Case Based Introduction to Radiation Oncology

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Cancer is Common
Estimated New Cancer Cases and Deaths by Sex, 2017

<table>
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<tr>
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<th>Men Incidence</th>
<th>Men Deaths</th>
<th>Women Incidence</th>
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<td>836,150</td>
<td>318,420</td>
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<td>60,490</td>
<td>12,240</td>
<td>Uterine</td>
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American Cancer Society, Surveillance Research, 2017

One in Three Americans will Develop an Invasive Non Skin Cancer in There Lifetime
Role of Radiation Therapy in the Management of Cancer

• At least 50% of cancer patients receive radiation therapy at some point during their management.

Basic Tumor Kinetics

• Tumors grow exponentially for a portion of their natural history
• Lower limit of detection about 1x10⁹ cells (1 cc³)
• A lethal volume of cancer is about 1x10¹² cells (1 kg). Most cancers have therefore completed about two-thirds of their natural life span before they are detected

The Cancer Team

• Multidisciplinary management is key for best outcomes
• The cancer team consists of:
  – Surgical Oncologist
  – Medical Oncologist
  – Radiation Oncologist
• Other supporting services
  – Radiology, nuclear medicine, pathology, social work, nursing…
Role of Radiation Oncologist

- Determine if a patient needs radiation therapy as a component of cancer care
- Recommend radiation type, dose, and fractionation schedule
- Inform patient of the rationale for radiation, side effects of treatment, and potential late toxicities
- Follow patient during and after treatment to assess outcomes

What is radiation?

Case #1 – Breast Mass

Introduction to External Beam RT
Case #1

- 42 yo woman presents to your office for a routine H&P
- On exam, you notice a 1 cm right breast mass in the UOQ
- Mammo confirms the presence of the mass and ultrasound guided biopsy is positive for breast cancer

What do you do?

- Treatment Options Include:
  - Mastectomy
  - Lumpectomy and radiation therapy
- The patient decides to have breast conserving therapy. Surgery goes well (T1 tumor, negative margins, negative nodes). Now she presents for routine post-op breast radiation.

Radiation Recommendation:

- 3D conformal external beam radiation therapy to the right breast
- Dose = 42.56 + 10 Gy boost
- Fraction size = 2 – 2.66 Gy per day

Huh?? What does this mean??
External Beam Radiation Therapy

- Aiming ionizing radiation at a tumor using beams that come from the outside
- Historical method
  - Gamma radiation with Co-60
- Current method
  - Megavoltage x-ray radiation using a linear accelerator

Definitions

- Ionizing radiation
  - Energy strong enough to ionize an atom
- Gamma ray vs x-ray
  - Gamma rays are photons emitted from radioactive materials as they decay
  - X-rays are photons produced by machine
    - High energy photons are produced by a linear accelerator when tungsten target bombarded by high energy electrons

Linear Accelerator

Courtesy of Dr. Jean Pouliot, UCSF
More Definitions – kV vs MV

• Kilovoltage (kV) - diagnostic radiology
  – Photoelectric effect creates sharp distinctions between tissue types
  – Energy range:
    – 25 kV – 150 kV (25,000 – 150,000 V)

• Megavoltage (MV) - radiation therapy
  – Intentionally ionizing
    – Compton effect and pair production
  – Energy range:
    – 4 MV – 20 MV (4,000,000 – 20,000,000 V)

“3D Conformal”

• A type of external beam radiation therapy
• Radiation plan based on CT scan of patient in the radiation position

• Other types of EBRT:
  – Conventional – simple fields, planning based on bony landmarks
  – IMRT – intensity modulated radiation therapy, computer-aided planning using multiple (~100) overlapping fields

Typical Breast Plan
Determining Dose

- Unit of dose = Gray (Gy)
- 1 Gy = 1 joule/kg, measure of energy deposited in the tissue treated
- Typical dose per day = 2 – 2.66 Gy

What is a “boost”?  

- The region of the tumor bed is the area at highest risk of recurrence
- So, additional radiation is given to the lumpectomy cavity

Typical Breast Boost Plan
**Rationale for Radiation in Breast Cancer**

If a patient opts for breast conserving therapy, radiation therapy should be given to reduce the risk of recurrence of cancer.

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**Case #2 – Sore Throat**

Introduction to IMRT

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**Case #2**

- 55 yo M, 40 pack year smoker, presents to your office complaining of sore throat

- On exam you see an ulcer in the right tonsil and you feel a rock hard 3 cm right neck node

- You realize this isn’t strep throat…
What do you do?

