Radiation Therapy for Breast and Prostate Cancer

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What do you know about radiation oncology?

1. Nothing

2. I know radiation is used to treat cancer, and not much more

3. I have seen patients receiving radiation therapy, and have seen some side effects from it

4. I am very familiar with the indications and various methods by which radiation is delivered

5. I can do BED calculations in my head for both early and late responding tissues while hopping on one leg
Overview

- Breast Cancer Overview
- Prostate Cancer Overview
- External Beam RT (Teletherapy)
  - 2D/3D
  - IMRT (intensity modulated radiation therapy)
  - Particles (Protons, Neutrons, Carbon ions, etc)
  - IGRT (image guided radiation therapy)
- Brachytherapy
  - Permanent: prostate implant
  - Temporary: accelerated partial breast irradiation, intraoperative
Breast Cancer
Breast Cancer

- Lifetime Risk: 1 out of 8 women in US
- 2nd leading cause of cancer death in women

2014:
- ~232,000 new cases of invasive cancer
- ~63,000 new cases of non-invasive cancer
- ~2,000 new cases in men
- ~40,000 deaths from breast cancer

- 2.8 Million breast cancer survivors
Breast Cancer – Risk Factors

- Genetics (BRCA, 1\textsuperscript{st} degree family history)
  - 85% of women w/ breast ca have \textbf{NO} family hx
- Being tall
- Other breast pathology (ADH, LCIS, dense breast)
- High endogenous estrogen (obesity, early menarche)
- Alcohol consumption
- Smoking
- Never/Late first full-term pregnancy
- Never breastfeeding a child
- Hormone replacement/OCP
- Risk models: Gail, Tyler-Cusick
Breast Cancer – Prevention

• Chemoprevention for high-risk women:
  – Tamoxifen/Raloxifene
    • Estrogen receptor antagonist/modulator
    • ~50% relative risk reduction
    • Risks: Blood clots, stroke, endometrial cancer
  – Aromatase Inhibitor

• Prophylactic Mastectomy
  – BRCA+ (60-80% lifetime risk of breast cancer)
Breast Cancer – Screening

• Mammogram
  – Screening starting at age 40 (ACS)
  – 3D (JAMA, June 2014):
    • 40% higher detection of invasive cancers
    • 16% less call backs

• MRI
  – ACS recommends for high-risk women
    • 20-25% lifetime risk
    • BRCA or other mutation with increased risk
    • Prior XRT to chest

• Clinical Breast Exam
External Radiation for Breast Cancer

• Usually given after surgery +/- chemotherapy
  – Decreases recurrence, improves survival
  – Post lumpectomy vs. post mastectomy

• Fractionation:
  – 5 days/week, 10-15min each day
  – Typical fractionation 6½ weeks
  – Hypofractionation 3-4 weeks
    • Delivers more dose each day

• Accelerated Partial Breast Irradiation
  – Discussed later, brachytherapy
External Beam for Breast Cancer
Acute Side Effects: Breast

- Fatigue
- Skin reactions
- Erythema/hyperpigmentation
  - aloe (non-alcohol) lotion
  - Steroid creams
- Dry desquamation
  - aquaphor
- Moist desquamation (not common)
  - aluminum acetate soaks
  - hydrogen peroxide rinse
  - non-adherent hydrogel wound pads
  - silver sulfadiazine
Radiation Reaction
Prostate Cancer
Prostate Cancer

• Lifetime risk: 1 in 7 men diagnosed in lifetime
• 2nd leading cause of cancer death in men
• 2014:
  – 233,000 new cases diagnosed
  – 29,480 men will die of prostate cancer
• 2.5 million survivors
Prostate Cancer – Risk Factors

• Age (60% diagnosed after 65yo, rare <40yo)
• Race (African-American)
• Family history
  – (BRCA gene)
• Obesity
• Smoking
Prostate Cancer - Screening

- PSA, Digital rectal exam (DRE)
- USPSTF, 2012 (Blunt, controversial):
  - Recommends against PSA-based screening for prostate cancer
- American Cancer Society (wordy):
  - Research has not proven that benefits of testing outweigh the harms of testing and treatment
  - At 50, men should talk to a doctor to decide if testing is the right choice, etc…
  - Start discussion at 45 if AA or father/brother diagnosed with prostate cancer < 65yo
Prostate Cancer - Screening

- American Urological Association (very wordy):
  - Recommends against PSA in men < 40yo
  - Does not recommend routine screening in men 40-54yo at average risk. For men younger than 55 at high risk, decision should be individualized
  - Strongly recommends shared decision-making at 55-69yo
  - Routine screening intervals of 2 years may be preferred over annual
  - Does not recommend PSA in men 70+ or <10-15y life expectancy. But some men 70+ in excellent health may benefit from screening
Prostate Cancer

