Post-Lumpectomy Radiation Techniques and Toxicities

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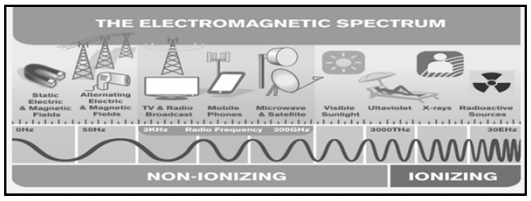
Learning Objectives

- How radiation therapy works
- Standard techniques
- Rationale behind adding radiation after lumpectomy
- Radiation options for patients after lumpectomy
- Radiation Toxicity

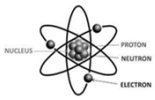
Photons

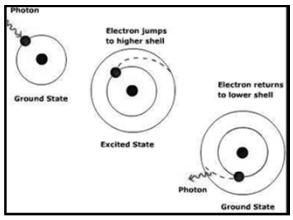
- Most commonly used particle for therapy throughout the world
- Elementary magnetic particle
- Zero rest mass
- Neutral charge



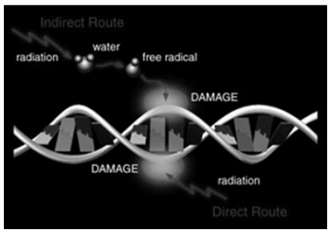
What Is Radiation Therapy?

- Particles accelerated to a therapeutic energy
- "Light" particles
  - Photons
  - Electrons
- "Heavy" particles
  - Protons
  - Carbon





How Does Radiation Kill Tumor Cells?



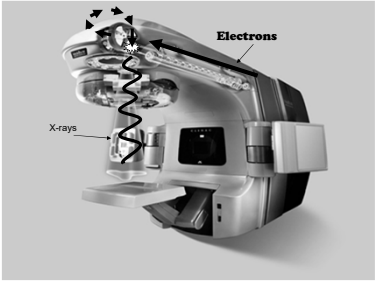
- Normal cells work to repair DNA damage
- Tumor cells have poor DNA repair and die

Radiation in Medicine

For decades, improvement in radiation therapy came mostly in building more powerful radiation machines that spared the skin.

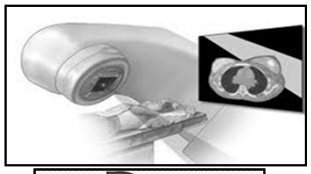
Modern Radiation Therapy

- Uses microwave technology to accelerate electrons in a part of the linac called the waveguide
- Accelerated electrons collide with a heavy metal target
- Photons produced from these collisions

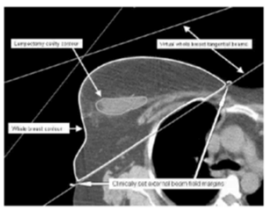


Traditional Whole Breast Radiation

Technique: Medial/Lateral tangential fields



Standard Technique



- Medial and lateral tangential fields to encompass **entire breast**
- 3D CT-based treatment plan, customized to fit individual patient anatomy
- Treat whole breast while sparing adjacent organs like heart and lungs

Radiation Set-up and Schedule

- Schedule
  - 3 to 6.5 weeks
  - Start 3-6 weeks after surgery or chemo
  - Monday through Friday
  - In radiation department for about 30 min/day
  - Beams on for 2-4 minutes
- Dose
  - 180 - 266 cGy/day x16 -28 fractions to whole breast
  - 200 - 250 cGy/day x4-5 fractions to lumpectomy cavity
  - Total of 5256 cGy - 6040 cGy in 20 - 33 fractions

Side Effects

- Radiation is focal therapy
  - Fatigue
  - Skin reaction: redness, peeling, itching
  - Fibrosis, soft tissue thickening
  - Lymphedema
  - Pneumonitis
  - Coronary artery disease
  - Small risk of secondary cancer

Risk of Radiation-Induced Cardiac Disease

- Cardiac volume exposed to RT (DVH)
- Use of potentially cardiotoxic systemic therapy
- Presence of independent risk factor (hypertension, DM, lipid disorders, smoking, age, CAD etc…)

A. Recht Editorial 2006

Late Cardiac Mortality and Morbidity in Early-Stage Breast Cancer Patients After BCT.
Harris EE, Correa C et al. JCO, September 2006.

