Disclosures/COI

- None
Audience Poll

• Dosimetrists?
• Nurses?
• Therapists?
• Physicians?
• NP or PAs?
• Medical assistants?
Background

• Why not one big dose of radiation?
  – Collateral Damage

• Early 1900s:
  – Smaller doses still treat cancer (1.8-2 Gy/fx)
  – Smaller doses better tolerated by normal tissue
Hypofractionation

- What is the conventional or standard?

Prostate SbRT

≥5 Gy/fx (UAB: 6.25-7 Gy)  1.8-2Gy/fx

Prostate hypofractionation

2-4 Gy/fx (UAB: 2.5 Gy)  1.8-2Gy/fx

https://www.foxchase.org/clinical-care/conditions/prostate-cancer/treatment/radiation-therapy-prostate-cancer/hypofractionation
Hypofractionation Defined

- Increase dose per fraction
- Decrease total # fractions
- E.g. prostate

**BACKGROUND**

Why hypofractionate?

- Improvements:
  - Tumor Imaging (e.g. MRI in prostate)
  - Radiation delivery (e.g. Stereotactic accuracy)
  - Radiobiology (e.g. radiation sensitivity depends on cancer growth rate)
Why hypofractionate?

• Advantages:
  – Complete RT much faster
  – Compete with other therapies
  – Increased compliance
  – Better tumor control

• Disadvantages:
  – Increased side effects
  – Can’t afford inaccuracy
  – Not “tried and true”

• Both
  – Cost
Which cancers?

- Prostate
- Breast
- Glioblastoma Multiforme (GBM)
- Bone
Questions before Shorten Treatments

• Standard Treatment?
• Hypofractionated Treatment?
• Evidence? Quality of Evidence?
  – ASTRO Guidelines
  – Outcomes, Side Effects/Toxicity
  – # of patients, randomized, length of follow-up
• Why change (or not)?
PROSTATE SbRT

≥5 Gy/fx (UAB: 6.25-7 Gy)  1.8-2 Gy/fx

PROSTATE hypofractionation

2-4 Gy/fx (UAB: 2.5 Gy)  1.8-2 Gy/fx
Standard Treatment?

Figure 1 | Radiotherapy fractionation schedules for the management of patients with prostate cancer. Fractionation of a prescribed radiation dose over several treatment sessions is used to protect nonmalignant tissues adjacent to the tumour. Technological developments have improved the precision of radiation delivery, enabling increased fraction doses and shorter treatment schedules without compromising efficacy but increasing patient compliance. Conventionally fractionated radiotherapy is usually delivered in 38–40 sessions of single 1.8–2 Gy fractions, resulting in an 8–9-week treatment duration. In moderate hypofractionation, 19–30 sessions of single 2.4–4 Gy fractions are given over a total of 4–6 weeks. Extremely hypofractionated radiotherapy consists of 4–5 treatment sessions of 6–10 Gy doses each and treatment is usually concluded after 1–2 weeks.
Hypofractionated Treatment?

Table 1. Accumulating Evidence From Randomized Trials on Hypofractionated Therapy for Prostate Cancer

<table>
<thead>
<tr>
<th>Trial, Predominant Risk Group</th>
<th>Conventional Dose, Gy</th>
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<th>Median Follow-up</th>
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<tr>
<td>PROFIT (N = 1,206), intermediate risk (JCO 2017)</td>
<td>78 Gy</td>
<td>60 Gy given in 3-Gy fractions</td>
<td>6 years</td>
<td>Moderate hypofractionation noninferior to standard</td>
<td>Overall, no significant differences except that GI toxicity more acute for moderate hypofractionation but more later for standard fractionation</td>
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<td>Regina Elena National Cancer Institute (N = 168), mostly high risk (JCO 2017)</td>
<td>60 Gy</td>
<td>62 Gy given in 3.1-Gy fractions</td>
<td>9 years</td>
<td>Moderate hypofractionation not superior to standard</td>
<td>Overall, toxicity similar, but greater macroscopic hematuria for moderate hypofractionation (P = .008)</td>
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<td>RTOG 0415 (N = 1,115), low to intermediate risk (JCO 2017)</td>
<td>73.8 Gy</td>
<td>70 Gy given in 2.5-Gy fractions</td>
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<tr>
<td>CHHP (N = 3,218), intermediate risk (Lancet Onc 2016)</td>
<td>74 Gy</td>
<td>60 Gy given in 3-Gy fractions and 57 Gy given in 3-Gy fractions</td>
<td>62 months</td>
<td>Moderate hypofractionation given in 3 Gy x 20 fractions is noninferior to standard</td>
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<td>76 Gy</td>
<td>70.2 Gy given in 2.7-Gy fractions</td>
<td>68.4 months</td>
<td>Moderate hypofractionation not superior to standard</td>
<td>No differences in late toxicity, although for patients with preexisting urinary symptoms, greater incidence of late grade 2 or higher GU toxicity</td>
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Abbreviations: CHHP, Conventional Versus Hypofractionated High-Dose Intensity-Modulated Radiotherapy for Prostate Cancer; FCCC, Fox Chase Cancer Center; GU, genitourinary; HYPRO, Hypofractionated Versus Conventionally Fractionated Radiotherapy for Patients With Localized Prostate Cancer; PROFIT, Prostate Fractionated Irradiation Trial; RTOG, Radiation Therapy Oncology Group.
# Evidence?

