Conventional Radiation Therapy: Historical Development

	Year	Process/Events	Specification	Comment	
X-Ray Radiotherapy	1895	Discovery of X-ray by Roentgen. Gas filled x-ray tubes	50 kV	Since the discovery of X-ray it was realized that it can be used for both diagnostic and therapeutic purposes.	Superseded
	1913	Present day x-ray techniques using vacuum tube with a hot tungsten cathode by W. D. Coolidge	Peak voltage of 140 kV with 5 mA current	X-rays generated by these tubes were fairly soft and hence disadvantageous, since, maximum dose would be delivered at the skin and rapidly fall off with depth in tissue. *So there was a continuous search for more penetrating radiation right from the beginning of radiation therapy. The early attention was focused on gamma emitting radionuclides.*	Superseded
	1937	X-ray tubes	400 kV, 5 mA 200 kV, 30 mA		
Gamma Ray Radiotherapy	1910	Radium needle	Radium-226 0.24 – 2.2 MeV gamma rays	The first device using harder radiation was radium cannon developed by Koenig for the treatment of pelvic cancer.	
	1951	Cobalt sources	Co-60 1.17-1.33 MeV gamma rays	Better depth-dose curve, maximum dose at about 5 mm below the skin surgace, thus markedly decreasing the skin dose. *Very soon it was accepted that future developments in radiotherapy would involve megavoltage therapy.*	
X-Ray Radiotherapy Electron Radio therapy	Early 1930's	Van de Graff Accelerator	Several MV accelerator	1937: The first machine (1 MeV air insulated), used in radiotherapy, was installed in Boston. 1940: The second one (1.25 MeV pressure insulated) was installed at the Massachusetts General Hospital also in Boston. 1946: High Voltage Engineering Corporation, founded by R. Van de Graff, began commercial production of 2-2.5 MeV machines. Total 40 such accelerators were built, until their production was discontinued in 1959.	Superseded

	1943	Betatron by D.W. Kerst	20-25 MeV	Dramatic increase in photon radiation energy 1949: The first patient was irradiated with x-rays generated by 20 MeV electrons from Kerst betatron in Urbana, USA. Several companies , like Allis-Chalmers in USA, Brown-Boveri , Siemens in Europe, started commercial production of 20-25 MeV betatrons for radiotherapy. *In the early 1970's about 200 betatrons were in medical use the worlds over. Betatrons produced x-rays with better properties, such as, higher depth dose and less side scatter.*	Superseded
	1953	Liner Accelerator	4-25 MeV	In mid 1960's, the rf linear accelerators rapidly took up the dominant position in the world market of medical accelerators. Due to its high dose rate (200-500 rad/min), large field (40 x 40) cm^2 and provision to rotate 360° around the patient, rf linear accelerator replaced the betatron from the medical market.	Still used

Main Parameters for Conventional Radiotherapy Beams:

Today, for modern radiotherapy 3-25 MeV electron linear accelerators are used. They are generally standing wave type, where electron acceleration energy is supplied by microwaves generated by a klystron (GHz). These accelerators are capable of producing:

- Beams of practically mono-energetic electrons, with energies varying between 3-4 MeV and 20-25 MeV and of cross section in the range of a few square cm and a few tens of square cm at the treatment distance of about 1 m.
- Photon beams, obtained by slowing down the electron beam in a heavy target (bremsstrahlung). These beams are characterized by a continuous energy spectrum and cross section similar to electron beams.

For electron, maximum range (in cm) is about half the initial energy of the beam (in MeV), so useful for superficial tumors.

Photon beams are characterized by the absorption of exponential type, after a maximum at about 3.5 cm depth for beams of 25 MeV energy. Due to this *build-up effect* the skin dose is relatively low. So, the high energy photon beam is suitable for deep seated tumors. Efficient technique of multiple beam entry point converging to the target is used to maximize the dose in the target and minimize dose in surrounding normal tissues. For this whole accelerating structure needs to rotate around the patient.

Reasons for the development of non-conventional Radiotherapy:

Some tumors, called radioresistant tumors, respond poorly to the photons. Sometimes even non-radioresistant tumors, located near critical body parts, can not be given a tumorocidal dose because of unavoidable dose to the surrounding normal tissues.

Hadronic radiotherapy (using neutrons, protons, pions, helium or heavier ions like carbon, argon etc.) developed to treat radioresistant tumors and tumors near critical body parts, like spinal cord etc. Initially, hadronic radiotherapy was researched using accelerators developed for basic physics experiments. At present there are about 34 dedicated facilities in operation and 22 facilities under construction. Hadronic radiotherapy specially concerns the patients with tumors in the brain and base of the skull region, sarcoma and prostate carcinoma.

