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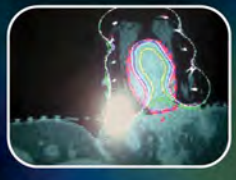
Practical RADIOTHERAPY & CHEMOTHERAPY Planning







Mirza Qaiser Baig

JAYPEE

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3 Principles of Radiation Therapy

Sir WC Roentgen was father of radiotherapy named after discovery of X-ray (Fig. 3.1). Physical considerations ionizing radiation is the energy that during absorption causes the ejection of an orbital electron. A large amount of energy is associated with ionization. Ionization radiation can be electromagnetic or particulate. Electromagnetic radiation may be considered as a wave and as a packet of energy (α photon). The packet of energy is large enough to cause ionizations, and these are distributed unevenly through tissues examples of particulate radiations are the subatomic particles: electrons, protons, alpha particles neutrons and atomic nuclei. All of these have been experimentally considered or are being used in radiation therapy.

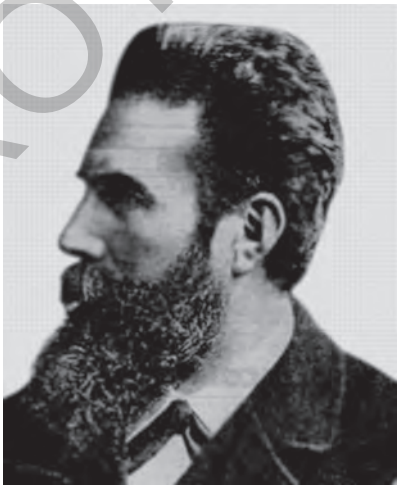

Fig. 3.1: Sir WC Roentgen—Father of radiotherapy

ELECTROMAGNETIC RADIATION

Electromagnetic radiation consists of roentgen and gamma radiation. They differ only in the way in which they are produced: gamma rays arc produced intranuclearly and roentgen rays are produced extranuclearly. In practice, this means that gamma rays used in radiation therapy are produced by decay of radioactive isotopes where as the Roentgen rays used in radiation therapy are produced by electrical machine, like linear accelerator (Fig. 3.2).

The intensity of electromagnetic radiation dissipates as the inverse square of the distance from the source. The dose of radiation 2 cm from a point source is 25% of the dose of 1 cm.

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Fig. 3.2: Linear accelerator

ABSORPTION MECHANISM OF ELECTROMAGNETIC RADIATION

The relative precalence of the three dominant absorption mechanisms of electromagnetic radiation depends on the energy of radiation.

Photoelectric Absorption

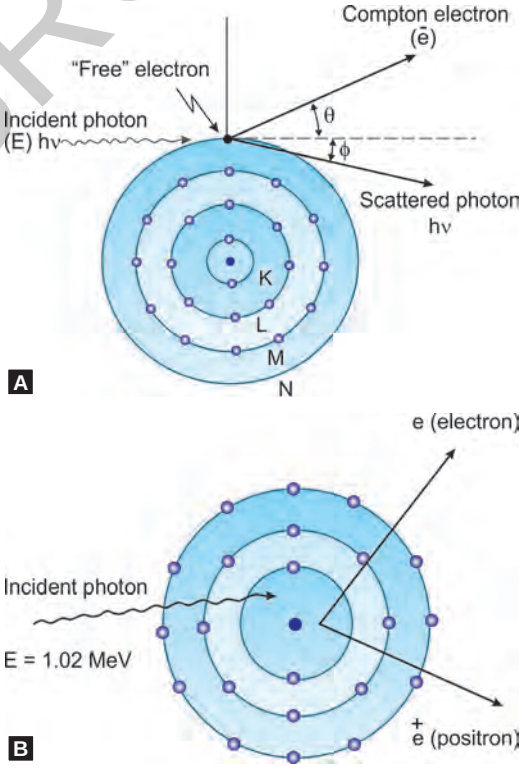
Photoelectric is a phenomenon in which a photon interacts with an atom and ejects from the orbital electrons from the atom. The vacancy left in the atomic shell is then filled by another electron falling from an outer shell of the same atom. Thus, leaving the atom in an excited state. Photoelectric absorption varies with the cube of the atomic number (Z3). This has significant practical implications because it explains why materials with high atomic numbers, such as lead are such effective shielding material.

Compton Effect

In this process, the photon interaction is with a distant orbital electron that has a low binding energy and the electron is termed as free. In this type of absorption, the photon does not give up all its energy to a single electron; an appreciable portion reappears as a secondary photon, which is created in the interaction. Since, the Compton effect involves essentially free electrons in the absorbing material, it is independent of atomic number Z, unlike photoelectric absorption (Fig. 3.3A).

