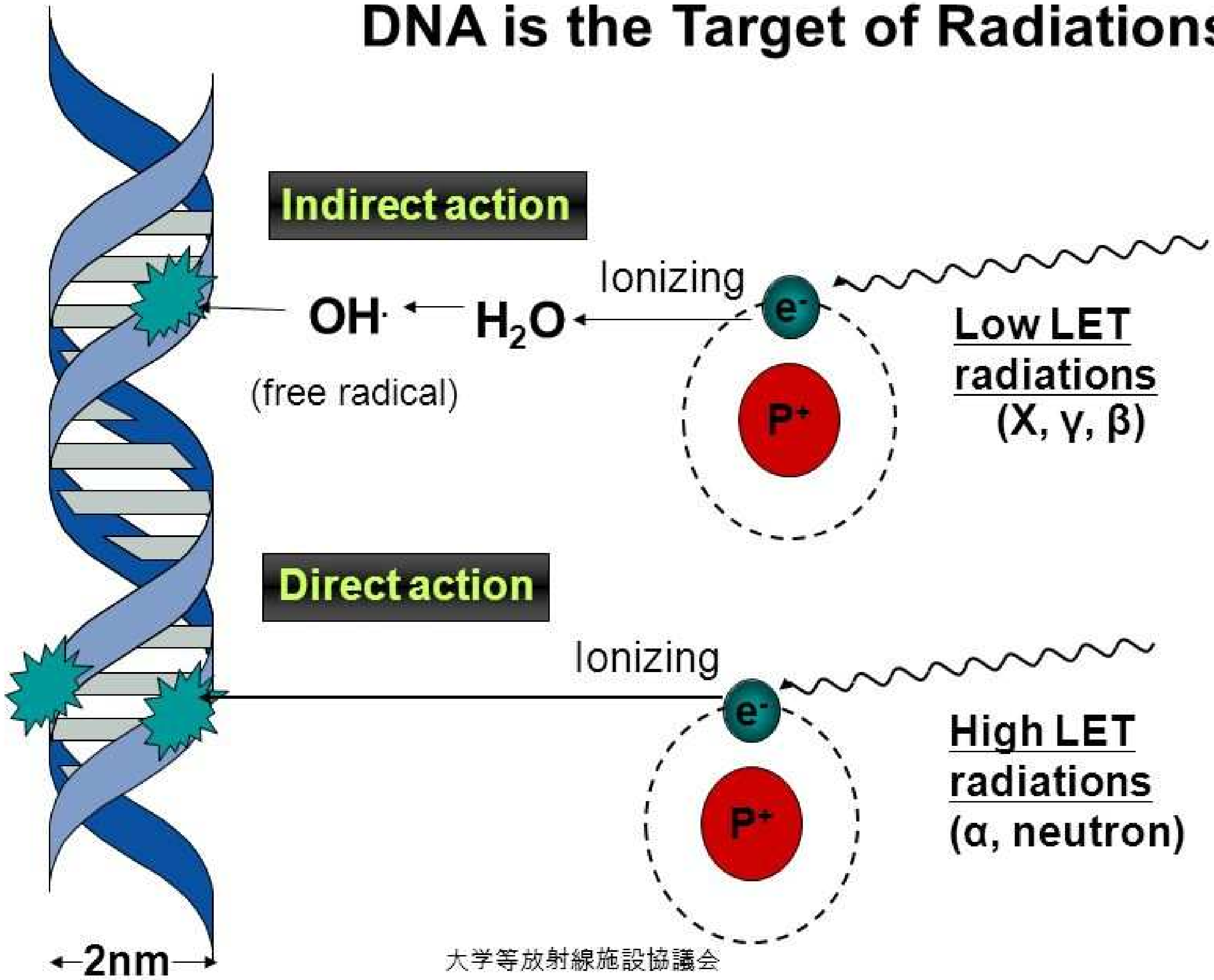
- In general, the photoelectric effect predominates at low photon energies, the Compton effect at intermediate energies and pair production at high photon energies.



Biological basis: Direct and indirect action

- Biologic effects of x-rays may be caused by direct action (the recoil electron directly ionizes the target molecule) or indirect action (the recoil electron interacts with water to produce a hydroxyl radical, which diffuses to the target molecule).