Three approaches appear very promising for further increase in selectivity of hadronic radiotherapy:

1. Proton therapy
2. Light ion radiotherapy (carbon)
3. Boron Neutron Capture Therapy (BNCT)

Proton beam has a finite range dependent on energy of the beam. By appropriate selection of distribution of energies, a depth dose curve can be flat at ~100% over the depth of interest and then falls of rapidly at the end to virtually zero over a distance ~0.6mm. Similarly lateral fall of dose is also quite steep. So the tumor can be irradiated more precisely than the conventional radiotherapy techniques.

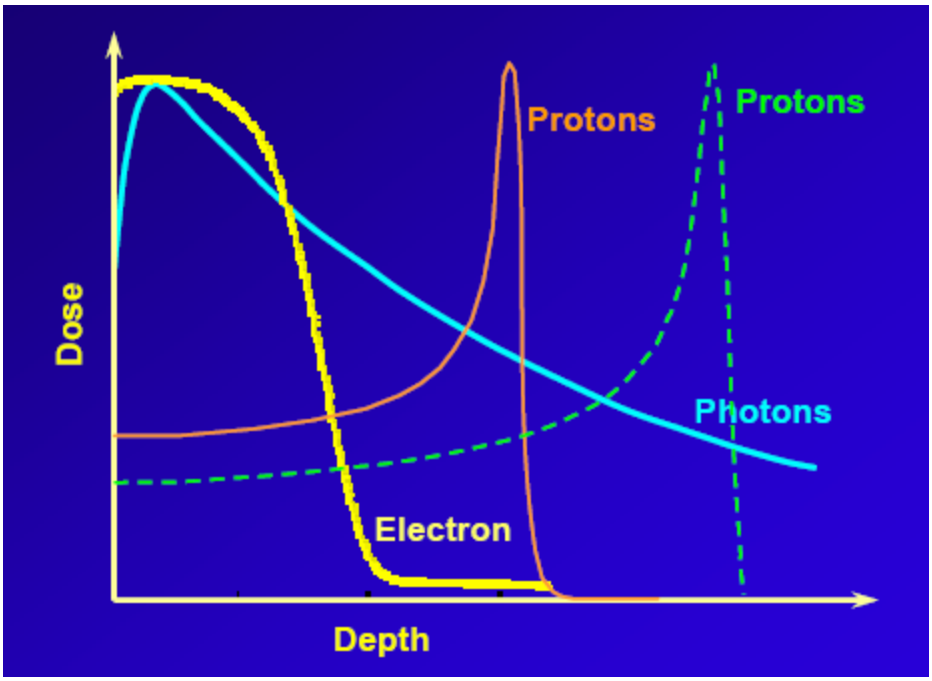

Fig: Depth dose curve (in arbitrary units) of photon, electron and proton beam.

Advantage of proton beam in cancer treatment

Proton therapy and radiation (x-ray therapy) both kill cancerous cells. In radiation therapy though, the radiologist is unable to adequately conform the irradiation pattern to the cancer causing nearby healthy tissue to receive a similar dose and be damaged. Consequently, a less-than-desired dose is frequently used to reduce damage to healthy tissues and avoid unwanted side effects.

In proton therapy, a higher dose of radiation can be directed at the cancerous cells, thereby sparing the surrounding tissue and causing the undesirable side effects.

All the radiation therapy works in following manner:

All tissues are made up of molecules with atoms as their building blocks. In the center of every atom is the nucleus. Orbiting the nucleus of the atom are negatively charged electrons.

When energized charged particles, such as protons or other forms of radiation, pass near orbiting electrons, the positive charge of the protons attracts the negatively charged electrons, pulling them out of their orbits. This is called ionization; it changes the characteristics of the atom and consequentially the character of the molecule within which the atom resides. This crucial change is the basis for the beneficial aspects of all forms of radiation therapy. Because of ionization, the radiation damages molecules within the cells, especially the DNA or genetic material. Damaging the DNA destroys specific cell functions, particularly the ability to divide or proliferate. Enzymes develop with the cells and attempt to rebuild the injured areas of the DNA; however, if damage from the radiation is too extensive, the enzymes fail to adequately repair the injury. While both normal and cancerous cells go through this repair process, a cancer cell's ability to repair molecular injury is frequently inferior. As a result, cancer cells sustain more permanent damage and subsequent cell death than occurs in the normal cell population. This permits selective destruction of bad cells growing among good cells.

Under certain circumstances, however, the cell is capable of repairing this damage. The challenge of radiation therapy is to administer the dose in such a way that tumour cells have no chance of repairing themselves, and, without exception, die off. Healthy cells, on the other hand, should suffer no major damage and be able to recover.