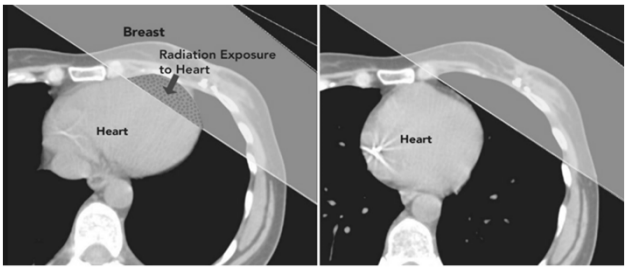
- 961 patients with early stage breast cancer
- In 2nd decade after radiation:
  - ↑ rate of cardiac deaths in left-sided patients
  - 6.4% for left-sided vs. 3.6% for right-sided patients
- Statistically higher rates of chest pain, CAD and myocardial infarction reported in left-sided patients

Deep Inspiration Breath Hold - Technique

Deep Inspiration Breath Hold – Patient is asked to take a very deep breath – usually for 15-25 seconds – so the breast area is as far from the heart as it can be.

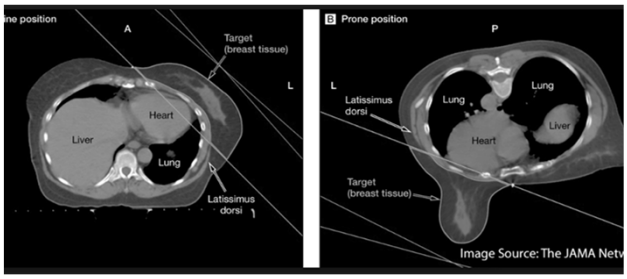
Then, during treatment, the patient takes and holds a deep breath in the same way as before, and when the breast area is in the same position as during planning, radiation beam turns on.

Respiratory Gating - Deep Inspiration Breath Hold



Standard Radiation Therapy Deep Inspiration Breath Hold

Prone positioning



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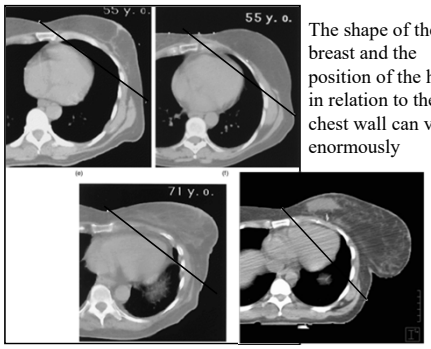


The shape of the breast and the position of the heart in relation to the chest wall can vary enormously

Cardiac dose reduction for tangentially irradiated breast cancer without compromising target coverage

Vikstrom et al, Acta Oncologica 2011

- 17 patients with early left-sided breast cancer
- Compared to free breathing, the deep inspiration breath hold gated patients obtained lower cardiac and pulmonary doses
- With the gated technique, the heart was completely out of the beam portals in 10 patients, while this could not be achieved in any of the 17 patients with free breathing

Stranzl et al, Strahlenther Onkol

- 22 left-sided breast patients
- Significant heart dose reduction using deep inspiration breath hold technique
- Mean dose to entire heart was 2.3 Gy for free breathing vs. 1.3 Gy for gated technique
- For free breathing, 1.4% of the heart received a dose of ≥ 20 Gy, reduced to 0.3% for respiratory gated technique

Korreman et al, Radiother Oncol 2005

- 17 left-sided breast cancer patients
- In left-sided breast cancer patients, the median heart volume receiving > 50% of the prescribed dose was reduced from 19.2% for free breathing to 2.8% for respiratory gated technique
- Median LAD coronary artery volume was decreased from 88.9% for free breathing to 22.4% for respiratory gated technique

Is radiation really needed after lumpectomy?

Reduction in Local Recurrence

	Lumpectomy	Lumpectomy + RT	Reduction
NSABP 06	36%	12%	67%
Uppsala	24%	9%	63%
Ontario	35%	11%	69%
Milan	24%	6%	75%
Swedish	14%	4%	71%

All trials show a reduction (~ 70%) in local recurrence with the addition of RT

Can We Omit Radiation in Elderly Patients?

Omission of RT for Elderly Patients: CALGB C9343

Age ≥70
Tumor ≤2cm
Clinically node negative
ER+ or unknown
BCS, no ALND

Tamoxifen
x 5 years

Tam + RT
(breast and low axilla,
45Gy + 14Gy boost)

Endpoints: LRR, mastectomy, DM, survival

Hughes, *NEJM* 2004

Omission of RT for Elderly Patients
CALGB C9343

	5 yr LRR	8 yr LRR	10 yr LRR
Tam + RT	1%	1%	2%
Tam	4%	7%	9%

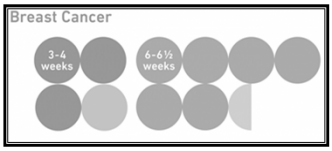
*No difference in overall survival

Bottom Line:
- Consider omitting RT for:
  - Age ≥ 70 withT1N0 tumors, ER+
  - Fit for and willing to take endocrine therapy for 5 years

Can Whole Breast Radiation Be Given Faster?