DNA is the Target of Radiations



大学等放射線施設協議会

Direct action in cell damage by radiation

- In direct action the radiation interacts directly with the critical target in the cell.
- The atoms of the target itself may be ionized or excited through Coulomb interactions, leading to the chain of physical and chemical events that eventually produce the biological damage.
- Direct action is the dominant process in the interaction of high LET particles and neutrons with biological material.

Indirect action in cell damage by radiation

- In indirect action the radiation interacts with other molecules and atoms (mainly water, since about 80% of a cell is composed of water) within the cell to produce free radicals, which can, through diffusion in the cell, damage the critical target within the cell.
- In interactions of radiation with water, short lived yet extremely reactive free radicals such as H_2O^+ (water ion) and OH•(hydroxyl radical) are produced. The free radicals in turn can cause damage to the target within the cell.
- About two thirds of the biologic damage by x-rays is caused by indirect action.

- DNA radicals produced by both the direct and indirect action of radiation are modifiable with sensitizers or protectors.
- DNA lesions produced by high-LET radiations involve large numbers of DNA radicals. Chemical sensitizers and protectors are ineffective in modifying such lesions.

Irradiation of a cell will result in one of the following nine possible outcomes:

- No effect..
- Division delay: The cell is delayed from going through division.
- Apoptosis: The cell dies before it can divide or afterwards by fragmentation into smaller bodies, which are taken up by neighbouring cells.
- Reproductive failure: The cell dies when attempting the first or subsequent mitosis.
- Genomic instability: There is a delayed form of reproductive failure as a result of induced genomic instability.

- Mutation: The cell survives but contains a mutation.
- Transformation: The cell survives but the mutation leads to a transformed phenotype and possibly carcinogenesis.
- Bystander effects: An irradiated cell can send signals to neighbouring unirradiated cells and induce genetic damage in them.
- Adaptive responses: The irradiated cell is stimulated to react and become more resistant to subsequent irradiation.

Cell Death

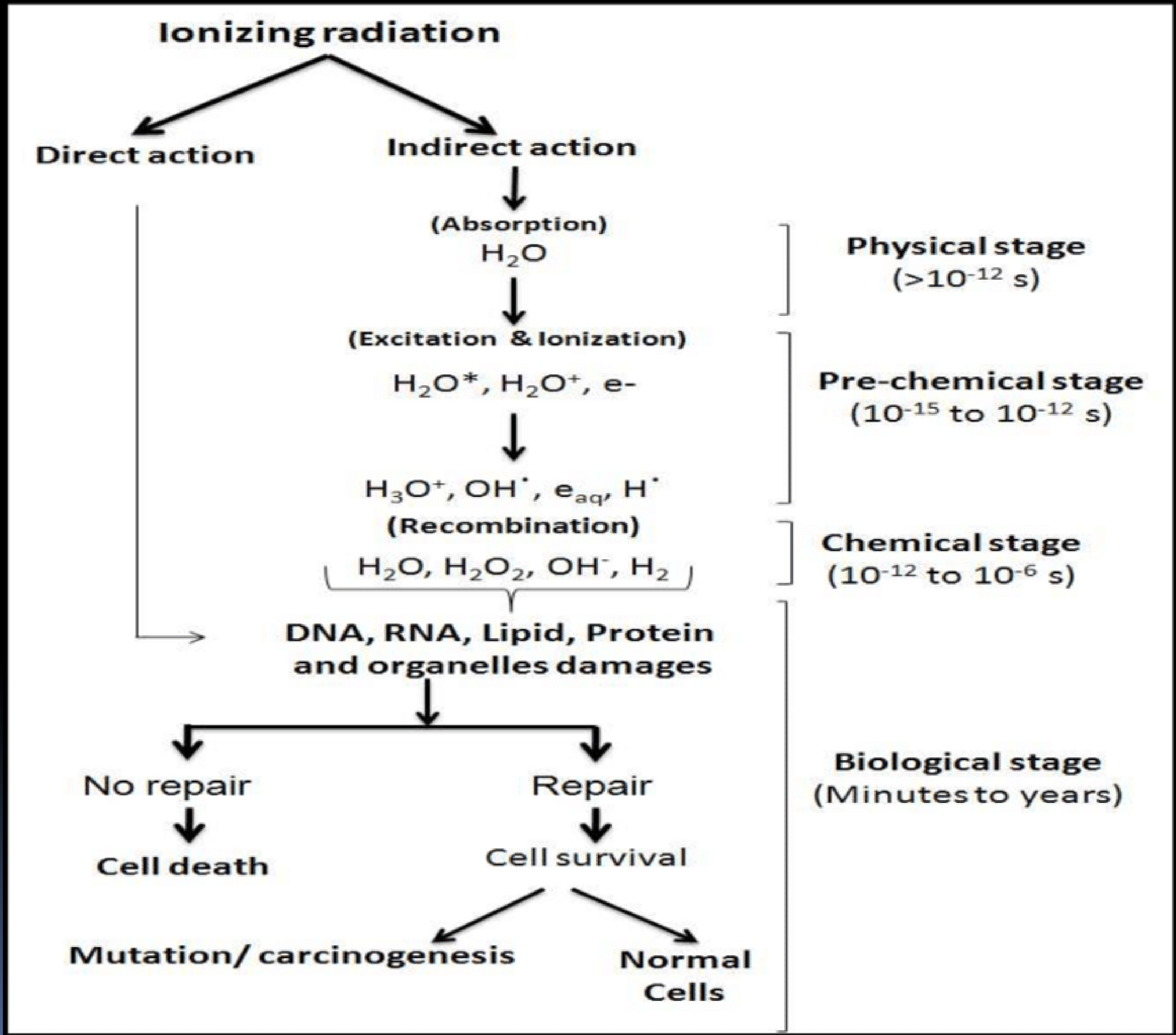
- Among the functional consequences of ionizing radiation, cell death is the most important one for radiation oncology. Cells can die in several ways by
- apoptosis, mitotic catastrophe, senescence, necrosis, necroptosis, and autophagy
- Most important for the effect of radiotherapy of solid tumors is the *mitotic catastrophe, which is caused by lethal chromosome* damage.

