The Role of Radiation Therapy

An Introduction to RT

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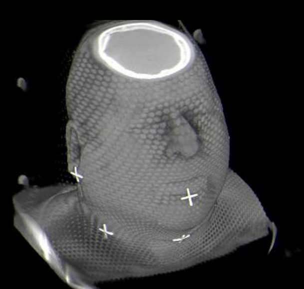
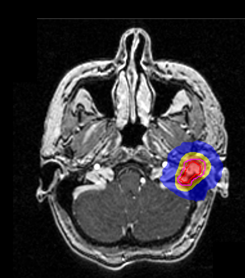
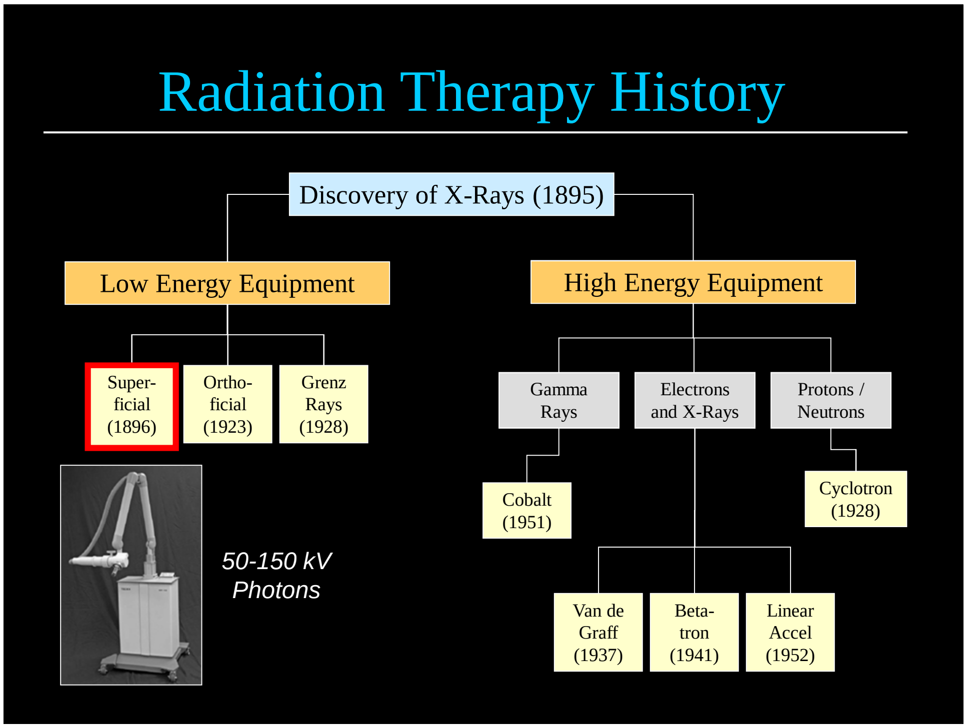
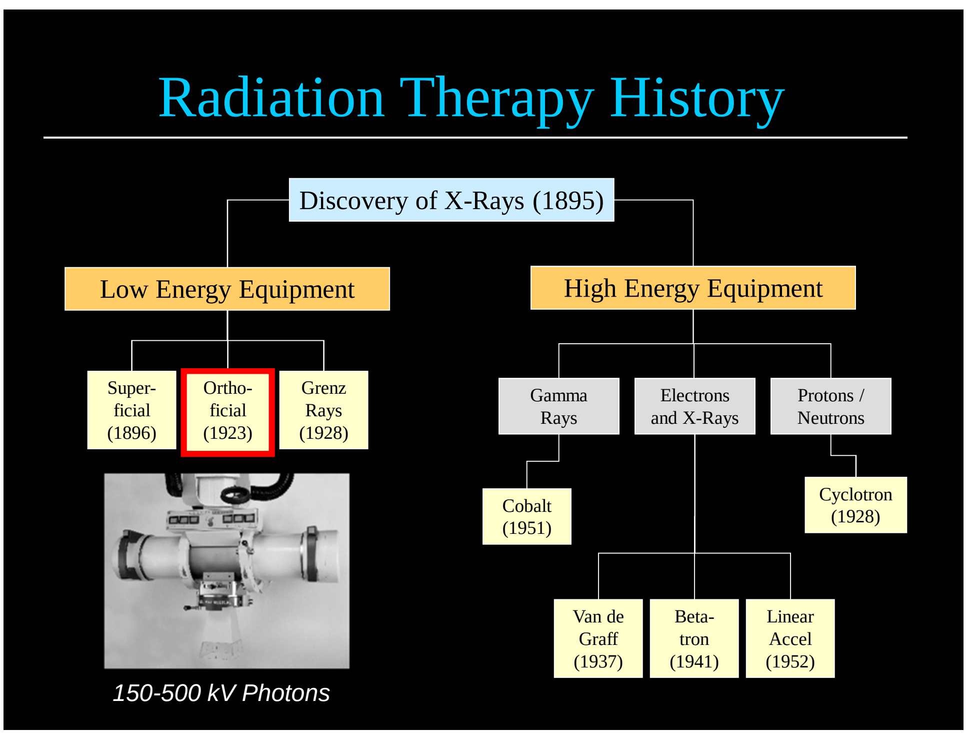
External-Beam Radiation Therapy





