PRINCIPLES and PRACTICE of RADIATION ONCOLOGY

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OUTLINE

- Physical basis
- Biological basis
- History of radiation therapy
- Treatment planning
- Technology of treatment delivery
- Future directions

Radiation

- Non-ionizing
  - visible light
  - IR, UV
- Ionizing
  - Directly
    - Charged Particles
  - Indirectly
    - x-rays, gamma, neutrons

Ionizing Radiation:
X-rays

- Result from extranuclear processes

    - characteristic radiation

    - bremsstrahlung radiation

Ionizing Radiation: Gamma Rays

- Intra nuclear process (RADIOISOTOPE)

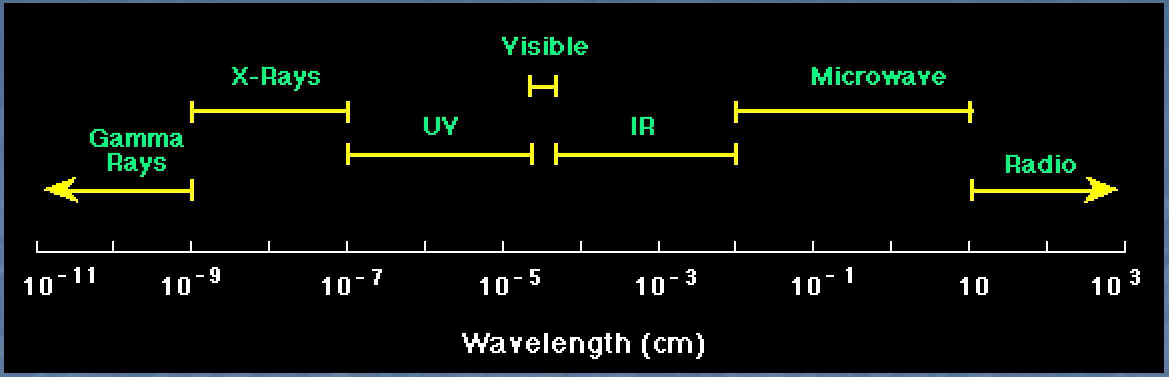
  - unstable (radioactive) nucleus decays towards ground state
  - parameters characterizing decay:

    $t_{1/2}$, decay constant, specific activity

Common Radioisotopes

Isotope	Half-Life	Energy
Co-60	5.26 yr	1.25 MeV
Cs-137	30 yr	0.661 MeV
I-125	60 d	28 keV
Pd-103	17 d	21 keV

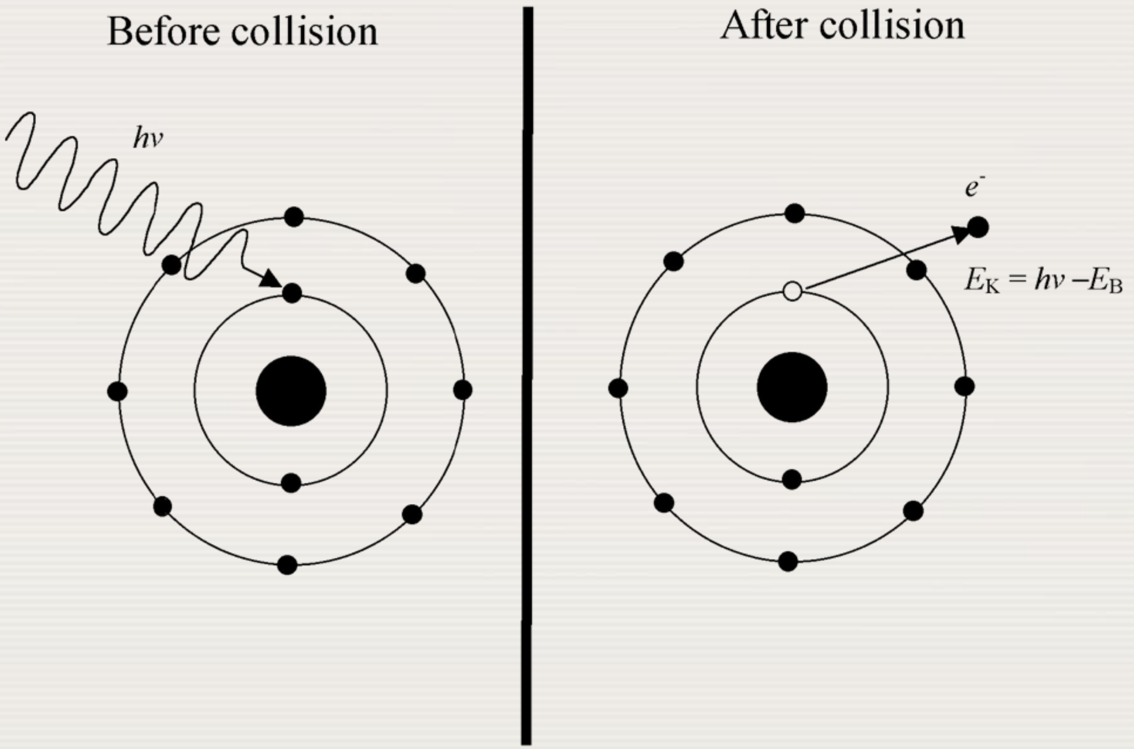
X Rays (photons)

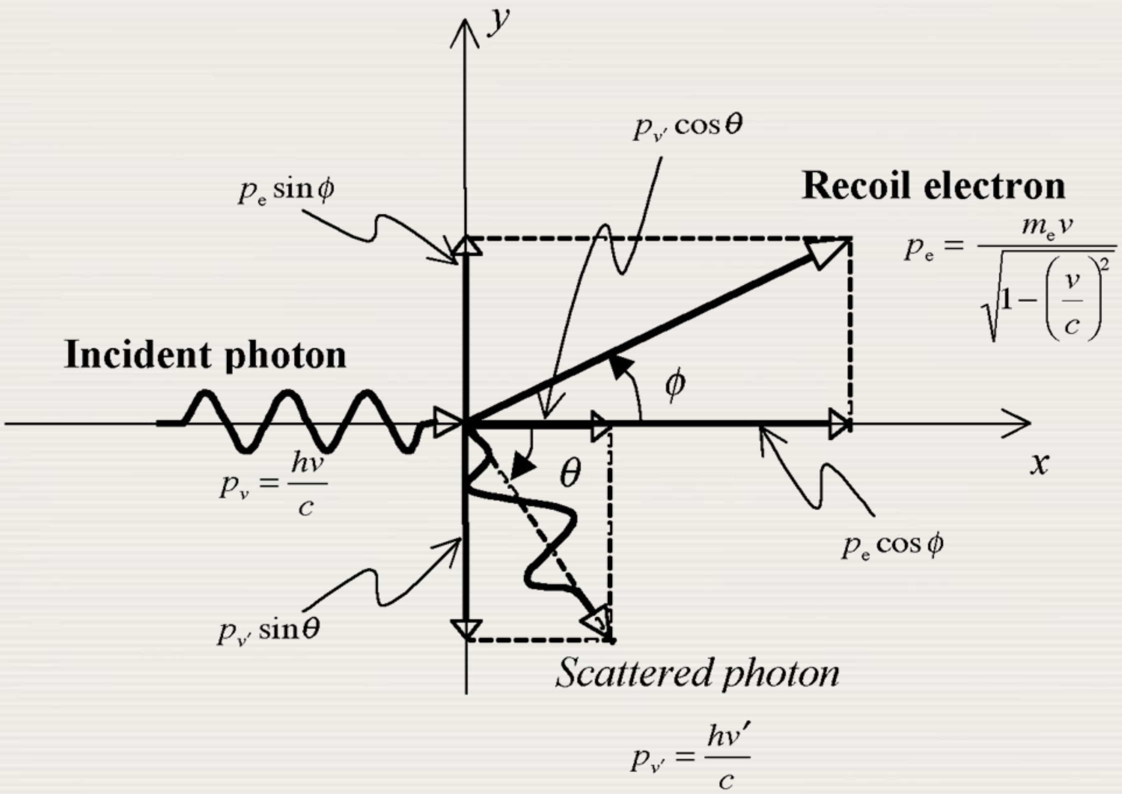


- Interact with matter in well characterized mechanisms:
  - photoelectric interaction
  - Compton interaction
  - pair production

- Infinite range, probability-based interactions

- Schematic diagram of the photoelectric effect
  - A photon with energy $h\nu$ interacts with a K-shell electron
  - The orbital electron is emitted from the atom as a photoelectron





Conservation of energy

$$h\nu + m_e c^2 = h\nu' + m_e c^2 + E_K$$

Conservation of momentum (x axis)

$$p_\nu = p_{\nu'}\cos\theta + p_e\cos\phi$$

Conservation of momentum (y axis)

$$0 = -p_{\nu'}\sin\theta + p_e\sin\phi$$

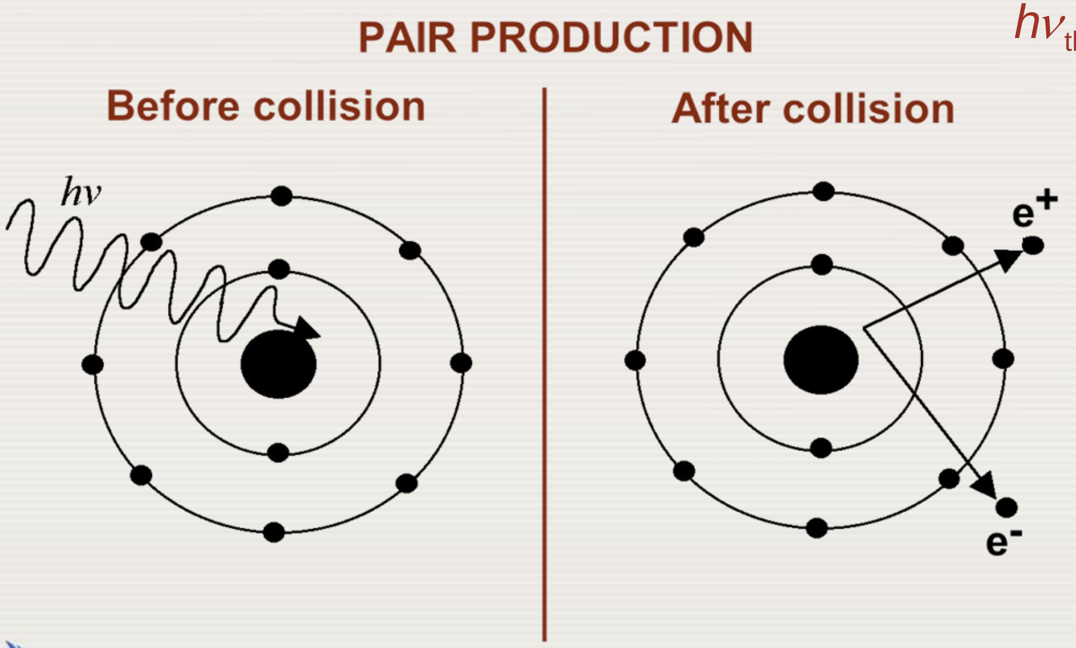
Compton expression:

