Principles and Applications of Radiotherapy

A Practical Introduction to Oncology

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Radiotherapy

Definition

Science & art of using ionising radiation for therapeutic purposes.

Aim

To deliver a tumoricidal dose to a target volume whilst sparing the surrounding normal structures

History of Radiotherapy

1895 Roentgen discovered X-Rays

1896 Lancet report of use of X-Rays for diagnostic purposes

1897 Freund treated a hairy mole

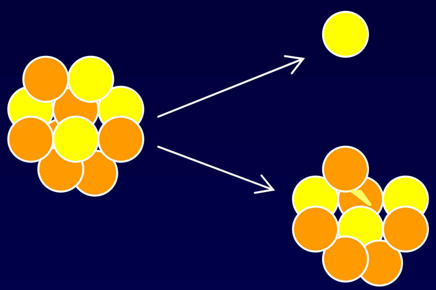
→ EXTERNAL BEAM RT

1898 Radium isolated by the Curies

1907 Uterine tumour treated with radium

→ BRACHYTHERAPY

Radioactivity



“Unstable” → “Stable”

Alpha particle (He+)
Beta particle (Electron)
Gamma ray - most commonly used in radiotherapy

Activity: Number of disintegrations per unit time of a radioactive isotope

S.I. Unit = Becquerel : 1 disintegration /sec

1 Curie : standard volume of radium = 3.7×10^{10} Bq

Tells us how radioactive the source is

Gives us no information about the dose the patient is actually receiving

Radiotherapy

Absorbed Dose : Energy absorbed from ionising radiation per unit mass

S.I. Unit: Gray = 1 J/Kg = 100 rads

Natural sources

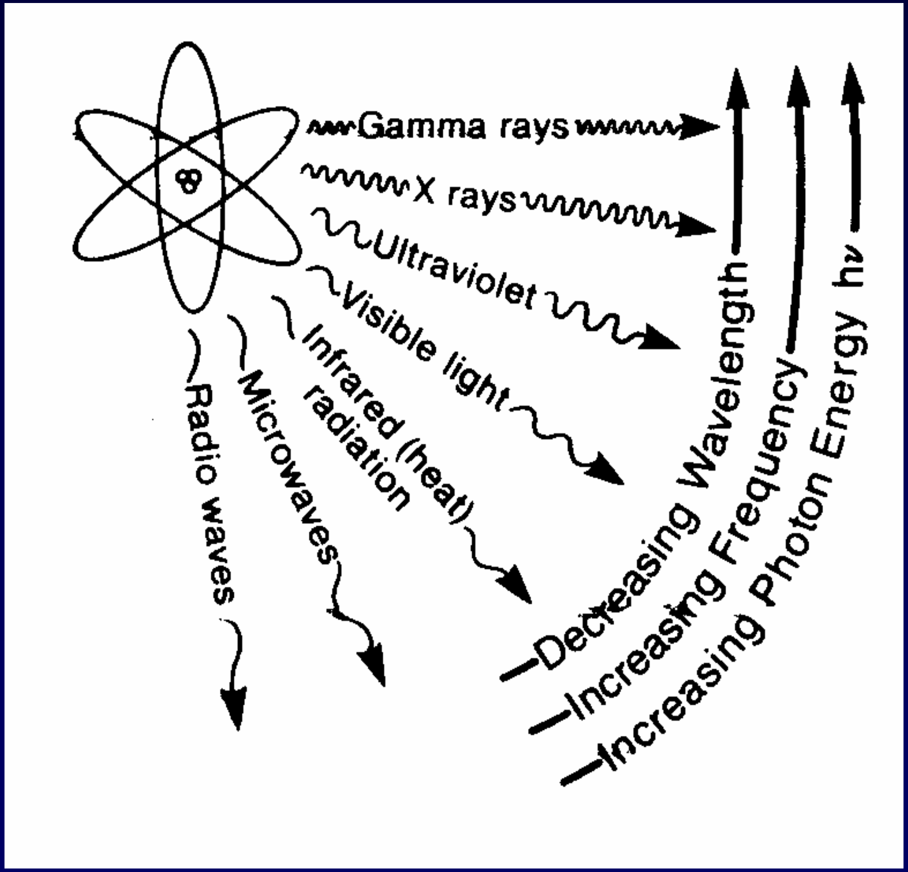
Cobalt – 60

Iridium – 192

Artificial sources

Linear accelerator

The Electromagnetic Spectrum



- EMR used in radiotherapy may be **x-rays or gamma rays**
- Both have identical physical properties
  - High frequencies
  - Short wavelengths
- High energies sufficient to break chemical bonds
- Photon energy E=hν
  - Diagnostic X-Ray 20-100kV
  - Therapeutic X Ray 6-20MV

Direct and Indirect Ionization

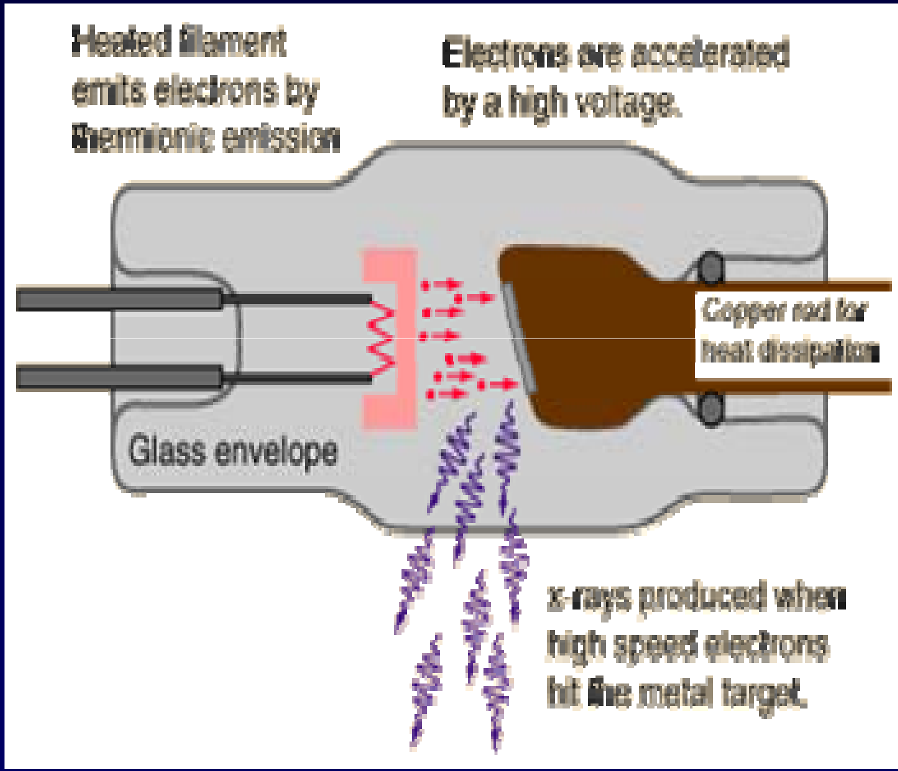
- The process by which a neutral atom acquires a positive or negative charge is called ionization.
- DIRECT IONIZATION: charged particles such as electrons, protons, α particles cause ionization by collision as they penetrate matter.
- INDIRECT IONIZATION: uncharged particles such as neutrons, photons liberate directly ionizing particles when they interact with matter.

Photons

- Non-ionizing radiation is absorbed evenly
- Ionizing radiation is absorbed unevenly in discrete packets (quanta, photons)
- It is the energy in each packet that can break chemical bonds, not the total energy
- A 4 Gray dose of x-rays can be lethal if given to the whole body. This involves the absorption of the same energy absorbed as heat from a sip of hot coffee!

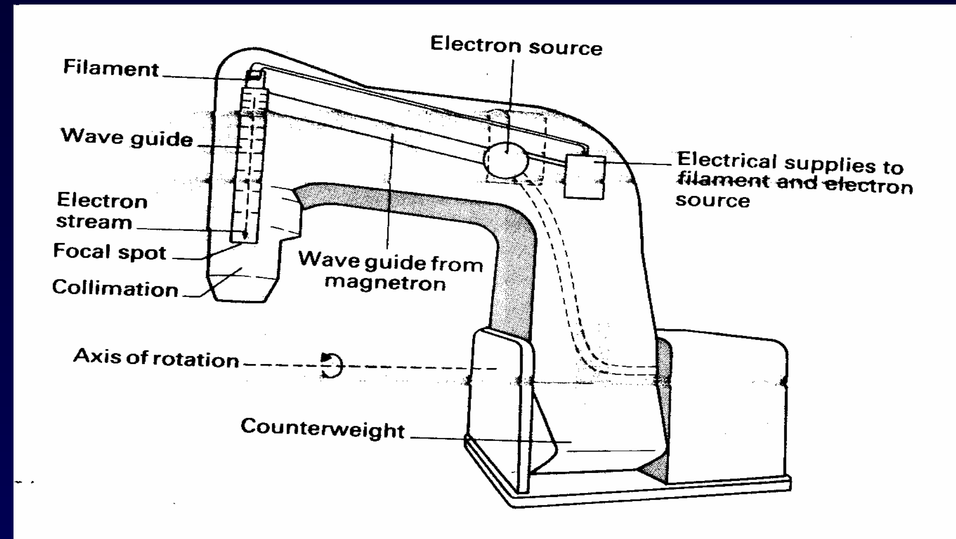
Production of X – rays.