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## Quality of Evidence?

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Prostate

Why change (or not)?

• Target Planning (from RTOG 0415):
  • [https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0415](https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0415)

![Table showing dose goals and constraints for two arms (ARM 1 and ARM 2)]

**ARM 1:** 73.8 Gy in 41 fractions. No more than 2% of the PTV may receive less than 73.8 Gy.
**ARM 2:** 70 Gy in 28 fractions. No more than 2% of the PTV may receive less than 70 Gy.

<table>
<thead>
<tr>
<th>Dose Goal (Prescription)</th>
<th>Minimum PTV dose (≥ 98% of PTV)</th>
<th>Minimum CTV dose (≥ 100% of CTV)</th>
<th>Maximum dose to PTV (No variation)</th>
<th>Maximum PTV dose to PTV (Minor variation)</th>
<th>Maximum PTV dose to PTV (Major variation)</th>
</tr>
</thead>
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<tr>
<td>ARM 1</td>
<td>73.8 Gy</td>
<td>73.8 Gy</td>
<td>79 Gy</td>
<td>81.2 Gy</td>
<td>&gt;81.2 Gy</td>
</tr>
<tr>
<td>ARM 2</td>
<td>70 Gy</td>
<td>70 Gy</td>
<td>74.9 Gy</td>
<td>77 Gy</td>
<td>&gt;77 Gy</td>
</tr>
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*The maximum dose must not be within an “Organ at Risk” such as the Rectum, Bladder, or Penile Bulb*
Why change (or not)?

- Constraint Planning (RTOG 0415):

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<th>Normal organ limit</th>
<th>No more than 15% volume receives dose that exceeds</th>
<th>No more than 25% volume receives dose that exceeds</th>
<th>No more than 35% volume receives dose that exceeds</th>
<th>No more than 50% volume receives dose that exceeds</th>
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<tr>
<td>Bladder Constraint</td>
<td>80 Gy</td>
<td>75 Gy</td>
<td>70 Gy</td>
<td>65 Gy</td>
</tr>
<tr>
<td>Rectum Constraint</td>
<td>75 Gy</td>
<td>70 Gy</td>
<td>65 Gy</td>
<td>60 Gy</td>
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<tr>
<td>Penile Bulb</td>
<td>Mean dose less than or equal to 52.5 Gy</td>
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<td>74 Gy</td>
<td>69 Gy</td>
<td>64 Gy</td>
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<tr>
<td>Rectum Constraint</td>
<td>74 Gy</td>
<td>69 Gy</td>
<td>64 Gy</td>
<td>59 Gy</td>
</tr>
<tr>
<td>Penile Bulb</td>
<td>Mean dose less than or equal to 51 Gy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prostate

73.8 Gy in 41 fx

70 Gy in 28 fx
Why change (or not)?

• Constraints at Duke and UAB (70 Gy/28):

<table>
<thead>
<tr>
<th>Organ at risk</th>
<th>Dose (Gy)</th>
<th>Volume (absolute or %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>65</td>
<td>15%</td>
</tr>
<tr>
<td>Bladder</td>
<td>40</td>
<td>35%</td>
</tr>
<tr>
<td>Rectum</td>
<td>70</td>
<td>&lt;10 cm³</td>
</tr>
<tr>
<td>Rectum</td>
<td>65</td>
<td>10%</td>
</tr>
<tr>
<td>Rectum</td>
<td>40</td>
<td>35%</td>
</tr>
<tr>
<td>Left femoral head</td>
<td>40</td>
<td>0%</td>
</tr>
<tr>
<td>Right femoral head</td>
<td>40</td>
<td>0%</td>
</tr>
<tr>
<td>Penile bulb</td>
<td>Mean dose &lt;50</td>
<td></td>
</tr>
<tr>
<td>Small bowel</td>
<td>40</td>
<td>1%</td>
</tr>
</tbody>
</table>

