Locoregional Therapy Update
from the 2019 SABCS

Mark Trombetta M.D., F.A.C.R.
Allegheny General Hospital
Professor of Radiation Oncology
Drexel University College of Medicine

No conflicts and no disclosures
Guiding decisions to omit radiation after breast conserving surgery for invasive breast cancer
Where are we now and where are we going?

Corey Spears MD PhD
University of Michigan

Oncotype DX was developed to quantify the likelihood of disease recurrence in estrogen positive breast cancer and was found to be useful in response to chemotherapy.
**SWOG-8814 (CTA 1995)**

Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Involved Axillary Lymph Nodes and Positive Receptors (Intergroup)

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**SWOG 8814: Post Mastectomy patients**

1-3 nodes +

*DX 0-17 (n=65); LRR 1.5%*

*DX 18+(n= 100); LRR 11.1%*  

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**SWOG 8814: Post Mastectomy patients**

> 3 nodes +

*DX 0-17(n=27); LRR 26%*

*DX 18+(n= 60); LRR 27%*
Non randomized studies ongoing

- IDEA: Individualized Decisions for Endocrine Therapy Alone (UMich)
- PRECISION: Profiling Early Breast Cancer for Radiation Omission (ProSigna Dana Farber)
- LUMINA-IHC: (Whelan/S Smith) 500 pts, Luminal A
- PRIMETIME- IHC4: (Cambridge) 2400 pts; Luminal A

Randomized phase III studies ongoing

- EXPERT: Examining Personalized Radiation Therapy for low risk breast cancer (IBCSG)

Randomized phase III studies ongoing

- MA 39: Tailor RT (Open at AHN)(Whelan CCTG)
  - >40 y
  - Oncotype ≤ 18
  - 1-3 positive nodes (macromets > 2mm with ALND); 1-2 pos with SNB
Randomized phase III studies ongoing

MA 39: Tailor RT
Both BCS and PM
+/- Comprehensive XRT

Randomized phase III studies ongoing

NRG Oncology

Guiding selection of RT approach after lumpectomy
Simona Shaitelman MD MDACC
EORTC Boost Trial

No boost vs boost

HR 0.65 in favor of boost greatest in age < 40 group but shown in all age groups

Evidence supporting hypofractionation
Level 1

Ontario Clinical Oncology Group

10 year f/u

Evidence supporting hypofractionation
Level 1

OCOG

1234 patients
T1-2; N0
50Gy in 25 fractions
vs
42.5 Gy in 16 fractions
Evidence supporting hypofractionation
Level 1

OCOG

50Gy in 25
IBTR 7%; OS 84%

42.5 Gy in 16
IBTR 6%; OS 85%

Evidence supporting hypofractionation
Level 1

OCOG

50Gy in 25
GR 2/3 skin tox 8%; Gr 2/3 sub Q
fibrosis:10%

42.5 Gy in 16
GR 2/3 skin tox 9%; Gr 2/3 sub Q
fibrosis:12%

Evidence supporting hypofractionation
Level 1

OCOG

Predictors of good/exc cosmesis

1. Age > 50; 1.64 odds ratio
2. Tumor size <2 cm vs > 2 cm; 1.26
3. Systemic CTX y/n; 0.89 (p=0.3)
Evidence supporting hypofractionation
Level 1

UK Start A and B

10 year f/u

4451 pts
pT1-T3 N0-N1
50% had bst
70% TMX
20% CTX

UK Start A

50Gy in 25
41.6 Gy in 13
39 Gy in 13
Evidence supporting hypofractionation
Level 1

UK Start A

50Gy; 7.4% IBTR; 80% OS
41.6 Gy in 13; 6.3% IBTR; 82% OS
39 Gy in 13; 9% IBTR; 80% OS

Evidence supporting hypofractionation
Level 1

UK Start B

50Gy in 25 vs 40 Gy in 15

Evidence supporting hypofractionation
Level 1

UK Start B

50Gy; 5.5% IBTR; 81% OS
40 Gy; 4.3% IBTR; 84% OS
Evidence supporting hypofractionation
Level 1

UK Start B

Breast shrinkage, telangiectasia and edema favored 40 Gy arm (all $p < 0.05$): induration ($p = 0.08$)

Evidence supporting hypofractionation
Level 1

Despite financial disincentive, hypofractionation has grown tremendously. 2013 ASTRO "Choosing Wisely"

Evidence supporting hypofractionation
Level 1

Hypofractionated breast irradiation in the United States: Changing the paradigm through 'socialised' data