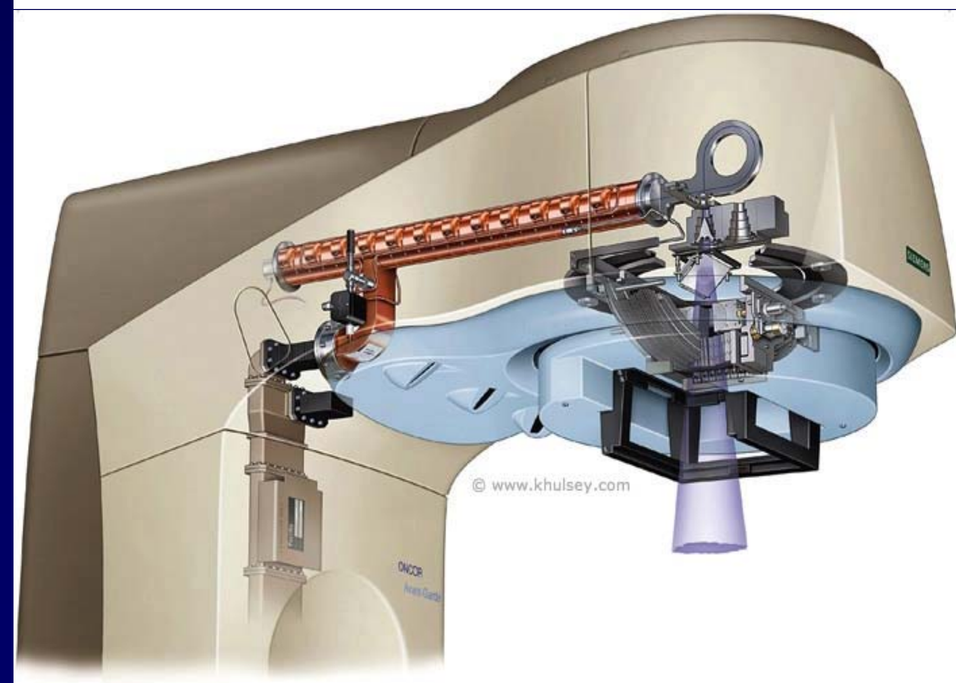
- Artificial production by electrical means
- Electrons are accelerated to a high energy and then stopped abruptly in a heavy metal target
- The kinetic energy of the electrons is converted into x-rays



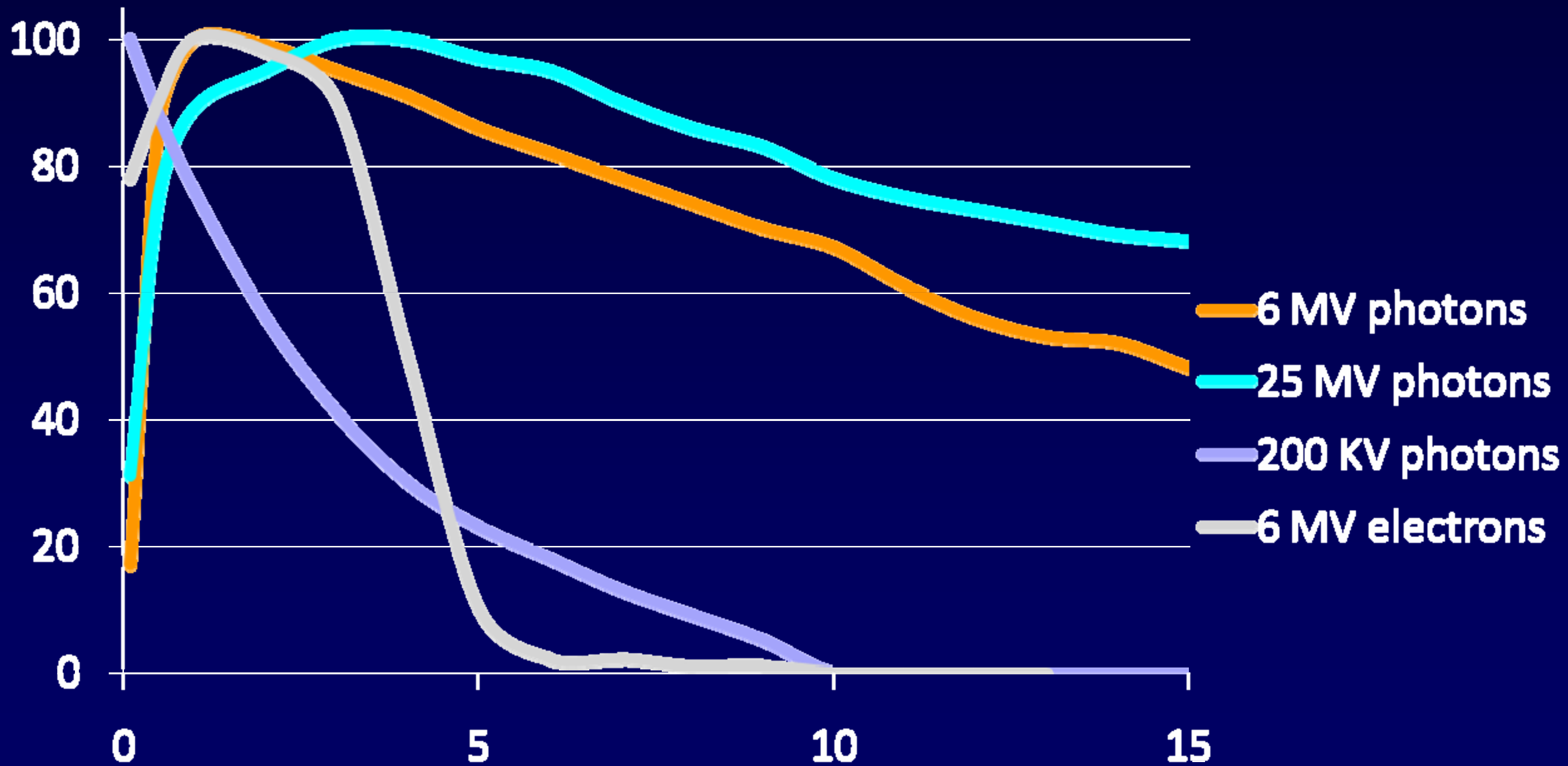
Types of X- Rays

- KILOVOLTAGE – Superficial X-rays.
- ORTHOVOLTAGE – Deep X-rays.
- MEGAVOLTAGE - X-rays are produced in a linear accelerator.

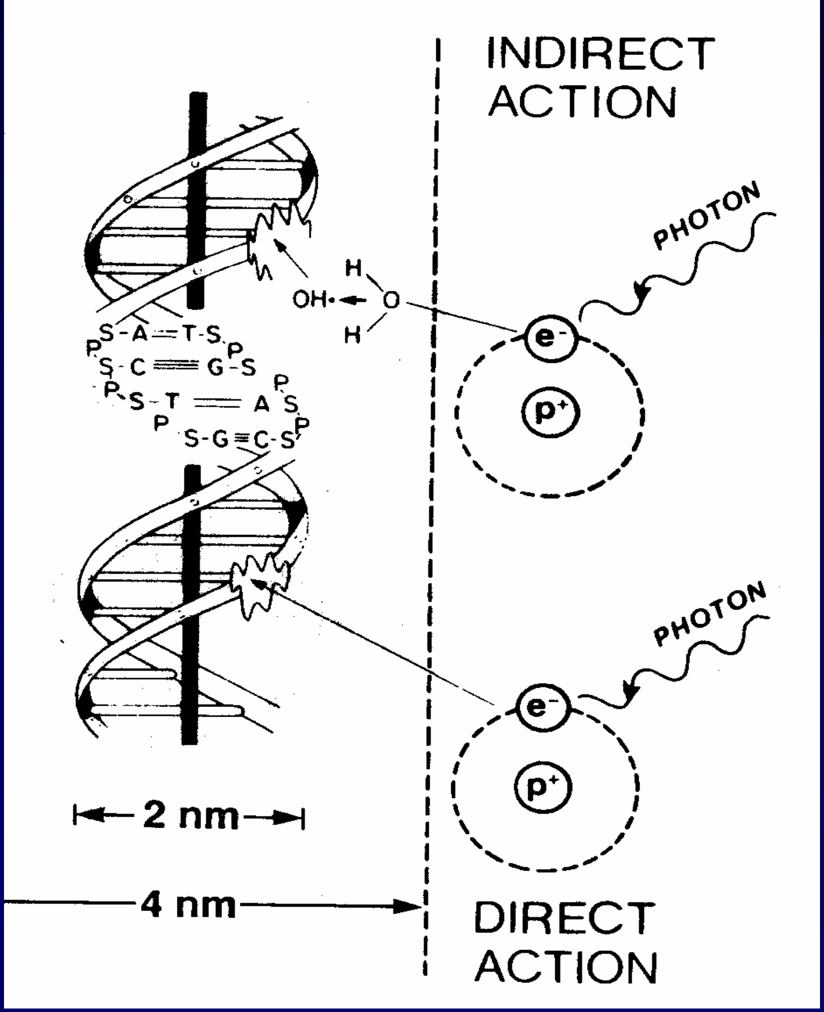




Beam characteristics of different radiotherapy beams



Mechanism of Action.



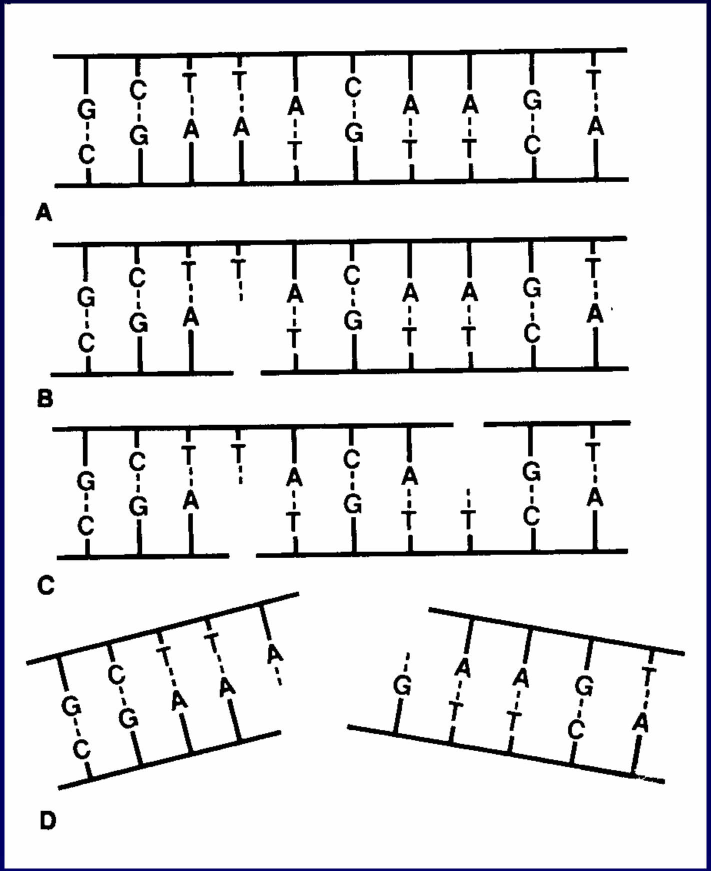
DIRECT ACTION

Electron interacts with DNA directly.