Pair Production

This type of absorption requires incident photon energy greater than 1.02 MeV. In this process, the photon interacts strongly with the electromagnetic field of an atomic nucleus and gives up all its energy in the process of creating a pair consisting of a negative electron (e^-) and a positive electron (e^+). Since, the rest mass energy of the electron is equivalent to 0.51 MeV. A minimum energy of the 1.02 MeV is required in order to create the pair of electron (Fig. 3.3B).



Figs 3.3A and B: (A) Compton effect; (B) Pair production

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Fundamental Quantity

Necessary to describe the interaction of radiation with matter is the amount of energy absorbed per unit mass. This quantity is called absorbed dose, and the rad was the most commonly used unit. Absorbed dose is measured in joules per kilogram; another name for 1 joule/kg is the Gray (1 Gray = 100 rad), which is now the recommended unit the roentgen (R) is a unit of roentgen rays or gamma rays based on the ability of radiation to ionize air. At the energies used in radiation therapy, 1 R of roentgen rays or gamma rays results in a dose of somewhat less than 1 rad (0. 01 Gy) in soft tissue on the energy increase depth of penetration of radiation increases after entering into radiation causes DNA damage into cell nucleus which is the prime target for radiation induce cell killing (Fig. 3.4).

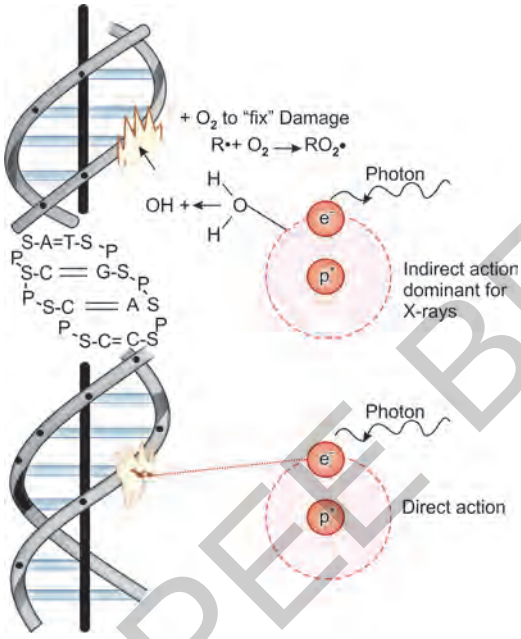

Fig. 3.4: Mechanism of radiation-induced cell killing

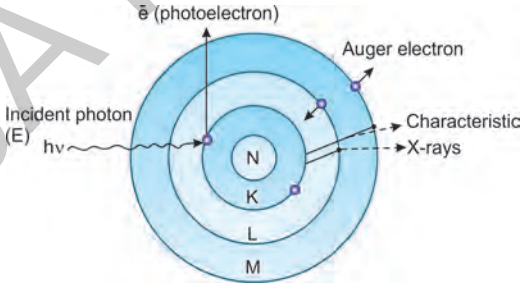

Fig. 3.5: Photoelectric effect

SPECTRUM OF ELECTROMAGNETIC RADIATIONS

The different ranges of electromagnetic radiations used in clinical practice are supervoltage radiation or roentgen from about 10–125 KeV; orthovoltage radiation or electromagnetic radiation between 125 and 400 KeV; and supervoltage or megavoltage radiation for energies above 400 KeV. As energy increases, the penetration of the roentgen rays increases, and at supervoltage energies, absorption in bone is not higher than that in surrounding soft tissues as is the case with lower energies. This is because at supervoltage energies, Compton absorption predominates.

MOVEMENT OF COBALT MACHINE

Compared with the orthovoltage, supervoltage radiation is skin sparing, meaning that the maximum dose is not reached in the skin, but instead occurs below the surface. The electrons created in the interaction travel some distance and do not attain full intensity until they reach some depth, resulting in a reduced dose to the skin (Fig. 3.8).

Radiation Techniques

Two general type of radiation techniques are used clinically, teletherapy and brachytherapy.

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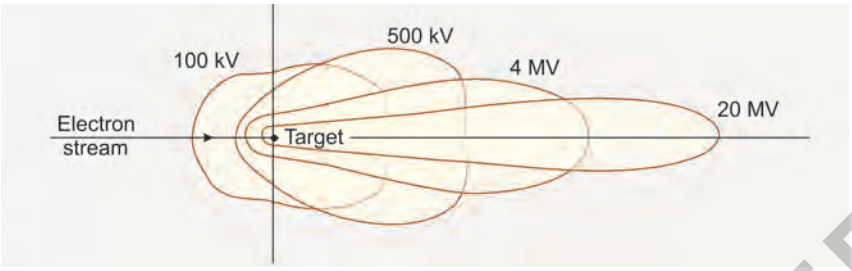

