Recent advances and current status of radiotherapy for breast cancer

Dr Gerry Hanna

Clinical Senior Lecturer in Radiation Oncology
Centre for Cancer Research and Cell Biology
Queens University Belfast

@gerryhanna
g.hanna@qub.ac.uk
Overview

• Defining the target volume
  • Surgical Clips
  • ESTRO consensus

• Fractionation

• Breast Boost

• IMRT

• Partial Breast Irradiation

• Cardiac Sparing

• Internal Mammary Chain Irradiation

• Safe Omission of Radiotherapy
Titanium Clips
Titanium Clips – Level III

2 clips on vein branch
At end of forceps
Titanium Clips

Introduced in UK via IMPORT Low Study
ESTRO consensus guidelines

ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer

Birgitte V. Offersen a,*, Liesbeth J. Boersma b, Carine Kirkove c, Sandra Hol d, Marianne C. Aznar e, Albert Biete Sola f, Youlia M. Kirova g, Jean-Philippe Pignol h, Vincent Remouchamps i, Karolien Verhoeven j, Caroline Weltens j, Meritxell Arenas k, Dorota Gabrys l, Neil Kopek m, Mechthild Krause n, Dan Lundstedt o, Tanja Marinko p, Angel Montero q, John Yarnold r, Philip Poortmans s
Delineating breast CTV: ESTRO Guidelines 1.1

## SCF Borders ESTRO guidelines 1.1

<table>
<thead>
<tr>
<th>SCF (level 3+4)</th>
<th>Level 3</th>
<th>Level 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cranial</strong></td>
<td>Includes cranial extent of subclavian artery</td>
<td>Includes cranial extent of subclavian artery</td>
</tr>
<tr>
<td><strong>Caudal</strong></td>
<td>5 mm caudal to the subclavian vein; if appropriate top of surgical ALND (start at clips)</td>
<td>Includes the subclavian vein with 5 mm, thus connecting to cranial border of the CTVn_IMN</td>
</tr>
<tr>
<td><strong>Ventral</strong></td>
<td>Major pectoral muscle</td>
<td>Sternocleidomastoid muscle, dorsal edge of clavicle</td>
</tr>
<tr>
<td><strong>Dorsal</strong></td>
<td>Up to 5 mm dorsal of axillary vein or to costae and intercostal muscles</td>
<td>Pleura</td>
</tr>
<tr>
<td><strong>Medial</strong></td>
<td>Junction of subclavian and internal jugular veins</td>
<td>Including the jugular vein without margin; excluding the common carotid and thyroid gland</td>
</tr>
<tr>
<td><strong>Lateral</strong></td>
<td>Medial side of the minor pectoral muscle</td>
<td>Includes the anterior scalene muscles and connects to medial border of CTVn_L3</td>
</tr>
</tbody>
</table>

ESTRO Guidelines 1.1

ESTRO Guidelines 1.1

- LN supraclavicular/ IV
- LN axilla level III
- LN axilla level II
- LN axilla Rotter
- LN axilla level I
- LN internal mammary

Heart

Hypofractionation
Dose and Fractionation

• START Trials
  • START A - 50 Gy/25F/5 weeks vs 39Gy/13F/5 weeks vs 41.6Gy/13F/5 weeks
  • START B - 50 Gy/25F/5 weeks vs 40Gy/15F/3 weeks
• No difference in OS or LRR or cosmesis
• Canadian Trial
  • 1234 pts 42.5/16F/22 days vs 50/25F/35days
• No diff in DFS/OS
START Trial Design and Endpoints

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

**Trial A**
- N=2236
  - 50Gy in 25 # (2.0Gy) 5 wks
    - N=749
  - 39.0Gy in 13 # (3.0Gy) 5 wks
    - N=750
  - 41.6Gy in 13 # (3.2Gy) 5 wks
    - N=737

**Primary endpoint:**
- local-regional relapse

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

**Trial B**
- N=2215
  - 50Gy in 25 # (2.0Gy) 5 wks
    - N=1105
  - 40Gy in 15 # (2.67Gy) 3 wks
    - N=1110

**Recruitment from 35 UK centres 1999-2002 with QA**

**Median follow-up:**
- 9.3 years (Trial A)
- 9.9 years (Trial B)
Trial B: Local Tumour Relapse

% of patients with no LR relapse

- 50 Gy (53/1105; 10yr rate 5.5%, CI 4.2-7.2)
- 40 Gy (42/1110; 10yr rate 4.3%, CI 3.2-5.9)