INDIRECT ACTION

Electron interacts with a water molecule to produce a hydroxyl radical which produces damage to the DNA.

DNA Strand Breaks



- Major biological target is DNA.
- Interactions cause chemical changes in structure of DNA.
- Double strand breaks are lethal lesions that lead to cell death

Biological Effects

Breakage of chemical bonds and subsequent biological damage may result in:

1. Cell Death
   - Hours, days, months
2. Carcinogenesis
   - Years
3. Genetic Mutations
   - Generations

Fractionation

Tumours have impaired repair mechanisms

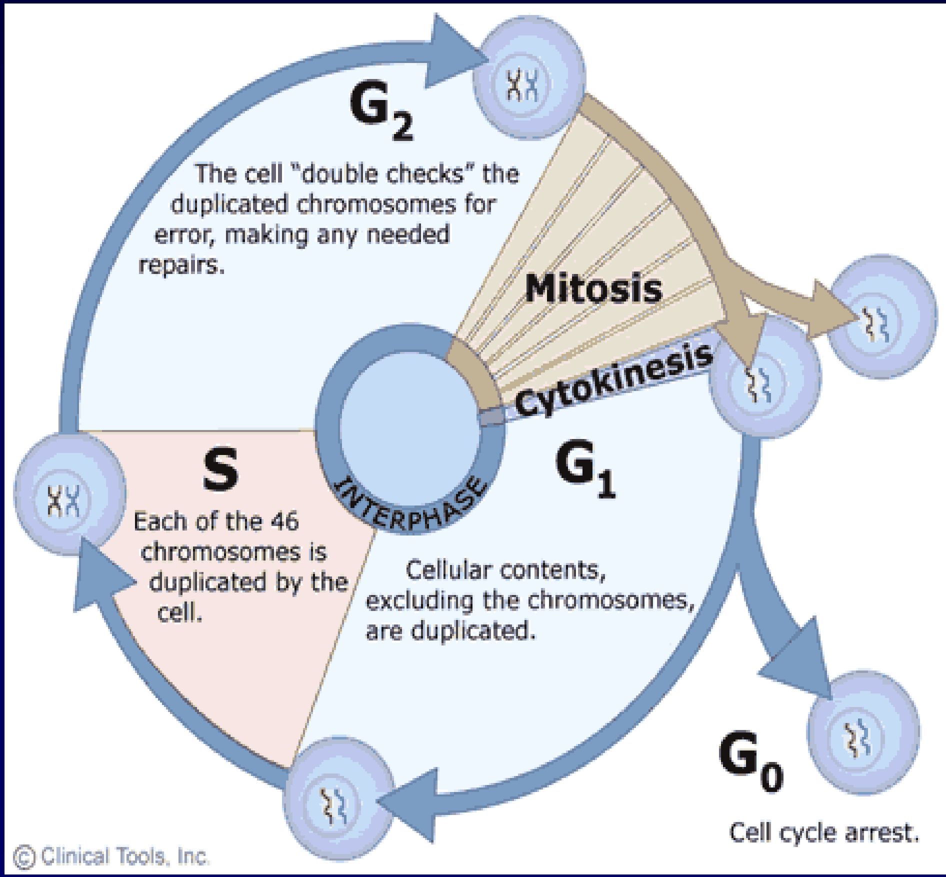
Multiple small fractions allow repair of normal cells and a higher total dose to tumour

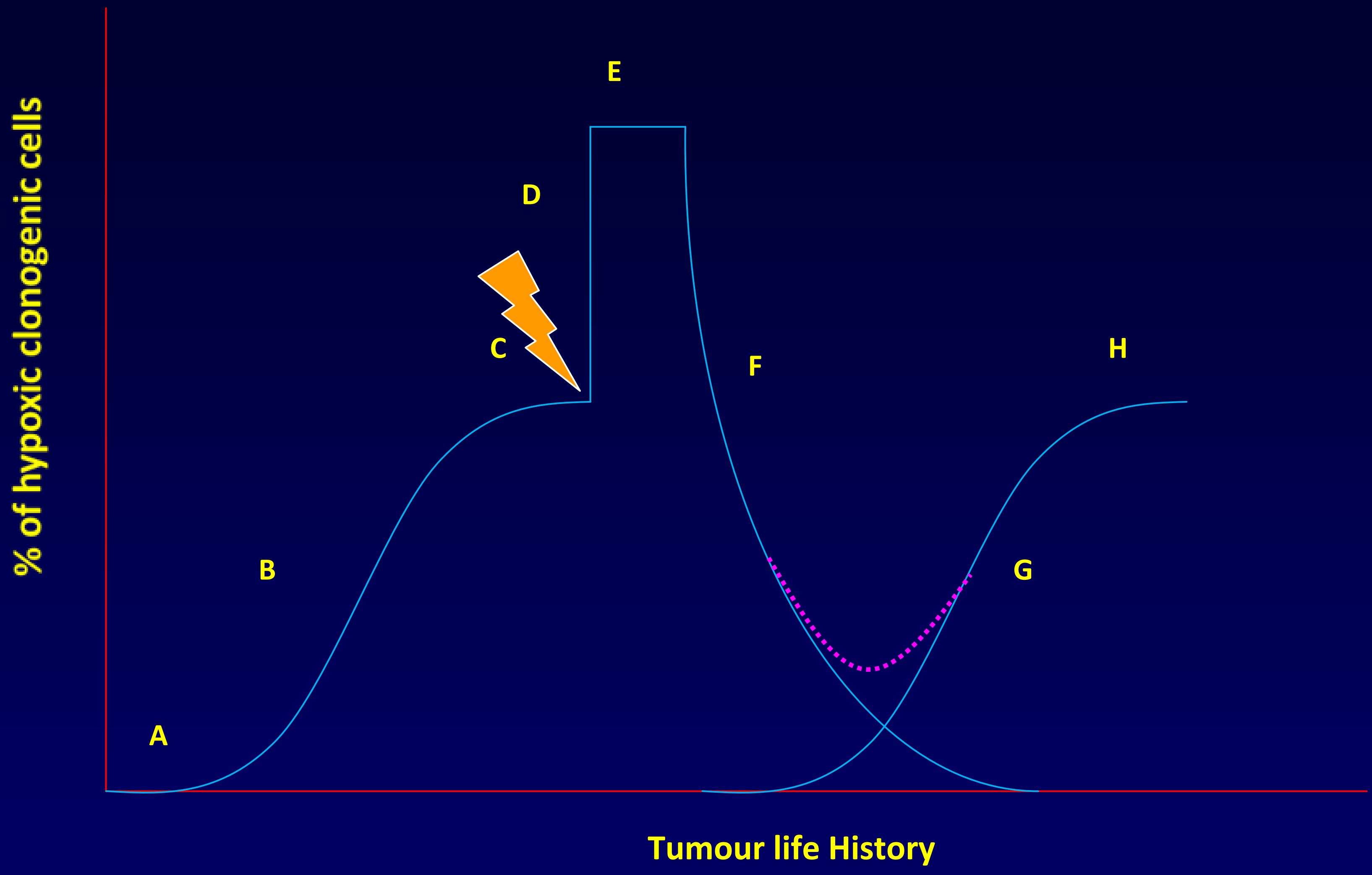
Incidence of long-term side effects is related to dose per fraction

Conventional RT given Mon-Fri for 5-7weeks

Fractionation.

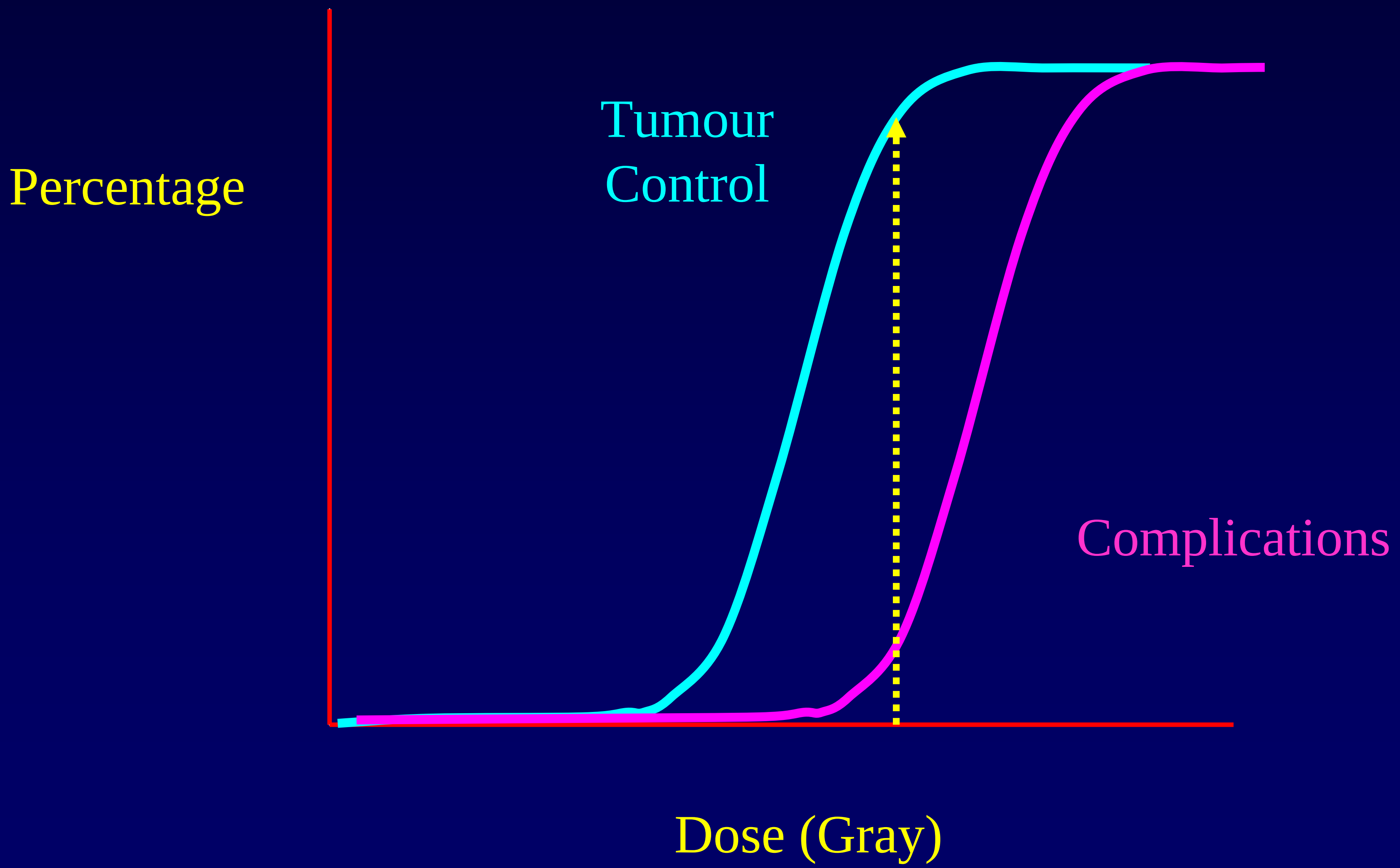
	Effect of Fractionation on	
	Tumor	Normal tissue
Repair	Bad	Good
Repopulation	Bad	Good
Reassortment	Good	Bad
Reoxygenation	good	Bad