• An ENT performs tonsil bx in the office and sends the patient for a FNA of the neck node

• Pathology shows poorly differentiated squamous cell carcinoma in both

Treatment Options

• Operable head and neck cancer has multiple treatment options:
  – Surgery followed by radiation
  – Radiation followed by surgery
  – Chemo-radiation with surgery reserved for incomplete response to therapy

• The patient wants to avoid surgery, decides to have definitive chemoradiation

Radiation Recommendation

• Intensity modulated radiation therapy to a total dose of 70 Gy to regions of gross disease

• Concurrent q 3 weekly cisplatin chemotherapy

• Post treatment imaging at 8 weeks to assess response to therapy
Conventional Radiation Fields

- A type of external beam radiation therapy
- Intensity of the radiation beam varies across the radiation field
- Based on CT anatomy
- Inverse treatment planning

IMRT
Extended Field IMRT

Designing an IMRT plan

- Radiation oncologist defines regions to treat and doses to give
  - Gross tumor, prophylactic coverage
- Radiation oncologist also defines regions to avoid
  - Parotid glands, spinal cord, eyes...
- Radiation physicist creates plan

Example IMRT plan

Lee, IJROBP, 57:49-60, 2003
Can you really give chemo and RT at the same time?

• Yes, you can!

• The combination has been proven to improve cancer control rates for many tumors, including:
  – Lung, rectum, pancreas, esophagus, anal, stomach, brain…

• What’s the downside? Increased toxicity

Overall Survival: Radiation Alone vs ChemoRT

Case #3 – Rising PSA

Introduction to brachytherapy
64 yo M presents to your office for routine H&P, you recommend some cancer screening tests including PSA.
PSA = 4.5, 2 years ago it was 1.3
Digital rectal exam WNL
Biopsy reveals prostate cancer.

**THERAPY OPTIONS**
**INTERMEDIATE RISK PROSTATE CANCER**

- Active Surveillance
- Radical Prostatectomy
- EBRT +/- ADT
- Brachytherapy +/- supplemental EBRT
- Other modalities:
  - Stereotactic body radiotherapy (SBRT)
  - Proton Radiotherapy
  - Cryotherapy
  - HIFU

What are the radiation options?

- External beam radiation therapy
  - Total dose around 78 Gy
  - Approx 40!! Treatments
  - Recent use of Hypofraction and SBRT
- Brachytherapy
  - Low dose rate (permanent)
  - High dose rate (temporary)
- Both +/- hormonal therapy
What is brachytherapy?

- Placement of radioactive materials into or immediately adjacent to the cancer
- Requires an invasive procedure
- May be done alone or in combination with external beam radiation therapy

HDR vs LDR

- Low dose rate (LDR)
  - Source may be placed temporarily or permanently
  - Radiation is delivered over days to weeks
  - Typical isotope for gyn cases = Cs-137
  - Typical isotopes for PPI cases = I-125 and Pd-103
- High dose rate (HDR)
  - Radiation source is temporarily placed in patient and then removed
  - Source is very “hot” so high doses of radiation given in minutes
  - Typical isotope = Ir-192

Permanent Prostate Implant

- Radioactive seeds are inserted into the prostate and remain there forever (LDR)
- Seeds are loaded into needles
- Needles directed thru the perineum and into the prostate under ultrasound guidance
Implant Dose

- Total dose = 144 Gy with I-125
- Total dose = 125 Gy with Pd-103
- The dose is very high because the radiation is given off slowly
- Half life for I-125 is 60 days
- Half life for Pd-103 is 17 days

How Successful is PPI?

MSKCC experience with 1,449 patients treated with PPI 1992-2000
Other types of brachytherapy

- Head and neck HDR
- Gynecologic LDR
- Gynecologic HDR
- Intraoperative brachytherapy
- Coronary brachytherapy
Case #4

Introduction to radiosurgery

Case #4

• Your breast cancer patient returns to your office 4 years after her initial diagnosis complaining of headache and nausea

• You order a MRI scan and it shows new brain metastases

What do you do?

• Treatment options:
  – Whole brain radiation therapy
  – Radiosurgery
  – Brain RT and radiosurgery boost
Radiosurgery

- Short course, high dose, very focused external beam radiation treatment

- Ways to perform radiosurgery:
  - Gamma knife
  - Linear accelerator based
  - Cyberknife

Gammaknife Radiosurgery

- Rigid patient immobilization, within 1 mm
- 201 cross-firing tiny radiation beams give extremely high doses to small points in the brain
- Accurate MRI based radiation treatment planning

Cyberknife Radiosurgery

- Miniature linear accelerator mounted on robot arm
- Can treat tumors located anywhere in the body
- Built-in ability to track moving tumor target
Case # 5

Introduction to Intraoperative Radiotherapy

Case # 5

- A 65 year old female presents with a clinical 1 cm/ER positive infiltrating ductal cancer.
- She lives far away from our Radiation Oncology Center and is seeking an alternative form of radiotherapy.