Cumulative hazard rate

- 50 Gy
- 40 Gy

Time from randomisation (years)

Hazard Ratio (95%CI)

- 40Gy vs. 50Gy 0.77 (0.51 – 1.16)

Absolute difference at 10 years (95%CI)

-1.2% (-2.6 to 1.0%)
Fast Study

The Fast Trialists Group. Radiother Oncol 2011;100:93–100
### FAST Forward Trial (N=4000)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>TD (Gy)</th>
<th># (Gy)</th>
<th>T (wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>15</td>
<td>40.0</td>
<td>2.67</td>
<td>3</td>
</tr>
<tr>
<td>Test 1</td>
<td>5</td>
<td>27.0</td>
<td>5.4</td>
<td>1</td>
</tr>
<tr>
<td>Test 2</td>
<td>5</td>
<td>26.0</td>
<td>5.2</td>
<td>1</td>
</tr>
</tbody>
</table>
Phase III randomised trial

Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3-week regimen delivered in the UK FAST-Forward Trial

A. Murray Brunt a,*, Duncan Wheatley b, John Yarnold c, Navita Somaiah d, Stephen Kelly e, Adrian Harnett f, Charlotte Coles f, Andrew Goodman f, Amit Bahl g, Mark Churn h, Rada Zotova h, Mark Sydenham i, Clare L Griffin i, James P Morden i, Judith M Bliss i, on behalf of the FAST-Forward Trial Management Group

![Graph showing percentage of patients by grade and weeks from starting radiotherapy]

Grade 3 toxicity reported at 4 weeks post-RT in 27 Gy/5F patient resolved to grade 1 one week later

**Fig. 1.** Acute toxicity substudy 2 – Prevalence of grade 1+, grade 2+ and grade 3+ CTCAE toxicity.
Patients with completely excised non-low risk DCIS and BCS, n=1600

RANDOMISE

Whole breast RT
No tumour bed boost

Arm 1
Standard WB fractionation
50 Gy/25 fractions/35 days

Arm 2
Shorter WB fractionation
42.5 Gy/16 fractions/22 days

Whole breast RT
plus tumour bed boost

Arm 3
Standard WB fractionation
50 Gy/25 fractions/35 days
Boost 16 Gy/8 fractions/10 days

Arm 4
Shorter WB fractionation
42.5 Gy/16 fractions/22 days
Boost 16 Gy/8 fractions/10 days
UK Consensus Statement on Hypofractionation

**STATEMENT:**

- There is no indication to use more than 15 fractions for the breast, chest wall or nodal areas
UK Consensus Statement on Hypofractionation

STATEMENT:
• There is no indication to use more than 15 fractions for the breast, chest wall or nodal areas

• 40 Gy in 15 fractions over 3 weeks (Breast, CW, Nodal)
• 13.35 Gy in fractions over 1 week (boost)
Breast Boost
Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

Harry Bartelink, Philippe Maingon, Philip Poortmans, Caroline Weltens, Alain Fourquet, Jos Jager, Dominic Schinazi, Bing Oei, Carla Rodenhuis, Jean-Claude Horiot, Henk Struikmans, Erik Van Limbergen, Youlia Kirova, Paula Elkuizen, Rudolf Bongartz, Raymond Miralbell, David Morgan, Jean-Bernard Dubois, Vincent Remouchamps, René-Olivier Mirimanoff, Sandra Collette, Laurence Collette; on behalf of the European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups

Breast RT Boost

UK Consensus statements

• A tumour bed boost should be considered for women less than 50 years old.

• For those over 50 years old with higher risk pathological features (especially Grade 3 and/or extensive intraductal component [EIC]), consider the benefit of boost in context of both local recurrence and normal tissue toxicity risks.

• Tumour bed clips should be considered the standard of care to improve planning (and delivery) of the boost.

• Photon boost using intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) is recommended, including simultaneous integrated photon boost (SIB).

• Electron and mini-tangents are acceptable alternatives when IMRT boost is not clinically appropriate.
Breast RT Boost

UK Consensus statements

• A tumour bed boost should be considered for women less than 50 years old.