A- Small tumour – no hypoxic cells
B-C – Increasing hypoxic cells as tumour grows
D – After dose of Radiotherapy all oxygenated cells die and hypoxic cells increase
F- The hypoxic cells decrease due to reoxygenation
G -Tumour re grows to establish proportion of hypoxic cells (H)

Dose Response Curve



Types of Radiotherapy

- External Beam Radiotherapy
  - Megavoltage (6 - 25MV)
  - DXT (2 - 300 KV)
  - Superficial (60 - 150KV)
  - Charged particle
    - Electrons, protons, neutrons
- Brachytherapy
  - Intracavitary
  - Interstitial
  - Targeted
  - Intraluminal

Uses of Radiotherapy

Loco-regional treatment

- surgical principles for target volumes
- Not limited by tissue planes
- Often in combination with surgery

Uses

Radical

Adjuvant

Neoadjuvant

Palliative

Benign disease

Radical Radiotherapy

- Primary treatment with curative intent
- When surgery likely to be inadequate or associated with significant functional or cosmetic morbidity
- Need for multidisciplinary approach
- Accept acute toxicity
- Often concurrent chemotherapy as radiosensitiser

Examples: ENT, cervix, prostate, oesophagus, lung, anus, bladder

Adjuvant Radiotherapy

- Treatment after primary modality if significant risk of microscopic disease
- Reduces risk of local recurrence
- Allows less radical surgery

Examples: Breast, head and neck, endometrium

Positive / close margins

Palliative Radiotherapy

- Unlikely to prolong survival
- Late toxicity less important
- Acute toxicity kept to minimum
- Short fractionation used if possible
- Significant benefit for symptom control

Examples:Spinal cord compression, bleeding, bone metastases, SVCO, fungation

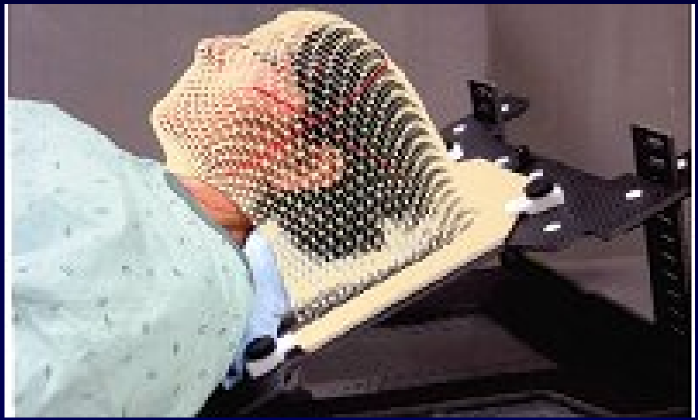
EXTERNAL BEAM RADIOTHERAPY

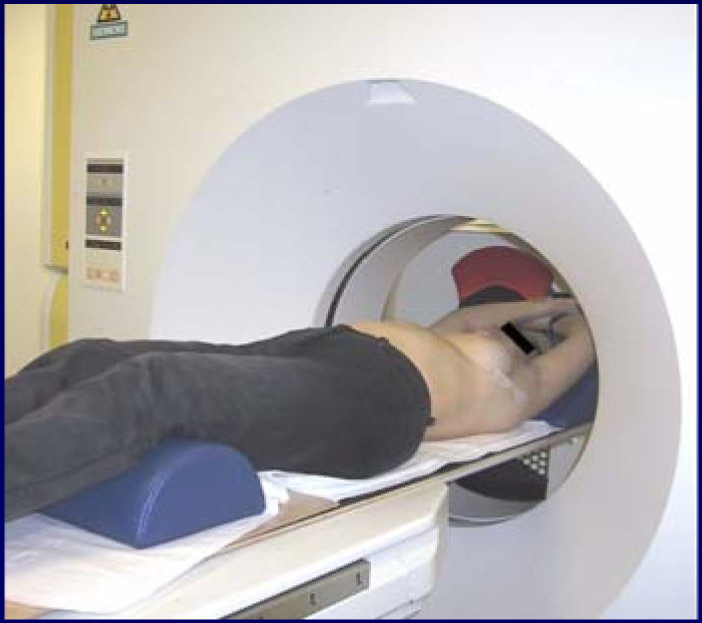
External Beam Radiotherapy
Steps in treatment process

1. Patient positioning
2. Target Volume localisation
3. Treatment Planning
4. Treatment delivery
5. Assess tumour response

Patient positioning

- Need to plan and treat the patient in a reproducible position
    - Flat bed, lasers
    - Patient tattoos / landmarks
- Immobilisation aids
    - Ankle / knee supports, chest boards
    - thermoplastic shells

