

INTRODUCTION TO RADIATION THERAPY



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BULGARIA



RUSE – OR JUST THE IDEA OF IT



Nothing in life is to be feared,
it is only to be understood.
Now is the time to understand
more, so that **we may fear less.**

– *Marie Curie*

AZ QUOTES



Marie Curie 1867-1934



- **What...is radiotherapy?**
- **Why....is radiotherapy needed?**
- **When....is radiotherapy used?**
- **How....does radiotherapy work?**
- **What....are the radiotherapy machines?**
- **Where....are the radiotherapy machines?**
- **How....do we measure, control and check their safty?**
- **Who....works in radiotherapy?**
- **What....is the workflow of radiotherapy?**
- **What....technics are used in radiotherapy?**
- **What....is the future of radiotherapy?**

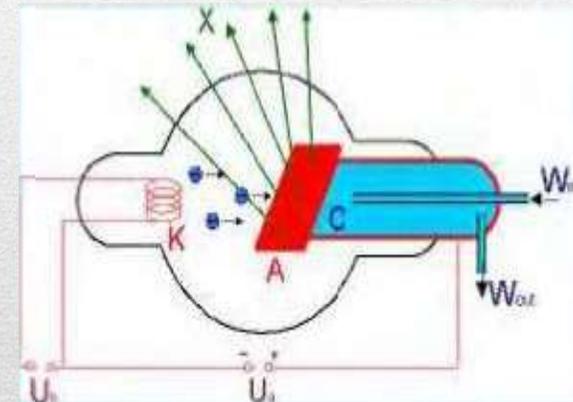
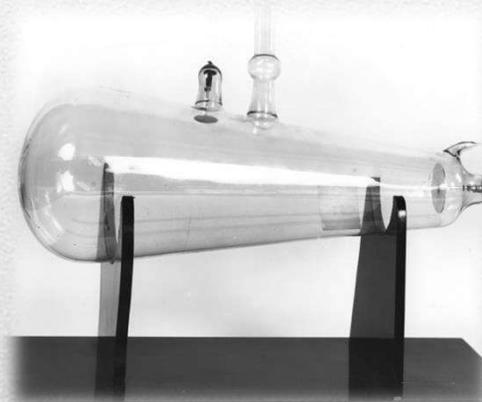
Overview



8th November 1895

Roentgen discovered new kind of rays:

X-rays - a form of high-frequency electromagnetic radiation produced in an X-ray tube.



The Beginning of Radiotherapy and Radiology



- 1896** Henry Becquerel reported the phenomenon of natural radioactivity of uranium
- 1896** Emil Grubbe – a medical student from USA was probably the first to treat breast carcinoma with X-rays
- 1898** Marie and Pierre Curie discovered radium and polonium and described natural radioactivity.
*THEY WERE THE FIRST TO SUGGEST
THAT RADIATION KILLS CANCER CELLS
BETTER THAN NORMAL CELLS*
- 1899** Tage Sjogren – a doctor from Sweden reported the first case of a skin tumor cured by use of radioactive source application
- 1934** Frederic and Irene Joliot-Curie discovered artificial radioactivity

Milestones in the History of Radiotherapy



1951 - First Co-60 Machine in Saskatoon, Saskatchewan, Canada



FIRST Co-60 MACHINE



1953 - First Linac Machine in London, UK



FIRST LINEAR ACCELERATOR (LINAC) MACHINE



Clinical Advances
Technologic Advances
Biologic Advances

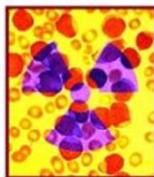
Fractionated radiation sterilizes ram's testes without major burns (11, 12) 1911

Cellular radiosensitivity depends on mitotic activities and levels of differentiation (47) 1906

Radiation intensity related to inverse square of distance from source 1903

Becquerel experiences skin burn while carrying radium in vest pocket (109) 1901

Leukemia cases reported in radiation workers (10) 1911



Radiosensitivity correlated with oxygen presence (52) 1923

How high-energy photons interact with tissue (Compton effect) (109) 1922

Hot-cathode x-ray tube invented (33) 1913

Roentgen adopted as standard exposure unit; radiation protection recommendations 1928

Head and neck cancers cured with fractionated X-rays (13) 1928

Air wall ionization chambers accurately measure radiation intensities 1924



Nobel Prize (Muller) for radiation-induced mutagenesis shown in *Drosophila* 1946

First self-sustaining nuclear chain reaction with uranium 1942

Plant root studies show importance of oxygen in radiotherapy (52) 1935

Dosage system for gamma ray (36) 1934

First patient treated with neutron beams 1938

Skin iso-effects governed primarily by total dose and overall treatment time (17) 1944



Cyclotron invented (37) 1932



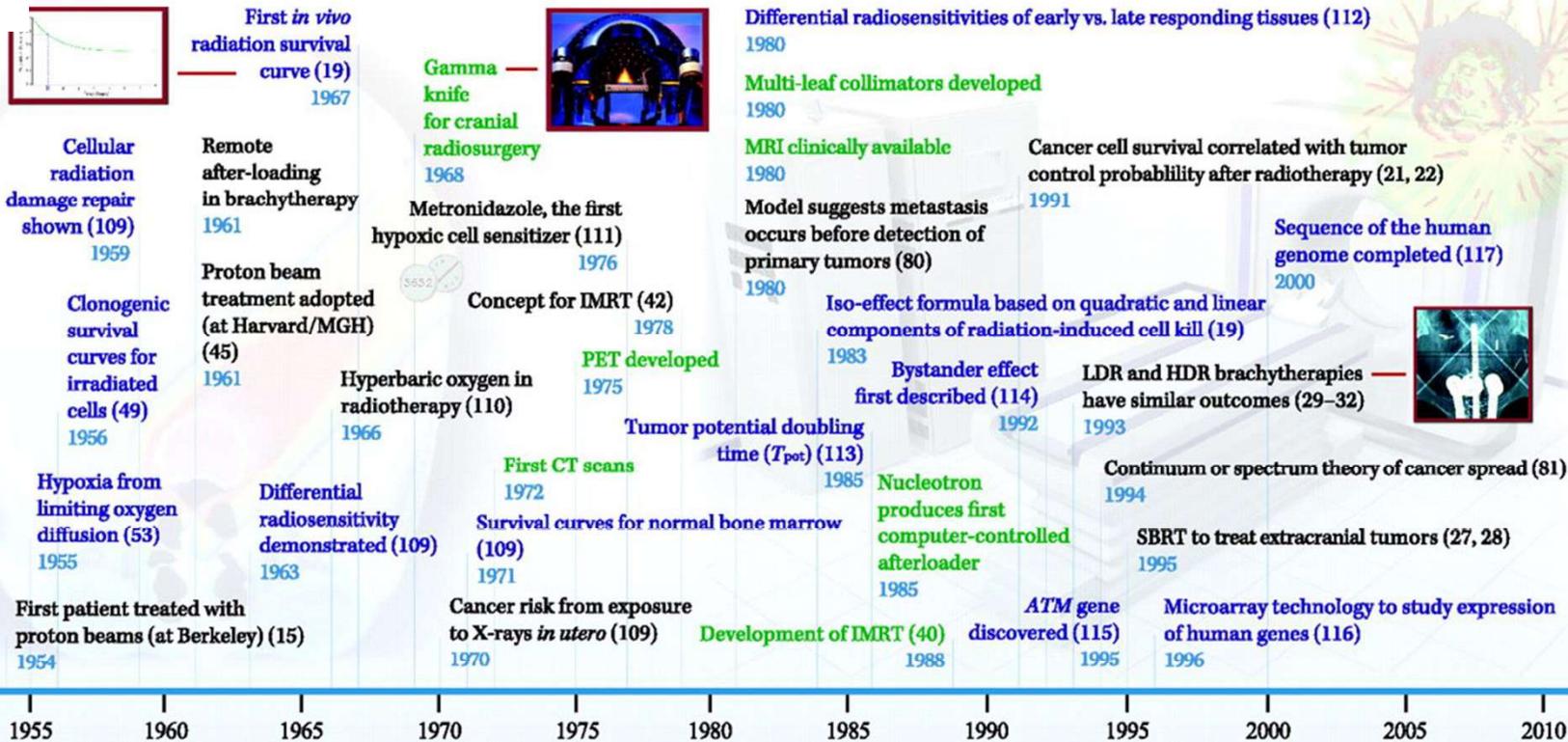
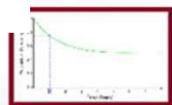
Experimental quantification of the oxygen effect (109) 1952

Cobalt-60 telotherapy units first used (15) 1951

AACR Centennial Series

Advances in Radiotherapy: 1900-1950

Philip P. Connell, and Samuel Hellman *Cancer Res* 2009;69:383-392



Cancer Research

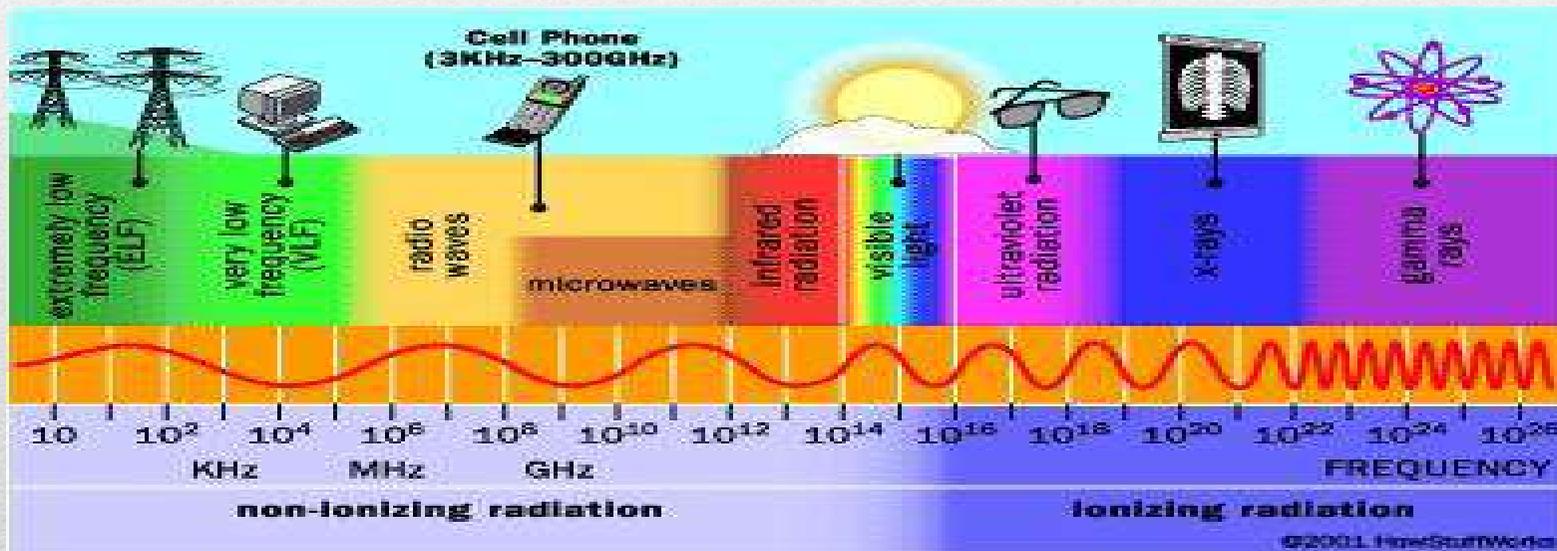
Advances in Radiotherapy: 1950-2010

Philip P. Connell, and Samuel Hellman Cancer Res 2009;69:383-392



Radiotherapy is the medical use of ionizing radiation as part of cancer treatment

Ionizing Radiation is energy flow released and spreading in the form of **charged particles or high energy photons (EM waves) or neutrons** which are capable to directly or indirectly ionize matter when interacting with its atoms.



What is Radiotherapy?



