PRINCIPLES and PRACTICE of RADIATION ONCOLOGY

Matthew B. Podgorsak, PhD, FAAPM
Department of Radiation Oncology
OUTLINE

- Physical basis
- Biological basis
- History of radiation therapy
- Treatment planning
- Technology of treatment delivery
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
<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-Life</th>
<th>Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-60</td>
<td>5.26 yr</td>
<td>1.25 MeV</td>
</tr>
<tr>
<td>Cs-137</td>
<td>30 yr</td>
<td>0.661 MeV</td>
</tr>
<tr>
<td>I-125</td>
<td>60 d</td>
<td>28 keV</td>
</tr>
<tr>
<td>Pd-103</td>
<td>17 d</td>
<td>21 keV</td>
</tr>
</tbody>
</table>
X Rays (photons)

- Interact with matter in well characterized processes:
  - photoelectric interaction
  - Compton interaction
  - pair production
- Infinite range, probability-based interactions
1.4 PHOTON INTERACTIONS

1.4.4 Photoelectric effect

- 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
Compton scattering
1.4 PHOTON INTERACTIONS

1.4.7 Pair production

- **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:
    
    $$h\nu_{\text{thr}} = 2m_e c^2 \left(1 + \frac{m_e c^2}{M_A c^2}\right) \approx 2m_e c^2$$

- $m_e$ electron mass
- $M_A$ mass of nucleus
- $m_e c^2 = 0.511 \text{ MeV}$
Charged Particles

- Interact via collisional and radiative mechanisms
- Predictable finite range
The general shape of the central axis depth dose curve for electron beams differs from that of photon beams.
Radiobiology

- Physical deposition of energy leads to a 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
  - mutation 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 $2.3 \times D_0$).

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 = $2.3 \times D_0$ 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
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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

The graph illustrates the probability of tumor control (TCP) versus normal tissue damage (NTCP) as a function of the delivered dose. The curves show how the probability of tumor control and normal tissue damage increases with higher delivered doses. At point A, the probability of tumor control is 10%. At point B, the probability of tumor control is 75%, and at point C, it reaches 90%. The NTCP curve also shows the probability of normal tissue damage increasing with dose.
Radiation Therapy History

- 1895 Roentgen discovers x-rays
- 1896 Becquerel discovers radioactivity (uranium)
- 1898 Marie Curie discovers Ra-226
- 1901 Pierre Curie self-induced radium burn on arm
- Biological effect of radiation exposure evident almost immediately
- Early radiation therapy using radium (interstitial, intracavitary, surface applicators)
Discovery of X-rays

On 8 Nov 1895, Wilhelm Conrad Röntgen (accidentally) discovered an image cast from his cathode ray generator.
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.
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
Dose distribution
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)
Post-Implant Dosimetry

Post-implant imaging for verification and dosimetry

Plane Film (2D)  CT (3D)
Other Brachytherapy

HDR esophagus

Typically 5 Gy/fx in 3-7 minutes
Other Brachytherapy

Base of tongue

Typically 1-4 day treatment
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
- Treatment 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
On the left is an MR image of a patient with a brain tumour. The target has been outlined and the result was superimposed on the patient’s CT scan. Note that the particular target is clearly seen on the MR image but only portions of it are observed on the CT scan.
Gamma Camera Scan

Liver metastasis from prostate carcinoma

IV administration of Tc99m

Accumulates in areas of increased blood flow due to active bone metabolism, oedema of inflammation or the angiogenesis associated with tumours
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
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
Dose distribution
Dose distribution
Dose distribution
Dose distribution
Dose distribution
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