University of Waterloo

PHYS 383: Medical Physics

Course Notes

Applications of physics in medicine. The course will address basic concepts of medical imaging, nuclear medicine and radiation isotopes, radiation therapy and biomedical laser applications. Nuclear structure and binding energy. Nuclear decays, radioactivity, and nuclear reactions. Interaction of radiation with matter.

Table of Contents

Key Equations **2**
Radiological Physics and Dosimetry **3**
Medical Imaging (CT) **39**
Radiation Biology **55**
Radiation Protection and Radiation Safety **82**
Imaging for Treatment Guidance and Monitoring **117**
Radiation Therapy **143**

Key Concepts

1. Types of ionizing radiation

Direct – electron, ions, charged particles → deposit energy directly

Indirect – Photons/neutrons → generate charged particles, then deposit damage

2. Interaction of Photon with Matter

Photoelectric interaction → high dependent on Z, low energy (50-100 keV) → for diagnostic

Compton interaction → less depend on Z, medium energy (100keV – 10 MeV) → treatment

Pair production → very high energy (1.022 MeV)

Rayleigh (coherent) scattering → low energy, high Z → no charged particle production

3. Interaction of Electron with Matter

Ionization → elastic or inelastic collision with electrons

Radiation → produces X-ray via bremsstrahlung → more E on high Z = efficient

4. BED Calculation

$$BED = \frac{E}{\alpha} = nd\,(1 + \frac{d}{(\frac{\alpha}{\beta})}) - \frac{\ln 2\,(T - T_k)}{\alpha T_d}$$

5. Exposure, Dose, Equivalent Dose, Effective Dose

Risk increases 5% per 1000 mSv

Physical quantity	SI unit	Non-SI unit	Relationship
Activity	becquerel	curie (Ci)	1 Bq=2.7x10^{-11} Ci 1 Ci=3.7x10^{10}Bq 1 mCi=37 MBq
Exposure	coulomb/kg	roentgen (R)	1 R=2.58x10^{-4} C/kg 1C/kg=3876 R
Absorbed dose	gray (=J/kg)	rad	1 Gy=100 rad 1 rad=1 cGy
Equivalent dose	sievert	rem	1 Sv=100 rem 1 rem=10 mSv
Effective dose	sievert	rem	1 Sv=100 rem 1 rem=10 mSv

6. Monitoring Units

For SAD set up: USE TPR for the depth

Dose(A, di) in cGy = Dose(Cal) in cGy *TPR(A, d6i)*RDF(x,y)*MU*WF

For SSD set up: USE PDD for depth

D(A, Di) in cGy = D(Cal) in cGy *PDD(A, Di)*RDF(x,y)*MU*WF

Radiological Physics and Dosimetry

Atomic and Nuclear Structure

- **Atom**: It is the basic unit of matter → Central core is called **nucleus**
    - Nucleus contains **protons** (positively charged) and **neutrons** (no charge)
    - **Nucleons**: Protons and Neutrons
- Surrounded by cloud of electrons moving in orbits around the nucleus
- **Thomson atomic model (Sir Joseph John Thomson)**
    - Earliest theoretical description of the inner structure of atoms proposed about 1900
    - Plum-pudding model of the atom
    - It is based on an assumption that the positive and the negative (electrons) charges of the atom were distributed uniformly over the atomic volume
- **Rutherford atomic model (Ernest Rutherford)**
    - The Thomson model was abandoned (1911) in favour of the Rutherford model on both theoretical and experimental grounds
    - Mass and positive charge of the atom are concentrated in the nucleus
    - Negatively charged electrons revolve about the nucleus in a spherical cloud on the periphery of the atom
- **Bohr atomic model (Niels Bohr)**
    - Proposed in 1913. Electrons revolve around the nucleus in well-defined, allowed orbits (planetary-like motion).
    - While in orbit, the electron does not lose energy despite being constantly accelerated (no energy loss while electron is in allowed orbit).
    - The angular momentum of the electron in an allowed orbit is quantized (quantization of angular momentum).
    - An atom emits radiation only when an electron makes a transition from one orbit to another (energy emission during orbital transitions).

- NOTATION: $^{A}_{Z}X$
    - X = Atomic symbol
    - A = Atomic mass number (A)
        - number of protons or electrons plus number of neutrons
    - Z = Atomic number (Z)
        - (number of protons) or (number of electrons in an electrically neutral atom)
    - Number of neutrons (N) = A – Z
- On the basis of different proportions of neutrons and protons in the nucleus, atoms are classified into:
    - **Isotopes**: Atoms which have the same number of protons but different number of neutrons
        - C-12: (6 protons, 6 neutrons), C-14: (6 protons, 8 neutrons)
    - **Isotones**: Atoms which have the same number of neutrons but different numbers of protons
        - K-19: (19 protons, 20 neutrons), Cl-37: (17 protons, 20 neutrons)
    - **Isobars**: Atoms which have the same number of nucleons (mass number) but different number of protons
        - Ar-40: (22 neutrons, 18 protons), Ca-40: (20 neutrons, 20 protons)
    - **Isomers**: Atoms with the same number of protons as well as neutrons.
        - They are identical atoms that differ in their nuclear energy states
- Number of atoms (Na) per mass m of an element

$$\frac{N_a}{m} = \frac{N_A}{A}$$

- Number of electrons (Ne) per mass m of an element

$$\frac{N_e}{m} = Z\frac{N_a}{m} = Z\frac{N_A}{A}$$

- Number of electrons (Ne) per volume V of an element

$$\frac{N_e}{V} = \rho Z \frac{N_a}{m} = \rho Z \frac{N_A}{A}$$

(Z: Atomic number of material, A: atomic mass of material; NA: Avogadro's Number = 6.022x1023 atoms/mol)

Classification of Radiation

- Radiation is classified into two main categories
  - **Non-ionizing radiation**: refers to any type of electromagnetic radiation that does not carry enough energy per quantum to ionize atoms or molecules (i.e. to completely remove an electron from an atom or molecule): e.g. infrared, laser, microwave
  - **Ionizing radiation**: consists of subatomic particles or electromagnetic waves that are energetic enough to detach electrons from atoms or molecules.
    - Directly ionizing radiation (charged particles): e.g. electron, protons, alpha particles, heavy ions
    - Indirectly ionizing radiation (neutral particles): e.g. photons (x-rays, gamma rays), neutrons
- Absorbed dose is a quantity applicable to both indirectly and directly ionizing radiations.
  - **Indirectly ionizing** radiation means: the energy is imparted to matter in a two step process.
    - In the first step (resulting in kerma), the indirectly ionizing radiation transfers energy as kinetic energy to secondary charged particles.
    - In the second step, these charged particles transfer a major part of their kinetic energy to the medium (finally resulting in absorbed dose).
  - **Directly ionizing** radiation means charged particles transfer a major part of their kinetic energy directly to the medium (resulting in absorbed dose).

- **Ionizing radiation**
  - **Characteristic x rays**
    - Results from electronic transitions between atomic shells.
  - **Bremsstrahlung x rays**
    - Results mainly from electron-nucleus Coulomb interactions.
  - **Gamma ray**
    - Results from nuclear transitions.
  - **Annihilation quantum** (annihilation radiation)
    - Results from positron-electron annihilation.
- **Alpha Particles (alpha)**
  - **Large mass**, highly charged, helium nuclei (2 protons, 2 neutrons)
  - Range: 1-2 inches in air
  - Shielding: Dead layer of skin, paper.
  - Biological Hazards: Internal, it can deposit large amounts of energy in a small amount of body tissue.
- **Beta particles (β)**
  - **Small mass**, electron size
  - Range: Short distance (one inch to 20 feet).
  - Shielding: Plastic
  - Biological Hazard: Internal hazard. Externally, may be hazardous to skin and eyes.
- **Neutrons (n)**
  - **Fairly large**. No charge. Has mass.
  - Range: Range in air is very far. Easily can go several hundred feet. High penetrating power due to lack of charge (difficult to stop).
  - Shielding: Water. Concrete. Plastic (high hydrogen content).
  - Biological Hazard: External whole body exposure.
- **Gamma (γ) or X-rays:**
  - **No mass**. No charge, Electromagnetic wave or photon. Range: Very far. It will easily go several meters. Very high penetrating power.

- Shielding: Concrete. Water. Lead.
- Biological Hazard: Whole body exposure. The hazard may be external and/or internal. This depends on whether the source is inside or outside the body

Exponential Attenuation

- Photons are attenuated via **Photoelectric effect, Raleigh, Compton scattering, or Pair production**
- Transfer of energy from photon to a medium takes place in two stages:
  - Involves the interaction of the photon with an atom, causing an electron or electrons to be set in motion
  - Involves the transfer of energy from the high energy electron to the medium through excitation and ionization
- **Fluence (I or Φ) – Number of photon per unit area**
  - **unit:** m^{-2}
  - It is the ratio of dN and dA, where dN is the number of particles incident on an imaginary sphere of cross-sectional area dA
  - Number of photons / area

$$I(x) = I(0)e^{-\mu x}$$

- **Fluence Rate (Φ) -** Number of photons that pass through unit area per unit time
  - **Unit:** $s^{-1}m^{-2}$
  - Number of photons / (time x area)
- **Energy Fluence (Ψ)** – energy per unit area
  - **Unit**: $J.m^{-2}$
  - ratio of dE and dA, where dE is the sum of the energies of all photons that enter a sphere of cross-sectional area dA
  - Energy / area
- Energy Fluence Rate (ψ) - The energy carried across unit area per unit time
  - **Unit**: $J.\ s^{-1}m^{-2}$
  - Energy / (time x area)

- **Linear attenuation coefficient (μ)**
  - **unit:** cm^{-1}
  - It is the probability per unit path length that a photon will interact with the absorbing medium. It depends on the photon energy and the atomic number of the medium
- **Half value layer (HVL)**
  - **Unit:** cm
  - Absorber thickness that attenuates the original intensity to 50 %.

$$\frac{Ln\ 2}{\mu}$$

  - Can have first, second, third, etc. HVLs
- **Tenth value layer (TVL)**
  - **Unit:** cm
  - Absorber thickness which attenuates the beam intensity to 10 %.

$$\frac{Ln\ 10}{\mu}$$

- **Mass Attenuation coefficient**
  - **Unit:** cm^2/g
  - μ/ρ
- **Atomic attenuation coefficient**
  - **Unit:** cm^2/atom
  - **No:** number of electrons per gram = N_A * Z / Atomic Weight

$$_{a}\mu = \frac{\mu}{\rho} * \frac{Z}{N_0}$$

- **Electronic attenuation coefficient**
  - **Unit:** cm^2/electron

$$_{e}\mu = \frac{\mu}{\rho} * \frac{1}{N_0}$$

Interaction of Ionizing Radiation with Matter

- Transfer of energy from photon to the medium takes place in two stages
    - Transfer E to an electron and gives it KE → KERMA
        - A photon is also scattered from a
    - The electron gives its energy via collision → Absorbed dose
        - Bremsstrahlung: between electron and a nucleus
        - Delta ray: violent electron-electron collision
        - Absorbed dose = KERMA – Bremsstrahlung energy
        - Max absorbed dose occurs at a range equal to the range of electron
- **Energy Transfer Coefficient (μtr)**
    - The fraction of photon energy transferred into kinetic energy of charged particles per unit thickness of the absorber including energy loss to bremsstrahlung
    - Etr is the average energy transferred from the primary photon with energy hν to kinetic energy of charges particles

$$\mu_{tr} = \mu \frac{\bar{E}_{tr}}{h\nu}$$

- **Mass Energy Transfer Coefficient**

$$\frac{\mu_{tr}}{\rho} = \frac{\mu}{\rho} * \frac{\bar{E}_{tr}}{h\nu}$$

- **Energy Absorption Coefficient (μab)**
    - The fraction of photon energy transferred into kinetic energy of charged particles per unit thickness of absorber excluding energy loss to bremsstrahlung
    - If Eab is the average energy absorbed in the absorbing medium

$$\mu_{ab} = \mu \frac{\bar{E}_{ab}}{h\nu}$$

- **Mass Energy Absorption Coefficient**

$$\frac{\mu_{ab}}{\rho} = \frac{\mu}{\rho} * \frac{\bar{E}_{ab}}{h\nu}$$

- The energy transfer coefficient and the energy absorption coefficient are related through the radiation fraction, i.e.

$$\mu ab = \mu tr * (1 - g)$$

  - g is the average fraction of the energy lost (to bremsstrahlung) in radiation interactions by the secondary charged particles, as they travel through the medium
- Also,

$$\frac{\mu_{ab}}{\rho} = \frac{\mu_{tr}}{\rho} * (1 - g)$$

- And

$$\frac{\mu_{ab}}{\rho} = \frac{\mu}{\rho} * \frac{\bar{E}_{tr}}{h\nu} * (1 - g)$$

- **Exposure**
  - It is a measure of ionization produced in air by photons
  - Define as the quotient of dQ by dm, where dQ is the total charge of the ions of one sign produced in air of mass dm

$$X = \frac{dQ}{dm}$$

  - **Roentgen (R)** is a unit of exposure
  - SI unit of exposure: coulomb per kg (C/kg)
    - 1R = 2.58x10-4 C/kg air
  - Applies only to X-ray and gamma rays (ie: ionizing radiation)
- **KERMA**
  - Kinetic Energy Released in the medium per unit Mass (in J/kg)
  - It is defined as the quotient dEtr by dm, where dEtr is the sum of the initial kinetic energies of all the charged ionizing particles liberated by uncharged particle in a material of mass dm

$$K = \frac{d\bar{E}_{tr}}{dm}$$

- For photon beams traversing a medium, Kerma is related to the **energy fluence** at that point in the medium by

$$K = \Phi * h\nu \left(\frac{\bar{\mu}_{tr}}{\rho}\right) = \Psi \left(\frac{\bar{\mu}_{tr}}{\rho}\right)$$

$$K = \Psi \left(\frac{\bar{\mu}_{en}}{\rho}\right) / (1 - \bar{g})$$

- quantity applicable to indirectly ionizing radiations, such as photons and neutrons
- The energy transferred to electrons by photons can be expended in two different ways:
  - Through collision interaction (soft and hard collisions): low z materials → collision KERMA (Kcol)

$$K_{col} = \Psi \left(\frac{\bar{\mu}_{en}}{\rho}\right)$$

  - Through radiation interactions (bremsstrahlung and e-p annihilation: high z materials → Radiation KERMA (Krad)

$$K_{rad} = \Psi \left(\frac{\bar{\mu}_{en}}{\rho}\right) * \frac{\bar{g}}{1 - \bar{g}}$$

  - K = Kcol + Krad
  - The average fraction of the energy which is transferred to electrons and then lost through radiative processes is represented by a factor referred to as the **radiation fraction (g)**.
    - Hence the fraction lost through collisions is (1-g).
  - A frequently used relation between collision kerma Kcol and total kerma K may be written as follows:

$$K\text{col} = K\ (1-g)$$

- **Absorbed Dose**
  - Energy absorbed in a medium per unit mass (in J/kg or Gr)

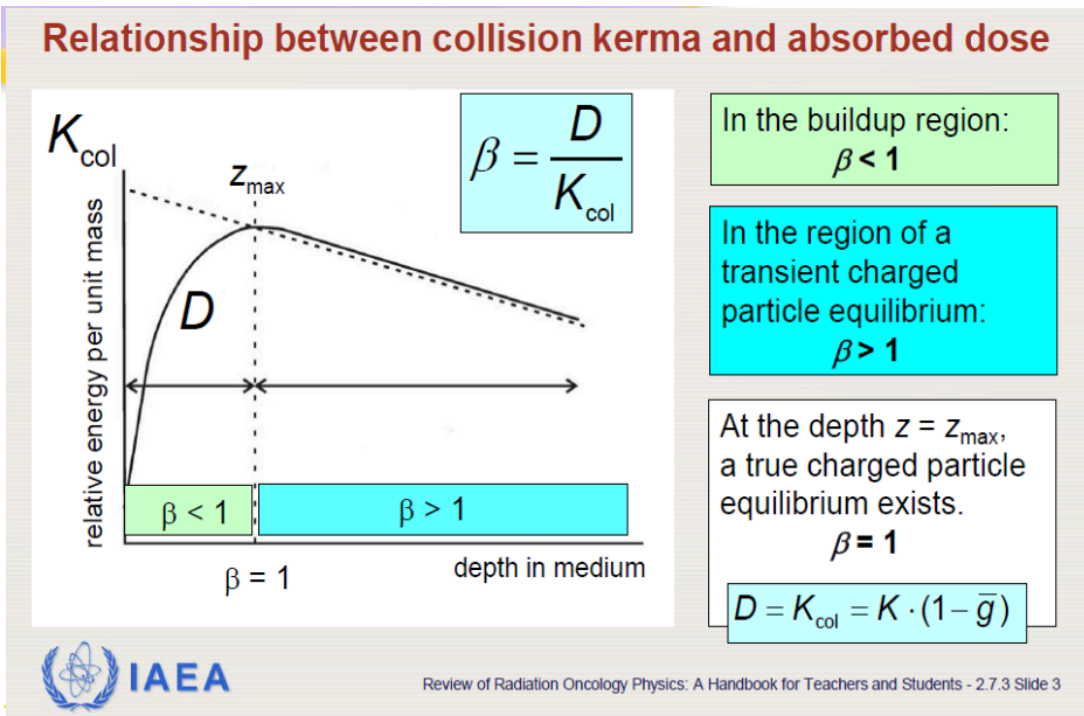
- quotient dEab by dm, where dEab is the energy absorbed in a material of mass dm

$$D = \frac{d\bar{E}_{ab}}{dm}$$

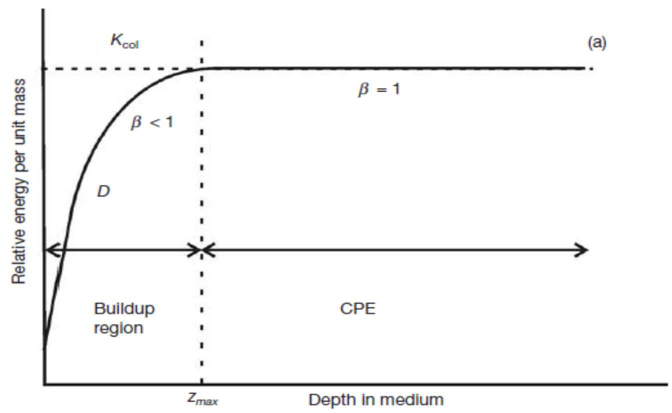
- For photon beams traversing a medium

$$D = \Phi * h\upsilon\left(\frac{\bar{\mu}_{en}}{\rho}\right) = \Psi\left(\frac{\bar{\mu}_{en}}{\rho}\right)$$

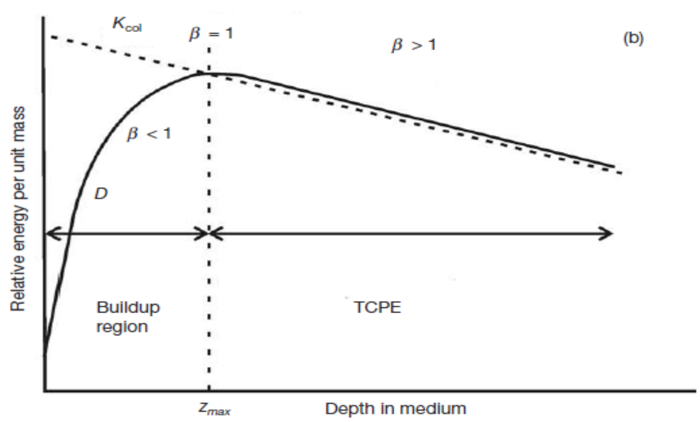
- **KERMA and Dose**



- Collision kerma and absorbed dose as a function of depth in a medium irradiated by a high energy photon beam for a hypothetical case of no photon attenuation or scattering
  - **Absorbed dose increases with depth** - **electronic equilibrium** is achieved, no attenuation of the primary.
  - Before the two curves meet, the electron buildup is less than complete, and beta<1
  - At **d-max**, if photon attenuation is negligible, then beta=1.



- Collision kerma and absorbed dose as a function of depth in a medium irradiated by a high energy photon beam for the realistic case of photon attenuation and scattering
  - Attenuation of the primary occurs. - **transient electronic equilibrium**
    - In the transient equilibrium region, beta >1



- **KERMA vs. Exposure**
  - Exposure is the ionization equivalent of the collision kerma in air.
  - multiply the collision kerma (Kcol) by (e/Wair)
    - number of coulombs of charge created per joule of energy deposited is the charge created per unit mass of air or exposure

$$X = (K_{col})_{air} \frac{e}{W_{air}}$$

It follows that

$$X = \Psi_{air} \left(\frac{\bar{\mu}_{en}}{\rho}\right) * \left(\frac{e}{W_{air}}\right)$$

W_{air} is about 33.97 eV/ion pair ($33.97 \times 1.602 \times 10^{-19}$ J/ion pair)

- The absorbed dose to a medium Dmed is related to the electron fluence in the medium as follows

$$D_{med} = \Phi * \left(\frac{S_{col}}{\rho}\right)_{\mathrm{med}}$$

    - $Scol$ / ρ is the unrestricted mass collision stopping power of the medium at the energy of the electron
    - This relation is valid under the conditions that:
        - photons escape the volume of interest
        - secondary electrons are absorbed on the spot
        - or there is **charged particle equilibrium (CPE)** of secondary electrons

Radioactive Decay

- Most stable atoms have an equal number of protons and neutrons
- Unstable atoms undergo a process called radioactive decay to reach a more stable state.
- Radioactive decay or Radioactivity: It is a process by which an unstable nucleus (parent) decays into a new nuclear configuration (daughter) that may be stable or unstable
- If the daughter is unstable, it will decay further through a chain of decays until a stable configuration is attained
- The decay energy emitted could be in the form of:
    - Electromagnetic radiation (i.e. gamma rays)
    - Kinetic energy of the reaction products
- Modes:
    - Alpha decay
        - if an unstable nucleus emits a helium nucleus (2 protons, 2 neutrons)

$${}_{Z}^{A}X \rightarrow {}_{Z-2}^{A-4}Y + {}_{2}^{4}He + Q \qquad {}_{88}^{226}Ra \rightarrow {}_{86}^{222}Rn + {}_{2}^{4}He + 4.87\,MeV$$

    - Beta decay
        - ejection of a positive or a negative electron from the nucleus
            - Beta plus decay
            - Beta minus decay

- Electron capture

$$ {}_{0}^{1}n \rightarrow {}_{1}^{1}p + {}_{-1}^{0}\beta + \bar{\upsilon} \; (\beta^{-} \; decay) \qquad {}_{15}^{32}P \rightarrow {}_{16}^{32}S + {}_{-1}^{0}\beta + \bar{\upsilon} \; (\beta^{-} \; decay) $$

$$ {}_{1}^{1}p \rightarrow {}_{0}^{1}n + {}_{+1}^{0}\beta + \upsilon \; (\beta^{+} \; \text{decay}) \qquad {}_{11}^{22}Na \rightarrow {}_{10}^{22}Ne + {}_{+1}^{0}\beta + \upsilon \; (\beta^{+} \; decay) $$

- Gamma decay
  - Pure gamma decay
  - Internal conversion
  - Auger effect

$$ {}_{27}^{59}Co + {}_{0}^{1}n \rightarrow {}_{27}^{60}Co + \gamma \; (\gamma \; \text{decay}) $$

- Spontaneous fission
  - a nuclear transformation by which a high atomic mass nucleus spontaneously splits into two nearly equal fission fragments
- Electron capture
  - a nuclear transformation in which a nucleus captures an atomic electron (K-shell), a proton is transforms to neutron and a neutrino is emitted
  - EX: Beryllium (Be) – Lithium (Li)

$$ {}_{Z}^{A}X + e^{-} \rightarrow {}_{Z-1}^{A}Y + v_{e} \qquad {}_{4}^{7}Be + e^{-} \rightarrow {}_{3}^{7}Li + v_{e} $$

- Internal conversion
  - a nuclear transformation in which a nuclear de-excitation energy is transferred to an orbital electron (K-shell).
  - The electron is emitted from the atom with a kinetic energy equal to the de-excitation energy less the electron binding energy.
  - Resulting shell vacancy is filled with a higher level orbital electrons resulting in characteristic photons or Auger electrons:
  - EX: Caesium - Barium

$$ {}_{Z}^{A}X^{*} \rightarrow {}_{Z}^{A}Y^{+} + e^{-} \qquad {}_{55}^{137}Cs \rightarrow {}_{56}^{137}Ba + e^{-} + v_{e} $$

- A radioactive decay which involves a transition from the quantum state of the parent to a quantum state of a stable daughter, the number of radioactive atoms at time (t) is related to the initial number of radioactive atoms at time (0) and λ the decay constant

$$\Delta N = -\lambda N \Delta t$$

$$N(t) = N_0 e^{-\lambda t}$$

- The **activity A(t)** of a radioactive substance at time t is defined as the product of the decay constant λ and the number of radioactive atoms N(t)
  - it is the total number of disintegrations (decays) per unit time (unit: Becquerel)

$$A(t) = \frac{dN(t)}{dt} = \lambda N(t)$$

$$A(t) = A_0 e^{-\lambda t}, \text{ Becquerel (Bq): } 3.7\times10^{10} \text{ Bq} = 1 \text{ Curie}$$

- **Specific activity**
  - It is the activity of the parent radioactive atom per unit mass
  - NA and A are the Avogadro's number and atomic mass number respectively

$$a = \frac{A(t)}{M} = \frac{\lambda N(t)}{M} = \frac{\lambda N_A}{A}$$

- **Half life**
  - It is the time during which the number of radioactive atoms decays from the initial value at time t=0 to half of the initial value

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

- **Mean Life (τ)**
  - average lifetime of all the radioactive nuclei.

$$\tau = \frac{1}{\lambda} = 1.443 T_{1/2}$$

- Table for half life of Radon (Rn-222), potassium (K-40), tritium (H-3), Colbolt-60 (Co-60), and iodine-125 (I-125)

Radionuclide	Half life	Source
Naturally occurring radionuclide:		
Radon-222 (Rn-222)	3.8 days	Radioactive decay of Radium-226 ($T_{1/2}$ 1620 yrs)
Potassium-40 (K-40)	1.248×10^9 yrs	Some food items i.e. banana
Tritium (H-3)	12 yrs	Interaction of cosmic radiation with gases in the upper atmosphere
Artificial radionuclide:		
Cobolt-60 (Co-60)	5.27 yrs	Interaction of cobolt-59 with neutrons in a reactor
Iodine-125 (I-125)	60 days	Neutron activation of Xeron-124 to produce Xeron-125 followed by electron capture

- Two types of radioactive decay
    - radioactive parent nucleus P decaying with a decay constant λp into a stable daughter nucleus D. The number of parent and activity of parent is:

$$N_p(t) = N_p(0)e^{-\lambda_p t} \qquad A_p(t) = A_p(0)e^{-\lambda_p t}$$

    - a radioactive parent nucleus P decays with a decay constant λP into a daughter nucleus D which in turn is radioactive and decays with a decay constant λD into a stable granddaughter G

$$\frac{dN_D}{dt} = \lambda_p N_p(t) - \lambda_D N_D(t) = \lambda_p N_p(0)e^{-\lambda_p t} - \lambda_D N_D(t)$$

The number of daughter nuclei at time t is

$$N_D(t) = N_p(0)\frac{\lambda_p}{\lambda_D - \lambda_p}\left(e^{-\lambda_p t} - e^{-\lambda_D t}\right)$$

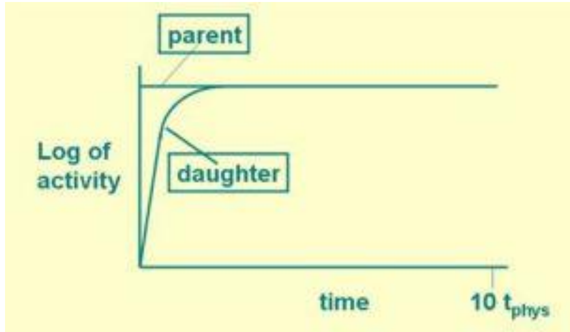
The activity of the daughter nuclei is:

$$A_D(t) = A_p(t)\frac{\lambda_D}{\lambda_D - \lambda_p}\left(1 - e^{-(\lambda_D - \lambda_p)t}\right)$$

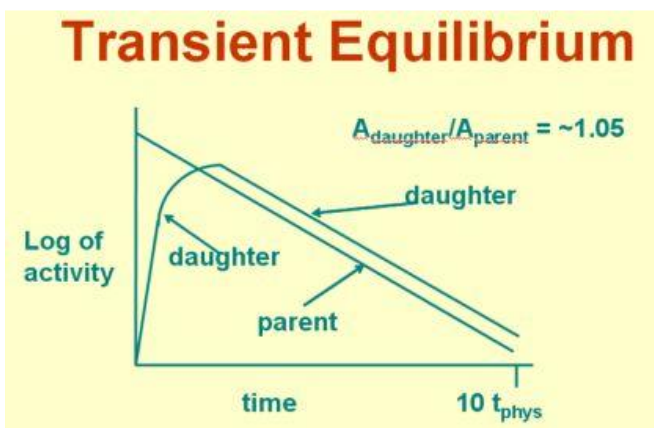
- At tmax, the parent and daughter activities are equal and the daughter activity reaches its maximum

$$t_{max} = \frac{Ln\,(\lambda_D/\lambda_p)}{\lambda_D - \lambda_p}$$

- **Equilibrium**
  - a condition established in a parent/daughter mixture when both parent and daughter are radioactive and when the daughter's half-life is shorter than that of the parent.
    - If the daughter's half-life exceeds that of the parent, equilibrium will never be reached
  - Two types
    - Secular Equilibrium
      - when the half life of the parent radioactive nuclei is many times greater than the half life of the daughter
      - EX: Ra226 (T1/2 =1620 yrs) ------> Rn222 (T1/2 =3.8 days)
      - At the point at which the activity of the parent and activity of the daughter become equal, equilibrium has been reached
      - It means in the equilibrium mixture, the daughter appears to decay with the half-life of the parent. When the daughter is isolated from the mixture, it has its expected half-life.
      - The simplest explanation for their appearing to be equal is that the daughter can't decay until it is formed, and so the rate of formation of the daughter equals the rate of decay of the parent, which is very slow. Therefore the parent and daughter appear to have the same half-lives.



- Transient Equilibrium
  - when the half life of the parent radioactive nuclei is approximately 10 times greater than the half life of the daughter radioactive nuclei.
  - Example: 99Mo/99mTc Generator, where the ratio of the half-lives is 67 hr/6 hr = 11:1
    - During a 60 hr period representing 10 half-lives of 99mTc , almost 50% of the 99Mo has disappeared. This represents a very significant amount, unlike the negligible amount in secular equilibrium.



- Times it takes to reach equilibrium
  - **Transient equilibrium** is reached in ~**4 t1⁄2 of daughter**. For Tc-99m, predicted length of time is 24 hours; actual time to equilibrium is 23 hr.
  - Secular equilibrium is reached in **~6 t1⁄2 of daughter**

- **Production of radioisotopes**
  - **Nuclear fission:** Nuclides with high atomic number are fissionable by neutron bombardment in a nuclear reactor. For example, iodine- 131, molybdenum-99 and xenon-133 can be produced in this way.
  - **Charged particle bombardment:** Radionuclides may be produced by bombarding target materials with charged particles in particle accelerators such as cyclotrons.
  - **Neutron bombardment:** Radionuclides may be produced by bombarding target materials with neutrons in nuclear reactors.
    - (n, gamma) Reaction: **Radiative Capture**
    - The product is an isotope of the target element itself and hence cannot be chemically separated
    - **EX:** Cobalt-60 (Co-60) and Molybdenum (Mo-99)

    Cobalt-60 (Co-60): Used in radiation therapy

$$^{59}_{27}Co + ^{1}_{0}n \rightarrow ^{60}_{27}Co + \gamma$$

    Molybdenum (Mo-99): Used in the production of Tc-99m

$$^{98}_{42}Mo + ^{1}_{0}n \rightarrow ^{99}_{42}Mo + \gamma$$

  - In each nuclear transformation a number of physical quantities must be conserved. The most important conserved physical quantities are:
    - Total energy
    - Momentum
    - Charge
    - Atomic number
    - Atomic mass number (number of nucleons)

Photon Interaction with Matter

- Indirectly Ionizing Radiations: Photon Beams
  - Photoelectric interaction
  - Compton interaction
  - Pair production

- Rayleigh (coherent) scattering

- **Photoelectric Interaction**
  - In this process a photon interacts with an atom (tightly bound electron) and ejects an orbital electron from the atom
  - This process involves bound electrons: Interactions of this kind takes place with electrons in the K, L, M and N shells
  - The entire energy of the photon is transferred to the electron to eject it from the atom
  - The kinetic energy of the ejected **photoelectron** is (hv-Eb)
  - Characteristic x-rays or probability of emission of Auger electrons
  - **Photoelectric cross section** (tau/rho) varies with photon energy approximately as 1/E3
  - The coefficient per electron or per gram varies with atomic number approximately as Z^3 for high Z materials and more nearly as $Z^{3.8}$ for low Z materials → high dependence on Z
  - The coefficient per atom for low Z materials varies with atomic number approximately as $Z^{4.8}$
  - Energy range: 50-100 keV

- **Compton Interaction**
  - In this process the photon interacts with an atomic electron as though it were a 'free' electron.
  - The photon transfers some energy to the electron ejecting it out of the atom with some kinetic energy.
  - The photon is scattered at an angle with a degraded energy.
  - Compton interaction is almost independent of atomic number
  - It decreases with increase in photon energy
  - In each interaction, some energy is scattered and some transferred to an electron, the amount depending on the angle of emission of the scattered photon and the energy of the photon

- On the average, the fraction of the energy transferred to KE per collision increases with increases in photon energy
- In **soft tissue**, the Compton interaction is much more important than either the photoelectric effect or pair production process for **photons in the range 100keV to 10MeV**
- Compton Shift, photon energy, and electron KE

$$\lambda' - \lambda = \lambda_c (1 - \cos\theta) \qquad \lambda_c = \frac{h}{m_o c}$$

➤ The scattered photon energy as

$$h\nu' = \frac{h\nu_o}{\left[\frac{h\nu_o}{m_o c^2}(1 - Cos\theta) + 1\right]} = \frac{h\nu_o}{[\alpha(1 - Cos\theta) + 1]}$$

$$\alpha = \frac{h\nu_o}{m_o c^2}$$

➤ The electron KE is:

$$E = h\nu_o \left[\frac{\alpha(1 - Cos\theta)}{\alpha(1 - Cos\theta) + 1}\right]$$

- **Direct Hit**
  - If the photon makes a direct hit with the electron, the electron will travel straight forward ϕ=0o and the scattered photon will be scattered straight back with θ=180 .
  - In such a collision the electron will acquire the maximum energy (Emax) and the scattered photon will be left with minimum energy hvmin.

$$h\nu'_{min} = h\nu \frac{1}{1 + 2\alpha}$$

$$E_{max} = h\nu \frac{2\alpha}{1 + 2\alpha}$$

- **Grazing Hit**
  - If the photon makes a grazing hit with the electron, the electron will be emitted at right angles ϕ=90o and the scattered photon will be scattered straight forward with θ=0 .
  - In such a collision the electron will acquire zero energy and the scattered photon will acquire the full energy of the incident photon.