Fig. 3.6: Increase in energy will lead increase in-depth

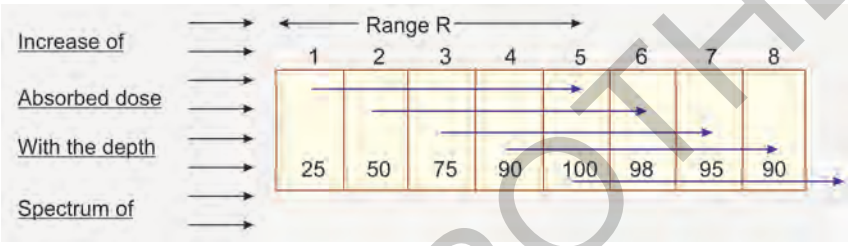

Fig. 3.7: Percentage of absorbed dose

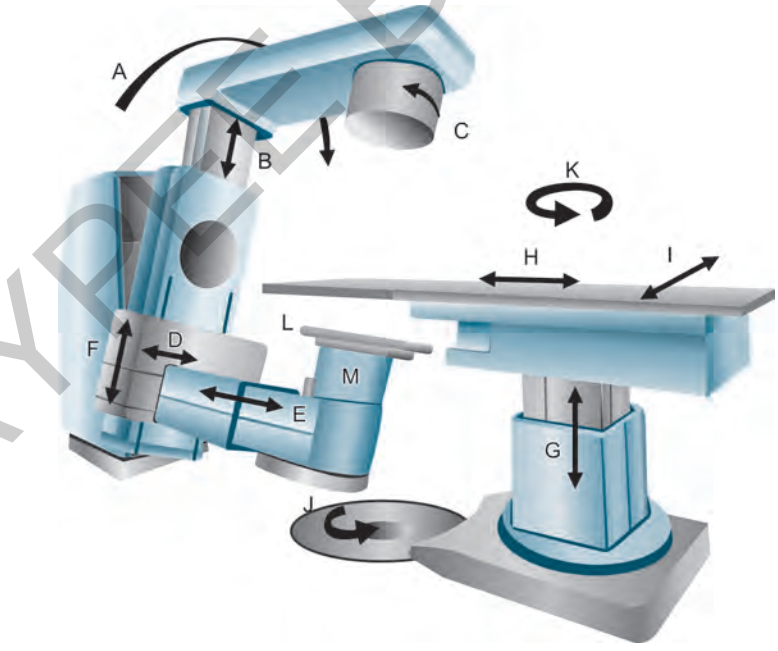

Fig. 3.8: Movement of cobalt machine

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Teletherapy

Mainly two type of teletherapy are in use for cancer treatment purpose cobalt machine and linear accelerator, cobalt machine is very common in India. It can move in various direction to treat cancer patients main part of cobalt machine is its head which accommodates its source.

Teletherapy uses a device located at a distance from the patient, as in the case in most orthovoltage or supervoltage machines, Gamma emitting radioactive isotopes may be used to produce a useful gamma ray beam for radiotherapy. It must be remembered that owing to the decay of activity, the source will need replacement from time to time. Anyone source is normally used for a period a little longer than one-half of the half-life of the isotope, i.e. when the activity has decayed to about two-thirds of the initial activity and the treatment times have increased by about one-half. Linear accelerator is another teletherapy unit which have both component X-ray and electron mode. X-ray mode useful for deep seated tumor and electron mode can be use for superficial tumor sliding scale compensator system are the equipment useful to assist radiotherapist in order to avoid unnecessary radiation reaction and proper dose delivery to tumor tissue.



Fig. 3.9: Curved caliper (45 cm)

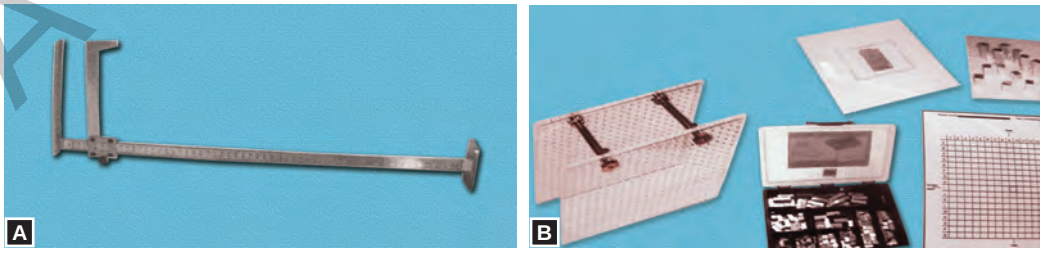
Early units using radium had the advantage of a long half-life (1620 years) and an effectively constant output dose rate. There were however three major disadvantages of radium.

Treatment head of linear accelerator X-ray mode and electron treatment mode:

1. Potential leakage of radon gas.
2. Low specific activity.
3. Very high photon energy making the protection on the source housing difficult These radium sources have been replaced with either Cesium-137 or Cobalt-60.