Mark Trombetta M.D.
Evidence supporting hypofractionation
Level 1

<table>
<thead>
<tr>
<th>ASTRO 2011</th>
<th>ASTRO 2018</th>
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</thead>
<tbody>
<tr>
<td>&gt; 50 y</td>
<td>Any</td>
</tr>
<tr>
<td>T 1-2</td>
<td>Any WBRT</td>
</tr>
<tr>
<td>CTX-None</td>
<td>CTX- Any</td>
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<tr>
<td>Dose +/- 7%</td>
<td>&gt; 105%</td>
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Royal College of Radiologists

"No indication for more than 15 fractions for standard adj XRT"

Boost: < 50 yr and > 50 yr with "high risk" features (high grade EIC, etc)

Evidence supporting APBI-Level 1

GEC-ESTRO Interstitial Multicath

LRR (5 year)

WBRT 0.92%
PBI 1.44%
Evidence supporting APBI-Level 1

**RAPID: Randomized Trial of Accelerated Partial Breast Irradiation**

> 40 yrs
IDC or DCIS
≤ 3 cm
Node neg

Evidence supporting APBI-Level 1

**RAPID: Randomized Trial of Accelerated Partial Breast Irradiation (Whelan)**

42.5 Gy in 16 fx or 50 Gy in 25 vs 38.5 Gy in 10 BID

Evidence supporting APBI-Level 1

**RAPID: Randomized Trial of Accelerated Partial Breast Irradiation**

5 year LRR
APBI 2.3%  WBRT 1.7%
8 year LRR
both essentially 3%
Evidence supporting APBI-Level 1

**NSABP B 39**

Similar to RAPID, but 1-3 + nodes allowed  
Also allowed brachytherapy 29% overall 
LRR 4.6% APBI 
LRR 3.9% WBRT

Evidence supporting APBI-Level 1

**NSABP B 39**

0.7%

Evidence supporting APBI-Level 1

**Import Low**

40Gy in 15 WBRT  
vs  
36 Gy in 15 with tangential “boost” to  
40Gy simultaneously  
vs  
40 Gy in 15 tangential less than WBRT
Evidence supporting APBI-Level 1

Import Low

40Gy in 15 WBRT
1.1% LRR
36 Gy in 15 with tangential "boost" to
40Gy simultaneously 0.2% LRR
vs
40 Gy in 15 tangential less than WBRT
0.5% LRR

Evidence supporting APBI-Level 1

Import Low

No statistically significant cosmesis noted
compared to mixed cosmesis in NSABP B 39
(vast majority still good to exc)

Evidence supporting APBI-Level 1

ASTRO Guidelines

Suitable

Age ≥50 (was 60)
Margins ≤2mm (same)
T1 or TIS (was T1 only; must be ≤ 2.5 cm
with ≥ 3 mm margins)
Evidence supporting APBI-Level 1

**ASTRO Guidelines**

**Cautionary**

- Age 40-49 (was 50-59)
- Margins < 2mm (same)
- DCIS < 3 cm (same but does not meet "suitable" criteria)

**Evidence supporting APBI-Level 1**

**ASTRO Guidelines**

**Unsuitable**

- Age < 40 (was < 50)
- Margins positive (same)
- DCIS ≥ 3 cm (same)

**UK RCR**

Consider APBI if Age ≥ 50; Grade 1-2; tumor < 3 cm; ER +; Her 2 not overexpressed; N0; ≥ 1 mm margin on invasive disease

Exclusions
- Lobular cancer
- LVI
APBI or WBRT following BCS in early stage breast cancer

10 year F/U of the APBI IMRT Florence Randomized phase III trial

APBI IMRT Florence Randomized phase III trial

(n= 520)
BCS
pT size < 25 mm
final margins ≥ 5 mm
Age > 40 years

APBI IMRT Florence Randomized phase III trial

APBI IMRT 30 Gy in 5 fractions (non consecutive vs 50 Gy in 25 fx + 10 Gy boost (5 fx)
APBI IMRT Florence Randomized phase III trial

Used mandatory minimum of 4 surgical clips to ID CTV
CTV Clips + 1.0 cm
PTV = CTV + 1.0 cm
Well matched cohorts

10 yr LRR 3.3% APBI
10 yr LRR 2.6 % WBRT
DM 3.1% both cohorts
OS (93%) and DSS (98%)*

*essentially the same

Cosmesis and acute reactions better in APBI group.