Imaging	Planning	Delivery
▪ CT	▪ Pencil Beam	▪ Photons (6-20 MV)
▪ MRI	▪ Convolution	▪ Electrons (4-24 MeV)
▪ PET/CT	▪ Monte Carlo	▪ Protons (50-300 MeV)


Radiation Therapy History
Discovery of X-Rays (1895)
Low Energy Equipment
High Energy Equipment
Super- ficial (1896)
Ortho- ficial (1923)
Grenz Rays (1928)
Gamma Rays
Electrons and X-Rays
Protons / Neutrons
Cobalt (1951)
Cyclotron (1928)
Van de Graff (1937)
Beta- tron (1941)
Linear Accel (1952)
50-150 kV Photons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Van de Graff (1937)
Beta- tron (1941)
Linear Accel (1952)
150-500 kV Photons

Radiation Therapy History

Discovery of X-Rays (1895)

- Low Energy Equipment
  - Super-ficial (1896)
  - Ortho-ficial (1923)
  - Grenz Rays (1928)
- High Energy Equipment
  - Gamma Rays
    - Cobalt (1951)
  - Electrons and X-Rays
    - Van de Graff (1937)
    - Beta-tron (1941)
    - Linear Accel (1952)
  - Protons / Neutrons
    - Cyclotron (1928)

10-15 kV Photons

Radiation Therapy History

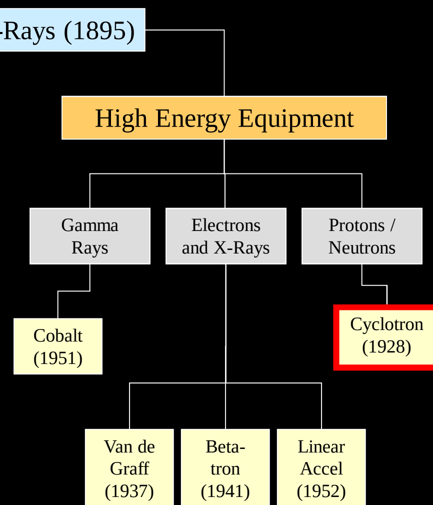
Discovery of X-Rays (1895)

- High Energy Equipment
  - Gamma Rays
    - Cobalt (1951)
  - Electrons and X-Rays
    - Van de Graff (1937)
    - Beta-tron (1941)
    - Linear Accel (1952)
  - Protons / Neutrons
    - Cyclotron (1928)

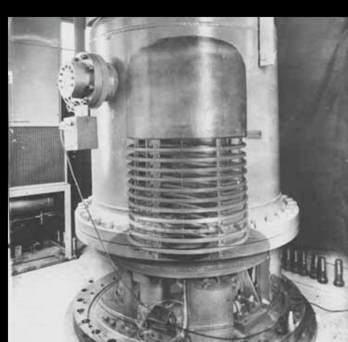
1.17 and 1.33 MeV Photons

Radiation Therapy History

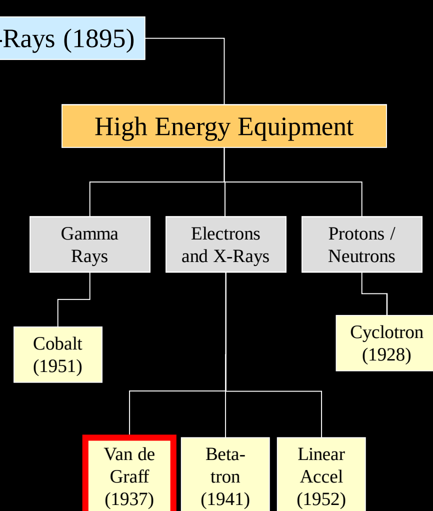
12 MeV Protons



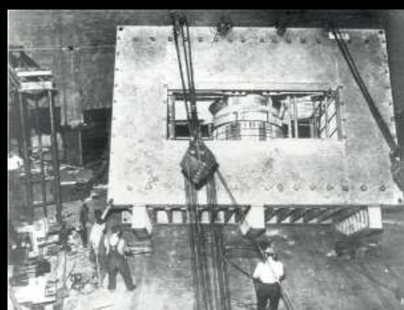
Radiation Therapy History



3 MeV Electrons



Radiation Therapy History



2 MeV Electrons

Discovery of X-Rays (1895)

High Energy Equipment

Gamma Rays

Electrons and X-Rays

Protons / Neutrons

Cobalt (1951)

Cyclotron (1928)

Van de Graff (1937)

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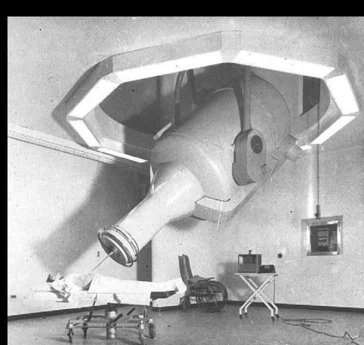
Linear Accel (1952)