The clinical target volume is the prostate in low-risk and favorable intermediate-risk patients and includes 10 mm of proximal seminal vesicles in patients with unfavorable intermediate-risk disease. A 3-dimensional expansion of the clinical target volume by 4 to 10 mm is used to create the planning target volume (PTV). A simultaneous boost technique is used to deliver 58.8 Gy in 28 fractions to the PTV including the proximal seminal vesicles. The maximum dose to the PTV cannot exceed the prescription dose by more than 7%; up to 10% is a minor, acceptable variation, and >10% is a major, unacceptable variation.
Why change (or not)?

• More side effects with hypofractionation?
• More long-term side effects with standard treatment?
• Studies not long enough?
  – Need 10 year data?
Take Homes

• Prostate hypofractionation is a reasonable treatment option
• Awaiting long-term follow-up
BREAST

Breast Cancer

- 3-4 weeks: 2.66 Gy/fx
- 6-6 1/2 weeks: 1.8-2 Gy/ fx
Standard Treatment?

- 23-25 2 Gy fractions to 46-50 Gy
- ± 5-8 fraction boost of 10-16 Gy
Hypofractionated Treatment?

- 40-42.5 Gy in 15/16 fractions (2.66 Gy/fx)
- ± 4-5 fraction boost of 10-12.5 Gy
Hypofractionated Treatment?

- **Accelerated Partial Breast Irradiation (APBI):**
  - 34 Gy in 10 fractions BID
  - 1 week
Hypofractionated Treatment?

- Mammosite Dosimetry:
- **PTV:**
  - Breast tissue bounded by expansion of balloon + 10 mm
  - Limited to **at least 5 mm from skin surface**
  - Limited by posterior breast tissue extent (chest wall and pectoralis muscles are not included)
  - 95% of prescribed dose covers 95% of PTV
  - Skin maximum: ≤ 125% prescribed dose
  - Rib maximum: ≤ 145% prescribed dose
  - Volume of breast receiving 150% of prescribed dose (V150): ≤ 50 cc
  - Volume of breast receiving 200% of prescribed dose (V200): ≤ 10 cc
Evidence?

- EBRT Hypofractionation:

Table 4. Characteristics of patients enrolled on clinical trials comparing hypofractionated whole breast irradiation with conventionally fractionated whole breast irradiation

<table>
<thead>
<tr>
<th></th>
<th>Canada (18, 19, 21) 1,234</th>
<th>RMH/GOC (17, 20) 1,410</th>
<th>START A (10) 2,236</th>
<th>START B (16) 2,215</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated with breast-conserving surgery</td>
<td>1,234 100%</td>
<td>1,410 100%</td>
<td>1,900 85%</td>
<td>2,038 92%</td>
</tr>
<tr>
<td>Age ≥ 50 years</td>
<td>929 75%</td>
<td>987 70%</td>
<td>1,727 77%</td>
<td>1,758 79%</td>
</tr>
<tr>
<td>pT1–2</td>
<td>1,234 100%</td>
<td>1,324 94%</td>
<td>Majority</td>
<td>Majority</td>
</tr>
<tr>
<td>pN0</td>
<td>1,234 100%</td>
<td>564 40%</td>
<td>1,547 69%</td>
<td>1,635 74%</td>
</tr>
<tr>
<td>Chemotherapy not used</td>
<td>1,098 89%</td>
<td>1,214 86%</td>
<td>1,443 65%</td>
<td>1,724 78%</td>
</tr>
<tr>
<td>Central axis inhomogeneity -7% to +7%</td>
<td>1,234 100%</td>
<td>1,410 100%</td>
<td>2,236 100%</td>
<td>2,215 100%</td>
</tr>
<tr>
<td>High tumor grade</td>
<td>233 19%</td>
<td>629 28%</td>
<td>509 23%</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CF = conventional fractionation; HF = hypofractionation; RMH/GOC = Royal Marsden Hospital/Gloucester Oncology Center; START = standardization of breast radiotherapy; WBI = whole-breast irradiation.
Evidence?

