Radiation Oncology 101:
A Whole Field, 120 Years, and 100’s of Diseases in Under 30 min

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Agenda

• Rad Onc as a Career: Advertisement for the Specialty.
• Uses of Radiotherapy in Clinical Medicine.
• Radiobiology 101.
• Radiation Physics 001.
• Radiation Treatment Modalities including Radiosurgery and Proton Therapy
• Patient Experiences through Treatment / Case Vignettes
Why am I a Rad Onc?

• 85 yo woman admitted with 1 week of inability to walk, bowel and bladder incontinence after three months of increasing back pain.
  – IDC, 1.5 years prior: pT3 pN3a (ER/PR 25%, Her2-)
  – Anastrozole / Femara / Tamoxifen intolerant due to “joint aches, back and shoulder pain”
Pre XRT
Paralyzed / Incontinent

3.5 years Post XRT
Ambulatory / Continent
Living Independently
Why am I a Rad Onc?

- I can cure many patients on my own.
- I relieve symptoms for many of those I cannot cure.
- Cancer care requires teamwork.
- I have the time to get to know my patients well, and form close relationships with them during critical and emotional milestones in their lives.
- I treat children and adults.
- I don’t just write prescriptions, I do procedures.
- I see fascinating biology and pathology each day.
- Our field strives for evidence-based care.
- It mixes art and science with rapidly advancing technology.
Use of Radiation Therapy

- First effective non-surgical anti-cancer treatment.

- Still the single most potent anti-cancer “drug”.

- 60-70% of all cancer patients will receive RT at some point in the course of their disease.

- Utilization is estimated to increase by 20% between 2010 and 2020.
# Uses of Radiation Therapy

<table>
<thead>
<tr>
<th>Use</th>
<th>Definition</th>
<th>% Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitive</td>
<td>Alone or in combination with sensitizers (cisplatin, 5FU, taxanes, Erbitux, androgen deprivation, etc.) to cure a cancer</td>
<td>33%</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>Before or after surgery (or less often chemotherapy) to kill regional microscopic disease for cure</td>
<td>33%</td>
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<tr>
<td>Palliative</td>
<td>Non-curable therapy to reduce or prevent symptoms from incurable cancer</td>
<td>33%</td>
</tr>
<tr>
<td>Benign Disease</td>
<td>Non-cancerous conditions</td>
<td>1%</td>
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Uses of RT – (NEO)ADJUVANT

ADJUVANT radiation is generally only given when risk of local/regional relapse after surgery or chemotherapy is:

1. ≥ 15% or would be very morbid
2. difficult or morbid to salvage
3. associated with cancer-specific mortality
4. supported by results of Phase 3 RCTs
5. “sanctuary” sites where chemotherapy cannot penetrate (brain / testes)
6. bulky disease

Generally, RCTs of adjuvant radiotherapy show:

- > 50% RELATIVE REDUCTION of risk of locoregional relapse
- 5-15% ABSOLUTE IMPROVEMENT in overall survival
Uses of RT: Definitive Radiotherapy

- Brain Tumors:
  - Meningiomas, Schwannomas, Germinomas
- Head and Neck Cancers:
  - Oropharynx, Larynx, Oral, Nasopharynx→Hypopharynx, Nasal Cavity
- Chest:
  - Lung, Esophagus
- GI:
  - Pancreas, Gallbladder, Bile Ducts, Anal
- GU:
  - Prostate, Penis, Urethra, Bladder
- GYN Cancer:
  - Cervix, Vagina, Vulvar, Uterine
- Non-melanoma Skin Cancer
  - Particularly on the face
- Lymphoma (alone or with chemotherapy)
- Pediatrics (usually with chemotherapy):
  - Rhabdomyosarcoma, Ewing’s, Lymphomas, …
Uses of RT - NEOADJUVANT

• NEOADJUVANT - BEFORE surgery to:
  – Downstage tumor to:
    • facilitate resection.
    • allow function-sparing surgery.
  – Minimize risk of positive margins and intraoperative tumor spread.
  – Minimize overall side effects of treatment as compared to radiation after surgery.
  – Maximize effectiveness of radiation by treating tumor before it is disrupted.