Radiation Therapy History



4 MeV Photons

Discovery of X-Rays (1895)

High Energy Equipment

Gamma Rays

Electrons and X-Rays

Protons / Neutrons

Cobalt (1951)

Cyclotron (1928)

Van de Graff (1937)

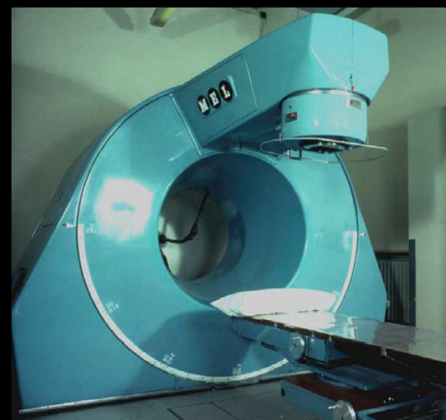
Beta-tron (1941)

Linear Accel (1952)

Early Linear Accelerators

In the 1960's the accelerating structures were positioned horizontally in the gantry

- The beam was deflected magnetically before striking the target
- In addition, the vacuum pump was positioned within the moving structure
- The MEL machine achieved the objective of full isocentric rotation with the center of rotation at a manageable height *(120–130 cm)* above the floor



4 MeV Photons

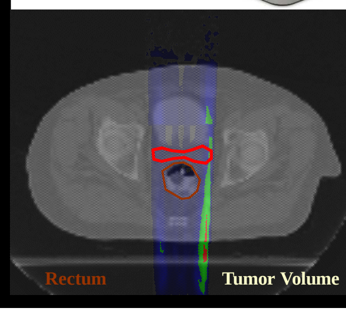
Modern Linear Accelerators

Today, linear accelerators are capable of electrons and photons

- Energy Range: 6 to 23 MV
- Automatic beam shaping
- Beam modulation
- On-board CT imaging
- On-board fluoroscopy
- Exit dosimetry measurements

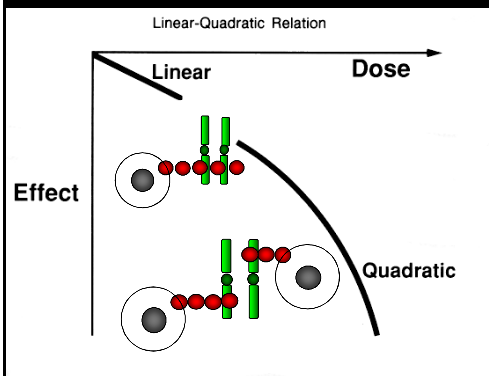
External-Beam Radiation Therapy

- External beam radiation therapy uses linear accelerators to treat cancer with x-rays or electrons
- Approximately 60% of all cancer patients will be treated with radiation therapy
- The radiation beams are precisely targeted from multiple directions centered on the cancer
- Radiation Therapy is typically delivered in 5 to 40 daily treatment sessions



External-Beam Radiation Therapy

How Does Radiotherapy Work?

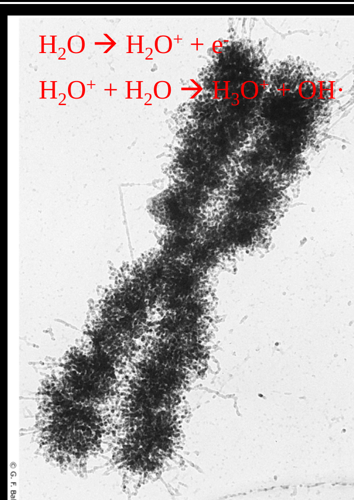


Direct Interaction

DNA Strand Breaks

- When Photons and Electrons interact with biological material, there is the potential for damage to a cell's DNA
- The atoms in the DNA may be DIRECTLY ionized or excited
- The radiation may interact with other atoms or molecules in the cell (*particularly water*) to produce free radicals
- These free radicals are capable of diffusion away from the interaction site

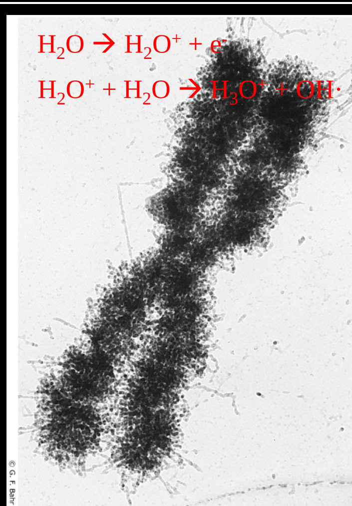
How Does Radiotherapy Work?



DNA Strand Breaks

- A free radical is a free (not combined) atom or molecule carrying an unpaired orbital electron in its outer shell
- An atom or molecule with an odd number of electrons has one electron in the outer orbit is associated with a high degree of chemical reactivity
- Since 80 percent of the cell is composed of water, the H_2O often becomes an ion radical

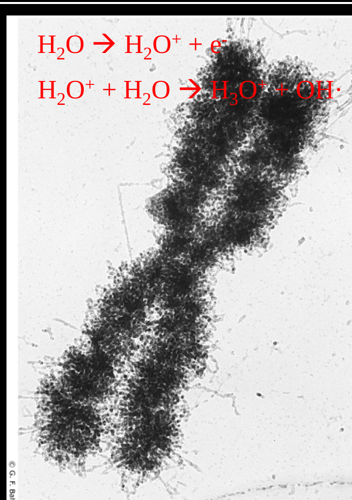
How Does Radiotherapy Work?