$$\Delta\lambda = \lambda_c(1-\cos\theta)$$

$$\lambda_c = \frac{h}{m_e c} = 0.24\ □$$

- In pair production
  - The photon disappears.
  - An electron-positron pair with a combined kinetic energy equal to $h\nu - 2m_e c^2$ is produced in the nuclear Coulomb field.
  - The threshold energy for pair production is:

$$h\nu_{thr} = 2m_e c^2 \left\{1 + \frac{m_e c^2}{M_A c^2}\right\} \approx 2m_e c^2$$



m_e electron mass

M_A mass of nucleus

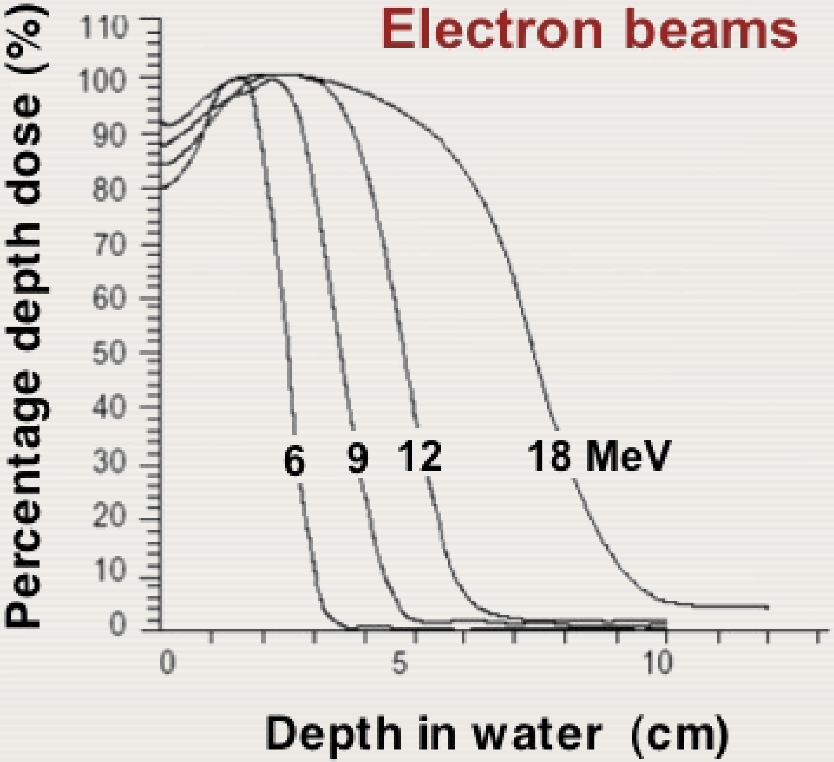
$m_e c^2 = 0.511$ MeV

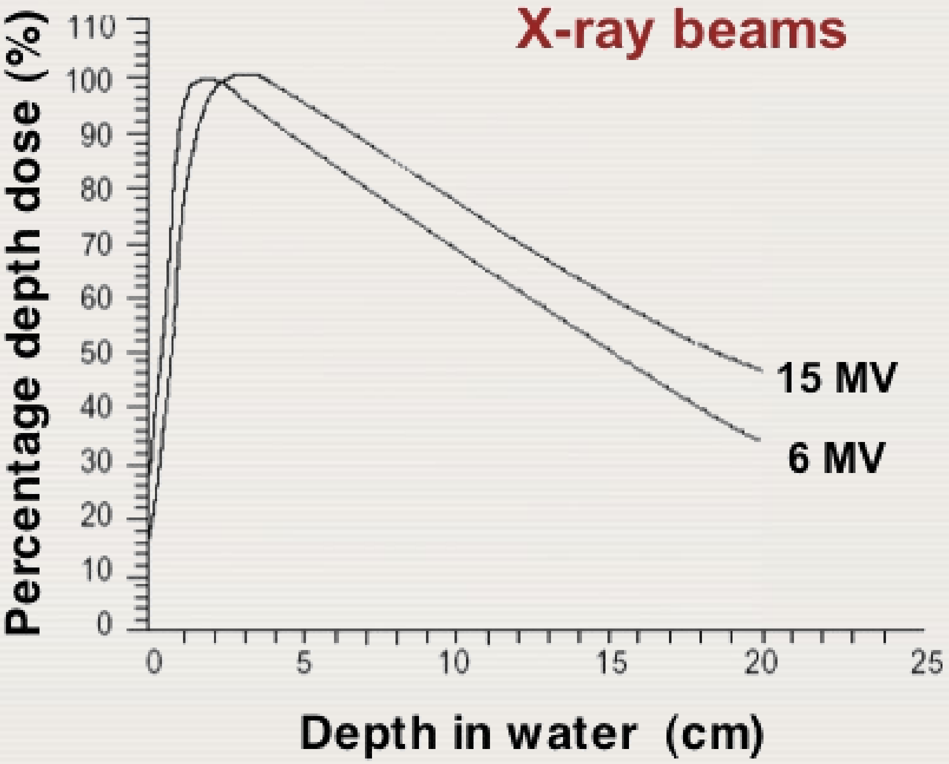
Charged Particles

- Interact via collisional and radiative mechanisms
- Predictable finite range

CENTRAL AXIS DEPTH DOSE DISTRIBUTIONS

- The general shape of the central axis depth dose curve for electron beams differs from that of photon beams.





IAEA

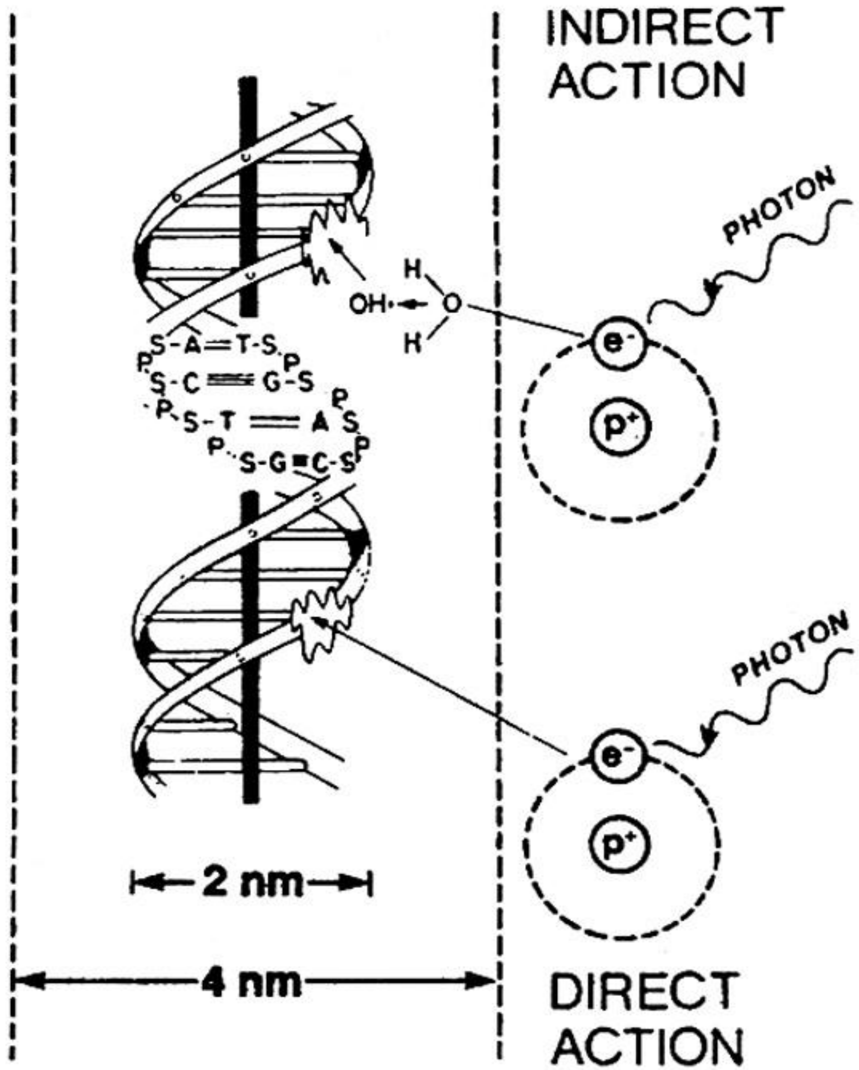
RadioBiology

- Physical deposition of energy leads to chain of reactions which ultimately lead to the observed clinical effect.
- Final energy transfer to material is via energetic electrons and positrons produced in a photon interaction.

Target Theory

- Cell killing is a multi-step process
- Absorption of energy in some critical volume is first step
- Deposition of energy as ionization or excitation in the critical volume leads to molecular damage
- Damage prevents normal DNA replication and cell division

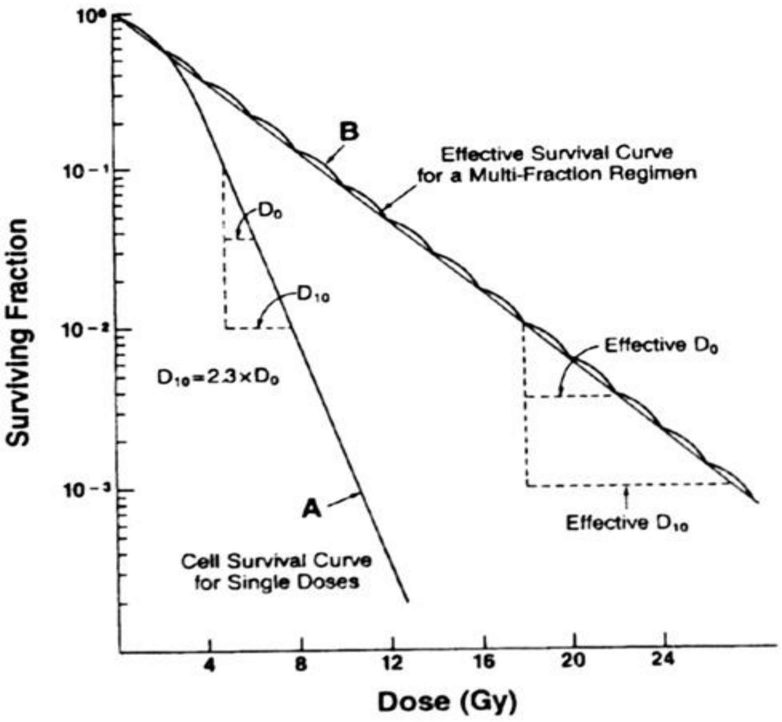
The two mechanisms of cell Kill



Cellular Response

- Loss of function
  - radiation mutagenesis and carcinogenesis
  - interphase cell death (apoptosis)
- Loss of reproductive ability

Cell Survival Curve



Curve A: Survival curve for mammalian cells. The dose required for to reduce survival by a factor of 10 (i.e. D_{10} is equal to 2.3 x D_0).

Curve B: Effective survival curve for cells exposed to a multifraction regimen, where doses are separated by a time interval sufficient for repair of sublethal damage. The effective survival curve is shallower than the single dose survival curve, i.e. D_0 effective is larger than D_0. Again the D_{10} effective = 2.3xDo effective.

