Current Indications for Breast Radiation

- Hypofractionated Whole Breast Radiation
- Accelerated Partial Breast Radiation
- Intraoperative Radiation
- Elimination of Radiation
- Proton Beam Irradiation

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Conflicts:

• I have no conflicts of interest to disclose
Background

– Conventional Fractionation-Whole Breast Irradiation (CF-WBI)
  • Whole breast: 45-50 Gy in 25-28 fractions
  • Boost: 10-16 Gy in 5-8 fractions

– Widely Embraced
– Accepted Standard of Care
– Long Term Follow-up on Efficacy and Toxicity
Local Relapse and BC Mortality Benefit: Randomized Trials of BCS compared to BCS +RT

Darby et al. Lancet 2011

Any first recurrence

Women with pNO disease (n=7287)

- 10-year gain 15.4% (SE 1.1)
- RR 0.49 (95% CI 0.45–0.55)
- Log-rank 2p<0.00001

Women with pN+ disease (n=1050)

- 10-year gain 21.2% (SE 3.4)
- RR 0.53 (95% CI 0.44–0.64)
- Log-rank 2p<0.00001

Breast cancer death

Women with pNO disease (n=7287)

- 15-year gain 3.3% (SE 1.3)
- RR 0.83 (95% CI 0.73–0.95)
- Log-rank 2p=0.005

Women with pN+ disease (n=1050)

- 15-year gain 8.5% (SE 3.4)
- RR 0.79 (95% CI 0.65–0.95)
- Log-rank 2p=0.01
Background

• **Limitations of CF-WBI**
  
  – Long overall treatment time
    • Patient inconvenience
    • Cost
  
  – Limited access in rural areas
  
  – Perhaps unnecessary toxicity due to irradiation of uninvolved portions of breast and normal tissue
Emerging Strategies

• Hypofractionated Whole Breast Irradiation (HF-WBI)
• Accelerated Partial Breast Irradiation (APBI)
• Intraoperative Radiation
• Elimination of Radiation
ASTRO Breast Guidelines

2009  Update 2016 to be published soon

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

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2011  Update ongoing publication expected 2017

FRACTIONATION FOR WHOLE BREAST IRRADIATION: AN AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) EVIDENCE-BASED GUIDELINE

Benjamin D. Smith, M.D.,* Soren M. Bentzen, Ph.D., D.Sc.,† Candace R. Correa, M.D.,‡
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Beryl McCormick, M.D., FACR.,# Julie R. McQueen, CHES., RHEd.,** Lori J. Pierce, M.D.,††
Simon N. Powell, M.D., Ph.D.,# Abram Recht, M.D.,§§ Alphonse G. Taghian, M.D., Ph.D.,¶¶
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WBI vs APBI: Target Volumes

[Diagram showing tumor and target volumes]

Whole Breast Target
WBI vs APBI: Target Volumes

Partial Breast Clinical Target Volume
HYPOFRACTIONATED WHOLE BREAST RT
Outcomes in Patients with Breast Cancer Who Received a Hypofractionated Regimen of Radiation Therapy as Compared with Standard Regimen

Hazard Ratios for Ipsilateral Recurrence of Breast Cancer in Subgroups of Patients

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50 yr</td>
<td>1.02 (0.62–1.70)</td>
<td>0.67</td>
</tr>
<tr>
<td>&lt;50 yr</td>
<td>0.77 (0.35–1.70)</td>
<td></td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 cm</td>
<td>0.99 (0.49–1.98)</td>
<td>0.90</td>
</tr>
<tr>
<td>&lt;2 cm</td>
<td>0.95 (0.55–1.64)</td>
<td></td>
</tr>
<tr>
<td>Estrogen-receptor status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>0.71 (0.41–1.23)</td>
<td>0.36</td>
</tr>
<tr>
<td>Negative</td>
<td>1.32 (0.62–2.82)</td>
<td></td>
</tr>
<tr>
<td>Equivocal</td>
<td>1.30 (0.22–7.81)</td>
<td></td>
</tr>
<tr>
<td>Tumor grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.70 (0.31–1.58)</td>
<td>0.01</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.57 (0.29–1.12)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>3.08 (1.22–7.76)</td>
<td></td>
</tr>
<tr>
<td>Systemic therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.86 (0.48–1.55)</td>
<td>0.65</td>
</tr>
<tr>
<td>Yes</td>
<td>1.06 (0.58–1.97)</td>
<td></td>
</tr>
</tbody>
</table>
Hypofractionated whole Breast