DNA Strand Breaks

- H_2O^+ is charged (i.e. an ion) and is also a free radical
- Ion Radicals have an extremely short lifetime, on the order of 10-10 seconds
- They decay to form free radicals, which are not charged but still have an unpaired electron
- In the case of water, the ion radical reacts with another water molecule to form the highly reactive hydroxyl radical (OH·)

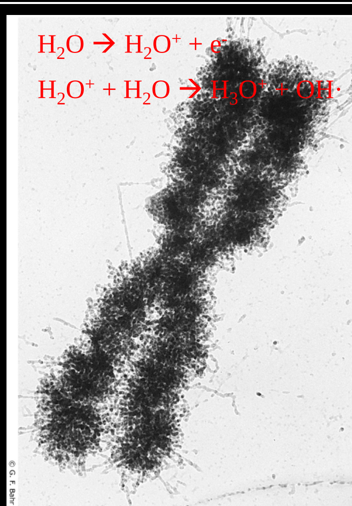
How Does Radiotherapy Work?



DNA Strand Breaks

- The hydroxyl radical (OH·) possesses nine electrons, so one of them is unpaired
- Hydroxyl has a long relatively long lifetime of 10-5 seconds
- This allow the hydroxyl time to diffuse a short distance through the cell to reach the DNA
- It is estimated that free radicals can diffuse as far as 4 nm (which is twice the diameter of DNA)

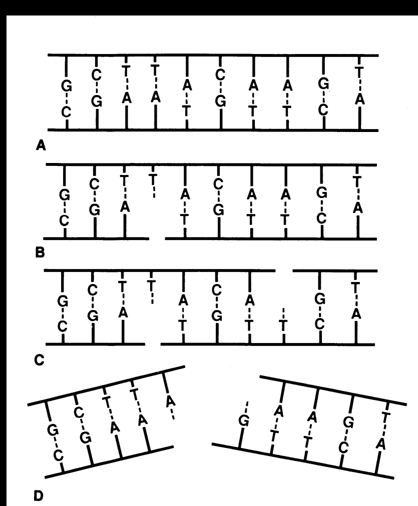
How Does Radiotherapy Work?



DNA Strand Breaks

- It is estimated that 2/3 of the x-ray damage in mammalian cells is due to the hydroxyl radical
- The best evidence for this estimate comes from experiments using free radical scavengers
- These scavengers have been shown to reduce the biological effectiveness of x-rays by a factor of three
- As such, free radical scavengers can also be used as radioprotectors

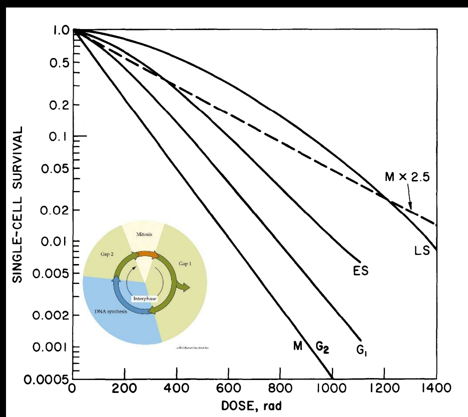
How Does Radiotherapy Work?



DNA Strand Breaks

- When cells are irradiated with x-rays, many breaks of a single stand occur (B)
- Single strand breaks are of little biological consequence (for cell killing) because they are easily repaired
- Because the DNA base pairs are complementary, the unbroken side is used as template to repair the damage
- Likewise, multiple single strand breaks that are well separated can also be repaired (C)

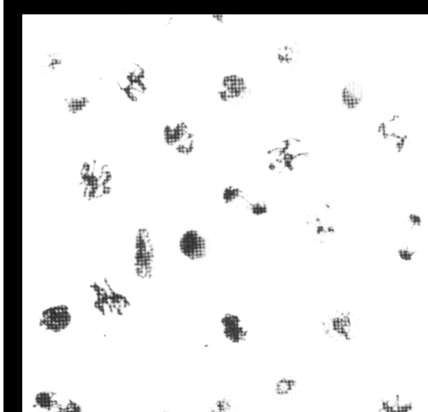
How Does Radiotherapy Work?