- EBRT Hypofractionation:

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<tr>
<th>Trial</th>
<th>Median Follow-up (years)</th>
<th>Time point for outcome reporting (years)</th>
<th>Dose (Gy)</th>
<th># Fr</th>
<th># Days</th>
<th>N</th>
<th>%</th>
<th>p</th>
<th>IBTR</th>
<th>Local-regional recurrence</th>
<th>Disease-free survival</th>
<th>Overall survival</th>
<th>%</th>
<th>p</th>
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<td>Canada (18, 19, 21)</td>
<td>12</td>
<td>10</td>
<td>50</td>
<td>25</td>
<td>35</td>
<td>612</td>
<td>7.5</td>
<td></td>
<td></td>
<td>7.4 &lt;.001*</td>
<td></td>
<td>84.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMH/GOC (17, 20)</td>
<td>9.7</td>
<td>10</td>
<td>42.5</td>
<td>16</td>
<td>22</td>
<td>622</td>
<td>7.4</td>
<td>&lt;.001*</td>
<td></td>
<td>7.4 &lt;.001*</td>
<td></td>
<td>84.6</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>START A (10)</td>
<td>5.1</td>
<td>5</td>
<td>50</td>
<td>25</td>
<td>35</td>
<td>749</td>
<td>3.2</td>
<td></td>
<td></td>
<td>3.6†</td>
<td>3.5†</td>
<td>89©</td>
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<tr>
<td>START B (16)</td>
<td>6.0</td>
<td>5</td>
<td>50</td>
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<td>1105</td>
<td>3.3</td>
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<td>35</td>
<td>612</td>
<td>7.5</td>
<td>7.4</td>
<td>.001*</td>
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<td>84.4</td>
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<td>84.6</td>
<td>.79</td>
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<tr>
<td>RMH/GOC (17, 20)</td>
<td>9.7</td>
<td>10</td>
<td>42.5</td>
<td>16</td>
<td>22</td>
<td>622</td>
<td>7.4</td>
<td>.001*</td>
<td></td>
<td></td>
<td>84.6</td>
<td>.79</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>START A (10)</td>
<td>5.1</td>
<td>5</td>
<td>50</td>
<td>25</td>
<td>35</td>
<td>749</td>
<td>3.2</td>
<td></td>
<td></td>
<td>3.6†</td>
<td>86</td>
<td>.33$</td>
<td></td>
<td>89</td>
<td>.81$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>START B (16)</td>
<td>6.0</td>
<td>5</td>
<td>40</td>
<td>15</td>
<td>21</td>
<td>1110</td>
<td>3.3</td>
<td></td>
<td></td>
<td>3.3†</td>
<td>86</td>
<td>.81$</td>
<td></td>
<td>89</td>
<td>.81$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Why change (or not)?

- ASTRO Guidelines (2010):

  **Purpose:** In patients with early-stage breast cancer treated with breast-conserving surgery, randomized trials have found little difference in local control and survival outcomes between patients treated with conventionally fractionated (CF-) whole breast irradiation (WBI) and those receiving hypofractionated (HF)-WBI. However, it remains controversial whether these results apply to all subgroups of patients. We therefore developed an evidence-based guideline to provide direction for clinical practice.

  **Methods and Materials:** A task force authorized by the American Society for Radiation Oncology weighed evidence from a systematic literature review and produced the recommendations contained herein.

  **Results:** The majority of patients in randomized trials were aged 50 years or older, had disease Stage pT1-2 pN0, did not receive chemotherapy, and were treated with a radiation dose homogeneity within ±7% in the central axis plane. Such patients experienced equivalent outcomes with either HF-WBI or CF-WBI. Patients not meeting these criteria were relatively underrepresented, and few of the trials reported subgroup analyses. For patients not receiving a radiation boost, the task force favored a dose schedule of 42.5 Gy in 16 fractions when HF-WBI is planned. The task force also recommended that the heart should be excluded from the primary treatment fields (when HF-WBI is used) due to lingering uncertainty regarding late effects of HF-WBI on cardiac function. The task force could not agree on the appropriateness of a tumor bed boost in patients treated with HF-WBI.

  **Conclusion:** Data were sufficient to support the use of HF-WBI for patients with early-stage breast cancer who met all the aforementioned criteria. For other patients, the task force could not reach agreement either for or against the use of HF-WBI, which nevertheless should not be interpreted as a contraindication to its use. Copyright © 2011 American Society for Radiation Oncology. Published by Elsevier Inc.

Breast cancer, Hypofractionation, Evidence-based guideline, Breast conserving therapy.
Why change (or not)?