Ephoton = Emax = hv ; Eelectron = 0

- **90 Degree Photon Scatter**
  - Any number of intermediate collisions are possible. For example if the photon is scattered <u>at right angles</u> to its original direction

$$h\nu^{/} = \frac{h\upsilon}{1+\alpha}$$

$$E = h\upsilon\frac{\alpha}{1+\alpha}$$

- **Pair Production**
  - In this process a photon interacts with the electromagnetic field of an atomic nucleus
  - The photon gives up all its energy in the process of creating a pair consisting of a <u>negative electron (e-) and a positive electron (e+)</u>.
  - The threshold energy for the pair production process is 1.02MeV.
  - The interaction process increases rapidly with energy above the threshold
  - The photon energy in excess of the threshold is shared between the two particles as kinetic energy.
  - The coefficient per atom varies approximately as Z^2
  - The coefficient per electron depends approximately on Z^1
  - The coefficient varies with energy as (alpha log E)
  - The energy transferred to KE is hυ - 1.022 MeV
  - Two annihilation photons, each of energy 0.511 MeV are produced per interaction and radiated from the absorber
- **Triplet Production (Electronic Pair Production)**
  - Photon disappears in the vicinity of an electron
  - An electron-positron is produced in the coulomb field of an orbital electron and a triplet leave the site of interaction
    - Two electrons
    - One positron
  - Threshold energy for triplet production is hυthr = 2.04MeV

- Cross section for pair production and triplet production is zero for photon energies below the threshold energy
- Cross section for pair production and triplet production increases rapidly with photon energies above the threshold energy

- **Rayleigh (Coherent) Scattering**
  - The interaction consists of an electromagnetic wave passing near the electron and setting it into oscillation.
  - The scattered x-rays have the <u>same energy</u> as the incident beam.
  - Probable in high atomic number materials and with photons of low energy

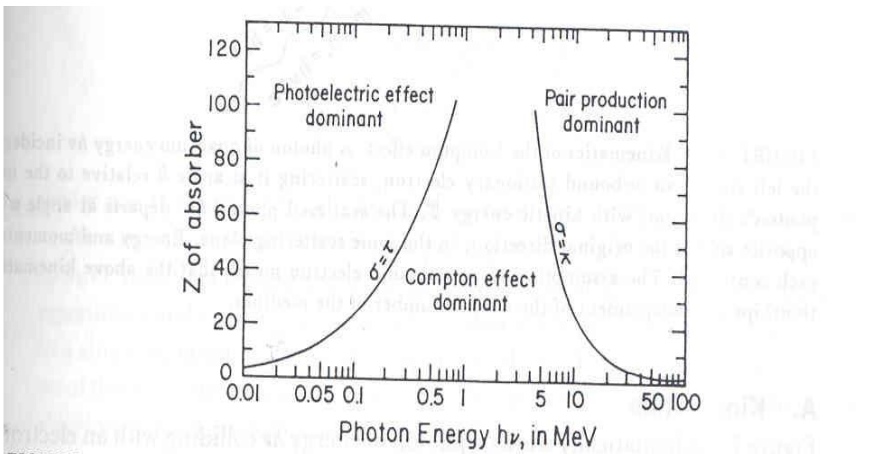


FIGURE 7.1. Relative importance of the three major types of γ-ray interactions. The curves show the values of Z and E_γ for which two types of effects are equal. (Reproduced from Evans (1955) with permission of R.D. Evans and McGraw-Hill Book Company.)

Electron Beam Interaction with Matter

- <u>Directly</u> Ionizing Radiations: Electrons
  - As electrons travel through a medium they loss energy through
  - **Inelastic** collisions with **atomic electrons**:
    - The incident electron is deflected from its original path and loses part of its kinetic energy to **ionization or excitation**
  - **Inelastic** collisions with **atomic nuclei**:
    - The incident electron is deflected from its original path and loses part of its kinetic energy in the form of **bremsstrahlung**
  - **Elastic** collisions with **atomic electrons**:

        - The incident electron is deflected from its original path but no energy loss occurs and characterized by **angular scattering power**
- **Inelastic collisions** with **atomic electrons** leading to **ionization or excitation**
    - Atomic ionization: Ejection of the orbital electron from the absorber atom.
    - Atomic excitation: Transfer of an atomic orbital electron from one allowed orbit (shell) to a higher level allowed orbit.
- Atomic ionizations and excitations result in **collision energy losses** experienced by the incident electron and are characterized by **collision (ionization) stopping power**
- **Inelastic** collisions with atomic nuclei results to **bremsstrahlung** (radiation loss) and characterized by radiation stopping power
- Energy loss by incident electron through inelastic collisions is described by the **linear stopping power S** (unit: MeV/cm)
    - The rate of kinetic energy loss <u>per unit path length</u> by charged particle

$$S = \frac{dE_K}{dx}$$

- The **mass stopping power** is the linear stopping power divided by the density of the medium (unit: MeV * cm^2/g)

$$\frac{S}{\rho} = \frac{dE_K}{\rho dx}$$

- **The linear energy transfer (LET)** (units: KeV/micrometre).
    - also known as the 'restricted' **collision stopping power**
    - defined as the <u>rate of energy loss per unit length</u> in collisions in which energy is 'locally' absorbed, rather than carried away by secondary electrons
- **Total Mass Stopping Power**
    - **Mass collision stopping power** resulting from electron-orbital electron interactions (atomic ionizations and atomic excitations), and

- **Mass radiation stopping power** resulting mainly from electron-nucleus interactions (bremsstrahlung production)

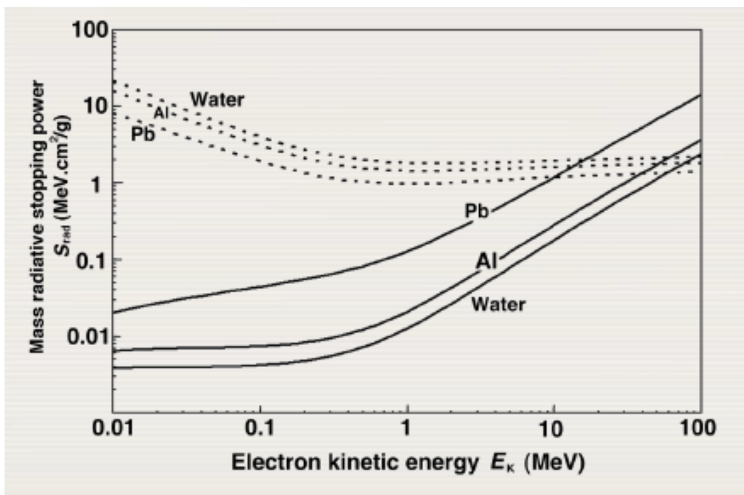
$$\left(\frac{S}{\rho}\right)_{tot} = \left(\frac{S}{\rho}\right)_{col} + \left(\frac{S}{\rho}\right)_{rad}$$

- For light charged particles both components contribute to the total stopping power
- For <u>heavy charged particles</u> the radiation stopping power is negligible

$$\left(\frac{S}{\rho}\right)_{tot} \sim \left(\frac{S}{\rho}\right)_{col}$$

- **Collision Interactions**
  - In low Z media (water or tissue), electrons loss energy through ionization and/or excitation
  - Rate of energy loss for collision interactions depends on
    - The electron density of the medium
    - Kinetic energy of the electron
  - The <u>rate of collision energy loss is greater</u> for <u>low atomic number (Z)</u> absorbers than for high Z absorbers.
    - High Z absorbers have lower electron density (fewer electrons per gram) E.g. Lead and Carbon........
    - High Z materials have more tightly bound electrons
  - Electron losses energy at about 2MeV/cm in water
  - Energy loss rate first decreases and then increase with increased electron energy
  - **Delta rays**: In the collision process with atomic electrons, if the KE acquired by the stripped electron is large enough for it to cause further ionization the electron is called a delta ray (δ-ray) or **secondary electron**
- **Radiative Processes**
  - In high Z media (lead) electrons loss energy through **bremsstrahlung production** (breaking radiation)
  - The rate of energy loss for radiation interactions is proportional to:

        - Kinetic energy of the electron
        - Square of the atomic number (Z^2) of the absorber
    - Bremsstrahlung production through radiative losses are efficient for higher energy electrons and higher atomic number absorbers (x-ray production: high energy with high Z material)
- **Total Energy Loss**
    - Depends on
        - Kinetic energy of the electron
        - Atomic number of the absorber
        - Electron density of the absorber



Cavity Theory

- Consider a point within a medium and within a beam of photon radiation. The absorbed dose at point P can be calculated by (s = stopping power)

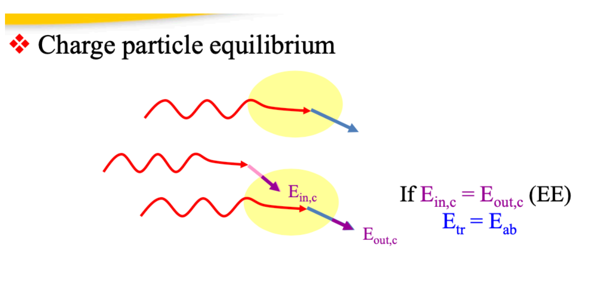
$$D_{med} = \hat{\Phi} * \left(\frac{S}{\rho}\right)_{\text{med}}$$

- In order to measure the absorbed dose at that point in the medium, a **dosimeter** can be introduced at that point
- Generally the sensitive medium will not be of the same material as the medium and if the Z and density are different then Dcav ≠ Dmed
- To determine Dmed from Dcav: **Bragg-Gray or Spencer-Attix theory**

- **Bragg-Gray Cavity Theory**
  - a relationship between the absorbed dose in a dosimeter and the absorbed dose in the medium containing the dosimeter
    - The absorbed dose to a medium at a point can be obtained from measured absorbed dose in a cavity and by multiplication with the **stopping power**

$$D_{med} = D_{cav} * \left(\frac{S}{\rho}\right)_{\text{med}} \Big/ \left(\frac{S}{\rho}\right)_{cav} = D_{cav} * \left(\frac{S}{\rho}\right)_{\text{med, cav}}$$

  - Assumptions
    - The cavity must be small when compared with the range of charged particles incident on it, so that its presence does not perturb the fluence of charged particles in the medium
      - The electron fluences are almost the same and equal to the equilibrium fluence established in the surrounding medium.
      - This condition can only be valid in regions of charged particle equilibrium



      - In reality → The presence of a cavity always causes some degree of fluence perturbation that requires the introduction of a fluence perturbation correction factor.
    - The absorbed dose in the cavity is deposited solely by those electrons crossing the cavity
      - Photon interactions in the cavity are assumed negligible and thus ignored.

        - All electrons depositing the dose inside the cavity are produced outside the cavity and **completely cross the cavity**.
        - **No secondary electrons** are produced inside the cavity (starters) and **no electrons stop** within the cavity (stoppers).
    - The Bragg-Gray cavity theory does not take into account the creation of secondary (delta) electrons generated as a result of the slowing down of the primary electrons in the cavity.
        - Some of these electrons released in the gas cavity may have sufficient energy to escape from the cavity carrying some of their energy with them out of the volume
        - This reduces the energy absorbed in the cavity and requires a modification to the stopping power of the electrons crossing the cavity
- Spencer-Attix Cavity Theory
    - modified Bragg-Gray cavity theory and changed stopping power to **restricted stopping power (L / rho)**.
    - Only include energy exchanges < 10 keV to eliminate delta rays that could travel outside the chamber carrying energy. High energy deltas are just added to the electron spectrum and dealt with through L once they slow down sufficiently
    - It operates under the same two conditions as used in the Bragg-Gray cavity theory
        - However, these conditions are now applied also to the fluence of the delta electrons
    - The cavity can be gaseous, liquid or solid medium, e.g. gas in ionization chambers
    - Taking into account all small perturbations, the dose in the medium is determined with a thin-walled ionization chamber in a high energy photon or electron beam by

$$D_{med} = \frac{Q}{m}\left(\frac{W_{gas}}{e}\right)\left(\frac{L}{\rho}\right)_{\text{med, cav}} P_{el}P_{dis}P_{wall}P_{elec}$$

where $\left(\frac{L}{\rho}\right)_{\text{med, cav}}$ = Spencer-Attix stopping power ratio

Wgas = the average energy expended in air per ion pair formed

Pel = the electron fluence perturbation correction factor

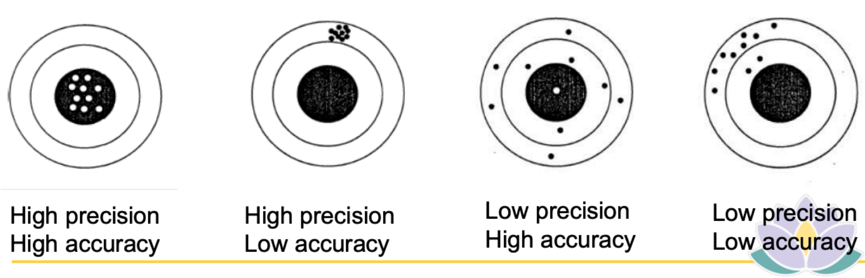
Pdis = correction factor for displacement of the effective measurement point

Pwall = wall correction factor

Pelec = correction factor for the central electrode

Radiation Dosimetry

- **Dosimeter**: A device that measures directly or indirectly the exposure, kerma, absorbed dose, equivalent dose etc
- **Dosimetry system**: Combination of the dosimeter and its reader
- A useful dosimeter exhibits the following properties
    - High accuracy and precision
        - **Accuracy and Precision**
            - **Accuracy**: specifies the proximity of the mean value of a measurement to the true value
            - **Precision**: specifies the degree of reproducibility of a measurement (small standard deviation)



    - Linearity of signal with dose over a wide range
        - Linearity → superlinearity → saturation
        - Linearity → saturation

- Small dose and dose rate dependence
  - The integrated responds of a dosimeter should not be dependent of the dose rate
  - The response should be constant for different dose rates
  - E.g. Linac dose rate 100MU/min – 600MU/min
- Flat Energy response
  - The responds of a dosimeter is generally a function of energy
  - **Calibration** is done at a specified beam quality, a reading should generally be corrected if the user's beam quality is not identical to the calibration beam quality
- Small directional dependence
  - Due to construction details and physical size, dosimeters usually exhibit a certain directional dependence
- High spatial resolution
  - Absorbed dose is a point quantity and the ideal measurements requires a point-like detector.
  - E.g. TLD, Film and gel (point defined by the resolution) , pin-point micro-chamber
- Large dynamic range

- **Absolute Dosimetry**
  - Aka. **Reference dosimetry**
  - Absolute dosimeter produces a signal from which the dose in its sensitive volume can be determined without requiring calibration in a known radiation field. e.g. Calorimetric, Chemical (Fricke), Ionization chamber dosimetry
    - Using **primary standard** in national standard laboratories
    - Physical constants and conversion factors are well characterised that dose determined without the need to calibrate the dosimeter
- **Absolute (calibrated) dosimetry**

- Requires calibration of its signal in a known radiation field. e.g. Ionization chamber dosimetry
- Using a dosimeter which has a known calibration factor, traceable to a primary standard
- Determination of absorbed dose (in Gy) at one reference point in a phantom
- Well defined geometry (example for a linear accelerator: measurements in water, at 100cm SSD, 10x10cm2 field size, depth 10cm)
- Follows protocols: TG-21 (old), TG-51
- If the absolute dosimetry is incorrect, everything will be wrong

- **Relative Dosimetry**
  - Requires calibration of its signal in a known radiation field. e.g. Film
  - Using a dosimeter which has a response proportional to the dose
  - Relates dose under non-reference conditions to the dose under reference conditions
  - Typically at least two measurements are required:
    - one in conditions where the dose shall be determined
    - one in conditions where the dose is known
  - If the absolute dosimetry is incorrect, everything will be wrong
- **Calorimetry**
  - Energy imparted to matter by radiation causes an increase in temperature ΔT
  - Dose absorbed in the sensitive volume is proportional to ΔT
  - Increase in temperature is measured with thermocouples or thermistors

$$D = \frac{dE}{dm} = \frac{C_p \Delta T}{1-\delta}$$

D = average dose in the sensitive volume

Cp = thermal capacity of the sensitive volume

δ = thermal defect

ΔT = temperature increase → ΔT (water, 1Gy) = 2.4 x 10-4 K

- **Chemical (Fricke) Dosimetry – reference dosimetry**

- Ionizing radiation absorbed in certain media produces a chemical change in the media and the amount of this chemical change in the absorbing medium may be used as a measure of absorbed dose
- The Fricke dosimeter relies on **oxidation of ferrous ions** (Fe2+) into ferric ions (Fe3+) in an irradiated ferrous sulfate FeSO4 solution.
- Concentration of ferric ions increases proportionally with dose and is measured with absorption of ultraviolet light (304 nm) in a spectrophotometer

$$D = \frac{\Delta M}{\rho G(Fe^{3+})}$$

ΔM - change in molar concentration of Fe3+

ρ - density of the Fricke solution

G(Fe3+) - chemical yield of Fe3+ in mol/J

- **Free Air Ionization Chamber – reference dosimetry**
  - Its sensitive volume is usually filled with ambient air and the dose related measured quantity is charge Q produced by radiation in the chamber sensitive volume
  - Charges are collected by electrodes
  - Sensitive volume and electron range limit radiations energies to about 0.3 MeV
- **Ionization Chamber – calibrated dosimetry**
  - Ionization chamber is the most practical and most widely used type of dosimeter for accurate measurement of machine output in radiotherapy
  - It may be used as an absolute or relative dosimeter
  - Its sensitive volume is usually filled with ambient air and the dose related measured quantity is charge Q produced by radiation in the chamber sensitive volume

$$D_{air} = \frac{Q}{m_{air}}\left(\frac{W_{air}}{e}\right)$$

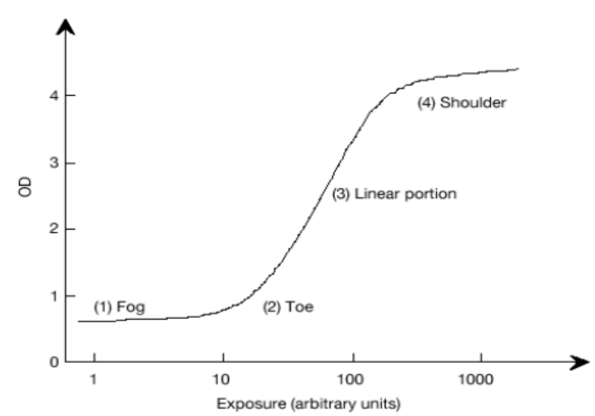
where $\left(\frac{W_{air}}{e}\right)$ is the mean energy required to produce an ion pair in air per unit charge e (33.97 eV/ion pair or 33.97 J/C)

- Basic design is of a **cylindrical farmer-type ionization chamber**
- It is a gas filled cavity surrounded by a conductive outer wall and having a central collecting electrode
- Can also be a **well type chamber**
- **Advantages**
    - Accurate and precise.
    - Recommended for beam calibration.
    - Necessary corrections well understood.
    - Instant readout
- **Disadvantages**
    - Connecting cables required.
    - High voltage supply required.
    - Many corrections required.

- **Radiographic Film – relative dosimetry**
    - A thin plastic base layer (200 mm) is covered with a sensitive emulsion of Ag Br-crystals in gelatine (10-20 mm).
    - During irradiation the AgBr is ionized, Ag+ ions are reduced to Ag (Ag+ + e --- Ag)
    - The elemental silver is black and produces the latent image
    - During development other silver ions are reduced
    - The rest of the silver bromide is washed away from the film during fixation process
    - Advantages
        - 2-D spatial resolution.
        - Very thin: does not perturb the beam
    - Disadvantages
        - Darkroom and processing facilities required.
        - Processing difficult to control.
        - Variation between films & batches.
        - Needs proper calibration against ionization chambers.

        - Energy dependence problems.
        - Cannot be used for beam calibration

- **H and D (Hunter and Driffield) Curve**
    - Gamma: slope of the linear part
    - Lattitude (contrast): Range of exposures that falls in the linear part
    - Speed (sensitivity): exposure required to produce an OD>1 over the fog Fog: OD of unexposed film



- **Thermoluminescent Dosimeter (TLD) – Relative dosimetry**
    - Must be calibrated
    - Before use, TLDs have to be annealed to erase any residual signal.
    - TLDs are available in various forms (e.g., powder, chip, rod, ribbon).
    - Must always be handled with care
    - TL dosimeters most commonly used in medical applications are based on their tissue equivalence
        - LiF:Mg,Ti
        - LiF:Mg,Cu,P
        - Li2B4O7:Mn
    - Other TLDs are (based on their high sensitivity):
        - CaSO4:Dy,
        - Al2O3:C
        - CaF2:Mn

- Advantage
  - Small in size: point dose measurements possible.
  - Many TLDs can be exposed in a single exposure.
  - Available in various forms.
  - Some are reasonably tissue equivalent.
  - Not expensive
- Disadvantage
  - Signal erased during readout.
  - Easy to lose reading.
  - No instant readout.
  - Accurate results require care.
  - Readout and calibration is time consuming.
  - Not recommended for beam calibration.

Dosimetry Phantom

- Phantom is a common name for materials that are used to replace the patient in studies of radiation interactions in patients
- Phantom material should meet the following criteria:
  - **Absorb photons** in the same manner as tissue.
  - **Scatter photons** in the same manner as tissue.
  - Have the **same density** as tissue.
  - Contain the same **number of electrons per gram** as tissue.
  - Have the same **effective atomic number** as tissue
- Water is the standard and most universal phantom material for dosimetry measurements of photon and electron beams
- EXAMPLES
  - SCANNING WATER PHANTOM
  - SOLD WATER PHANTOMS (SLABS)
  - Anthropomorphic phantom
  - Rando Phantom – Allow placement of TLDs in the phantom

Calibration of Photon and Electron Beams

- With ionization chambers
- Radiotherapy relies on accurate dose delivery to the prescribed target volume
- ICRU recommends an overall accuracy in tumour dose delivery of **5 %**
- Accurate dose delivery to the target with external photon or electron beams is governed by a chain consisting of the following main links
    - Basic output calibration of the beam
    - Equipment commissioning and quality assurance.
    - Treatment planning
    - Patient set-up on the treatment machine
- Output for a clinical beam is usually stated as
    - Dose rate at a point in **Gy/min** for kilovoltage machines
    - Dose rate at a point in **Gy/MU** for Linear Accelerators (Linacs)
    - At a reference depth zref (often the depth of **dose maximum** zmax)
    - In a water phantom for a nominal source to **surface distance** (SSD) or source to **axis distance** (SAD) 100 cm
    - At a **reference field size** on the phantom surface or the isocentre (usually 10×10 cm2)
- **TG-51 Protocol**
    - The TG-51 protocol is based on '**absorbed dose to water**' calibration (in a Co-60 beam). It is based on an in-water calibrated **Farmer-type ionization chamber**
        - National Calibration Lab – NRC
        - Standard source : Co-60
        - Stated calibration factor : ND,W
        - Dose per unit reading in water
    - The calibrated chamber can be used in **any beam modality** (photon or electron beams) and any energy, in water.
    - The formalism is simpler than the TG-21, but it is applicable in water only.

- Step:
  - OBTAIN AN ABSORBED-DOSE TO WATER CALIBRATION FACTOR
    - Dose to water per unit charge (reading)

$$N_{D,w}^{^{60}Co} \equiv \frac{D}{M}\left(\frac{Gy}{C\ or\ rdg}\right)$$

  - Determine the type of beam needed:

❖ In a Co-60 beam:

$$D_w^{^{60}Co} = M\, N_{D,w}^{^{60}Co} \quad (M\ is\ corrected)$$

❖ In any other photon beam Q: (only cylindrical chamber allowed at present)

$$D_w^Q = M\, k_Q\, N_{D,w}^{^{60}Co}$$

Converts beam quality (energy) from *Co-60* to *Q*.

- In any electron beam R_{50}: (both cylindrical and parallel-plate chambers allowed)

$$D_w^Q = M\, P_{gr}^Q\, k'_{R_{50}}\, k_{ecal}\, N_{D,w}^{^{60}Co}$$

Gradient correction for cylindrical chambers

Converts modality from *photon* to *electron*.

Converts electron energy from *ecal* to R_{50}.

Corrected charge

$$M = P_{ion}\, P_{TP}\, P_{elec}\, P_{pol}\, M_{raw}$$

Polarity correction $\quad P_{pol} = \left|\frac{\left(M_{raw}^{+} - M_{raw}^{-}\right)}{2M_{raw}}\right|$

Press/temperature $\quad P_{TP} = \frac{T + 273.2}{273.2 + 22} \times \frac{101.33}{P}$

Electrometer correction $\quad P_{elec}$

Ion recombination correction $\quad P_{ion}(V_H) = \frac{1 - \frac{V_H}{V_L}}{\frac{M_{raw}^H}{M_{raw}^L} - \frac{V_H}{V_L}}$

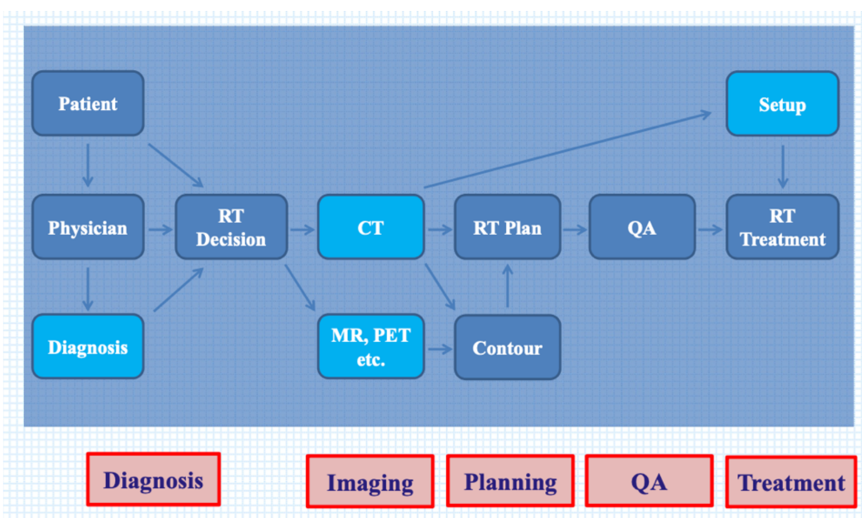
Medical Imaging (CT)

Medical Imaging

- Computed Tomography (CT or CAT)
- Magnetic Resonance Imaging (MR or MRI)
- Positron Emission Tomography (PET or PET/CT)
- Single Photon Emission Computed Tomography (SPECT)
- Ultrasound (US)
- X-Ray

Medical Imaging in Radiation Therapy

- CT: Diagnostic, Contouring, **Planning**, Setup
- MRI: Diagnostic, Contouring,
- US: Diagnostic, Contouring, Positioning
- PET: Diagnostic, Contouring
- SPECT: Diagnostic, Contouring
- X-Ray: Diagnostic
- CBCT/kV/MV: Setup



Computer Tomography (CT)

- Diagnostic
    - Is it cancer? Could be other methods involved
- Contouring

- tumor and organ delineation. Might with the help of images from other modalities.

- Planning
  - beam setup and dose calculation
- Setup
  - duplicate imaging position

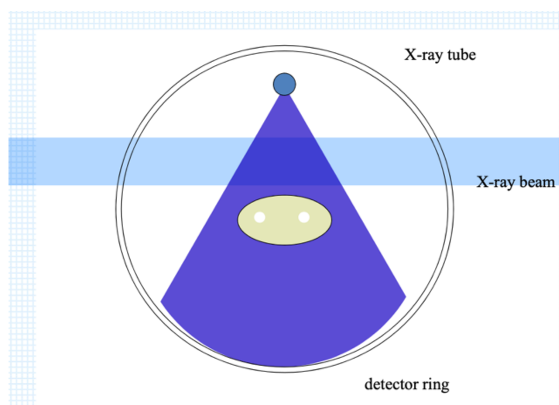
CT Milestones

- 1895: Roentgen discovers a new kind of radiation, which he named X-ray
- Hounsfield and Ambrose publish the first clinical scans with an EMI head scanner

Wilhelm Conard Roentgen (1845 – 1923)

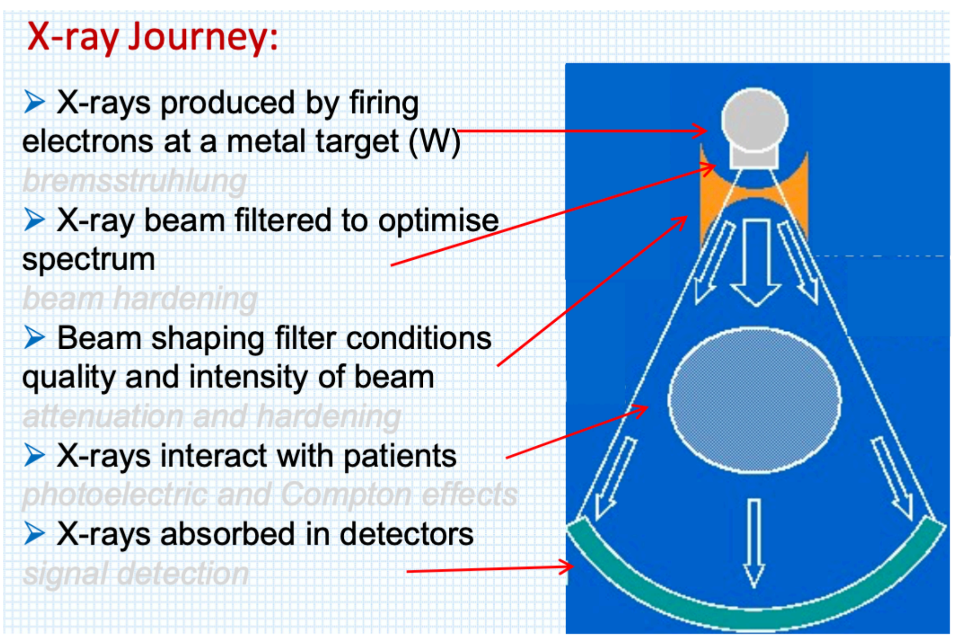
- German physicist
- Nov. 8, 1895: produced and detected electromagnetic radiation in a wavelength range known as **X-rays** or **Röntgen rays**
- 1901: first Nobel Prize in Physics: "in recognition of the extraordinary service he has rendered by the discovery of the remarkable rays subsequently named after him"
- 2004: International Union of Pure and Applied Chemistry (IUPAC) named element 111, roentgenium, after him.
- Unit for **exposure** from photon beams, **Roentgen**: One electrostatic unit of charge (3.33*10-10 C) in 1 cm^3 of air at STP. 1R=2.58*10-4 C/kg=0.876 cGy (in air).