  – DISADVANTAGES:
    • Pathological information from surgical specimen is not available.
    • May result in over-treatment of some patients whose disease is less extensive than preoperative imaging evaluation suggests.
Uses of RT: Neoadjuvant Treatment

- Lung Cancer:
  - NSCLC (especially Pancoast Tumor)
- GI Cancers:
  - Rectal
  - Esophageal
  - Pancreatic
  - Gastric
- Soft Tissue Sarcoma
Uses of RT - ADJUVANT

**ADJUVANT** - AFTER definitive surgery to:

- Minimize risk of *loco-regional recurrence* by sterilizing disease in:
  - unresected draining lymph nodes.
  - the margins of a resection, especially positive margins.
- Contribute to **overall survival**.
Uses of RT: Adjuvant Treatment

• Brain
• Head and Neck
• Lung
• Breast
• GI Cancers: Gastric, Rectal
• GU: Prostate
• Soft Tissue Sarcoma
• Skin
• Pediatrics:
  – Brain, Rhabdomyosarcoma, Wilm’s, Neuroblastoma, …
Uses of RT: Consolidative/Prophylactic RT

• Lymphoma
• Prophylactic Cranial or Craniospinal Irradiation
  – “Sanctuary” due to blood-brain barrier
  – Small Cell Lung Cancer
  – Leukemia / Lymphoma
  – Medulloblastoma and other Pediatric CNS Tumors
Uses of RT - PALLIATIVE

- **PALLIATIVE** – Relieve symptoms in incurable disease.
  - Pain:
    - Bone mets, uncontrolled head & neck, skin, chest wall, or extremity disease.
  - Neurological Impairment:
    - Brain metastases, spinal cord compression.
  - Obstructions:
    - Airway, bowel, vessels (eg SVC syndrome, extremity edema), dysphagia
  - Hemostasis:
    - Hemoptysis, vaginal bleeding, hematochezia
  - **Success Rate:** ≥ 80% for bone pain relief, ≥ 70% for other indications
  - **Onset:** within days to weeks
  - **Duration of response:** Weeks to Years (usually months)
Uses of RT – BENIGN DISEASE

BENIGN DISEASE –

- Inflammatory or Other Etiologies:
  - Heterotopic ossification prophylaxis after hip arthroplasty.
  - Keloids
  - Trigeminal neuralgia
  - AVMs
  - Grave’s Ophthalmopathy
  - Pyronie’s Disease
  - Hypersalivation

- Benign Tumors
  - Acoustic neuromas, Schwannomas, Meningiomas
  - Desmoid tumors
Radiation Toxicities

DETERMINISTIC:

– Will occur when a given tissue is exposed to given amount of radiation.
– Different tissues have differing susceptibilities.
– Result from cell death, scarring/fibrosis, or physiologic changes.
– May be influenced by medical comorbidities
  • DM, IBD, genetic radiation sensitivities (ataxia telangiectasia, xeroderma pigmentosa, …)
– Depend on functional organization of an organ.
Radiation Toxicities

**STOCHASTIC:**
- No absolute dose-response relationship.
- May be caused by even very-low dose exposures, e.g.

- **Radiation-induced second primary malignancies**
  Risk increases with:
  - Younger age at treatment.
  - Large volume of body treated.
  - Higher dose delivered.
  - Latency of > 7 years
Radiation Side-Effects

• Limited to the area treated, except:
  – Fatigue
  – Nausea (usually only with abdominal treatments)

• ACUTE:
  – Normal and expected.
  – Build up slowly over course of radiation.
  – Peak 7-10 days after completion of therapy.
  – >90% resolved 3-4 weeks after treatment.
Radiation Side-Effects

• Common Chronic:
  – Slowly manifest over 1-2 years after treatment.
  – Usually of mild intensity, such as:
    • Brain: Short-term memory loss
    • Prostate: Obstructive urinary symptoms (eg slow stream, nocturia, frequency, ...), erectile dysfunction
    • Head & Neck: Dry mouth, fibrosis
    • Abdomen: Frequency, intermittent diarrhea, intolerance of fatty foods
    • Breast: Tissue fibrosis.
Radiation Side-Effects

• CHRONIC:
  – SEVERE complications such as bowel obstruction, fistulae, radionecrosis, strictures, etc. are RARE (<5%)
  – Risk increases with higher-dose, larger fields
  – Retreatment (Reirradiation)
  – Concurrent chemotherapy
  – Diabetes, Smoking, Procedures in Treated Areas
  – Genetic Predispositions (ATM, XP, etc.)
Mechanism of Action
Maximizing Therapeutic Ratio - Fractionation Radiobiology