• ASTRO Guidelines - Dosimetry:
  – Central axis dose homogeniety within 7% of prescription dose
  – No stipulation on dose outside of central axis
  – Canadian trial excluded those with chest wall separation along central axis >25 cm
  – Exclude heart from treatment fields
Why change (or not)?

- **Advantages:**
  - Complete RT faster
  - Compete with other therapies
  - Increased compliance

- **Disadvantages:**
  - Not “tried and true”
  - Only certain cases
  - Not for post-mastectomy or nodal RT

---

Choosing Wisely. ASTRO 2013.
### Evidence?

- **Accelerated Partial Breast Irradiation (APBI):**

<table>
<thead>
<tr>
<th>Applicator</th>
<th>Trial Type</th>
<th>Total (Treated)</th>
<th>Lumen</th>
<th>5-year LR</th>
<th>5-year IBTR</th>
<th>Long-Term Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MammoSite Initial Trial</td>
<td>Prospective</td>
<td>70 (43 treated)</td>
<td>Single-Lumen</td>
<td>0%</td>
<td>1.5%</td>
<td>9.3% infection, 33% seroma, 12% symptomatic seroma, 4 patients with fat necrosis, 83% excellent/good cosmesis</td>
</tr>
<tr>
<td>MammoSite Registry</td>
<td>Prospective</td>
<td>1449</td>
<td>Single-Lumen</td>
<td>3.8%</td>
<td>1.5%</td>
<td>91% excellent/good cosmesis, 9.6% infection, symptomatic seroma 13%, 13% telangiectasias, 2.5% fat necrosis</td>
</tr>
<tr>
<td>External Beam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSABP B-39/RTOG 0413; 2011</td>
<td>Randomized</td>
<td>1367</td>
<td>3D-CRT</td>
<td>6%</td>
<td></td>
<td>3% Grade 3+ fibrosis</td>
</tr>
<tr>
<td>RAPID</td>
<td>Randomized</td>
<td>2135</td>
<td>3D-CRT</td>
<td>6%</td>
<td></td>
<td>Increased adverse cosmesis with APBI, Grade 3 toxicity, 1.4%, increased grade 1/2 toxicity with APBI</td>
</tr>
<tr>
<td>University of Florida</td>
<td>Randomized</td>
<td>520</td>
<td>IMRT</td>
<td>0%</td>
<td></td>
<td>Reduced acute and chronic toxicity with APBI, improved cosmetic outcome with APBI</td>
</tr>
<tr>
<td>RTOG 0319</td>
<td>Prospective</td>
<td>52</td>
<td>3D-CRT</td>
<td>6%</td>
<td></td>
<td>64% excellent/good cosmesis at 3 years, 5.8% grade 3 toxicity</td>
</tr>
<tr>
<td>William Beaumont Hospital</td>
<td>Retrospective</td>
<td>192</td>
<td>3D-CRT</td>
<td>0%</td>
<td></td>
<td>81% excellent/good cosmesis, 7.5% grade 3 fibrosis, 7.6% telangiectasias</td>
</tr>
<tr>
<td>Tufts University</td>
<td>Retrospective</td>
<td>60</td>
<td>3D-CRT</td>
<td>3%</td>
<td></td>
<td>8% grade 3/4 fibrosis, 82% excellent/good cosmesis</td>
</tr>
<tr>
<td>University of Michigan</td>
<td>Prospective</td>
<td>34</td>
<td>3D-CRT</td>
<td>3%</td>
<td></td>
<td>73% excellent/good cosmesis, 0% grade 3 fibrosis</td>
</tr>
</tbody>
</table>

Quality of Evidence?

- **Accelerated Partial Breast Irradiation (APBI):**

Why change (or not)?