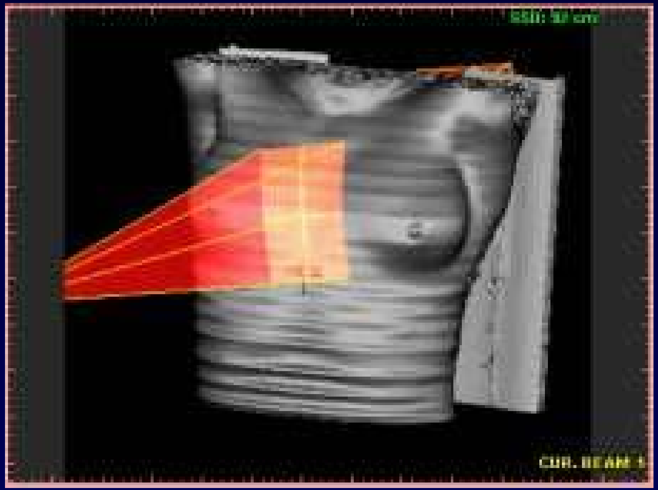




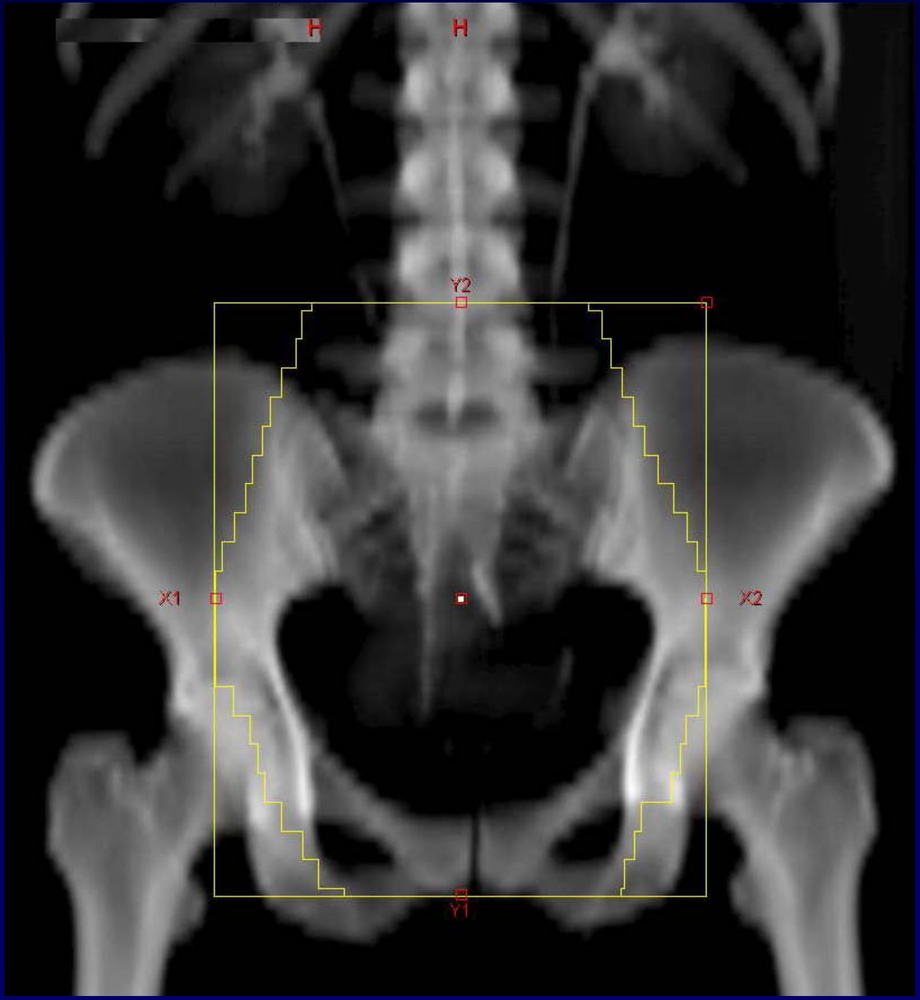
Target volume localisation

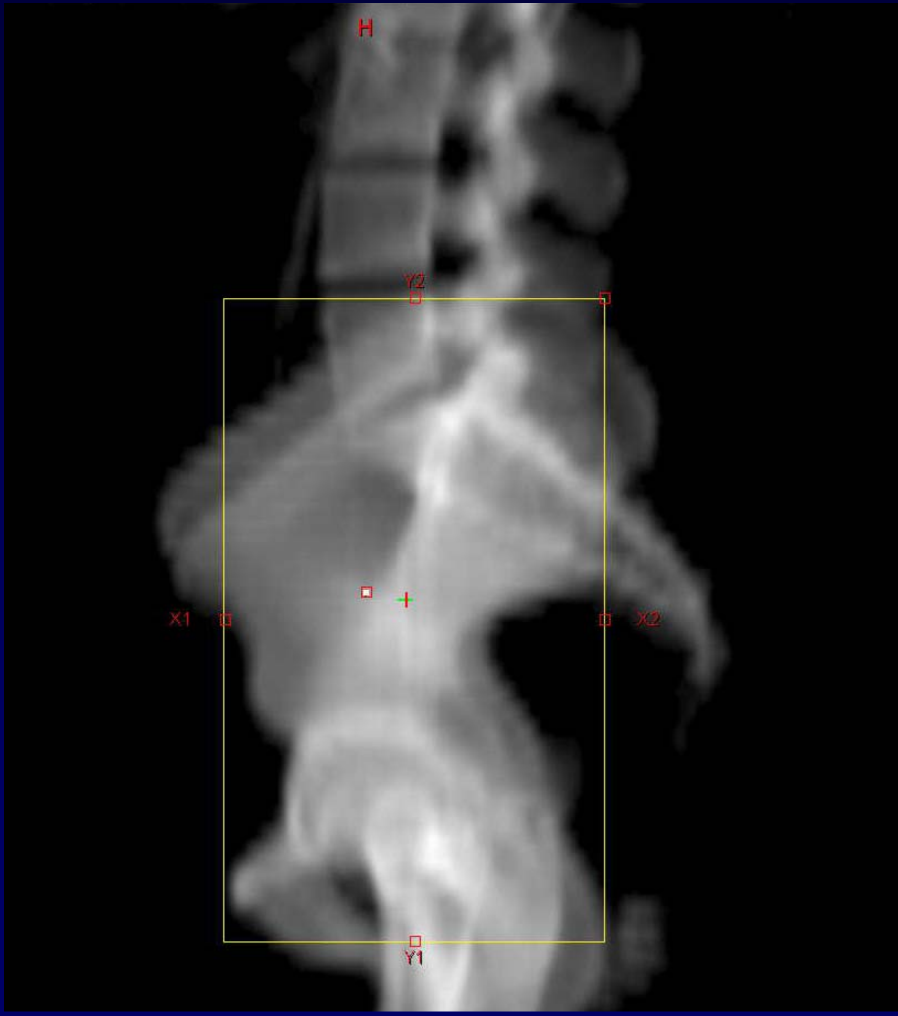
Define volume required to be treated
Prescribe required dose to each target

Methods to localise
Clinical – eg skin tumours, breast
Conventional – simulator
Image based