• For those over 50 years old with higher risk pathological features (especially Grade 3 and/or extensive intraductal component [EIC]), consider the benefit of boost in context of both local recurrence and normal tissue toxicity risks.

• Tumour bed clips should be considered the standard of care to improve planning (and delivery) of the boost.

• Photon boost using intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) is recommended, including simultaneous integrated photon boost (SIB).

• Breast boost standard in <50 yr olds and those with high risk features
IMPORT High

Control Arm
- 40Gy/15Fr
- 56Gy/23Fr*
- Sequential dose escalation
- 23 (15+8) fractions

Test Arm 1
- 36Gy/15Fr
- 40Gy/15Fr
- Concomitant dose escalation
- 15 fractions

Test Arm 2
- 36Gy/15Fr
- 40Gy/15Fr
- 48Gy/15Fr
- Concomitant dose escalation
- 15 fractions

[Medical images and diagrams related to radiation therapy and dose distributions]
Breast IMRT
Breast IMRT

2 partial isocentric arcs
2D Versus 3D Forward Planned IMRT

- Randomised trial - demonstrated clinical benefit of using 3D forward planned IMRT

Donovan et al. Radiother Oncol 2007;82:254-264

<table>
<thead>
<tr>
<th></th>
<th>Year 2 assessment</th>
<th>Year 5 assessment</th>
<th>P-value (from GEE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standard 2D</td>
<td>IMRT 3D</td>
<td>Standard 2D</td>
</tr>
<tr>
<td>Centre of the breast</td>
<td>33/122 (27%)</td>
<td>19/117 (16%)</td>
<td>37/117 (32%)</td>
</tr>
<tr>
<td>Pectoral fold</td>
<td>32/119 (27%)</td>
<td>13/113 (12%)</td>
<td>34/118 (29%)</td>
</tr>
<tr>
<td>Inframammary fold</td>
<td>35/121 (29%)</td>
<td>18/113 (16%)</td>
<td>28/116 (24%)</td>
</tr>
<tr>
<td>Boost site</td>
<td>65/120 (54%)</td>
<td>44/118 (37%)</td>
<td>70/114 (61%)</td>
</tr>
</tbody>
</table>
Randomized Controlled Trial of Intensity-Modulated Radiotherapy for Early Breast Cancer: 5-Year Results Confirm Superior Overall Cosmesis

Simple Forward Planned IMRT is now standard of care in breast RT
Partial Breast RT
Types of Partial Breast Irradiation

• EBRT
  • Photons
    • 3D Conformal
    • IMRT
  • Electrons

• Mammosite

• Interstitial Brachytherapy

• Intra-operative
Partial Breast Irradiation

Suggested benefit of partial breast irradiation is comparable tumour control, yet reduced acute and late toxicity with subsequent improvement in cosmesis.
Partial Breast RT

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>APNI</th>
<th>Total</th>
<th>WBNI</th>
<th>Total</th>
<th>U-E Variance</th>
<th>Weight</th>
<th>Hazard Ratio Exp[O-E / V], Fixed, 95% CI</th>
<th>Hazard Ratio Exp[O-E / V], Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1.1 Four years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaiyaa 2010</td>
<td>6</td>
<td>1113</td>
<td>5</td>
<td>1119</td>
<td>1.365</td>
<td>2.727</td>
<td>100.0%</td>
<td>1.65 [0.50, 5.41]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1113</td>
<td>1119</td>
<td>5</td>
<td>1119</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>1.65 [0.50, 5.41]</td>
</tr>
<tr>
<td>Total events</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.83 (P = 0.41)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **1.1.2 Five years** |      |       |      |       |              |        |                                          |                                          |
| Rodriguez 2013     | 0    | 51    | 0    | 51    | 0            | 1      | 22.9%                                   | 1.00 [0.14, 7.10]                       |
| Veronesi 2013      | 21   | 651   | 4    | 654   | 6.598        | 3.36   | 77.1%                                   | 7.13 [2.45, 20.76]                      |
| Subtotal (95% CI)  | 702  | 705   | 4    | 705   |              |         | 100.0%                                   | 4.54 [1.78, 11.61]                      |
| Total events       | 21   | 4     |      | 4     |              |         |                                          |                                          |
| Heterogeneity: Chi² = 2.97, df = 1 (P = 0.08); I² = 66% |      |       |      |       |              |        |                                          |                                          |
| Test for overall effect: Z = 3.16 (P = 0.002) |      |       |      |       |              |        |                                          |                                          |