Cell Survival Curve (con’t)

- Inherent radiosensitivity
- Oxygen concentration
- Repair processes
- Repair of potentially lethal damage (PLD)
- Cell cycle phase dependence
- Cell proliferation status

Parameters

- Linear Energy Transfer (LET)

  amount of energy deposited per unit path length

- Relative Biologic Effectiveness (RBE)

  measures efficiency of radiation in producing biological response relative to a standard radiation (250 kVp)

Parameters (con't)

- Oxygen Enhancement Ratio (OER)
  - oxygenated cells more sensitive to radiation damage
  - anoxic cells radioresistant
- Radioprotectors
- Radiosensitizers

Tumor Response

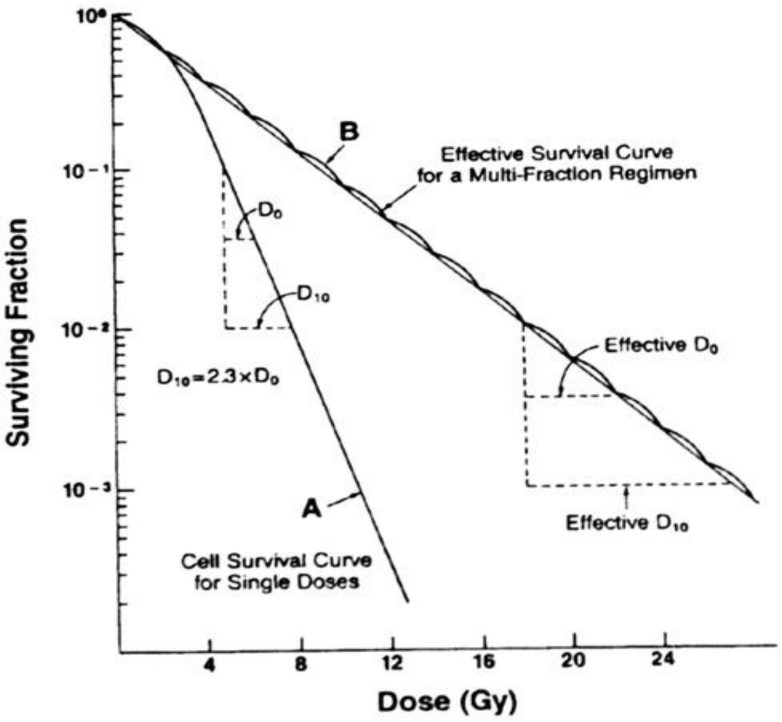
- Repair
- Repopulation
- Reoxygenation
- Reassortment

→ 4 R's of Radiobiology

Dose Fractionation

- Dividing a dose into a number of fractions
  - spares normal tissues
    - repair of sublethal damage
    - repopulation of normal cells
  - increases damage to tumor cells
    - reoxygenation can occur
    - reassortment into radiosensitive phases of cell cycle

Cell Survival Curve



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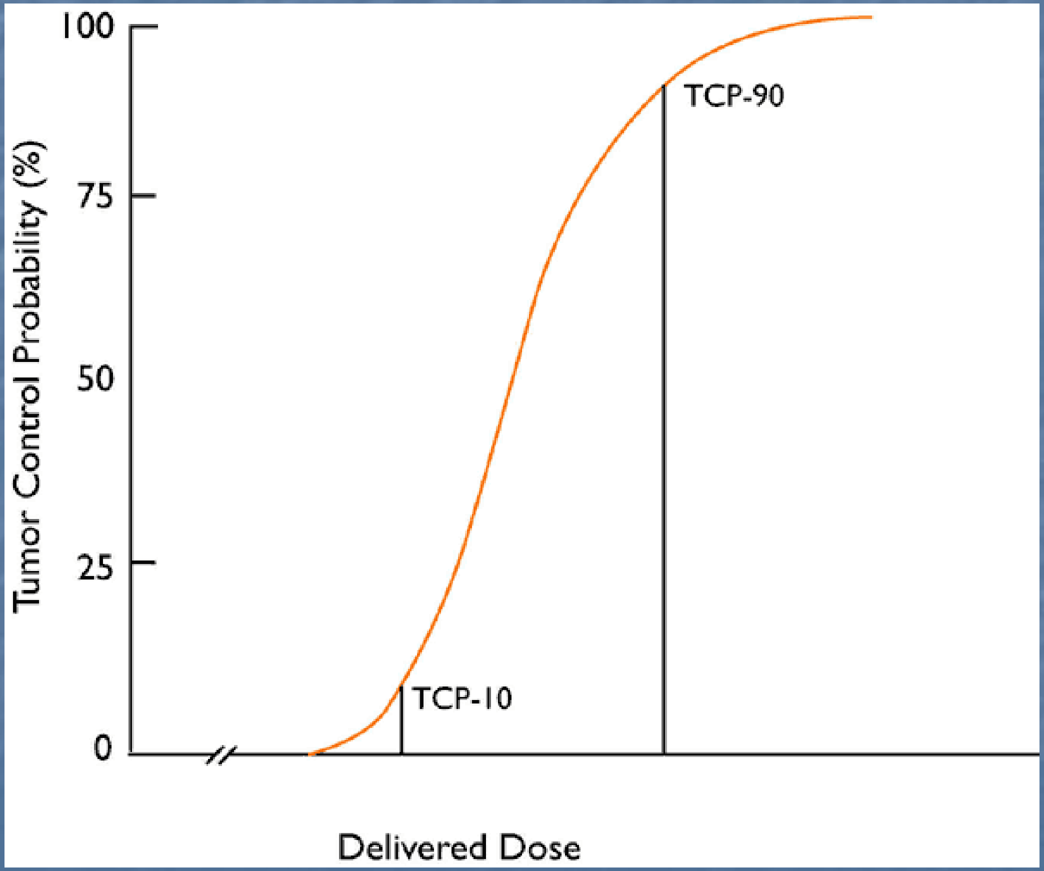
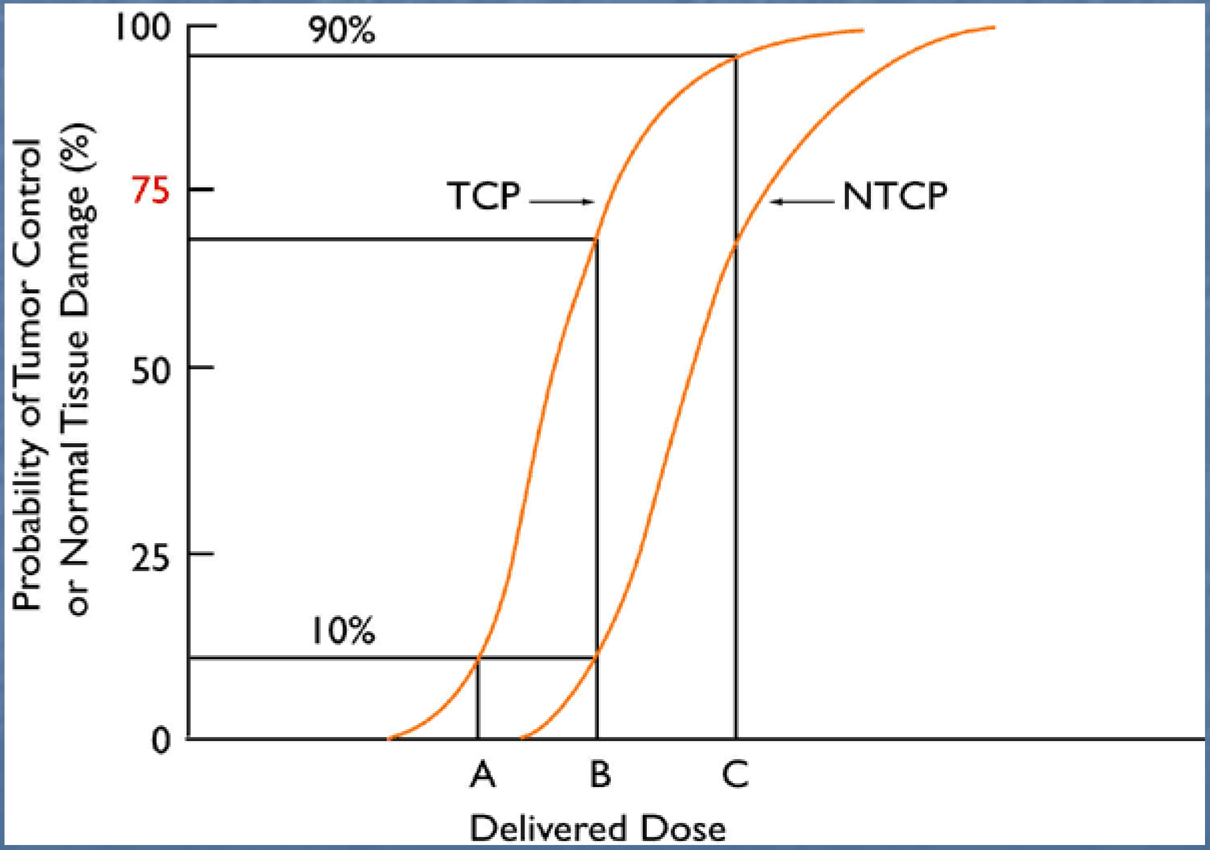
Tissue and Organ Response

- TCP – Tumor Control Probability
  - likelihood of controlling tumor growth
- NTCP – Normal Tissue Complication Probability
  - likelihood of normal tissue complications

Tumor Control Probability (TCP)



TCP vs. NTCP

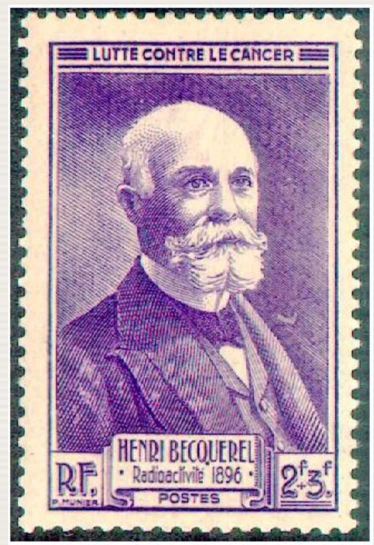


100
90%
75
TCP
NTCP
50
25
10%
0
A
B
C
Delivered Dose
Probability of Tumor Control or Normal Tissue Damage (%)