CT Simulator



- An X-ray device capable of cross sectional imaging
- Generating images of slices through the patient.
- Component
  - Doughnut shaped gantry
  - Moving couch
  - Lap lasers
  - Control console
  - Recon computers

- **X-ray journey**
    - X-rays produced by firing electrons at a **metal target** (W) → bremsstruhlung
    - X-ray beam **filtered** to optimise spectrum → beam hardening
    - Beam shaping filter (**Bow-tie Filter**) conditions quality and intensity of beam → attenuation and hardening
    - X-rays interact with patients → photoelectric and Compton effects
    - X-rays absorbed in detectors → signal detection
        - Detector and tube rotate around the patient
        - Detector arrangement
            - Single detector, detector row, detector ring, or detector matrix
        - Types:
            - Early detectors scintillators, e.g. NaCl
                - Low max count rate leads to long scanning time
            - Xenon gas detectors
                - Pressurised Xe gas: higher count rates, but lower detection efficiency
            - Modern ceramic scintillators
                - Coupled to photodiodes, offer **best all round performance**



CT Scanner Evolution

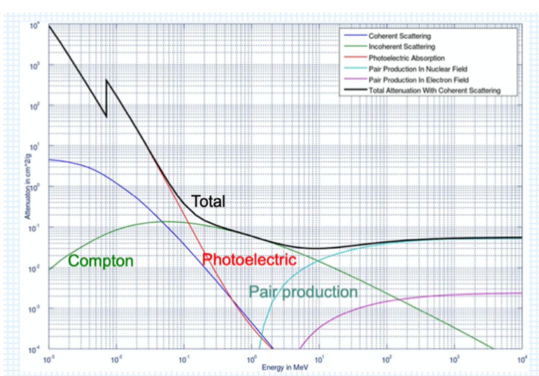
- 1st generation: Rotate-Translate, Pencil Beam
    - Produced a thin **focused beam of X-rays** known as "**pencil beam**"
    - The pencil beam passing through the patient onto a **single detector**
    - CT tube and detector moved across the patient from left to right rotating 1 deg
    - Total scan time about 5 min per image
- 2nd generation: Rotate/Translate Narrow Fan Beam
    - **Fan beam**
    - **Multiple detectors** in a straight **line**
    - Tube and detector move across the patient then rotate 5 deg
    - Total scan time about 20s per image
- 3rd generation: Rotate/Rotate, Wide Fan Beam
    - Fan beam
    - **Multiple detectors** along a **curve**
    - Tube and curved array of detectors rotate around the patient
    - Total scan time about 1s per image
- 4th generation: Rotate/Stationary, Closed Detector Ring
    - Fan beam
    - **Multiple detectors** <u>encircle the patient</u> but do not rotate
    - Tube rotates around the patient
    - Total scan time < 1s per image
- 5th generation: Stationary/Stationary, Electron Beam Rotate
    - Fan beam
    - Both target and detectors encircle the patient <u>w/o rotating</u>
    - **Incident electron beam rotates**
    - Total scan time < 1s per image
- 6th generation: Helical CT, Tube Rotate + Couch Translate, Single Detector Row
    - Continuous Couch Translation with Tube/Detector Rotation
    - Fan Beam

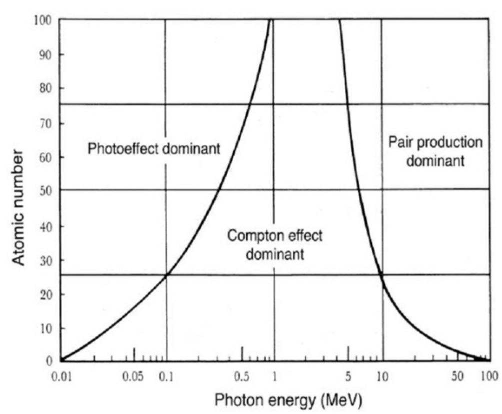
- Single Detector Row
- 7th generation: Multiple Detector Array, Helical Scanning
  - Continuous Couch Translation with Tube/Detector Rotation
  - Wide fan beam
  - Multiple detector array

Electron Interactions

- Ionization → delta rays, converted mainly to heat
  - Electrons follow erratic paths in matter as a result of multiple scattering events
  - The ionization track is sparse and nonuniform
- Radiation
  - **characteristic radiation** by ejecting a shell electron
  - Bremsstrahlung, the **X- rays generating interaction**
    - **The higher e- energy, the higher efficiency in X-ray generation from Bremsstrahlung**
  - Extreme case of bremsstruhlung. Electron full stop and **photon receives all energy** → defines kVp
- **Stopping Power**
  - The rate of energy loss per unit charged particle track length.
- Collision Stopping Power (Sion)
  - Energy loss by ionization → mainly to heat
- Radiative Stopping Power (Srad)
  - Energy loss by radiation
  - In **kV range**, Srad << Sion. **X-ray production is very inefficient**. For 100 keV e-beam, >99% lost to heat.
    - CT is usually operated at 80-140 kVp, which means that the incident electron energy for generating X-rays is in the range of 80-140 keV.
- **Photoelectric Effect**
  - Probability jumps up when hv ~ **bounding energy EB**
  - Probability

        - $1/(hv)^3$ → low energy range dominate
        - $Z^{3\text{-}4}$ → high dependence on atomic number
        - density
    - **dominates for 10's keV range** → for water (Zeff = 7.42), 10-26 keV
- **Compton Effect**
    - Probability
        - drops off as energy increases
        - not (very) dependent on Z
        - electron density
    - Dominates interactions for **> 10's keV to MeV energies**, such as radiography, nuclear medicine, and radiotherapy → for water (Zeff = 7.42), 26 keV – 25 MeV
- **Pair Production**
    - Threshold photon energy 1.022 MeV
    - Probability: increases w/ photon energy; ~ Z^2; ~ density
    - Positron is eventually annihilated
    - for water (Zeff = 7.42), 25 MeV – 100 MeV

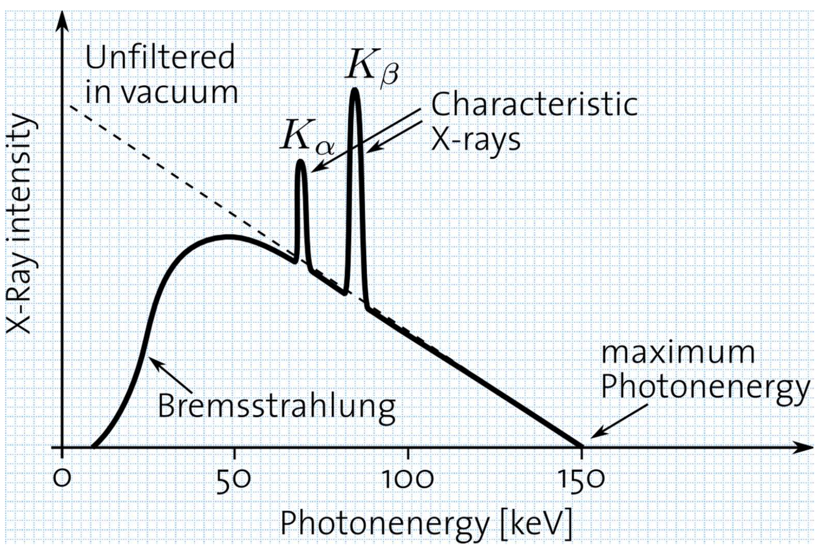




- We use kV X-rays for medical imaging, as bone, muscle, and fat have different Zeff → mass absorption coefficient ratio is different for all three
    - High Z = high absorption at kV range for photoelectric effect
    - Most tissue contrasts

X-Ray Production

- accelerated electron beam bombards a rotating anode (the target) with a small target angle → rotary design for dissipation of heat
- Incident e- energy for CT: 80 keV --- 140 keV → interaction: ionization and radiation
    - Only the radiation part becomes X-ray
- Target: Tungsten (W), Z=74, A=184
    - Melting point: 3422 deg → as this method is inefficient, it generates a lot of heat → it has to have a high melting point
- CT machines are very inefficient X- ray generator. The lower the energy, the less efficient.
    - e.g. 100 kVp: >99% lost to heat
    - We still use this due to the usefulness of the energy of the X-ray generated
- For 150 kVp X-ray (ie: max photon energy at 150 keV) Spectrum



- For MV beams, X-ray intensity peaks forward, i.e., the e- incident direction
- For kV beams, X-ray intensity peaks away from the e- incident direction

X-Ray Attenuation

- **The linear attenuation coefficient, μ**, between the X-ray tube and the detector
- The linear attenuation coefficient is a measure of how rapidly are X-ray attenuated

- the fraction of photons that interact <u>per unit thickness</u> of attenuator. The unit thickness must be chosen small enough so that the attenuated fraction is small compared to 1.0

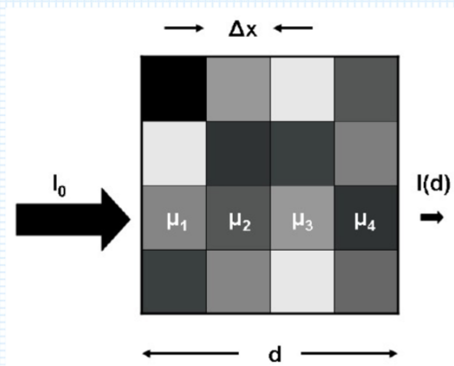
$$\mu = -\tfrac{\Delta I}{I}/\Delta x$$

$$I = I_0 e^{-\mu x}$$

$$I = I_0 e^{-\sum_i \mu_i \Delta x}$$

Projection:

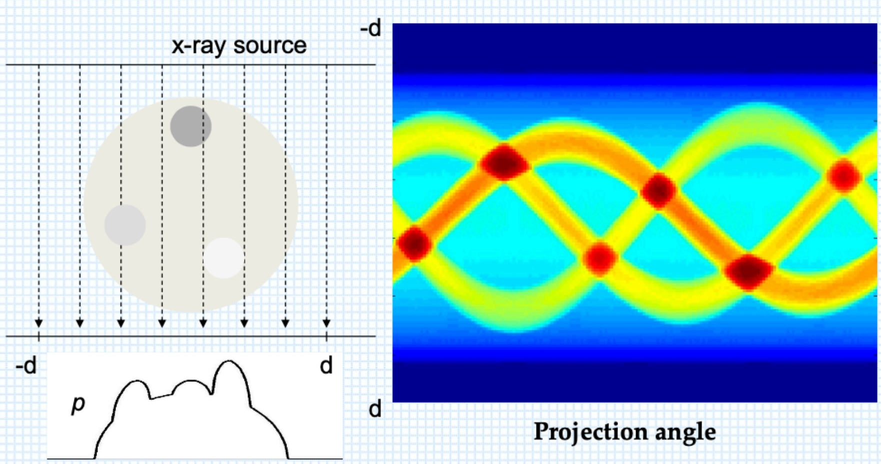
$$p = \sum_i \mu_i \Delta x = -\ln \frac{I}{I_0}$$



Reconstruction

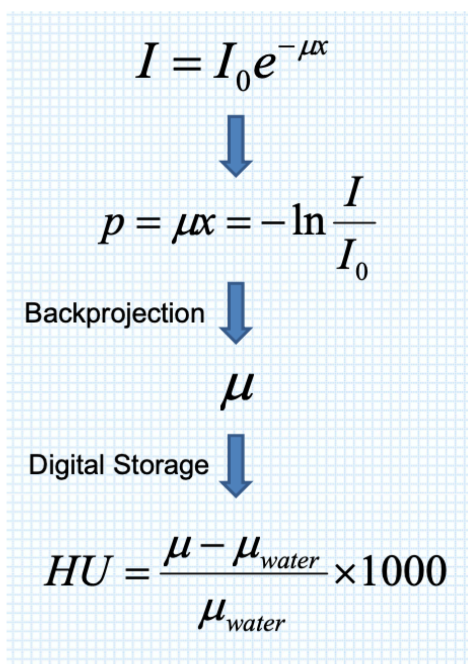
- **Sinogram** → take 3D and project it into 2D

• projections $p = \sum_i \mu_i \Delta x = -\ln \frac{I}{I_0}$ • I, I_0 - intensities



- **Algorithms**
    - Computer based
        - simple back-projection → 1/r blurring
        - filtered back-projection
            - simple back-projection produces blurred images
            - projection data need to be filtered before reconstruction
            - different filters can be applied for different diagnostic purposes
                - **smoother** filters for viewing **soft** tissue
                - **sharp** filters for **high resolution** images
            - back-projection is the same as before
        - iterative techniques
    - reverse the process of measurement using projection data to reconstruct an image
    - each projection is uniformly distributed across the reconstructed image
- **Back-Projection**
    - After back-projection, the result is a **matrix of attenuation coefficients**

CT Number / Hounsfield Number (HU)



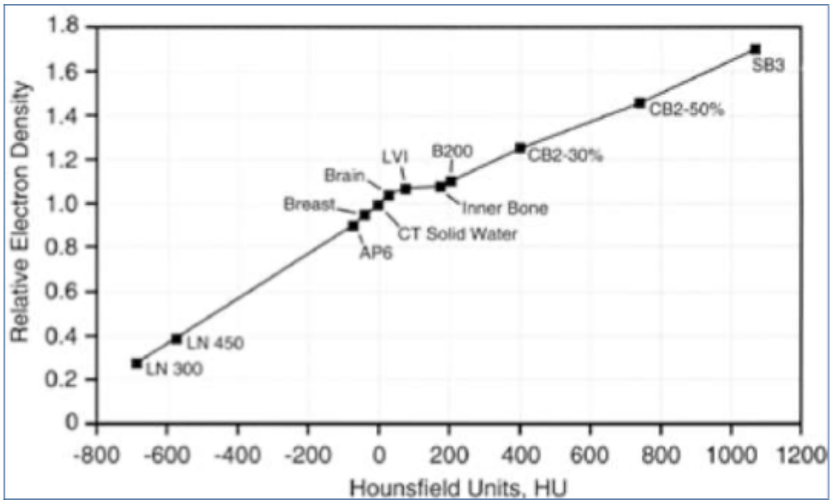
- **Sir Godfrey Newbold Hounsfield (Aug.28, 1919 -- Aug. 12, 2004)**
    - 1979 Nobel Prize winner for Physiology or Medicine for developing the diagnostic technique of computerized tomography (CT).
    - In 1958, he helped design the first commercially available all-transistor computer made in Great Britain: the EMIDEC 1100
    - Oct.1, 1971, CT scanning was first introduced into medical practice with a successful scan on a cerebral cyst patient at Atkinson Morley Hospital in Wimbledon, London.
    - In 1975, Hounsfield built a whole-body scanner.
- HU for different medium
    - Water: 0 HU
    - Air/Vacuum: -1000 HU
    - Bone: 1000 --- 3000 HU

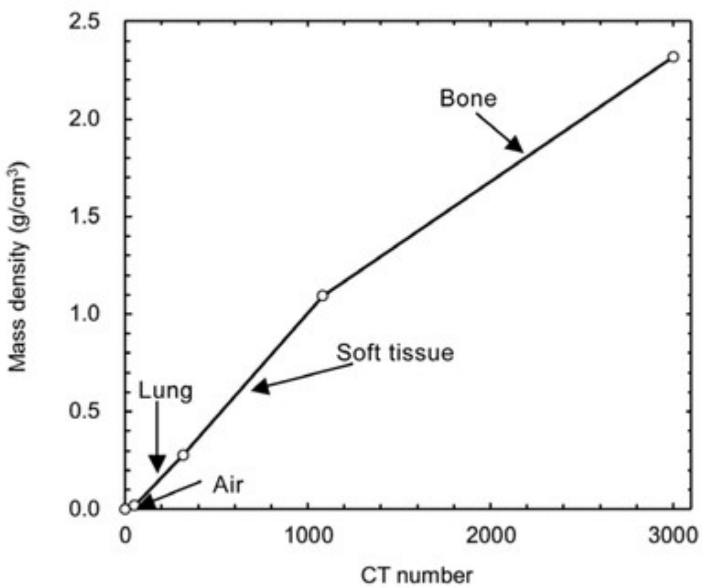
TABLE 11.1. TYPICAL HU VALUES AND RANGES OF VALUES FOR DIFFERENT TISSUES AND MATERIALS[a]

Substance	HU
Compact bone	+1000 (+300 to +2500)
Liver	+60 (+50 to +70)
Blood	+55 (+50 to +60)
Kidneys	+30 (+20 to +40)
Muscle	+25 (+10 to +40)
Brain, grey matter	+35 (+30 to +40)
Brain, white matter	+25 (+20 to +30)
Water	0
Fat	–90 (–100 to –80)
Lung	–750 (–950 to –600)
Air	–1000

- Storing HUs
    - Integer storage assigned to each voxel: 12 bits
        - 2^{12} = 4096; Starts from -1024, ends at 3071. Covering most clinically relevant tissues.
    - Stored in **DICOM format**: 0 – 4095, but clearly indicated w/ an **offset -1024**.
    - For covering high density materials, extents to 14 bits (16384).
- Display HUs
    - CT usually visualized on a monitor capable of discriminating **256 (2^8) grey values**
    - Human eyes can optimally discriminate 700-900 shades of gray.
    - CT images are of 4096 (2^12) values
    - Each pixel HU value has to undergo a linear mapping to a 'window' of 8 bit values.
    - Capable of using appropriate window size for optimal visualization of the tissues of interest
    - Window size: (HUmax --- HUmin)
    - Window level: (HUmax + HUmin)/2
- Dose Calculation
    - CT number → linear attenuation coefficient → density → dose
    - **CT to density table** specific to the CT scanner is required

Electron density Plug material	Physical relative to water	density, g/cm³
CT Solid Water	.99	1.02
True water	1.00	1.00
Lung (LN300)	0.28	0.30
Lung (LN450)	0.40	0.45
Adipose (AP6)	0.90	0.92
Breast	0.96	0.99
Brain	1.05	1.05
Liver (LV1)	1.07	1.08
Inner bone	1.09	1.12
Bone (B200)	1.11	1.15
Bone (CB2-30% mineral)	1.28	1.34
Bone (CB2-50% mineral)	1.47	1.56
Cortical bone (SB3)	1.69	1.82





CT Image Definition and Formation

- CT Digital Storage
  - In DICOM (Digital Imaging and Communication in Medicine) format
  - **One slice** is **one DICOM** file
  - CT image dataset contains many DICOM files
  - Each DICOM file contains
    - patient information
    - scanning parameters (kVp, mA, sec, exposure, recon) slice location & image position,
    - slice thickness

        - pixel numbers and spacing
        - pixel data (0--4095) with intercept -1024 clearly indicated

- **Image Quality**
    - Four basic factors
        - Spatial resolution
        - Image noise
        - Image contrast
        - Artifacts → Cannot avoid this
    - The factors interact to determine sensitivity and visibility of details.
    - Increasing CT image quality generally results in the increase of CT Dose.
        - Medical imaging's contribution to collective effective dose increased dramatically
        - CT itself contributes about half of the dose from medical imaging
        - For effective dose < 100 mSv, there is no data supporting it is helpful/harmful to human health yet. (Effective dose ~ 10 mSv per CT exam)
        - But we assume it is harmful to human body
        - We also assume that the detriment to human body linearly increase with dose, no matter how small dose amount (i.e. Linear Non-Threshold).
        - CT patients with caution: only when it is necessary and only when it is doing more good than harm.
        - When doing CT, minimize patient dose while maintaining reasonable image quality (balance)
- **Spatial Resolution**
    - the ability to distinguish small, closely spaced objects on an image
    - Generally limited by the size and spacing of the detectors
    - Usually expressed as line pair per cm
- **Noise**
    - Variation in CT number in image of a uniform object

- Associated with the # of X-rays contributing to each detector measurement
- Due to the use of limited # of photons to form the image. Result of random processes involved in X-ray interactions and detection.
- measured using the **standard deviation of the image CT number**.
- Is **important** when looking at **low contrast images**.

- **Contrast**
  - Contrast = difference in signal.
  - For CT: difference in CT# between an object and the surrounding tissue (CTB – CTA)
  - CT contrast is determined by differential attenuation
    - Differences in X-ray attenuation in different types of tissue resulting in differences in X-ray intensity reaching detectors
    - **Compton scattering** dominates (due to kVp, filtration, & tissue type) for **soft tissue**
      - Soft tissue contrast in CT comes mainly from **physical density**
    - **Bone** is of higher Z, more **photoelectric** effect; and of higher density, too.
      - CT images provides very good contrast to compact bones
  - When looking at objects which have CT number close to background (ie: low contrast), noise can mask detail.
- Scanning Parameters that affect quality
  - **mA**:
    - high tube current gives more intense X-ray beam
  - **Scan time**:
    - long scan time → more X-rays to detectors
  - **kVp**:
    - high kVp X-rays more penetrating
  - **Slice thickness**:
    - wide slice → more X-rays
  - **Pitch**:

        - couch travel with respect to tube rotation
    - More, such as artifacts, patient composition: **small patients less attenuation**
    - **mAs**
        - mAs: mA -- tube current, s -- exposure time, at a given tube voltage
        - mAs (or mA ` s) proportional to # of photons generated per rotation
        - mAs increase → photon fluence increase → **noise decrease** → more detail in image but higher dose
    - **kVp**
        - determined by **tube voltage**. Together with filters, it governs the X-ray spectrum.
        - Higher kVp, higher mean photon energy, **increased penetration**
        - Controls **contrast** in a CT image
        - But highly increased the dose delivered to patients
    - **Slice thickness**:
        - the number of mm's of information used for reconstructing one CT slice at a certain table position.
        - Single slice CT --- beam collimation width in the axial direction;
        - Multi-slice CT --- detector width in the axial direction.
        - Increasing slice thickness:
            - Increase the amount of anatomy covered
            - Decrease the noise on the image
            - Decrease the resolution
            - Could lead to partial volume artifacts
        - Selecting a suitable slice thickness is a balance between edge definition and noise, because of their mutual offsetting effects
            - Soft tissues: **Thicker** slices give **less noise** & **better contrast**
            - Bony structures: **Thinner** slices give better **spatial resolution**

- **Pitch**
  - Increased pitch → faster scanning → greater anatomical coverage in less time → decreased patient dose
  - Pitch = (couch travel per tube rotation) / (collimated beam width)
    - Pitch < 1: beam overlap
    - Pitch = 1: no beam overlap and no beam gap
    - Pitch > 1: beam gaps
    - Pitch <=2: no skipping anatomy
    - Pitch > 2: spiral defects

- Summary Table for Scanning Parameters

Effects	Slice Thickness	Pitch	mAs	kVp
Contrast	Unchanged	Unchanged	Unchanged	May increase or decrease
Resolution	Decrease	May decrease	Unchanged	Unchanged
Noise	Decrease	May increase	Decrease	Decrease
Dose	May decrease	Decrease	Increase	High increase. 15% increase in kV = 50% increase in dose

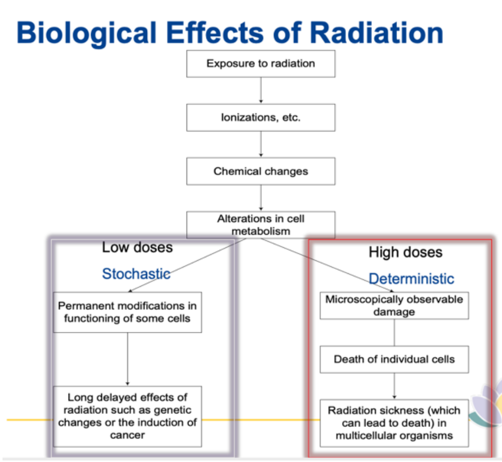
Radiation Biology

Cancer Risk Factors

- **Breast Cancer**: Family history, defects in DNA repair genes, previous radiation, years of hormones (lower risk with later menarche, 1st child before 30, earlier menopause, shorter estrogen supplementation)
- **Prostate Cancer**: Age; African-American race; Geography (Scandinavia-high, Asia-low); Family history; Dietary fat
- **Lung Cancer**: Smoking (~80% of cancers), genetic factors, radon, asbestos, air pollution
- **Head & Neck Cancer**: Tobacco + Alcohol (oral cavity, pharynx, larynx), sun (oral cavity), HPV (oral cavity), radiation (salivary glands), throat irritants (sinuses, nasal cavity), age (nasopharynx bimodal - teens, elderly)
- **Lymphoma**: Age 15 to 35 and > 55, male, genetics, HIV

Biological Effects of Radiation

- Ionizing Radiation can directly and indirectly damage DNA
    - DNA double-strand breaks
    - Chromosome damage
    - Depending on the type of radiation, total dose, dose rate, cell type and cell environment, resultant effects can:
        - Manifest as acute (early) and/or chronic (late) reactions
        - Mild (skin redness) or severe (death)
        - Affect exposed individual or progeny



Radiation Biology (Radiobiology)

- Radiation Biology: Study of the action of **ionizing radiations** on **living things**.
    - Ionization: Eject one or more orbital electrons
    - Ionizing Radiation: Localized release of energy, Biological basis of radiation oncology

Ionizing Radiation

- Electromagnetic Radiation
    - X-rays (produced **extra**-nuclearly) and γ-rays (produced **intra**-nuclearly) do not differ in nature or in properties, only in the way they are produced
- Particulate
    - These types of radiation occur in nature and also are used experimentally, in radiation therapy and diagnostic radiology
        - Electrons (beta radiation)
        - Protons
        - α-Particles
        - Neutrons
        - Deuterons
        - Heavy charged particles

X-Rays

- All forms of electromagnetic radiation have the same velocity, but different wavelength, and therefore different frequencies
- X-rays may be thought of as electromagnetic waves and-alternatively- as streams of photons, or "packets" of energy
- Each energy packet contains an amount of energy equal to **E=hν**, where h is Planck's constant and ν is the frequency
- If a radiation has a long wavelength, it has a small frequency ($\lambda\nu=c$), and so the energy per photon is small. Conversely, radiation with short wavelength will have a large frequency and hence the energy per photon is large.

- In their biological effects, electromagnetic radiations are considered to be ionizing if they have a photon energy in excess of **124 eV**, which corresponds to a wavelength shorter than about 10^{-6} cm.

Alpha Radiation (α)

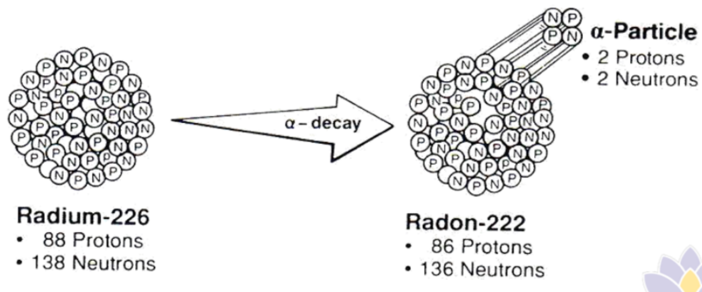
- Nuclei of helium atoms
- 2 protons and 2 neutrons
- Heavy, slow, +2 charges
- Can be accelerated in electrical devices similar to those used for protons
- High linear energy transfer (LET)
- Low penetrability
- They are also emitted during the decay of heavy naturally occurring radionuclides:

$$^{210}_{84}\text{Po} \rightarrow \, ^{206}_{82}\text{Pb} + \, ^{4}_{2}\text{He}$$

- Alexander Litvinenko was a former officer of the Russian Federal Security Service (FSB) and KGB. The 210Po was administered with activity of approximately 2 GBq (50 mCi) which corresponds to about 10 micrograms of 210Po. He died 3 weeks later. That is 200 times the median lethal dose of around 238 µCi or 50 nanograms in the case of ingestion.
- Direct Ionizing Radiation
    - they carry a charge and can interact directly with atomic electrons through Coulombic forces (i.e. same charges repel each other; opposite charges attract each other).

Decay of a heavy radionuclide by the emission of an α particle

- The emission of an α-particle (two protons and two neutrons) <u>decreases</u> the **atomic number by two** and the **mass number by four**. note that the radium has changed to **another chemical element**, radon, as a consequence of the decay.



Beta Radiation

- Electron emitted from nucleus
- Light, Fast, -1 charge
- Can be accelerated to high energies in **betatron** or **linear accelerator**. Widely used in cancer therapy
- Can travel several feet in air and has a medium penetrability
- The range of beta particle is considerably greater than an alpha particle
- Beta particle may transfer energy through ionization, excitation and it can produce a **Bremsstrahlung radiation** (X-rays)
- **Direct Ionizing Radiation**
    - they carry a charge and can interact directly with atomic electrons through Coulombic forces (i.e. same charges repel each other; opposite charges attract each other).

Neutrons (N)

- Neutral particle
- Classified by energy:
    - Thermal neutrons - E < 1eV
    - Fast neutrons - E > 10 keV
- **Indirectly** ionizing (no electrical charge). Ionization is caused by charged particles, which are produced during collisions with atomic nuclei
- Neutrons are also emitted as byproducts of fission of heavy unstable radioactive atoms. With the exception of 209 Bi (Bismuth) each nucleus with an atomic number greater than 82 is unstable.

- Neutrons interaction depends on the neutron energy and the material of the absorber:
  - Scattering: elastic and inelastic
    - Elastic collision
      - Neutrons lose their energy by elastic collision with **nuclei of similar mass**. In soft tissues interaction of a fast neutron with the **hydrogen nuclei** (protons) is the dominant process of energy transfer.
      - Part of the energy of the neutron is given to the proton as kinetic energy. Deflected neutron proceeds with reduced energy.
    - Inelastic collision / Spallation
      - At energies above 6MeV inelastic scattering contributes to energy loss in the absorbing material.
      - The neutron may interact with carbon or oxygen nucleus to produce **three or four α-particles**. These are known as **spallation products** which are very important at higher energies.
  - Capture
    - Boron neutron capture Therapy (BNCT)
      - To deliver a drug containing boron that localized only in tumors and then to treat with low-energy thermal neutrons that interact with **boron** to produce a particles

$$ {}^{10}_{5}B + {}^{1}_{0}n \rightarrow {}^{4}_{2}He + {}^{7}_{3}Li $$

Interaction of Photons with Matter

- Photons have zero mass, zero charge, and a velocity that is always "c", the speed of light;
- They do not steadily lose energy via coulombic interactions with atomic electrons as charged particles;
- Photons travel considerable distance before transferring the photon energy to electron energy;

- Photons are far **more penetrating** than charged particles of similar energy.
- The process by which x-ray photons are absorbed depends on the **energy of the photons** and the chemical composition of the absorber.
- Absorption of X-ray photon by Compton process
  - At high energies (100 keV-10 MeV), characteristic of a cobalt-60 unit or a linear accelerator used for radiotherapy, the Compton process dominates
  - Part of the photon energy is given to the electron as kinetic energy. The photon proceeds with reduced energy
- Absorption of X-ray photon by photoelectric process
  - The photon gives up its energy entirely; the electron is ejected from the atom. The vacancy is filled either by an electron from an outer orbit or by a free electron from outside the atom. **The change in energy is emitted as a photon of characteristic x-rays.**
  - It is a predominant mode of photon interaction at:
    - Relatively low photon energies
    - High atomic number Z
- Absorption of X-ray photon by pair production process
  - For energies greater than twice the rest mass energy of the electron (1.022 MeV) pair production may occur and will be the dominant type of interaction at energies above several MeV. The incident photon is converted to an electron-positron pair. The positron eventually annihilates with an electron producing two 511 keV photons.

Radiation Interaction with Water

- The body is composed of 80% water.
- The ultimate result of radiation interaction with water molecule is the formation of an **ion pair (H+, OH-) and free radicals (H radical, OH radical)**. Free radicals have an unpaired electron in their outer shell, a state which confers a high degree of reactivity.
- Free radicals initiate chemical reactions that lead to the production of damage via indirect action in the cell.

- X-ray photon → fast electron (e) → ion radical → free radical → chemical changes → biologic effect

Direct and Indirect Action of Ionizing Radiation

- When ionizing radiation interacts with a cell, ionizations and excitations are produced either in **critical biological macromolecules** (e.g. DNA) or in the **medium** in which the cellular organelles are suspended (e.g. water, HOH).
- Based on the site of these interactions, the action of radiation on the cell can be classified as either **direct** or **indirect**.
    - Direct: Charged particles (electrons, protons, etc.) → physical
        - Deposit does directly
        - DSB / SSB
    - Indirect: uncharged particles (photons, neutrons) → chemical
        - Produce charged particles (such as electrons) via interaction, then deposit does
        - DSB / SSB
- Sequence of events in indirect action

$T_{1/2}$ in sec	Incident X-ray photons
	↓
10^{-15}	Fast electrons
	↓
10^{-5}	Ion radicals
	↓
10^{-5}	Free radicals
	↓
	Macromolecular changes from breakage of chemical bonds
	↓
	Biological effects
days	- cell killing
generation	- mutation
years	- carcinogenesis

Dose Response Relationships

- Low does
    - DSB caused by one single electron
    - Probability of an interaction is proportional to dose
- High dose
    - DSB caused by two separate electrons
    - Probability is proportional to the square of the dose

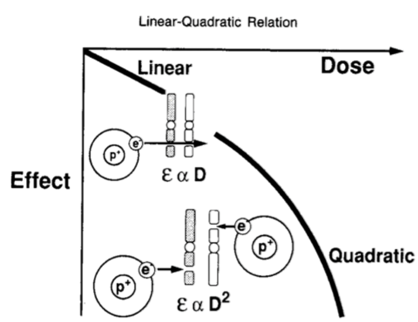
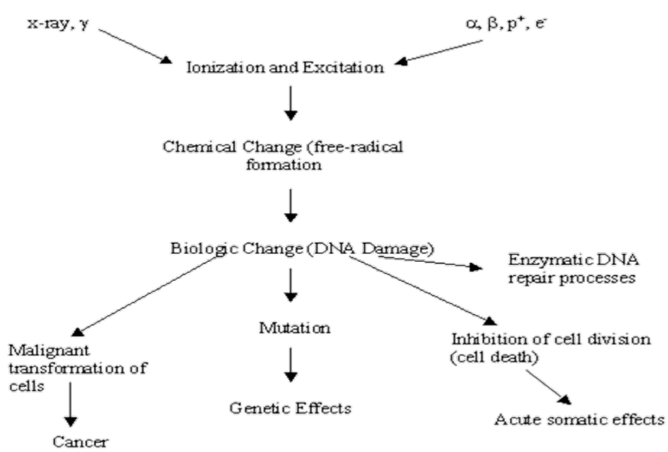


Figure 3.6. Relationship between chromosome aberrations and cell survival. Cells that suffer exchange-type chromosome aberrations (such as dicentric) are unable to survive and continue to divide indefinitely. At low doses, the two chromosome breaks are the consequence of a single electron set in motion by the absorption of x- or γ-rays. The probability of an interaction between the breaks is proportional to dose; this is the linear portion of the survival curve. At higher doses, the two chromosome breaks may result also from two separate electrons. The probability of an interaction is then proportional to the square of the dose. The survival curve bends if the quadratic component dominates.

Development of Radiation Injury



The Cell Cycle

- **Cell cycle time Tc**: Time between successive divisions (mitoses)
- G1 → S → G2 → M → G1
- Mitosis is a process of cell division which results in the production of two daughter cells from a single parent cell.

- M (mitosis) and S (DNA synthesis) portions of the cell cycle are separated (followed) by **two periods (gaps)** G1 and G2 when, respectively
- Cell cycle time for **mammalian cells** is of the order of **10 – 20 hours**:
    - S phase is usually in the range of 6 – 8 hours.
    - M phase is less than 1 hour.
    - G2 is in the range of 2 – 4 hours.
    - G1 is in the range of 1 – 8 hours.
- Cell cycle time **for stem cells** in certain tissues is up to **10 days**
- In general, cells are **most radio-sensitive in the M and G2 phases**, and **most radio-resistant in the late S phase**.
- Cell cycle time of malignant cells is shorter than that of some normal tissue cells, but during **regeneration after injury** normal cells can proliferate faster.
- Exponential growth of cell

N = No exp(lambda x t)

Lambda = fractional growth per unit time

Cell Death

- Cell death of non-proliferating (static) cells is defined as the loss of a specific function.
    - **Cell death = No reproduction**.
- Cell death for stem cells and other cells capable of many divisions is defined as the loss of reproductive integrity (**reproductive death**).
- Cell reproduction needs DNA.
    - Damage DNA (DSB / SSB) may stop the reproduction→ Cell death.
- Q: How does the radiation reaction interact to cause cellular damage and death?
    - Ans: By depositing **charged particles** (electrons, radicals, or ions)

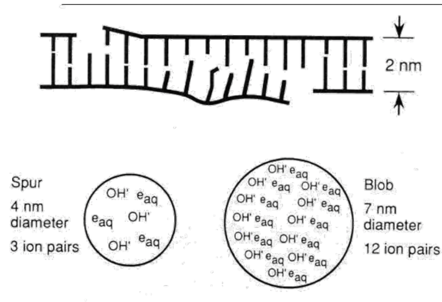


FIGURE 2.3 ● Illustration of a locally multiply damaged site. Energy from x-rays is not absorbed uniformly but tends to be localized along the tracks of charged particles. Radiation chemists speak in terms of spurs and blobs, which contain a number of ion pairs and which have dimensions comparable to the DNA double helix. A double-strand break is likely to be accompanied by extensive base damage. John Ward coined the term *locally multiply damaged site* to describe this phenomenon.