Cesium-137: It has a long half-life (30 years) and is an attractive alternative to radium. Unfortunately, it has a low specific activity (like radium) as well as a low gamma ray constant. The advantages of cesium over radium are that it requires less shielding and is less hazardous in microsphere form. The disadvantages of cesium, however, outweigh its advantages and it is now rarely found in teletherapy units. It is widely used as a radium substitute in brachytherapy.

Cobalt-60: The effective photon energy of cobalt-60 is only slightly lower than that of radium and its half-life is relatively short (5.26 years), but despite this, cobalt-60 is the most widely used isotope in gamma ray beam units. The main advantage of cobalt-60 is its high specific activity. Cobalt-60 is produced by neutron bombardment of cobalt-59 and decays to nickel-60 by emitting a beta particle and two gamma rays of 1.17 and 1.33 MeV.



Figs 3.10A and B: (A) Sliding scale; (B) Compensator system used during radiation

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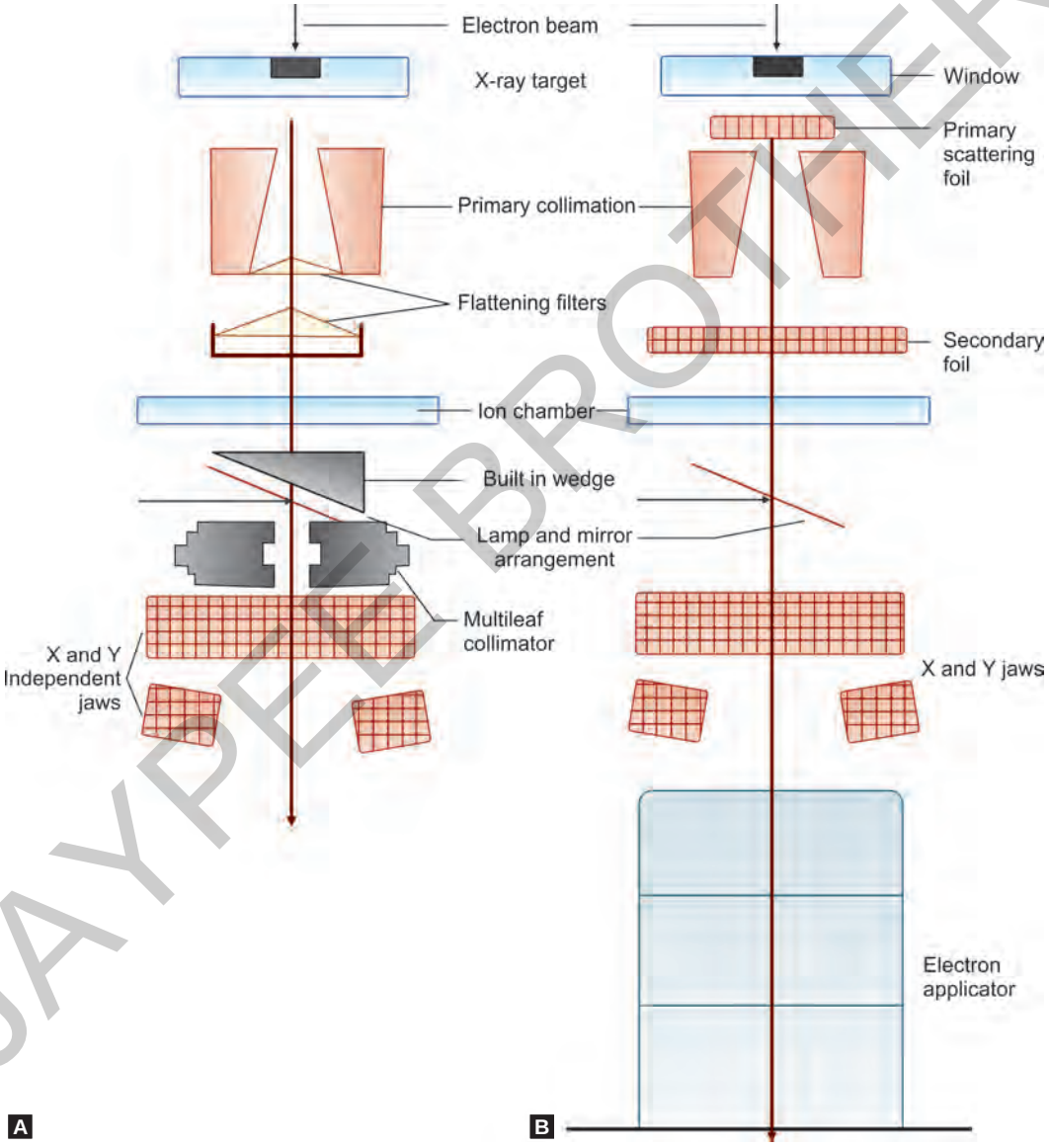
Concepts of Brachytherapy

- Bell in 1903 first suggested implanting the radioactive source directly into tumor.
- Forshell in 1931 coined term brachytherapy.
- Initially radium was used as brachytherapy source.
- Nowadays radium is not used because:
  - By product of radium is radio-toxic.
  - Radon gas emission is always a threat.
    - Contamination can cause great problem.
    - Low specific activity therefore requires large source size.