- The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials.
  - Haviland et al. Lancet Oncology 2013

- Hypofractionated whole breast irradiation: the preferred standard of care?
  - Haffty and Buchholz Lancet Oncology 2013
The UK START Trials

START Trials: design and endpoints

Women with completely excised invasive breast cancer, T1-3 N0-1 M0

Primary endpoint:
- local-regional relapse

Secondary endpoints include:
- normal tissue effects
  (assessed by physicians, photographs & patients)
- disease-free & overall survival

Recruitment from 35 UK centres 1999-2002

Median follow-up:
9.3 years (Trial A)
9.9 years (Trial B)
COSMETIC OUTCOME: START B

Trial B: Any moderate/marked effect in the conserved breast (physician assessments)

- 40 Gy (332/1005; 10yr rate 37.9%, CI 34.5-41.5)
- 50 Gy (394/1001; 10yr rate 45.3%, CI 41.7-49.0)

% of patients with no moderate / marked effect in the breast

Time from randomisation (years)

Hazard Ratio (95%CI) Absolute difference at 5 years (95%CI) Absolute difference at 10 years (95%CI)

40Gy vs. 50Gy 0.77 (0.66-0.89) -6.0% (-9.0 to -2.8%) -8.1% (-12.4 to -3.7%)
Normal Tissue Effect: START B

Trial B: Normal tissue effects – individual endpoints (physician assessments)

- Change in photographic breast appearance (5 yrs)
- Breast shrinkage
- Breast induration
- Breast oedema
- Telangiectasia
- Shoulder stiffness
- Arm oedema

Hazard Ratio (95% CI)

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Local-regional Control: START B
Issue of High Grade and Hypofractionation

• This really should no longer be an issue.
• As previously noted in the Canadian trial for unclear reasons the local recurrence seemed higher in the hypo-fractionation arm for high grade tumors.
• This was not found to be the case in the START trials.
• Further analysis of the Canadian Trial Did Not Confirm that Grade was a Significant Factor upon central review.
Hazard ratios for local recurrence of breast cancer in subgroups of patients.

HF-WBI: Clinical Data

- **Majority of patients in all trials:**
  - Treated with breast conserving surgery
  - Age ≥ 50 years
  - pT1-2 pN0
  - Chemotherapy not used
  - Homogeneity within +/- 7%

Patient group for whom data to support HF-WBI is strongest!!

However, this does not imply that this is the only group in whom HF-WBI can/should be used!!
Hypofractionated Whole Breast

- Strong Phase III data that this is acceptable as an alternative to whole breast
- Remains some controversy regarding selection of higher risk patients, patients requiring a boost, younger patients, and patients who have received chemotherapy
- Improvements in technology, allowing more homogenous dose distribution throughout the breast, and allowing for simultaneous boost, will likely further advance and encourage the use of hypo-fractionated whole breast treatment
- However, long term follow-up and patient experience is still much more immature and less extensive compared to experience with conventionally fractionated whole breast treatment
PARTIAL BREAST IRRADIATION
Rationale for Partial Breast Radiation

• The majority of all local recurrences occur within the region of initial lumpectomy
• Why do we need to radiate the whole-breast
• Early Phase I/II data on partial breast irradiation appears promising for selected patients
Potential Advantages of APBI

• All local therapy completed prior to chemotherapy

• Treatment of tissue at most increased risk of sub-clinical disease – rather than healthy breast tissue/skin may actually improve cosmesis
Potential Disadvantages

• Local relapses may be higher
• Fibrosis with larger fractions may be significant with longer follow-up
• Prospective randomized data proving its effectiveness is lacking
APBI-Treatment Approaches

• Multi-catheter Interstitial
• Single Catheter Balloon Based
• External Beam
• Intraoperative
Multi-Catheter Brachytherapy placement – US, Stereotactic mammography, or CT guidance
APBI: Interstitial Brachytherapy

Key Study
William Beaumont
N=199
82% stage I
100% negative margins
10-yr in-breast recurrence: 3.8%
Excellent/good cosmetic outcome: 99%