Dual Radiation Action (DRA) Theory

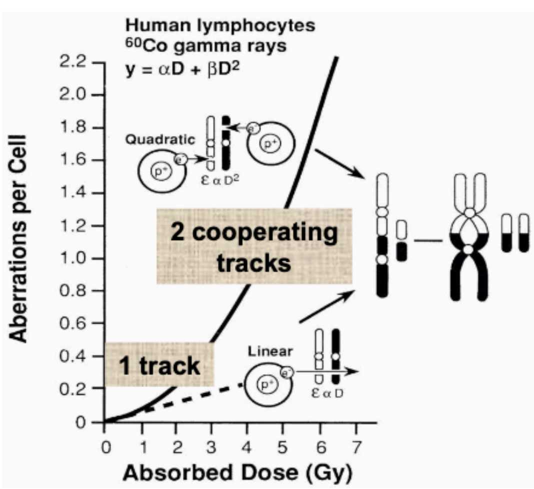
- Kellerer and Rossi, 1972
- Biological effect is based on a linear term and a quadratic term
- Damage Formats:
    - Single-strand breaks (SSB)
    - Double Strand Breaks (DSB)
    - Base damage: Single Base modification can have profound effects on protein function
- **Cell Survival**

$$S = \exp(-n) = \exp(-(\text{alpha} \times D + \text{beta} \times D^2))$$

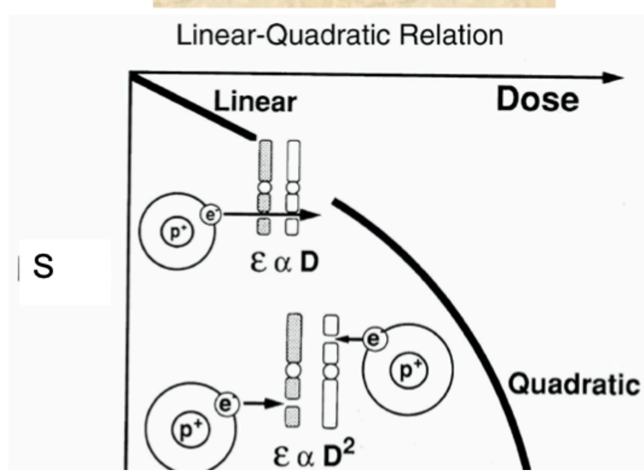
n = number of fatal chromosome aberrations

Linear Quadratic (LQ) Model

- α – Initial slope at **low Dose** susceptibility to **single-track damage**
- β – Adds curvature to the final slope (**larger Dose**) susceptibility to **dual-track damage**.
    - affected by dose rate and interim chromosome Repair
- α/β – **Dose** at which the two cell-killing effects are **equal**.

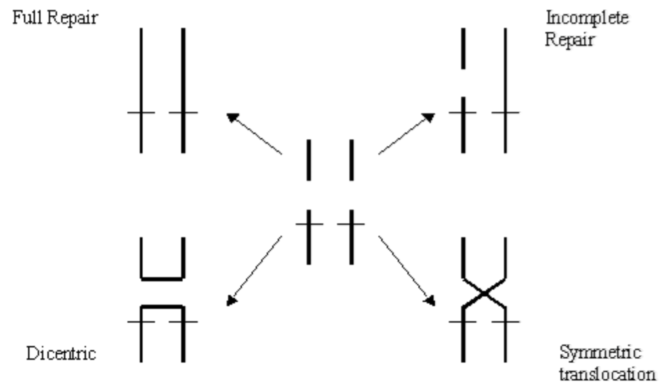


$$S(D) = e^{-\alpha D - \beta D^2}$$

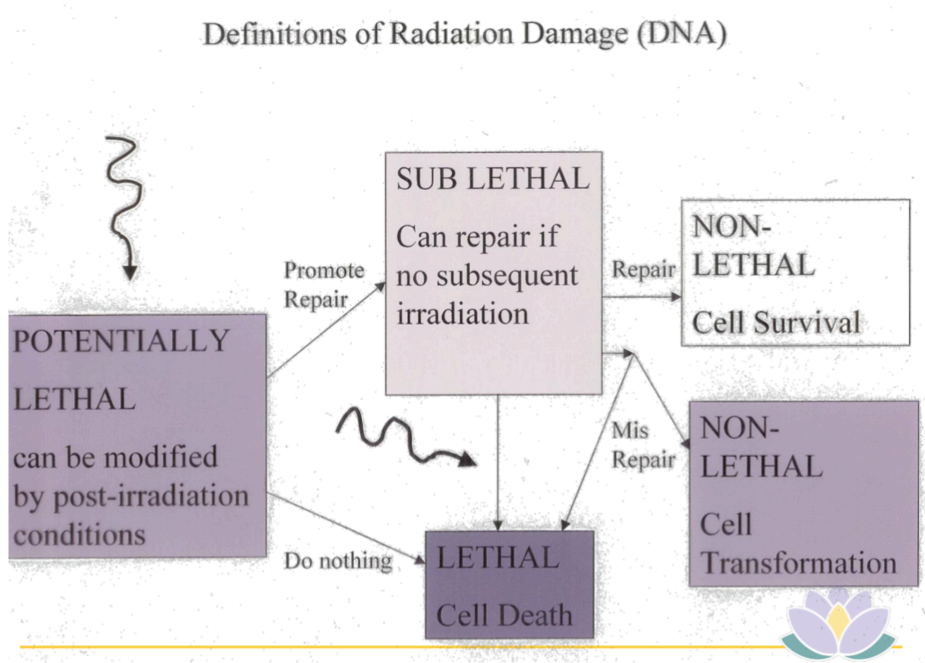


Radiation Damage

- Ionizing radiation produces **sublethal lesions**
- Sublethal lesions may combine to form **lethal lesions**



- From DNA damage to critical chromosome damage
    - Most DNA breaks are repaired !
    - Some are not repaired or misrepaired
    - Breaks lead to chromosome aberrations which interfere with
        - cell proliferation
        - cell normal functions



The *in vitro* cell survival curve

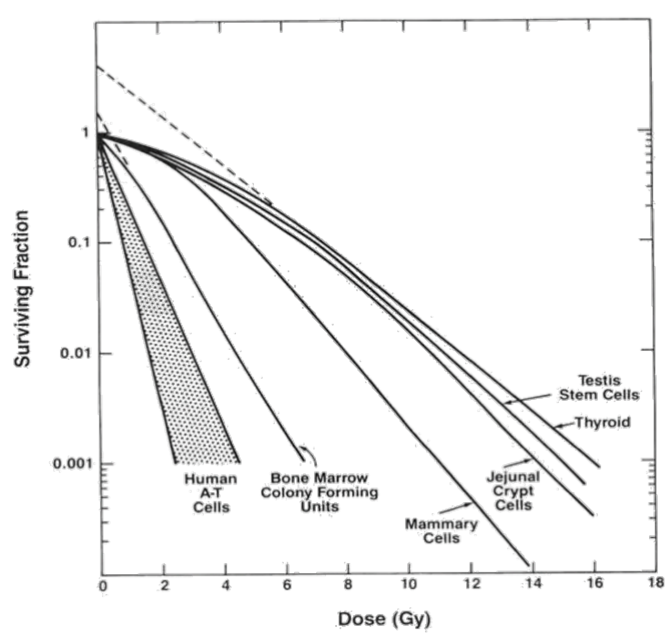
- Colony
  - represents the progeny of single ancestor – ~ 100 cells seeded: 50 - 90 colonies
- Plating efficiency (PE)
  - % of cells seeded that produce colonies → N1/No
  - PE needed in calculation of surviving fraction

$$PE = \frac{\#\,of\ colonies\ for\ D=0}{\#\,of\ cells\ plated\ \ for\ D=0}$$

- Surviving Fraction:
  - Survival:
    - capacity to divide indefinitely so as to produce a colony
  - colonies counted/(cells seeded * PE)

$$S = \frac{\#\,of\ colonies\ for\ D}{\#\,of\ cells\ plated\ \ for\ D \times PE}$$

- Cell Survival Curves: Survival vs. dose
  - Aim: To measure survival of cells to radiation dose.



Theory of Dual Radiation Action (DRA)

- Molecular Theory of Cell Inactivation (Chadwick and Leenhouts, 1981)
- Cell inactivation results from **unrepaired DNA double-strand breaks (DSB)**.
- At low-LET, a ?/?=d DSB can result from either a single event (linear component) or two separate events (quadratic component).
- Cell inactivation results from chromosome aberrations.
  - Some aberrations are produced by a single event.
  - Some aberrations are produced by two separate breaks.

Linear-Quadratic Hypothesis

- The linear quadratic model assumes that a cell can be killed in two ways.
  - Single lethal event
  - Accumulation of sublethal events
- If these modes of cell death are assumed to be independent

$$S=S^1S^n$$

Where S1 is the single event killing, And Sn is the two even killing

- The most common expression is

$$S = e^{-(\alpha d + \beta d2)}$$

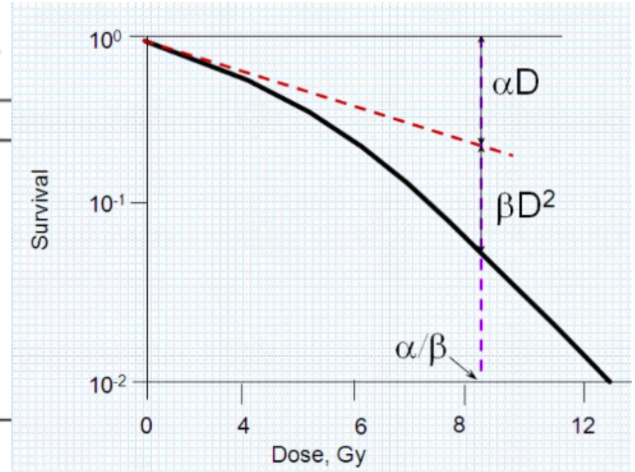
Where S is the fraction of cells surviving a dose D and α and β are constants.

- Survival curves show **continuously increasing curvature**, following a linear portion. This continuously bending curve reflects
- A component of cell kill proportional to dose (DSBs)
- A component proportional to dose^2 (SSBs).
  - $S = e^{-(\alpha d + \beta d2)}$, Where α and β are constants.
- These two components may progress at **different rate**.
- When two components are equal: α/β=d

Alpha/Beta Radio for some tissues

TABLE 22.1. *Ratio of Linear to Quadratic Terms From Multifraction Experiments*

Reactions	α/β, Gy
Early	
Skin	9–12
Jejunum	6–10
Colon	10–11
Testis	12–13
Callus	9–10
Late	
Spinal cord	1.7–4.9
Kidney	1.0–2.4
Lung	2.0–6.3
Bladder	3.1–7



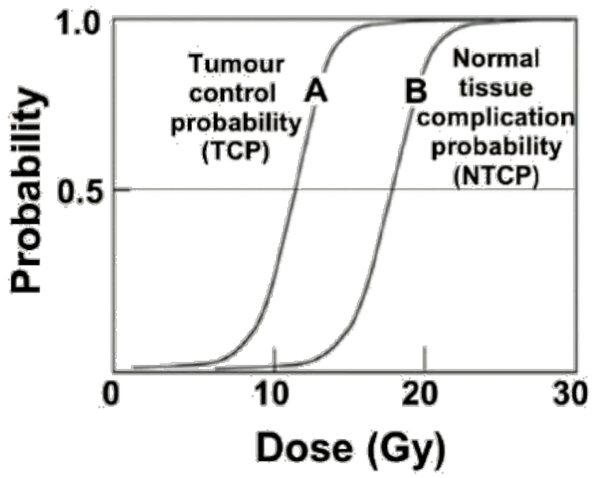
Properties of Cell Survival Curves

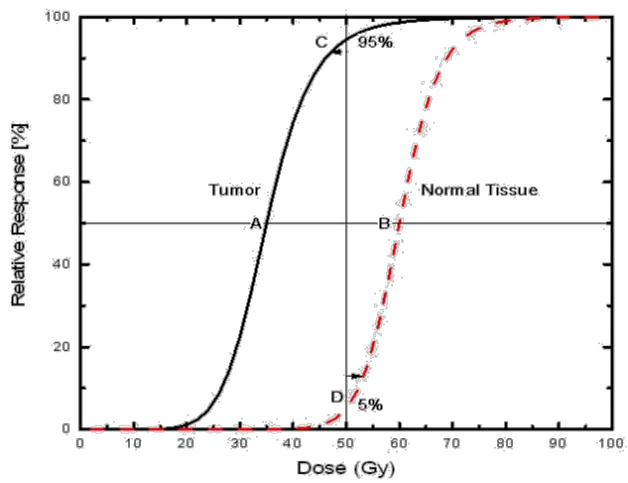
- For **late responding tissues** the survival curves (dose response curve) are **more curved** than those for early responding tissues (since beta contribution is higher)
  - For **early** effects the **ratio is large**; for **late** effects it is **small**.
  - For early effects, linear dominates at low doses.
  - For late effects quadratic term has an influence at doses lower than for early responding tissues.
- The alpha and beta ratio of mammalian cell killing are equal at the following doses:
  - 10 Gy for early responding tissues.
  - 2 ~ 3 Gy for late responding tissues.
- Late responding tissues more sensitive to change in **fractionation**.
- **Fraction size** is dominant factor determining late effects.

Normal and Tumour Cells Therapeutic Ratio

- Principle of radiotherapy is usually illustrated by plotting two sigmoid curves:
  - For tumor control probability (TCP) → DA
  - For normal tissue complication probability (NTCP) → DB
- **Therapeutic ratio = DB / DA**
- Optimum choice of radiation dose delivery technique in treatment of a given tumor is such that it **<u>maximizes</u> the TCP and simultaneously <u>minimizes</u> the NTCP**.

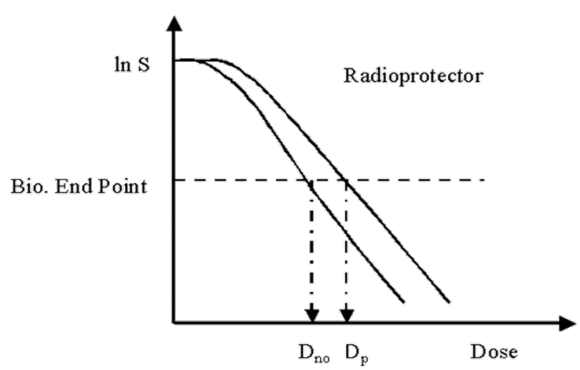
- The **TCP** curve for regional control of certain tumors never reaches a value of 1.0 as a result of microscopic or **metastatic spread** of the disease beyond the primary tumor site.
- It is imperative that the doses to normal tissues be kept lower than the doses to tumors in order to:
    - Minimize treatment complications.
    - Optimize treatment outcomes.





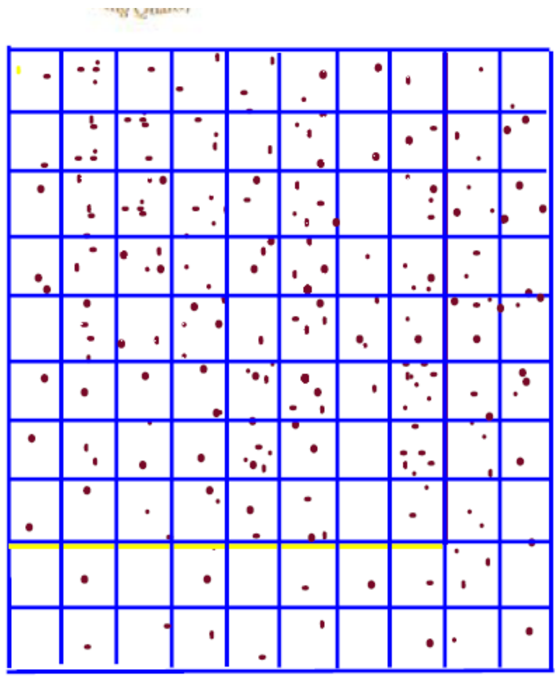
Radiosensitizers and radioprotections

- Chemical Modification
- Dose Modifying Factor (DMF)
    - DMF=Dp/Dno
- DMF > 1 for radioprotectors (normal tissue)
- DMF < 1 for radiosensitizers (tumor)
- Oxygen is a radiosensitizer



Single Hit / Single Target Model

- Poisson Distribution → on average, how many critical hits per cell at a given dose?

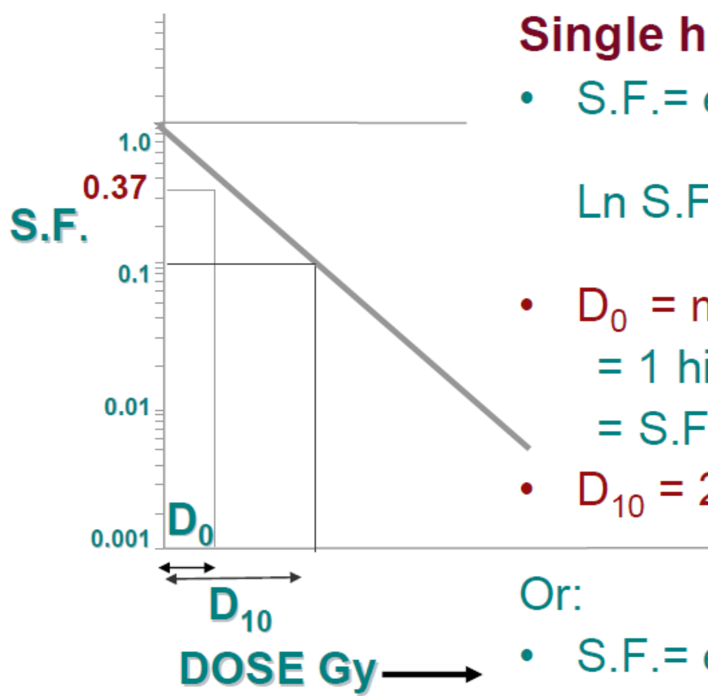


From the Poisson Distribution
P of x = $e^{-m}.m^x/x!$
where m = mean # hits

<u>P survival (x = 0)</u>

100 targets 100 hits	**e^{-1}=0.368**
100 targets 200 hits	**e^{-2}=0.137**
100 targets 300 hits	**e^{-3}=0.05**

- Cell Survival Fraction
  - Do: radiation at which on average, one hit per target → reducing survival fraction to 1/e = 0.37



Single hit, single target model

- S.F.= e^{-D/D_0}

  Ln S.F. = $-D/D_0$

- D_0 = mean lethal dose
  = 1 hit per target
  = S.F. of 36.8%
- $D_{10} = 2.3 \times D_0$

Or:

- S.F.= $e^{-\alpha D}$, i.e. $D_0=1/\alpha$

Mean Inactivation Dose (Do)

- Use to delay growth or sterilize

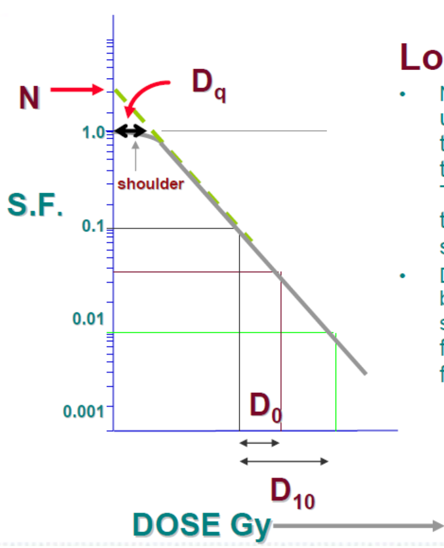
Mean Inactivation Dose (Do)

- Virus D_0 approx. = 1500 Gy
- E. Coli D_0 approx. = 100 Gy
- Mammalian bone marrow cells D_0 = 1 Gy
- Generally, for mammalian cells D_0 = 1-1.5 Gy

FOOD TYPE	DOSE (Gy)	EFFECT
Meat, Poultry, Fish, Shellfish, some vegetables	20,000 - 70,000	Sterilization. Storage at room temperature
Spices, etc.	8,000 - 3 0,000	Reduces micro-organisms and insects
Meat, Poultry, Fish	1,000 - 10,000	Delays spoilage. Kills salmonella.
Strawberries and some other fruits	1,000 - 4,000	Delays mold growth
Grain, Fruit, Vegetables	100 - 1,000	Kills some insects
Bananas and other non-citrus fruits	250 - 350	Delays ripening
Pork	80 - 150	Inactivates trichinae
Potatoes, Onions, etc.,.	50 - 150	Inhibits sprouting

Quasi-threshold Dose (Dq)

- Measure size of shoulder
- Repeated between fractions if enough time is left for repair



$\text{Log}_e N = D_q/D_0$

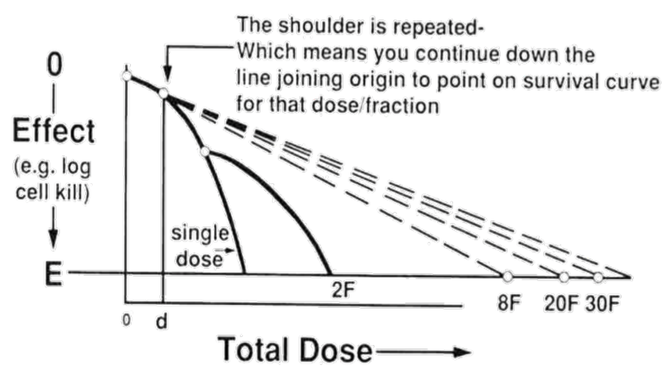
- N = extrapolation dose, which used to be thought to reflect the number of targets that had to be inactivated to kill a cell. This is not true. In a sense, it is the measure of the size of the shoulder.
- Dq (quasi-threshold dose) is a better measure of the size of the shoulder. It is repeated between fractions if enough time is left for repair.

4 Rs in Radiation Biology

- Repair → for healthy cells
  - DSB is repaired by enzymes ~ hours
- Redistribution (Reassortment) → for tumour cells
  - Cell cycle effect ~ day
  - To make the cell become more sensitive to radiation (after S phase)
- Repopulation → for healthy cells
  - Cell "growth" ~ week
- Reoxygenation → for cancer cells
  - Oxygen effect ~ 0.25 – 1 day

Fractionation → repeat the shoulder

- **Dividing** dose in number of fractions spares normal tissues.
  - Repair normal tissue
  - Repopulation of normal tissue
- Dividing dose in number of fractions increases damage to tumour.
  - Reoxygenation
  - Redistribution into radiosensitive phases



Fractionation in LQ Model

- Fractionated cell survival rate

$$S = [e^{-(\alpha d + \beta d^2)}]^n$$

$$S = e^{-nd(\alpha + \beta d)}$$

Where d = dose/fraction; n = number of fractions

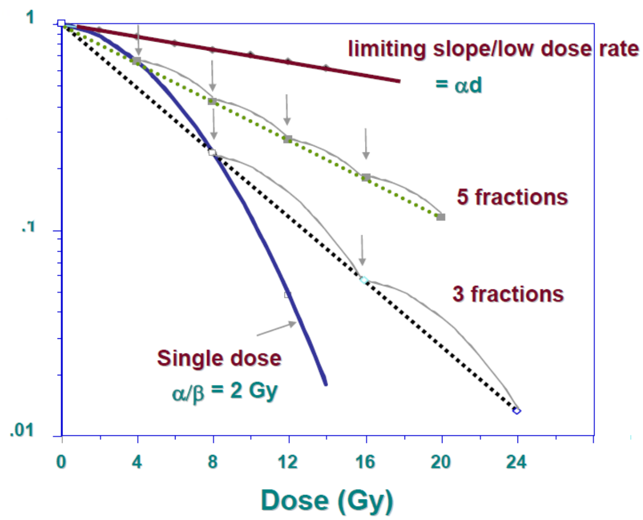
- Effect (Response Level)

E = − ln S = n d (alpha + beta d)

- Biologically Effective Dose (BED)

$$BED = \frac{E}{\alpha} = nd\left[1 + \frac{d}{(\frac{\alpha}{\beta})}\right]$$

- Different fractionation will give you different response (ie: effect or survival)



Time Factor in Fractionated LQ Model

- Related to **tumour doubling time** or **normal tissue proliferation.**
- Late responding normal tissues have **negligible** or small time factors since they are very slowly proliferating tissues.
- T = overall treatment time.
- Tk = time at which **rapid proliferation** sets in.
- Td = tumour **doubling time**.

E=nd(alpha+beta d)−lambda(T−Tk)

Lambda = ln(2) / Td

- The New BED:

$$BED = \frac{E}{\alpha} = nd\left(1 + \frac{d}{(\frac{\alpha}{\beta})}\right) - \frac{\ln 2(T - T_k)}{\alpha T_d}$$

- Treatment styles:
  - General treatment: 50 Gy/25 fx, 2 Gy/fx, 1 fx/day, 5 fx/week.
  - **Hyperfractionation**: 2 or more fractions per day.
  - **Hypofractionation**: 2 or more Gy per fraction.

Repair of Sublethal Damage

- Tends to improve cell survival.
- Repair occurs during interval between fractions.
- Time between fractions for most tissues should be 6 hours if possible
- Even then some tissues such as CNS may have incomplete repair and twice-a-day (BID) treatment is inadvisable
- Estimated repair times of late effects tissues may be 2.5-4.5 hours

Reassortment of Cells within the Cell Cycle

- Tends to reduce cell survival.
- Cells move to more radiosensitive phase in the cell cycle between fractions.
- M and G2 most sensitive phases.
- Late S most resistant phase.

Reoxygenation

- Hypoxic cells become oxygenated after a dose of radiation is termed reoxygenation
- Tumors contain a mixture of aerated and hypoxic cells. A dose of X-rays kills a greater proportion of aerated than hypoxic cells, because they are more radiosensitive.
- **Immediately after radiation, most cells in the tumor are hypoxic**. But the pre-irradiation pattern tends to return because of reoxygenation.
- If the radiation is given in a series of fractions separated in time sufficiently for reoxygenation to occur, the presence of hypoxic cells does not greatly influence the response of the tumor.

Repopulation

- Tends to increase cell survival.
- Occurs when fraction interval length **greater** than cell cycle doubling time.

- In acute responding tissues, regeneration (repopulation) has a considerable sparing effect
- The lag time prior to regeneration varies with the tissue
- Acute responding tissue may become dose-limiting as treatment time is reduced

Benefits of Dose Fractionation

- Repair of sublethal damage
  - spares late responding normal tissue preferentially
- Reassortment/Redistribution of cells in the cell cycle
  - increases tumor damage, no effect on late responding normal tissue
- Repopulation
  - spares acute responding normal tissue, no effect on late effects, danger of tumor repopulation
- Reoxygenation
  - increases tumor damage, no effect in normal tissues

Dose Rate Effect

- **Decrease in dose rate** (1Gy/min to 0.3 Gy/h) → **reduction in cell killing**.
  - Sublethal damage repair.
- Brachytherapy
  - Putting radioactive sources to the tumor.
  - "short" distance treatments.
  - Continous irradiation.
- Full repair at very low dose rates (< 5 cGy/h).
- No repair with single fraction high dose rate.
- Brachytherapy is somewhere in between high and very low dose rates.
- **Inverse-dose rate effect**
  - Decreasing dose rate enhances cell killing
  - Reason: Cell cycling
    - halts at high dose rates → decrease the dose reduce this effect

        - progresses at low to G2 → Cells can pile up in G2 and be irradiated - a sensitive phase

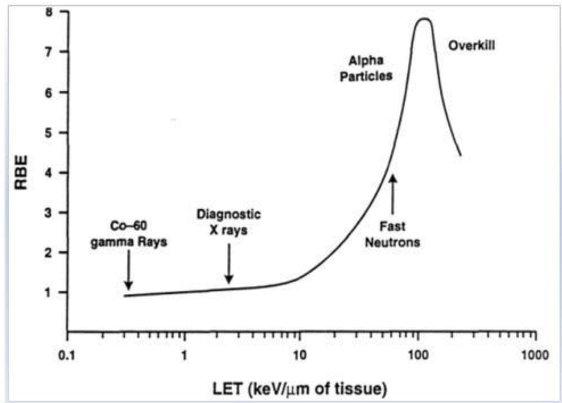
Relative Biological Effectiveness (RBE)

- Standard radiation is 250 keV x-ray → RBE = 1.0
- Used to compare the effects of different types of radiation.
- Depends on dose, species and effect used for the determination
- RBE = dose from <u>standard radiation</u> to produce a given bio effect / dose from the <u>test radiation</u> to produce the same bio effect
- High RBE = more damage at a given a given dose when compared to standard

Linear Energy Transfer (LET)

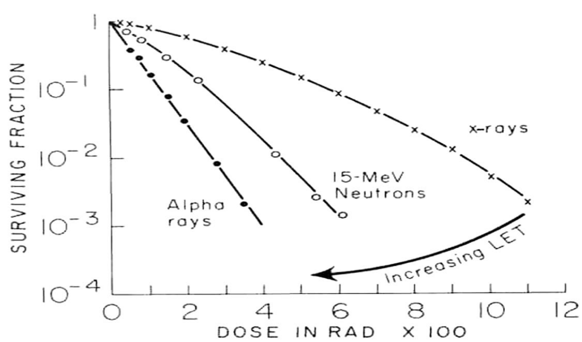
- the amount of **energy deposited** in tissue **per unit track length**. (keV/micro metre).
    - used to describe the rate at which energy is deposited as a charged particle travels through matter.
- Most **high LET** (densely ionizing) radiation e.g. neutron and alpha-particles is more efficient in producing **cell inactivation.**
- LET used to account for the biological effectiveness of different types of radiation.
    - Heavy charged particles have higher LET.
- LET is a function of the medium, the mass and charge of the particle.
- **The higher the LET, the less likely cellular repair**.
- LET of about **100 keV/µm** is optimal in terms of producing a biologic effect.
    - At this density of ionization, the **average separation in ionizing events** is equal to the **diameter of DNA double helix** which causes **significant DSBs**. DSBs are the basis of most biologic effects.
    - The probability of causing DSBs is low in sparsely ionizing radiation such as x-rays that has a low RBE.
- For low LET radiation, ==> RBE proportional to LET, for higher LET the **RBE increases to a maximum**, the subsequent <u>drop</u> is caused by the **overkill effect**.
    - These high energies are sufficient to kill more cells than actually available!

- In the case of sparsely ionizing X- rays, the probability of a single track causing a DSB is low, thus **X-rays have a low RBE**. At the other extreme, densely ionizing radiations (ex. LET of 200 keV/ um) readily produce DSB, but energy is "wasted" because the ionizing events are too close together. Thus, RBE is lower than optimal LET radiation.



Comparing Radiations

- Survival curves for cultured cells of human origin exposed to 250-kV X-rays, 15-MeV neutrons, and 4-MeV alpha-particles.
    - As the LET of the radiation increases, the survival curve changes: the slope of the **survival curves gets steeper** and the **size of the initial shoulder gets smaller**.



- Because the RBE of more densely ionizing radiations, such as neutrons, varies with the dose per fraction, the RBE for a fractionated regimen with neutrons is greater than for a single exposure, because a fractionated schedule consists of a number of small doses and the RBE is large for small doses.
- For a surviving fraction of 0.01 the RBE for neutrons relative to X-rays is 2.6 (was 1.5 at single exposure). This is a direct consequence of the larger shoulder for X-ray curve that

is repeated for each fraction. The width of the shoulder represents a part of the dose that is “wasted”; the larger the number of fractions, the greater the extent of the wastage. Neutrons curve-almost no shoulder.

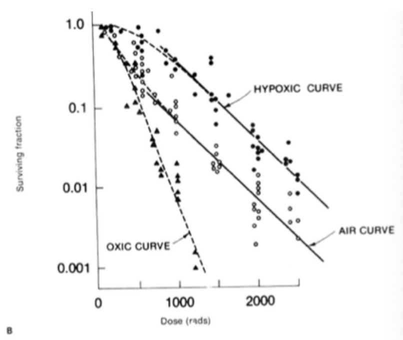
- Result: **neutrons** become progressively **more efficient than X-rays** as the **dose per fraction is reduced** and the number of fractions is increased.
- Further, the neutron RBE is larger at a low dose rate than for an acute exposure, because the effectiveness of neutrons decreases with dose rate to a much smaller extent than is the case for x- or γ-rays.

Oxygen Effect (Oxygenation)

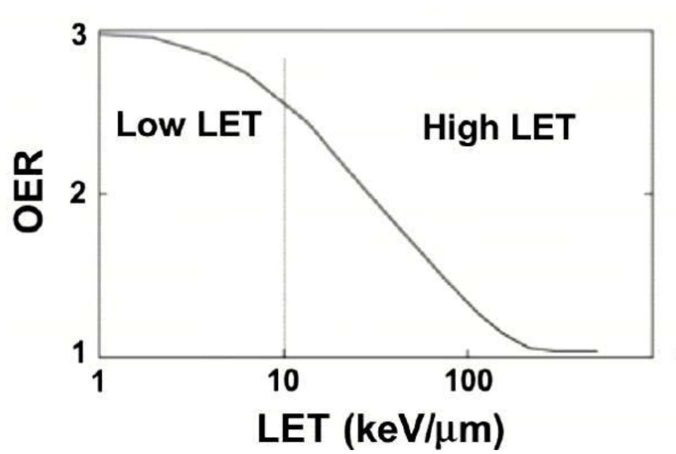
- O2 binds to radicals from radiation → Enzymes cannot “fix” DNA when it is contaminated with O2 type radicals.
- Oxygen Enhancement Ratio (OER):

  OER = Dose for a given effect without O2 / Dose for the effect with 1atm of air
- Common OER

Radiation Type	OER
x-rays and γ rays	2 - 3.5
Neutrons	1.5
α-particles	1.0

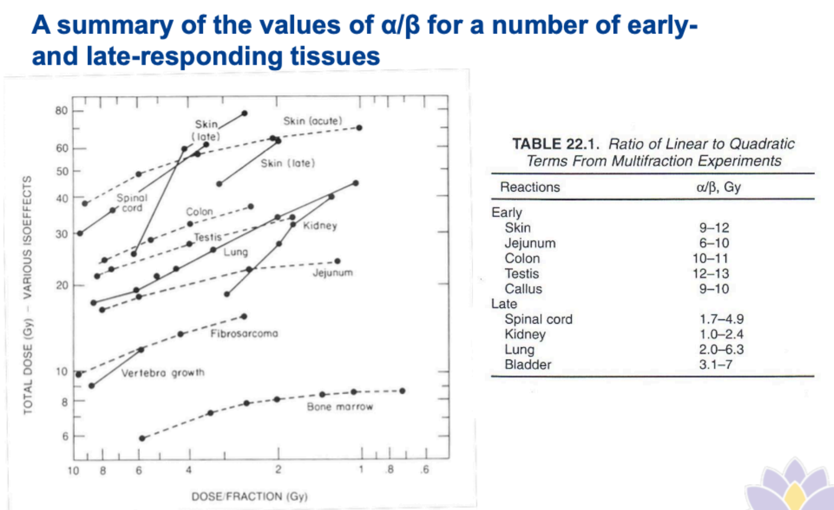


- OER and LET



Early Reacting and Late Reacting Tissue

- Dose-response is more curvy for late effects than early effects.
- Early responding tissues (including tumour) alpha/beta ~ 10 Gy.
- Late responding tissues alpha/beta ~ 2-3 Gy.
- Late responding tissues more sensitive to change in fractionation.
    - Fraction size is dominant factor determining late effects.



Acute Radiation Syndrome

- Signs and symptoms experienced by individuals exposed to **acute whole body irradiation**.
- Data collected largely through Japanese atomic bomb survivors at Hiroshima and Nagasaki.
- Limited number of accidents at nuclear instillations.
- Clinical radiotherapy.
- Well-characterized animal data base.
- **LD50 dose of human is ~4 Gy**.
- Source:
    - Animal experiments
    - Human exposures
        - A-bomb survivors
        - Uranium miners

        - Nuclear Fallout
        - Radium dial painters
        - Accidents
            - 400 accidents, 120 deaths from 1944-1999
        - Medical exposures
        - Occupational exposures
- Problem with Data
    - Controlled animal data
        - Not clear how this scales to humans
        - "Mouse to Man" debate
    - Human exposures
        - Unethical to study explicitly
        - Accidents are not controlled (by definition)
            - Retrospective analysis of dose is uncertain
        - Assumptions
            - Poor dose information (to part or whole body ?)
            - Unknown co-existing conditions (prior cancer)
            - Poor statistics (small numbers of individuals)
            - Dose Rate variations (minutes, hours, days,...)