Hypofractionation

- Larger daily fractions given over a shorter period of time
- Possibly increased tumor control (particularly for more radioresistent tumors like melanoma)
- Long-term side effects likely related to fraction size



Ontario Clinical Oncology Group Trial of Accelerated Hypofractionated Whole Breast Irradiation

1,234 patients
T1-2, N0
With clear margins
>50 yo

R → 50 Gy/25 fxs – 5 weeks
R → 42.56 Gy/16 fxs – 3 weeks

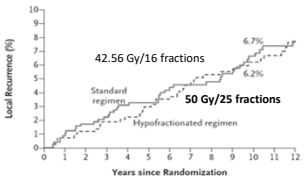
Median FU 10 years

- No boost given
- 11% received chemo
- Breast size ≤ 25cm (large breasted women excluded)
- 2D planning (older technique)

Whelan, JNCI 2002

Results

Cosmesis good/excellent
50 Gy = 71%
42.56 Gy = 70%



Conclusion: The shorter radiation fractionation schedule of 42.56 Gy/16 fractions was as good as a more traditional schedule of 50Gy/25 fractions in terms of local breast cancer recurrence (6.2 vs. 6.7%) and cosmesis at 10 years

Note: Cosmesis rated good/excellent 70% of patients in both arms

Whelan, NEJM 2010

ASTRO Guidelines 2018

Table 1

Patients for whom consensus supports use of HF-WBI. A comparison of the 2011 and 2018 ASTRO Guidelines*

Factor	2011 Guideline	2018 Guideline
Age	≥50 years	Any
Stage	T1-2 N0	Any stage provided intent is to treat the whole breast without an additional field to cover the regional lymph nodes
Chemotherapy	None	Any chemotherapy
Dose homogeneity	±7% in the central axis	Volume of breast tissue receiving >105% of the prescription dose should be minimized regardless of dose-fractionation

Acute and Short-Term Toxic Effects of Conventionally Fractionated vs. Hypofractionated Whole Breast Irradiation

JAMA ONCOLOGY, August 2015

- Similar results for the following:
  - Somewhat or more lack of energy (HF-WBI, 38% vs. CF-WBI, 39%)
  - Somewhat or more trouble meeting family needs (HF-WBI, 10% vs. CF-WBI, 14%)
- Differing results for the following *during radiation*:
  - Maximum physician-reported acute dermatitis (HF-WBI, 36% vs. CF-WBI, 69%)
  - Pruritis (HF-WBI, 54% vs. CF-WBI, 81%)
  - Breast pain (HF-WBI, 55% vs. CF-WBI, 74%)
  - Hyperpigmentation (HF-WBI, 9% vs. CF-WBI, 20%)
  - Fatigue (HF-WBI, 9% vs. CF-WBI, 17%)

-HF-WBI = Hypofractionated whole breast irradiation
-CF-WBI = Conventionally fractionated whole breast irradiation

Acute and Short-Term Toxic Effects of Conventionally Fractionated vs. Hypofractionated Whole Breast Irradiation

JAMA ONCOLOGY, August 2015

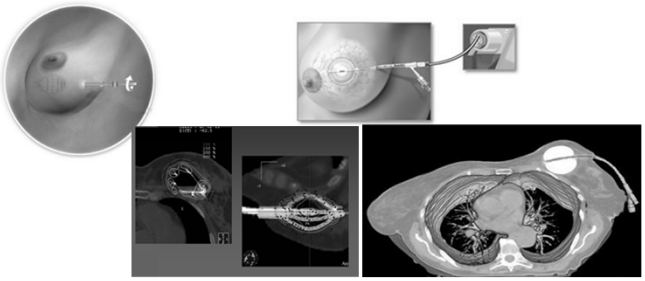
- Results 6 months after RT:
  - Fatigue (HF-WBI, 0% vs. CF-WBI, 6%)
  - Lack of energy (HF-WBI, 23% vs. CF-WBI, 39%)
  - Trouble meeting family's needs (HF-WBI, 3% vs. CF-WBI, 9%)

CONCLUSIONS AND RELEVANCE Treatment with HF-WBI appears to yield lower rates of acute toxic effects than CF-WBI as well as less fatigue and less trouble meeting family needs 6 months after completing radiation therapy. These findings should be communicated to patients as part of shared decision making.

Accelerated Partial Breast Irradiation (APBI)

- The question has arisen as to whether the whole breast needs to be treated or just the lumpectomy bed
- With smaller treatment volume a higher dose could be given, and treatment time could be cut down to just one week
- Can be accomplished by external beam radiation or brachytherapy

Accelerated Partial Breast Irradiation



Rationale for Accelerated Partial Breast Irradiation

- Most recurrences after breast conserving surgery occur in tumor bed region
- "Elsewhere" recurrences in breast are rare after lumpectomy alone or followed by RT
- Whole breast RT may not be necessary in appropriately selected patients

Thank You!

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