Randomized Trial (Strnad et al. Lancet, 2016)
- Randomized Trial: Whole Breast vs. Interstitial Brachytherapy
- At 5 yrs, No difference in local relapse, survival, toxicity
Randomized Trial: Brachy APBI vs Whole Breast

Local Relapse

Overall Survival

- Local recurrence (%)
- Difference at 5 years: 0.52% (95% CI: 0.44 to 1.75)
- p = 0.42 (Fine and Grey)

- Number at risk
  - APBI: 633, 626, 616, 606, 601, 573, 429
  - WBI: 551, 543, 535, 522, 511, 490, 381

- Overall survival (%)
- Difference at 5 years: 1.72% (95% CI: 0.44 to 3.88)
- p = 0.11 (log-rank)
APBI: Interstitial Brachytherapy

Limitations

- Invasive
- Risk of infection
- Operator-dependent
- Limited diffusion
- Heterogeneous clinical outcomes
Ideal Case for Balloon Based Brachy

Placed by Surgeon or Rad Onc - at the time of lumpectomy or post lumpectomy

Target conforms to balloon surface
IntraCavitary Applicators
APBI: Balloon-based

Key Study
ASBS Mammosite Registry
N=1,449
>90% stage I
ER Negative associated with higher IBTR
5-yr in-breast recurrence: 3.8%
Excellent/good cosmetic outcome: 90.6%

APBI: Balloon-based

Limitations

• Invasive
• Risk of infection and seroma
• Short follow up
• Not appropriate for superficial lesions
APBI: External Beam

Key Study
RTOG 0319
N=53
92% stage I
100% negative margins
3-yr in-breast recurrence: 6% (95% 0-12%)

APBI: External Beam

Limitations

• Very short follow up
• Few patients treated
• Uncertainty in target delineation
• ?Uncertainty day to day setup
• Increased integral dose to breast
### Stratification

- **Age:** < 50, ≥ 50
- **Histology:** DCIS, invasive disease
- **Tumour size:** < 1.5 cm, ≥ 1.5 cm
- **ER status:** +ve, -ve
Summary of RAPID/JCO 2014

- 2135 women randomized to WBRT vs APBI
- Whole breast (50 Gy/25 Fractions) or Canadian (42.5 Gy/16 fractions) +/- Boost
- APBI 3.85 BID to 38.5 Gy all External Beam Conformal
- Cosmesis assessed by Study Nurse and Patient:
- Cosmesis also assessed by panel of trained radiation oncologists unaware of tx arm using digital photos
- Planned interim analysis based on nurse assessment at 2.5 years
- DSMC recommended release of results based on highly significant findings
# Adverse Cosmetic Assessment

## 3 Independent Measures

<table>
<thead>
<tr>
<th></th>
<th>Whole Breast</th>
<th>APBI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse Assessment</td>
<td>18.6%</td>
<td>31.5%</td>
<td>.0001</td>
</tr>
<tr>
<td>Patient Assessment</td>
<td>18.4</td>
<td>26.2</td>
<td>.004</td>
</tr>
<tr>
<td>RO Panel Assessment</td>
<td>16.6</td>
<td>35.1</td>
<td>.0001</td>
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### ASTRO - Suitable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Finding</th>
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<tbody>
<tr>
<td>Age</td>
<td>( \geq 60 )</td>
</tr>
<tr>
<td>T-stage</td>
<td>T1</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>( \leq 2 \text{ cm} )</td>
</tr>
<tr>
<td>Margins</td>
<td>&gt; 2 mm</td>
</tr>
<tr>
<td>Grade</td>
<td>Any</td>
</tr>
<tr>
<td>LVI</td>
<td>No</td>
</tr>
<tr>
<td>ER Status</td>
<td>Positive</td>
</tr>
<tr>
<td>Multicentricity</td>
<td>Unifocal ( \leq 2 \text{ cm} )</td>
</tr>
<tr>
<td>Histology</td>
<td>IDC or favorable</td>
</tr>
<tr>
<td>EIC</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Pure DCIS</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Nodes</td>
<td>pNO</td>
</tr>
<tr>
<td>Neoadjuvant Chemo</td>
<td>Not allowed</td>
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## ASTRO - Cautionary