Radiation-Induced Mutagenesis

- Radiation DOES NOT produce new, unique mutations, but <u>increases the incidence</u> of the same mutations that occur spontaneously.
- Mutation incidence in humans is <u>DOSE and DOSE-RATE dependent</u>.
- A dose of **1 rem (10 mSv) per generation** increases background mutation rate by **1%**.
- Information on the genetic effects of radiation comes almost entirely from animal and IN VITRO studies.
- Children of A-bomb survivors from Hiroshima and Nagasaki <u>fail</u> to show any significant genetic effects of radiation.

Radiation Carcinogenesis

- A **stochastic** late effect.
- No threshold, an all or none effect.
- Severity is <u>not dose related</u>.
- <u>Probability</u> of carcinogenesis is <u>dose dependent.</u>
- Leukemia has the shortest latency period of ~5 years. Solid tumors have a latency period of ~20 to 30 years.
- Total cancer risk for whole body irradiation is **one death per 104 individuals** exposed to **1 rem**.
- For every leukemia induced there are 3 to 4 sarcoma induced in the same irradiated population.

Dose-response for Deterministic and Stochastic Effects

- Deterministic (Non-stochastic)
    - Threshold dose
    - Severity increases with dose
- Examples
    - Cataracts (eye opacity)
    - Erythema (skin reddening)
    - Epilation (loss of hair)
- Stochastic Effect
    - Carcinogenesis, severity non-dose related

Radiation Protection and Radiation Safety

Review of Electromagnetic Waves

- Sir Isaac Newton 1642-1726 (light is made of particles or corpuscules: reflection, propagation straight line)
- Christiaan Huygens 1629-1695 (light explained by wave: interference, refraction, diffraction)
- James Clerk Maxwell 1831-1879 showed light to be an electromagnetic wave.
- Beginning of 20th century, wave theory of light prevalent.
- Some phenomena could not be explained by the wave theory :
    - Black body radiation
        - A "black body" is a body that only absorbs and emits light, but does not reflect it. A black body emits light with a continuous spectrum. Attempts to explain theoretically the shape of the spectrum of the black body radiation based on classical theory had failed, especially for small wavelengths.
        - Max Planck 1858-1947 was able to explain the entire spectrum, by assuming that energy could only be absorbed or emitted in discrete units called quanta.
    - Photoelectric effect
        - When light is incident on the (metallic) cathode, electrons are emitted.
        - No electrons emitted if the frequency of the incident light is lower than a certain value, called the "cutoff frequency".
        - The maximum kinetic energy of electrons increases linearly with light frequency.
        - Above the cutoff frequency, the maximum number of photoelectrons is proportional to the light intensity
        - Electrons are emitted almost instantaneously (10^{-9} s after beginning of illumination)
        - Einstein's explanation

        - A light beam consists of quanta, each of energy (Planck's hypothesis) E=h ν , traveling at the speed of light c.
        - Each photon gives all its energy instantaneously to an electron in the metallic cathode.
        - If, and only if, the photon's energy is higher than the minimum binding energy in the metal (called the work function,Φ), an electron is emitted.
        - The maximum kinetic energy of an electron is: KEmax =hν-Φ
  - Compton effect
    - Arthur H. Compton (1892-1962)
    - Interaction of electromagnetic radiation with "free" electrons.
    - Frequency of scattered radiation depends only on scattering angle.
    - Photons undergo inelastic collisions with "free" electrons.
    - The shift in wavelength, can be explained using the laws of conservation of relativistic energy and momentum need to be applied.
  - Atomic spectra
    - Atomic spectra are discrete (appear as lines)
    - Johannes Rydberg (1854-1919): The prediction of electromagnetic radiation wavelengths emitted due to change in electron level was found empirically to satisfy: $\frac{1}{\lambda} = R_H\left(\frac{1}{m^2} - \frac{1}{n^2}\right) \quad n > m$
- Rutherford model of the atom
  - Ernest Rutherford (1871-1937): Following gold foil experiment (Rutherford scattering) Model of the atom. The electrostatic force acts as the centripetal force
  - Limitation with Rutherford's model:
    - According to electromagnetic theory, orbiting electrons would radiate light continuously at the frequency they rotated, and in doing so they

would lose energy, and eventually fall onto the nucleus but this phenomenon was never observed.

- Bohr's model of the hydrogen atom
  - The hydrogen atom has only one electron, the nucleus consists of one proton.
  - Neils Bohr (1922-1962) started from Rutherford's model, which assumed the negatively-charged electron to gravitate around the positively charged proton on a circular orbit with electrostatic attraction force acting as the centripetal force.
  - Bohr's additional hypotheses
    - Certain orbits (radii) are stable. No radiative loss of energy occurs for these orbits.
    - The allowed (stable) orbits are those for which the orbital angular momentum has values given by $L=nh/2\pi$.
    - Electrons can jump from one orbit to another. Only when such a jump occurs energy is either emitted or absorbed, in the form of a photon

Discovery of Radiation and Radiation Hazards

- Wilhelm Conrad Röntgen discovered X-rays November 8, 1895.
- A few months later, X-ray dermatitis was observed in several countries. E.g. radiation damage to the hands and fingers of early experimental investigators.
- Antoine Henri Becquerel (1896) discovered spontaneous radioactivity. (Nobel Prize in Physics 1903)
- 1897 : Discovery of Electrons by J . J . Thompson Received Nobel Prize in Physics 1906
- 1898: Discovery of Radium and Polonium (Marie and Pierre Curie shared 1903 Nobel prize in physics with Becquerel)
- The idea of inflicting radiation damage at will on selected tissues also paved the way for radiation therapy.
- 1899 : Cure of Skin Cancer reported in Stockholm
- 1899: Discovery of α & β particles (E. Rutherford) 1900: Proposal of Radioactive Decay & Half life Received Nobel prize in Chemistry 1908 for "Disintegration theory " of elements

- 1900 : Discovery of γ-rays by Paul Ulrich Villard while studying radiation emitted from radium. Villard's radiation was named "gamma rays" by Ernest Rutherford in 1903
- 1900: Discovery of energy quanta by Max Planck (Nobel prize in Physics 1918)
- 1905 : Photoelectric effect explained by Albert Einstein (Nobel prize in Physics 1921)
- 1911 Rutherford's model of the atom (nucleus), later 1920 proposed "proton" for the positively charged particles.
- 1913: Hot Cathode tube ~ W D Coolidge • Peak voltage of 140 kV
- 1920s-1930s : Case of "Radium Girls"
- 1922: Discovery of Compton Scattering (Nobel Prize in Physics 1927)
- 1929 : Invention of Cyclotron Ernest Lawrence received Nobel 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
- 1932 : Discovery of Neutron James Chadwick received Nobel prize in Physics 1935
- 1934 : Artificial Radioactivity Irène and Frédéric Joliot Curie shared Nobel prize in Chemistry 1935
- 1940 : Betatron (Donald W Krest)
- 1945: (Monday, August 6, at 8:15 AM) the Atomic Bomb " Little Boy" was dropped on Hiroshima by an American B-29 bomber, the Enola Gay directly killing an estimated 80,000 people
- 1951 : First Cobalt 60 machine in Saskatoon ,Canada
- 1953: First Linear Accelerator
- 1958: Computerized treatment planning introduced
- 1968: Computer-assisted Tomography Shared Nobel Prize in Medicine 1979 between Allan M Cormack Godfrey N. Hounsfield
- 1973: Magnetic Resonance Imaging, Nobel prize in Medicine 2003 to Paul C. Lauterbur and Sir Peter Mansfield for their discoveries

Discovery of X-Ray

- On 8 Nov 1895, Wilhelm Conrad Röntgen (accidentally) discovered an image cast from his cathode ray generator. Röntgen was investigating various vacuum tube equipment when an electrical discharge is passed through them.
- Nov 1895, the invisible cathode rays caused a a small cardboard (painted with barium platinocyanide) to fluoresce.
- New rays termed "X-rays".

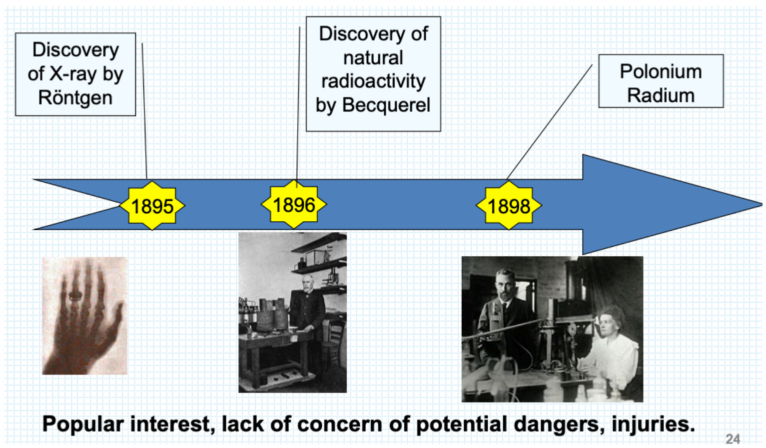
Radioactivity

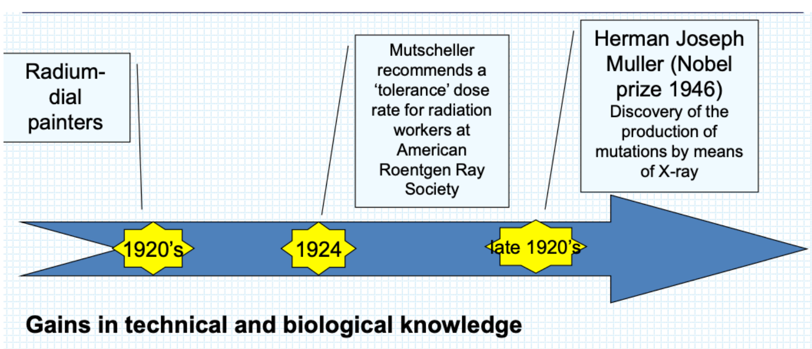
- In 1896, while Henri Becquerel was experimenting with uranium salts and photographic plates, he discovered that radiation was coming from the uranium (spontaneous radioactivity).
- Pierre and Marie Curie investigated radioactivity. In 1898 discovered polonium and months later radium (used term "radioactivity").

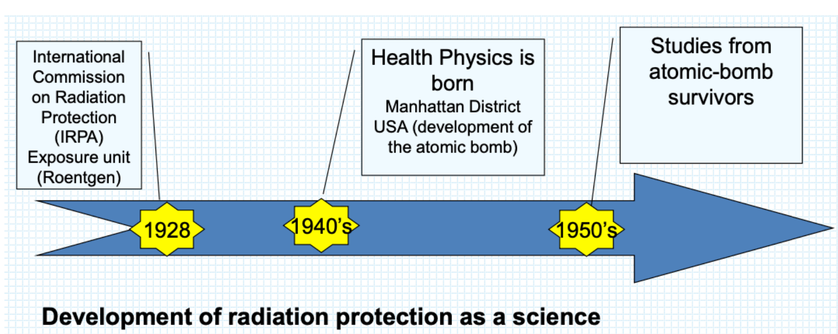
Radiation History

- Since discovery of radiation and radioactivity, the philosophy surrounding radiation and radiation protection standards have evolved.
- New data and information as well as changing attitude as to what is acceptable for dose limit drive the standards in radiation protection.
- Soon after radiation discovery, people were unaware of the deleterious biological effects of high radiation dose
- **The first radiation instrument** to measure output of an x-ray tube was **skin reddening (erythema)**
  - Early 1900s, a radiologist (Dr Kassabian) documented the progressive injury to his hands from chronic exposure to x-rays
- **Shoe-fitting fluoroscope**
  - 1920's until about 1970s
  - Customer and operator would look through a viewing porthole down at the x-ray view of the feet and shoes.

- **Fluorescent Lamp of Edison**
    - Thomas Edison did not experiment long with x-rays, fearing they were too dangerous.
    - His assistant Clarence Dally died in 1904 from an x-ray overdose
    - "I started in to make a number of these lamps, but I soon found that the X-ray had affected poisonously my assistant, Mr. Daily, so that his hair came out and his flesh commenced to ulcerate. I then concluded it would not do, and that it would not be a very popular kind of light, so I dropped it..." (Edison His Life and Inventions by Dyer and Martin)







Effect of Radiation

- Early1900's, animal studies show that x-rays can produce **cancer and kill living tissues**
- Most vulnerable organs are skin, blood-forming organs and reproductive organs
- Tragedy of radium-dial painters
  - Around1920s,Radiumpaintwasusedforglow-in- the-dark applications (radioluminescent).
  - "radium girls" would lick their brushes, ingesting radium. Women would experience anemia, osteonecrosis, death.
  - "In 1924, a woman named Mae Keane was hired at a factory in Waterbury, Conn. Her first day, she remembers, she didn't like the taste of the radium paint. It was gritty.
  - "I wouldn't put the brush in my mouth," she recalled many years later.
  - After just a few days at the factory, the boss asked her if she'd like to quit, since she clearly didn't like the work. She gratefully agreed."

Standards for Protection

- Paper in 1925 by Mutscheller "Physical Standards of Protection Against Roentgen Ray Dangers"
- F.M. Sievert (similar conclusions for tolerance doses)
- Units of roentgen, rad, rem
- Data from the two Nuclear bombs
- Data from survivors of high dose medical procedures
- 1949 Chalk River conference (USA, Canada, Great Britain) on permissible doses
- Studies on fruit flies and mammals showed genetic changes could be induced
- This leads to standards for **annual dose limits** to public.
- Early Data on survivors of atomic-bomb was incorrect and genetic human changes have never been observed
- 1906: Law of Bergonie And Tribondeau, **radiosensitivity** of a tissue is directly proportional to the **reproductive activity** and inversely proportional to the **degree of differentiation**

- 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 number of treatment sessions.
- 1975 : Concept of 4 Rs of Radiobiology (H.R. Withers)

Medical Health Physics

- The safe use of x-ray, gamma ray, neutron, electron, and other charged particle beams or radionuclides in medicine (for diagnostic or therapeutic purposes).
- The instrumentation required to perform appropriate radiation surveys.
- The medical physicist often serves as radiation safety officer

Types of Radiation

- Non-ionizing
    - Infrared
    - Laser
    - Microwaves
    - Radio waves
    - Ultrasound
- Ionizing → produce ion + high energy electron
    - A) directly (charged particles)
        - E.g. electron, proton, heavy charged particles, alpha, pions (π+ or π-)
    - B) indirectly (neutral particles)
        - photons (gamma, x-ray), neutrons

Ionizing Radiation of High Energy Photons with Matter

- Photons are electrically neutral
- Photons can penetrate the matter some distances before interacting with atoms
- <u>Penetration distance</u> depends on <u>photon energy</u> and the interacting <u>matter</u>.
- When photon interacts with matter it can be <u>scattered, absorbed (disappears).</u>
- Transfer energy to electrons

- Photoelectric effect (absorption)
  - Photon is absorbed by atom
  - Electron is excited or ejected
- Compton effect (scattering)
  - Photon scatters off an electron
- Pair production
  - Photon interacts in electric field of nucleus and produces an e+ e pair. Requires photons above 1.022 MeV

- Rayleigh (coherent) scattering
  - It is an elastic scattering i.e. no loss of energy. Only significant for low energy photons <50 keV.
- Photonuclear interaction
  - Significant at very high energy
- Linearattenuation coefficient μ (cm-1)

$$dN = \mu N \, dx$$

- Exponential attenuation of the number of photons N of a narrrow beam

$$N = N0 \, e^{-\mu x}$$

Electron Interaction (beta particles) interaction with matter

- Radiation(Bremsstrahlung): Slowing down of electrons around nucleus
  - energy emitted as photons
- Ionization (CharacteristicX-rays): impact with orbital
  - electron release → vacancy fill → energy emitted as Characteristic x-rays
- Any electron can lose a small or large fraction of its energy, and be deflected by a small or large amount. This leads to large variation among incoming electrons in their path into the tissue (range-straggling)
- Beta particle range varies due to scattering events, bremsstrahlung-producing collisions, etc
- The beta range is often given as the **maximum distance** the most energetic beta can travel in the medium.

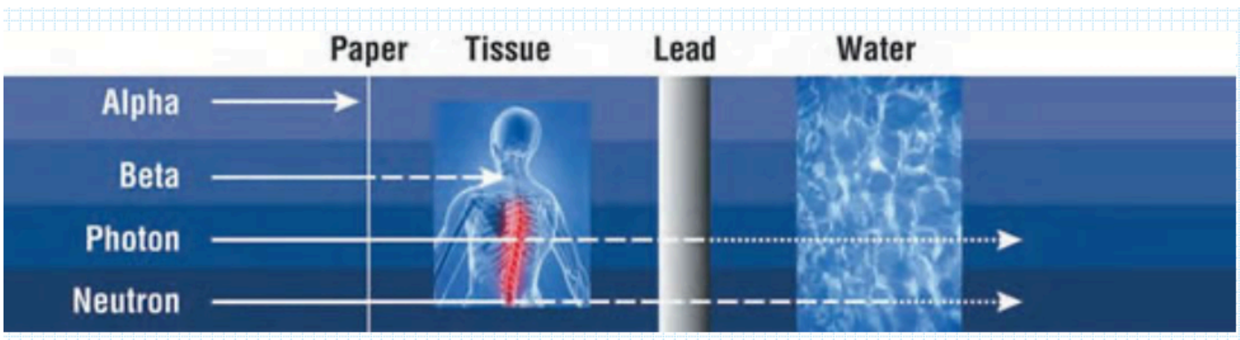
- The range of beta particles in tissue is on the order of **mm's**

Neutron Interaction with Matter

- Electrically neutral
- Neutrons travel **appreciable distances** in matter without interacting
- Neutrons interact with the **atomic nucleus** (inelastic scattering, elastic scattering and absorption)
- Mass similar to protons, great interaction with **Hydrogen** (Human, water content → hazardous)

Alpha Particle Interaction with Matter

- He nucleus (2 protons + 2 neutrons)
- Electrical charge of 2 units
- Energy loss through electronic **excitation** and **ionization**
- Strong interaction with matter → alpha particle have a **short range**
- A few centimeters of air can stop them
- The range of an alpha particle emitted in tissue is on the order of **µm's**.



Background Radiation

- The natural radiation that is always present in the environment.
  - As opposed to artificial sources of ionizing radiation which can be classified as **medical or non-medical** and are a result of human activities
- Can be either terrestrial or extra-terrestrial.
  - Terrestrial sources

        - Naturally occurring radioactive material found in **rocks and soil** such as some with long half-life in millions of years: Uranium-235, Uranium-238, Neptunium-237, Thorium-232. And more.
        - **Radon** released in the atmosphere from these rocks. Can accumulate in basement of poorly-ventilated buildings. In fact Radon is responsible for a significant portion of annual irradiation that an average person would receive (U.S.A. data, same here).
    - Extra-terrestrial (Cosmic and Solar radiation)
        - Generated from **sun** and the **geo-magnetically trapped particles** associated with it.
        - Also from other **stars** many light years away –pulsars and black holes in particular – that provide X-rays and gamma rays.
        - Amount of extra-terrestrial radiation reaching the surface varies with atmospheric thickness, altitude and latitude.
        - E.g. Pilots and flights attendants and those who live in Denver (Colorado) are subjected to higher extra-terrestrial radiation than those who live at sea-level. Higher levels of exposure are also seen in polar regions where the earth's atmosphere is thinner (Fairbanks, Alaska and Reykjavik, Iceland).
    - Food Chain
        - E.g. Potassium-40 may be present in **Lima beans, plantains, tomatoes, bananas**. → internal radioactivity
            - Radioactivity in diet: lead-210; polonium-210; potassium-40
        - Radium and polonium isotopes from radioactive decay in the ground can leach into water and end up in vegetable roots such as beets

Source of Radiation Exposure

- World average of **3.01 mSv/year from all sources**.

- The average radiation dose from all natural sources **is around 2.4 mSv/year** (as a global average) and corresponds to slightly less than 80% of the total average dose received by humans.
- The rest of the dose comes from artificial sources, with medical radiation use being responsible for just under 20% of the total average dose (**0.6 mSv/year**).
- The remaining 0.40% consists of dose contributions from nuclear weapons testing fall-out, occupational exposure, nuclear power plant discharges and radiation from the Chernobyl accident.

Artificial Sources of Ionizing Radiation

- Non-medical sources
    - E.g. Granit ecountertops with naturally occurring radioactive materials thorium, uranium, potassium,...), smoke detectors with Americium-241, glazed ceramics with Uranium and Thorium, older watches and clocks with Radium 226 (newer with Tritium of Promethium 147), etc...
- Medicalsources
    - Radioactive sources (sealed and unsealed) used in Nuclear medicine, Radiation oncology. X-ray emitting devices CT scanners, Radiographic Units. Medical linacs, etc...

Aim of Radiation Protection

- Prevent **deterministic** harmful tissue effects
- Limit the probability of **stochastic** effects to levels deemed acceptable.

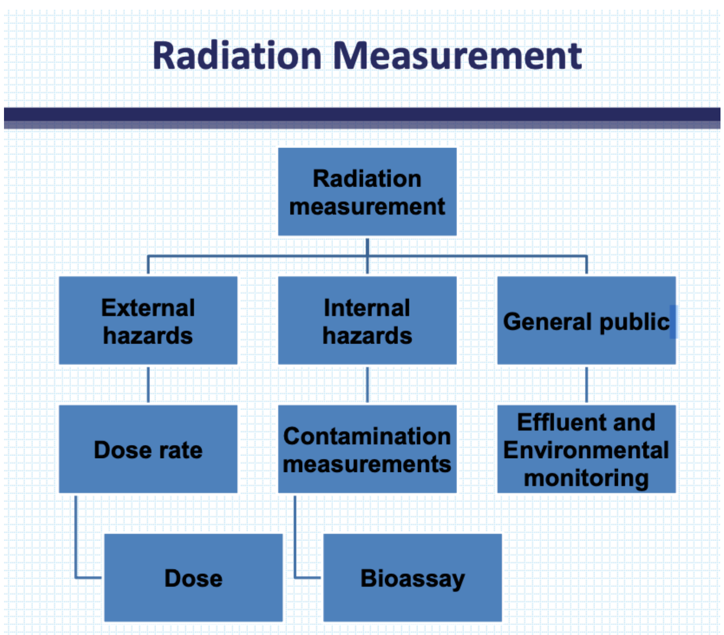
Radiation Instruments

- Operation depends how radiation interacts with matter. For a detector to be, radiation shall deposit part of its energy within some material (solid, liquid, or gaseous).
    - Deposition of energy causes events such as **ionization and excitation of the atoms in the detector** and we are able to observe or measure these effects.
- Can measure rate at which the events occur, which is related to intensity of the radiation.
- Alternatively, events can be stored or integrated over a period of time.

- The expression dosimeter is frequently used for a device that measures directly or indirectly: Exposure, absorbed dose, equivalent dose or other related quantities.

Monitoring

- Personal instruments
  - Issued to workers in the active areas, used to measure external dose ("personal dosimeters" or "badges")
- Survey instruments
  - Normally portable instruments to measure radiation hazards in the particular area.
- Installed instruments
  - Located at **fixed positions** to monitor radiation hazards around the station. E.g. to measure gamma dose-rate or airborne contamination.



Radiation Detection Instruments

Radiation Effect	Dosimetric method
Ionization in gases	Gas filled ionization chamber
Ionization in liquids	Liquid filled ionization chamber
Ionization in solids	•Semiconductors (diodes, MOS-FETs) •Diamond detectors
Luminescence	•Thermoluminescence dosimetry (TLD) •Optically stimulated luminescence dosimetry
Fluorescence	Scintillation counters
Chemical transitions	•Radiographic film •Radiochromic film •Chemical dosimetry •Gel dosimetry
Heat	Calorimetry
Biological effects	Erythema Chromosome damage

64

Ionization Chamber

- With a proper electrical circuit, a tiny current will pass from one electrode to the other, indication of the rate at which radiation is striking the chamber.
- In other words, the current reading would be proportional to the dose rate and the chamber would then be operating as a dose rate meter. A voltage is required to collect current (can use battery).
- Condenser Chamber:
    - A condenser type ionization chamber, instead of having a steady voltage applied at all times, the ionization chamber is **charged up to a known voltage V**. When the chamber is then irradiated, the charge collected will discharge the chamber to a lower voltage. They are used as a dosimeter, measure total dose.
- Gas Multiplication
    - If the voltage applied to an ionization chamber is increased, it is found that the number of ions collected increases with the voltage applied; although the radiation intensity has remained the same.

- This is caused by the fact that the "primary" ions produced by the radiation are accelerated by the applied voltage and gain sufficient energy to cause "secondary" ionization. With sufficiently high applied voltage, se secondary ions can also gain energy to produce further ionization. This is called gas multiplication and results in "avalanche" of secondary ions being collected.

- Proportional counters
  - Proportional detectors or counters, the applied voltage is kept constant such that the number of secondary ions collected is more or less proportional to the number of primary ions, which in turn, is proportional to the energy deposited in the counter by the radiation. The pulses of charge produced in a proportional counter, therefore provide us with
    - Number of pulses counted: measure of intensity of the radiation
    - Size of the pulses: amount of energy deposited in the counter by the radiation.
  - In general, different types of radiation have different specific ionizations, they will produce pulses of differing sizes. E.g. alpha particles passing through a counter will create many more ions than a beta particle. This property enables us to identify and measure radiation with high specific ionization such as alpha particles in the presence of other types such as beta, gamma.
  - In the proportional region there is an amplification of the primary ion signal due to ionization by collision between ions and gas molecules (charge multiplication). This occurs when, between successive collisions, the primary ions gain sufficient energy, in the neighborhood of the thin central electrode, to cause further ionisation in the detector. The amplification is about 103-fold to 104-fold.
  - • Proportional counters are more sensitive than ionisation chambers and they are suitable for measurements in low intensity radiation fields. The amount of charge collected from each interaction is proportional to the amount of energy deposited in the gas of the counter by the interaction.

- Neutron detectors
  - **Thermal neutrons** (~0.025 eV) are captured (radiative capture) in certain materials e.g. B10, He3 or Li6 and the compound nucleus disintegrates by emission of either a proton or an alpha particle. Boron-10 isotope emits a high energy alpha particle.
  - Proportional counters filled with boron trifluoride gas BF3 or with a boron lining on the counter will detect thermal neutrons. The alpha particles produced will cause dense ionization in the counter and the pulses can be easily counted even in the presence of a high gamma background.
  - For higher energy neutrons, counters are surrounded with materials that will slow neutrons down to thermal region. Suitable materials for this purpose are paraffin wax or polyethylene. Cadmium for fast neutrons.
  - Neutron area survey meters operate in the proportional region so that the photon background can be easily discriminated against.
  - Thermal neutron detectors usually have a coating of a boron compound on the inside of the wall or else the counter is filled with the BF3 gas. A thermal neutron interacts with boron-10 nucleus causing an (n,α) reaction and the alpha particles can be detected easily by their ionizing interactions.

- **Geiger counters**
  - If the voltage applied to a counter is further increased, the gas multiplication increases until eventually a point is reached where the number of ions collected remains almost constant. This occurs quite abruptly at a threshold voltage.
  - Over a limited range of voltage above the threshold, called the **Geiger plateau**, the counter is delivering the maximum number of secondary ions it can produce. Each pair of primary ions generate about 109 secondary ions.

    - The pulse of charge collected from a geiger counter is constant and independent of the energy of the initial ionizing event. The pulses of charge are so large that they are easily counted so they are **sensitive to low levels of activity**.
    - Finally if the voltage is further applied to the counter, a continuous discharge occurs making the counter insensitive to any further ionizing events and probably cause permanent damage to counter.
- **GM (Geiger-Muller) Counters**
    - In the GM region the discharge spreads throughout the volume of the detector and the pulse height becomes independent of the primary ionisation or the energy of the interacting particles. In the GM counter detector the gas multiplication spreads along the entire length of the anode.
    - Large charge amplification (9 to 10 orders of magnitude). GM survey meters are widely used at very low radiation levels.
    - GM counters are considered "indicators" of radiation.

Gas Filled Detectors

- Principles
    - The ionizing particle passes through the gas that fills the condenser, creating positive ions and electrons.
    - Either parallel plate, spherical or cylindrical geometry. E.g. a cylindrical condenser would have a central anode for collecting electrons and an outer cathode for collecting positive ions.
- Types
    - Ionisation chamber counters
        - no secondary ions are produced
    - Proportional counters
        - secondary ions are produced but the number is proportional with initial energy of the radiation
    - Geiger-Müller counters

        - secondary ions are produced in large numbers and the number of ions is no longer proportional with radiation energy
- Properties
    - Depending upon the voltage applied the detector can operate in one of three regions:
        - Ionization region B
        - Proportional region C
        - Geiger-Müller (GM) region E

Scintillation Detectors / Fluorescence

- Detectors based on **scintillation (light emission)** are known as scintillation detectors and belong to the class of **solid-state detectors**. Certain organic and inorganic crystals contain activator atoms and emit scintillations upon absorption of radiation. High atomic number phosphors are mostly used for the measurement of gamma rays, while the plastic scintillators are mostly used with beta articles.
- Scintillating phosphors include solid organic materials and plastic scintillators as well as thallium-activated inorganic phosphors, such as NaI(Tl) orCsI(Tl).
- A photomultiplier tube (PMT) is optically coupled to the scintillator to convert the light pulse into an electric pulse. Some survey meters use photodiodes in place of photomultiplier tubes.
- A “scintillation” is in reality a very brief shower tiny light flashes, each flash resulting from the resettlement of the electrons in an ionized atom
- Basic Components
    - A scintillator, e.g. a phosphor in the form of crystal, which emits a tiny flash of light when ionizing radiation strikes it (e.g. NaI, BGO).
    - A photomultiplier tube detects flash of light then produces current pulses.

Semiconductor Detectors

- acts like a solid state ionization chamber.
- The radiation interacts with the atoms in the sensitive volume of the detector to produce ionization. The collection of the ions produces a pulse of electrical charge.

- In air, it requires and energy of 35 eV to produce an ion pair; whereas only 3.5 eV is required in a silicon semiconductor detector.
- Silicon Diode Dosimetry Systems
  - A silicon diode dosimeter is a positive-negative junction diode.
  - The diodes are produced by taking n-type or p-type silicon and counter-doping the surface to produce the opposite type material.
  - The depletion layer is typically several mm thick. When the dosimeter is irradiated, **charged particles** are set free allowing a signal current to flow.
  - Diodes can be operated with and without bias. In the photovoltaic mode (no bias), the generated voltage is proportional to the dose rate.
- **MOSFET dosimetry**
  - A MOSFET dosimeter is a Metal-Oxide Semiconductor Field Effect Transistor.
  - Ionizing radiation generates charge carriers in the Si oxide.
  - The charge carriers moves towards the silicon substrate where they are trapped.
  - This leads to a charge buildup causing a change in threshold voltage between the gate and the silicon substrate.
  - MOSFET dosimeters are based on the measurement of the threshold voltage, which is a linear function of absorbed dose.
  - The integrated dose may be measured during or after irradiation.

Luminescence Dosimetry

- Principle
  - Thermoluminescence
    - Luminescence released when heated following radiation absorption
  - Optically stimulated luminescence
    - Luminescence released when illuminated following radiation absorption
- Types of detection materials
  - Lithium Fluoride
  - Calcium Fluoride
  - Lithium Borate

    - • $Al_2O_3:C$
- Types of luminescence
    - Fluorescence (very short time delay between the stimulation and the emission of light at 10^{-10} to 10^{-8} s)
    - Phosphorescence (relatively long delay > 10^{-8} s
- Thermoluminescence dosimeter (TLD) and optically stimulated dosimeter (OSLD)
    - Luminescence explained with two energy bands model where the valence and conduction are separated by a forbidden gap. Defects purposely introduced into the material during fabrication act as local energy bands with levels within the forbidden gap, called traps.
    - When ionizing radiation hits the material, electron-hole pairs are created. Electrons move up to the conduction band and holes move to the valence band.
    - Electrons travel in the crystal lattice until they either cross back towards the valence band and recombine with a hole or if near near a defect, it can fall into the energy trap. The electron is now prevented from recombining with a hole until it can gain enough energy to once again reach the conduction band.
    - In the case of <u>TLDs,</u> **heat is used as stimulation** to release trapped electrons. It follows a recombination of electrons with holes where light is emitted, proportional to the amount of radiation received.
    - For <u>OSLDs</u>, **optical photons** (instead of heat) are used for the stimulation.
    - TLD Glow Curve / thermogram
        - The TL intensity emission is a function of the TLD temperature T
        - Keeping the heating rate constant makes the temperature T proportional to time t and so the <u>TL intensity can be plotted as a function of t</u>.

Radiographic Film

- A thin plastic base layer (200 mm) is covered with a sensitive emulsion of Ag Br-crystals in gelatine (10-20 mm).
- The **amount of darkening** depends on the **amount of radiation exposure**.

- Traditional radiographic films (silver film emulsion) must be carefully packaged otherwise they will be blackened by daylight. These type of films have to be developed, fixed, washed and dried.
- There is an energy dependence.
- **Filters** (lead, tin,..) can be made from different materials and depending on the combination to estimate dose form gamma, beta and also thermal neutrons (cadmium filter). E.g. for Beta dose to the skin, the film package would be uncovered by filters (open window).
- Fast neutron dose would require extra thick emulsion to knock a proton out of a molecule in the emulsion. Proton loses its energy by causing ionization. Proton 'tracks" become visible under microscope.

During **irradiation**, the following reaction is caused (simplified):

- Ag Br is ionized
- Ag^+ ions are reduced to Ag: $Ag^+ + e^- \rightarrow Ag$
- The elemental silver is black and produces a so-called **latent** image.

During the **development**, other silver ions (yet not reduced) are now also reduced in the presence of silver atoms.

That means:
If **one silver atom** in a silver bromide crystal is reduced, all silver atoms in this crystal will be reduced during development.

The rest of the silver bromide (in undeveloped grains) is the washed away from the film during the fixation process.

- Optical density (OD)

Light transmission is a function of the film opacity and can be measured in terms of optical density (OD) with devices called densitometers.

The *OD* is defined as $OD = \log_{10}\left(\frac{I_0}{I}\right)$ and is a function of dose, where

I_0 is the initial light intensity.
I is the intensity transmitted through the film.

Film gives excellent 2-D spatial resolution and, in a single exposure, provides information about the spatial distribution of radiation in the area of interest or the attenuation of radiation by intervening objects.