Figs 3.11A and B: Components of treatment head of a medical linear accelerator. (A) X-ray therapy mode; (B) Electron therapy mode

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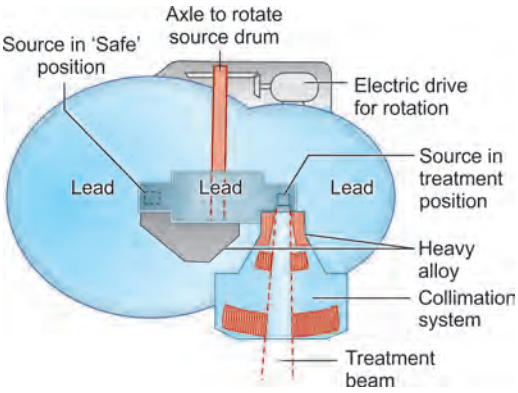

Fig. 3.12: Treatment head of cobalt-60

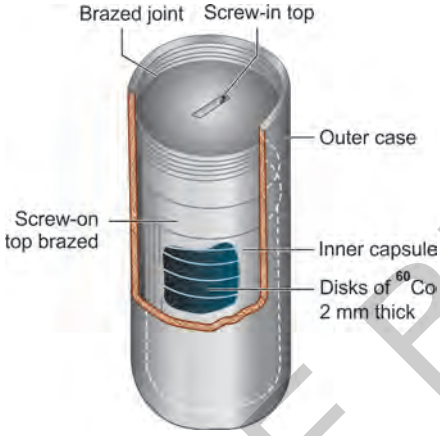

Fig. 3.13: Cobalt source



Fig. 3.14: Teletherapy unit cobalt-60

– High-cost
– Disposal problem.

Above problem with radium as a brachytherapy source leads to discovery of many other radioactive isotopes.



Fig. 3.15: Syed/Neblett prostate template

IDEAL BRACHYTHERAPY SOURCE

Should be γ emitter with energy 200 KeV preferably monoenergetic.

Large should have half-life for temporary implant and short half-life for permanent implant.

- No gaseous by product
- High specific activity
- Insoluble and chemically non-toxic
- Should be molded in various size and shape
- Low-cost.

Brachytherapy source is available in various physical forms such as needle, tube pellets, seeds wire which facilitates their application in the patient.

Forms of Applications

- Intracavitary
- Interstitial brachytherapy templet system use in (Figs 3.15 and 3.16).
- Intraluminal
- Surface molds.

Sources (Table 3.1)

- Co-60 → Source available needle, tube, pellets for high dose rate (HDR) after-loading.
- Cs-37 → Needle, tube, beads for after-loading.

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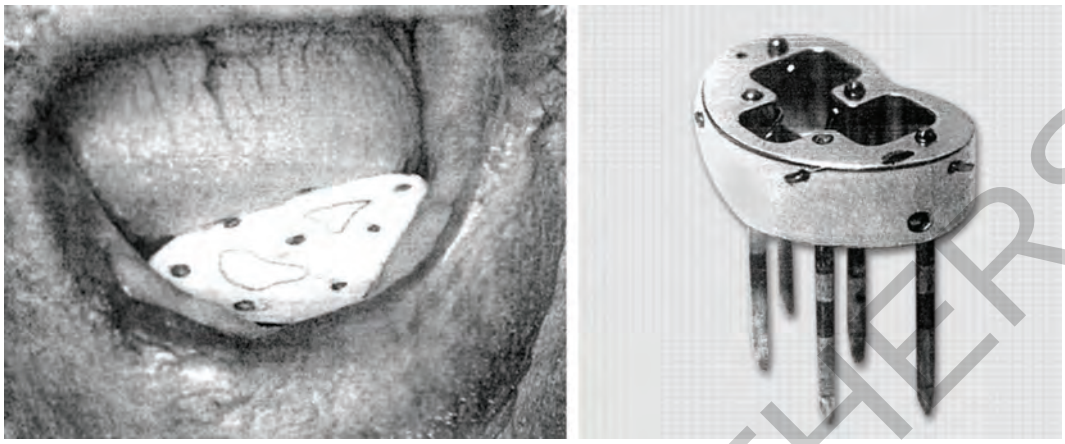