- Neoplastic hematopoietic or lymphatic cells often die from radiation-induced *Apoptosis via the intrinsic,caspase9–dependent pathway.*
- *Radiation-induced senescence plays an important role for development of normal tissue damage—for example, fibrosis, but occurs also in response to nonlethal stress as in tumor cells. Cells survive and are metabolically active but lose their replicative potential.*

- *Necrosis is an unregulated process of cell* destruction by the release of intracellular components. This is usually the consequence of pathophysiologic conditions such as ischemia and inflammation.
- Necroptosis, the prototype of regulated necrosis, is a caspase-indepenform of programmed cell death and kills apoptosis-deficient cells.
- Autophagy is a form of non apoptotic and nonnecrotic cell death that is related to lysosomal degradation of proteins and cell organelles that are then utilized for the production of new cells.

- By far the most important target for the biologic effects of ionizing radiation is the DNA
- Exposure of cells to about 1 Gy causes approximately 3,500 DNA injuries, 1,500 to 2,500 of which are damaged bases, 1,000 single-strand breaks (SSBs), 40 DSBs

- Importantly, it also has to be considered that different types of radiation treatment can cause different extent of damage to the DNA in a tumor cell.
- Low LET IR generates about 30% of DNA DSBs of this form, whereas for *α-particles, it is >90%.*
- Besides effects on DNA, ionizing radiation also evokes biologically important responses on proteins (e.g., transmembrane receptors) and on lipids.


Ionizing radiation
Direct action
Indirect action
(Absorption)
H2O
(Excitation & Ionization)
H2O*, H2O+, e-
H3O+, OH˙, eaq, H˙
(Recombination)
H2O, H2O2, OH-, H2
DNA, RNA, Lipid, Protein and organelles damages
No repair
Cell death
Repair
Cell survival
Mutation/ carcinogenesis
Normal Cells
Physical stage
(>10-12 s)
Pre-chemical stage
(10-15 to 10-12 s)
Chemical stage
(10-12 to 10-6 s)
Biological stage
(Minutes to years)

- For all IRs, the density is especially high at the end of the electron tracks.
- For high LET radiations, such as *a-particles, ionization is dense all along and close to tracks,* which number about 4 per Gy.