Radiation Therapy History

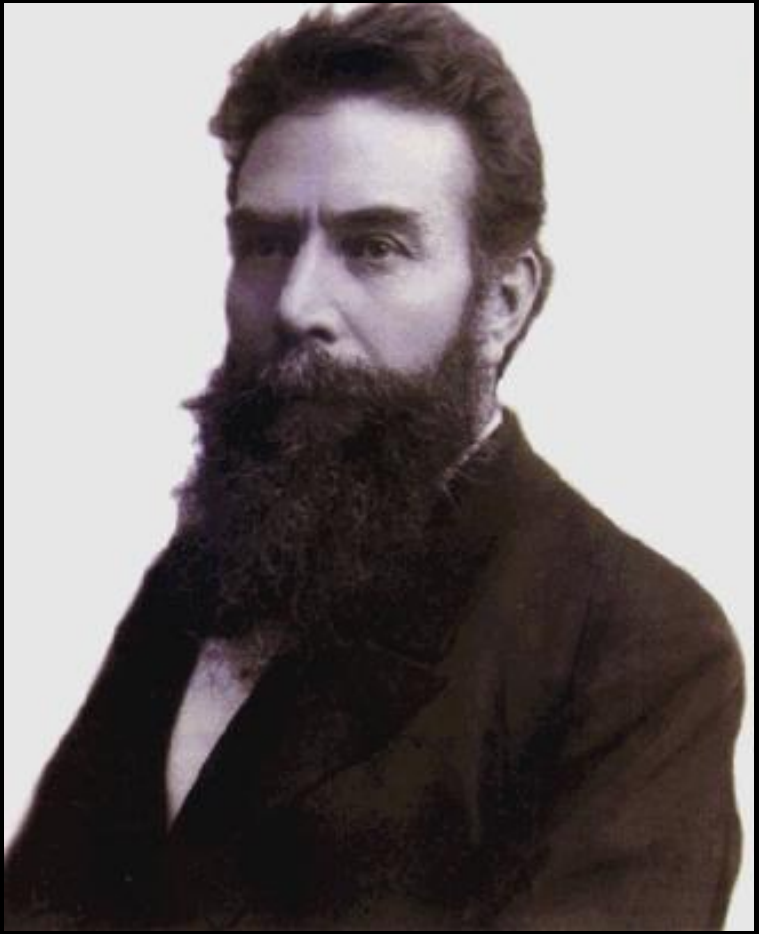
- 1895 Roentgen discovers x-rays
- 1896 Becquerel discovers radioactivity (uranium)
- Biological effect of radiation evident almost immediately
- 1901 Pierre Curie self-induced radium burn on arm
- Early radiation therapy using radium (interstitial, intracavitary, surface applicators)

- The study and use of ionizing radiation in medicine started with three important discoveries:
  - X rays by Wilhelm Roentgen in 1895.
  - Natural radioactivity by Henri Becquerel in 1896.
  - Radium-226 by Pierre and Marie Curie in 1898.

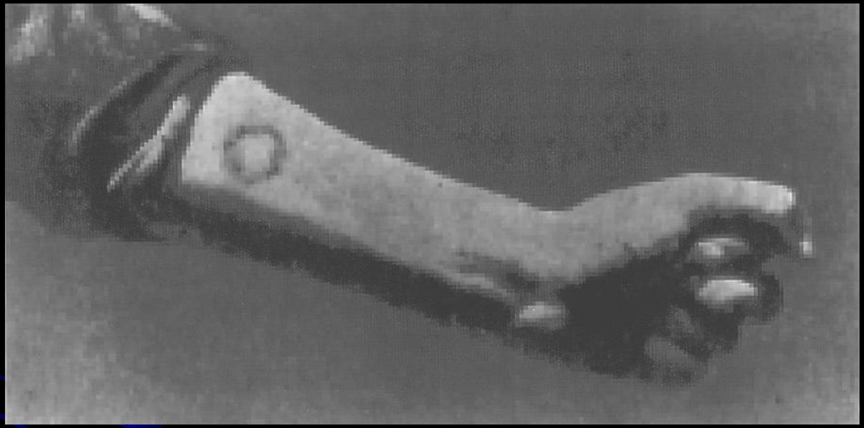


Discovery of X-rays

On 8 Nov 1895, Wilhelm Conrad Röntgen (accidentally) discovered an image cast from his cathode ray generator.



Guinea Pig Physicist!

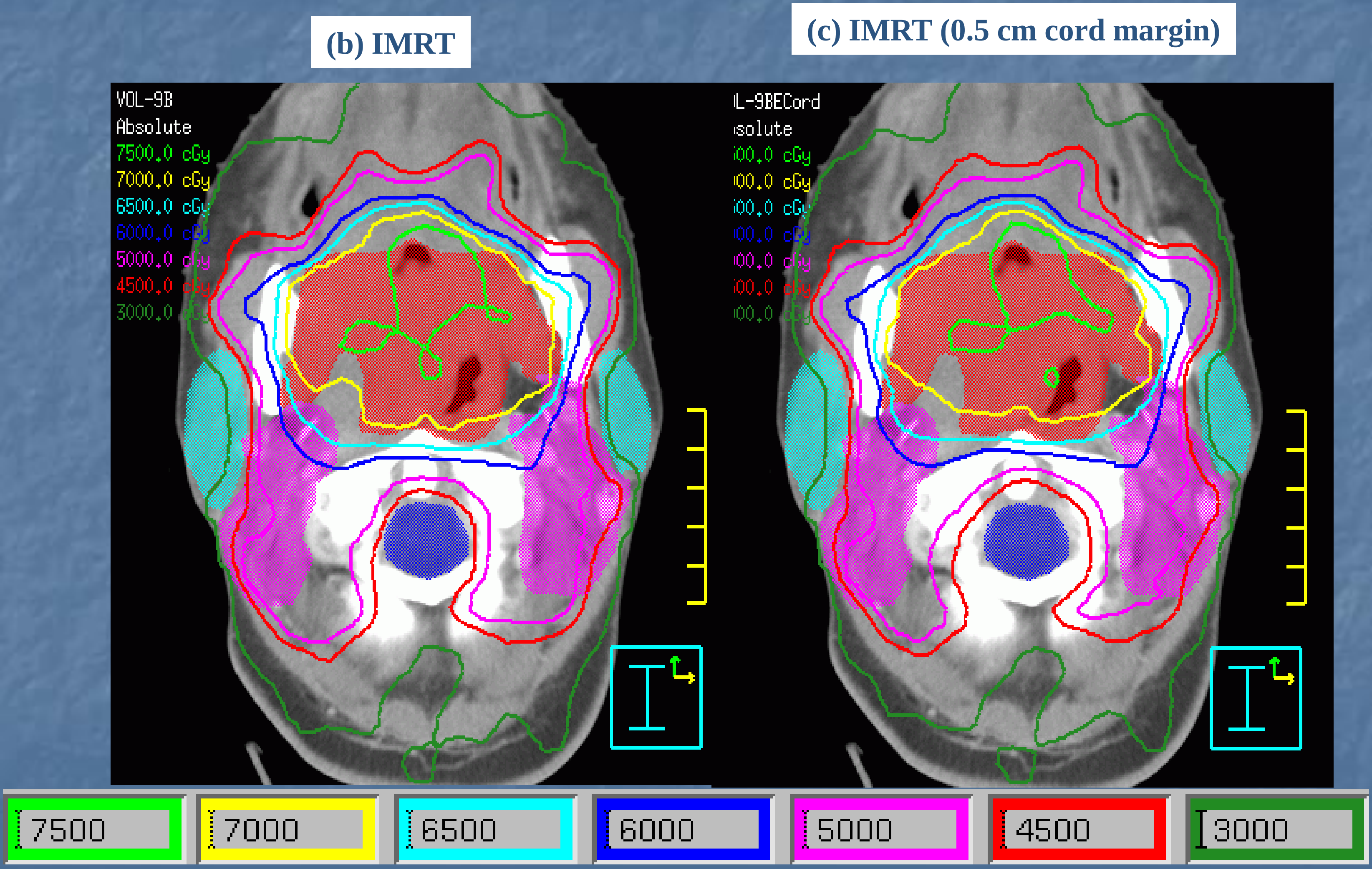


- Self induced radiation burn on Pierre Curie's arm, 1901
- Experiment with biological application of radioactivity…first indication of biological effect?

Early Radiation Therapy

- Early surface applicator, 1922
- Lack of rigorous quantitative dosimetry
- Disregard for radiation safety procedures

IMRT plan: Head & Neck ca



Modern Radiation Therapy Team

- Radiation Oncologist / Resident
- Medical Physicist / Resident
- Dosimetrist
- Radiation Therapist
- Nurse
- Social Worker
- Administrator

Goal of radiation therapy

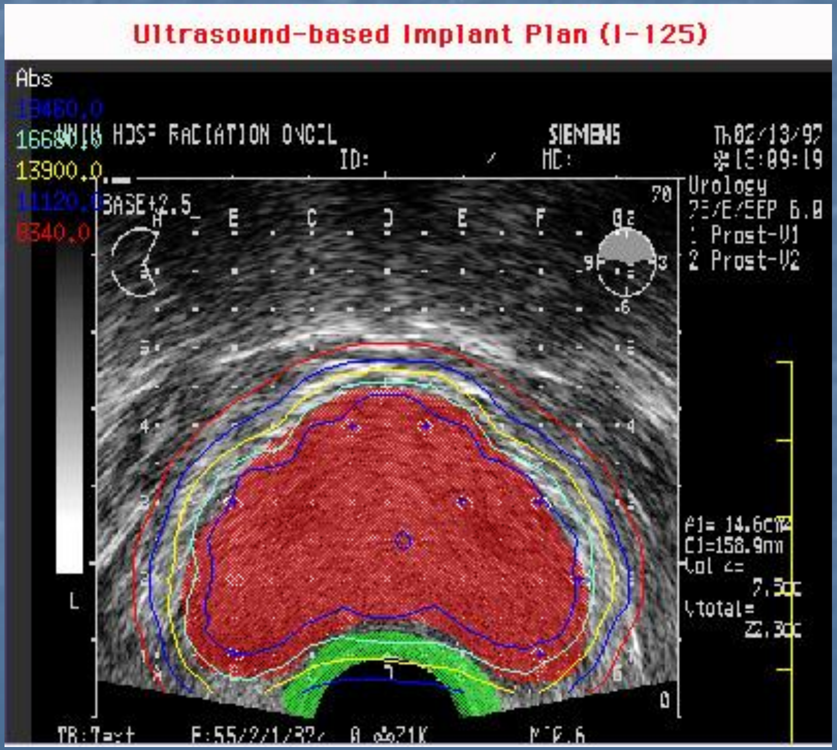
- “concentrate dose to target tissues and minimize dose to healthy tissues”

Radiation Therapy

- Brachytherapy – therapy at a short distance
  - sources placed directly into tumor volume
- Teletherapy – therapy at a large distance
  - source outside body

Review of Brachytherapy Principles

- Highly localized dose to target with sharp fall-off in surrounding tissues
- The ultimate conformal therapy?
- Inherent inhomogeneity and hot spots

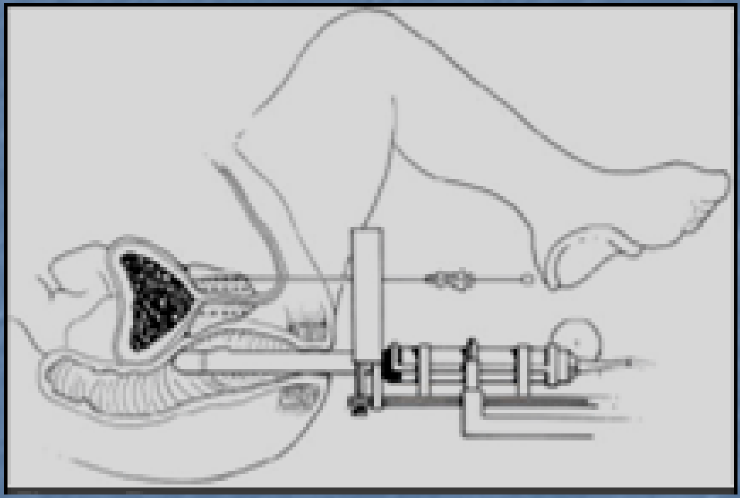


Brachytherapy Clinical Applications

- Historically, brachytherapy has been applied clinically to many anatomical sites
- e.g., eye, head and neck, brain, skin, bronchus/lung, esophagus, breast, prostate, female pelvis (gyn), soft tissue (sarcoma), and others...