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<th>Finding</th>
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<tr>
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<td>50-59</td>
</tr>
<tr>
<td>T-stage</td>
<td>T0 or T2</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>2.1-3.0 cm</td>
</tr>
<tr>
<td>Margins</td>
<td>Close &lt; 2 mm</td>
</tr>
<tr>
<td>Grade</td>
<td>NA</td>
</tr>
<tr>
<td>LVI</td>
<td>Limited/focal</td>
</tr>
<tr>
<td>ER Status</td>
<td>Negative</td>
</tr>
<tr>
<td>Multicentricity</td>
<td>NA</td>
</tr>
<tr>
<td>Histology</td>
<td>Invasive lobular</td>
</tr>
<tr>
<td>EIC</td>
<td>≤ 3 cm in size</td>
</tr>
<tr>
<td>Pure DCIS</td>
<td>≤ 3 cm in size</td>
</tr>
<tr>
<td>Nodes</td>
<td>NA</td>
</tr>
<tr>
<td>Neoadjuvant Chemo</td>
<td>NA</td>
</tr>
</tbody>
</table>
## ASTRO - Unsuitable

<table>
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<th>Variable</th>
<th>Finding</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 50</td>
</tr>
<tr>
<td>T-stage</td>
<td>T3 or T4</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>&gt; 3 cm</td>
</tr>
<tr>
<td>Margins</td>
<td>Positive</td>
</tr>
<tr>
<td>Grade</td>
<td>NA</td>
</tr>
<tr>
<td>LVI</td>
<td>Extensive</td>
</tr>
<tr>
<td>ER Status</td>
<td>NA</td>
</tr>
<tr>
<td>Multicentricity</td>
<td>Present</td>
</tr>
<tr>
<td>Histology</td>
<td>NA</td>
</tr>
<tr>
<td>EIC</td>
<td>If &gt; 3 cm in size</td>
</tr>
<tr>
<td>Pure DCIS</td>
<td>If &gt; 3 cm in size</td>
</tr>
<tr>
<td>Nodes</td>
<td>pN1, pN2, pN3</td>
</tr>
<tr>
<td>Neoadjuvant Chemo</td>
<td>If used</td>
</tr>
</tbody>
</table>
Future Directions in APBI: Exploring Ultra-short Fractionation
Europeans accumulating large body of maturing data with intraoperative single fraction treatment.

- TARGIT
- ELIOT
TARGIT: radiobiological considerations

• 5 Gy at 1 cm distance?

• 50 kV source increases RBE (1.5 at 1 cm), but still low.

• Intraoperative alters lumpectomy microenvironment?
Update on the TARGIT-A trial

- 3451 randomized patients, median fup 2.5 years; 2020 with 4 yr fup, 1222 with 5 yr fup

- Pre vs post-pathology strata (pre-path: 21% recd whole breast RT)

- 5-year ipsilateral breast recurrence: 3.3 vs 1.3% (p=0.042).
Update on the TARGIT-A trial
Update on the ELIOT trial

- 1184 randomized women, median fup 6 yrs

- No “remedial” whole breast RT

- 5-year ipsilateral breast recurrence: 4.4 vs 0.4% (p<0.0001)

- Fat necrosis rate: 14.5% (versus 2-3% with device-based 5 day APBI)

- Only 23% of patients “suitable” for APBI, 33% (387/1184) “unsuitable”.
Limitations of intraoperative APBI

- Treatment triage occurs before permanent path review (no margin/LN eval)
- 20% of patients selected for intraop got additional WBI (TARGIT-A, but not ELIOT)
- Logistics (increase OR time, coordinate schedules (surgeon/rad onc/dedicated path to do intraop assessment)
- Treatment planning is NOT image based
- Dosimetry/radiobiology not validated
Fraction-escalating “Overnight” study (short-course 2 Day APBI)

– Concept: women with early stage, low risk breast cancer can receive adjuvant RT in 2 days; women living remote from treatment center can stay “overnight” close to facility and return home on day 2

– Eligible women:
  • age ≥ 50 years
  • unifocal invasive or in situ tumors
  • less than 3.1 cm/+ Hormone Receptors
  • excised with negative margins
  • negative lymph nodes
Treatment planning
Treatment schedule

- 3 cohorts of 30 patients each with predefined stopping criteria for toxicity and a 6 month observation period between cohorts
- Radiobiology modeling by Prof Roger Dale (Imperial College UK)
  - 7 Gy times 4
  - 8.25 Gy times 3
  - 10.5 Gy times 2
Update on Phase II “Overnight” study:  
Khan, Arthur, Vicini, Haffty  
Sponsor: Cianna Medical (Alisa Viejo, CA)

• 3 cohorts of 30 patients (n=90) with predefined stopping criteria for toxicity.