- Dose-OD Relationship (H&D curve)

Ideally, the relationship between the dose and *OD* should be linear.

Some emulsions are linear, some are linear over a limited dose range, and others are non-linear.

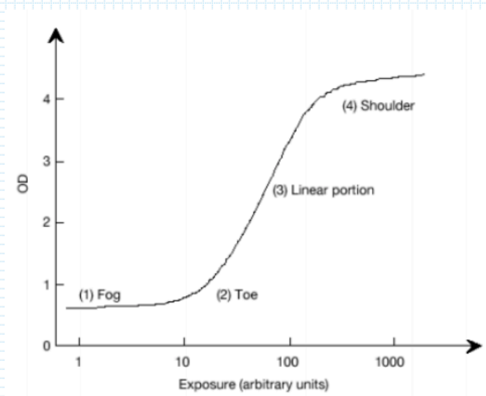
For each film, the dose versus *OD* curve
(known as sensitometric curve or as characteristic or H&D curve, in honour of Hurter and Driffield)
must therefore be established before using it for dosimetry work.

Gamma: slope of the linear part

Latitude: Range of exposures that fall in the linear part

Speed: exposure required to produce an *OD* >1 over the fog

Fog: *OD* of unexposed film



- Film Dosimetry
  - Silver halide film with a range of filters to distinguish exposures from beta, X-ray, gamma and thermal neutrons.
    - Dose is determined by degree of blackening (optical density) and comparing it with calibrated films.
    - Provides permanent record of an individual's dose. Their drawbacks are shorter shelf life, adverse effects of light and heat and require dark room facilities.
  - Change takes place in silver halide grains when the photographic emulsion is exposed to light, x rays, or charged particles.
  - Adequately exposed grains will be developed and the remainder are left largely undeveloped with the exception of a small fraction that creates a low level darkening on the film referred to as "fog."

- While the mechanism that permits the formation of latent images is not fully understood, some in-direct processes the transformation of silver bromide to atomic silver indicate that the latent image is a formation of silver atom aggregates inside the grain.
- Film developing includes four steps: developing, fixing, washing, and drying. In the development process the latent image is reduced to metallic silver grains.

- **Radiochromic Film**
  - a newer type of film
  - This film type is self-developing. Radiochromic effects involve the **direct coloration of a material** by the absorption of energetic radiation, <u>without requiring latent chemical, optical, or thermal development or amplificatio</u>n.
  - Radiochromic film contains a special dye that is polymerized and develops a blue color upon exposure to radiation.
  - Similarly to the radiographic film, the radiochromic film dose response is determined with a suitable densitometer.

Dose Concepts

- Absorbed Dose
  - Radiation energy absorbed per unit mass of a substance (Gy)
- Equivalent dose
  - Absorbed dose weighted for the degree of biological effeteness of different radiations (Sv)
- Effective Dose
  - Equivalent dose weighed for the sensitivities of different tissues (Sv)

Equivalent Dose (HT)

- The equivalent dose is simply the **absorbed dose** <u>multiplied</u> by a **radiation weighting factor**
- represent the <u>stochastic health effects</u> (probability of cancer induction and genetic damage).

- The radiation weighting factor helps to account for the different levels of biological damage caused by different types of radiation
- Equivalent dose allows us to compare radiation doses from different types of radiation.
    - 1 mSv of equivalent dose from gamma radiation is comparable to 1 mSv of equivalent dose from beta or alpha radiation, in terms of biological damage
- The unit of equivalent dose is the millisievert (mSv)

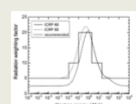
H_T is the equivalent dose absorbed by tissue T

$D_{T,R}$ is the absorbed dose in tissue T by radiation type R

w_R is the radiation weighting factor

$$H_T = \Sigma_R \, w_R \times D_{T,R}$$

- Weighting Factors

Radiation type and energy	Radiation weighting factor W_R
Photons, Electrons, Muons	1
Protons and charged pions	2
Alpha particles, fission fragments, heavy nuclei	20
Neutrons	(Some continuous function)  $w_R = \begin{cases} 2.5 + 18.2e^{-[\ln(E_n)]^2/6}, & E_n < 1 \text{ MeV} \\ 5.0 + 17.0e^{-[\ln(2E_n)]^2/6}, & 1 \text{ MeV} \leqslant E_n \leqslant 50 \text{ MeV} \\ 2.5 + 3.25e^{-[\ln(0.04E_n)]^2/6}, & E_n > 50 \text{ MeV} \end{cases}$

Effective Dose

- equivalent dose multiplied by a tissue weighting factor
    - Risk related parameter, taking **relative radiosensitivity of each organ and tissue** into account and calculate an overall effect
- The tissue weighting factor helps to account for the varying sensitivities to radiation exposure of the different tissues and organs

- Effective dose accounts for the type of radiation and the tissue or organ irradiated
- The unit of effective dose is the millisievert (mSv)
  - 1 mSv of effective dose is just 1 mSv, regardless of whether the dose was delivered to the lungs, thyroid, bone marrow, or any other tissue.
- Unfortunately, mSv is the unit equivalent dose as well as effective dose though they are not equal

$$E(Sv) = \Sigma_T \, w_T \times H_T$$

w_T : tissue weighting factor for organ T

H_T : Equivalent dose received by organ or tissue T

- Tissue Weighting Factors

Tissue	Tissue weighting factor, w_T	Sum of w_T values
Bone-marrow (red), colon, lung, stomach, breast, remainder tissues[a]	0.12	0.72
Gonads	0.08	0.08
Bladder, oesophagus, liver, thyroid	0.04	0.16
Bone surface, brain, salivary glands, skin	0.01	0.04
Total		1.00

[a] Remainder tissues: Adrenals, extrathoracic (ET) region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate (♂), small intestine, spleen, thymus, uterus/cervix (♀).

- Equivalent vs. effective dose
  - Equivalent dose is the unit used to assess **doses to individual tissues** or extremities
    - Tissues are treated separately
    - There are equivalent dose limits for skin, hands and feet
  - Effective dose is the unit used to assess doses on the scale of **the whole body**
    - Tissue doses are weighted to indicate effect on the body as a whole
  - Note that these quantities are <u>not directly measurable</u>. In practice for monitoring areas or personal, other operational quantities are used.

Unit Conversion (Activity, Exposure, Absorbed dose, equivalent dose, and effective dose)

Physical quantity	SI unit	Non-SI unit	Relationship
Activity	becquerel	curie (Ci)	1 Bq=2.7×10^{-11} Ci 1 Ci=3.7×10^{10}Bq 1 mCi=37 MBq
Exposure	coulomb/kg	roentgen (R)	1 R=2.58×10^{-4} C/kg 1C/kg=3876 R
Absorbed dose	gray (=J/kg)	rad	1 Gy=100 rad 1 rad=1 cGy
Equivalent dose	sievert	rem	1 Sv=100 rem 1 rem=10 mSv
Effective dose	sievert	rem	1 Sv=100 rem 1 rem=10 mSv

Radiation effects

- Ionizing radiation interacts at the cellular level (ionization, chemical changes, biological effects).
- Outcome of a cell exposed to radiation: Damage to DNA will make the cell either unviable, viable (mutation is repaired), or cancer (cell survives but mutated).
- The effects of exposure to radiation can be divided into two categories:
  - Hereditary (genetic) Effect
    - those which do not become apparent until future generations are born
    - Possible result of radiation induced damage to the DNA molecule in the germ cells (sperm, ova).
    - In human: from the nuclear bomb explosions in Japan:
      - Hereditary effects such as **leukemia** and **developmental delays** have only been seen in those children who were <u>heavily irradiated while still in their mother's womb</u>

        - Children conceived <u>after the explosion</u> have shown <u>no change in the natural mutation rate</u>
            - The findings are not statistically sound
    - Somatic (body) effect
        - those which are experienced directly by the people exposed to the radiation
        - There are two types of somatic effects:
            - Stochastic effects
                - radiation exposure <u>increases the likelihood</u> of developing a disease such as cancer
                - The greater the exposure, the greater the likelihood
                - We can never be certain that an effect will occur
            - Deterministic effects

DNA Damage

- When radiation interacts with living tissue, molecular bonds can be broken and cell function altered
- If a DNA molecule is damaged:
    - The body may be able repair the DNA
    - The cell may die; or
    - The DNA is not repaired properly resulting in a <u>mutated cell</u> with altered function

Mutation Effect

- A radiation dose has a certain <u>probability</u> of causing a mutation in a cell.
- A mutation might bring about cell destruction.
- A mutation could affect cell behaviour and <u>increase the rate of cell divisions</u>.
    - The new cells will have the mutation causing them to also divide before reaching their mature state.
    - They will provide no beneficial function to the body.
    - These cells form a tissue called a **tumour**.
        - If the cells <u>do not invade surrounding tissues</u>, the tumour is **benign**.

        - If the tumour invades neighbouring tissues it is **malignant**.
            - A malignant tumour is cancer which may or may not be fatal

Radiation Induced Cancers

- Early radiation scientists
    - Many died from skin, bone, and blood cancers.
- Radium watch dial painters 1920s
    - Many died of bone cancer 8 to 40 years later.
- UK X-ray treatment for **ankylosing spondylitis** (1935-1957)
    - 13 914 were treated for ankylosing spondylitis with x-rays.
    - In 1992, 60 leukemia death (relative risk average increase of 7 for 1Gy irradiation)
- Japanese bomb survivors (80,000 people)
    - 350 cancer deaths, double the expected figure.

Latency Period

- There is a delay between exposure to the radiation and the onset of cancer.
- This delay is known as the latency period.
    - For leukemia, it is about **8 years**.
    - For other cancers, it can be much longer.

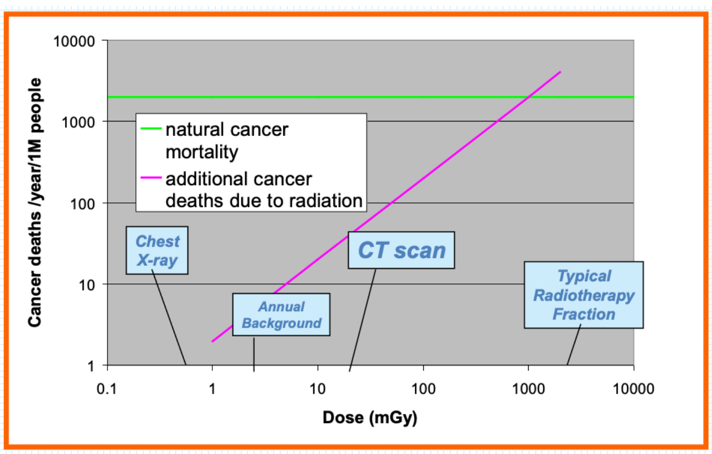
Risk: Cancer from radiation

- The risk of developing a fatal cancer as a result of exposure to radiation is thought to be approximately **5% per 1000 mSv**
- Consider a person who worked for 50 years and received 20 mSv per year
    - This person's total lifetime radiation dose would be 1000 mSv
- This person could have an extra 5% chance of developing a fatal cancer

How do we know all these

- Epidemiology (observations of humans)
    - LIFE SPAN STUDY (Hiroshima and Nagasaki)
        - Only ~5% of 7,800 deaths from cancer or leukaemia due to radiation
    - Other evidence (examples)

        - 131-I thyroid exposures in Scandinavia (1950s- 60s fallout from nuclear testing in Soviet Union)
        - Radium dial painters 1920s
        - Chernobyl 1986
        - Air plane crews
        - many other studies
- Experimental radiobiology (studies on animals)
- Cellular and molecular radiation biology
- Yet, we do not know what happens at lower doses
    - Cell culture and animal data difficult to extrapolate to humans
    - Human experience
        - Not randomized controlled
            - Otherwise would be highly unethical
        - Many assumptions in Life time study
            - Poor dose information (to part or whole body)
            - Unknown co-existing conditions
            - Poor statistics (small numbers)
- Linear No-Threshold Hypothesis / Risk Model
    - the risk of cancer proceeds in a <u>linear fashion at lower doses</u> without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans.



Comparison of Radiation Worker Risks

	Mean death rate 1989 (10^{-6}/y)
Trade	40
Manufacture	60
Service	40
Government	90
Transport/utilities	240
Construction	320
Mines/quarries	430
Agriculture	400

Safe industries (Trade, Manufacture, Service, Government)
~ 2 mSv/y

Hazard	Risk of Death Per Year
Accidents on the road	1 in 5,000
Accidents at home	1 in 11,000
1 mSv per year legal limit (dose limit for public)	1 in 20,000
Accidents at work	1 in 24,000
0.05 mSv per year	1 in 400,000

Exposure Limits

- Limits have changed with time
- Biological information
    - Genetic risks are smaller, carcinogenic risks are larger than thought in 1950s
- Social philosophy
- Ability to control exposures

Radiation on Fetus / Embryo

- Fetus/embryo is more sensitive to ionizing radiation than the adult human
- Increased incidence of spontaneous abortion a few days after conception
- Increased incidence → deterministic

    - Mental retardation
    - Microcephaly (small head size) especially 8-15 weeks after conception
    - Malformations: skeletal, stunted growth, genital
- Higher risk of cancer (esp. leukemia) – Both in childhood and later life → stochastic effect

Acute Exposure

- Exposure to a high dose delivered within seconds, minutes or days
- Possible deterministic effects
    - Blood changes
    - Nausea
    - Diarrhea
    - Hair-loss
    - Malaise
    - Death
- The rapidly reproducing cells are most affected by acute radiation:
    - The skin
    - The blood-forming tissues
    - The gonads
    - The digestive system lining (the gastrointestinal tract or GI tract)

Effects related to a whole body acute dose

LD_{50} (Lethal dose that would kill 50% of the population)

Dose (mSv)	Effects
0 – 200	No measurable short-term effects
200 – 500	- measurable changes in blood composition - some chromosome aberrations - no fatalities (typical cancer therapy dose)
3000	LD_{50}/60 days without medical care
10000	LD_{100}/15 days

Objectives of Radiation Protection

- To prevent clinically significant radiation induced **deterministic** effects by adhering to dose limits that are below the apparent or practical threshold (dose limit).
  - Deterministic Effects
    - Threshold value
    - • Severity of the effect increases with dose
    - • Cataract, erythema, impaired fertility, cell depletion of bone marrow
- To limit the risk of **stochastic effects** (cancer and heritable effects) to a reasonable level in relation to societal needs, values and benefits gained (ALARA)
  - Stochastic Effects
  - No Threshold value
  - Probability of occurrence is proportional to the dose
  - Severity is independent of dose
  - Cancer and genetic effects
- The principles behind protecting individuals revolve around the concepts of
  - Time
    - Minimize time of exposure to the source
    - **Radiation Dose = Dose Rate x Time**
  - Distance
    - Increase distance from the source
    - For a point source of radiation, Inverse Square Law can be invoked.
  - Shielding
    - Use a radiation shield (attenuating material)
  - Contamination Control (if used of Radioactive Materials is involved).
- Adherence to these four principles will help minimize radiation exposure.

Guiding Radiation Protection Principle: ALARA

- "As Low As Reasonably Achievable"
- which means making every reasonable effort to maintain exposures to ionizing radiation as far below the dose limits as practical, consistent with the purpose for which the

licensed activity is undertaken, taking into account the state of technology, the economics of improvements in relation to state of technology, the economics of improvements in relation to benefits to the public health and safety, and other societal and socioeconomic considerations, and in relation to utilization of nuclear energy and licensed materials in the public interest.

- An approximated overall risk coefficient of 5% Sv^{-1} can be used for radiation protection purposes

International Commission on Radiological Protection (ICRP)

- The aim of the ICRP recommendations is to contribute an appropriate level of protection for people and the environment against the detrimental effects of radiation exposure without unduly limiting the desirable human actions that may be associated with such exposure.
- The ICRP dose limits are intended to serve as a boundary condition that will prevent deterministic effects and limit the probability of stochastic effects.
- Occupational dose limit and public dose limit were derived by examining data from models and experiments, studies on animal and on human, Japanese A-bomb cohort.

Dose limits recomended by ICRP in planned exposure situations (2007)

Type of limit	Occupational, mSv in a year	Public, mSv in a year
Effective dose	20, averaged over 5 years, with no more than 50 mSv in any one year	1 (exceptionally, a higher value of effective dose could be allowed in a year provided that the average over 5 years does not exceed 1 mSv in a year)
Equivalent dose to lens of the eye	150	15
Equivalent dose to skin	500	50
Equivalent dose to hands and feet	500	—

Personnel Dosimeters

- To ensure compliance with the regulatory limits on occupational dose, individuals working with ionizing radiation or radioactive material must be monitored.
- In the past photographic film encased in small badge-like housings "film badges" with the lower limit of sensitivity of film-based dosimeter of about 0.1 mSv
- Improved technology is the thermoluminescent-based dosimeter (TLD), chip of lithium fluoride, which when heated, emits in the visible range. Cumulated radiation dose proportional to the integrated light output during the heating period.
- A variation of TLD is the optically stimulated dosimeter (OSD), in which a laser beam generates the light output instead of heating. For both TLD and OSD the lower limit of sensitivity is about 0.01 mSv.
- Limitations of all forms of personnel dosimeters is the fact that <u>it measures its own dose</u> (not to the wearer). Dose has to be <u>converted to effective dose to the wearer</u>.

Shielding

- Linear Accelerator Bunker
    - Protective barriers must protect against primary radiation (**primary barrier**) and scatter and leakage radiation (**secondary barrier**)
- For an idealized case of "good" narrow beam geometry, the radiation intensity (I) decreases after it passes through a uniform attenuating material, mathematically described by the equation:

$$I = Io \exp(-ux)$$

Io is the intensity before the shielding material

u is its linear attenuation coefficient

x is the thickness of the material (perpendicular to the ray's direction of travel).

- The thickness of material which reduces the incident intensity to half its original value is the so-called **half-value layer (HVL).**
- In real-world conditions, broad beam geometry is more applicable.

$$I = B\, Io \exp(-ux)$$

B is the build-up factor, B> 1, and is the ratio of the intensity of the scattered + primary beams to the primary beam alone.

- Shielding from radiation of intensity P0 . Shielding goal P (e.g. P=0.1 mSv/yr), The **primary barrier transmission factor** Bpri (Bpri =P/P0) is calculated from the following relationship:

$$B_p = \frac{Pd^2}{WUT}$$

P is the weekly design dose limit derived from the annual limit appropriate for the type of space protected by the barrier (Sv/wk).

d is the distance from the target to the point of measurement (m)

W is the workload (Gy/wk)

U is the use factor

T is the occupancy factor

The TVL is the thickness required to attenuate the beam to one tenth of its original intensity.

$$TVL = \frac{log_e 10}{\mu}$$

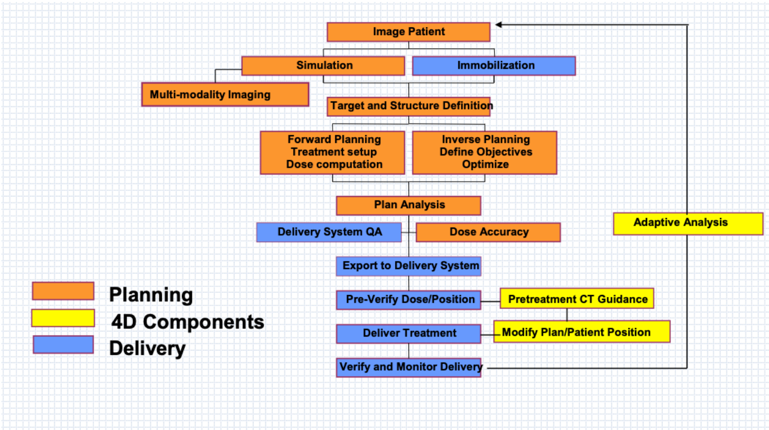
International Organization of Radiation Safety

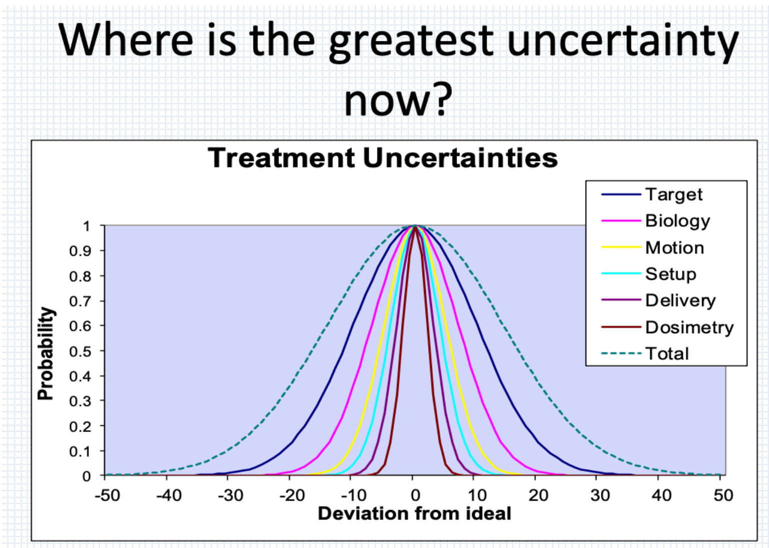
- Committees that formulate the concepts for use in radiation protection and recommend maximum permissible levels (law makers):
  - ICRP (International Commission of Radiological Protection)
  - ICRU (International Commission of Radiological Units and Measurements)
  - NCRP (National Council on Radiological Protection and Measurement) USA
  - **CNSC (Canadian Nuclear Safety Commission) Canada**
- Legal max permissible occupational dose in Canada

Person	Period	Effective Dose (mSv)
Nuclear energy worker, including a pregnant nuclear energy worker	(*a*) One-year dosimetry period	50
	(*b*) Five-year dosimetry period	100
Pregnant nuclear energy worker	Balance of the pregnancy	4
A person who is not a nuclear energy worker	One calendar year	1

Imaging for Treatment Guidance and Monitoring

Radiation Therapy Workflow





Motion and Motion Management

- Radiation therapy goal deliver high dose to tumour while minimizing dose to healthy tissue.
  - Clinical uncertainties (delineating the target)
  - Setup uncertainties (patient positioning/immobilization, reproducibility)
  - **Motion interfraction and intrafraction** (respiration, filling status of internal organs)
- Without account of motion, possibility to underdose tumour and/or overdose organs at risk.

- Strategies to deal with some of the uncertainties
    - adding margins,
    - immobilization,
    - abdominal compression
    - breath hold,
    - organ filling/emptying
    - Dynamic tracking

Intrafraction Motion

- Intrafraction motion is an issue that is becoming increasingly important in the era of image-guided radiotherapy.
- Intrafraction motion can be caused by
    - the respiratory,
    - skeletal muscular,
    - cardiac, and
    - gastrointestinal systems

Types of Errors

- Systematic errors
    - Reproducible inaccuracies consistently in the <u>same direction</u>
    - Due to persisting problem
- Random errors:
    - caused by unknown and unpredictable changes
    - Statistical fluctuations in <u>either direction</u>
    - Calculation:
        - Based on series of measurements of a given quantity x
        - Calculate the **mean** from this data and the standard deviation σ

Tumour Delineation and Margins

- **Gross Tumor Volume (GTV)**
    - "Gross demonstrable extent and location of the malignant growth"

- Primary tumor
- Involved nodes
- Metastatic disease

- Adequate dose must be delivered to <u>whole GTV</u> to achieve aim of therapy
- May not be possible to define GTV after surgical intervention
- Determining GTV
  - Clinical examination
  - Various imaging techniques

- **Clinical Target Volume (CTV)**
  - "Tissue volume that contains a demonstrable GTV and/or subclinical malignant disease that must be eliminated"
  - CTV delineated based on GTV with <u>expansion for microscopic disease</u>
  - Expansion based on clinical knowledge of spread of disease
  - May be multiple CTVs, each with its own prescription – CTV I, CTV II, CTV III, etc
  - Delineation of GTV and CTV based on general oncological principles, independent of any therapeutic approach
  - Definition of GTV and CTV must precede selection of treatment modality and treatment planning procedures
  - <u>It is not appropriate to modify GTV and CTV based on result of dose calculation</u>
- **Internal Target Volume ITV = CTV + IM**
  - CTV + internal margin (IM)
  - to compensate for <u>all movements</u>
    - Respiration
    - Bladder and rectum fillings
    - Swallowing
    - Cardiac motion
    - Bowel motion
  - Expansion of CTV based on knowledge of internal motion
    - Population-based expansions

            - Explicit expansions based on motion studies
- **Planning Target Volume (PTV) = CTV + IM + SIM**
    - A geometrical concept used for treatment planning, defined to select appropriate beam sizes and beam arrangements to ensure that the prescribed dose is <u>actually delivered to the CTV</u>"
    - PTV is ITV + **setup margin (SM)** to account for setup uncertainties
        - Expansion of ITV based on knowledge of setup uncertainties
        - Immobilization devices
        - On-line imaging
    - It is not appropriate to modify setup margin based on result of dose calculations
    - PTV <u>does not include margin for penumbra</u>
        - Penumbra margin added when treatment portal is defined
- **Organ at Risk (OAR)**
    - "Normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose"
    - Planning Organ at Risk Volume (PRV): PRV = OAR + IM + SM

Source of Uncertainty → why may the target be elsewhere

- Mispositioning (interfraction)
- Organ motion (intrafraction)
- Shape change (interfraction)
- May result in absorbed dose in the volumes of interest and organs at risk that do not correspond to the theoretical dose planned.
- As a result, we employ immobilization systems (which is not always enough)
- How can we know the position of the target? → IGRT

Image Guided Radiation Therapy (IGRT)

- Radiation therapy has evolved and it is now possible to produce highly conformal radiation dose distribution by using techniques such as **intensity-modulated radiation therapy (IMRT)**

- Dose conformity necessitates enhanced patient localization and beam targeting techniques.
- Components affecting the reproducibility of target position during and between subsequent fractions of radiation therapy: organ filling, motion etc.
- IGRT uses advanced imaging technology to better define the tumor target
- Goal is to reduce and ultimately eliminate the uncertainties
- Treatment Planification
    - Patient simulation → planning (volume of interest + dose distribution) → treatment
- IGRT is the use of the image in the actual treatment room as a tool for tracing and verification of the tumour volume immediately before or during treatment.
- IGRT Solutions
    - Biological imaging to better define tumor
    - Time-resolved (4D) imaging for modeling intra-fraction organ motion
    - On-board imaging systems (attached to treatment delivery system) for intra-fraction patient localization
    - New treatment planning and delivery schemes incorporating new imaging systems
- By imaging frequently and adapting the treatment accordingly based on these images, the precision of the treatment can be increased
- As the technology for delivering radiation dose and image guidance improves, these margins can be reduced.
- There are a range of image guidance methods

Tumour Target Definition

- CT (X-ray computed tomography)
    - High spatial integrity
    - High spatial resolution
    - excellent bony structure depiction,

- ability to provide relative electron density information used for radiation dose calculation.
    - recent development of ultra-fast multi-slice CT allows time-resolved (4D)
- MRI (Magnetic Resonance Imaging)
    - superior soft tissue discrimination, especially for central nervous system (CNS) structures and within the abdomen and pelvis, and has been widely
- Ultrasound
    - soft tissue localization
    - Can be hampered with large observer errors.
    - 3D ultrasound, potential to reduce those errors

Biological Imaging

- CT and MRI provide snapshot of patient's anatomy (no biological information)
- Biological imaging is in vivo characterization **of biological processes** at the cellular and molecular level. E.g.
    - MRSI (Magnetic Resonance Spectroscopy Imaging)
    - PET (Positron Emission Tomography)

Image Fusion

- Combining multimodality images to examine or delineate the anatomical or physiological features from the datasets
- Hybrid PET/CT is a hardware-based fusion technology
- Computer-aided fusion tools

Types of Organ Motion

- Rigid-body displacements (rotation, translation)
- Tissue deformation (distorted)

Intra-fractions: Managing Respiratory Motion

- 4D CT imaging
- Breath-hold and respiratory gating
- Tumor tracking

- Methods:
    - Immobilization :
        - Voluntary Deep Inspiration Breath-Hold (DIBH)
            - A reproducible state of maximum breath-hold (DIBH)
            - It significantly reduces tumor motion and internal anatomy changes
        - Active Breathing Control (ABC)
    - Gating:
        - Turn radiation on/off at a specific breathing phase
    - Tracking:
        - Real time target localization
    - Optimize free-breathing PTV
        - 4DCT integration of respiratory motion into treatment planning (ITV)

Inter-fraction: Organ Movement

- Megavoltage image with electronic portal imaging device (EPID)
- Cone-beam CT (CBCT) with either kV or MV x- rays

Cyberknife

- Small linac (6MV x-ray) mounted on a robot allows complete freedom to position the radiation within a space about the patient. The system can deliver radiation from many different directions in a feasibly short treatment time. (Claimed accuracy = 0.5 mm)
- An image guidance system is an essential item in the CyberKnife system. X-ray imaging cameras are located on supports around the patient allowing instantaneous X-ray images to be obtained.
- A computer algorithm determines what motion corrections have to be given to the robot because of patient movement.

CT and 4D CT

- CT (computed tomography)
    - 3D image generated from the reconstruction of using x-ray images acquired around an axis of rotation

- 4D CT
    - large number of individual CT scans obtained at various phases of the respiratory cycle
    - Multislice CT scanners allow efficient acquisition of 4D data
- CT Image Reconstruction
    - X-ray projection data are acquired at many different angles around the patient
    - A mathematical process is used to generate images from these projections
    - Result: CT - Digitally Reconstructed Radiograph (DRR)
- EX: Siemens 4D CT
    - The 4DCT scan is made up of many 3D CT sets obtained at various breathing phases
    - Images are tagged with breathing signals
    - Images are sorted based on the corresponding breathing signals

Respiratory Gating

- Amplitude-based gating allows automatic gating based on the absolute position of the marker block on the patient's thorax or abdomen, regardless of the phases in the patient's respiratory cycle.
- Uses infrared tracking camera and a reflective marker

Portal Imaging

- International Commission on Radiation Units and Measurements (ICRU) suggest that the inaccuracy in dose delivery be < 5%
- Accurate patient positioning and field placement is required
- **Set up Error Occurs Imaging** is a solution (for localization and verification)
    - Portal Films
    - **Electronic Portal Imaging Devices** EPID
        - Matrix-Ion Chamber
        - Active Matrix Flat Panel Imagers (AMFPI)
            - Amorphous Silicon
            - Amorphous Selenium

        - X-Ray Converter
            - Metal Plate (Copper or Steel)
        - Detector
        - Clinical Uses
            - Error Detection/Correction
                - Patient Setup Verification
                - Patient Treatment Modification
                - Organ/Target Motion
            - Advanced Applications
                - Compensator design/verification
                - Complex treatment QA
                - Patient dosimetry
    - Cone Beam CT (CBCT): MV-CBCT or kV-CBCT
        - In CBCT imaging, the rotating x-ray source produces a divergent pyramidal- or cone-shaped source of ionizing radiation directed through the middle of the area of interest onto an area x-ray detector on the opposite side.
        - Regular CT uses fan-shaped source
        - Advantages: <u>shorter examination time</u>, some reduction of image distortion due to patient movements, and increased x-ray tube efficiency.
        - Disadvantage: with larger FOVs<u>, limitation in image quality</u> related to noise and contrast resolution because of the detection of large amounts of scattered radiation
        - MV-CT vs. kV CT
            - Compton effect
                - Proportional to the number of electrons per gram
            - Photoelectric process is the predominant mode of photon interaction
                - At relatively low photon energies

- High atomic number
- MV CT
  - Megavoltage CT imaging
  - Metal artifact reduction

Ultrasound in Radiotherapy

- High-frequency sound waves to view soft tissues.
- Subjectivity, requires highly trained operators with experience in ultrasound image interpretation, time consuming and inefficient.
- Advances in 3D ultrasound will minimize some of these subjectivity issues.

Motion Management through Gating and Coaching

- Methods to manage breathing motion
  - Gating
  - Turn radiation on/off at a specific breathing phase
  - Tracking
  - Synchronize beam motion with breathing motion
  - Immobilization
  - Voluntary deep inspiration breath-hold
  - Active Breathing Control
  - Optimize-free breathing PTV (Planning Target Volume)
- **Respiratory Gating**
  - Why
    - Patients can breath regularly and periodically with/without? proper voice coaching
    - Organ motion such as lungs, kidneys, pancreas and liver are related to the motion of an external marker
    - <u>Target motion</u> is also related to the motion of an <u>external marker</u>

- 2 types
  - Prospective or triggering
    - Simplest and best for acquiring a desired threshold, if known ahead of time by physician
    - Takes a series of snapshots at the proper moment, moves the couch to the next position, takes more snapshots, and so on. Basically, prospective 4D-CT results in one volumetric sequential CT acquisition collected at a specific threshold of the respiratory cycle.
  - Retrospective
    - Most efficient for acquiring multiple phases simultaneously with large volumes
    - Acquired in volume mode with low pitch spiral
    - Data put in bins according to the time stamp correlation of respiratory trace

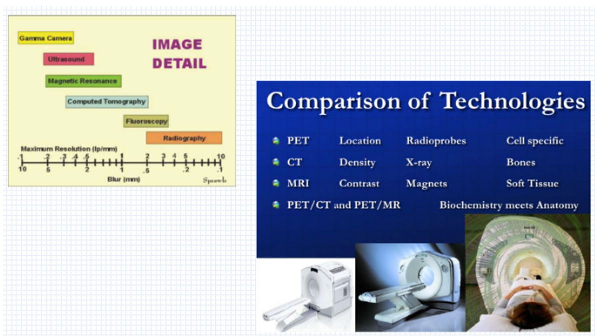
- Deep Inspiration Breath-Hold (DIBH)
  - Technique for Left Breast Treatment
  - Breast adjuvant radiotherapy improves local control but increases the risk of cardiovascular mortality and pulmonary complications
  - Cardiac perfusion defects correlate with volume of heart in the field during tangential field radiotherapy.
  - DIBH to <u>increase the distance between the heart</u> and the chest wall for left breast or left chest wall patient.
  - For younger women this can be a primary concern with regard to life expectancy.

Summary

- Geometrical uncertainties limit the precision of radiotherapy (RT)
- 2D,3D and 4D image registration and guidance increases the precision of RT allowing margin reduction and dose escalation
- Adaptive RT further individualized treatment delivery

Image Guidance in Medicine

- Radiation treatment guidance
- Computer-assisted surgery
- Different modalities:
  - CT
  - MRI
  - PET
  - Ultrasound
  - And more...