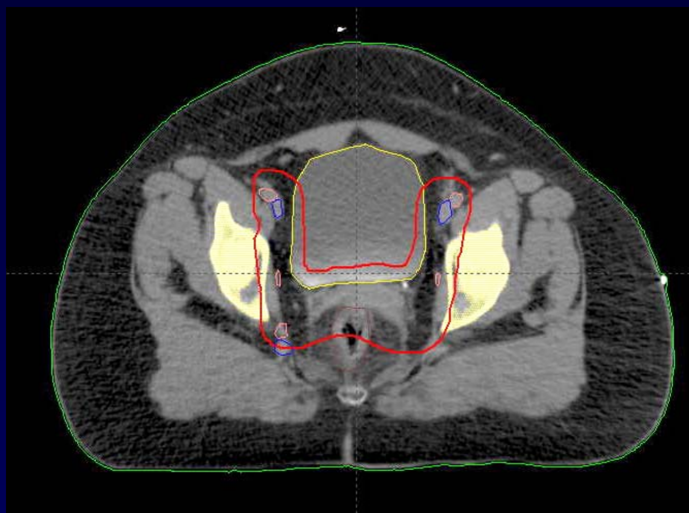


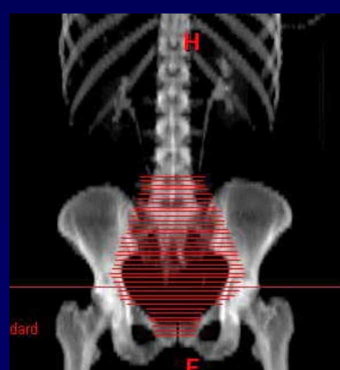
Conventional Radiotherapy

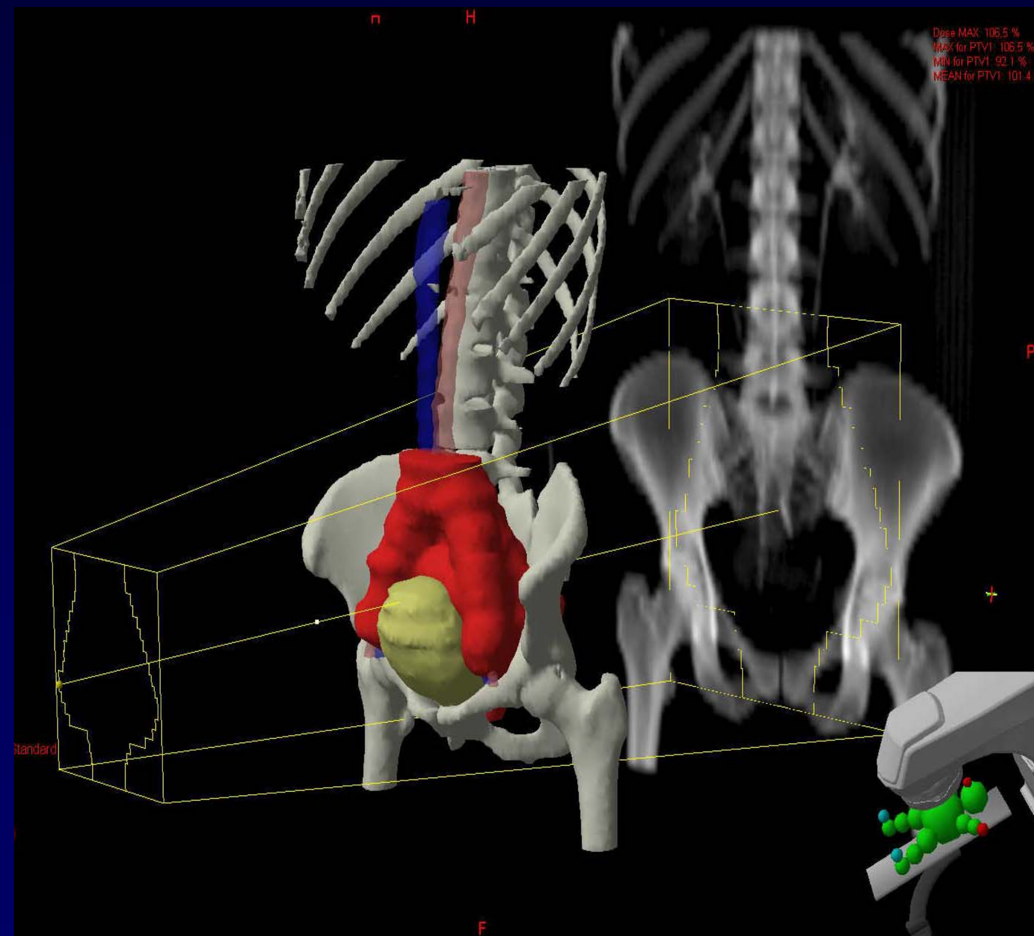


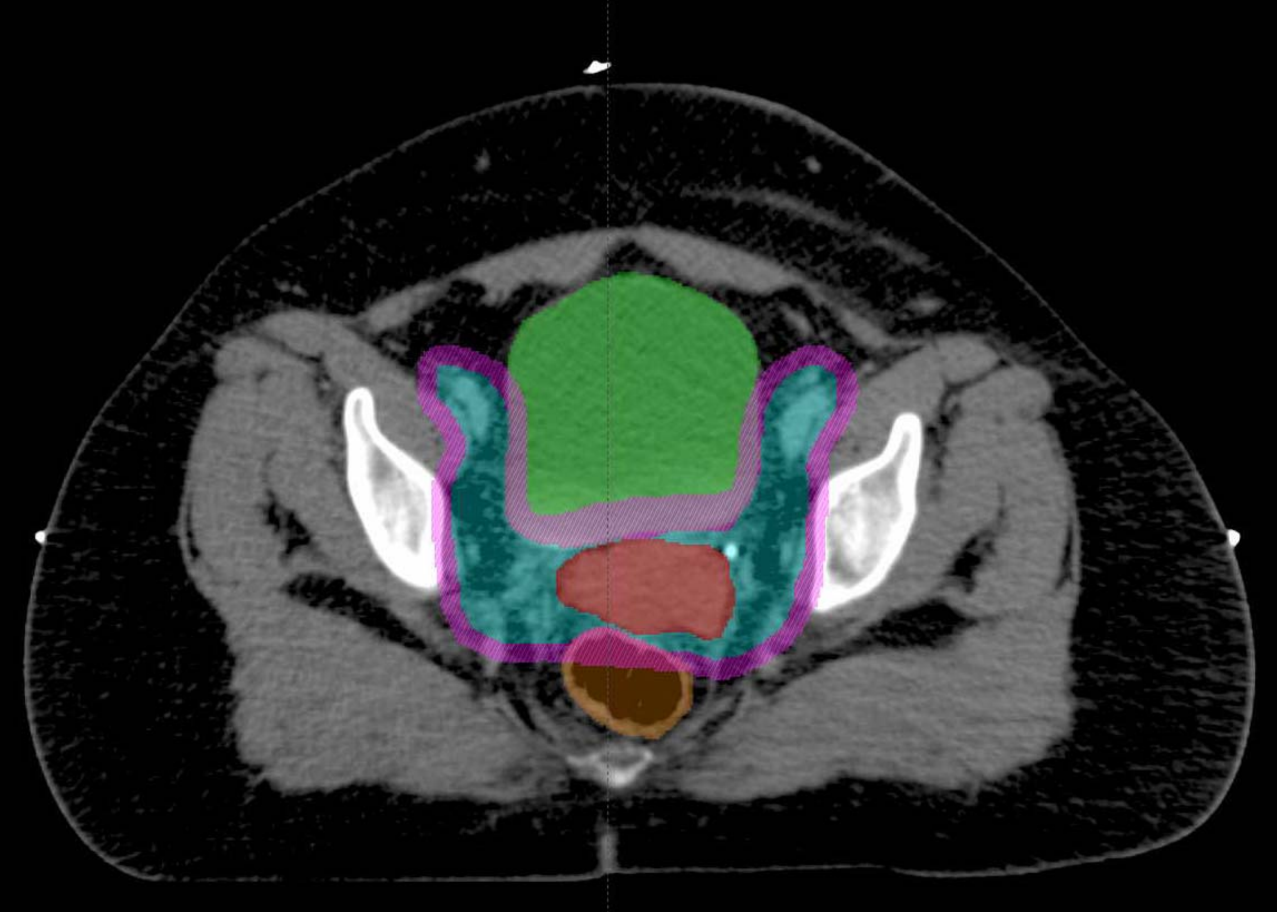


3-Dimensional Planning

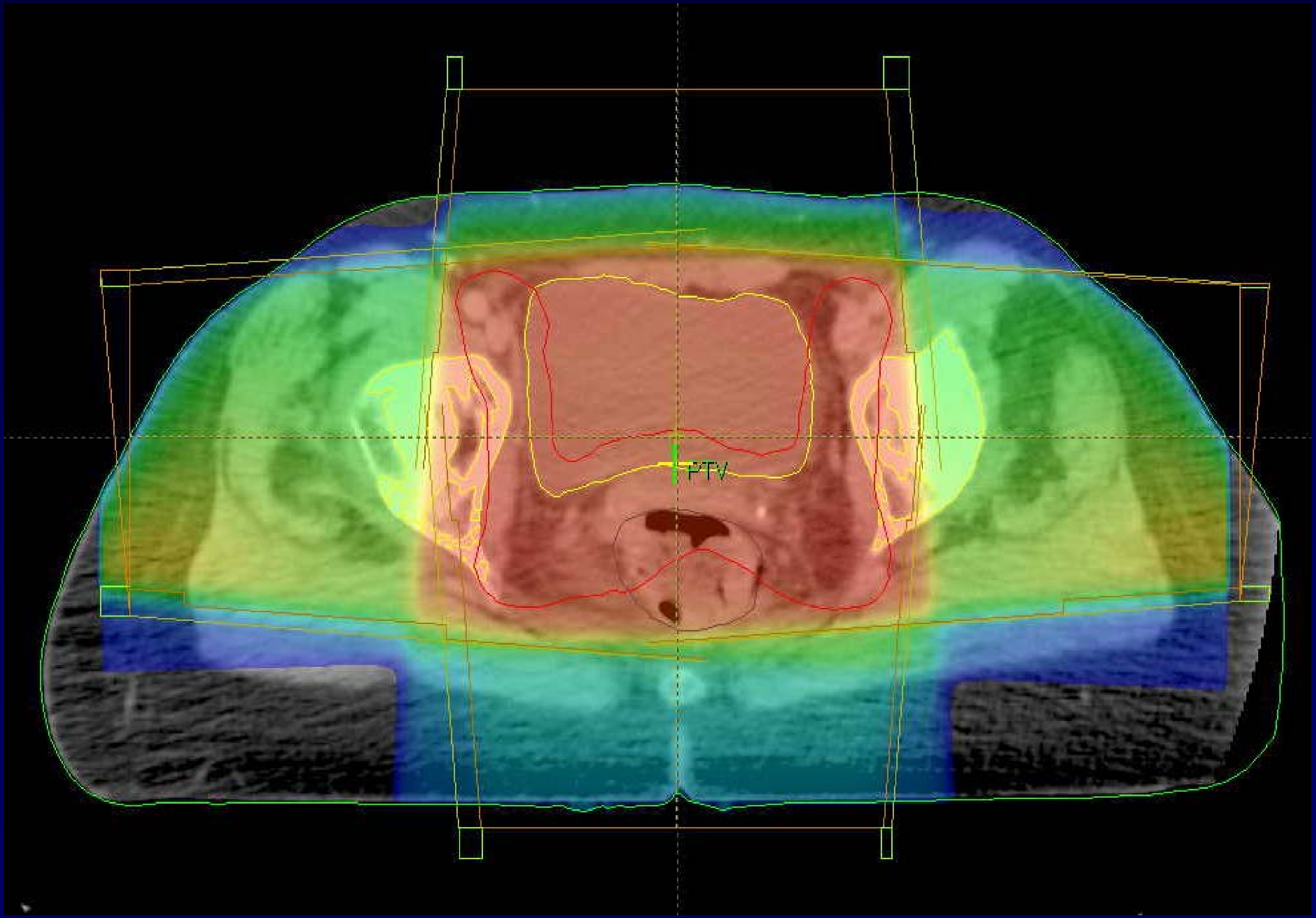




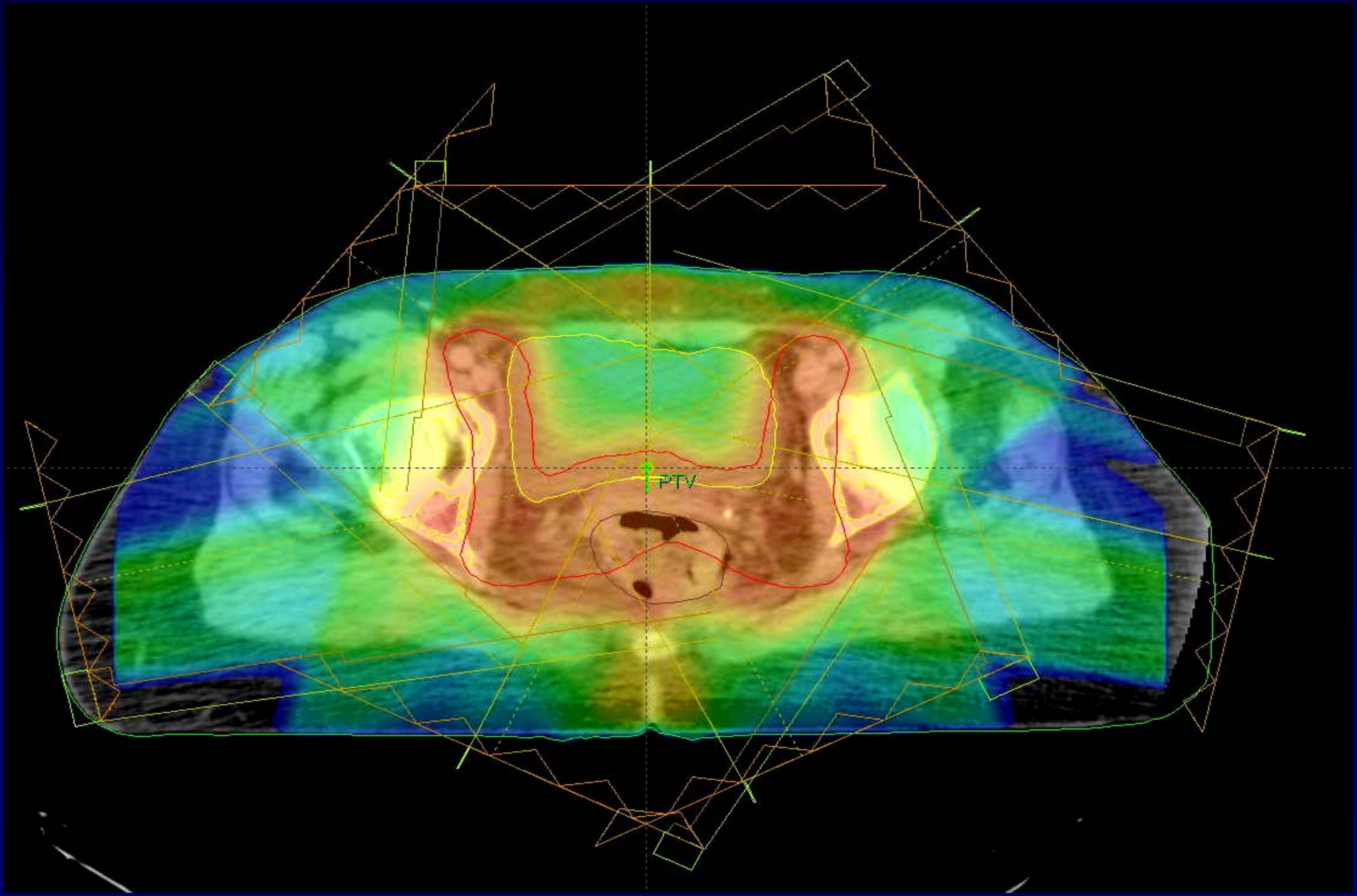




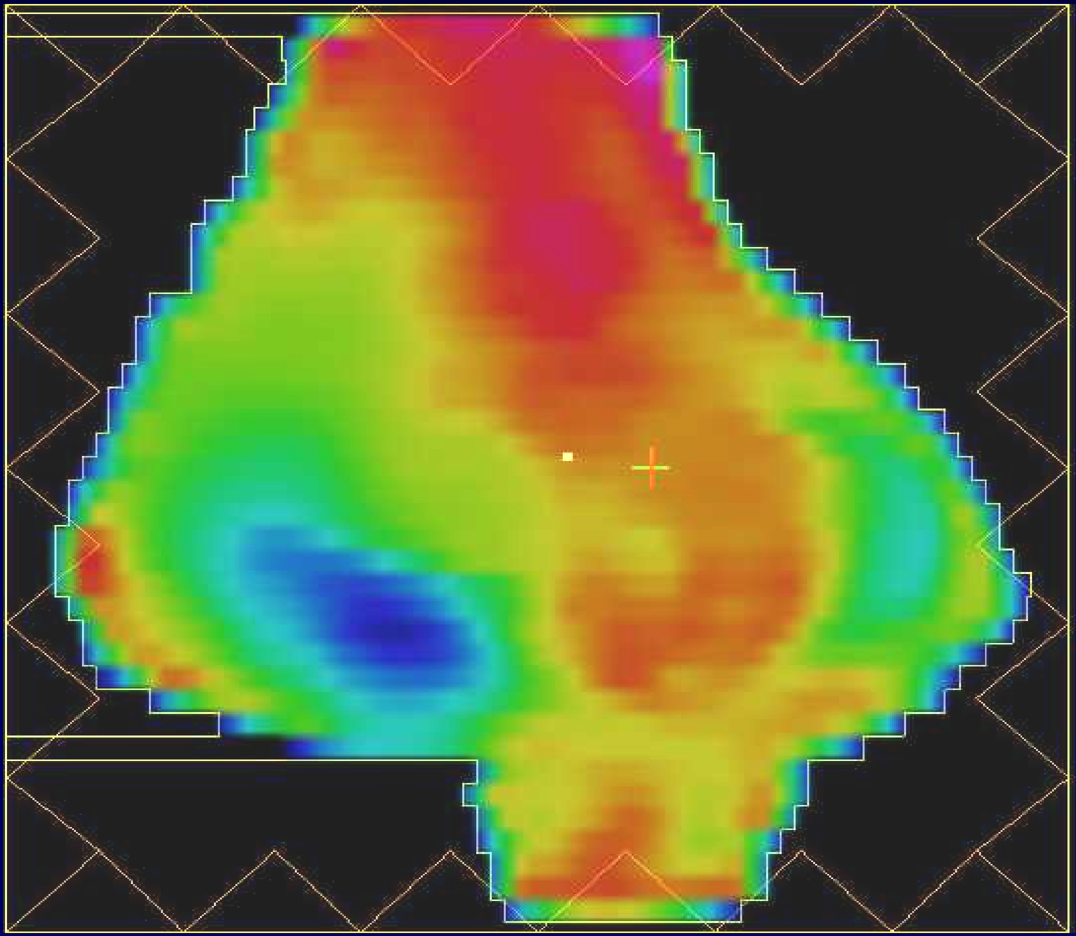
Conformal RT



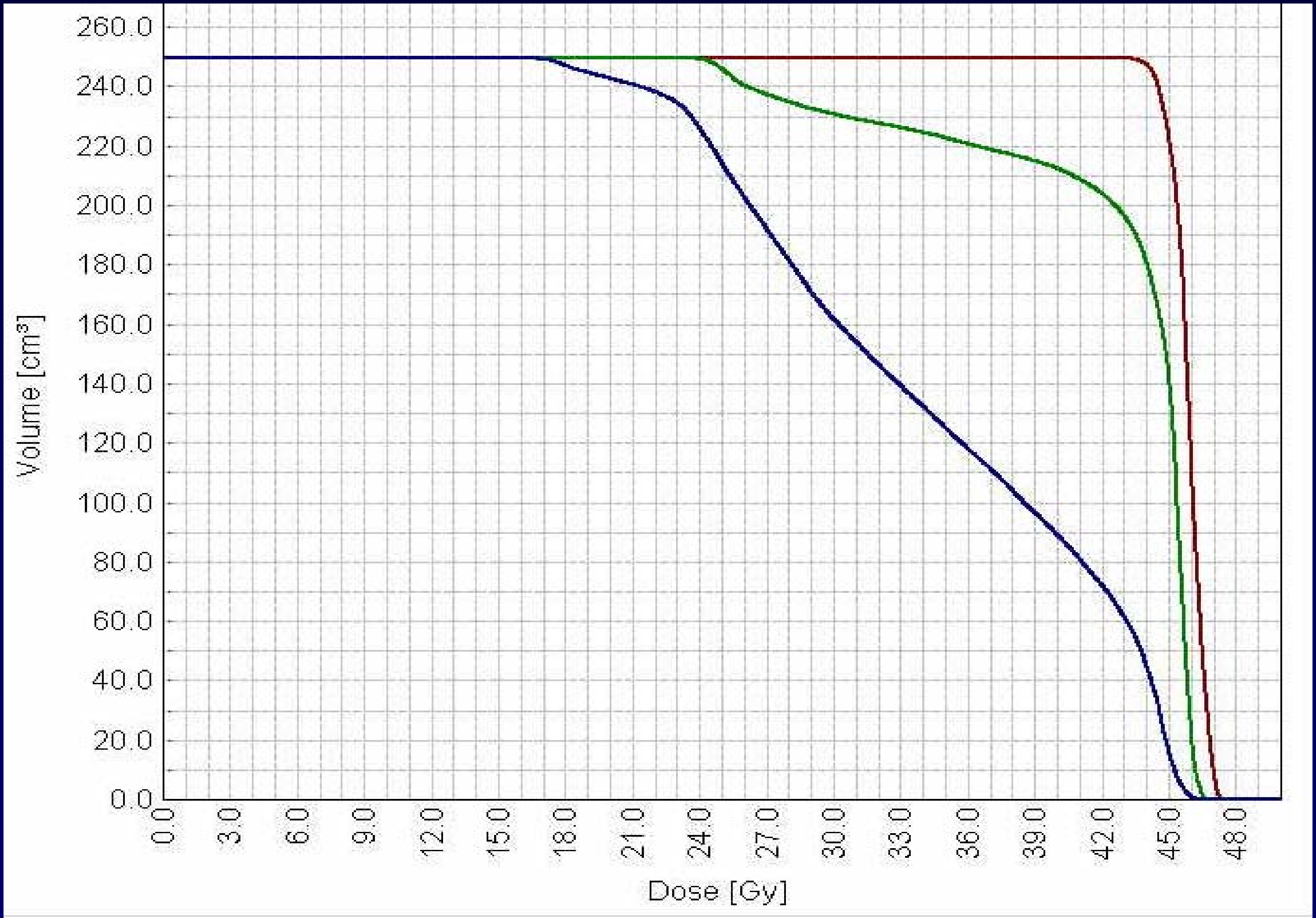
IMRT



Intensity-modulated Radiotherapy

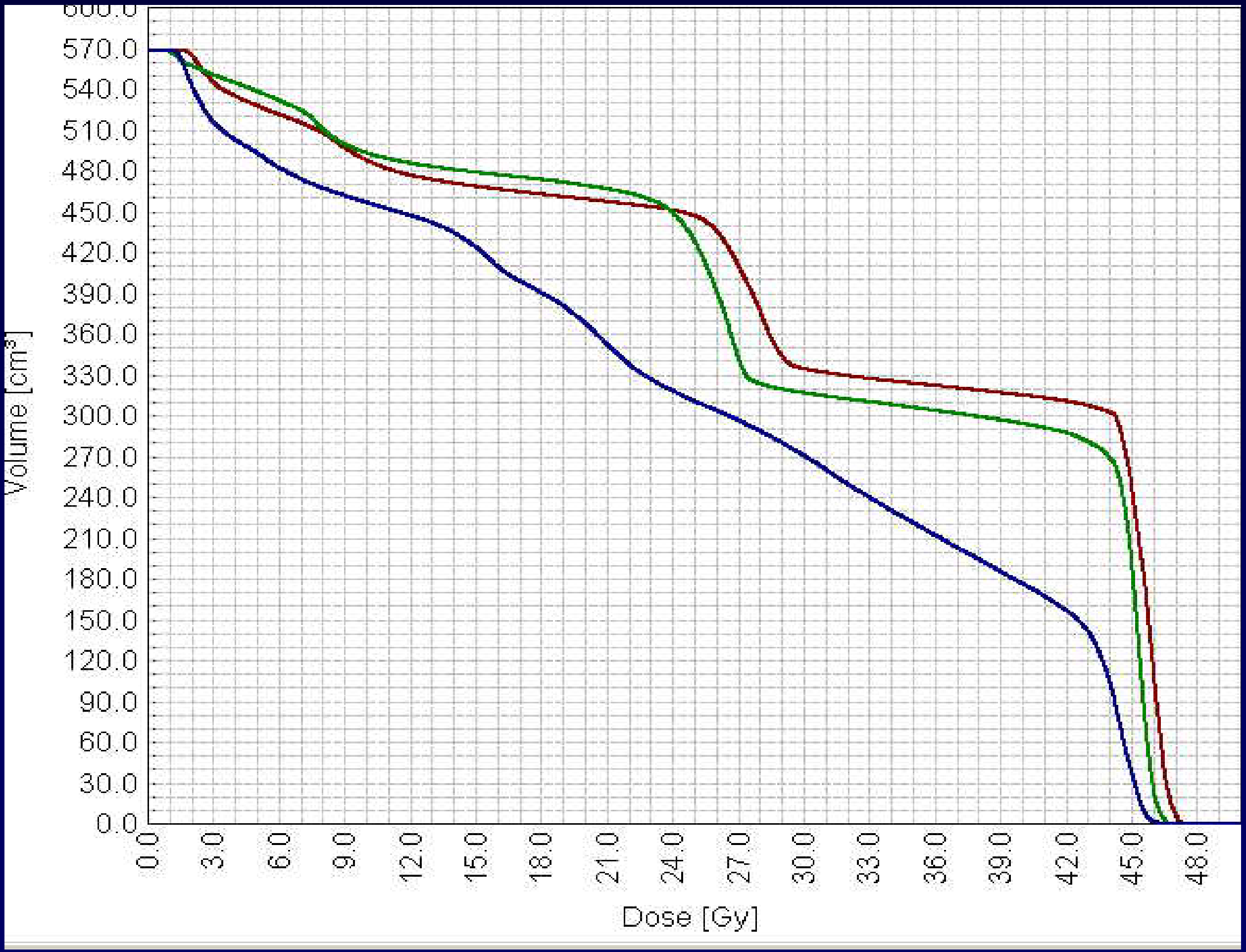


DVH - Bladder



260.0
240.0
220.0
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
Volume [cm³]
0.0
3.0
6.0
9.0
12.0
15.0
18.0
21.0
24.0
27.0
30.0
33.0
36.0
39.0
42.0
45.0
48.0
Dose [Gy]

DVH - Bowel


600.0
570.0
540.0
510.0
480.0
450.0
420.0
390.0
360.0
330.0
300.0
270.0
240.0
210.0
180.0
150.0
120.0
90.0
60.0
30.0
0.0
Volume [cm³]
0.0
3.0
6.0
9.0
12.0
15.0
18.0
21.0
24.0
27.0
30.0
33.0
36.0
39.0
42.0
45.0
48.0
Dose [Gy]

Treatment planning

- Defined target volumes
- Dose prescription:
  - Total dose to each volume
  - Number of fractions

- Specify dose limits for organs at risk

Normal Tissue Tolerance

Ovary	10Gy (50% risk)
Small Intestine	45Gy (5% risk)
Rectum	60Gy (5% risk)
Bladder	65Gy (5% risk)
Kidney	20Gy (5% risk)
Spinal cord	48Gy (0.5% risk)
Liver	<30Gy for 66% volume (5%)