Linear Energy Transfer and Relative Biologic Efficiency

- The rate at which a charged particle, such as an electron or proton, deposits its energy along its track is described as its LET
- The heavier the particle, the higher its LET.
- Thus, electrons are predominantly low LET, protons slightly higher, neutrons even higher and heavily charged particles the highest LET of clinically used radiations.

- *As the LET of radiation increases, the ability of the radiation to produce biological damage i.e. its biologic efficiency (RBE) also increases., although the increase is most rapid and peaks around 100 to 150 kv/µm.*

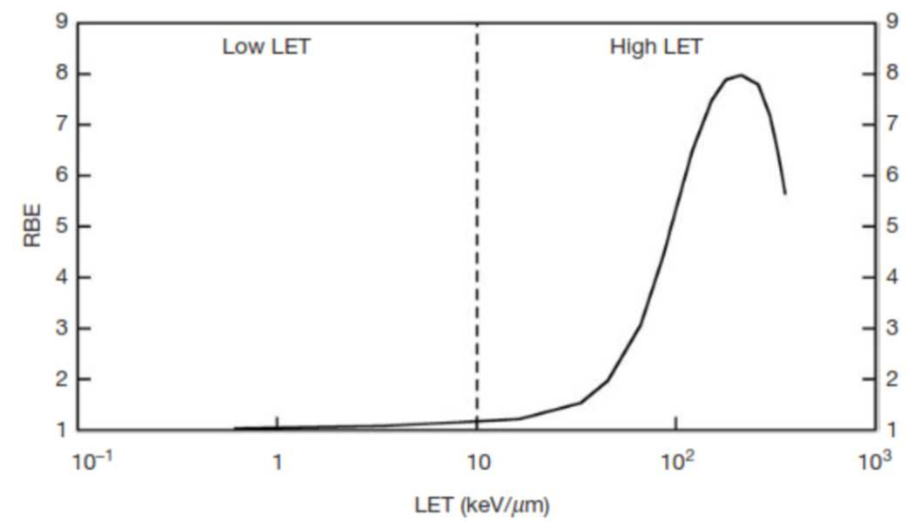
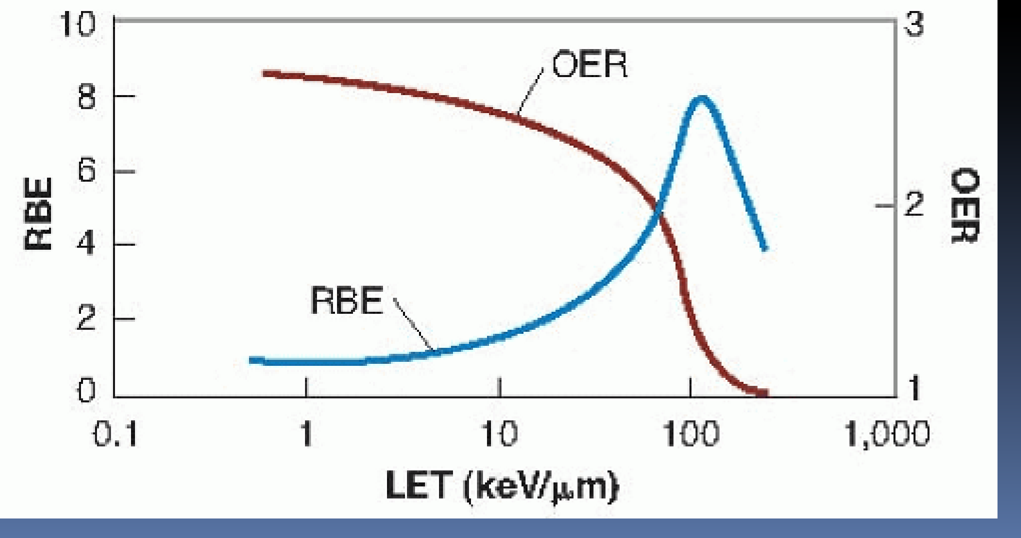
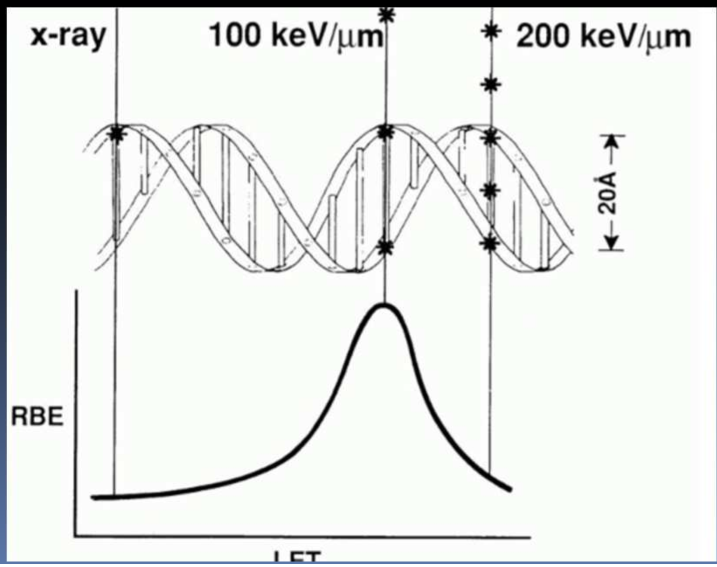