Prostate Brachytherapy

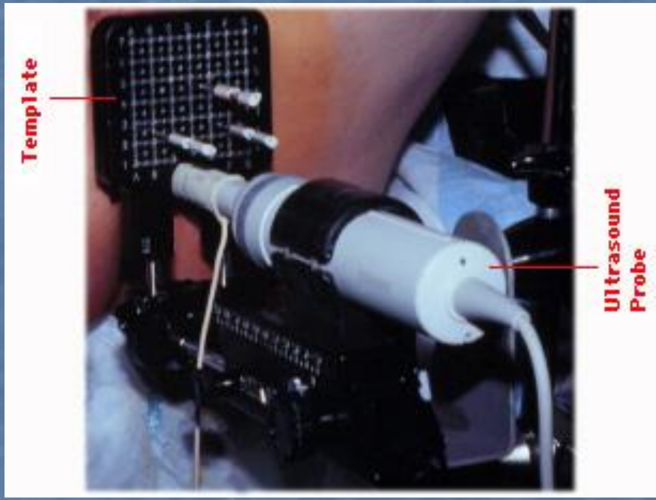
1970's MSKCC

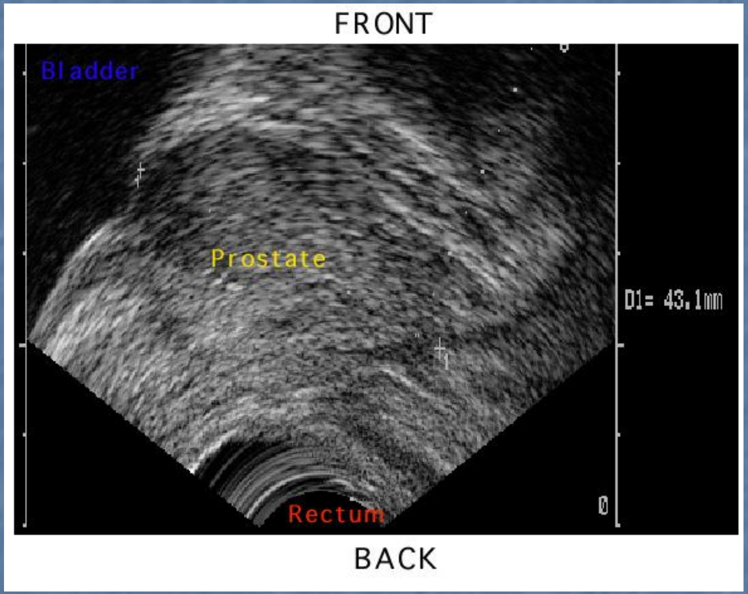


TRUS-guidance (early '90's)

Prostate Brachytherapy

TRUS Imaging and implant needle placement





Post-Implant Dosimetry

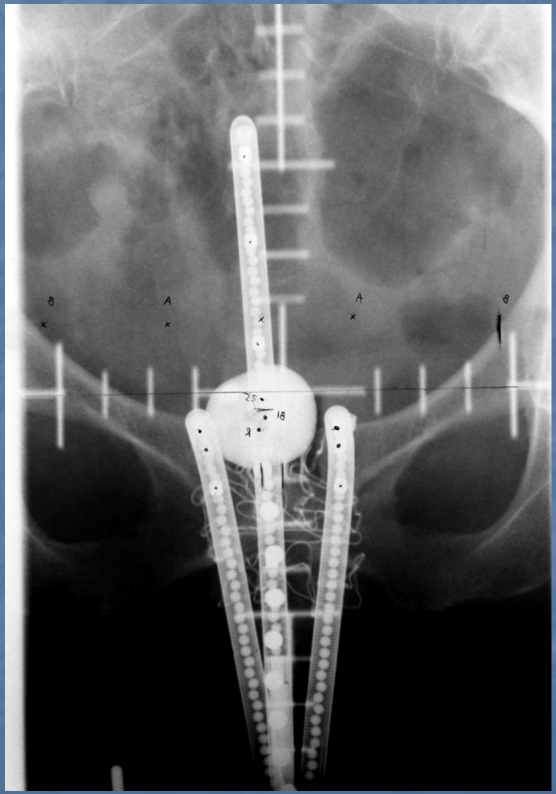
Post-implant imaging for verification and dosimetry

Plane Film (2D)

CT (3D)

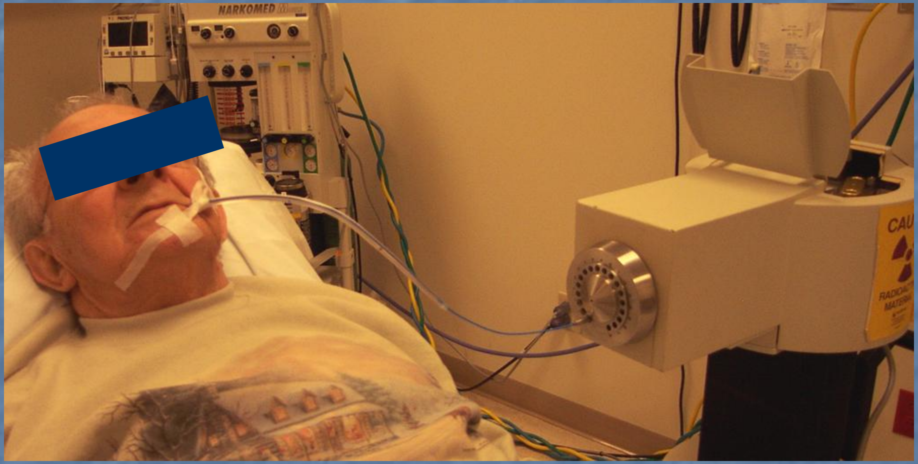
GYN Brachytherapy

LDR Remote Afterloader procedure



Other Brachytherapy

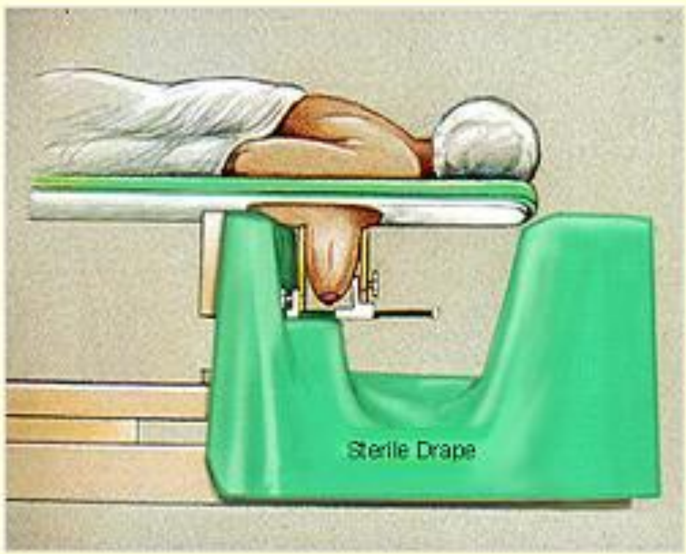
HDR esophagus



Typically 5 Gy/fx in 3-7 minutes

Other Brachytherapy

HDR breast



[redacted] Mammography equipment draped and aligned with template.

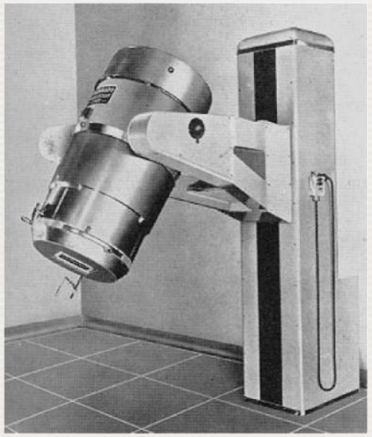
[redacted] The breast under each hole is completely anesthetized prior to catheter insertion.

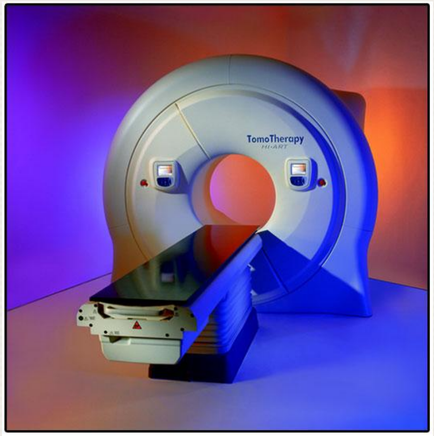
Teletherapy
Energy Categories

- Superficial (10 – 80 kVp)
- Orthovoltage (100 – 500 kVp)
- Megavoltage (Co-60 – 35 MV)

Equipment for dose delivery

- **1895** X-ray machine: Crookes type.
- **1913** X-ray machine: Coolidge type.
- **1940s** Van de Graaff generator and betatron.
- **1950s** Cobalt-60 teletherapy
- **1960s** Linear accelerator (linac) and Gamma Knife.
- **2000s** Tomotherapy machine and Cyberknife.



Superficial / Orthovoltage (x-ray tube)

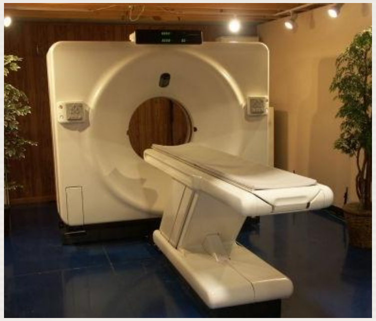
Medical Linear Accelerator

Patient flow in radiation therapy

- Consultation / Informed consent
- Conventional / Virtual simulation
- Treatment planning
- Simulation check / port film
- *in vivo* dosimetry

Imaging for target localization

- **1970s CT scanner**
  - **Allan Cormack**
  - **Godfrey Hounsfield**
    - **Nobel Prize 1979**



- **1973 PET scanner**
  - **Edward J. Hoffman**
  - **Michael E. Phelps**

- **1980s MR scanner**
  - **Paul C. Lauterbur**
  - **Peter Mansfield**
    - **Nobel Prize 2003**

