It’s estimated that approximately 66% of patients will receive radiation therapy during their cancer trajectory. This session will bring you up to speed on how radiation therapy works, which cells it affects, and the various types of treatment delivery. At its end, you’ll be able to explain how radiobiology and fractionation impact radiation therapy outcomes, and identify the differences between external beam and internal radiation. Your new knowledge will help you to assess and manage the early and late effects of radiation therapy.

Content Area: Education

Content Level: Intermediate

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Penn Medicine. Employer
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Objectives:
At the end of this session, participants will be able to:
1. Explain how radiobiology and fractionation impact radiation therapy outcomes.
2. Distinguish the differences between internal and external beam radiation.

Content Outline:
I. Introduction
   A. Definition

II. Radiobiology
   A. Fractionization
   B. Radiosensitizers
   C. Radioprotectants

III. Process of radiation therapy
   A. Consultation
   B. Simulation
      1. Tools of the trade
   C. Treatment planning
   D. Treatment delivery

IV. Methods of delivery
   A. Teletherapy
      1. Kilovoltage
      2. Orthovoltage
      3. Megavoltage
   B. Brachytherapy
      1. Unsealed
      2. Sealed

V. Radiation safety/quality improvement

VI. Early side effects/management

Bibliography:


Indications for Radiation Therapy

It is estimated that 60% of cancer patients will receive radiation for the management of their cancer.

- Primary
- Neoadjuvant
- Concurrent
- Adjuvant
- Palliative

Ionizing Radiation

- Shortest wavelength & greatest energy of the electromagnetic spectrum
- Capable of imparting its energy to the body and causing chemical changes
- Ionizing radiation is emitted by
  - Radioactive materials
  - Some devices such as x-ray machines

Radiobiology

- Study of events that occur after ionizing radiation is absorbed by a living organism
- Some devices such as x-ray machines
- The deposit of RT into the cell causes physical, chemical & biochemical changes that result in direct or indirect damage to DNA causing cell death
- RT exerts damage to tissue by colliding with ionizing particles @ small intervals along the path through tissue
- Both normal & cancer cells are able to recover from RT injury
- Bio-effects of radiation on tumors & normal tissue are dependent on the 4 basic principles called the 4”R’s”

Reapportion

- Effect is to reduce cell survival over a fractionated course of radiation.
- Cells move to more radiosensitive phase in the cell cycle between fractions.
- M and G2 most sensitive phases.
- Late S most resistant phase.

Reoxygenation

- Effect is to reduce cell survival over a fractionated course of radiation.
- Pool of hypoxic cells diminishes after each fraction.
- Oxygenated cells more sensitive.

Repair of Sublethal Damage

- Effect is to increase cell survival over a fractionated course of radiation.
- Repair occurs during interval between fractions.
- Needs 2 hour interval for maximal effect.

Fifth R: Radiosensitivity & Factors

- Inherent – some cell lines & diseases are more sensitive to RT e.g. lymphocytes, ataxia telangiectasia, scleroderma
- Radiosensitizers- chemical/pharmacologic agents given with RT to increase damage to sensitive cells (e.g. fluoropyrimidines, taxanes, platinum compounds)
- Radioprotectors- chemical agents that minimize normal tissue damage from RT without compromising local tumor control (e.g. ethylol)
Radiation Dose

- Absorbed dose = the amount of energy adsorbed per unit mass
  - Correlates directly to energy of beam
  - Accurate measurement is critical
- Old measurement
  - Rad: 1rad = 1cGy
- New measurement
  - Gray: 100 cGy = 1Gray (Gy)

Moore-Higgins (2007)

Fractionation

- Standard
  - Single fraction 5 days a week
- Hyperfractionation
  - Smaller doses given more than once a day
- Accelerated fractionation
  - Shorter overall treatment time
  - Standard doses with increased number of fractions per day
  - Concomitant boost

Multidisciplinary Team

- Radiation Oncology
  - Radiation doctors
  - APRNs/PAs
  - Radiation nurses
  - Protocol nurses
  - Medical physicists
  - Dosimetrists
  - Radiation therapist
  - Engineers
- Support services
  - Social workers
  - Nutrition
  - Rehabilitation therapists
  - Pain management
  - Receptionists
  - Secretaries
  - Transport
  - Orderly
  - Pastoral care

Radiation Oncology

- Medical Oncology
- Surgical Oncology

Pediatric Considerations

- Psychosocial
  - Patient (child) & family centered care
  - Stages of childhood development
  - Child life specialist program
- Technical
  - Immobilization
    - Sedation
    - Specialized imaging and treatment delivery techniques
    - Dose/Fractionation schedule
  - Biologic
    - Side effects differ significantly between adult & pediatric populations
    - Acute side effects
      - Early & severe
      - Recover quicker
    - Late side effects
      - Greater
      - Immature & developing tissue more sensitive to RT
      - Greater risk of developing 2nd cancer
    - Survivorship
      - 60-70% of adults surviving a childhood cancer will develop at least one health related complication