FIG. 14.7. RBE against LET. The vertical dashed line separates the low LET region, where RBE ≈ 1, from the high LET region, where the RBE first rises with the LET, reaches a peak of about 8 for LET ≈ 200 keV/µm, and then drops with a further increase in the LET.

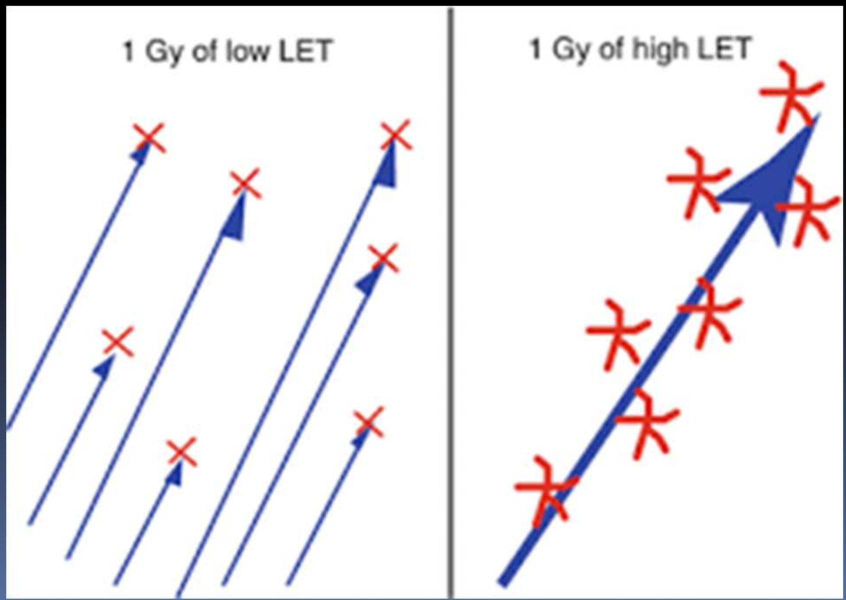
- As LET increases, OER decreases inversely with biologic effectiveness (i.e.,oxygen is not needed as much to cause damage),and the impact of variations in cell cycle–related radiosensitivity become less.
- At high LET, single-hit, non repairable cell killing increases relative to that from accumulation of SLD



- Radiation with an LET of about 100 keV/µm is optimal in terms of producing a biologic effect.
- At this density of ionization, the average separation between ionizing events just about coincides with the diameter of the DNA double helix (20 Å, or 2 nm).
- Radiation with this density of ionization has the highest probability of causing a double-strand break by the passage of a single charged particle,



- In the case of x-rays, which are more sparsely ionizing, the probability of a single track causing a double-strand break is low, and in general more than one track is required. As a consequence, x-rays have a low biologic effectiveness
- . At the other extreme, much more densely ionizing radiations (with an LET of 200 keV/μm, for example) readily produce double-strand breaks, but energy is “wasted” because the ionizing events are too close together