Fig. 3.16: Cardboard templates

Table 3.1: Half-lives and radiation energy released by various radioisotopes

Isotope	*Half-life*	*Av. Photon energy (meV)*	*Exp. Rate constant (R cm²/ mCi-r)*
Ra-226	*1622 years*	*0.832*	*8.25*
Co-60	*5.26 years*	*1.25 (Av)*	*13.07*
Cs-137	*30 years*	*0.662*	*3.226*
Ir-192	*74.2 days*	*0.38 (Av)*	*4.62*
Au-198	*2.7 days*	*0.412*	*2.327*
I-125	*60 days*	*0.028 (Av)*	*1.208*
Pd-105	*17 days*	*0.21 (Av)*	
Samarium-145	*340 days*	*0.41 (Av)*	

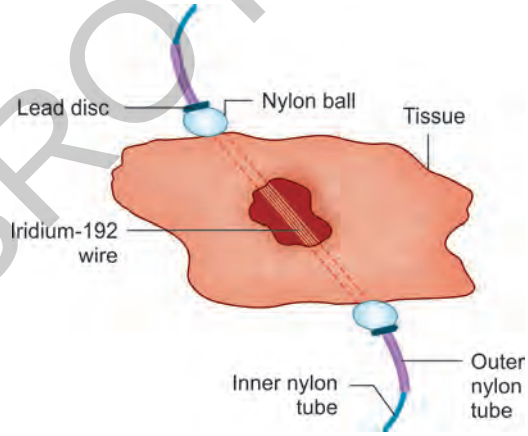

Fig. 3.17: Source train—manual after-loading

- Ir-192 → As wire, pins for manual after-loading.
  As pellets for remote after-loading
- I-125 → Seeds for permanent implant for surface applicator
- Cs-137 → Largely replaced radium as nuclide of choice.

Alkaline material, compound of cesium chloride/sulfate is chemically stable.

Recommended working half-life is 10 years.

All sources have recommended working life beyond which manufacture will not guarantee the integrity of sources.

Cesium (Cs) is available in needle form or tube or small pellet for remote after-loading machine.

- Iridium
- Currently widely use
- High specific activity
- Flexibility—acquire the shape of tumor.
- Available in 0.8 mm diameter, 4.5 mm length
- Au-198/I-125 can be used for permanent implantation short half-life.
- Surface or mold application.
- Now replaced by electron treatment of linac.

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- Co-60—High specific activity is constant
- Make it attractive use for HDR.
- Au-198, available in grains/seeds/wires.
- With the help of implantation guns directly fit in tumor area.
- Use as permanent implantation purpose also in malignant plural effusion and malignant ascites.
- I-125 available in seeds form
- As permanent implant or plaque.

Directly applied in tumor area as in case of treatment of single solitary retinoblastoma.

PRACTICAL ASPECTS IN BRACHYTHERAPY

Activity of a source is the apparent activity because real activity of source is attenuated because of source encapsulation thus true activity is always greater than this activity.

Exposure rate constant (γ-rays constant of source) is defined as dose rate cGY/hr at a distance of 1 cm from millicurie activity of point source; this is however redefined because of source encapsulation (attenuation effect).

Point Source

From a single point source, a γ-ray is emitted isotropically. It follows inverse square law therefore intensity of radiation will decrease with square of the distance from the source.

The dose rate will be proportional to activity of source as well as inverse square of the distance from source.

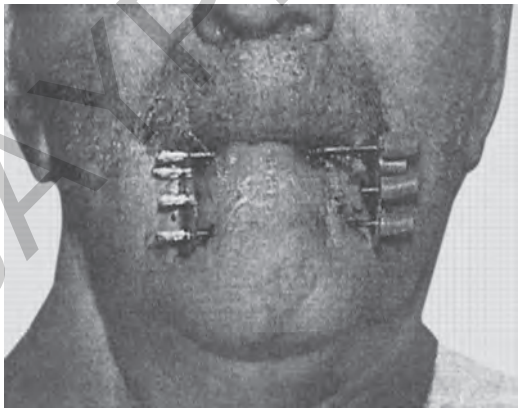

Fig. 3.18: Interstitial brachytherapy in lip cancer

Multiple Sources

Five equally spaced line of the source.

Each emits γ-ray in all direction producing complex pattern of isodose distribution.

It has been seen that point close to source in the same horizontal axis will receive high dose and point between the two sources will receive low dose.

Uniformity of the dose further improved by increasing the activity of source at the end of the line.

Methods of Application of Brachytherapy

- Pre-loading method
- Manual after-loading
- Remote after-loading.

Pre-loading: Sources are loaded in applicator before they are inserted into patient. Because of radiation exposure to medical and para-medical staff leads invention of after-loading method.