Treatment delivery – linear accelerator

BRACHYTHERAPY

Brachytherapy

- Implanting radioactive sources into or near tumour
- High doses can be given to the tumour with relative sparing of surrounding normal tissues
- Can be sole treatment (eg prostate) or boost to macroscopic disease (eg cervix)
- Inverse square law applies:
  - Dose is inversely proportional to square of the distance from the source
- Dose rate:
  - Low dose rate (LDR) = 0.4-2 Gy/hour
  - High dose rate (HDR)= >12Gy/hour

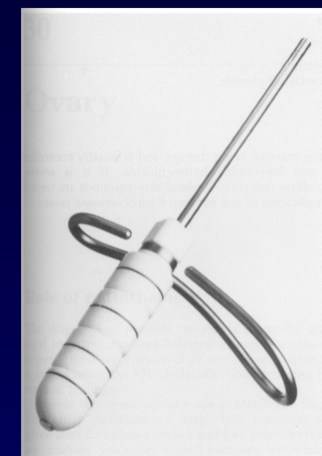
Brachytherapy

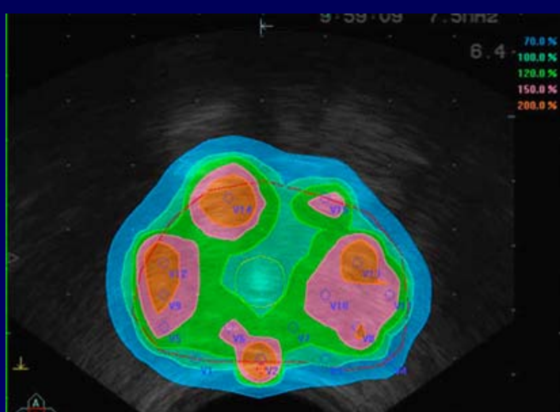
- Intracavitary brachytherapy
  - Gynaecological cancer
  - Oesophagus
  - Bronchus
  - Bile duct
  - Vascular stents
- Interstitial brachytherapy
  - Iridium-192 wires: tongue, lip, breast,
  - Gold-198 or I-125 seeds : prostate
  - Yttrium implants – craniopharyngioma, GBM

Isotopes used for brachytherapy

	half-life	emission	use
Radium-226	1620 yrs	(α,β,γ	n/a
Caesium-137	30 yrs	γ	LDR
Iridium-192	74 days	γ	HDR
Iodine-131	8 days	β	thyroid
Gold-198	2.7 days	β	seeds
Yttrium-90	2.7 days	β	
Iodine-125	60 days	Auger	seeds

HDR Brachytherapy





Targeted radiotherapy

- Injection of radioactive substance into blood
  - Iodine-131 in thyroid cancer
  - Radio-labelled monoclonal antibodies in leukaemia
  - MIBG in neuroblastoma
  - SIRTEX.
- Considerable uncertainty in doses
  - Estimates of absorbed dose only
  - Prescribed in terms of radioactivity (Bq)

Side Effects of Radiotherapy

Toxicity - Risk Factors

- RT dose – total dose and dose per fraction
- RT volume

- Performance status
- Previous surgery
- Diabetes
- Hypertension
- Concurrent drugs: e.g. chemotherapy

Acute Toxicity

- Occurs during course of RT or within 6 weeks of completion
- Mechanism: RT damages rapidly proliferating normal cells
- Usually resolves within 4-6 weeks

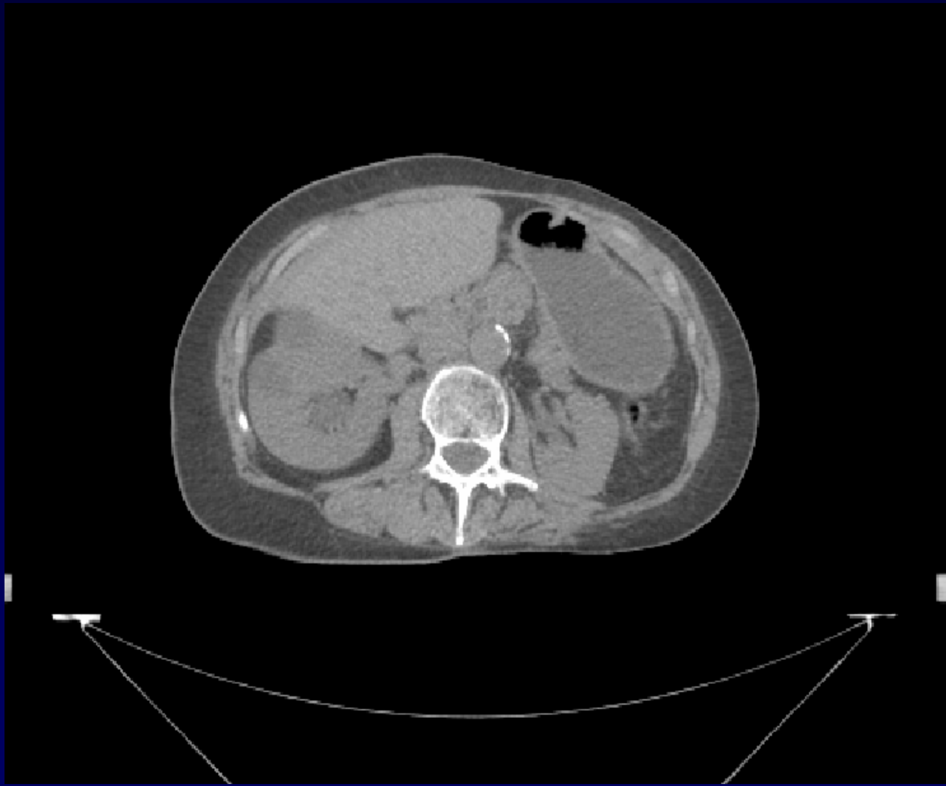
- Patients reviewed weekly during treatment

Acute Toxicity

- Depends on treatment area – affects rapidly dividing cells
  - Skin erythema / desquamation
  - Cystitis
  - Proctitis
  - Small Bowel Enteritis - diarrhoea
  - Lethargy
  - Nausea / vomiting
  - Hair loss in treated area

Late Toxicity

- Occurs 6 months to years after treatment
- Vascular changes / fibrosis
- Irreversible and serious
- Tolerance of each normal tissue is defined
- Determines maximum dose that can safely be delivered



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Late Toxicity

Proctitis
Fistula
Vaginal Stenosis
Lymphoedema
Lumbosacral plexopathy
Psychosexual dysfunction
Second malignancy

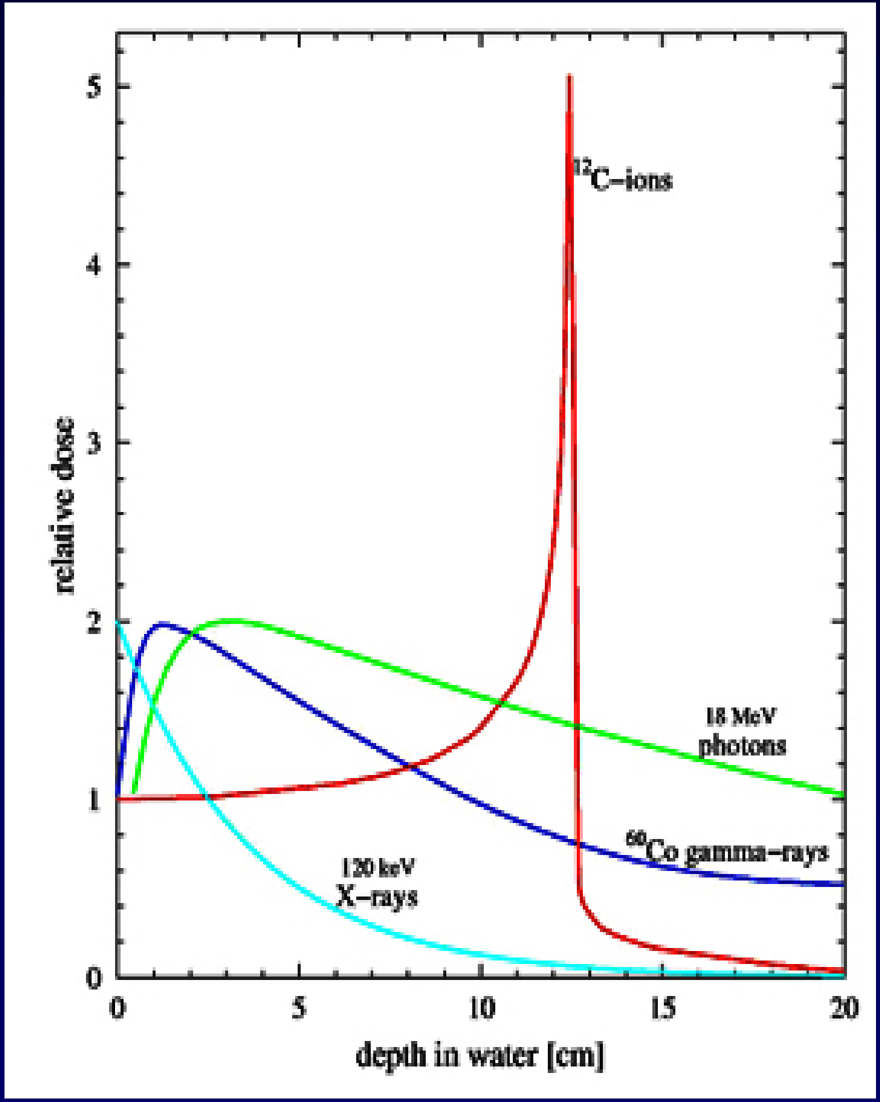
Ureteric stricture
Small Bowel Obstruction
Haemorrhagic Cystitis
Insufficiency fractures
Impaired healing

Grading systems: RTOG, LENT SOMA, Franco-Italian Glossary, CTC, CTCAE

SOME EXAMPLES

Heavy charged particles.

- Depends on the particle charge & velocity.
- The peaking of dose deposition at the end of the range is called BRAGG peak.
- This has the advantage of high tumour dose and less normal tissue dose.



Summary

- 60-70% of patients with cancer will receive radiotherapy
- Aim to treat target volume while reducing dose to normal structures
- Recent developments in imaging and technology likely to impact on survival