### Respiratory Gating

- Synchronized treatments to breathing pattern
  - Helps to manage tumor or target motion
    - Maximizes dose to tumor
    - Minimizes dose to surrounding tissue
  - Respiratory cycle must be modeled prior to radiation delivery
  - Use of 4-D CT imaging (real time)
  - Radiation beam turned on/off to sync with Pt’s respiratory cycle
  - Lung, breast, liver, pancreas, kidney

### Organs at Risk (OAR)

- Normal tissues whose radiation sensitivity may significantly affect prescribed dose & treatment planning
  - “Emami paper”- published radiation tolerance doses for various organs (1/3, 2/3, or the whole organ)
  - Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC)
  - Dose-Volume Histograms (DVH)

### Definition of Treatment Volumes

- **GTV** = Gross tumor volume = All areas of gross disease
- **CTV** = Clinical tumor volume = GTV + margin: microscopic disease
- **PTV** = Planning target volume = CTV + margin: variation in internal organ motion
- **Treatment portal** = Additional margin to account for variation in set-up

**Haas, M.L. (2011)**

### Methods of Delivery

#### Teletherapy (External Beam)
- Kilovoltage
- Orthovoltage
- Megavoltage

#### Brachytherapy (Interstitial, intracavitary)
- Sealed sources
- Unsealed sources

### External Beam Radiation Therapy (EBRT)

- Ionizing radiation
  - Photons (x-rays and gamma rays)
  - Particle radiation (electrons, protons, neutrons, carbon ions, alpha and beta particles)

### EBRT

#### 3D-Conformal Radiation Therapy (3D-CRT)
- 3D-imaging for targeting tumor
- Minimizes normal tissue damage
- Maximizes RT dose to tumor

#### Intensity Modulated Radiation Therapy (IMRT)
- Enhanced imaging capability
- Modify intensity of beams during treatment
- Enhanced precision of dose
- Volumetric Modulated Arc Therapy (VMAT)
**Image-Guided Radiation Therapy (IGRT)**
- Repeated imaging scans during treatment delivery
- Increases accuracy and precision in treating tumor
- Reduces RT to normal tissue

**Stereotactic Radiosurgery (SRS)**
- Small tumors treated with one or more large radiation dosages
- Brain tumors, head & neck cancers, lung

**Stereotactic Body Radiation Therapy (SBRT)**
- Spine, liver, pancreas, kidney, lung, prostate cancer
- Highly focused treatment delivery from different angles
- Gamma Knife, CyberKnife, Clinac, X-Knife

**Internal Radiation Therapy**

**Sealed**
- Localized treatment
- Radioisotope placed implanted inside or close to tumor
- Ambulatory care setting

**Unsealed**
- Systemic treatment
- Radiopharmaceutical agents ingested or administered intravenously
- Inpatient setting

**Brachytherapy**
- BRACHY (short distance)
- THERAPY (treatment)
- Precise targeting of tumor/target
- Higher radiation dosages over shortened treatment course

**Brachytherapy**
- Sealed radioactive isotopes implanted
  - (iridium, palladium, iodine)
- Interstitial or intracavitary approach
- Temporary or permanent
- Treatment delivered directly to tumor

**Brachytherapy Guidelines**
- Published guidelines
  - Appropriate patient selection criteria
  - Treatment delivery
- American College of Radiology (ACR)
- American Society for Therapeutic Radiology and Oncology (ASTRO)
- American Brachytherapy Society (ABS)
- American Society of Clinical Oncology (ASC)

**Types of Brachytherapy**

**Permanent Seed**
- Low dose rate (LDR)
- Seeds permanently implanted into tumor/target organ
- Low levels of radiation emitted over few days/months

** Temporary Seed**
- High dose rate (HDR)
- Temporary implant of radioactive source for the duration of treatment
- High intensity radiation delivered in minutes

Used alone as monotherapy or as a boost combined with external beam radiation therapy
Cancers Treated with Brachytherapy

- Prostate
- Breast
- GU (penis, bladder, urethra)
- Head & Neck
- Gynecological (uterus, cervix, vagina, vulva)
- Lung
- GI (esophagus, bile duct, gallbladder)
- Rectal/Anal
- Ocular
- Pediatric tumors
- Skin/soft tissue
- Other cancers