  - 7 Gy x 4
  - 8.25 Gy x 3
  - 10.25 Gy x 2

• 30 women on cohort 1, COMPLETE ACCRUAL.

• 30 women on cohort 2, COMPLETE ACCRUAL.

• No > grade 2 toxicity events, no safety events
What About No Radiation?

• All randomized studies show a benefit to radiation in reducing local relapse
• In some higher risk patients, this benefit translates to improvements in relapse free or even overall survival
• However, some subsets of patients are at so low risk that radiation can be avoided
• This is the subject of several trials, completed, ongoing and developing
Local Relapse and BC Mortality Benefit: Randomized Trials of BCS compared to BCS +RT

Darby et al. Lancet 2011

**Women with pNO disease (n=7287)**

- **Any first recurrence**
  - 10-year gain 15.4% (SE 1.4)
  - RR 0.49 (95% CI 0.45-0.55)
  - Log-rank 2p < 0.00001
  - BCS 31.0%, BCS + RT 22.5%

- **Breast cancer death**
  - 15-year gain 3.3% (SE 1.3)
  - RR 0.83 (95% CI 0.73-0.95)
  - Log-rank 2p = 0.005
  - BCS 20.5%, BCS + RT 12.7%

**Women with pN+ disease (n=1050)**

- **Any first recurrence**
  - 10-year gain 21.2% (SE 3.4)
  - RR 0.53 (95% CI 0.44-0.64)
  - Log-rank 2p < 0.00001
  - BCS 63.7%, BCS + RT 53.7%

- **Breast cancer death**
  - 15-year gain 8.5% (SE 3.4)
  - RR 0.79 (95% CI 0.65-0.95)
  - Log-rank 2p = 0.01
  - BCS 51.3%, BCS + RT 42.8%
From Darby et al. Meta-analysis of BCS+/-RT

These are the only groups that benefit!

Figure 5: Absolute reduction in 15-year risk of breast cancer death with radiotherapy (RT) after breast-conserving surgery versus absolute reduction in 10-year risk of any (locoregional or distant) recurrence
Participant flow schema.

- Participated in the RCT (N = 769)
- TMA available for 501 samples
- 6-marker panel ER, PR, HER2, CK5/6, EGFR, Ki-67
  - Luminal A (n = 265)
  - Luminal B (n = 165)
    - Luminal HER2 (n = 22)
    - HER2 enriched (n = 13)
    - Basal like (n = 30)
    - TN-non-basal (n = 6)
  - Luminal A, age > 60, T1, and grade 1/2 (n = 151)
  - Grade missing (n = 9)
  - Others (n = 341)

Fei-Fei Liu et al. JCO 2015;33:2035-2040
Cumulative incidence of ipsilateral breast relapse in the combined cohort for (A) luminal A, (B) luminal B, and (C) luminal human epidermal growth factor receptor 2 (HER2), HER2-enriched, basal-like, and triple-negative–nonbasal tumors.

Fei-Fei Liu et al. JCO 2015;33:2035-2040
Posoperative Radiotherapy In Minimum-risk Elderly--PRIME II

• 1,326 pts between 2003-2009 randomized to WLE and adjuvant hormonal tx +/- WBI in women ≥ 65 yrs
  – T1-2 (up to 3cm)N0M0, ER+ or PR+, clear margins (at least 1mm), N0, margins ≥ 1mm
  – Exclusion: grade 3 + LVSI
  – RT (40-50Gy in 15-25fxn)
  – 98 centers in 6 countries
  – Median f/u 5 years

Kunkler, Lancet Oncol, 2015
## PRIME II

### Time to first local recurrence

<table>
<thead>
<tr>
<th></th>
<th>Local recurrence</th>
<th>5 yr actuarial rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>No RT (n=668)</td>
<td>26</td>
<td>4.1%</td>
</tr>
<tr>
<td>RT (n=658)</td>
<td>6</td>
<td>1.3%</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