Radiation Fractions

- The effectiveness of cell killing/survival is dependant on damage to the DNA
- During S phase, the DNA doubles as the genome is checked and replicated
- As such, this is the period of minimum radiosensitivity
- Just before mitosis, the chromosomes appear to condense into discrete entities, which increases the radiosensitivity
- In addition, levels of free-radical scrubbers vary during the cell cycle, which affects radiosensitivity

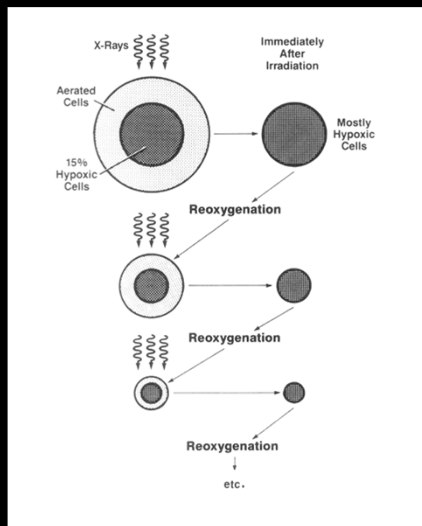
How Does Radiotherapy Work?



Radiation Fractions

- When a single dose is delivered to a population of asynchronous cells, the effect will depend on the phase of the cell cycle
- Cells that are at (or close) to mitosis will be killed at a greater rate
- Radiation tend to synchronize the cell population in the resistant phase
- Fractions of radiation therapy are given in time intervals so that the cancer cells are irradiated at or near mitosis

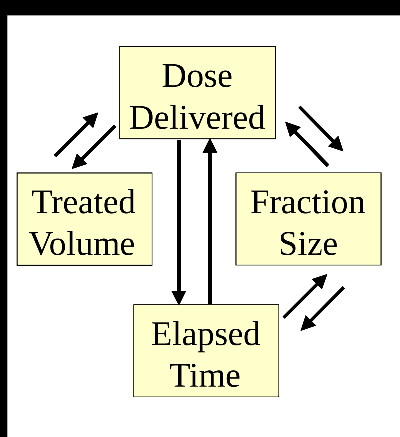
How Does Radiotherapy Work?



Radiation Fractions

- Oxygen must be present during the microseconds after exposure
- Regions of acute hypoxia develop in tumors as a result of the temporary closing of a particular blood vesicle
- At the moment of the first irradiation, a portion of the tumor cells will be hypoxic
- As these cells die off, reoxygenation occurs
- The next fraction of radiation then damages the previously radioresistant cells

How Does Radiotherapy Work?

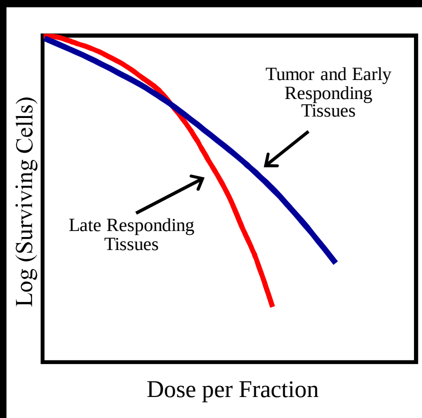


The Four R's of Radiobiology

- Repair of Sublethal Damage
- Reassortment of the cell cycle
- Repopulation
- Reoxygenation

- The basis of fractionation in radiation therapy is the dividing of doses so that normal tissues have time to repair the sublethal damage
- In addition, increasing the number of fractions increases damage to the tumor because of reoxygenation and reassortment

How Does Radiotherapy Work?



The Four R's of Radiobiology

- Not all tissue types respond the same to doses of radiation
- The effects of radiation have been subdivided into three groups
  - Acute responses occurs within the first 6 months
  - Subacute responses occurs within the second 6 months
  - Late responses occur after the first year
- The type of response depends on the cell kinetics (slow vs. fast) and the dose

Radiotherapy Treatment Delivery

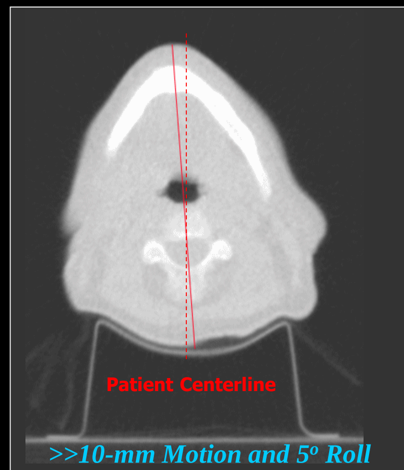
Patient Setup

- Radiation therapy patients are typically positioned for treatment using external lasers that are mounted on the walls of the treatment room
- Marks are drawn or tattooed on the patient during the patient's initial setup and are aligned with lasers
- The goal is to correlate the internal position of the tumor to these external marks, which may or may not correspond to the internal target position over the course of therapy

Radiotherapy Treatment Delivery

Patient Setup

- Without proper immobilization, the patients will move between treatment and during treatment
- In this example, a patient was treated without immobilization
- The patient was aligned with the in-room lasers, but note the severe misalignments over the course of treatment
- Note the variability in the position of the patient on the head rest



Radiotherapy Treatment Delivery

Patient Setup

- In radiation therapy, custom immobilization masks are made of thermoplastics
- A thermoplastic is a polymer that turns to a liquid when heated and freezes to a very glassy state when cooled sufficiently
- The thermoplastic material is heated and molded around the bony anatomy of the patient such as the nose and chin