- The RBE varies not only with the type of radiation but also with the type of cell or tissue, biologic effect under investigation, dose, dose rate and fractionation
- These uncertainties are magnified further when considering radiations that have a Bragg peak, where the RBE can vary markedly and rapidly over small tissue areas

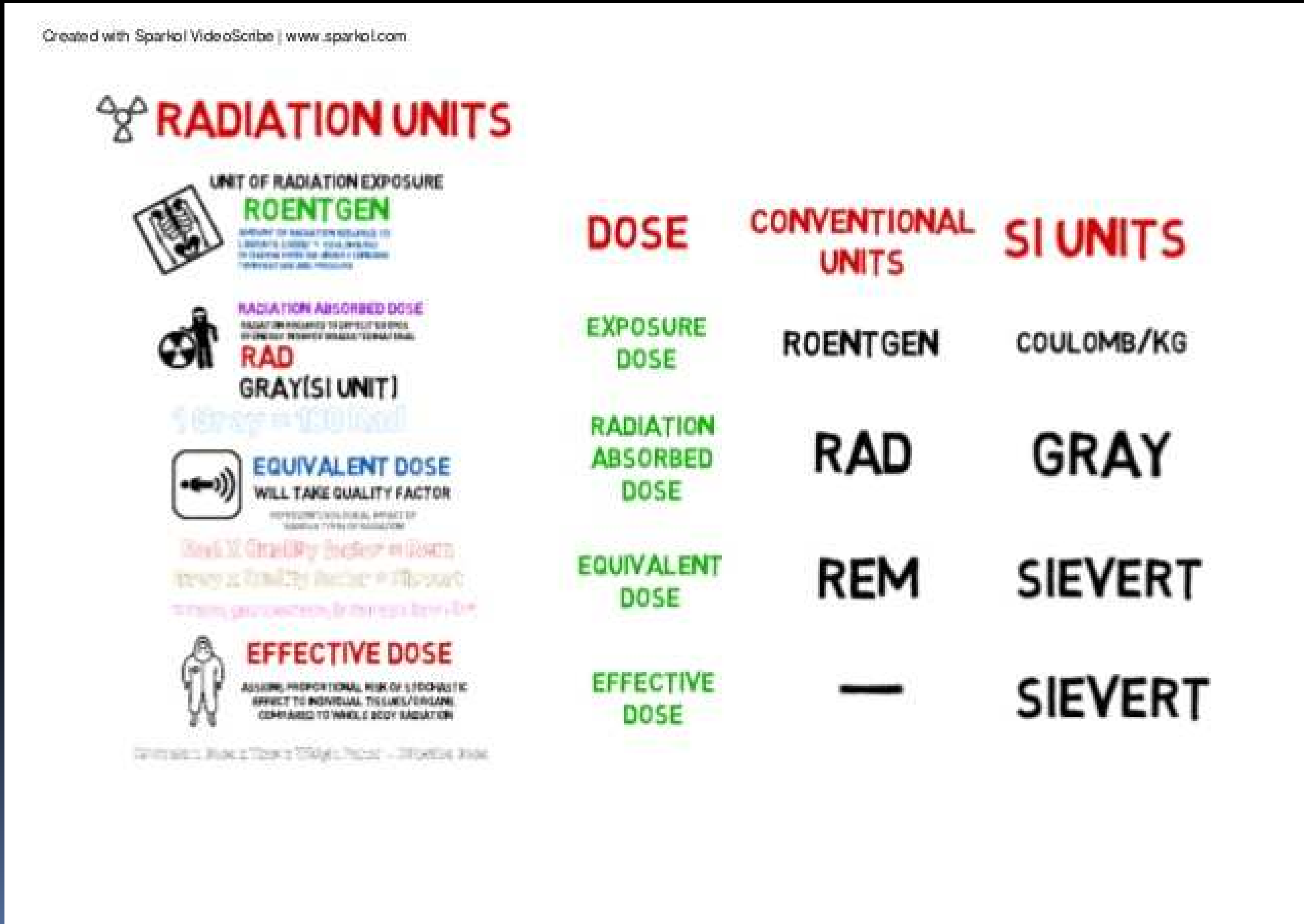
1920s : Radiation dosimetry

R . Sievert

E.Quimby

So, ionization and energy absorption are the starting point for radiation dosimetry