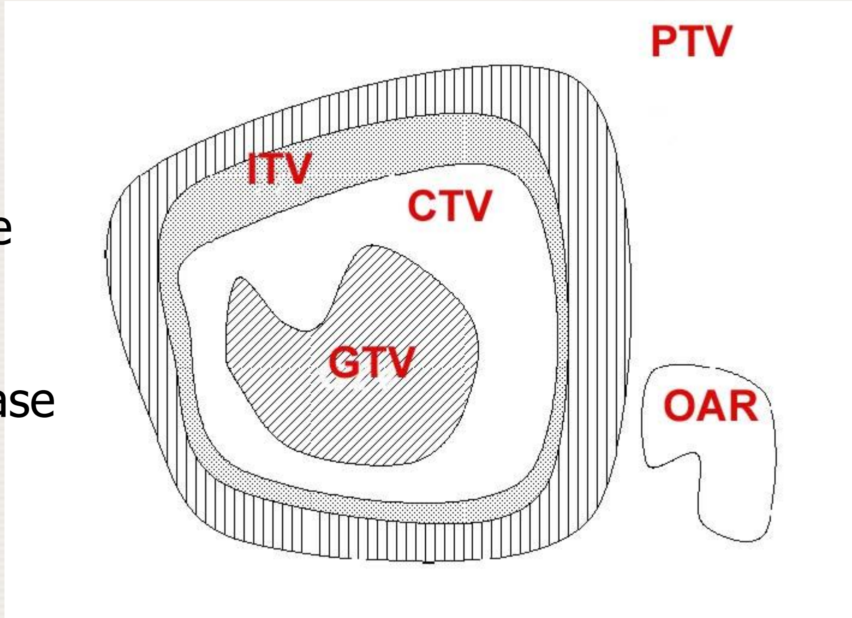
TREATMENT VOLUME DEFINITION

GTV – gross tumor volume
palpable or visible extent of disease

CTV - clinical target volume
GTV + subclinical microscopic disease

ITV - internal target volume
CTV + margin for organ motion
e.g., breathing

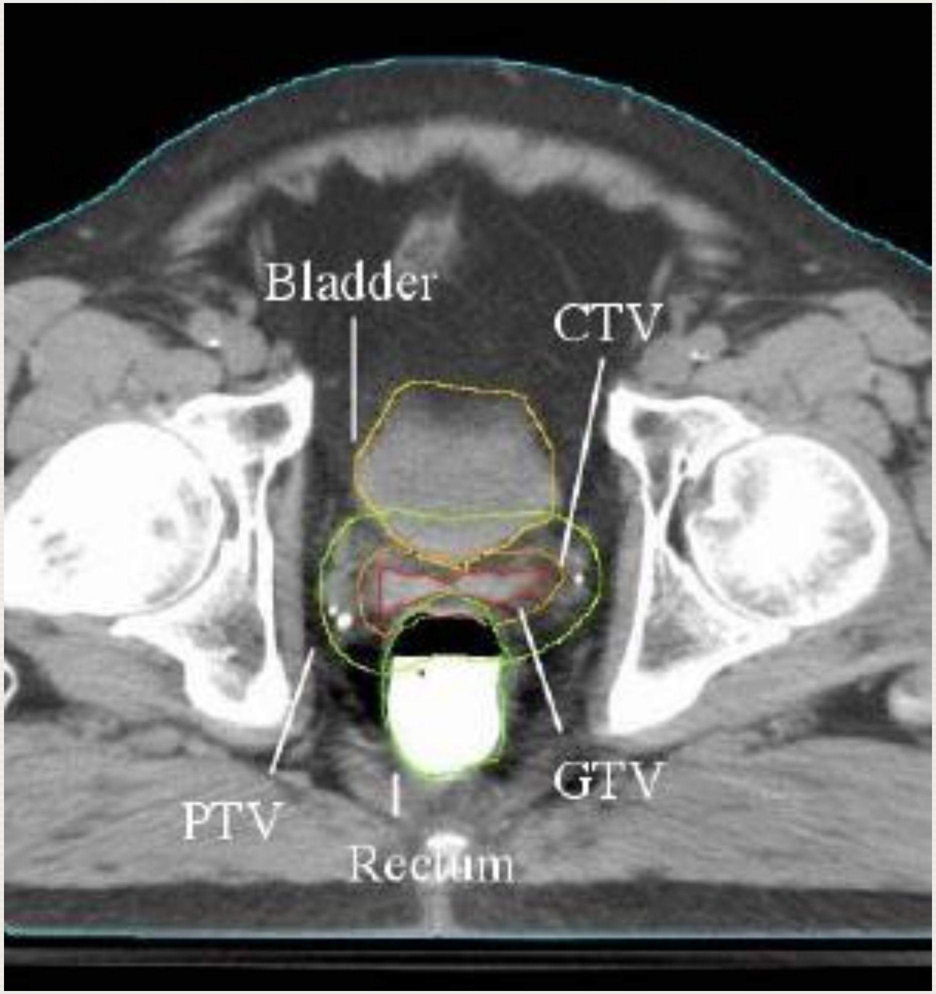
PTV - planning target volume
ITV + margin for setup errors and
treatment machine tolerances



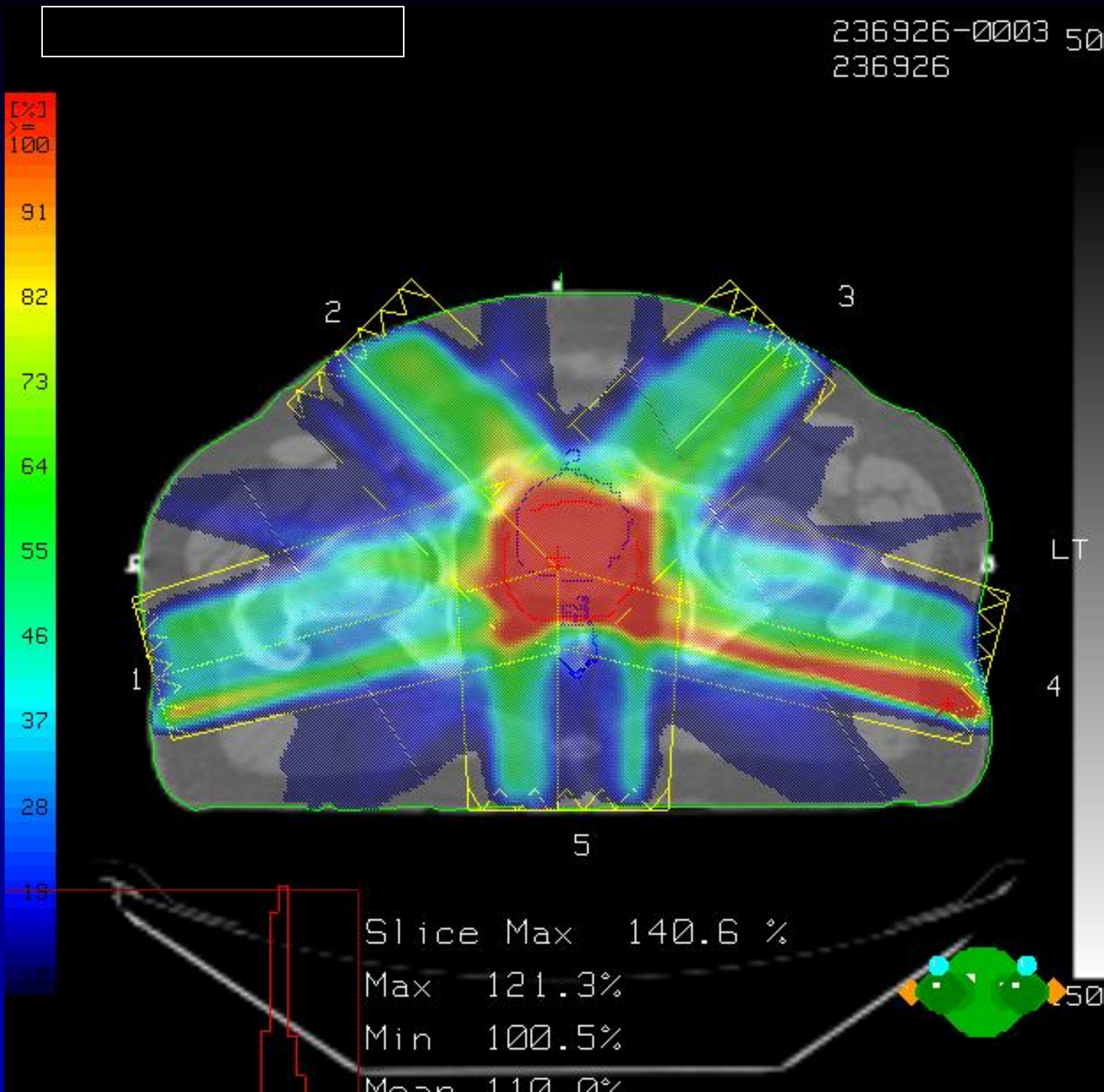
MALE PELVIC CONTOURING

Contours for different volumes have been drawn on this CT slice for a prostate treatment plan:

- GTV
- CTV
- PTV
- organs at risk (bladder and rectum).



Treatment Planning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>=
100
91
82
73
64
55
46
37
28
19
1
2
3
4
5
LT
Slice Max 140.6 %
Max 121.3%
Min 100.5%
Mean 110.0%