Radiotherapy is divided into:

■ External RT or Teletherapy

which is treatment of cancer with radiation beams delivered by a machine outside the body

- ❖ Photon RT
- ❖ Particle RT

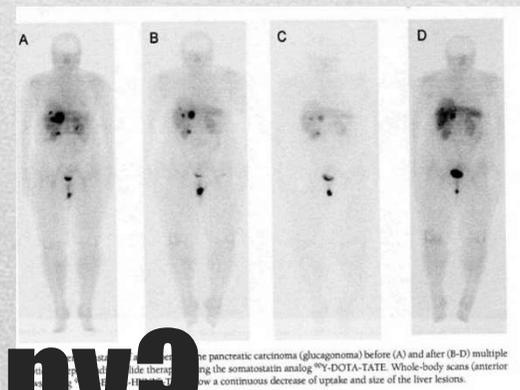
■ Internal RT or Brachytherapy

which is treatment of cancer with sealed radioactive sources placed very close up to the tumor

- ❖ Intracavitary BT
- ❖ Intrastitial BT
- ❖ Intraluminal BT
- ❖ Surface BT
- ❖ Intravascular BT
- ❖ Intraoperative BT

■ Systemic RT or Metabolic RT

which is provided by unsealed radioactive sources injected or swallowed by the patient

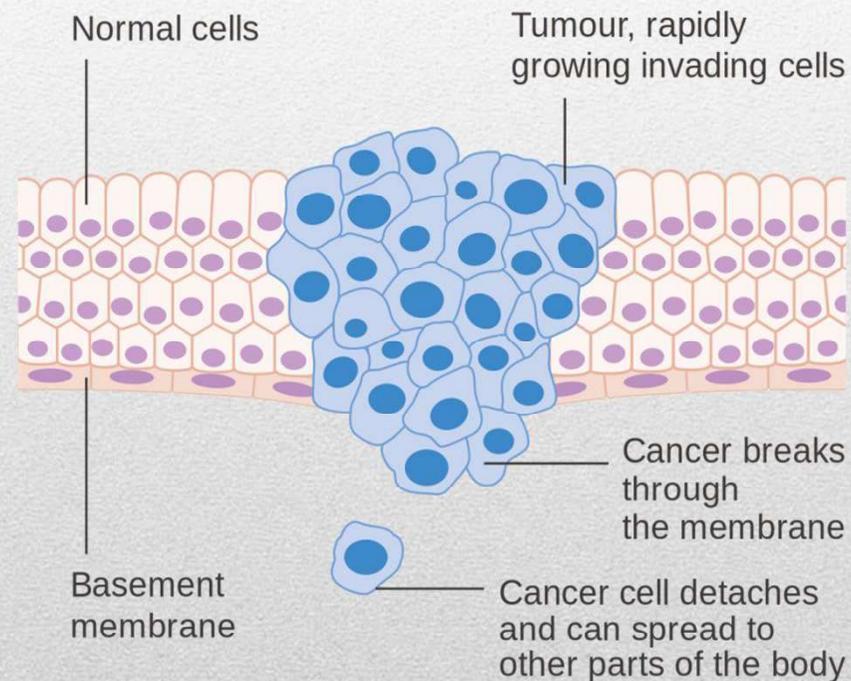


What is Radiotherapy?



What is Cancer?

- Cancer is out of control growth of cells.
- As a result they do not perform their intended function.
- There are four main medical **methods** to treat cancer:
 - ❖ Surgery
 - ❖ Chemotherapy
 - ❖ Radiotherapy
 - ❖ Hormone therapy
- The **choice** of treatment depends on a number of factors including type, size, location and stage of the tumor.

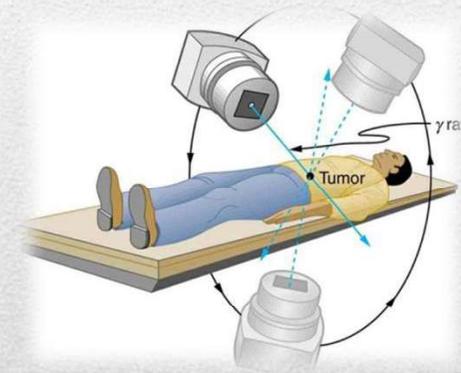


Why is Radiotherapy Needed?



The **ultimate purpose** of radiotherapy is to cause maximum targeted damage to the cancerous cells with minimum risk to surrounding healthy tissue.

- Radiotherapy may be used as the primary therapy or in combination with other methods.
- The treatment purpose might be:
 - ❖ curative
 - ❖ adjuvant
 - ❖ therapeutic
 - ❖ palliative
- More than 60 percent of patients diagnosed with cancer will receive radiotherapy as part of their treatment



Why is Radiotherapy Needed?



Common cancers curable at early stages with radiotherapy alone:

- Prostate carcinomas
- Head & neck carcinomas
- Non-small cell lung carcinomas
- Squamous and basal cell skin cancers
- Hodgkin lymphomas
- Uterine cervix carcinomas

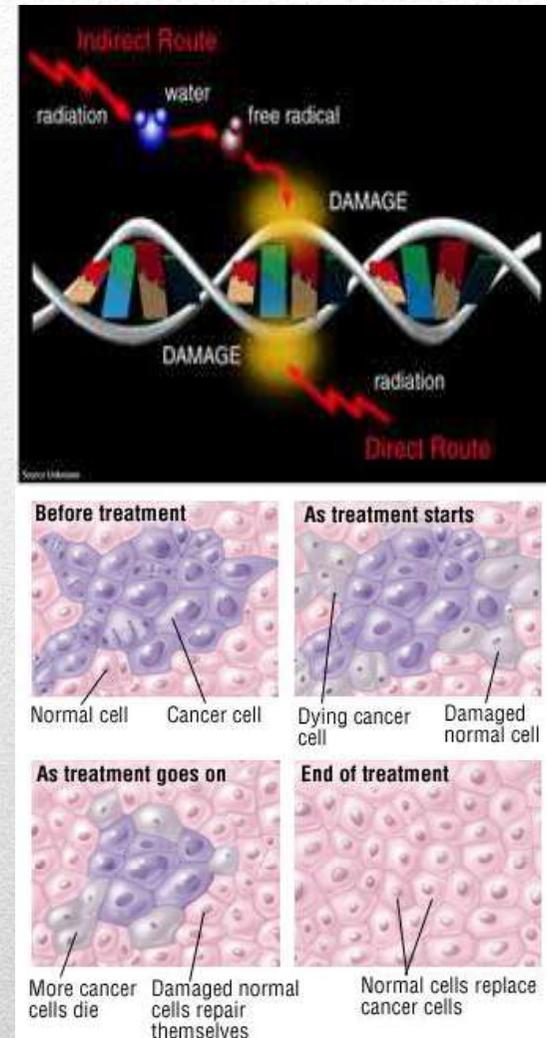
Additional common cancers curable with regimens that include radiotherapy:

- Breast carcinomas
- Locally advanced lung carcinomas
(non-small cell and small cell)
- Seminomas
- Endometrial carcinomas
- Locally advanced uterine cervix
- Several CNS tumors
(e.g., ependymoma, glioma)
- Soft tissue sarcomas
- Rectal and anal carcinomas
- Lymphomas (Hodgkin and non-Hodgkin)
- Advanced head & neck carcinomas
- Bladder carcinomas
- Numerous pediatric malignancies
(e.g., Wilms tumor, medulloblastoma,
neuroblastoma, Ewing's sarcoma,
rhabdomyosarcoma)

Why is Radiotherapy Needed?



- Radiation therapy uses regulated doses of high-energy radiation targeted at the cancer cells to damage directly or indirectly their DNA and thus destroying their ability to reproduce
- Both normal and cancer cells can be affected by radiation, but cancer cells have generally limited ability to repair this damage, leading to cancer cell death, unlike healthy cells
- All tissues have a tolerance level, or maximum dose, beyond which irreparable damage may occur



How does Radiotherapy Work?



- Differences in repair abilities of normal and cancer cells is in the basis of dividing the total dose into small daily fractions over several days or weeks, which is called Fractionation.
- Fractionation spares normal tissue through **repair** and **repopulation** while increasing damage to tumor cells through **redistribution** and **reoxygenation**

Fractionation:

A Basic Radiobiologic Principle



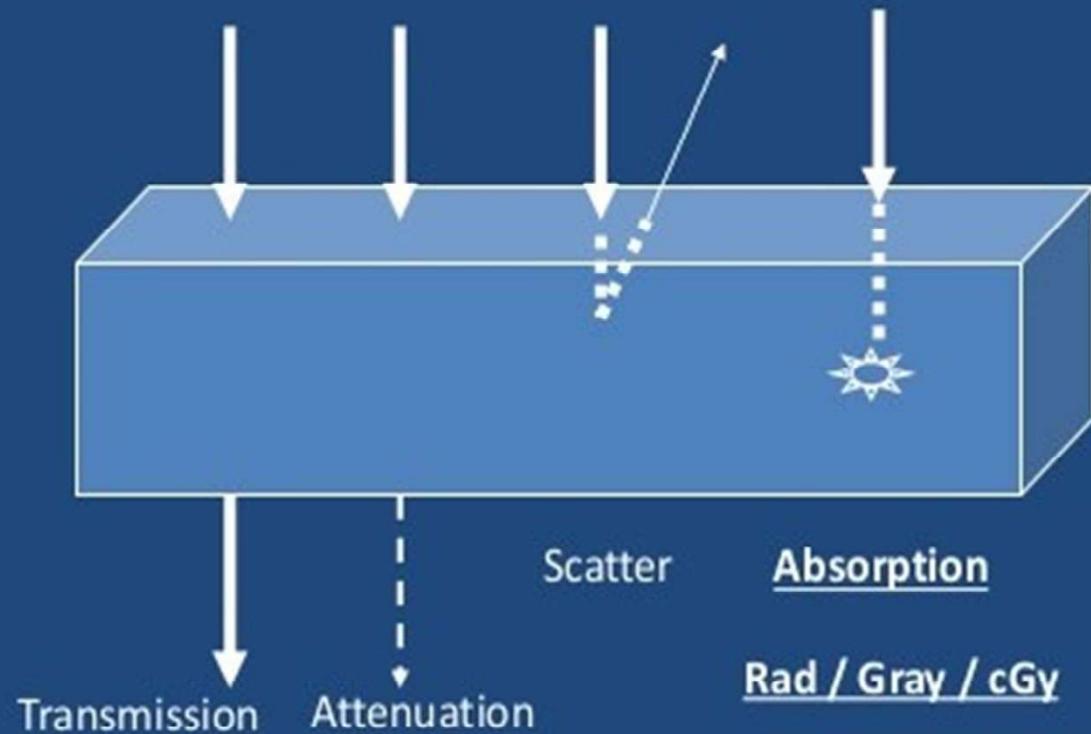
Side effects during the treatment vary depending on site of the treatment and affect usually tissues in the radiation field:



Side Effects of Radiotherapy



Interaction of Radiation with matter

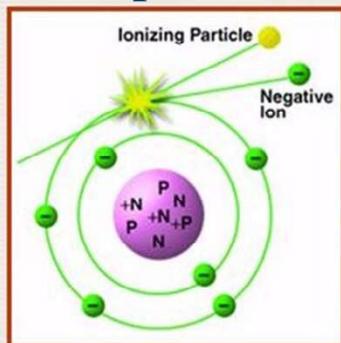


How does Radiotherapy Work?