Quantities and Units



Unit of Exposure X

- Measure of ionization produced in air by photons
- Cannot measure photon energies more than 3 MeV
- The actual amount of energy that reaches the body

- Exposure = $\dfrac{\text{Total no. of ions of one sign}}{\text{mass of air}}$
- SI unit is C/kg
- Special unit is Roentgen

Absorption Dose D

- Physical Dose
- Amount of energy deposited in a unit mass of human tissue or medium
- Original unit is rad

$$1 \text{ rad} = 100 \text{ erg/g}$$

- SI unit is Gray

$$1 \text{ Gray} = 1 \text{ J/kg}$$

$$1 \text{ Gray} = 100 \text{ rad}$$

Equivalent Dose H

- Biological dose/effective dose/committed dose
- Represents stochastic biological effects of ionising radiation
- It is a weighted average of absorbed dose taking into account both the type f ionising radiation and the type of medium
- Conversion factor is the Q factor
-

x rays and gamma rays	1
alpha rays	20
neutrons	5 – 20

Equivalent dose H

$$H = Q \text{ factor} \times D$$

- cgs unit is rem (roentgen equivalent in man)
- SI unit is sievert
- 1 sievert = 100 rem

Effective Dose

- Some tissues and organs are more sensitive to radiation than others.
- The equivalent dose, HT, in each tissue, T, is multiplied by a tissue-weighting factor, wT. The effective dose, E, is then the sum of HTwT for all exposed tissues.
- Effective dose is a risk averaged dose that serves as a measure of risk including adjustments for both the type of radiation, wR, and the tissues exposed, wT.
- Effective dose is expressed in sievert (Sv) when the absorbed dose is measured in Gy, or in rem when the dose is measured in rads; 1 Sv = 100 rem.

NORMAL AND TUMOUR CELLS: THERAPEUTIC RATIO

- The aim of radiotherapy is to deliver enough radiation to the tumour to destroy it without irradiating normal tissue to a dose that will lead to serious complications (morbidity).
- The principle is usually illustrated by plotting two sigmoid curves, one for the tumour control probability (TCP) (curve A) and the other for the normal tissue complication probability (NTCP) (curve B).

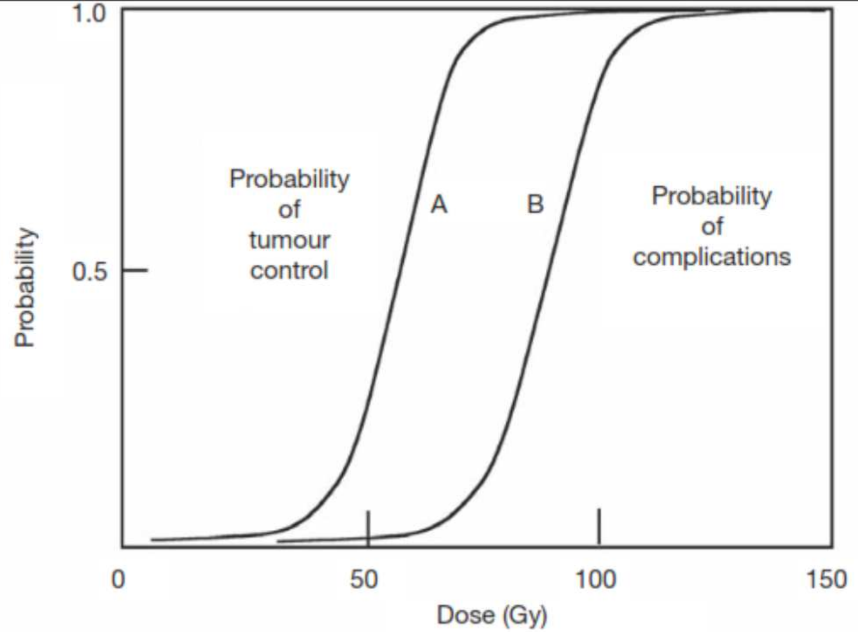


FIG. 14.4. The principle of therapeutic ratio. Curve A represents the TCP, curve B the probability of complications. The total clinical dose is usually delivered in 2 Gy fractions.