Protons are positively charged particles – the nucleus of the hydrogen atom. Free protons are produced by ionisation of hydrogen atoms (the electrons are displaced from the atom-shell). The free protons are then accelerated to high speed. This is done in proton cyclotrons or synchrotrons by strong electrical fields (in so called cavities). In radiotherapy they enter the human body at a pre-selected energy level and continue in a straight line up to a precisely calculated depth. While moving, they release very little energy. Toward the end of their trajectory they slow down, coming to rest at the Bragg peak (called after the physicist of that name), where they release most of their energy. Behind the Bragg peak the dose reduces to nil after a few millimetres. This physical profile is the reason for using protons in radiotherapy. It permits deep-seated tumours to be treated without overshooting the mark.

The Proton pencil beam

As protons are elementary particles which carry a positive charge they can be deflected and focused in magnetic fields, and the beam can be shaped as desired, preferably as thin as a pencil. In contrast to photons, which are generally used today for radiation therapy, protons have a quite specific and precisely limited depth of penetration into the body.

The Bragg peak

Photons deliver the largest dose immediately after penetration into the body. Thus the healthy tissue is unnecessarily strongly irradiated. The range of the protons depends on their initial speed and on the material in which they are absorbed. Between the surface of the body and the point where they stop, the material absorbs only a relatively low dosage, causing the velocity of the protons to fall continuously. At the end of their range they stop moving and release their maximum energy dosage. This generates a dosage peak, the Bragg peak. Beyond this point the dosage drops to zero within a few millimeters.

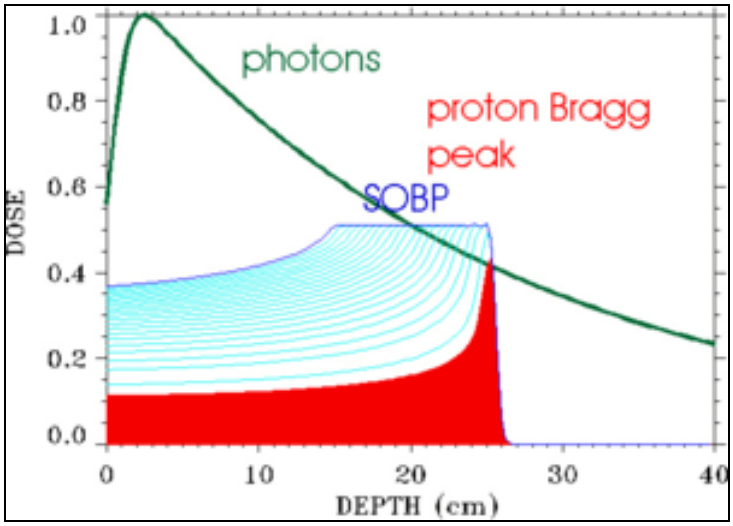

Figure: Figure shows the dosage curve for a monoenergetic thin pencil beam of protons. This is compared with a depth dose curve of a photon beam (the modality used today in hospitals for radiation therapy), with characteristic exponential decrease of the dose with depth.

Through the weighted superposition of proton beams of different energies (Bragg peaks with different proton ranges) it is possible to deposit a homogenous dose in the target region using only a single proton beam direction. The resulting (range-modulated) proton beam distribution is called Spread Out Bragg Peak (SOBP). The picture shows that the protons deposit a substantially smaller dosage than photons. Behind the target volume, the tissue is still essentially irradiated, with protons it's absolutely not.

The radiation dose is a measure of the energy absorbed in a material, such as body tissue. The biological effect of radiation however, depends not only on how much energy is deposited in the cells, but also how it is deposited. In each case, it is the energy dose which is measured in Gray (Gy). A typical therapy dose for the destruction of a tumour amounts to

approximately 60 to 70 Gy. It is transferred in individual fractions in several successive days (approx. 30 fractions in total)

In order to further improve treatment PSI has developed the spot-scanning technique which works in complement to the physical advantages of protons.

With the new treatment technique at PSI a pencil beam (7mm diameter) of protons is regulated by computer controlled magnets in such a way that the high-dose spot can be positioned very precisely, for an exactly specified period of time and at any desired location within a tumor. By superimposing many individual spots – more than 9000 within a volume of one litre – we can impose the desired radiation dose uniformly within a tumour, with the dose being individually monitored for each single spot. This enables extremely precise and homogeneous irradiation, ideally adapted to the shape of the tumour, which is in most cases irregular.