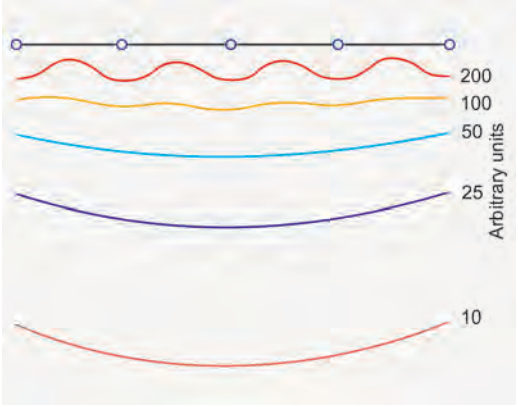

Fig. 3.19: Inference drawn from above figure is that of dose achieved depends on both distance from source and spacing between the sources

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Fig. 3.20: Selectron low-dose rate (LDR)

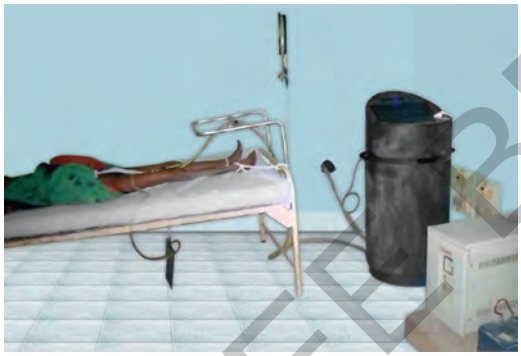

Fig. 3.21: Low-dose rate brachytherapy



Fig. 3.22: Cancer cervix patient during brachytherapy

Manual after-loading: First applicator are in patient then sources are manually inserted into applicators. Remote after-loading—each

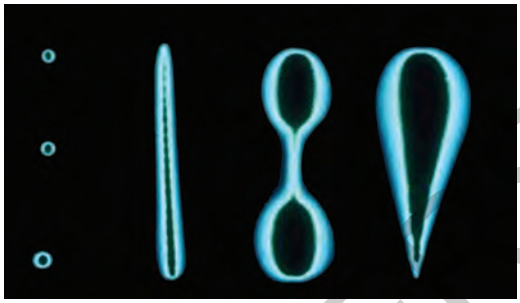

Fig. 3.23: Optimization of dose distribution adjusting the dwell times of the source

applicator is fixed in the patient and check X-ray carried out to localize dummy source in applicator, many remote after-loading machine life selectron (HDR) now available for the purpose of remote after-loading treatment.

Source Movement

- Combination of various source trains with option to choose.
- Small miniature source with spacer enabling the operator to create his own source configuration.
- By single source with option of different (dwell times) → (How much dose to be delivered at different site) at various position simulating either as many point
- Optimization of dose distribution—adjusting the dwell times of the source

INTERSTITIAL IMPLANT

It is important to clearly define target volume and to have preplanned number and distribution of radioactive sources to be used.

Homogeneous dose distribution is very important because high dose around each source cab cause neurosis low dose between the sources could result in recurrence.

Rules of Interstitial Implant

- Active source should be parallel and straight.

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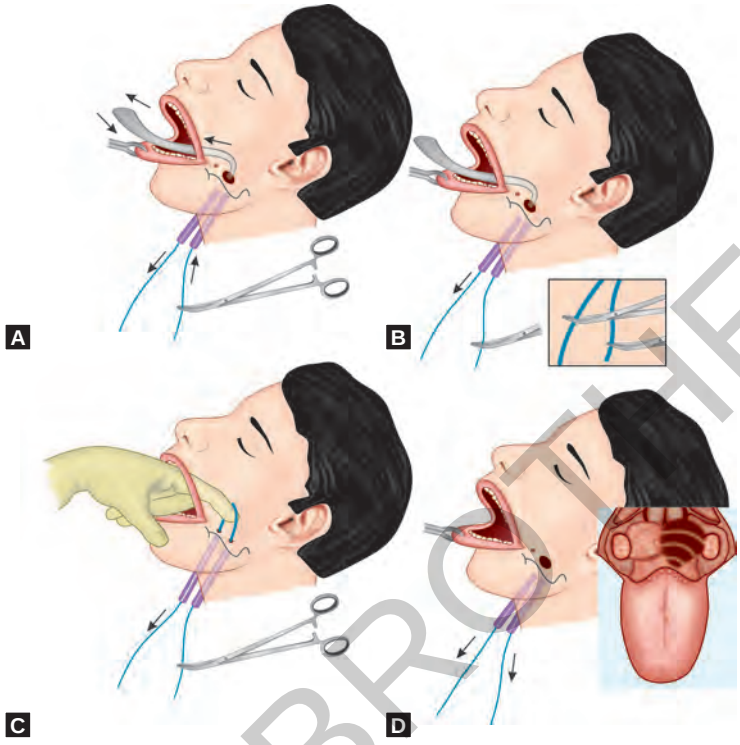

Figs 3.24A to D: Loop techniques of implant

- Line should be equidistant.
- Line or plane on which the midpoint of the source lies should be at right angle to axis of the source.
- Linear activity of the source should be uniform along the length of each line.
- Separation between sources may vary from one implant to other implant. But minimum 8 mm separation is acceptable for smallest volume rising to 20 mm largest.
- Average length of active wire should be larger than target volume by 25–30%.