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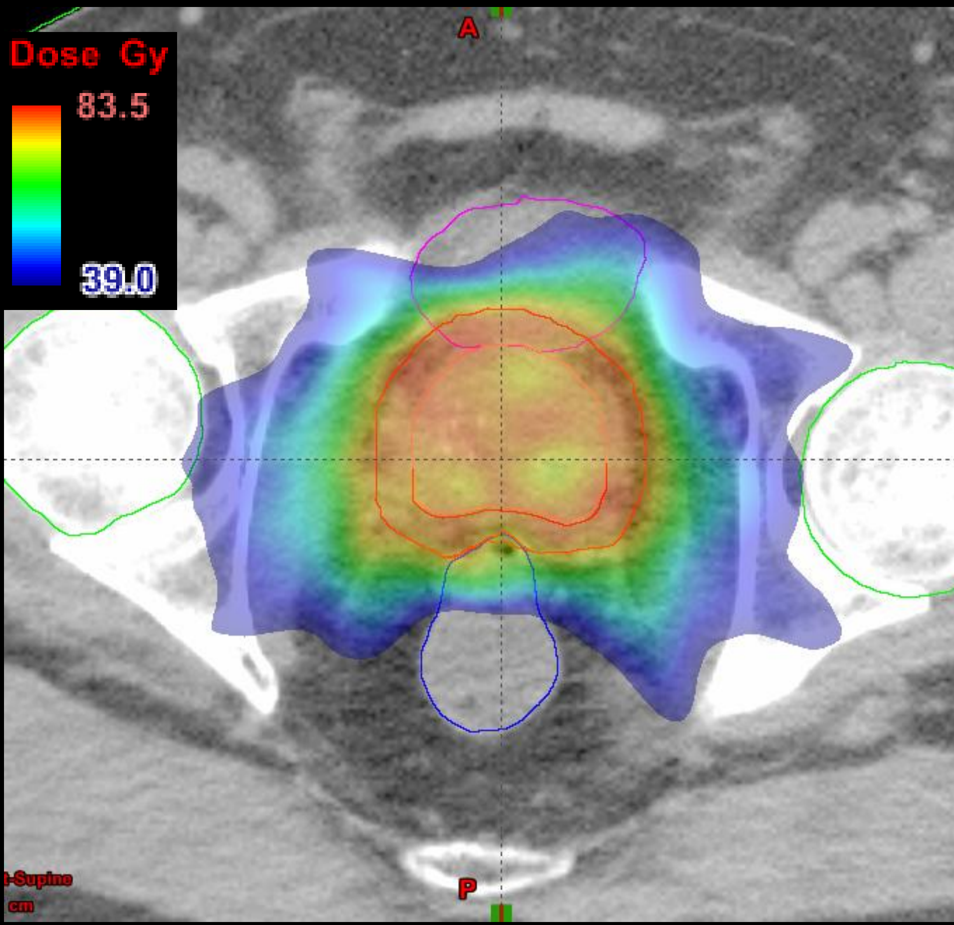
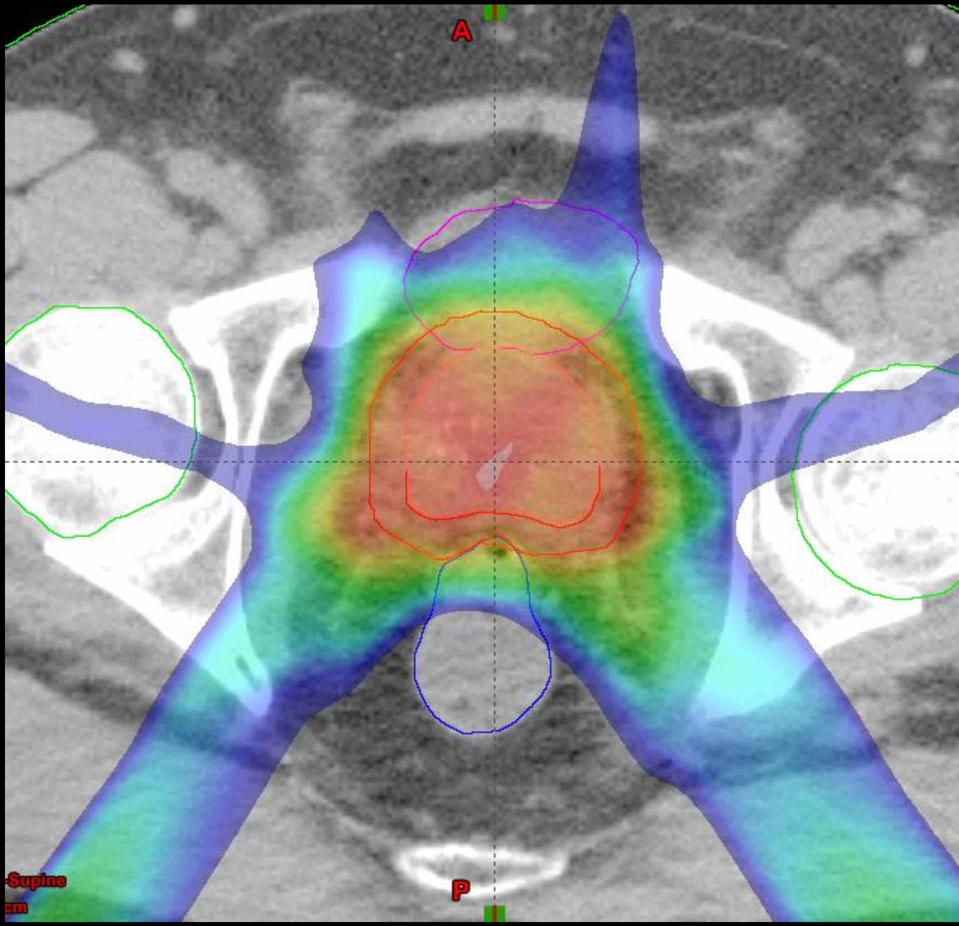
IMRT Quality



RapidArc Single arc IMRT **603 MU**



Conventional 5-field IMRT **915 MU**

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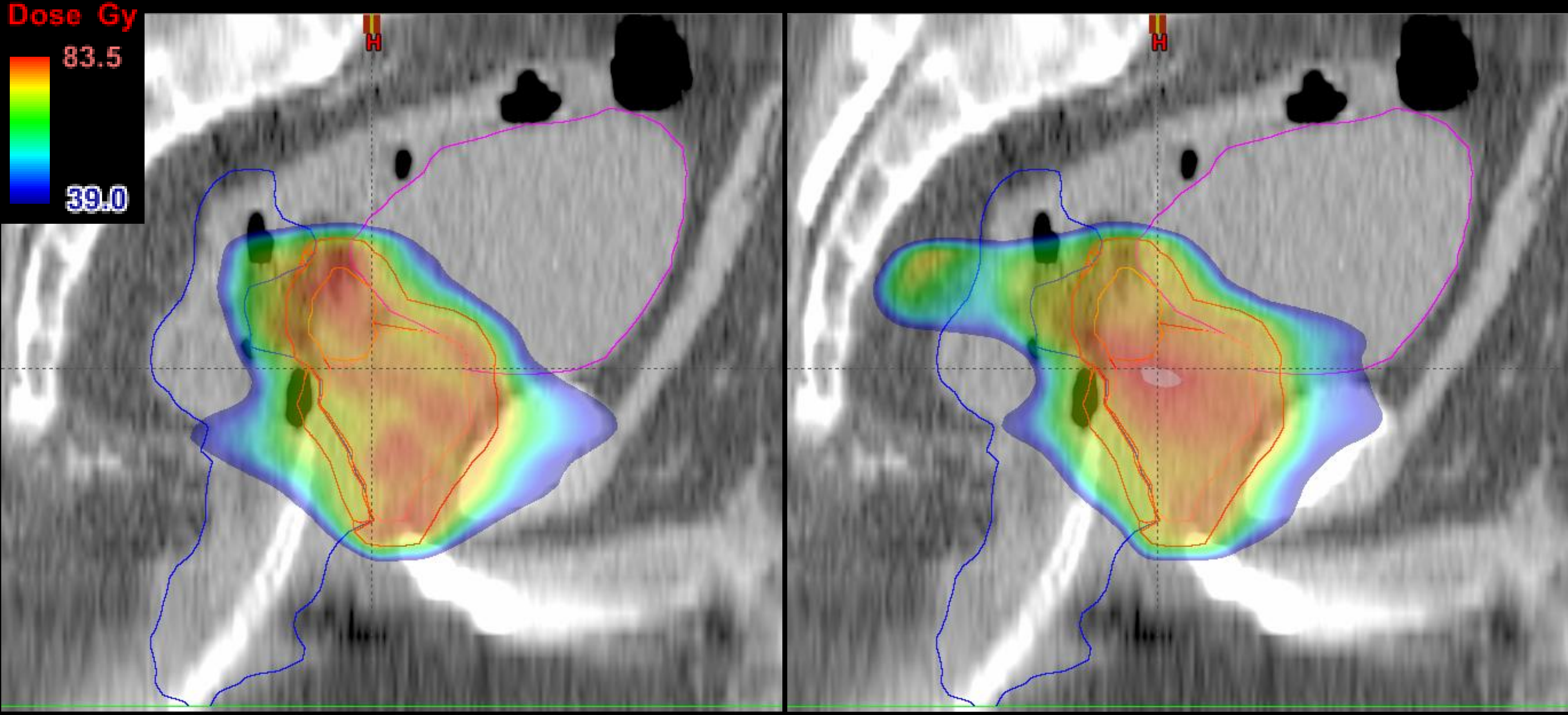
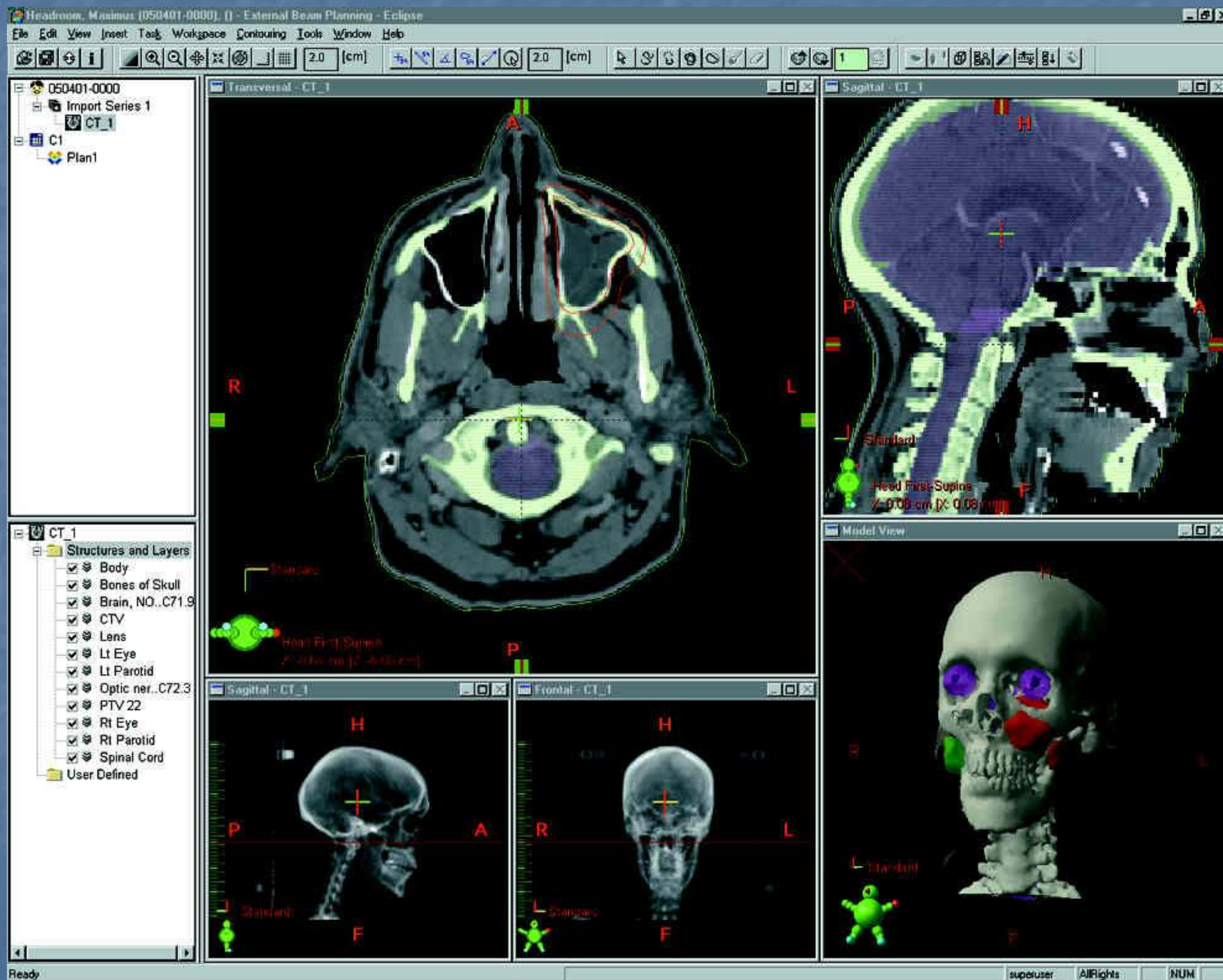
IMRT Quality