- The optimum choice of radiation dose delivery technique in the treatment of a given tumour is such that it maximizes the TCP and simultaneously minimizes the NTCP. For a typical good radiotherapy treatment, TCP ≥ 0.5 and NTCP £ 0.05.

Classification of radiation damage

Radiation damage to mammalian cells is divided into three categories:

● Lethal damage, which is irreversible, irreparable and leads to cell death;

● Sublethal damage, which can be repaired in hours unless additional sublethal damage is added that eventually leads to lethal damage;

● Potentially lethal damage, which can be manipulated by repair when cells are allowed to remain in a non-dividing state.

1911 : Concept of fractionation

Sterilization of ram's testis without excessive skin reactions using fractionated radiation (Claude Regaud)

1934 : Time –dose factor concept

Henri Coutard showed that both skin and mucosal reactions depended on the dose, the treatment time and the no. of treatment sessions.

FRACTIONATION

- Fractionation of radiation treatment so that it is given over a period of weeks rather than in a single session results in a better therapeutic ratio.
- The basis of fractionation is rooted in five primary biological factors called the five Rs of radiotherapy:

1975 : Concept of 4 Rs of Radiobiology

H Rodney Withers

Withers also quantified stem-cell numbers and survival of normal cells .

- Radiosensitivity. Mammalian cells have different radiosensitivities.
- Repair. Mammalian cells can repair radiation damage. This is a complex process that involves repair of sublethal damage by a variety of repair enzymes and pathways.
- Repopulation. Cells repopulate while receiving fractionated doses of radiation.

- Redistribution. Redistribution in proliferating cell populations throughout the cell cycle phases increases the cell kill from a fractionated treatment relative to a single session treatment.
- Reoxygenation. Reoxygenation of hypoxic cells occurs during a fractionated course of treatment, making them more radiosensitive to subsequent doses of radiation.

Conventional fractionation

- Division of dose into multiple fractions spares normal tissues through repair of sublethal damage between dose fractions and repopulation of cells. The former is greater for late reacting tissues and the latter for early reacting tissues.
- Concurrently, fractionation increases tumour damage through reoxygenationion and redistribution of tumour cells.

- A balance is achieved between the response of tumour and early and late reacting normal tissues, so that small doses per fraction spare late reactions preferentially, and a reasonable schedule duration allows regeneration of early reacting tissues and tumour reoxygenation to likely occur.

- The current standard fractionation is based on five daily treatments per week and a total treatment time of several weeks.
- Other fractionation schemes are being studied with the aim of improving the therapeutic ratio. Some of these are hyperfractionation, accelerated fractionation and CHART:

AIM

- The aim of radiation therapy is to deliver a precisely measured dose of irradiation to a defined tumor volume with as minimal damage as possible to surrounding healthy tissue resulting in
  1. Eradication of the tumor
  2. A high quality of life
  3. Prolongation of survival
  4. Palliation of symptoms

At a reasonable cost.

Therapeutic uses of ionizing radiation alone or in combination with other treatment modalities

- Surgery
- Chemotherapy, biologic and immunologic therapies
- Oxygen, radiosensitizers and radioprotectors
- Heat.

In 1962, Buschke defined our role

- We examine the patient personally,
- Review the microscopic material
- Take a biopsy if necessary.
- On the basis of this thorough clinical investigation we consider the plan of treatment and suggest it to the referring physician and to the patient.

- We reserve for ourselves the right to an independent opinion regarding diagnosis and advisable therapy and if necessary the right of disagreement with the referring physician
- During the course of treatment, we ourselves direct any additional medication that may be necessary… and are ready to be called in an emergency at any time

- In contrast to other medical specialties that rely mainly on the clinical knowledge and experience of medical specialists, radiotherapy, with its use of ionizing radiation in the treatment of cancer, relies heavily on modern technology and the collaborative efforts of several professionals whose coordinated team approach greatly influences the outcome of the treatment.

- Radiation oncologists, in general, have two techniques at their disposal. The first, *teletherapy, has a similar etymology to telephone, telegraph, and telepathy.* It refers to the projection of radiation through space.
- Brachytherapy is the other important technique of radiation therapy. The word brachytherapy shares an etymology with words such as brachycephaly and brachydactyly. It refers to short or slow therapy

- THANK YOU