**SINGLE DOSE RT**

- 100%
- 10%
- 1%
- 0.1%
- 0.01%

**FRACTIONATED RT**

- 100%
- 10%
- 1%
- 0.1%
- 0.01%

**Tumor**

**Normal Tissue**

- Single Dose 8Gy
- Fractionated Dose 8Gy
- Fractionated Dose 18Gy
### Conventional RT Schedules

<table>
<thead>
<tr>
<th>Schedule Type</th>
<th>Example Cancer Type</th>
<th>Dose Details</th>
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</thead>
<tbody>
<tr>
<td>Definitive RT Alone</td>
<td>Prostate Cancer</td>
<td>200 cGy/d, 50 Gy to pelvis boost prostate to 80Gy</td>
</tr>
<tr>
<td>Adjuvant RT</td>
<td>Breast Cancer</td>
<td>200 cGy, 50 Gy to whole breast boost lumpectomy bed to 60Gy</td>
</tr>
<tr>
<td>Definitive Chemo RT</td>
<td>Head &amp; Neck Cancer</td>
<td>200 cGy/d, 50 Gy to neck, boost gross tumors to 70Gy</td>
</tr>
<tr>
<td>Palliative Hypofractionated RT</td>
<td>Cord Compression, Bone Pain, Hemorrhage, Brain Mets</td>
<td>300 cGy x 10 OR 250 cGy x 14 OR 400 cGy x 5 OR 800 cGy x 1</td>
</tr>
</tbody>
</table>
SENSITIVITY and RESPONSIVENESS

How SENSITIVE to Killing

More
- Squamous Cell (H&N, Anus)
- Lymphoma
- Small Cell
- Lung/Colon

Less
- Sarcoma
- Melanoma / Renal Cell

How FAST does tumor Shrink

Fast
- Lymphoma
- Squamous
- Small Cell

Slow
- Melanoma / Sarcoma
- Renal Cell / Colorectal
Radiosurgery

- Focus 1-5 massive doses of radiation on a tumor or organ.
- Non-invasively kill nearly everything in the target volume.
- Forfeit most radiobiological sparing of normal tissues.
- More like surgery, RFA or cryotherapy.

- Rely on physics, imaging, and technology to maximally focus radiation on target and AVOID normal tissues.

- Radiobiology of large single dose treatment may induced more death of tumor neovasculature to result in better tumor killing.
RADIOSURGERY = RADIATION ABLATION

Definitive RT Alone (eg 80 Gy to prostate in 40 fx daily)

Radiosurgery (eg 38 Gy in 5 fx)

Keep the prostate
Kill the cancer.

Radiosurgical Prostatectomy

Radiosurgery Schedules

OR

OR

OR

OR
Maximizing Therapeutic Ratio

• How do I FOCUS it?  PHYSICS
  – External Beam and/or Brachytherapy
  – Alphabet Soup:
    IGRT, IMRT, Tomotherapy, Protons, HDR, LDR, SBRT, SRS, Cyberknife, TrueBeam, Novalis, Vero, …
Simulation

• Position patient as they will be treated.
• Fabricate immobilization devices (mask, arm-rest, body cradle, leg-rest, abdominal compression belt to minimize respiratory motion).
• Obtain treatment-planning CT scan of the target area.
• Place marks (often tattoos) as reference for repositioning.
Planning

• Rad Onc works with team to define treatment:
  – Fuse different imaging modalities to the planning CT
  – Draw targets and normal structures to avoid
  – Specify Dose-Volume Constraints, for example:
    • Max dose to spinal cord < 50 Gy
    • No more than 27% of lungs to get 20 Gy
    • Lowest dose in PTV should be 95% of the prescription
  – Work with team to optimize treatment
  – Quality assurance
Image-Guided IMRT - Delivery
Linear Accelerator
Manipulator
X-ray Sources
ROBOTIC DELIVERY SYSTEM
IMAGING SYSTEM
TARGETING SOFTWARE
Image Detectors
Brachytherapy – Implant Types

• Temporary
  – “Applicator” = device or catheters placed within tumor-bearing tissue to hold radioactive sources.
  – Applicator removed at end of therapy.

• Permanent
  – Permanent implantation of radioactive seeds into tumor which decay to inert metal.
Brachytherapy – Dose Rate

- **Low Dose Rate**
  - Low activity radioactive seeds slowly deliver radiation over days to months.

- **High Dose Rate**
  - High activity source pushed in & out of applicator by robot (Afterloader)