Paris System of Dose Calculation

It is based on the distribution of sources in the central plane—that is, the plane which is at right angles to the axis of the mid-point of the sources.

The basal dose rate represents the dose in the center of the implanted volume, and is defined as the dose rate at a point in the middle of a pair or group of sources where the dose rate is lowest.

In the case of a large implant, there may be several pairs of groups of sources arranged in triangle or squares. For these, a mean basal dose rate is taken for the implant as a whole.

The basal dose rate, a point is the summation of dose contributions from each source obtained from graphs of dose rate variations with distance from the source. Once the basal dose rate in the center of the implant has been defined, the reference dose rate is taken as 85% of the basal dose rate (BDR). This serves to calculate the duration of the implant, and the 85% is dose defines the treated volume.

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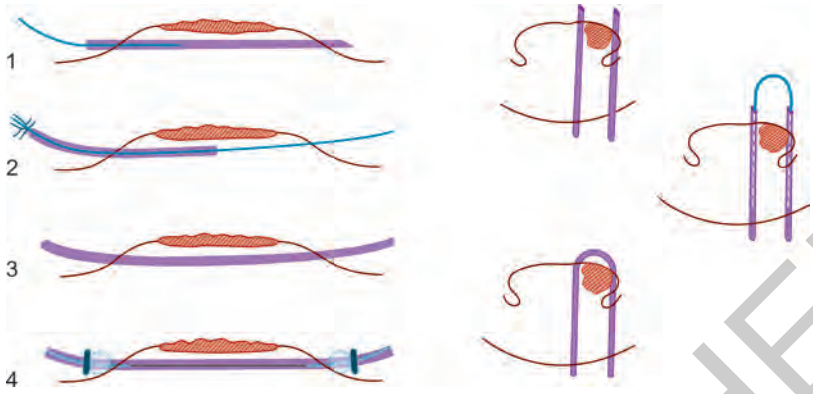


Fig. 3.25: Methods of implant

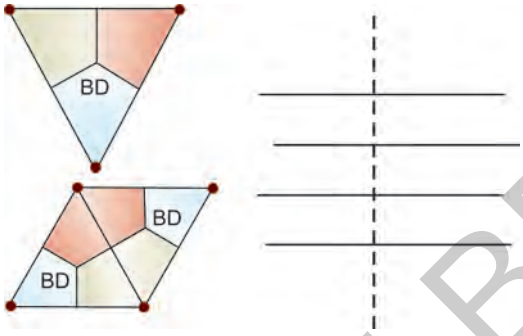
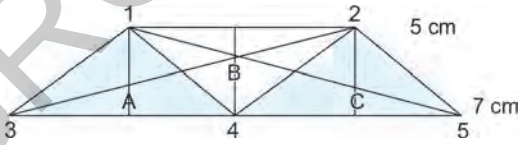


Fig. 3.26: Basal dose rate

Two-plane implant to deliver 2.5 Gy
Superficial plane = 5 cm wires × 2
Deep plane = 7 cm wires × 3
Separation between sources = 18 mm
Activity of wire (midway through treatment)
= air kerma rate 0.5 μGy/h/mm at 1 m (0.1193 mG/mm)



Wire	*A*		*B*		*C*	
	Distance (mm)	*Dose rate (Gy/h)*	*Distance (mm)*	*Dose rate (Gy/h)*	*Distance (mm)*	*Dose rate (Gy/h)*
1	10.4	0.1245	10.4	0.1245	20.8	0.0465
2	20.8	0.0465	10.4	0.1245	10.4	0.1245
3	10.4	0.1340	20.8	0.0555	27.5	0.0365
4	10.4	0.1340	10.4	0.1340	10.4	0.1340
5	27.5	0.0365	20.8	0.0555	10.4	0.1340
Total		0.4755		0.4940		0.4755

Mean basal dose rate = $\frac{0.4755 + 0.4940 + 0.4755 \text{ Gy/h}}{3}$
= 0.4817 Gy/h
Reference (85%) dose rate = 0.4817 × 0.85
= 0.4095 Gy/h

Treatment time = $\frac{25.00}{0.4095}$
= 61.05 h
= 2 days 13 h

Fig. 3.27: Calculation of dose

A value of 85% has been chosen to provide an is dose contour that reasonably covers the target volume with an acceptable variation between the dose at the center and that at the periphery of the target volume. The time for which at implant must be left in place is derived by dividing the prescribed dose by the reference dose rate.

Rationale of Low-dose Rate Brachytherapy

It has been known for many decades that lowering the dose rate generally reduces radiobiologic damage. The explanation of this effect, relating to sublethal damage repair, also has been long understood.

Increasing the dose rate will increase late effects much more than it will increase tumor

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