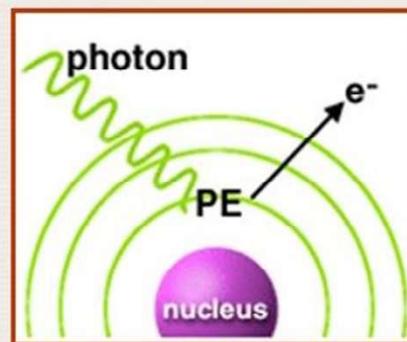


Ionizing radiation is divided into two categories:

Directly Ionizing
alpha and beta
and protons



Indirectly Ionizing
photons and neutrons



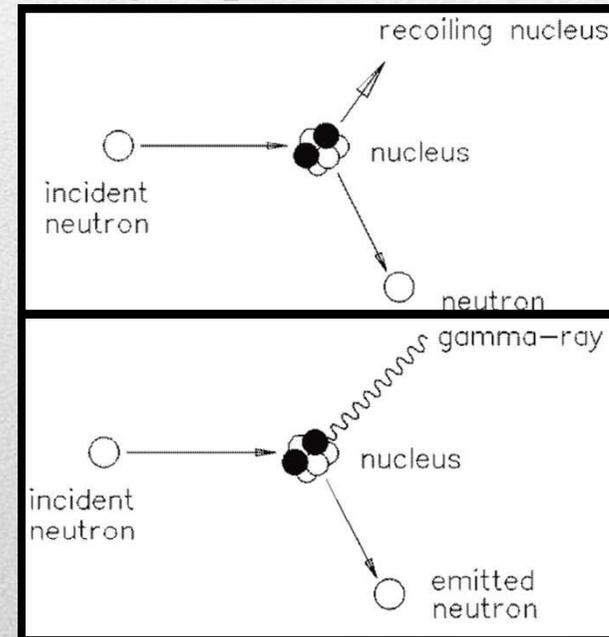
Gamma rays and neutrons release charged particles in matter which are themselves directly ionizing.



How does Radiotherapy Work?



- The major forms of interaction of **directly ionizing charged particles such as protons and electrons** with matter are:
 - ❖ COLLISIONAL LOSS due to ionization and excitation
 - ❖ RADIATIVE LOSS due to interaction with the nucleus
- **Neutrons are indirectly ionizing uncharged particles,** which interact only with the nucleus:
 - ❖ ELASTIC SCATTERING
 - ❖ CAPTURE REACTIONS – emission of n and γ , p or α
 - ❖ INELASTIC SCATTERING – emission of n and γ
 - ❖ NUCLEAR FISSION

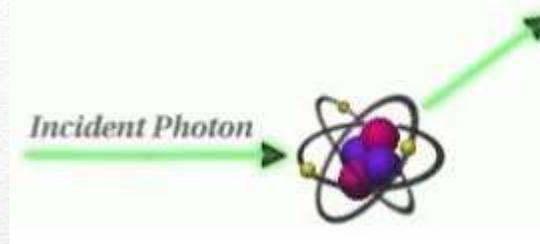


How does Radiotherapy Work?

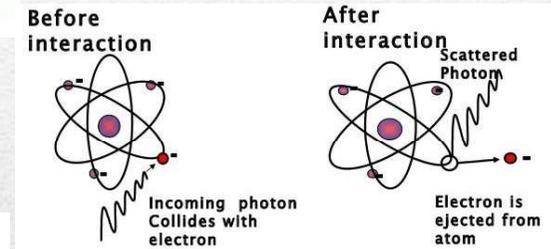


The major forms of interaction of **photon radiation** with matter, which are of clinical importance in radiotherapy are:

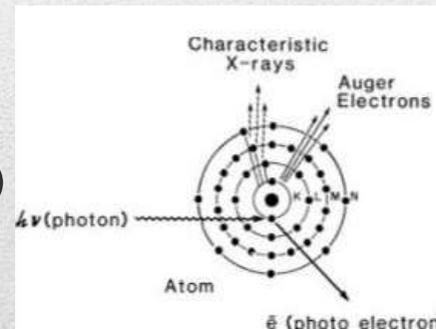
- Coherent scattering



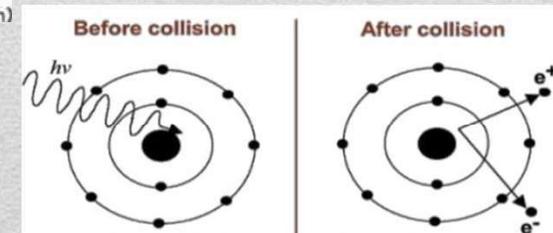
- Compton effect
(Most important in modern-day megavoltage RT)



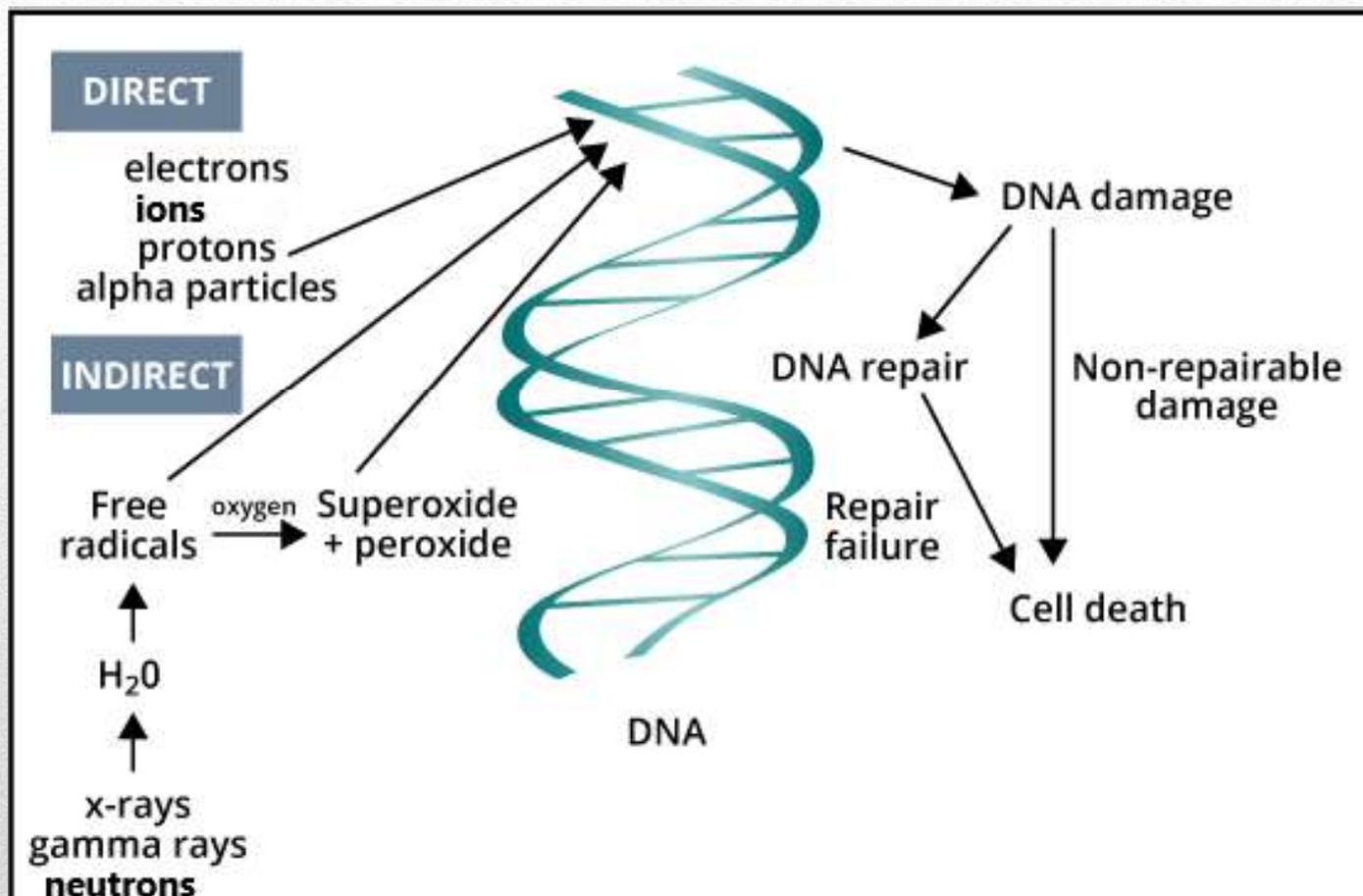
- Photoelectric effect
(Most important in radiology)



- Pair production



How does Radiotherapy Work?



How does Radiotherapy Work?



Direct and indirect ionizing radiation **imparts energy** to the material with which it interacts through any of the described forms.

- The mean energy imparted per unit mass of the absorbing material is defined as **Absorbed Dose**, measured in *Gray (Gy) defined as 1 J/kg*
- The amount of radiation given to the patient or the **Patient Total Dose** has to be accurately calculated so that the damage is limited to the cancerous cells only.

How does Radiotherapy Work?



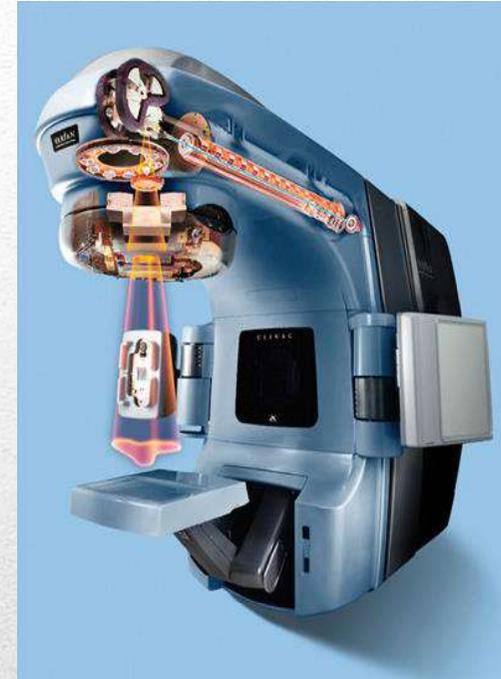
■ Photon RT Machines

- ❖ γ - rays (gamma rays): Emitted from a nucleus of a radioactive atom
 - Cobalt treatment machine and GammaKnife
 - Radioisotopes used in brachytherapy
- ❖ X – rays: Generated by a Roentgen tube or a linear accelerator when accelerated electrons hit a target

■ Particle Beams Machines

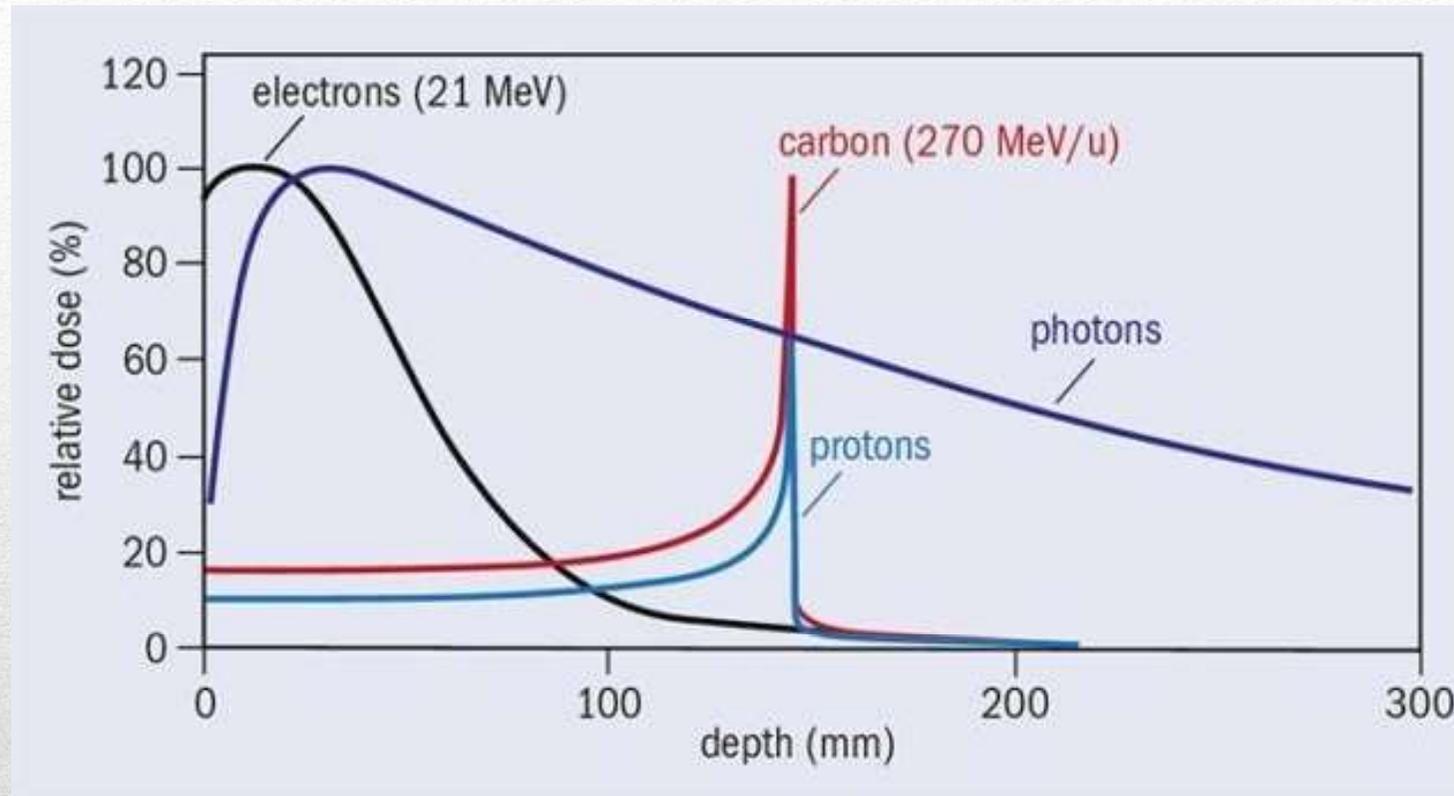
- ❖ Protons
- ❖ Neutrons
- ❖ Electrons
- ❖ Ions

What are the Sources of Ionizing Radiation?