- RT usually given for *definitive* treatment
  - instead of surgery

- Definitive EBRT

- Definitive PSI

- Combination PSI + EBRT

- Concurrent androgen deprivation
## Prostate Risk Groups

<table>
<thead>
<tr>
<th></th>
<th>D’Amico</th>
<th>MSKCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td>PSA &lt; 10, and GS 2-6, and T1c-T2a</td>
<td>PSA &lt; 10, and GS 2-6, and DRE &lt; T2c</td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td>PSA 10.1-20, or GS 7, or T2b</td>
<td>PSA &gt; 10, or GS &gt; 6, or DRE &gt; T2b</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>PSA &gt; 20 or GS 8-10, or T2c</td>
<td>2 or 3 unfavorable features noted above</td>
</tr>
</tbody>
</table>
Prostate EBRT Fractionation

• Standard fractionation
  – Tx five days/week
  – Approximately 8 to 8.5 weeks
  – 1.8-2.0Gy to total of 75-80Gy
  – ~15 minutes each treatment

• Hypofractionation (SBRT)
  – 5 total treatments, every day or every other day
  – 7.0-7.25Gy to total 35-36.25Gy
  – ~1 hour each treatment
Acute Side Effects: Pelvis

- Nothing!!
- Bladder irritation
  - antispasmodics
- Urinary hesitancy
  - tamsulosin
- Rectal irritation
  - hydrocortisone cream
  - HC suppository
- Diarrhea
  - antimitotility agents
What is Radiation Therapy?
History of Radiation

• 1895: William Rontgen discovered/named x-rays
  – 2 months later it was proposed to be used for treatment of diseases

• 1986: Becquerel discovered uranium emitted radiation

• 1898: Marie Curie discovered radium and coined the term “radioactivity”

• By 1900: Used to treat skin cancers
Types of Radiation Therapy

• Teletherapy – “Distance therapy”
  – external beam
  – linear accelerator
  – essentially no radiation exposure to caregivers

• Brachytherapy – “Short (close) proximity”
  – “seeds”, “sources”
  – “radiation implant”
  – exposure to caregivers (physicians, nurses, physicists)
Brachytherapy implants
External Beam Radiation
External Beam Radiation
Progression to IMRT

• Surface anatomy

• 2D = fluoroscopy
  – made possible by x-rays

• 3D = CT based reconstruction / visualization
  – made possible by CT-scanners

• IMRT = intensity modulation
  – made possible by faster computer processing
  – inverse planning
2D – Fluoroscopy
3D – CT-based planning
IMRT: Intensity Modulation
What cancers are treated with IMRT?

- Head and neck (most convincing data)
  - normal tissue sparing
- GI (gastric, pancreas, anal)
- Prostate (widely adopted)
- Pelvis, re-irradiation
- Any site where sharp dose gradient is necessary
IMRT: Caution!

- Higher risk of missing the tumor
  - sharp dose gradient
  - patient immobilization and/or tumor tracking is critical (IGRT)
Radiation - Protons

- Protons are not magical treatments for cancer
- First used to treat cancer in 1950’s at Harvard
- Loma Linda opened first Hospital-based proton center in 1990
- Bragg Peak
- Range uncertainty
- Medicare approved coverage in 2002
Bragg Peak

Graph showing dose relative to mm for different types of radiation:
- Electrons
- Protons
- Photons

The graph indicates that Bragg Peak is a phenomenon in radiation therapy where the dose is concentrated at a specific depth, showing a sharp rise and then a rapid drop-off.
**IMRT vs. Protons**

- No difference in biological effectiveness  
  - Same effect on cancer
- Do protons have less side effects? Probably not
- Do protons have more side effects? Probably not
- Studies show protons may be slightly better or worse  
  - Any differences are very small  
  - Doctor/Dosimetrist/Biology – much greater factors  
  - Michelin vs. Goodyear
- Future combinations of proton/photon concepts might be a little better (biology and motion still trumps)
IMRT vs. Protons – Harvard Study
Image Guided Radiation Therapy (IGRT)
IGRT - What is it?

You see what you treat!
IGRT Methods

- Ultrasound based
- X-ray based
- CT based
IGRT: Ultrasound

- Used mostly for prostate cancer
- 3-D ultrasound visualization
- Real-time optical tracking
- Adjust table position each day based on location of prostate, bladder, and rectum
Ultrasound Based IGRT
IGRT: X-ray/CT

- Daily orthogonal x-rays or limited CT’s
- Can track bony markers or soft tissues
- Can be used for all sites
- Table adjusted for every treatment as needed
X-ray Based IGRT
CT Based IGRT
Why bother?

• What’s the purpose of IMRT, IGRT, etc.?