Multimodality Imaging / Image Fusion

- In medicine, combining images from different modalities can provide useful anatomical and physiological information.
- E.g.
  - CT (xray) provide anatomical information, high resolution
  - MR good soft tissue contrast
  - PET functional imaging

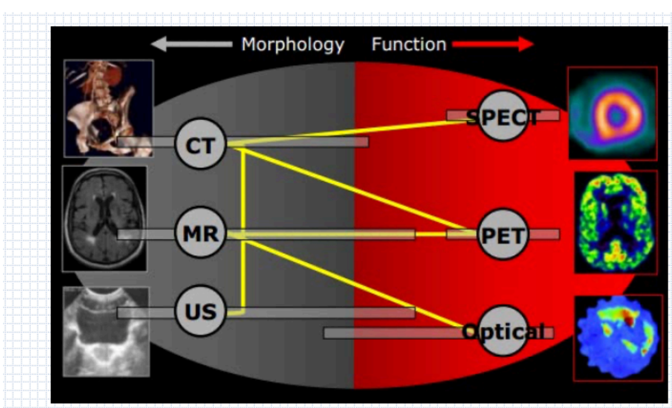


Image Registration

- Alignment of a target image with a reference image using a transformation to find the space coordinates to relate corresponding features in the images.
- Could be done with or without 'rigid body' assumption
    - Rigid (rotations, translations, scaling)
    - Deformable (non-rigid)

PET-CT, MR-CT Image Fusion

- CT – Bony landmarks
- MRI – soft tissue
- Image fusion
    - Image registration/fusion: enhances diagnosis and localization of pathological lesions by combining single or multi-modality images into a registered or fused image.
        - 'Registration' as applied to images connotes a process of correlating different image data sets to identify corresponding structures or regions

Multimodality-Imaging in RT

- **Computed tomography (CT)** is the primary modality for image based treatment planning
- Other imaging modalities can provide unique information which may improve overall patient management
    - Magnetic resonance Imaging (MRI) and Spectroscopy (MRS)
    - Single Photon and positron Emission computed tomography (SPECT and PET)
    - Ultrasound (US)
    - Molecular Imaging
- The goal is to biologically characterize and accurately delineate a tumor and to predict the response to the planned course of therapy at the earliest time
- Registration Techniques
    - Surface based registration
        - Internal

        - External
    - Image-based registration
    - Point-based registration
    - Automatic and semi-automatic computer assisted methods

MRI-CT Fusion-Registration

- MRI
    - Excellent soft tissue contrast allows better differentiation between normal tissues and many tumors
    - Not limited to imaging in axial planes
- Disadvantages:
    - Susceptible to spatial distortions
    - Image intensity values do not relate to physical or electron density

PET Imaging for RT

- Provides information about <u>physiology</u> rather than anatomy
    - Tumor metabolism
    - Differentiation between tumor recurrence and radiation necrosis
    - Regional lung function
- Poor resolution
    - Difficult to delineate target and organ boundaries
    - Difficult to appreciate external contours
- 18F-FDG is the primary agent used in oncology imaging
- PET-CT Fusion / Image Registration
    - Lack of anatomical definition makes a registration with CT image a necessity
    - Combined PET/CT scanners can simplify the process
    - Setup reproducibility a concern
    - Might require deformable image registration

More Multimodality Imaging

- Combination or fusion of images from different modalities (CT, PET, MRI, SPECT) can be accomplished using hybrid systems or with mathematical tools (image registration)
    - CT
    - SPECT
    - MRI
    - PET
    - SPECT/CT
    - PET/CT
    - PET/MRI
    - ....

2D Images and 3D Images and Coordinate Systems

- How can we localize in 3D, interpret the images?
- Need some system to figure out the **coordinate systems**. Start with some fiducial markers or landmarks.
- A good example is the stereotactic frame used for surgery application and for radiosurgery (surgery with radiation).

Current Technology

- Gamma Knife® by Elekta
    - Uses 192 to 201 beams of highly-focused gamma rays
        - All beams aim at target region
- Linear accelerator (LINAC) machines
    - Deliver high-energy x-rays = photons
    - Uses **microwave technology** to accelerate photons
        - Novalis TxTM by Brainwave AG
        - XKnifeTM by Integra
        - AxesseTM by Elekta
        - CyberKnife® by Accuray
- Proton beam machine

Stereotaxis

- Derived from the Greek stereo- for "three- dimensional" and -taxic for "an arrangement," was coined by Horsley and Clarke in 1908.
- It was their use of a **three-dimensional Cartesian coordinate system** that provided the basis for all stereotactic systems used in modern day neurosurgery.

Stereotactic Procedures (SRT – Stereotactic Radiation Therapy)

- Radiosurgery:
    - The use of radiation as a "surgical" Tool
- Small volumes of tissues within the brain are treated with large doses delivered in a single fraction
- Normal tissues are protected by the rapid dose falloff and by delivering the treatment with high precision
- Where to aim?
    - Determining the exact coordinates of the tumour
    - Target (anatomy) localization
        - Common problem for all SRS modalities
            - SRS (Stereotactic radiation surgery) Frame Placement
    - Stereotactic Frames Provide
        - patient immobilization
            - rigid fixation of cranial anatomy
        - target localization
            - precise identification of target coordinates in a stereotactic coordinate frame
    - treatment setup
        - patient setup must guarantee accurate placement of target coordinates to the nominal isocenter of the linac
    - DSA images are registered to CT/MR through **stereotactic localization**.
    - **Angiography** helps identification of the nidus position and differentiation from
    - feeding arteries and draining veins, not easily identifiable on CT or MR images

- Can you hit what you are aiming at?
  - Dose Localization
  - Procedure, process, equipment, technique specific
- Treatment Applications
  - Brain tumors
    - Cancerous and non-cancerous
    - Primary and metastatic – spreading
  - Arteriovenous malformations (AVMs)
    - Tangling of expanded blood vessels
      - Limits blood flow
  - Trigeminal neuralgia
    - Nerve disorder in face
  - Parkinson's disease
  - Tremors
  - Epilepsy
  - ...

Digital Subtraction Angiography (DSA)

- X-ray images of vessels in isolation from their background (bone and soft tissue).
- Two images are acquired from exactly the same anatomical region before and after injection of a contrast medium.
- Subtraction of the logs of the transmission.
  - Mask signal It
  - Contrast signal Ic

2D Images and Stereotactic Frame

- Projection of markers, e.g. 2 plates attached to stereotactic frame (plate on each side of head), 4 markers each.

Homogeneous Transformation Matrices

- 3D → 3D
- 3D→2D (with a 4x3 matrix). DSA images acquired with the 8 markers

- Acquire 2 projections or images (AP and LAT).
- Transformation matrix has 12 unknowns (4x3).
- 2 images from different directions projections, means 2 equations. Need at least 6 markers to solve for the 12 unknowns of the transformation matrix.

Fractionated Stereotactic Radiation Therapy

- Fractionated Stereotactic Radiation Therapy (SRT) combines the <u>target and dose localization</u> characteristics of SRS with the biologic advantages of <u>dose fractionization</u>

Evolution Imaging for Treatment Verification

- 1980's port films
- 1990's MV portal imagers, In-room ultrasound localization, Marker-based localization, Fluoroscopic tracking
- 2000's Flat panel imaging, KV digital imaging, CBCT, MV CBCT, CT 'on rails'
- Emerging electromagnetic localization and tracking, surface tracking, in-room MRI

MRI

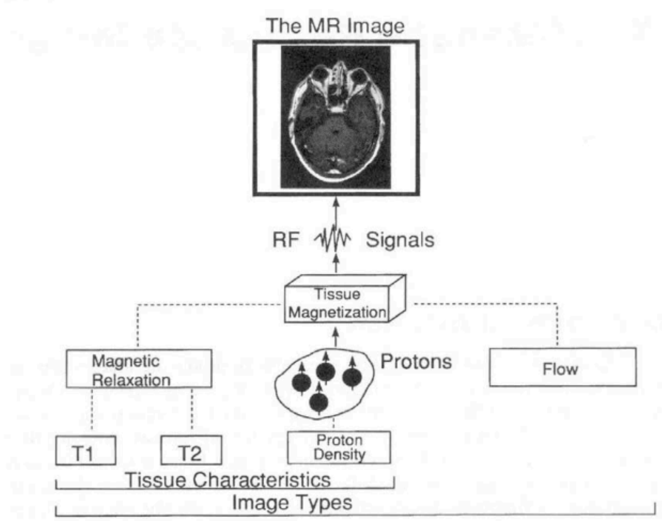


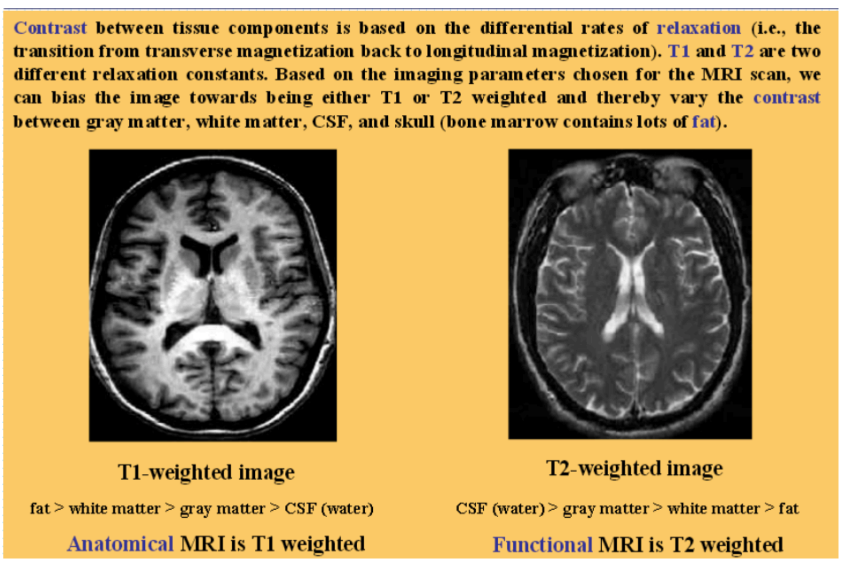
Figure 28-1 Physical Characteristics of Tissue That Are Displayed in the Magnetic Resonance Image

- Angular Momentum
  - J = mω=mvr
- A Single Proton
  - There is electric charge on the surface of the proton, thus creating a small current loop and generating magnetic moment μ.

- The proton also has mass which generates an angular momentum J when it is spinning.
- Thus proton "magnet" differs from a magnetic bar in that it also possesses angular momentum caused by spinning.

- Protons in a magnetic field
  - Parallel (low energy)
  - Anti-parallel (high energy)
- Protons Align with field
  - spins tend to align parallel or anti-parallel to B0
  - net magnetization (M) along B0
  - spins precess with random phase
  - no net magnetization in transverse plane • only 0.0003% of protons/T align with field
- Boltzman Equation
  - the population ratio of the two energy states: $N-/N+ = e^{-E/kT}$
  - Larger B0 produces larger net magnetization M, lined up with B0
  - Thermal motions try to randomize alignment of proton magnets
  - At room temperature, the population ratio is roughly 100,000 to 100,006 per Tesla of B0
- Energy Difference Between States
  - Larmor Frequency: $\gamma/2\pi$ = 42.57 MHz / Tesla for proton
- Procession
  - Precession of the quantum expectation value of the magnetic moment operator in the presence of a constant external field applied along the Z axis. The uncertainty principle says that both energy and time (phase) or momentum (angular) and position (orientation) cannot be known with precision simultaneously.
  - $d\mu/dt = \gamma (\mu \times Bo)$

- RF Excitation
    - Excite Radio Frequency (RF) field
    - transmission coil: apply magnetic field along B1 (perpendicular to B0)
    - oscillating field at Larmor frequency
    - frequencies in RF range
    - B1 is small: ~1/10,000 T
    - tips M to transverse plane – spirals down
    - analogy: children's swing set
    - final angle between B0 and B1 is the flip angle
- Signal Detection via RF Coil
- T1 and T2 relaxation
- Spin-Echo Pulse Sequence
- T1 and T2 weighted Image



Images

- Turning people into numbers!
- How do we get the numbers?
    - Image acquisition and reconstruction
        - MR, CT, PET, US, and radiography
- How good are the numbers?
    - Image quality

        - Accuracy, noise, spatial resolution, ...
- A few ways the numbers are important:
    - Detection, localization, and segmentation (Interpreting the numbers)
    - Registration (Aligning the numbers)
    - Transformation (Turning one set of numbers in to another)

Ultrasound Imaging

- <u>Pressure waves</u> that propagate through matter via compression and expansion of the material 20kHz+
- Measure the reflectivity of tissue to sound waves
- **Doppler imaging**: measure velocity of moving objects, e.g. blood flow
- Characteristic impedance of a medium Z (kg/m2s or rayleigh), speed c.
- Plane or spherical wave. Reflection, refraction at an interface. Scattering and absorption. Beam reflected at tissue-interface (99%), need to couple with gel.
- Ultrasound produced and detected with a transducer. Transducer made of a piezoelectric crystal. Alternative current applied to crystal causes it to vibrate and produce the ultrasounds. Reverse effect to detect (mechanical energy from sound vibrating the crystal converted to electrical energy).
- 3D ultrasound (waves send from different angles then reconstructed).
- Use for diagnosis (visualize heart, breats abdomen, fetus,...).
- Guidance
    - Some application for image guidance in therapy e.g. transrectal ultrasound to guide permanent radioactive seed implant in the prostate (brachytherapy, permanent implant).

Hybrid Linac MRI System

- recent developments
- The first whole body clinical linac MRI hybrid (linac-MR) began installation in 2013 at the CCI, Edmonton AB, Canada. The linac-MR integrates into one machine, **a linac and an MRI.**

- The linac-MR consists of an isocentrically mounted **6 MV linac** that rotates in-unison with a biplanar 0.5 T MRI in transverse plane. The MRI's Bo field and the central axis of the 6 MV beam are parallel to each other.
- (other groups also working on their version of such hybrid machines).

Digital Imaging and Communications in Medicine (DICOM)

- It's a file format definition and a network communications protocol.
- A standard for handling, storing, printing, and transmitting information in medical imaging.

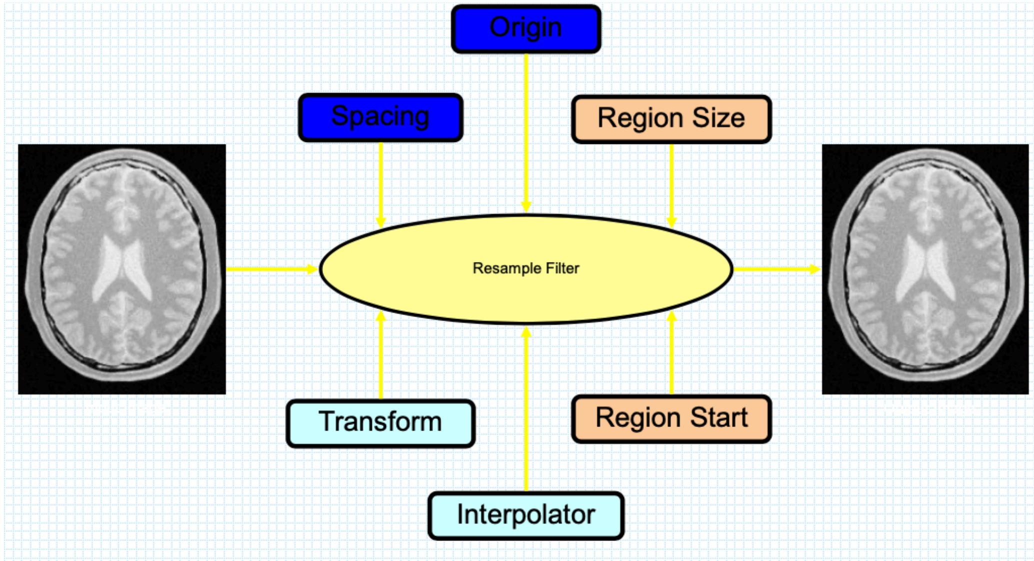
Image Processing

- Enhancement
- Visualization
- Segmentation
- Registration
- Quantification

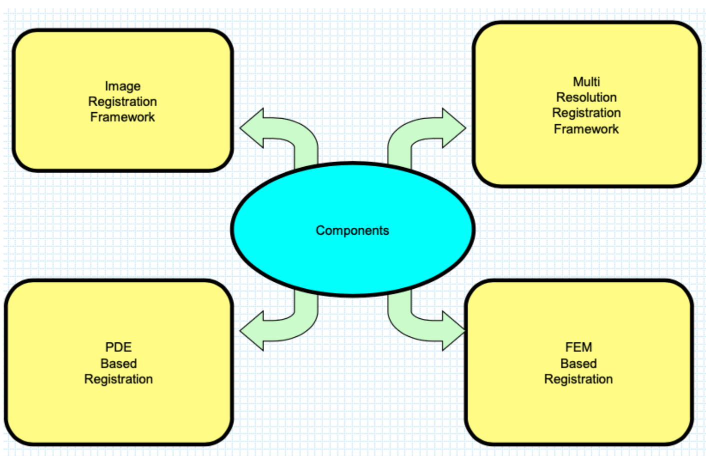
Insight Segmentation and Registration Toolkit (ITK)

- Open-source, cross-platform system that provides developers with an extensive suite of software tools for image analysis.
- Image Pixel → index to physical coordinates
- Key Ideas
    - Image Resampling
    - Registration Framework
    - Multi-Modality
    - Multi-Resolution
    - Deformable registration

- Resampling



- Registration



- Components

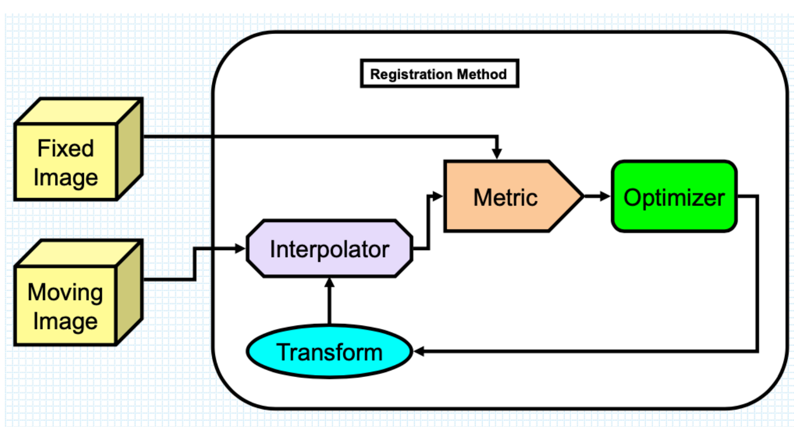


Image Metrics

- Mean Squares
- Normalized Correlation
- Mean Reciprocal Square Difference
- Mutual Information
  - Viola-Wells
  - Mattes
  - Histogram based
  - Histogram normalized

Transforms

- Translation
- Scaling
- Rotation
- Rigid3D
- Rigid2D
- Affine
- BSplines
- Splines: TPS, EBS, VS

Optimizers

- Gradient Descent
- Regular Step Gradient Descent
- Conjugate Gradient
- Levenberg-Marquardt
- One plus One Evolutionary Algorithm

Interpolators

- Nearest Neighbor
- Linear
- BSpline

Image Registration

- Fixed Image
- Moving Image
- Registered Moving Image

Image Similarity Metrics

- How similar is Image A to B?
- Does Image B matches A better or C?
- Match(A , B) Simplest Metric: **Mean Squared Differences**
    - Difference(index) = A(index) – B(index) Sum += Difference(index) 2
    - Match(A , B) = Sum / numberOfPixels
- Then evaluating the matches and plotting the matches via mean squared differences in a transform parametric space

Image Metrics

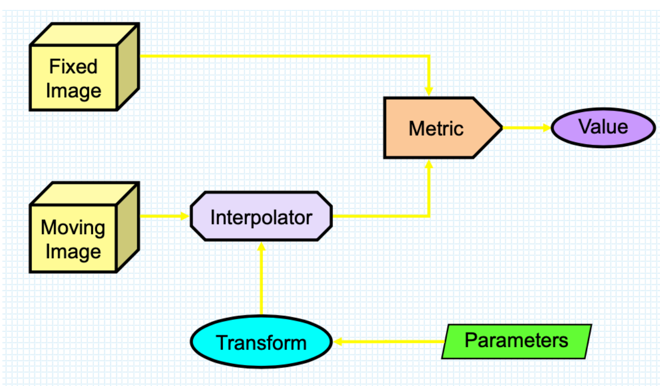
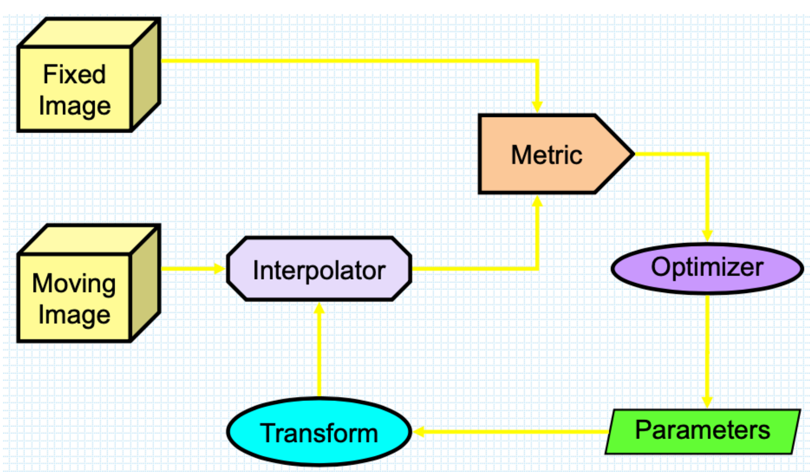


Image Registration Framwork → Gradient Decent Optimizer



Multi-Modality Registration

Radiomics

- Mining of quantitative image features from medical imaging to enable data to be extracted and applied to help clinical evaluation for diagnostic, prognostic, or prediction purposes.

Radiation Therapy

Introduction

- Oncology
  - Three primary specialties for treatment of cancer: Radiation oncology, medical oncology and surgical oncology
- Radiation therapy or radiotherapy
  - Abbreviated as RT, RTx, or XRT,
  - Utilizes high-energy ionizing radiation to control or kill malignant cells.
  - May be part of a <u>curative treatment</u> in several types of cancer.
  - May also be part of a palliative treatment to <u>control symptom</u> such as pain or progression of disease.
  - Radiation is used to kill cancer cells by damaging their DNA.
  - Both normal and cancer cells can be damaged with radiation. Therefore, treatment must be carefully planned to minimize radiation exposure to normal organs.
  - The radiation used for cancer treatment may come from a machine
    - External to the body (**External-beam Radiation Therapy**)
    - Radioactive material placed in the body near tumorcells (**Brachytherapy**)
    - Radiopharmaceutical injected / ingested (**Systemic Radiation Therapy or Nuclear Medicine**)
  - A patient may receive radiation therapy **before, during, or after surgery**, depending on the type of cancer being treated.
  - Some patients receive **radiation therapy alone**, and some receive radiation therapy in **combination with chemotherapy and/or surgery**.
- Successful radiotherapy requires a uniform dose distribution within the target (tumour).
- Criteria of a uniform dose distribution within the target:
  - Recommendations regarding dose uniformity, prescribing, recording, and reporting of photon beam therapy are set forth by the **International Commission on Radiation Units and Measurements (ICRU)**.

    - The ICRU report 50 and 62 recommends a target dose uniformity within **+7% and –5%** relative to the **dose delivered** to a well defined **prescription point** within the target.

Techniques

- Radiotherapy is carried out with a variety of
    - Beam energies
    - Beam types
    - Field sizes
    - Delivery modes (Static, Dynamic or Rotational)
- Uses one of two set-up conventions:
    - **a constant source to surface distance (SSD)** for all beams or
    - an **isocentric** set-up with a **constant source to axis distance (SAD)**

SSD

- Distance from the source to the surface of the patient is kept constant for all beams.
- Each beam require repositioning of patient.

SAD

- Center of the target volume is placed at the machine isocentre, i.e., the distance from source to the target point is kept constant
- In contrast to the SSD technique, the SAD technique requires no adjustment of the patient setup when turning the gantry from one field to the next field.

Beam Characteristics

- Primary Beam Modifier
    - Flattening Filter
        - Used to render beams flat across.
        - Usually achieved at a depth of 10cm in water.
- Different **field sizes** are often achieved with;
    - Collimator jaws
        - Two sets of jaws
        - X (X1 & X2) and Y (Y1 & Y2)

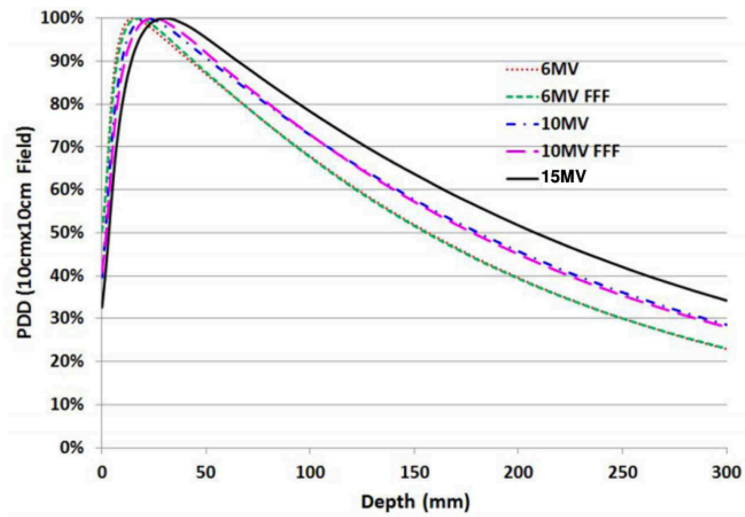
- Custom blocks
  - Poured or lead shaped blocks
- Multi-Leaf Collimator (MLC)
  - Tungsten leafs (2.5mm – 1cm widths)
  - Typically 60 -120 leafs depending on vendor and system

- Additional beam modifiers may be required;
  - Wedges (physical or dynamic)
    - Physical – wedge shaped attenuator
    - Dynamic – uses the sweeping jaw (Y) to shape the beam
  - Compensators
    - Beam modifying devices used to even out the skin surface contour to create dos homogeneity
  - Bolus materials
    - Tissue equivalent materials used to compensate for missing tissue.
    - To improve dose coverage to skin.

Photon Beam

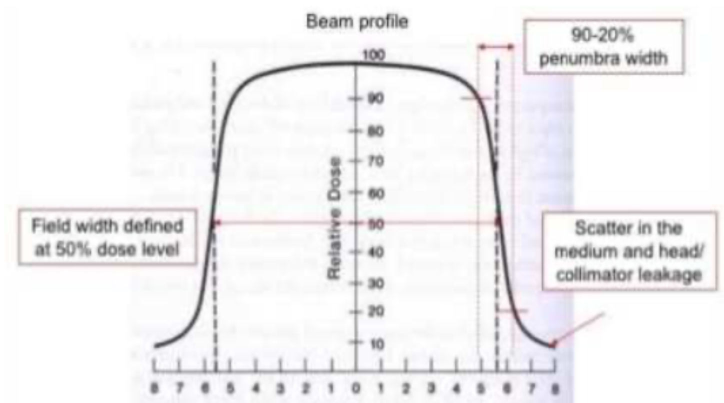
- Beam energies used in external beam photon radiotherapy:
  - Superficial (30 kVp to 80 kVp)
  - Orthovoltage (100 kVp to 300 kVp)
  - Megavoltage (Co-60 to 25 MV)
- **Dmax** = depth at maximum dose
  - 6MV=1.5cm; 10MV=2.5cm; 15MV=3cm → increase with beam energy
  - 6MV-FFF= 1.2cm; 10MV-FFF= 2.0cm
- **Percentage Depth Dose (PDD)**
  - Ratio of <u>dose</u> at a specified depth to dose at Dmax.
  - Measured at an **SSD setup** (i.e. constant SSD)
  - Gradient of curve increases with energy
  - <u>Do not</u> vary significantly with field size

- Percentage depth dose (PDD)

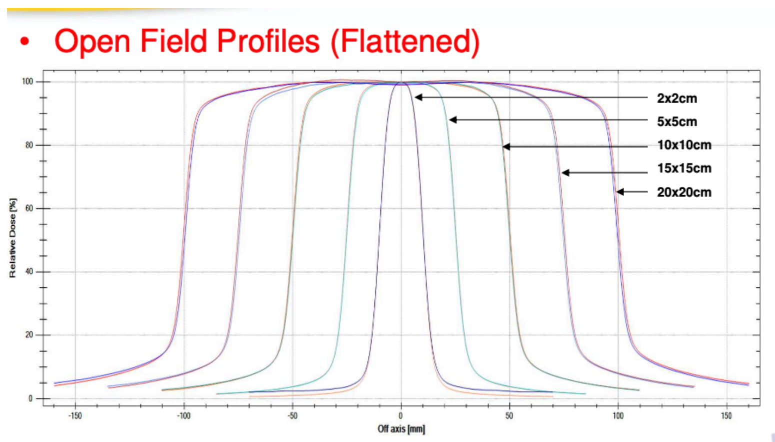


- **Tissue Phantom Radio (TPR)**
  - ratio of <u>dose</u> at a specified depth to <u>dose</u> at reference depth.
  - at **SAD setup** (SSD changes with each depth).
  - depends on Energy, Depth and <u>Field size</u>.
  - **Tissue Maximum Ratio (TMR)** if reference depth is Dmax.
- **Relative Dose Factor (RDF)**
  - ratio of <u>dose</u> for the specified <u>field size</u> to dose at a <u>reference field size</u> (10x10cm)
  - two components
    - Collimator factor (Sc)
    - Phantom factor (Sp)
- **Wedge Factor (WF)**
  - ratio of dose with <u>wedge</u> to dose <u>without wedge</u> (open field)
- **Transmission Factor (TF)**
  - ratio of dose with an <u>attenuator</u> to dose without.
- **Beam profile**
  - Relative dose across the beam
  - **Penumbra** is defined as the <u>90-20% distance</u>

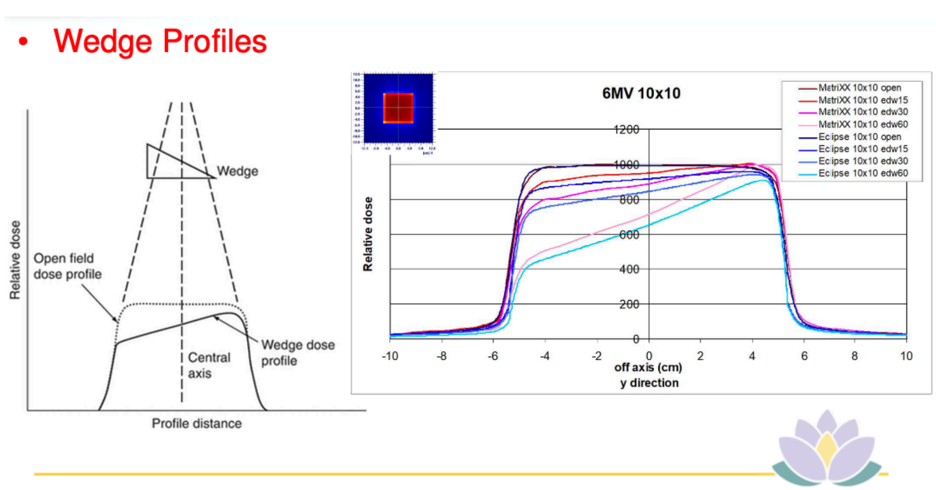
- **Field width** is defined as the width at the 50% dose level
- Phantom and Collimator Scatter, and leakage results in the tail of the profile
- Profiles are characterized by their **flatness** and **symmetry**



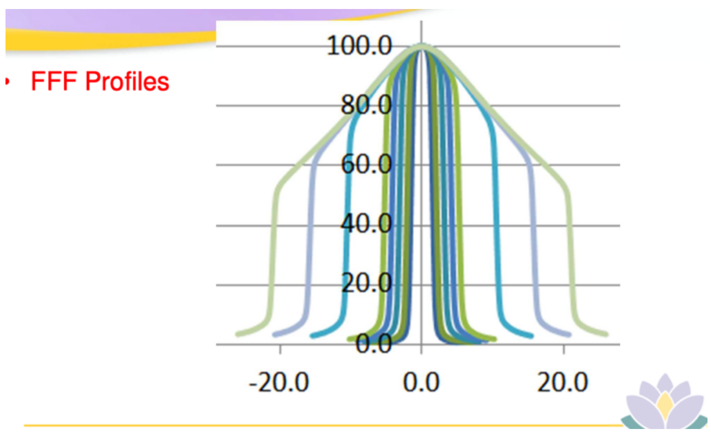
- **Open Field Profiles**



- **Wedge Profiles**

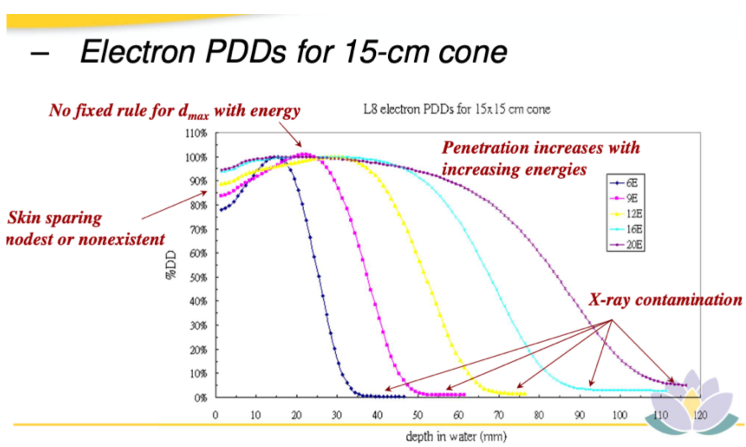


- **Flattening-Filter Free Beams (FFF)**
    - Available on newer TrueBeam Linacs
        - 6FF and 10FFF
    - These are photon beams <u>without</u> flattening filters
    - Capable of **higher dose rates** (up to 2400MU/min compared to 600MU/min for flattened beams)
    - Profiles <u>peaks</u> in the <u>middle</u>
    - Have **limited useful open field size** (max of 20x20cm compared with 40x40cm for flatten beams)



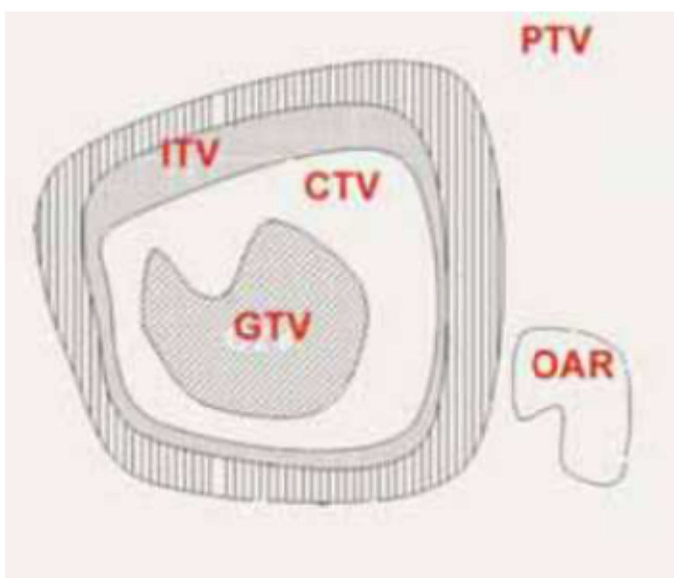
Electron Beams

- Percentage Depth Dose (PDD) Curve
    - Most useful depth given by 90% depth dose
    - Rapid dose drop-off after 90% depth dose
    - X-ray contamination increases with energy



Volume Definition

- The ICRU 50 and 62 Reports define and describe several target and critical structure volumes
- **The Gross Tumor Volume (GTV)** is the gross visible or palpable malignant growth.
- **Clinical Target Volume (CTV)** is the tissue volume that contains the GTV and/or microscopic malignant disease.
- **The Planning Target Volume (PTV)** includes the internal target margin and an additional margin for:
  - Set-up uncertainties
  - Machine tolerances
  - Intra-treatment variations.
  - The PTV is often described as the **CTV plus a fixed or variable margin**.
- **Organ at Risk (OAR)** is an organ whose sensitivity to radiation is such that the dose received from a treatment plan may be significant compared to its tolerance. (e.g. Spinal cord)
  - May require a change in the beam arrangement or a change in the dose.
  - Specific attention should be paid to organs that, even though not immediately adjacent to the CTV, have a <u>very low tolerance dose</u>. (e.g. Lens of the Eye).