Facts

Whole breast irradiation reduces local recurrence rate from 30-40% to < 10%

Tumors < 1cm without RT 16.5% Local recurrences

90% local recurrences are in the index quadrant independent of applied radiotherapy
The TARGIT Technique

PRS400 (Intrabeam)
A miniature electron generator and accelerator
Accurately delivers radiotherapy
from within the breast
in about 25 minutes.

The TARGIT Procedure

Lumpectomy Placement of X-Ray Source Boost Irradiation

Spherical Applicators
2.5 cm Diameter (100 uses each) Mounted Applicator
These graphs are restricted to 4 years as less than 420 (<20%) patients have a follow-up beyond this point; however, all patients (with a maximum follow-up of 10 years) are included in the analysis. As recommended by Pocock et al. Lancet 2002; 359(9318): 1686-9.

1.2% (95% CI 0.53 – 2.71)  
0.95 (95% CI 0.39 – 2.3)  
log rank test p = 0.41

Image Guided Radiation

Radiation Safety

- ALARA =  
  - As Low As Reasonably Achievable!

- Time  
  - Minimize the amount of time you are exposed

- Distance  
  - $1/R^2$, 2 times the distance is 4 times less dose

- Shielding
Typical Radiation Doses

- Conversions: 10 mSv = 1 rad = 1 rem = 1 cGy
- Natural background, radon = 2 mSv/year
- Natural background, other (cosmic, etc) = 1 mSv/year
- Commercial flight, USA to Europe = 0.05 mSv
- CXR = 0.02 - 0.05 mSv
- CT scan = 6.34 - 7.8 mSv (depending on part of body scanned)
- PET scan = 11 mSv
- Fluoroscopy = 3-20 R/minute surface dose (this is why cardiologists are the only one who ever go over tolerance limits!!)
- Public exposure limit, continuous/frequent = 1 mSv/year
- Public exposure limit, infrequent = 5 mSv/year

Summary

- The radiation oncologist is an important member of the cancer team
- Common radiation treatments include:
  - External beam radiation
    - Conventional, 3D conformal, IMRT
  - Brachytherapy
    - HDR, LDR
  - Radiosurgery

Summary

- Radiation can be used:
  - Before surgery
  - After surgery
  - Alone
  - In combination with chemotherapy
- Goals of radiation:
  - Cure cancer
  - Palliation in incurable patients
Role of The Medical Student/Intern

Two Lessons to Learn

There exist 2 different definitions regarding radiotherapy toxicity: (1) effects directly attributable to radiotherapy or (2) any adverse events after radiotherapy. Unfortunately the second definition is used frequently and is always inappropriate.

Typical Scenario

- Sixty Four year old gentleman who has undergone an APR for a low rectal cancer. Stage T3N1M0. Post-operative combined chemotherapy and radiotherapy is recommended. Patient subsequently is admitted to the hospital in July with complaints of severe abdominal cramping and diarrhea. The house staff calls Radiation Oncology to notify us that the patient has been admitted with “Severe Radiation Enteritis”.

I inform the house staff that it is unlikely that the patient has Radiation Enteritis and receive harsh criticism that Radiation is “bad for the small intestine” and that the “patient has all the clinical and radiographic features of radiation enteritis.”

My reason for suspecting the radiotherapy is not contributing to the current situation….

The Patient has yet to start Radiotherapy !!!!!!!
LESSON NUMBER ONE
Radiation Toxicity Only Occurs if Radiotherapy has been delivered.

Case #2.
Patient undergoes a mastectomy for an early breast cancer and develops a local recurrence which is treated with excision and radiotherapy in 1997. Approximately 9 years later she develops pain and paraesthesias in the arm. She is referred to neurology, does not see the treating radiation oncologist, and is diagnosed with a radiation brachial plexopathy.

Case # 2
Patient’s symptoms continue to progress – she develops “treatment related lymphedema”, worsening pain and near complete paralysis of the extremity. I saw the patient in consultation, patient has a large supraclavicular recurrence, axillary DVT. Review of the previous radiotherapy fields note the supraclavicular fossa was not originally irradiated. No note in the neurology chart that the radiotherapy fields were reviewed.
LESSON NUMBER TWO

Radiation Toxicity Only Occurs if Radiotherapy has been delivered to the area in question

The most important factor to determine if a patient is having a radiation toxicity is determining the area radiated and the dose.

Please think before you write.