---

**RT**

- No RT
- RT

![Graph showing cumulative failure and time to first local recurrence](http://example.com/graph.png)

**Cumulative failure (%)**

**Time (years)**

**p=0.002**
## PRIME II: Unplanned Subgroup Analysis

<table>
<thead>
<tr>
<th>ER</th>
<th>Local Recurrence N (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No RT</td>
<td>RT</td>
<td>p-value</td>
</tr>
<tr>
<td>High</td>
<td>20/593 (3.3%)</td>
<td>5/601 (1.2%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Low</td>
<td>6/65 (10%)</td>
<td>0/55 (0.0%)</td>
<td>0.026</td>
</tr>
</tbody>
</table>

High ER = ER positive, ER ≥ 7, fmol >20, staining >20%, and +++
All others = Low ER
Prime II

- On MVA, only factor associated with increased risk LR: omission of RT and low ER status
- NS difference RR, DM, OS, contralateral breast cancer
- Conclusions:
  - Omission of RT in women $\geq 65$, pT1-T2 (up to 3cm) pN0, ER+ or PR+ breast cancer s/p BCS with endocrine therapy: 5yr IBTR 4.1% (vs. 1.3%)
  - *RT does reduce IBTR, but the absolute reduction is small*
  - Omission of RT does not impact OS (not surprising)
Ongoing/Planned Studies of Observation in Low Risk Breast Cancer

- Jagsi (Michigan)–Multi-institution Prospective Single Arm Study of Observation in Patients Age 50-69 with Luminal A and Low Oncotype
- Fyles et al (Canada)-Single Arm Prospective Study of Observation in Patients with Luminal A, Low Ki-67
- Bellon (Harvard)-Multi-institution Prospective Single Arm Study of Observation in Patients with Luminal A, Favorable PAM50
• Protons are just another way of delivering radiation
• The Beam Characteristics with no “exit” dose allow for advantages in some situations
• However, the technology is more expensive currently such that one must clearly demonstrate a benefit to justify its use to the “payers”
• A “better dosimetric plan” on paper can not always serve as justification for the use of proton beam
• While it can be used to deliver partial breast irradiation, it can be difficult currently to justify its routine use in this setting given the excellent dose distributions that can be achieved using other methods (interstitial, balloon based, external beam, intraoperative).
Ideal dose distribution

15MV Photons vs SOBP Protons

Protons Stop!

Photons Keep Going.
Clinical Benefit: Avoid collateral dose

Pediatric Medulloblastoma

% Dose Rec’d
Fig. 1. Dose distribution and dose volume histogram of (a) single proton beam and (b) two field proton beam using the anterior oblique angle in the axial plane. Lumpectomy cavity (pink); PTV (red); ipsilateral breast (cyan); lung (orange); and heart (yellow) ar...

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**Phase II trial of proton beam accelerated partial breast irradiation in breast cancer**


http://dx.doi.org/10.1016/j.radonc.2013.06.008
Proton Beam for regional nodal and post-mastectomy Radiation

• In certain situations where one needs to treat the breast/chest wall and regional nodes, including the internal mammary nodes there may be an advantage with protons, particularly when patient anatomy results in relatively high doses to the heart/lungs

• Currently, with conventional radiation, 3-D planning, breath holding and other technical advances, acceptable doses to normal tissues can be achieved.

• Current ongoing trial for patients in whom regional nodal irradiation is indicated: Randomized Trial of Protons vs. Photons with cardiac events/toxicity as endpoint
PROTONS vs. Photons/Electrons in PMRT

(a) Protons

(b) Photons/Electrons

RCA
LAD, D-1, D-2

Photons minus protons = excess dose
Conclusions

• Hypofractionated Whole Breast is a Reasonable Option for a majority of women with early stage breast cancer
• Partial Breast Irradiation is a reasonable option for selected patients
• Interstitial, Balloon Based or External Beam are all reasonable options when applied appropriately
• Intraoperative is also an option in selected cases, preferably on prospective trials
• Elimination of radiation is reasonable in selected cases, preferably on prospective trials
• Proton Beam may offer advantages in selected cases where regional nodal irradiation is indicated. This should be evaluated on the ongoing prospective randomized trial
Thank you for your attention!

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