Dose Specification

- The complete prescription of radiation treatment must include:
  - Definition of the aim of therapy
    - Palliation
    - Curative
- Volumes to be considered
  - GTV, CTV and PTV
- Prescription dose and fractionation
  - Prostate - 7800cGy in 39 fractions
  - Breast - 4250cGy in 16 fractions
  - Lung - 6000cGy in 30 fractions
  - Lung (SABR)- 4800cGy in 4 fractions
  - Brain (SRS) - 2000cGy in 1 fraction

Patient Data

- The patient information required for treatment planning depends on which system is used:
  - Two dimensional system
  - Three dimensional system
- 2D Treatment Planning
  - A **single patient contour**, acquired using lead wire or plaster strips, is transcribed onto a sheet of graph paper, with reference points identified.
  - **Simulation radiographs** are taken for comparison with port films during treatment.
  - SSDs as well as depths of interest can be determined at simulation.
  - **Organs at risk** can be identified and their depths determined on simulator radiographs.
- 3D Treatment Planning
  - CT dataset of the region to be treated is required with a **suitable slice spacing**
    - typically 0.1 – 0.5 (depending on disease site and planning technique).

- An **external contour** (representative of the skin or immobilization mask) must be drawn on every CT slice used for treatment planning.
- Tumor and target volumes are drawn on CT slices.
- **Organs at risk** and other structures of importance should be drawn in their entirety, if their doses are to be estimated.
- **MRI** or other imaging modalities such as **PET** may be required for image fusion (co-registration)
    - E.g. MRI for brain, PET for lung
- With many treatment planning systems, the user can choose:
    - To ignore for inhomogeneities (often referred to as **heterogeneities**).
    - To perform **bulk corrections** on outlined organs.
    - To use the CT data itself (with an appropriate conversion to electron density) for **point-to-point correction**.
- CT images can be used to produce **digitally reconstructed radiographs (DRRs)**
- CT images and/or DRRs can be used to verify patient set up during treatment.

- Patients may require an **external immobilization** device for their treatment:
    - To immobilize the patient during treatment.
    - To provide reliable means of reproducing the patient position from treatment planning and simulation to treatment, and from one treatment to another.
    - The immobilization may include;
    - Masking tape, Velcro belts ,elastic bands, or even a sharp and rigid fixation system attached to the bone (**stereotactic frame**), head rest, vacuum-based devices, breast board.

CT Simulation

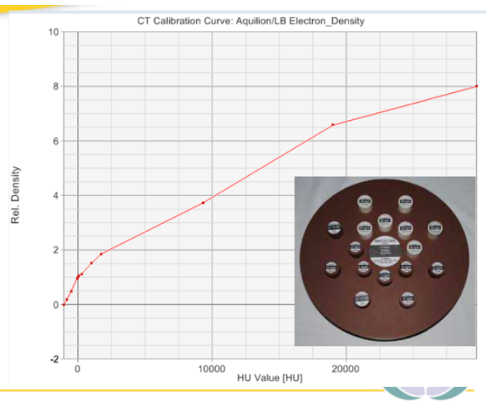
- Modern simulation systems are based on
    - Computed Tomography Simulator (CT-Sim) or
    - Magnetic Resonance Simulator (MR-Sim)
- CT simulation can provide
    - Patient **treatment position**

- Marking of **reference isocenter**.
- **Electron density**
- Localization and contouring of **targets** and **critical structures**
- 3D dose calculation
- Follow-up
    - Tumour response
    - Normal tissue response

Relative Electron Density (RED) Curve

- CT Scan of phantom
    - Phantom has materials of known electron densities
    - For each scanning protocol (kVp)
        - Determine the mean HU for each material
        - Plot **HU v Electron density**

Material[1]	Electron Density
Lung Inhale	0.190
Lung Exhale	0.489
Adipose	0.952
Breast	0.976
Water	1.000
Muscle	1.043
Liver	1.052
Bone 200	1.117
Bone 800	1.512
Bone 1500	1.859
Titanium[2]	3.735



Dose Calculation Algorithm

- Measurements are performed for:
    - Fixed square fields
    - Fixed depths
    - **Homogenous medium (water)**
    - Flat surface
- Types of algorithm
    - Semi-empirically based
    - Model based

    - Direct Monte Carlo
    - Hybrid
- Calculation Algorithms for TPS (photons)
    - Elekta XiO
        - Clarkson
        - FFT Convolution
        - Multigrid Convolution
        - Superposition
        - Fast Superposition
    - Phillips Pinnacle
        - Collapsed Cone Convolution
        - Pencil Beam
    - Varian ECLIPSE
        - AAA Collapsed Cone Convolution
        - Pencil Beam

Clinical Considerations

- For photon beams:
    - Isodose curves (lines of equal dose)
    - Wedges
    - Bolus
    - Compensators
    - Corrections for contour irregularities
    - Corrections for tissue inhomogeneities
    - Beam combinations

Beam Combination

- **Single Photon Beam – one beam**
    - Often used for palliative treatments or for relatively superficial lesions (depth < 5-10cm depending on energy)
    - Higher dose at the surface near Dmax when used for deep-seated lesions.

- **Parallel Opposed Beams – two beams**
    - suited for a variety of targets that covers the depth of the patient - often in palliative situations.
- **Multiple Co-Planar Beams** – 3 beams / 4 beams
    - 3 field technique using wedges
    - High dose delivered at the intersection of the beams
    - Characteristics

Multiple co-planar beams: General characteristics

- Wedge pair:
  Two beams with wedges (often orthogonal) are used to achieve a trapezoid shaped high dose region. This technique is useful in low-lying lesions (e.g., maxillary sinus and thyroid lesions).
- 4-field box:
  A technique of four beams (two opposing pairs at right angles) producing a relatively high dose box shaped region. The region of highest dose occurs in the volume portion that is irradiated by all four fields. This arrangement is used most often for treatments in the pelvis, where most lesions are central (e.g., prostate, bladder, uterus).
- Opposing pairs at angles other than 90°:
  also result in the highest dose around the intersection of the four beams, however, the high dose area here has a rhombic shape.

Multiple co-planar beams: General characteristics

- Occasionally, three sets of opposing pairs are used, resulting in a more complicated dose distribution, but also in spread of the dose outside the target over a larger volume, i.e., in more sparing of tissues surrounding the target volume.
- The 3-field box technique is similar to a 4-field box technique. It is used for lesions that are closer to the surface (e.g., rectum). Wedges are used in the two opposed beams to compensate for the dose gradient of the third beam.

Plan Evaluation

The following tools are used in the evaluation of the planned dose distribution:

- Isodose curves.
- Orthogonal planes and isodose surfaces.
- Dose distribution statistics.
- Differential Dose Volume Histogram.
- Cumulative Dose Volume Histogram.

From the location of matrix points within an organ and from the calculated doses at these points, a series of statistical characteristics can be obtained.

These include:

- Minimum dose to the volume.
- Maximum dose to the volume.
- Mean dose to the volume.
- Dose received by at least 95% of the volume, D95%
- Volume irradiated to at least 95% of the prescribed dose, V95%

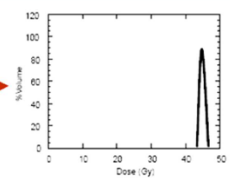
- Dose Volume Histograms (DVHs)

Dose volume histograms (DVHs) summarize the information contained in a three-dimensional treatment plan.

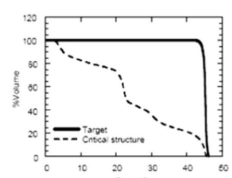
- This information consists of dose distribution data over a three-dimensional matrix of points over the patient's anatomy.
- DVHs are extremely powerful tools for quantitative evaluation of treatment plans.

Two types of DVHs are in use:

- Direct (or differential) DVH



- Cumulative (or integral) DVH
Definition: The volume that receives at least the given dose and plotted versus dose.



Monitor Unit

- Output for a radiotherapy machine is usually calibrated stated as follows:
  - In a water phantom
  - As the dose Di for a point P at a reference depth dref
  - For a nominal source-surface distance (SSD) or source to axis distance (SAD)
  - For a reference field size Aref (often 10x10 cm2) on the phantom surface or at the isocentre
  - At the calibration point, 1MU = 1cGy

- Reference Condition for calibration of a Linac
  - Electron
    - Field Size = 10x10cm2
    - Depth = Dmax or Reference Depth (energy dependent)
    - SSD
  - Photon
    - Field Size = 10x10cm2
    - Depth = Dmax (energy dependent) or at a Reference depth
    - SAD
- **Inverse Square Law**
  - Intensity of the radiation at a distance from the source follows the Newton's Inverse Square Law
  - Intensity is inversely proportional to the distance from the source.
  - For two intensities at two location from the source;

$$I1 * d1^2 = I2 * d2^2$$

  - Similarly for two areas;

$$A1 * d1^2 = A2 * d2^2$$

- The dose at prescription point (di):
  - For SAD set up: USE TPR for the depth

    Dose(A, di) in cGy = Dose(Cal) in cGy *TPR(A, d6i)*RDF(x,y)*MU*WF
  - For SSD set up: USE PDD for depth

    D(A, Di) in cGy = D(Cal) in cGy *PDD(A, Di)*RDF(x,y)*MU*WF
- For multiple fields, divide the required dose by the number of fields to get the dose per field

- RDF for 6MV photons

13. Relative Dose Factors: 6 MV Photons

Data for collimator setting at Source-Axis Distance = 100.0 cm
Normalised to a 10 x 10 cm field size

	Y Jaw →									
X Jaw ↓	5	8	10	12	15	20	25	30	35	40
5	0.943	0.963	0.971	0.977	0.983	0.990	0.994	0.998	1.001	1.003
8	0.956	0.981	0.991	0.999	1.007	1.017	1.023	1.027	1.030	1.033
10	0.960	0.988	1.000	1.008	1.017	1.028	1.035	1.040	1.044	1.046
12	0.964	0.993	1.005	1.014	1.024	1.035	1.043	1.048	1.052	1.056
15	0.968	0.998	1.011	1.021	1.031	1.044	1.052	1.058	1.063	1.067
20	0.971	1.003	1.017	1.027	1.039	1.053	1.062	1.069	1.074	1.079
25	0.974	1.006	1.021	1.032	1.044	1.059	1.069	1.076	1.082	1.087
30	0.975	1.008	1.023	1.035	1.048	1.064	1.074	1.082	1.088	1.093
35	0.976	1.010	1.025	1.037	1.050	1.067	1.078	1.086	1.093	1.098
40	0.976	1.011	1.026	1.039	1.052	1.069	1.080	1.089	1.096	1.101

- TPR for 6MV Photons

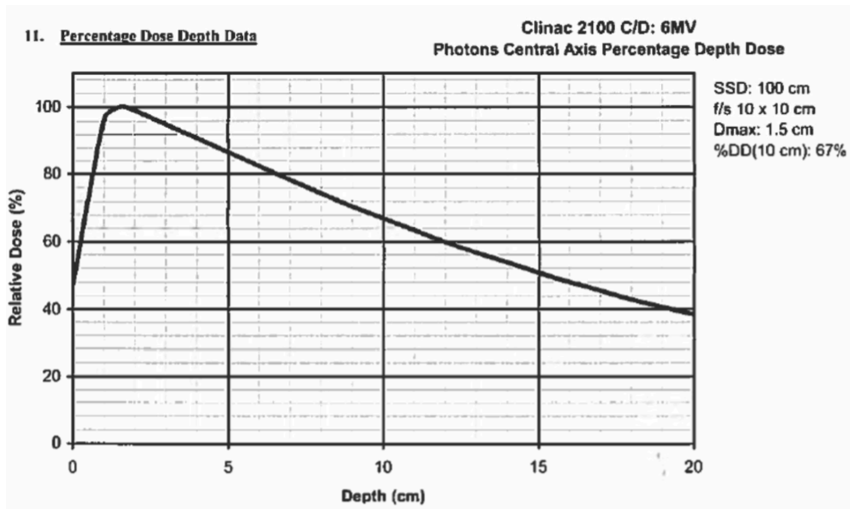
12. Tissue Phantom Ratio: 6 MV Photons

Source-Axis Distance = 100.0 cm
Field Size defined at 100.0 cm
Data normalized at 2.0 cm

	Field Size (cm)						
Depth (cm)	5x5	10x10	15x15	20x20	25x25	30x30	40x40
0.0	0.094	0.156	0.214	0.266	0.314	0.357	0.428
1.0	0.964	0.971	0.978	0.983	0.988	0.991	0.996
2.0	1.000	1.000	1.000	1.000	1.000	1.000	1.000
3.0	0.969	0.975	0.977	0.979	0.980	0.981	0.983
4.0	0.938	0.950	0.956	0.960	0.962	0.964	0.967
5.0	0.922	0.937	0.932	0.938	0.953	0.945	0.950
6.0	0.872	0.895	0.907	0.915	0.921	0.925	0.931
7.0	0.837	0.867	0.883	0.892	0.899	0.904	0.912
8.0	0.803	0.837	0.855	0.868	0.876	0.883	0.891
9.0	0.770	0.808	0.829	0.843	0.853	0.860	0.869
10.0	0.754	0.793	0.803	0.819	0.840	0.837	0.846
11.0	0.707	0.750	0.775	0.793	0.805	0.814	0.826
12.0	0.675	0.722	0.750	0.768	0.782	0.791	0.805
13.0	0.645	0.694	0.723	0.744	0.758	0.768	0.782
14.0	0.617	0.666	0.697	0.720	0.735	0.746	0.759
15.0	0.604	0.653	0.673	0.695	0.724	0.723	0.738

- PDD for 6MV Photons

11. Percentage Dose Depth Data



Correction for Tissue Inhomogeneities

- Tissues with densities and atomic numbers that are different from those of water are referred to as tissue inhomogeneities or heterogeneities.
- Inhomogeneities in the patient result in:
    - Changes in absorption of the primary beam and associated scattered photons.
    - Changes in electron fluence.
- Importance of each effect depends on the position of the point of interest relative to the inhomogeneity.
- Correct inhomogeneities:

In the megavoltage range the Compton interaction predominates and its cross-section depends on the electron density (in electrons per cm^3).

The following four methods are used to correct for the presence of inhomogeneities within certain limitations:

- TAR method
- Batho power law method
- Equivalent TAR method
- Isodose shift method

- **Tissue Air Ratio (TAR)**
    - the ratio of the dose to water at a given depth to the dose in air at the same location (with a buildup cap).

TAR (Z, Rd) = Dose in Tissue/Dose in Air

Where Rd is the field size R at a depth Z, at point d.

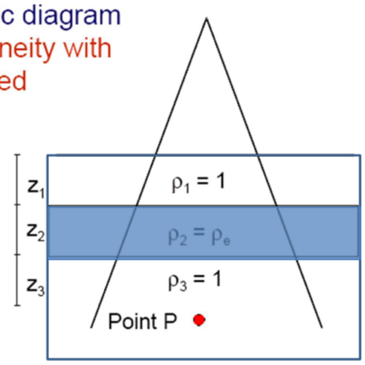
- TAR is dependent on the following factors;
    - TAR increases with the Beam energy
    - TAR increases with the Field size
    - TAR decreases with the Depth
    - TAR is independent of SSD

- The dose at each point is corrected by the factor CF:

Dinhom = CF x Dwater

The four methods for inhomogeneity correction are studied using the schematic diagram which shows an inhomogeneity with an electron density ρ_e nested between two layers of water-equivalent tissue.

$$D_{inhom} = C_F \times D_{water}$$



TAR method

The dose at each point is corrected by the factor C_F:

$$C_F = \frac{\mathrm{TAR}(z', r_d)}{\mathrm{TAR}(z, r_d)}$$

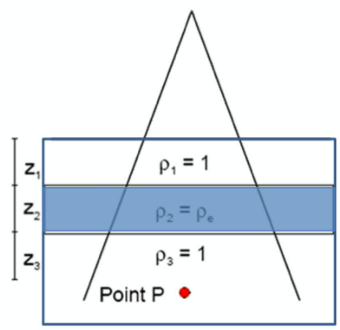
where

the total effective depth

$$Z' = \rho_1 Z_1 + \rho_2 Z_2 + \rho_3 Z_3$$

and the total actual depth

$$Z = Z_1 + Z_2 + Z_3$$



- Batho Power-Law Method:

Batho Power-law method

Dose at each point is corrected by correction factor C_F:

$$C_F = \frac{\mathrm{TAR}(z', r_d)^{\rho_3 - \rho_2}}{\mathrm{TAR}(z, r_d)^{1-\rho_2}}$$

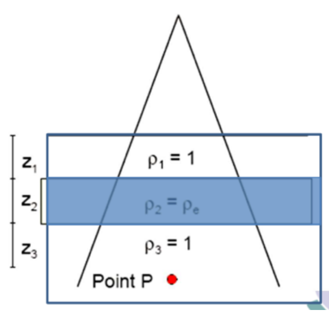
where

the total effective depth

$$Z' = \rho_1 Z_1 + \rho_2 Z_2 + \rho_3 Z_3$$

and the total actual depth

$$Z = Z_1 + Z_2 + Z_3$$



- Equivalent TAR Method

Equivalent TAR method

The method is similar to the TAR method. The field size parameter r_d is now modified into r'_d as a function of density and the correction factor C_F is:

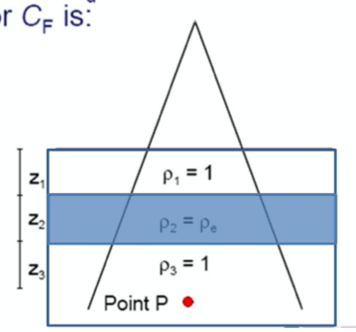
$$C_F = \frac{TAR(z', r'_d)}{TAR(z, r_d)}$$

Where the total effective depth

$$Z' = \rho_1 Z_1 + \rho_2 Z_2 + \rho_3 Z_3$$

and the total actual depth

$$Z = Z_1 + Z_2 + Z_3$$



- Isodose shift method
    - Isodose Shift Factors is a factor determined for tissue types/density and used to determined the dose shift at various points beyond the inhomogeneity.
    - These factors are energy dependent but do not vary significantly with field size
    - Isodose Shift Factors for 6MV:
        - Air cavity = -0.6; lung=-0.4; hard bone=0.5

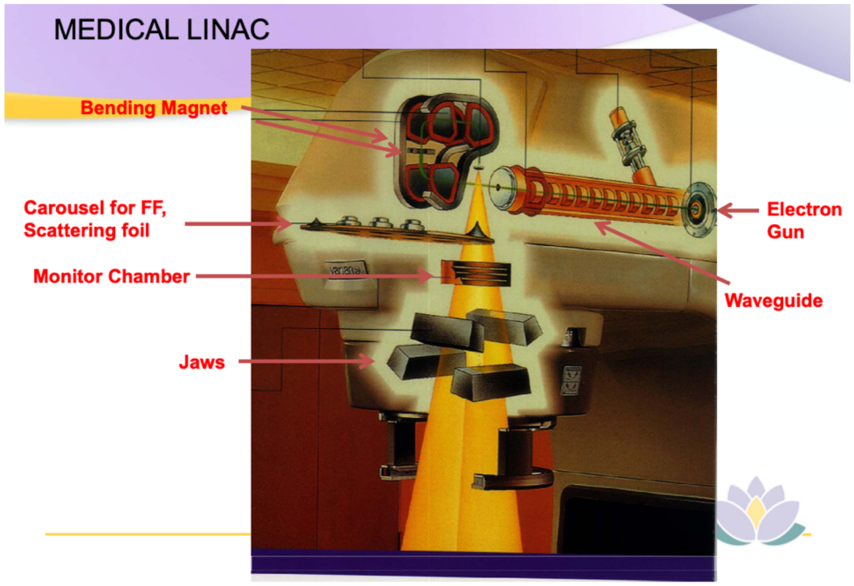
          Total Isodose Shift = Z' * Isodose Shift Factor
    - Shift is away from surface when negative.

Linear Accelerator (LINAC)

- Linear accelerators consist of two basic elements:
    - the accelerating structure and
    - the particle beam.
- The accelerating structure depends on type of Linac.
    - DC Linacs, like Van de Graaf,
        - Structure consists of some kind of column of electrodes.
        - DC electric field to **accelerates a continuous stream of particles**.
        - • LimitedtoafewtensofMeV.
    - Induction Linacs
        - The accelerating electric fields.
        - Obtained according to Faraday's law, from changing magnetic fluxes.

        - Generally used in medium-energy high-current pulsed applications.
    - RF Linacs
        - Can be categorized as:
            - low frequency (UHF), microwave frequency (L, S, C, or Xband), or laser frequency;
            - Continuous Wave or Pulsed;
            - traveling-wave or standing-wave;
            - Room temperature or superconducting.
        - Used for:
            - Circular accelerators,
            - High-energy accelerators such as SLAC,
            - Medical accelerators
- In all these cases, the structure is a conducting array of gaps, cavities or gratings along which RF waves with an electric field parallel to the beam and can be supported and built up through some resonant process
- The particle Beam
    - Types
        - Electrons (or positrons)
        - Protons (Hydrogen)
        - Ions
    - beam dynamics that must be considered;
        - Longitudinal bunching and stability (pulse)
        - Focusing and transverse stability
        - Steering and transport to a target
        - Shaping and modulation

Medical LINAC



Components of LINAC

- The Electron Gun
  - Where electron acceleration begins
  - the cathode of the electron gun is a Barium aluminate ("thermionic" material).
  - has a negative electrical charge usually created by heating the cathode.
  - the electrons "boil" near the surface of the cathode.
- The gate
  - is an anode that acts like a switch
  - consists of a copper screen or "grid"
  - has surface with a positive electrical charge
  - every 500 ms the gate is given a strong positive charge that causes electrons to fly toward it from the cathode
- The Buncher
  - the purpose of the buncher is to accelerate the pulsing electrons as they come out of the electron gun and pack them into bunches
  - the buncher receives powerful **microwave** radiation from the klystron or magnetron.

- The accelerating waveguide
    - receives additional RF power to accelerate the electrons.
- Bending magnet
    - Deflects electrons from accelerator structure and loops the electrons around to strike the target
    - Two types of arrangement
- Target
    - High Z material used to produce x-rays through bremsstrahlung interactions
- Flattening filter
    - Make photon beam intensity more uniform
- Scattering foil
    - Thin metallic foil used to broaden electron beam to a useful-sized field
- Treatment head
    - Monitor chamber
        - Set of two ion chambers to monitor the beam
            - beam output
            - beam Flatness
            - beam Symmetry
    - Collimator system
        - Primary collimator
            - To provide the maximum field size
        - Secondary collimator
            - (Jaws, MLC, stereotactic cones)

Cyberknife System

- Optimized to deliver stereotactic radiosurgery and stereotactic body radiation therapy (SRS/SBRT) non-invasively throughout the body.
- Robotic system
    - ability to track and automatically correct for tumor motion during treatment
    - enables delivery of high doses of radiation with extreme accuracy.

- Uses cones (interchangeable)

Gamma Knife System

- Gamma knife radiosurgery is a single treatment.
- 200 radiation beams from cobalt-60 sources converge with high accuracy on the target.
- A Radiosurgery therapy

Tomotherapy System

- A fully integrated IMRT/3D conformal RT
- optimized beamlet-based delivery
- unique helical design
- 6MV
- No Flattening Filter
- CT gantry
- Slice delivery

Brachytherapy

- Brachytherapy treats cancer by placing radioactive sources directly into or next to the area requiring treatment.
- Enables delivery of high dose to tumor with minimal dose to surrounding healthy tissues.
- Require applicator(s)/catheter(s) through which the Radioactive source is positioned at/near the treatment site.
- Sites:
    - Prostate cancer
    - Breast cancer
    - Lung cancer
    - Esophageal cancer
    - Gynecologic cancers
    - Anal/Rectal tumors
    - Sarcomas
    - Head and neck cancers

    - Skin
- Techniques
    - Low Dose Rate (LDR)
        - uses a lower strength radioactive source
        - dose rate = 0.4 - 2Gy/h
        - longer treatment times (for the one-time treatment).
        - E.g., prostate radioactive **seed implant**
            - involves permanent placement of tiny radioactive seeds (iodine-125) in prostate tissue.
        - Historically LDR has been used in the treatment of other sites such as gynaecological and head & neck
            - low activity sources are temporarily placed for several days & then removed.
    - High Dose Rate (HDR)
        - Uses a higher strength radioactive source contained within an **afterloader device.**
        - The afterloader delivers the source for a brief period of time through catheters, needles, or other applicators placed in or near the tumor site.
        - Dose = 2-12Gy/h
        - Per treatment, HDR is a much shorter procedure (minutes vs. days) than LDR
        - Require multiple treatments.
        - Increasingly more common, HDR techniques have replaced LDR techniques for most body sites.
    - Pulse Dose Rate (PDR)
        - Utilizes HDR sources to deliver LDR treatment
        - Involves short pulses of radiation,
        - Typically, once per hour
        - To simulate an overall LDR dose rate and effectiveness

- Sites include Gynaecological and Head & Neck cancers

Radiation Sources

Radionuclide	Type	Half-life	Energy
Cesium-131 (^{131}Cs)	Electron Capture, ε	9.7 days	30.4 keV (mean)
Cesium-137 (^{137}Cs)	β⁻- particles	30.17 years	0.662 MeV
Cobalt-60 (^{60}Co)	β⁻- particles	5.26 years	1.17, 1.33 MeV
Iridium-192 (^{192}Ir)	γ-rays	73.8 days	0.38 MeV (mean)
Iodine-125 (^{125}I)	Electron Capture, ε	59.6 days	27.4, 31.4 and 35.5 keV
Palladium-103 (^{103}Pd)	Electron Capture, ε	17.0 days	21 keV (mean)
Ruthenium-106 (^{106}Ru)	β⁻- particles	1.02 years	3.54 MeV
Radium-226 (^{226}Ra)	β⁻- particles	1599 years	0.74 MeV (mean)

Stereotactic Radiosurgery (SRS)

- Focal Irradiation technique
- Deliver radiation to stereotactically localized lesion
  - 3D superposition of a fixed coordinate system on a given organ
- Prescribed dose in order of several thousand cGy
- PTV are small (1-35cm^3)
- Stereotactic frames **rigidly attached** to the patient is used
- Delivery
  - Stereotactic brachytherapy with radioactive sources
  - External Beam Stereotactic irradiation
    - Gamma knife, Cyber knife, Linacs
- Diseases treated
  - About 50% involved arteriovenous malformation (AVM)
    - Typical dose of 25Gy
  - Benign lesions, primary malignant tumors, solitary metastasis
  - Functional disorders

Respiratory Gated Radiation Therapy

- Method to manage breathing motion
  - Gating
    - Turn radiation on/off at a specifies breathing phase

- Tracking
  - Synchronized beam motion with breathing motion
- Immobilization
  - Voluntary deep inspiration breath-hold
  - Active Breathing Control
- Optimize-free breathing PTV

- Clinical Sites
  - Lung
  - Liver
  - Pancreas
  - Breast
  - Lymphoma
- Respiratory Gating System
  - Reflective external marker placed on abdomen or chest
  - Infrared illuminator/CCD camera
  - Computer system for processing signal and generate trigger for CT/Linac

Total Body Irradiation (TBI)

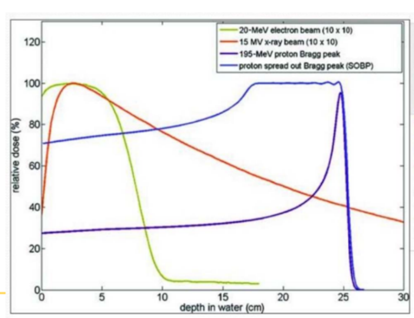
- Bone marrow transplantation (BMT)
  - Mostly to irradiate malignant diseases but also autoimmune or genetic disorders
    - Leukemia, lymphomas, multiple myeloma aplastic anemia, autoimmune diseases, AIDS
- To irradiate recipient's native bone marrow prior to transplantation.
  - TBI can be sequenced to either precede or follow chemotherapy
- Requirement for TBI
  - To deliver a whole-body irradiation to within +/-10% of prescribed dose.
- High dose TBI: 12Gy/6 (2 Fraction per day)
- Low dose TBI: Half body + nodes

Intraoperative Radiotherapy (IORT)

- Combination of surgery and radiation therapy
- Deliver in a single session 10 to 20Gy to a surgically exposed internal organ or tumor bed.
- To destroy microscopic tumor cells left behind from surgery
- Traditionally uses electron or orthovoltage beam
- More recently HDR brachytherapy sources have also been used

Photon Beam Therapy

- Proton therapy is an advanced form of radiation therapy that uses a high-energy proton beam for cancer treatment.
    - Proton beam delivers its energy within a **small range** inside the tumor, known as the **Bragg peak**
    - Resulting in reducing adverse effects to adjacent healthy tissues.
    - Cyclotrons is used to accelerate protons to an extremely high speed
    - Beam is steered and focused through a series of magnetic fields to generate a controlled beam
    - Beam is delivered very precisely in the treatment rooms, through a nozzle, to the targeted tumor.
- With proton therapy, there is significant potential to reduce side effects, improve overall outcomes in cancer treatment and offer a better quality of life to patients.
    - Specifically useful in younger patients
- Low entrance dose (plateau)
- Maximum dose at depth (Bragg peak)
- Rapid distal dose fall-off



Proton Beam Therapy

- Proton Accelerators
  - Linear Accelerator
  - Cyclotron
    - Fixed energy, continuous monoenergetic beam (250MeV), high dose rate.
  - Synchrotron
    - Selectable energy, limited dose rate especially for larger fields
  - High gradient Electrostatic Accelerator
  - Laser Plasma particle accelerator
- For a clinically useful proton beam, the pencil beam is modified either by;
  - **Scattering** Beam technique
    - Uses a range modulation wheels of variable thickness of acrylic glass or graphite steps.
  - **Scanning** Beam technique
    - Magnetically steering in the lateral direction to deliver a treatment field
    - Intensity may be modulated as the beam is moved across the field to create an IMPT (intensity modulated proton therapy) technique

Quality Control / Assurance

- IAEA
  - Guidelines
- AAPM
- Task group reports
- COMP & CAPCA
  - Standards and Technical Quality Control (TQC) Guidelines
    - In late 1990's
    - Canadian Association of Provincial Cancer Agencies (CAPCA), along with COMP
    - Identified the need to develop a set of Technical Quality Control (TQC) standards

        - Details of quality control tests for specific radiotherapy equipment and software.
        - Based on expert opinion and best practices
- Institution
    - Local CC policies and procedures

CPQR

- 2010
- The Canadian Partnership for Quality Radiotherapy
- An alliance among the national professional organizations involved in the delivery of radiation treatment in Canada
    - Canadian Association of Radiation Oncology – CARO,
    - Canadian Organization of Medical Physicists – COMP,
    - Canadian Association of Medical Radiation Technologists – CAMRT,
    - Canadian Partnership Against Cancer – CPAC.
        - strategic and financial support
- Mandate of CPQR
    - to support the universal availability of high quality and safe radiotherapy for all Canadians
    - through system performance improvement and
    - the development of consensus-based guidelines
    - indicators to aid in radiation treatment program development and evaluation

Acceptance testing and commissioning

- Following the delivery and installation of any equipment or technique is an
    - Acceptance Testing
        - Vendor specific process and specifications.
        - To ensure that the unit meets vendor specifications;
        - To ensure the equipment meets specifications specified in the tender document;

    - To establish baseline parameters for the future quality control program; and
    - To familiarize the users with operation of the unit
  - Commissioning
    - For subsequent operating/performance calculations, for example, involving radiation dose;
    - To establish baseline parameters for future quality control program.

Phantom Systems and Water Tanks

- Anthropomorphic Phantoms
  - **Humanlike phantoms**
  - Full or Partial body
  - Anatomic specific
  - Slices or whole piece
  - Dosimetry capable
  - Optimized for setup or imaging
  - Infant, adult, male or female
- Chambers (Ion or diode)
  - Single chamber for 1D
  - Cylindrical or parallel plate – 2D Array of chambers
  - ArcCheck for VMAT
- Water Tanks
  - Used in obtaining comprehensive dosimetry data during commissioning.
  - PDD, TPR, Profiles etc.
  - Has translational motion in all three axis
  - Typically 48cmx48cmx48cm
  - Smaller version used for absolute dose calibration (TG51)
- Water and Tissue Equivalent
  - Suitable for both kV and MV
  - Many sizes and shapes,

  - Molded or machined
  - cavities to house dosimeters.
  - Water equivalent (WT1)
  - Tissue equivalent
    - Adipose (AP7)
    - Breast (BR12)
    - Hard Cortical Bone (SB5)
    - Inner Bone (IB7)
    - Rib or Average bone (RB2)
    - Lung (LN10)
    - Soft Tissue (ST1)
    - Kidney (KD1) & Liver (LV1)
- Imaging phantoms
  - CATPHAN
    - CT performance and image quality verification
  - AAPM CT performance Phantom
    - CT performance and image quality verification
  - RMI Phantom
    - Used for electron density calibration
  - ISOCUBE
    - Linac Image Guided RT (IGRT) QA
    - Linac isocentre verification
- 3D printing
  - Growing Interest in utilization of 3D printing in RT.
  - Patient accessories – Bolus
    - Much more conformal
    - Better fit to patient’s surface
    - Inexpensive

- QA Tools – Phantoms
    - Inexpensive
    - Easy to make
    - Control of some of the density with infill
    - Challenging to print much denser material composition
- Small parts or components.