Radiotherapy Treatment Delivery

Patient Setup

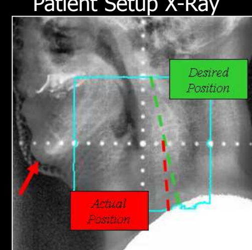
- Vacuum cushions are used to provide customized support and immobilization of the body
- Vacuum cushions are filled with tiny polystyrene beads that forms a rigid mold when a vacuum is pulled
- A cellophane sheet can also be placed over the patient and attached to a vacuum cushion
- The vacuum pump can then be used to generate up to 1200+ lbs per square foot around the patient

Radiotherapy Treatment Delivery

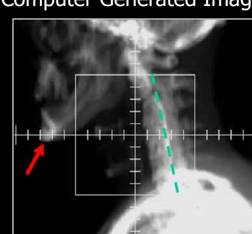
Pre Treatment Imaging

- With the patient immobilized, the location of the tumor must be correlated to external laser marks on the patient’s skin
- In conventional radiation therapy, the positioning of the patient is verified using orthogonal radiographic imaging
- An x-ray image acquired on the linear accelerator is typically compared with a computer-generated reference image
- Historically, this comparison was performed visually by the radiation oncologist

Patient Setup X-Ray



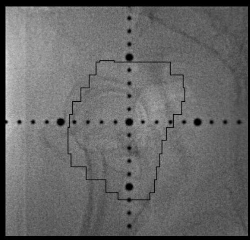
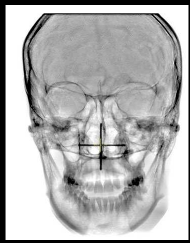
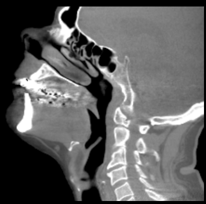
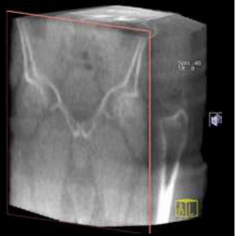
Computer Generated Image



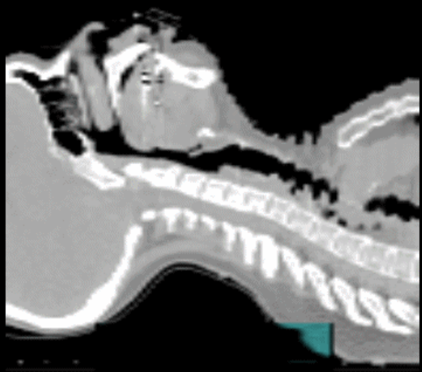
Radiotherapy Treatment Delivery

Pre Treatment Imaging

- Image-Guided Radiation Therapy (IGRT) is a treatment technique that uses imaging immediately before treatment to place the patient in the correct position
- There are a wide-range of imaging techniques that are used to position patients for treatment
  - *Electronic Portal Imaging*
  - *Orthogonal Imaging*
  - *Cone Beam CT*
  - *Tomotherapy*

Radiotherapy Treatment Delivery

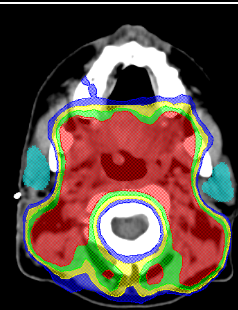


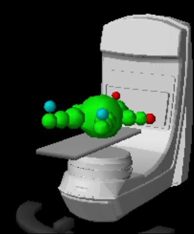

- IGRT CT images are acquired daily and fused with the treatment planning CT images to determine patient setup corrections
- The patient is then positioned for treatment with an accuracy of 0.6-mm

Radiotherapy Treatment Delivery

Treatment Delivery

- Intensity modulated radiation therapy (IMRT) is a treatment technique where the uniformity of the treatment is dynamically adjusted to deliver complex dose distributions
- The goal of IMRT is to shape the radiation dose around normal tissues from multiple gantry angles
- There are multiple techniques for delivering IMRT, including Physical Compensators, Step-and-Shoot, Sliding Window, IMAT, VMAT, RapidArc, Serial Tomotherapy and Helical Tomotherapy

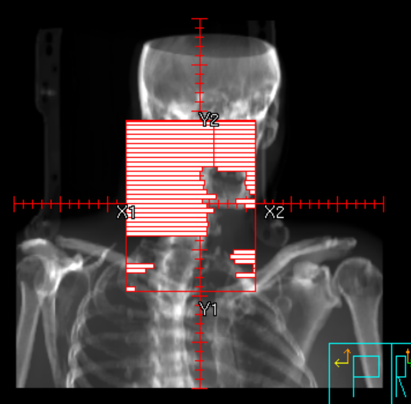




Radiotherapy Treatment Delivery

Treatment Delivery

- Step-and-Shoot (also known as Multiple Static Segments) is a commonly used technique for head and neck IMRT
- The radiation beam is turned on for each “segment” and off as the tungsten collimators “step” to the next shape
- Complex dose distributions are created by superimposing leaf shapes from 5 or more gantry angles