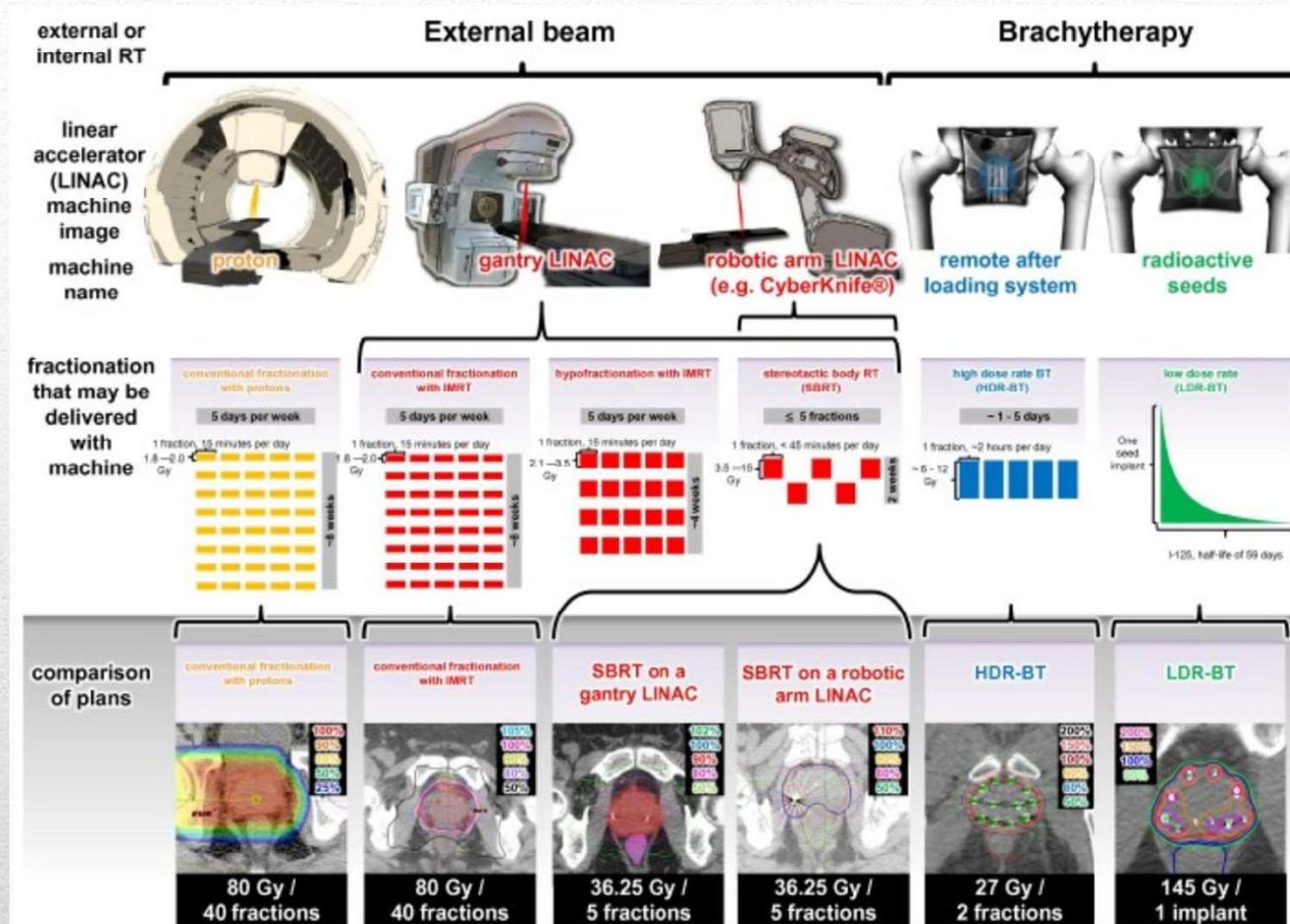


Most external beam radiation treatments use photons generated by a linear accelerator.

Source: Varian Medical Systems Inc.



Relative Depth Dose Deposition Comparison for Photon, Electron, Proton and Carbon Ion Beams



Typical Equipment, Fractionation and Dose Distributions



TYPE OF EXTERNAL RADIOTHERAPY ACCORDING TO ENERGY	ENERGY RANGE	TARGET DEPTH IN TISSUE	SSD Source-to-Surface Distance
Grenz-ray Therapy or ultrasoft Bucky Therapy	10-30 kV	surface of skin	< 1 cm
Contact Therapy	40-50 kV	1-2 mm	< 2 cm
Superficial Therapy	50-150 kV	< 5 mm	15-20 cm
Orthovoltage Therapy	150-500 kV	3-5 cm	50 cm
Supervoltage Therapy	500-1000 kV	7-8 cm	50-80 cm
Megavoltage Therapy with Telegamma Cobalt-60 Machine, GammaKnife	1.25 MV	> 0.5 cm	80 cm
Megavoltage Therapy with FF Linac, FFF Linac, Tomotherapy, MRI Linac, CyberKnife	4-25 MV	> 1,5 cm	100 cm 65-100 cm

What are the Types of External Photon Radiotherapy?



■ Grenzray or Bucky
External X-ray Therapy



■ Superficial
External X-ray Therapy



■ Orthovoltage
External X-ray Therapy

What are the Machines for External Photon Radiotherapy? X-Ray MACHINES



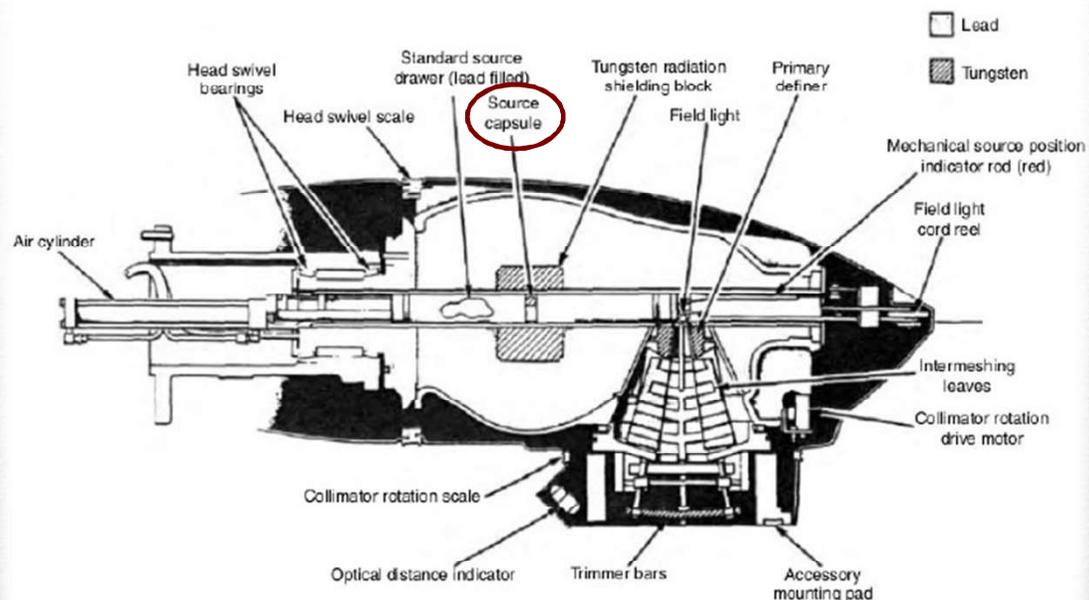
Co-60 (Terabalt) machine in Ruse Oncology Center