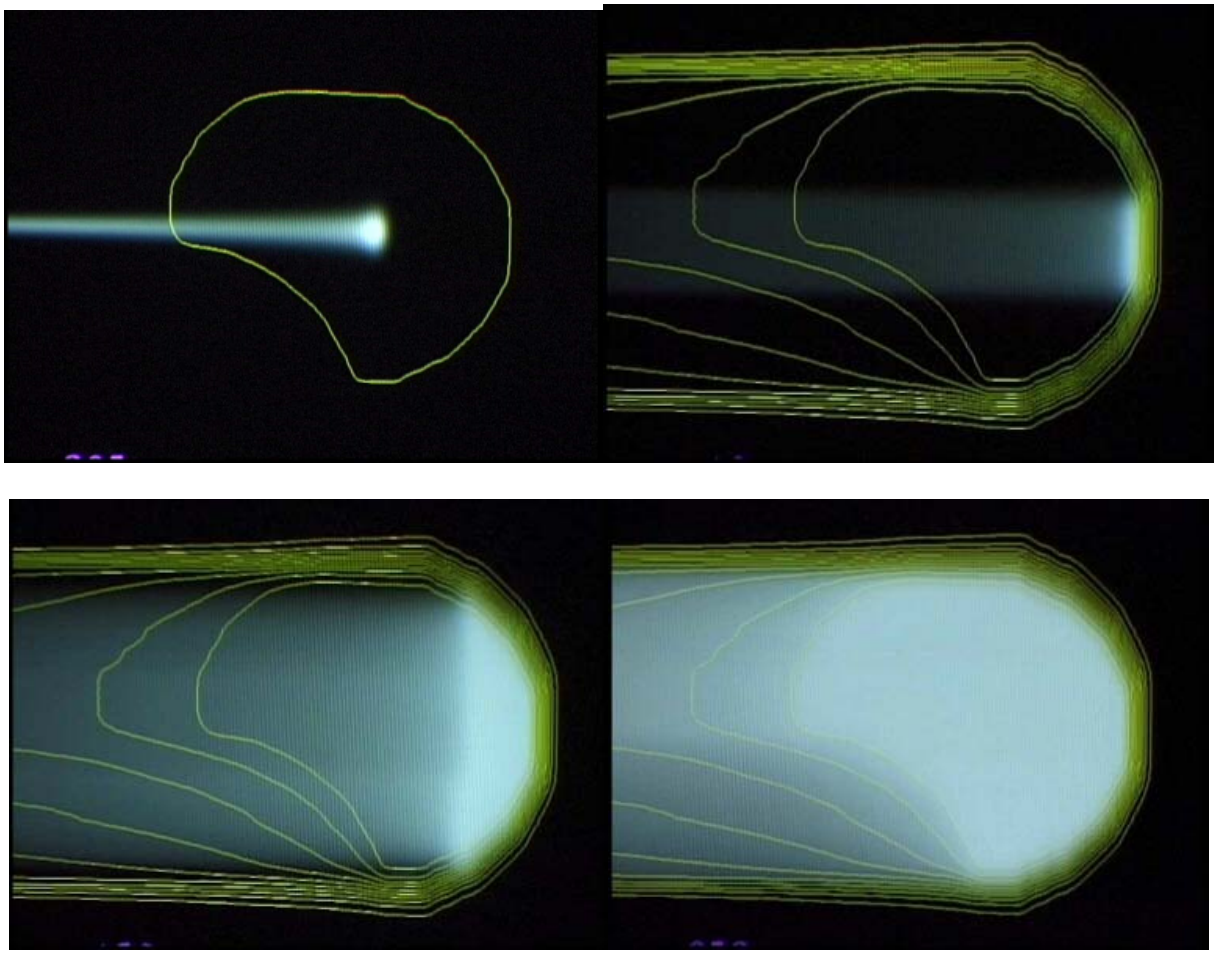

Figure 4: Spot-Scanning Technique for extremely precise and homogeneous irradiation.

Accelerators for Proton Therapy

The medical use of proton requires high energy accelerator suitable in hospital environment. Pioneering institution had to work with complex accelerators designed for research in nuclear physics. But the scenario is changing and a number of proton therapy systems, specifically designed for hospital environment are either under installation or operational. The most essential requirement for a medical facility is high reliability and availability of the complete system and especially the application of superconducting coils in a cyclotron design offer advantages which help to enhance the total reliability and availability of the accelerator.

	Cyclotron	Synchrotron	Linear Accelerator
Possibility of intensity control	Very good	Good	Good
Injection energy (MeV)	0.01-0.1	1-5 Pre accelerator is needed	Pre accelerator is needed
Quality factor (>25%)	Very good	Very good	Average
Power (kW)	35	150	350
Duty factor (% beam on time)	100% or CW	20% at 0.5Hz	0.1% at 300 Hz
Dimension (square meter)	Small (25) ~6 m diameter	Medium (50) ~10 m Diameter	Large (150) ~150 m length
Control possibility	Good	Average	Poor
Safety	Good	Good	Poor
Cost	Average	Average	large

Reference:

1. Wioletta Wieszczycka and Waldemar H. Scharf, Warsaw University of Technology, Poland, “Proton Therapy Accelerators”, World Scientific.