Less high-dose radiation to normal tissues allows

More high-dose radiation to tumor

(better tumor control)
Brachytherapy
Prostate Seed Implant
Prostate Seed Implant: Isotopes

- Most commonly used are iodine-125 (I-125) and palladium-103 (Pd-103)
  - I-125
    - higher energy = better dose homogeneity
    - half-life ~60 days
  - Pd-103
    - shorter half-life (~17 days) = faster delivery of dose to prostate
    - possibly more effective for aggressive tumors
- No proven clinical difference in efficacy or toxicity
Prostate Seed Implant: Isotopes

- Cs-131
  - highest energy (best dose homogeneity)
  - shortest half-life ~9.7 days
    - may be the “optimal” half-life for biologic effectiveness
    - less exposure to family members
  - FDA approved in 2003
  - ongoing phase II study for combination therapy

Accelerated Partial Breast Irradiation

- Multicatheter interstitial brachytherapy
  - traditional method for PBI
  - operator dependent
- Balloon brachytherapy
- Intraoperative (Intrabeam)
- External beam
Why do APBI?

• Convenience
  – 2 treatments/day x 5 days (10 total treatments)
  – Intraoperative single treatment

• Toxicity
  – smaller volume of breast tissue and skin being irradiated (may be good or bad…)
Multicatheter interstitial brachytherapy
Balloon brachytherapy

Radioactive source

MammoSite catheter
Balloon brachytherapy
Intrabeam
Intrabeam
## Balloon APBI: Limited Follow-up

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Median followup (months)</th>
<th>Cosmetic results (%good/exc)</th>
<th>Local recurrence (%)</th>
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<tbody>
<tr>
<td>Keisch et al</td>
<td>43</td>
<td>29</td>
<td>84</td>
<td>0</td>
</tr>
<tr>
<td>Tufts/VCU</td>
<td>28</td>
<td>19</td>
<td>93</td>
<td>0</td>
</tr>
<tr>
<td>St. Vincent’s</td>
<td>32</td>
<td>11</td>
<td>86</td>
<td>0</td>
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<tr>
<td>Rush Univ.</td>
<td>30</td>
<td>18</td>
<td>93</td>
<td>0</td>
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<tr>
<td>Kaiser</td>
<td>40</td>
<td>13</td>
<td>97</td>
<td>0</td>
</tr>
<tr>
<td>ASBS</td>
<td>1400</td>
<td>5</td>
<td>92</td>
<td>0.1</td>
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</tbody>
</table>
APBI: Phase III Clinical Trials

• NSABP B39/RTOG 0413
  – multicatheter, targeted radiation therapy, or 3D-EBRT
  – all ages
  – ≤3 cm
  – all invasive histologies and DCIS
  – margins negative
  – pN0–pN1, no ECE

• GEC-ESTRO
  – multicatheter only
  – ≥40 years-of-age
  – ≤3 cm
  – all invasive histologies & DCIS w/ VNPI <8
  – margins negative 2–5 mm depending on histology
  – pN0–pN1 mic
TARGIT-A

- First randomized clinical trial comparing APBI and standard whole-breast RT
- Update published online, Lancet, Nov 11, 2013
- 1451 women randomized

<table>
<thead>
<tr>
<th></th>
<th>Intrabeam (%)</th>
<th>Whole Breast (%)</th>
<th>P</th>
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<tbody>
<tr>
<td>5y LR all</td>
<td>3.3</td>
<td>1.3</td>
<td>0.042</td>
</tr>
<tr>
<td>5y LR pre-pathology*</td>
<td>2.1</td>
<td>1.1</td>
<td>0.31</td>
</tr>
<tr>
<td>Overall Mortality</td>
<td>3.9</td>
<td>5.3</td>
<td>0.099</td>
</tr>
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</table>
APBI: Patient Selection

• American Brachytherapy Society* (ABS)
  – age >45
  – Infiltrating ductal histology
  – size <3cm
  – negative margins
  – negative nodes

• American Society of Breast Surgeons** (ASBS)
  – age >50
  – infiltrating ductal or DCIS
  – size <2 cm
  – negative margins >2 mm
  – negative nodes

• Contraindications (both societies)
  – lobular histology
  – positive margins
  – positive nodes

APBI: Patient Selection

- ASTRO – “suitable”
  - ≥ 60yo, BRCA negative
  - ≤ 2cm tumor, T1 stage
  - Negative margins by 2mm+
  - No LVSI
  - ER positive
  - Unicentric
  - Invasive Ductal
  - No pure DCIS or EIC
  - Node negative
  - No neoadjuvant therapy

- Others are considered “cautionary” or “unsuitable”
Other Cancer Sites
Acute Side Effects: Head/Neck

- Irritation of mucosa
  - artificial saliva solution
  - viscous lidocaine mixtures
  - narcotic pain meds

- Dry mouth (permanent)
  - ethyol
  - pilocarpine hydrochloride
  - acupuncture

- Fungal infections of mouth
  - antifungal

- Skin reactions

- Loss of taste
Acute Side Effects: Lung/Thorax

- Fatigue
- Esophageal irritation
  - viscous lidocaine mixtures
    - Maalox
    - nystatin
    - diphenhydramine
    - tetracycline
    - GI cocktail
  - narcotic pain med
- Skin reactions
Acute Side Effects: Abdomen

- Nausea
  - antiemetics
  - lorazepam
  - dexamethasone

- Diarrhea
  - antimotility agents

- Concurrent chemo side effects
Questions?