- Accelerated Partial Breast Irradiation (APBI):

```
<table>
<thead>
<tr>
<th>Patient group</th>
<th>Risk factor</th>
<th>Original</th>
<th>Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitability</td>
<td>Age</td>
<td>≥60 y</td>
<td>≥50 y</td>
</tr>
<tr>
<td></td>
<td>Margins</td>
<td>Negative by at least 2 mm</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td>T stage</td>
<td>T1</td>
<td>Tis or T1</td>
</tr>
<tr>
<td></td>
<td>DCIS</td>
<td>Not allowed</td>
<td>If all of the below:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Screen-detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Low to intermediate nuclear grade</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Size ≤2.5 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Resected with margins negative at ≥3 mm</td>
</tr>
</tbody>
</table>

Cautionary

| Age | 50-59 y |

Pathologic factors:

- Size 2.1-3.0 cm
- T2
- Close margins (<2 mm)
- Limited/focal LVSI
- ER(-)
- Clinically unifocal with total size 2.1-3.0 cm
- Invasive lobular histology
- Pure DCIS ≤3 cm if criteria for "suitable" not fully met
- EIC ≤3 cm

Unsuitable

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;50 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margins</td>
<td>Positive</td>
</tr>
<tr>
<td>DCIS</td>
<td>&gt;3 cm</td>
</tr>
</tbody>
</table>

* The size of the invasive tumor component.

* Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

Why change (or not)?

- **Advantages:**
  - Complete RT in 1 week
  - Convenient

- **Disadvantages:**
  - New Procedure (compared to whole breast irradiation)
  - ?Worse cosmesis
  - New, not “tried and true”
  - Only certain cases (T1, >50 yo, negative margins)
  - Benefit to treatment in this cohort?
  - Final RTOG/NSABP results not out
Take Homes

- Breast hypofractionation is a reasonable treatment option *for appropriate patients*
- Acute side effects may be better with hypofractionation
- Not for advanced cases, e.g. regional nodal RT or post-mastectomy
Standard Treatment?

- 60 Gy in 30 fractions with concurrent TMZ
Hypofractionated Treatment?

- Suggested as option if >60 yo and/or lower KPS
- Various Regimens:
  - 3 week regimen: 40 Gy in 15 fractions
  - 2 week regimen: 34 Gy in 10 fractions
  - 1 week regimen: 25 Gy in 5 fractions
Evidence?

- 3 week option:
  - 40 Gy x 15 fractions
  - >60, KPS >50

Results

All patients had died at the time of analysis. Overall survival times measured from randomization were similar at 5.1 months for standard RT versus 5.6 months for the shorter course (log-rank test, \( P = .57 \)). The survival probabilities at 6 months were also similar at 44.7% for standard RT versus 41.7% for the shorter course (lower-bound 95% CI, –13.7). KPS scores varied markedly but were not significantly different between the two groups (Wilcoxon test, \( P = .63 \)). Low completion rates of the FACT-Br (45%) precluded meaningful comparisons between the two groups. Of patients completing RT as planned, 49% of patients (standard RT) versus 23% required an increase in posttreatment corticosteroid dosage (\( \chi^2 \) test, \( P = .02 \)).

Evidence?

- 2 week option:
  - 34 Gy x 10 fractions
  - >60, KPS >50
Evidence?

- 1 week option:
  - 25 Gy x 5 fractions
  - >60, KPS >50
Quality of Evidence?

- 3 randomized trials for each 3-, 2-, and 1-week regimen
- Smaller numbers (n=100, n=342, and n=98)
Why change (or not)?

- **Advantages:**
  - Allows completion of RT
  - Similar outcomes in selected patients
  - ?Increased compliance

- **Disadvantages:**
  - Potentially undertreating patients
  - Age only surrogate for performance status?
Take Homes

• Hypofractionation is effective treatment for patients that are not good candidates for 6 weeks of RT
• These patients may be more frail requiring more assistance with completing treatment
Standard Treatment?

- 30 Gy in 10 fractions
- 20 Gy in 5 fractions
Hypofractionated Treatment?

- 8 Gy x 1 fraction
Evidence?

- RTOG 9714
- 30 Gy/10 vs 8 Gy/1
- Primary outcome: Pain at 3 mo

- Grade 2-4 acute toxicity:
  - 30-Gy arm (17%)
  - 8-Gy arm (10%)
  - P = 0.002
Quality of Evidence?

• RTOG 9714
  – Prospective, RCT
  – 455 patients

• Dutch trial: 1171, similar results
Why not change?

• Advantages:
  – Quicker
  – Pain control appears equivalent

• Disadvantages:
  – Higher re-treatment rate with 8Gy arm (18% v 9 %, p<0.001)
Bone Mets

Take Homes

- 8 Gy x 1 fraction is reasonable option for patients who cannot undergo 10 fractions
  - Live far away
  - Poor performance status
- May have flair of pain in first few days but should resolve after 1-2 days
- Consider adding dexamethsone to reduce pain flare
Future

• Post-Mastectomy?
Summary

- Hypofractionation is a well-studied radiation treatment for Prostate, Breast, GBM, and Bone Metastases
- Using hypofractionated radiation depends on appropriate patient selection and patient preference
Acknowledgements

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