**What are the Machines
for External Photon Radiotherapy?
Co-60 MACHINE**



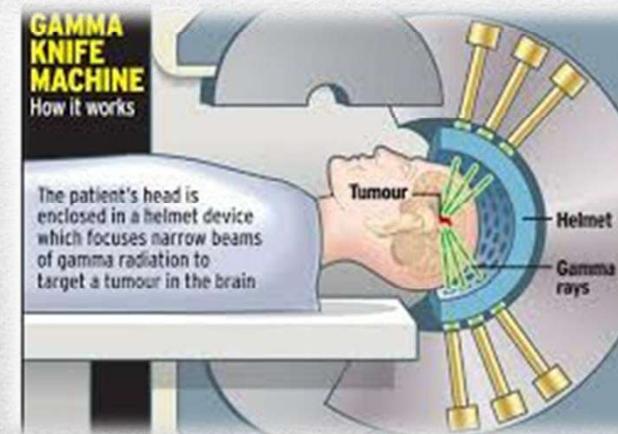
Co-60 Gantry Head Design



What are the Machines for External Photon Radiotherapy? Co-60 HEAD DESIGN



Elekta Leksell GammaKnife



**What are the Machines for
External Photon Radiotherapy?
GammaKnife**



Elekta Synergy LA machine at Ruse Oncology Center



**What are the Machines for
External Photon Radiotherapy? LINAC**



KOU - PYGE

Varian Edge Radiosurgery LA



Varian Halcyon LA



Elekta Versa HD Radiosurgery LA



Mitsubishi Vero LA



Accuray Radixact



Accuray TomoTherapy

What are the Machines for External Photon Radiotherapy? LINACS



ViewRay MRIdian MRI LINAC

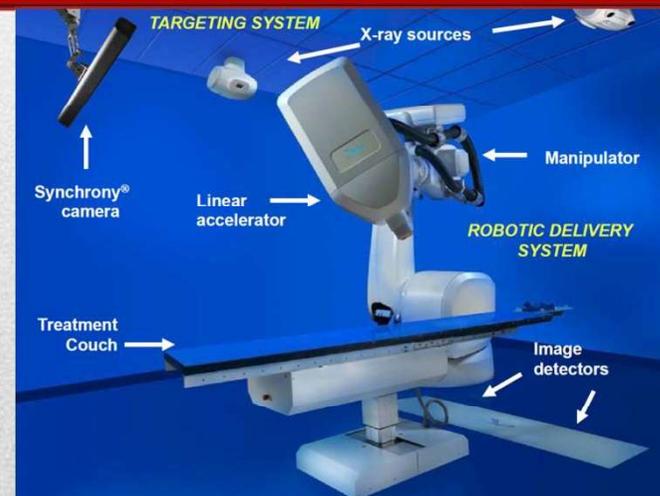


Elekta Unity MRI LINAC

What are the Machines for External Photon Radiotherapy? MRI LINACS



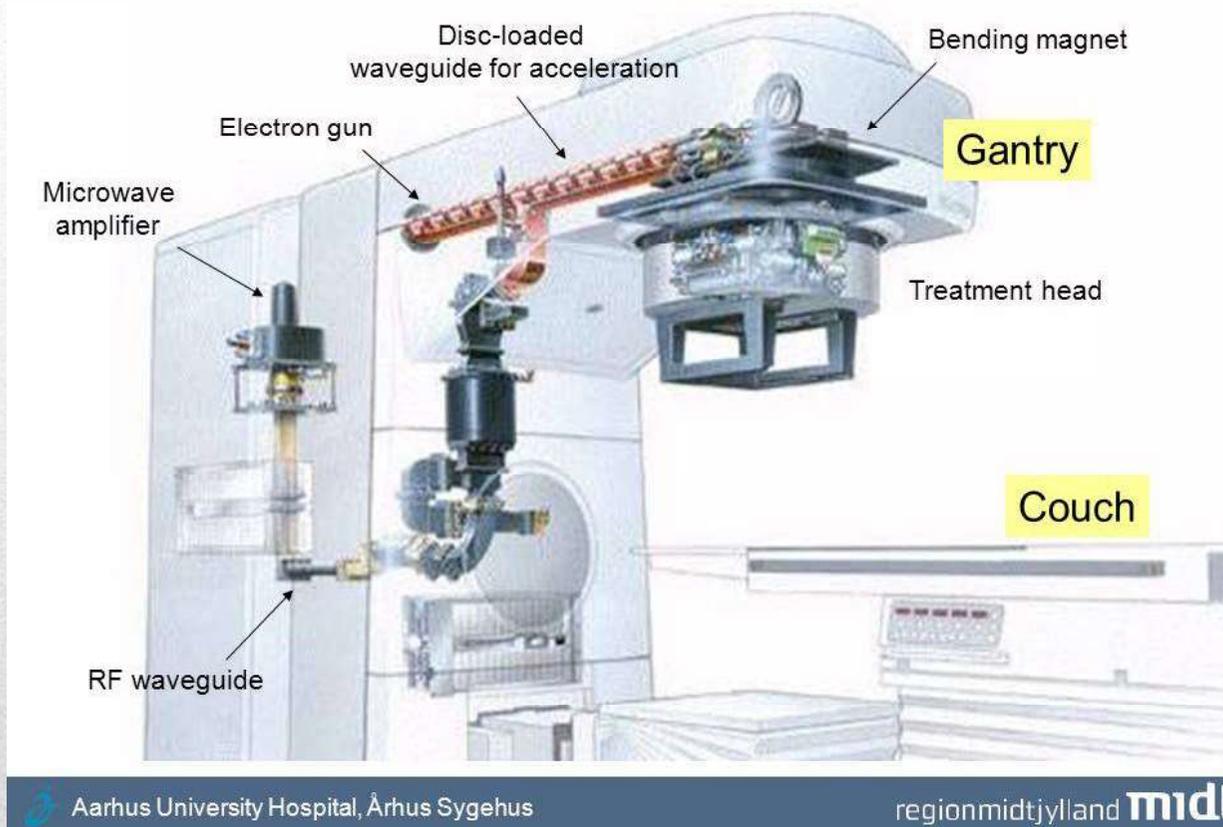
Accuray CiberKnife



**What are the Machines
for External Photon Radiotherapy?
ROBOTIC LINAC SiberKnife**



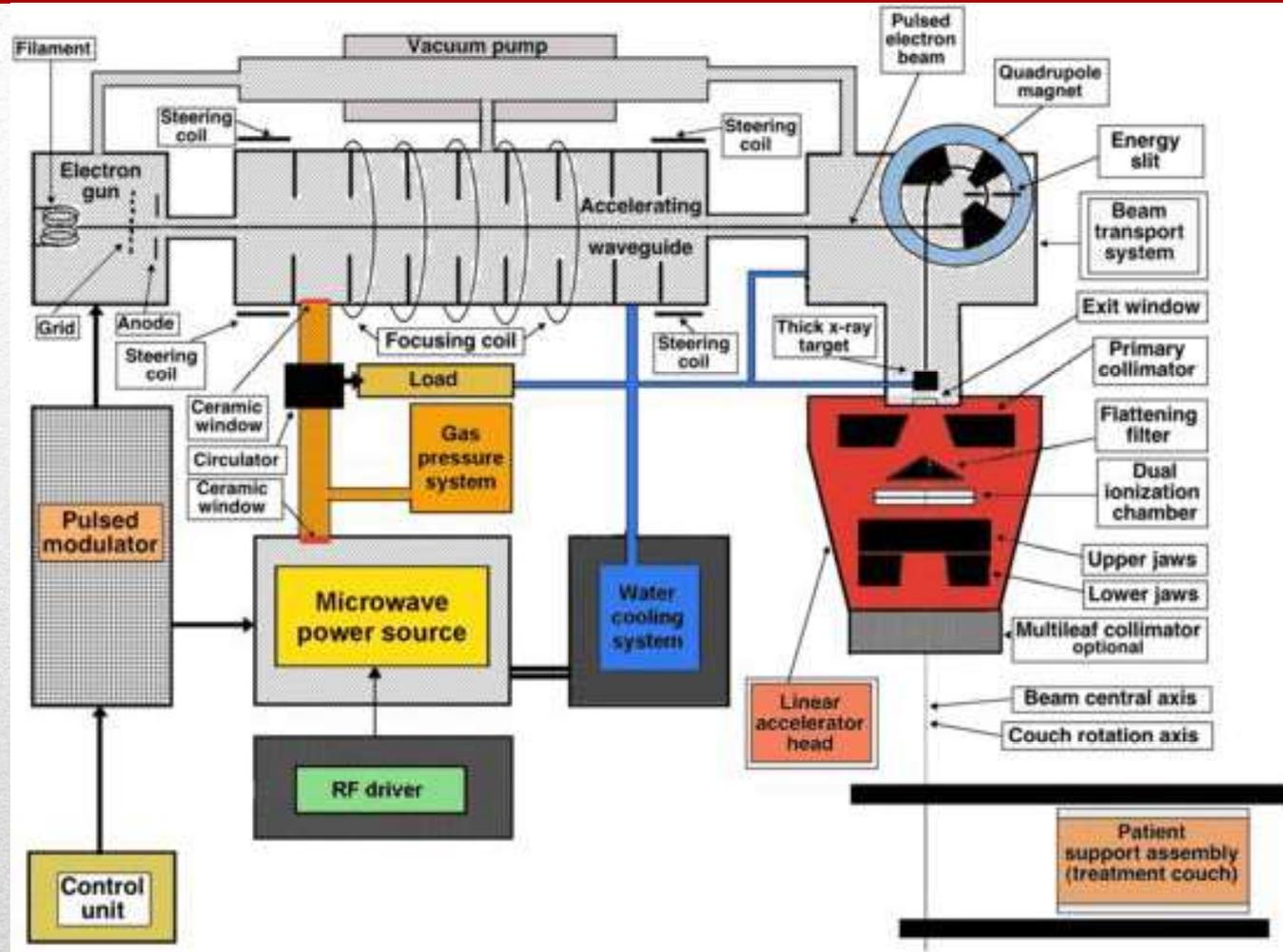
Main components of medical linac



Aarhus University Hospital, Århus Sygehus

regionmidtjylland midt

What are the Machines for External Photon Radiotherapy? LINAC DESIGN



What are the Machines for External Photon Radiotherapy? LINAC DESIGN



- The aperture of each radiation field matches the projected shape of the tumor which allows for
 - ❖ 3D Conformal Radiotherapy (3D CRT)

- Dynamic MLC, static or dynamic gantry and collimator rotation, varying radiation dose with time and angle and thus modulating the radiation intensity within the field allow further for:
 - ❖ Intensity Modulated Radiotherapy (IMRT),
 - ❖ Volumetric-Modulated Arc Therapy (VMAT)
 - ❖ Radiosurgery

- These technical capabilities and irradiating technics allow for
 - ❖ even better sparing of normal tissue and organs at risk– reduce normal tissue complication probability (NTCP)
 - ❖ maximizing dose to tumor – increase tumor control probability (TCP)



What are the Machines for External Photon Radiotherapy? MLC DESIGN



Varian ProBeam Proton Therapy



IBA Proteus Proton Therapy



Neutron Therapy, USA

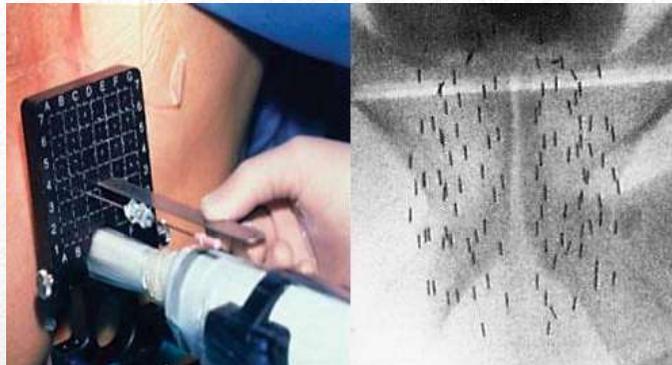
courtesy Wikipedia



Carbon Ion Therapy, Heidelberg, Germany

courtesy Richard Cameron , NationalCompass

What are the Machines for External Particle Radiotherapy? PROTON, NEUTRON AND CARBON ION THERAPY MACHINES