RapidArc
Single arc IMRT **603 MU**

Conventional
5-field IMRT **915 MU**

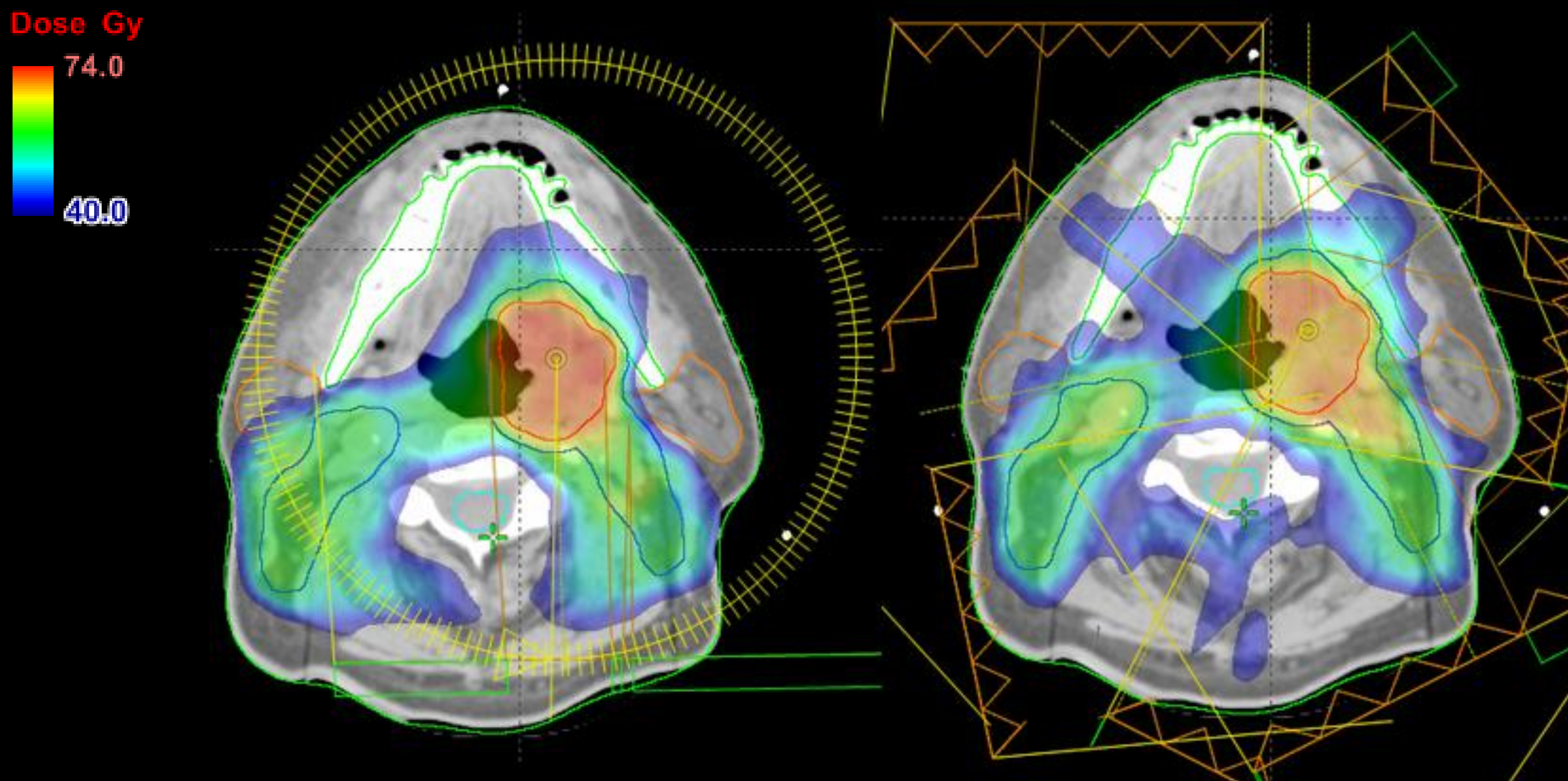
Treatment Planning (con't)



Radiation Therapy: State-of-the-art and future directions

- IMRT – Intensity Modulated Radiation Therapy
- VMAT – Volumetric Modulated Arc Therapy
- Tomotherapy – Image at time of therapy

IMRT Quality



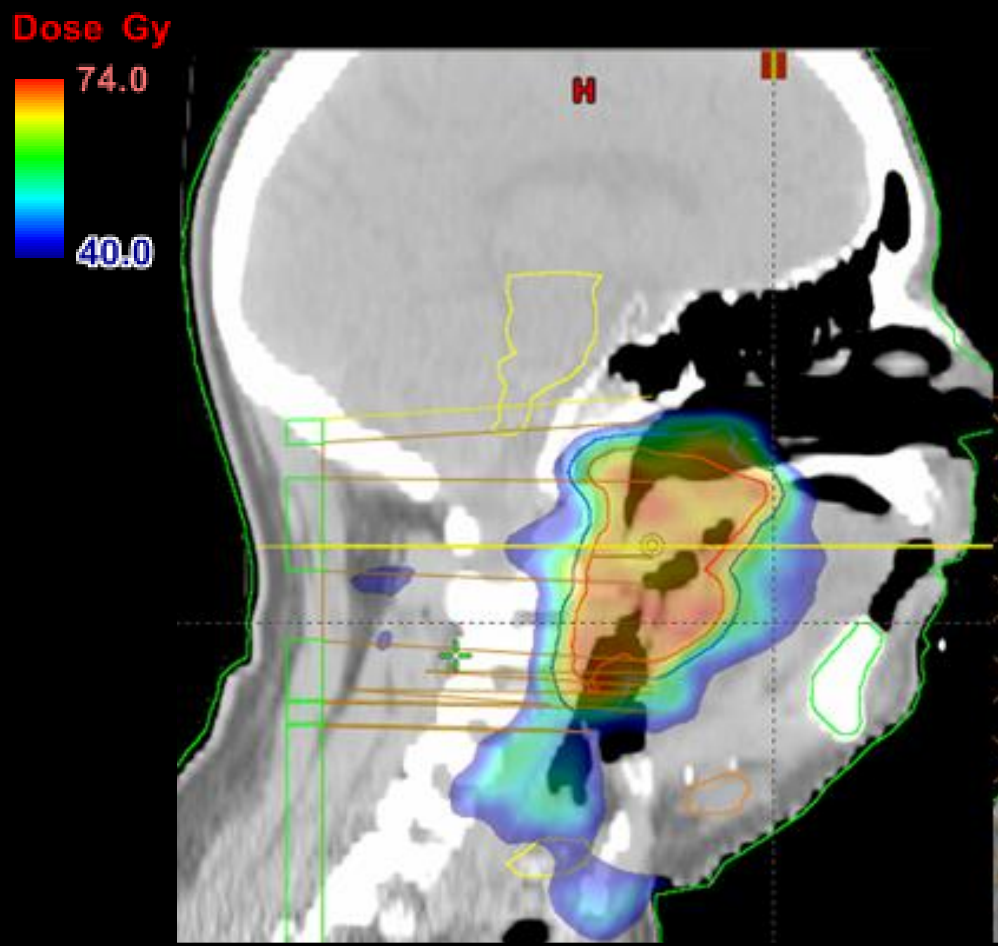
RapidArc
Single arc IMRT

496 MU

Conventional
7-field IMRT

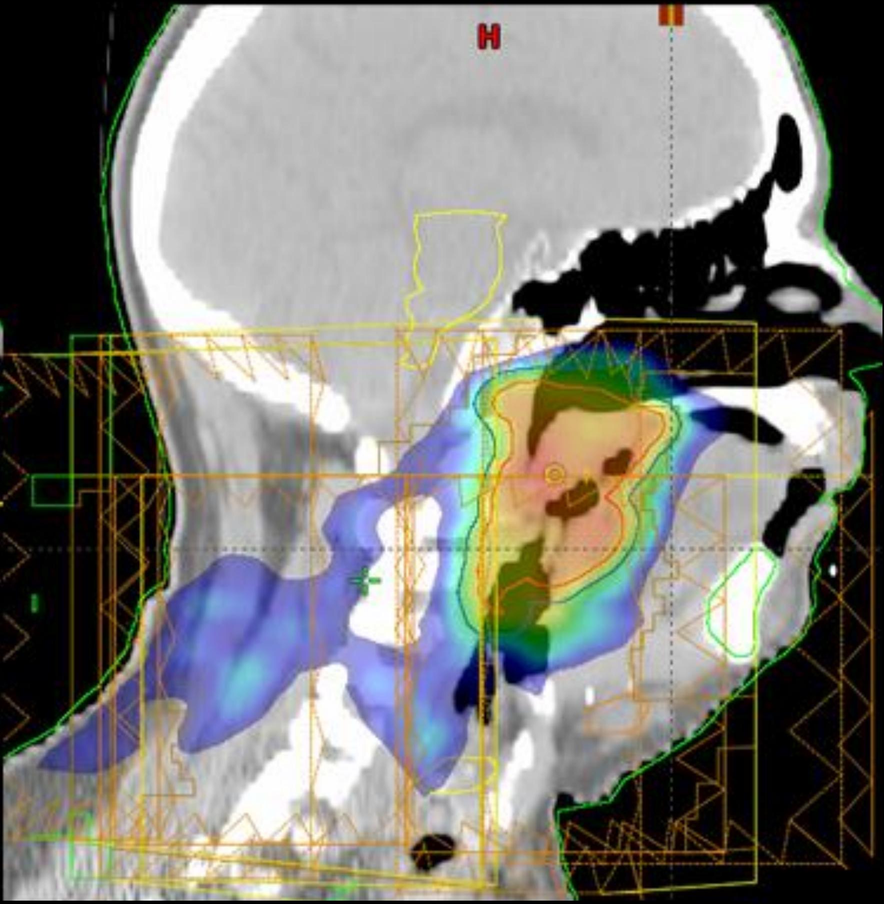
1685 MU

IMRT Quality



RapidArc
Single arc IMRT

496 MU



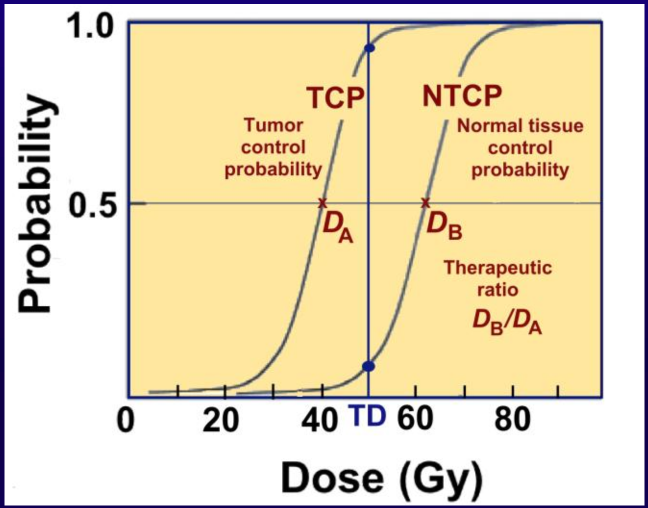
Conventional
7-field IMRT

1685 MU

GOALS of MODERN RADIOTHERAPY

To improve tumor control

through an increase in tumor dose,
i.e., through an increase in TCP



To reduce morbidity

through decreased dose to normal tissue,
i.e., through a decrease in NTCP

Using
(1) **More complex treatment techniques**
and
(2) **New technology**