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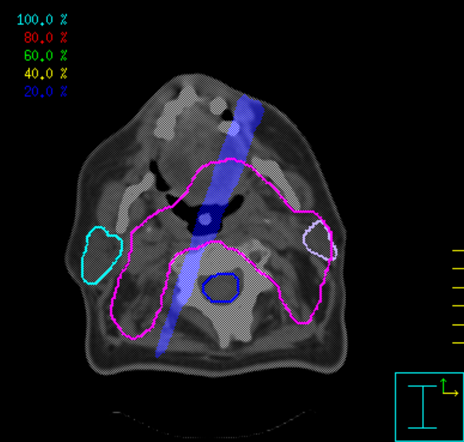
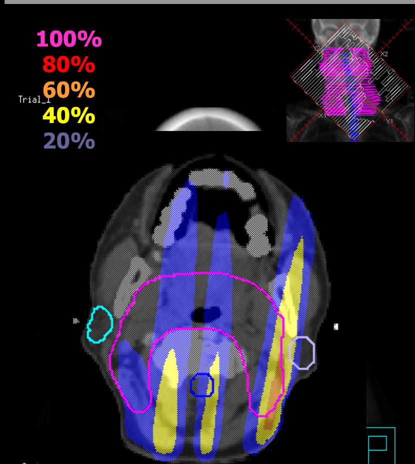


Radiotherapy Treatment Delivery

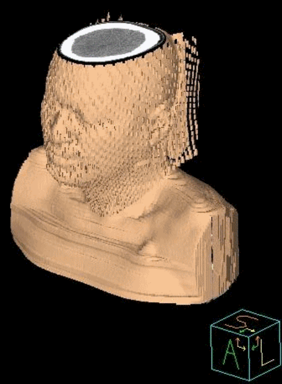
Treatment Delivery

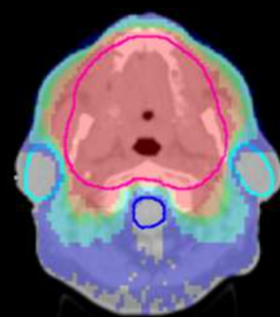
- Volume Modulated Arc Therapy (VMAT) is defined as modulated treatment delivery with continuous gantry motion
- During the gantry motion the field shape changes in order to modulate the treatment beam
- In addition, the gantry and/or dose rate of the radiation will speed up or slow down to assist in the shaping of the radiation dose

Volume Modulated Arc Delivery



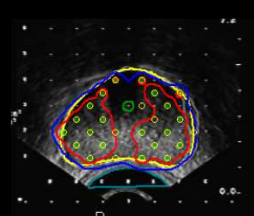
Radiotherapy Treatment Delivery





The primary goal of IMRT and VMAT in head & neck patients is to spare the parotid glands

Brachytherapy



Isotopes

- Iodine
- Iridium
- Palladium

Planning

- Pre-Operative
- Intra-Operative

Implanting

- Temporary
- Permanent

What is Brachytherapy

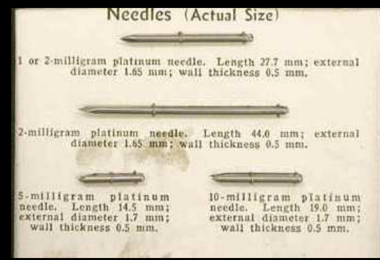
- Brachytherapy is a special procedure in therapeutic radiology that utilizes the irradiation of a target with radioactive sources placed at short distances from the target
- The sources can be implanted in the target tissue directly (interstitial brachytherapy) or are placed at distances of the order of a few millimeters from the target tissue (intracavitary brachytherapy), or externally on structures (surface plaques or molds)

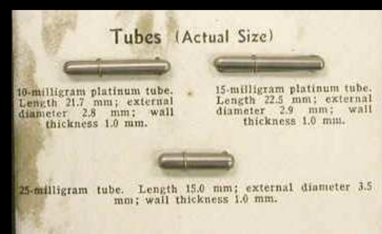
What is Brachytherapy

- Most brachytherapy uses gamma-emitting radionuclides
- Many use radionuclides such as ^{137}Cs and ^{192}Ir, which emit high-energy gammas, that penetrate deeply and also require heavy shielding for radiation protection of the personnel and the patient's family
- Whenever possible, brachytherapy with low-energy gamma emitters, like ^{125}I and ^{103}Pd is preferred because it requires minimal shielding for radiation protection
- Beta-emitting sources are commonly used as unsealed sources for systemic brachytherapy similar to nuclear medicine diagnostic procedures

Brachytherapy History

- ^{226}Ra and ^{222}Rn were the first brachytherapy sources used to treat cancer
- Radium decays into radon, with a half-life of about 1622 years; radon is a heavy, inert gas that in turn disintegrates into its daughter products
- The radioactive material was supplied mostly in the chemical form of radium sulfate or radium chloride loaded into cells about 1 cm long and 1 mm in diameter
- They are virtually unused today, primarily because of the hazards of chemical and radioactive toxicity of radium and its by-products





Brachytherapy History

- ^{137}Cs is a by-product of nuclear fission and is generated in nuclear reactors
- It has a half-life of about 30 years and emitts a photon energy of 662 keV
- ^{137}Cs sources are less hazardous and require less shielding compared to that required for ^{226}Ra sources
- Although the half-life of ^{137}Cs is much less than that of ^{226}Ra, some of the cesium sources may have to be replaced after about 7 years