Low Dose Rate Permanent Brachytherapy

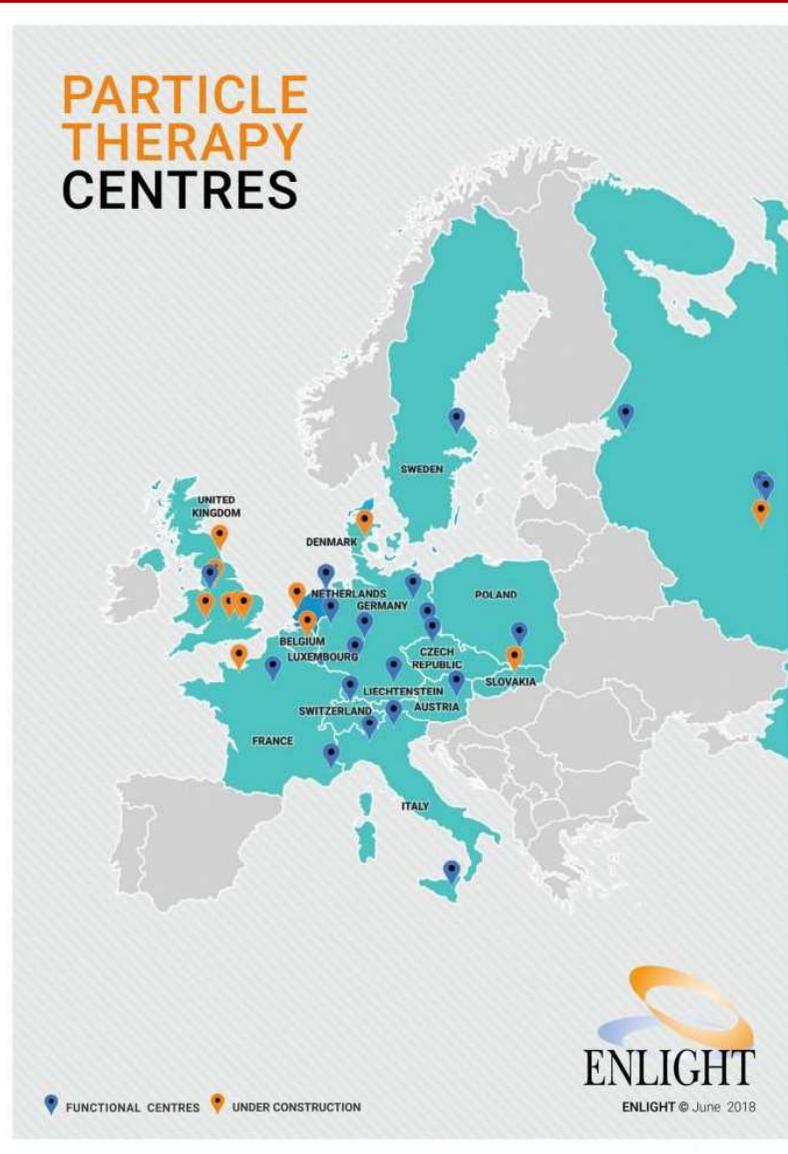
High Dose Rate Temporary Brachytherapy



What are the Machines for Internal Photon Radiotherapy? **BRACHYTHERAPY**



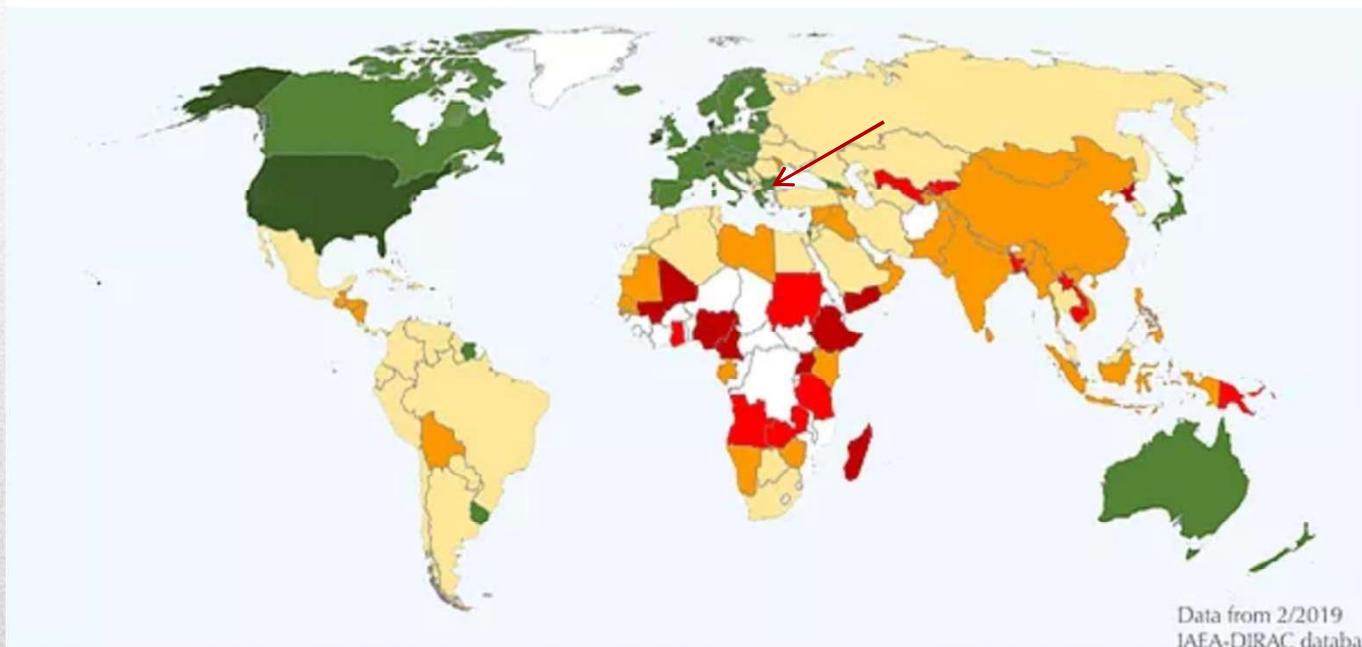
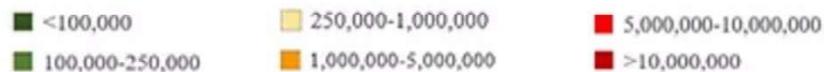
Where are the Radiotherapy Machines – Particle Therapy?





2019 Global Radiotherapy Access

People served per machine



**Where are the Radiotherapy Machines –
Linacs, Cobalt-60 and HDR Brachytherapy?**



Map of RT Centers in the Bulgarian Cancer Hospital Net

BIG STARS– 1 National RT Center and 4 University RT Centers: Sofia, Plovdiv, Varna, Pleven;
SMALL STARS– 11 Regional RT Centers – Varna, Ruse, Schoumen, Veliko Turnovo, Vratza, Plovdiv, Panagyuriste, St Zagora, Burgas, Haskovo, Blagoevgrad;



- 1 Accuray CyberKnife
- 1 Accuray Tomotherapy
- 1 Varian Halcyon
- 14 Varian Clinac
- 1 Elekta Versa
- 7 Elekta Synergy
- 2 Elekta Platform
- 4 Terabalt Co-60 machines
- 1 Rocus Co-60 machine

Where are the Radiotherapy Machines in Bulgaria?

Linacs, Cobalt (Co-60) and Brachytherapy units are shown.

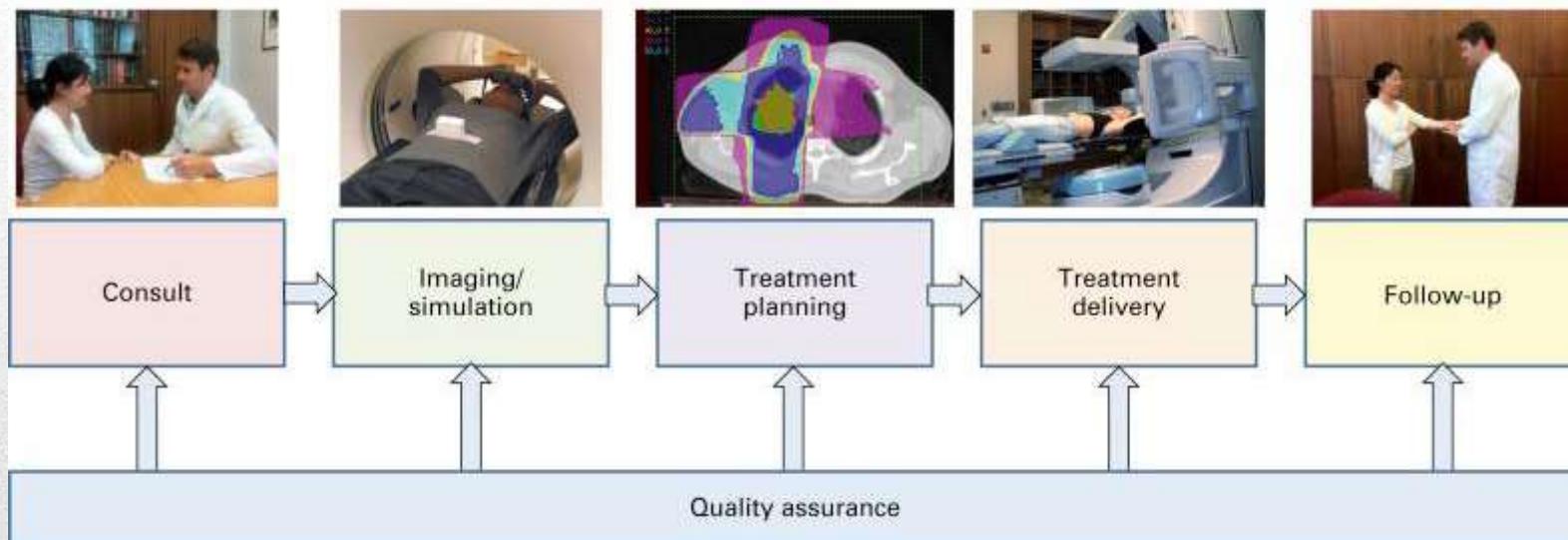


- **Radiation Oncologist** - the oncology doctor who prescribes and oversees the radiotherapy treatment of cancer patients with radiation for either cure or palliation
- **Medical Physicist**- ensures that treatment dosimetric plans are properly tailored for each patient and is responsible for the calibration, accuracy and safety of treatment equipment and for the radiation protection of patients and staff
- **Engineer** - ensures first line technical support
- **Dosimetrist** - works with the radiation oncologist and medical physicist to calculate the proper dose of radiation given to the tumor
- **Radiation Therapist** - administers the daily radiation under the doctor's prescription and supervision
- **Radiation Oncology Nurse** - interacts with the patient and family at the time of consultation, throughout the treatment process and during follow-up care

Who Works in Radiotherapy? or THE RADIATION ONCOLOGY TEAM



Who Works in Radiotherapy or the Radiation Oncology Team in Bulgaria



What is the Workflow in External Radiotherapy?



- Patient is set up in treatment position on a dedicated CT scanner
 - ❖ Immobilization devices may be used to assure patient daily correct positioning
 - ❖ Reference marks or “tattoos” are placed on patient
- CT simulation images are often fused with PET or MRI scans for treatment planning



Workflow - Simulation



CT room dedicated to children

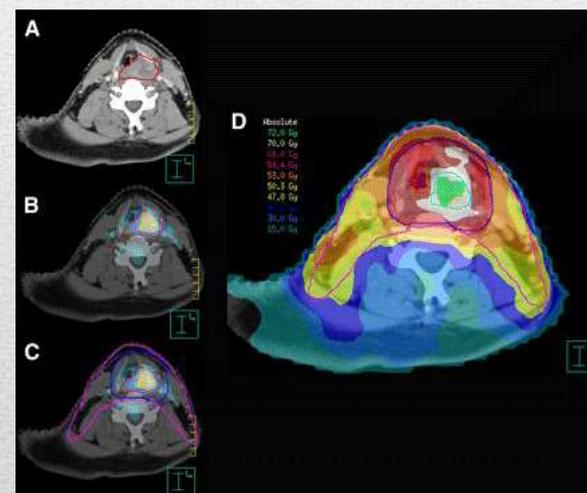
Immobilization masks for children



Workflow - Simulation



- Radiation oncologist outlines the target and organs at risk creating the anatomotopographic treatment plan
- Medical physicist
 - ❖ uses sophisticated software to carefully create an appropriate dosimetric treatment plan
 - ❖ computerized algorithms enable the treatment plan to spare as much healthy tissue as possible
- Radiation oncologist reviews and approves final treatment plan



Workflow - Treatment Planning



The type of treatment depends on the location, size and type of cancer.



- *External radiotherapy or Teletherapy* typically delivers radiation using a linear accelerator

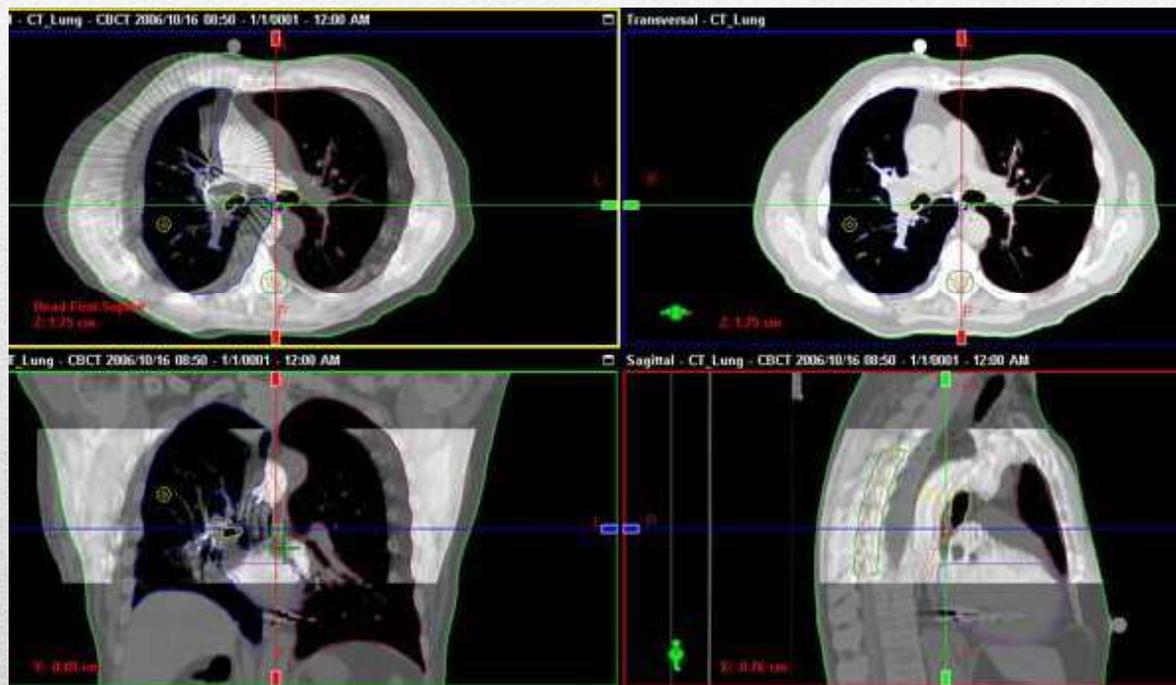
- *Internal radiotherapy or Brachytherapy* involves placing permanently or temporarily radioactive sources into or near the tumor



Workflow - Delivery of Radiotherapy



Image-guided Radiotherapy (IGRT) is frequent use of medical imaging techniques to match and verify patient positioning and tumor location for daily set-up accuracy.