Radioembolization

- Palliative treatment of liver cancer
- Prolongation of life
- Indications
  - Primary liver cancer
  - Inoperable liver cancer
  - Tumors that metastasize to liver
- Minimally invasive technique
- Radioactive particles inserted via angiogram
- Particles travel through bloodstream to lodge near the liver blocking blood flow to tumor

Selective Internal Radiation Therapy: SIR-Spheres Microspheres

**Indications**
- Targeted liver-cancer therapy
- Inoperable primary and metastatic liver cancer
- Permanent single-use implant

**Contraindications**
- Prior EBRT to liver
- Ascites
- Clinical liver failure
- Disseminated extra-hepatic malignant disease

TheraSphere (Yttrium-90)

- Radioactive glass beads injected into hepatic artery
- Radiation emitted over several weeks
- Minimal impact to non-targeted tissue
- Further therapeutic intervention possible
- Approved for use with portal vein thrombosis

Unsealed Sources

**Benign Conditions**
- Hyperthyroidism

**Malignant Conditions**
- Post thyroidectomy

Radioactive Iodine

- Liquid or capsule ingested
- Liquid form absorbed/concentrated by thyroid gland
- Thyroid tissue destroyed
- Healthy tissue spared
Radiopharmaceuticals

- Palliation of osseous pain related to metastases
- Administered intravenously
  - Strontium-89 Chloride (Metastron)
  - Samarium 153 Lexidronam (Quadramet)
  - Radium-223 dichloride (Xofigo)

Radiation Safety: Patient

EBRT
- No special precautions
- Minimal exposure time
- Image quality control
- Shielding
- Beam collimation
- Avoid imaging retakes

Brachytherapy
- HDR (temporary implant)
  - No special precautions
- LDR (permanent implant)
  - Special precautions
  - (Pregnant women, strain urine, condom)
- Radiopharmaceuticals
  - Excreted through urine, sweat, saliva, stool

United States Nuclear Radiation Commission [U.S.NRC, 2013]

Radiation Safety: Employee

Awareness
- Potential hazards
- Operating and emergency procedures
- ALARA principles

Compliance
- Radiation Safety Committee/Officer
- Training of personnel
- Wear personal dosimetry monitoring (film badges)
- Current annual dose limit 5,000 millirem
- Recommended < 500 millirem/year

Quality Assurance

- Calibration and periodic inspection
- Quality management program
- Physician peer review
- Staffing levels
- Continuous quality improvement initiatives
- Weekly assessments by radiation oncologist and support staff
- Treatment summary

American College of Radiology (2013)

Radiation Induced Side Effects

- effect of radiation on normal tissues
- dependent on total RT dose, fractionation schedule and size of treatment area
- 2 types of side-effects
  1. Acute (early): during & up to 6 months after RT
  2. Chronic (late): occur 6 months to years after RT
- May be more intense and may begin sooner with combined therapies (chemo & RT)
- Classification of side effects
  1. General
  2. Site-specific

General Side Effects

- Fatigue
- Skin
- Weight loss
- Myelosuppression (dependant on treatment area)
### Acute Site-Specific Side Effects

**Brain/Spine**
- Nausea / Vomiting
- Headaches
- Seizures
- Alopecia
- Skin reactions
- Transient exacerbation of pretreatment symptoms

**Breast**
- Skin reactions
- Swelling/tenderness
- Itching

**Head/Neck**
- Difficulty swallowing
- Sore mouth
- Dry mouth
- Taste changes
- Voice changes
- Skin reactions

**Chest**
- Difficulty swallowing
- Skin reactions
- Cough/hiccups

**Abdomen**
- Loss of appetite
- Nausea
- Vomiting
- Diarrhea
- Constipation

**Pelvis**
- Irritable bladder symptoms (↑ frequency, urgency, nocturia)
- Urinary Tract Infections
- Blood in urine
- Unable to urinate
- Rectal irritation/bleeding
- Skin reactions
- Sexuality changes

### Recommended Websites

- Oncology Nursing Society
  [http://www.ons.org](http://www.ons.org)
- ONS Radiation Special Interest Group
  [http://radiation.vc.ons.org](http://radiation.vc.ons.org)
- American Brachytherapy Society (ABS)
  [http://www.americanbrachytherapy.org](http://www.americanbrachytherapy.org)
- American Society for Therapeutic Radiology and Oncology (ASTRO)
- Radiation Therapy Oncology Group (RTOG)
  [http://www.rtog.org](http://www.rtog.org)

- The Radiosurgery Society
  [http://www.therss.org](http://www.therss.org)
- Radiological Society of North America (RSNA)
- Children’s Oncology Group
  — Survivorship guidelines
- Onco Link: Cancer resources for patients and healthcare professionals
  [http://www.oncolink.org](http://www.oncolink.org)