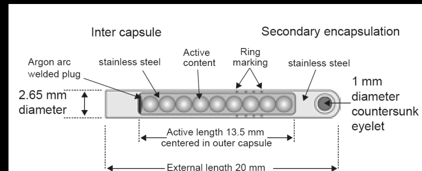
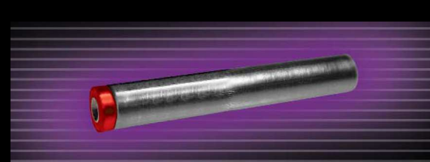
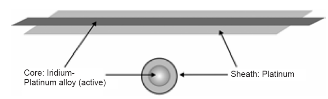


Fig. 1.1 Diagrammatic representation of a caesium-137 tube similar to an Amersham 'J-Type' tube.



HDR Brachytherapy

- ^{192}Ir is produced in a nuclear reactor via neutron capture by stable 1^{91}Ir
- ^{192}Ir has a half-life of 73.83 days and has a very complicated gamma-ray spectrum with an average energy of about 0.38 MeV
- Because the gamma-ray energy is lower than ^{226}Ra or ^{137}Cs, ^{192}Ir sources require less shielding
- Another advantage of 192Ir is its high activity per unit mass, which means that you can make a small source that emits a large number of photons



	Wire	Hairpins
Core diameter:	0.1 mm	0.4 mm
Sheath Thickness:	0.1 mm	0.1 mm
Overall Diameter:	0.3 mm	0.6 mm

Fig. 1.3 Diagrammatic representation of iridium-192 wire.

Table 2. Exposure Rates from an Exposed 10 Ci 192Ir Source

Typical situation	Distance [m]	Dose equivalent rates [Sv/h]	Time to receive 10 Sv (Likely injury)	Time to receive 0.05 Sv (Annual body limit)
In Patient	0.01	4.6R/(mCi h) × 0.966 rem/R = 444 Sv/h	1.35 minutes	0.007 minutes 0.4 seconds 0.67 minutes
Handling with Kelly Clamps	0.1	4.44	2.3 hours	(6.8 minutes for hand limit)
Handling with Kelly Clamps	0.3	0.5	20 hours	0.10 hour 6 minutes
Standing near	1	0.044	9.5 days	1.1 hours
Standing far	2	0.011	37.5 days	4.5 hours

HDR Brachytherapy

- Since ^{192}Ir brachytherapy is associated with high radiation exposure rates, it is only used in well-shielded bunkers
- Depending on distance and usage factors, 1 to 2 feet of concrete shielding or its equivalent in other materials is required
- Treatment is delivered by High Dose Rate (HDR) remote-control techniques rather than manual loading
- Treatments to be given in only a few minutes on an outpatient basis

HDR Brachytherapy

Partial Breast Irradiation

- Six modern, prospective randomized trials have shown no significant difference between conservative surgery + radiation vs. mastectomy
- Multiple randomized trials have been shown that RT cannot be omitted after breast conserving surgery
- Up to 40% of patients who are candidates for breast conservation therapy do not receive it

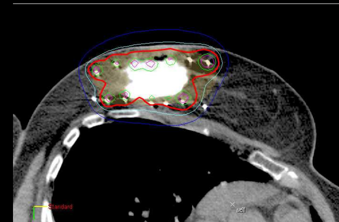
Why the preference for mastectomy?

- Physician bias
- Patient choice
- More complex and prolonged treatment course
  - 6 weeks – daily treatment Monday to Friday
  - Can be inconvenient or prohibitive for those with poor access to a radiation facility, the elderly and working women.

HDR Brachytherapy

Partial Breast Irradiation

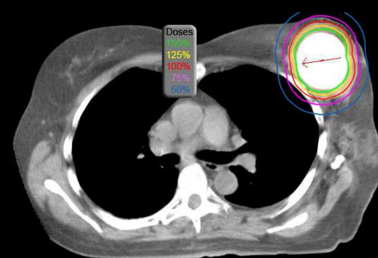
- Accelerated partial breast irradiation is a technique where only the lumpectomy cavity is irradiated
- Treatments are given twice per day for a total of ten treatment fraction
- The radiation is typically delivered using HDR Breachytherapy
- In interstitial HDR, hollow needles are placed through breast and the ^{192}Ir “dwells” at multiple locations to build the desired dose distribution



HDR Brachytherapy

Partial Breast Irradiation

- Intra-lumen accelerated partial breast irradiation is a technique where a balloon catheter is placed in the lumpectomy cavity
- The balloon catheter is filled with saline and distends the cavity
- The ^{192}Ir source is then placed in the center of the catheter for a single dwell position
- After the completion of the ten fractions, the balloon is deflated and removed



Radiation Therapy Summary

- Radiation therapy is used in the treatment of 60% of all cancer patients in the United States
- These patients are typically treated in combination with surgery and chemotherapy
- Most hospitals in the U.S. will have a radiation therapy department that delivers external beam treatments and brachytherapy treatments