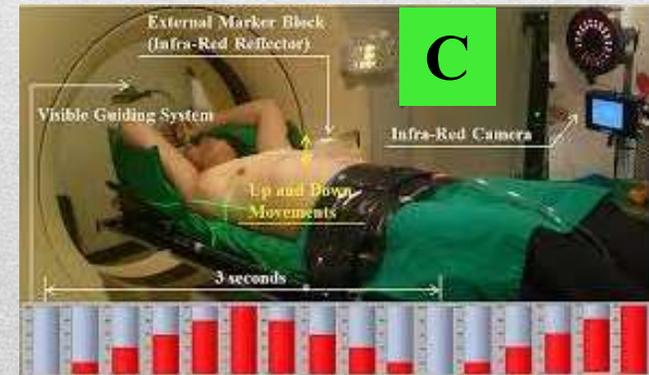
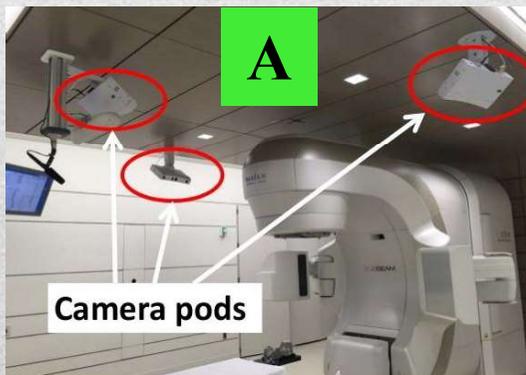


Workflow – Image Guided Radiotherapy



Types of imaging technics for IGRT:

- Ultrasound based image matching
- Video-based 3D surface image matching (pic.A)
- kV or MV planar image matching (MV-MV, kV-kV or kV-MV matching) (pic.A)
- kV or MV Cone beam CT (CBCT) volumetric image matching (pic.A)
- kV or MV Fan beam CT (FBCT) volumetric image matching (pic.B)
- MRI based volumetric image matching
- Respiratory Gating Technics for tracking motion of tumors (pic.C)

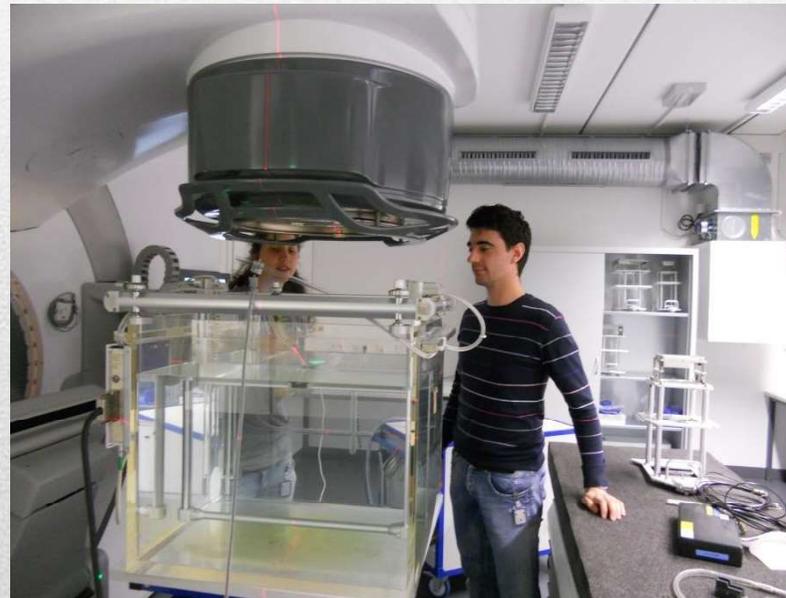


Workflow – Image Guided Radiotherapy



Both radiotherapy equipment and each patient treatment plan go through many safety checks complying with national regulations

Dosimetry equipment: Phantoms, Detectors, Electrometers



Workflow - Safety and Quality Assurance



- External Megavoltage Radiotherapy (energy > 1 MV)
 - ❖ Two-dimensional Radiotherapy (2D RT)
 - ❖ Three-dimensional Radiotherapy (3D RT)
 - ❖ Three-dimensional Conformal Radiotherapy (3D CRT)
 - ❖ Intensity Modulated Radiotherapy (IMRT)
 - ❖ Volumetric Modulated Arc Therapy (VMAT)
 - ❖ Adaptive Radiotherapy (ART)
 - ❖ Total Body Irradiation Radiotherapy (TBI RT)
 - ❖ Image Guided Radiotherapy (IGRT)
 - ❖ Respiratory Gated Radiotherapy (RGRT)
 - ❖ Intraoperative Radiotherapy (IORT)
 - ❖ Stereotactic Body Radiotherapy (SBRT)
 - ❖ Stereotactic Radiosurgery (SRS)

**What are the Technics
of External Megavoltage Radiotherapy?**



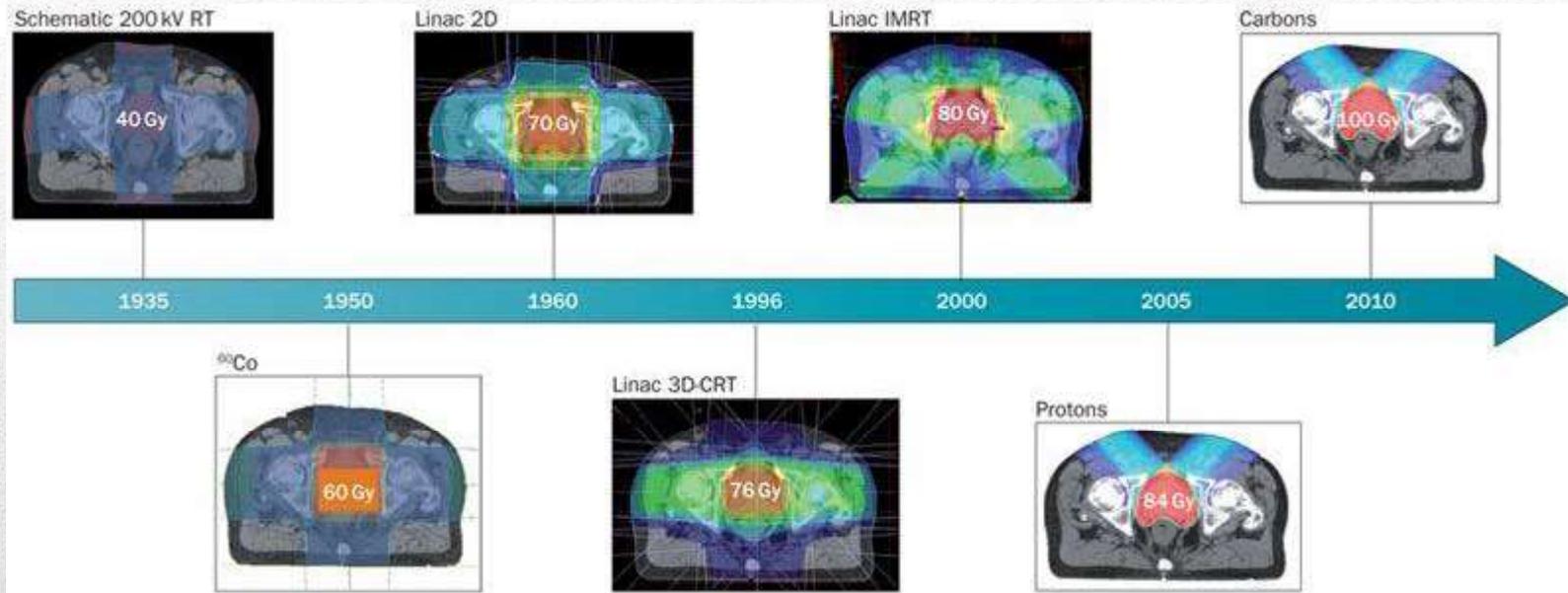
Types of Particle Beam Therapy:

- Hadron Therapy (protons and ions)
- Fast Neutron Therapy (FNT)
- Neutron Capture Therapy (NCT)
- Electron Therapy

Advantages:

- Charged particles deposit most of their energy at a given depth, minimizing risk to tissues beyond that point
- Allows for highly specific targeting of tumors located near critical structures
- Most commonly used in treatment of pediatric, central nervous system and intraocular malignancies

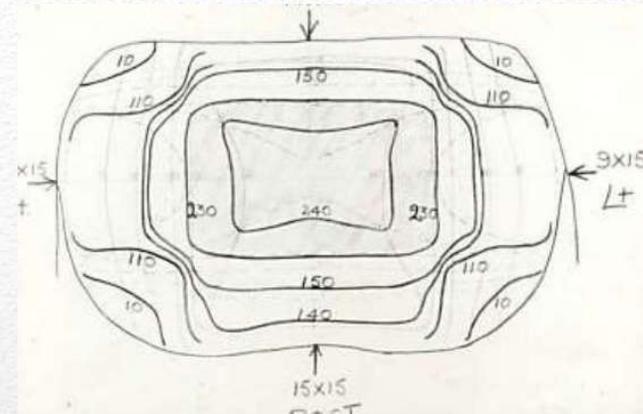
What are the Types of External Particle Therapy?



Evolution of Dosimetry Planning



- Uses patient CT scans to create a 3D picture of the patient anatomy to delineate precisely tumor and surrounding organs at risk
- Utilized with MLC equipped machines

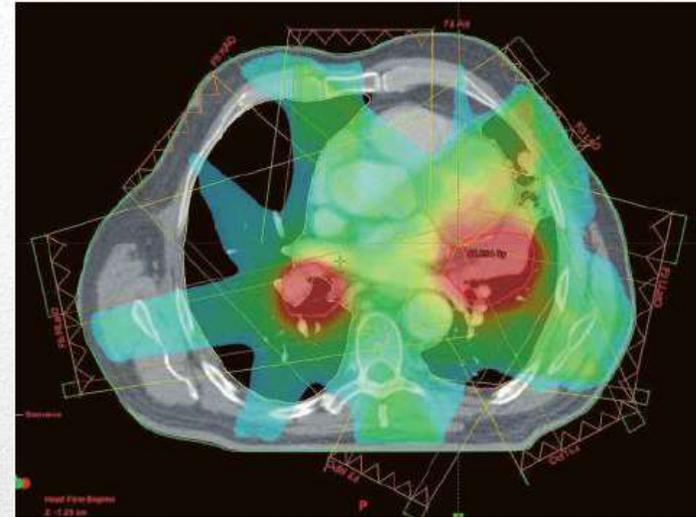


- Uses computer software algorithm for computing dose volume distribution for a multifield plan
 - ❖ Improved precision than 2D planning with rectangular fields used with Co-60 machines,
 - ❖ Decreased normal tissue damage

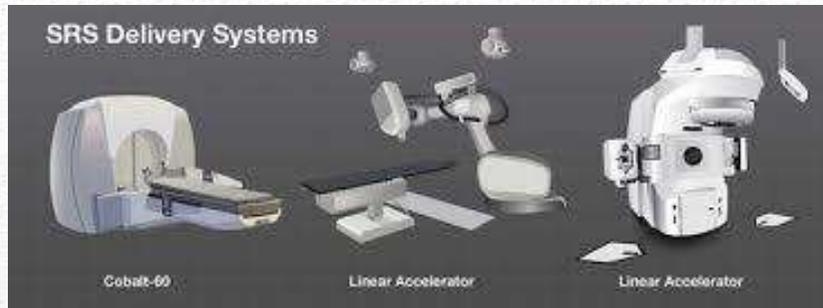
Three-Dimensional Conformal Radiation Therapy (3D CRT)



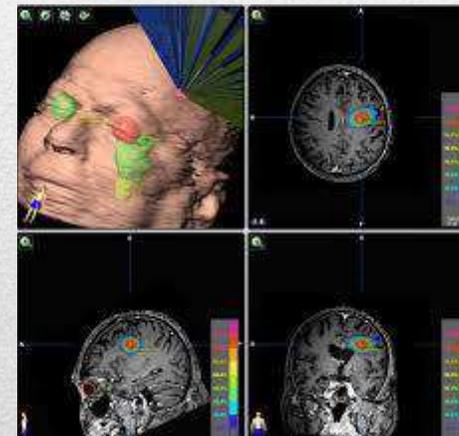
- IMRT and VMAT are highly sophisticated radiotherapy technics allowing radiation to be shaped more exactly to fit the tumor
- Radiation is delivered by multiple fields or one or multiple arcs divided into segments with adjusted intensity through dynamic varying MLC, dose and gantry and colimator rotation
- IMRT and VMAT allows higher doses of radiation to be delivered to the tumor while sparing more healthy surrounding tissue



Intensity Modulated and Volumetric Modulated Arc Radiotherapy (IMRT and VMAT)



SRS and SBRT are specialized types of external beam radiation that use focused radiation beams targeting a well-defined tumor in the head or in the body.



Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT)



Internal RT or Brachytherapy is treatment of cancer with **sealed radioactive sources** such as ^{125}I , ^{103}Pd , ^{192}Ir , ^{137}Cs inserted very close up to the tumor.

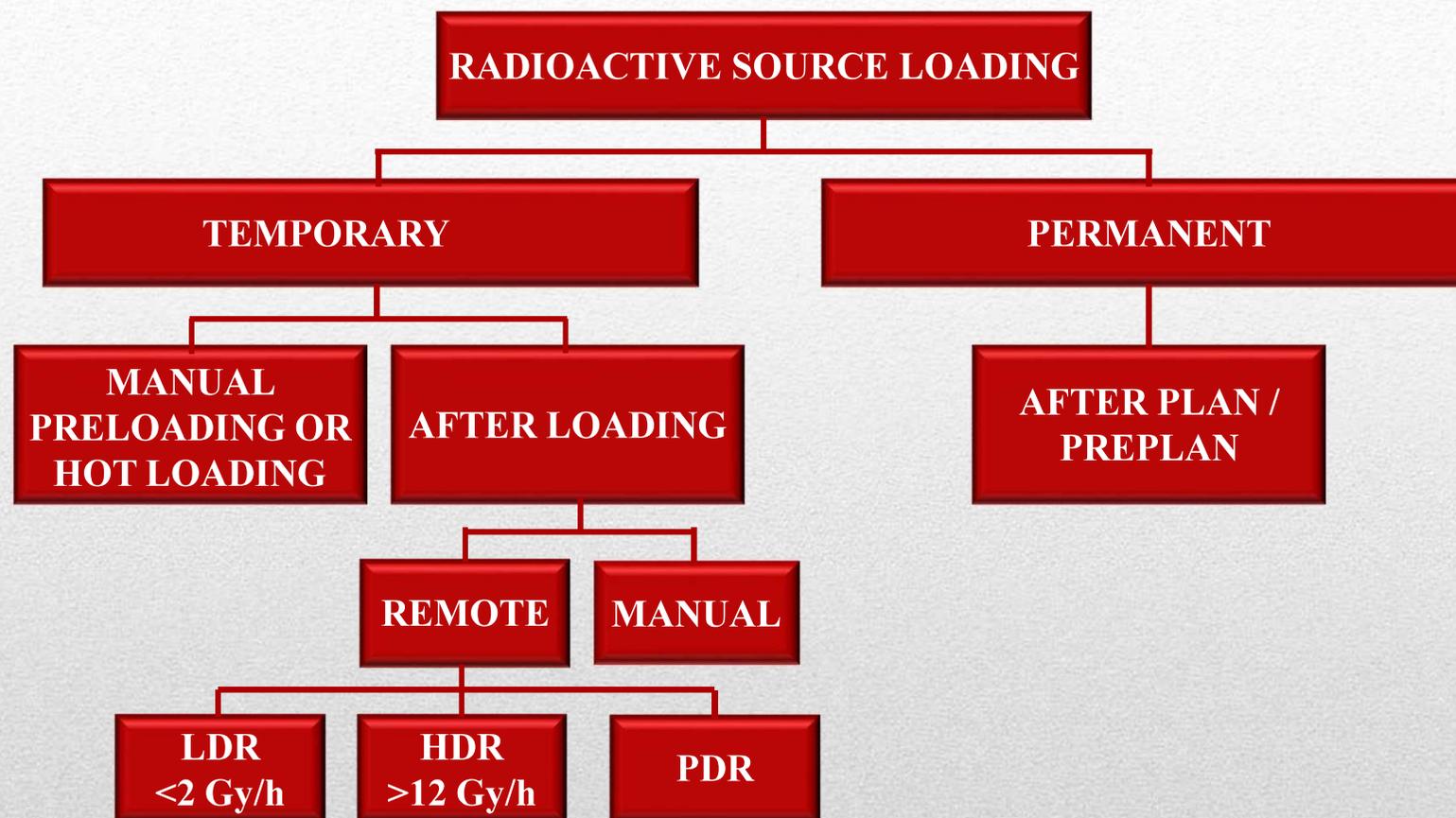
According to location of radioactive implant it might be:

- ***Intracavitary brachytherapy*** - the source is inserted into a body cavity such as the vagina or uterus
- ***Interstitial brachytherapy*** - the sources are placed directly into the tissue (prostate, vagina)
- ***Intraluminal brachytherapy*** - the source is placed within intraluminal space such as the esophagus or trachea
- ***Surface (mould) brachytherapy*** - moulds are attached to the surface of the skin
- ***Intravascular brachytherapy*** - the source is placed within blood vessels
- ***Intra-operative implants*** – the surface applicator is in direct contact with the surgical tumor bed

What are the Types of Internal Radiotherapy or Brachytherapy?



According to way of loading of radioactive implant it might be:



What are the Types of Internal Radiotherapy or Brachytherapy?



IORT delivers a concentrated dose of radiation therapy to a tumor bed during surgery



Intraoperative Radiation Therapy (IORT)



Radiation can also be delivered by injecting or swallowing **unsealed radiopharmaceuticals**.
Some of the locations and radioisotopes used are:

- For treating bone metastases radioactive isotopes absorbed primarily by cancer cells may be used such as Metastron ($^{89}\text{Strontium}$), Quadramet ($^{153}\text{Samarium}$) and Xofigo ($^{223}\text{Radium}$)
- For treating thyroid cancer radioactive iodine (I^{131}) is used
- For treating lymphomas radioactive isotopes may be attached to an antibody targeted at tumor cells (Zevalin, Bexxar)
- For treating primary or metastatic liver cancer radioactive “beads” may be used (Y^{90} -Microspheres)



Systemic or Metabolic Radiotherapy

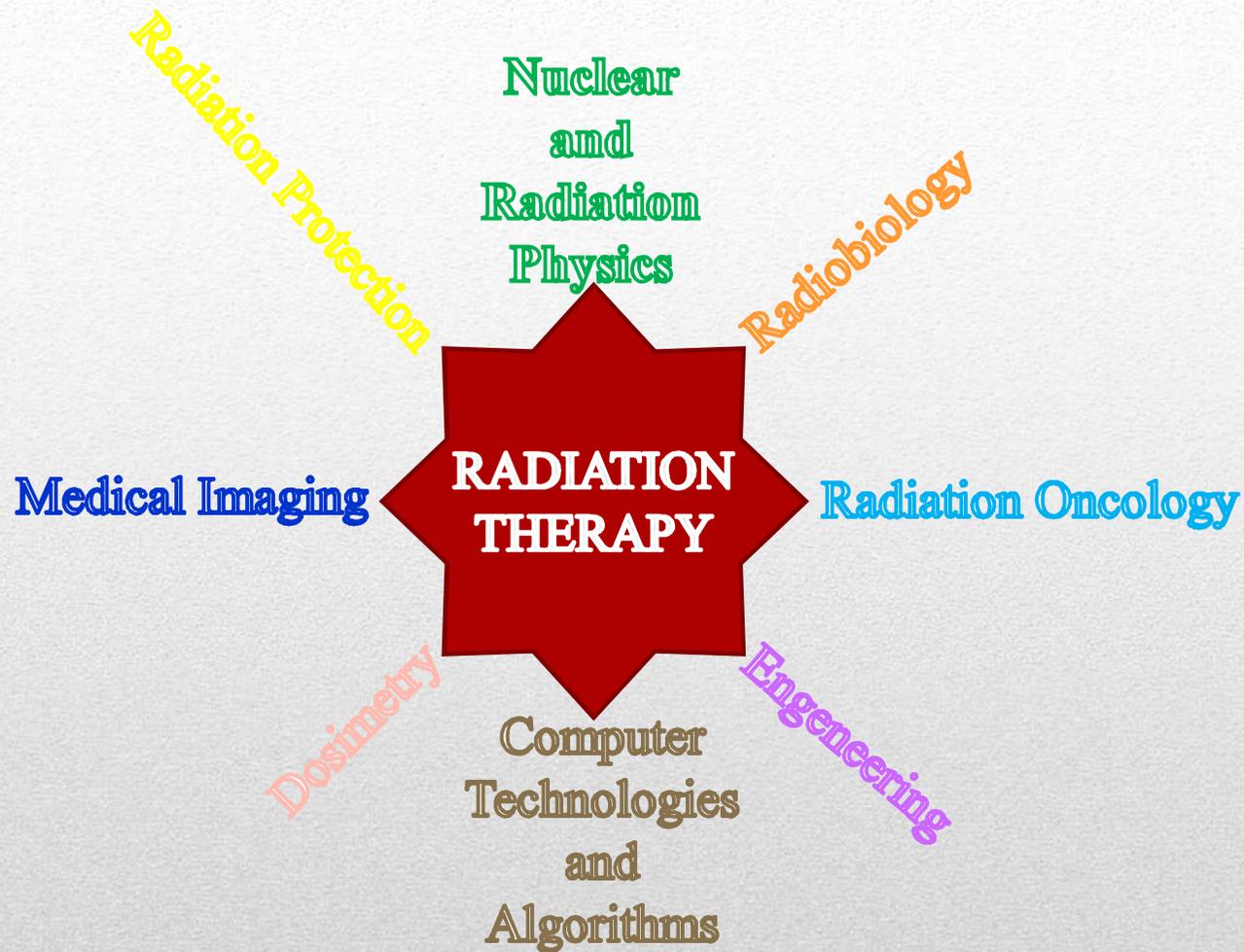


Though ionizing radiation remains one of the most effective tools in the therapy of cancer cure, answers to a number of questions remain:

- Further ways to optimize the effectiveness of radiation therapy in combination with other modalities of treatment?
- Further ways for precise and accurate treatment delivery by more precise and accurate tumor localisation in treatment planning and delivery? Real-time IGRT advances?
- Further ways to lower side effects to normal tissues? Adaptive RT advances?

Answers to these and other questions together with ongoing advancements in radiation therapy technology and techniques will ultimately lead to continued improvement in cancer treatment.

What is the Future of Radiotherapy?



Multidisciplinary Approach



- Radiation therapy is a well established modality for the treatment of numerous malignancies
- Radiation oncology team are specialists trained to treat cancer with a variety of forms of radiation
- Treatment delivery is safe, quick and painless due to sophisticated technology, irradiation technics and computing algorithms

Summary



Ruse Complex Oncology Center



“Theory is when you know everything but nothing works.

Practice is when everything works but no one knows why.

In our lab, theory and practice are combined: **nothing works and no one knows why.”**

Combining Theory with Practice



**KEEP
CALM
AND
BEAM
ON**

**THANK YOU
FOR YOUR ATTENTION!**