| **1.1.3 Seven years** |      |       |      |       |              |        |                                          |                                          |
| Ribeiro 1993       | 69   | 353   | 39   | 355   | 16.672       | 24.916 | 100.0%                                   | 1.95 [1.32, 2.89]                       |
| Subtotal (95% CI)  | 353  | 355   | 39   | 355   |              |         | 100.0%                                   | 1.95 [1.32, 2.89]                       |
| Total events       | 69   | 39    |      | 39    |              |         |                                          |                                          |
| Heterogeneity: Not applicable |      |       |      |       |              |        |                                          |                                          |
| Test for overall effect: Z = 3.34 (P = 0.0008) |      |       |      |       |              |        |                                          |                                          |

| **1.1.4 Eight years** |      |       |      |       |              |        |                                          |                                          |
| Dodwell 2005       | 10   | 84    | 4    | 90    | 3.03         | 2.857  | 100.0%                                   | 2.89 [0.91, 9.21]                       |
| Subtotal (95% CI)  | 84   | 90    | 4    | 90    |              |         | 100.0%                                   | 2.89 [0.91, 9.21]                       |
| Total events       | 10   | 4     |      | 4     |              |         |                                          |                                          |
| Heterogeneity: Not applicable |      |       |      |       |              |        |                                          |                                          |
| Test for overall effect: Z = 1.79 (P = 0.07) |      |       |      |       |              |        |                                          |                                          |

| **1.1.5 Ten years** |      |       |      |       |              |        |                                          |                                          |
| Polgar 2013        | 69   | 353   | 39   | 355   | 16.672       | 24.916 | 100.0%                                   | 1.95 [1.32, 2.89]                       |
| Subtotal (95% CI)  | 353  | 355   | 39   | 355   |              |         | 100.0%                                   | 1.95 [1.32, 2.89]                       |
| Total events       | 69   | 39    |      | 39    |              |         |                                          |                                          |
| Heterogeneity: Not applicable |      |       |      |       |              |        |                                          |                                          |
| Test for overall effect: Z = 3.34 (P = 0.0008) |      |       |      |       |              |        |                                          |                                          |

Partial Breast RT

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>APN Events</th>
<th>WBN Events</th>
<th>U-E Variance</th>
<th>Weight</th>
<th>Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I.1.1 Four years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaiyya 2010</td>
<td>6</td>
<td>1113</td>
<td>1113</td>
<td>2.727</td>
<td>1.65 [0.50, 5.41]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>6</td>
<td>1113</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>6</td>
<td>1119</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.83 (P = 0.41)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **I.1.2 Five years** |            |            |              |        |                                          |
| Rodriguez 2013     | 0          | 51         | 0            | 1      | 1.00 [0.14, 7.10]                       |
| Subtotal (95% CI)  | 702        | 705        |              |        |                                          |
| Total events       | 21         |            |              |        |                                          |
| Heterogeneity: Chi² = 2.97, df = 1 (P = 0.08); I² = 66% |
| Test for overall effect: Z = 3.16 (P = 0.002) |

| **I.1.3 Seven years** |            |            |              |        |                                          |
| Ribeiro 1993       | 69         | 353        | 355 (16.672) | 24.916 | 1.95 [1.32, 2.89]                      |
| Subtotal (95% CI)  | 353        | 355        |              |        |                                          |
| Total events       | 69         |            |              |        |                                          |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 3.34 (P = 0.0008) |

| **I.1.4 Eight years** |            |            |              |        |                                          |
| Dodwell 2005       | 10         | 84         | 90 (3.03)    | 2.857  | 2.89 [0.91, 9.21]                      |
| Subtotal (95% CI)  | 84         | 90         |              |        |                                          |
| Total events       | 10         |            |              |        |                                          |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.79 (P = 0.07) |

| **I.1.5 Ten years** |            |            |              |        |                                          |
| Polgar 2013        | 69         | 353        | 355 (16.672) | 24.916 | 1.95 [1.32, 2.89]                      |
| Subtotal (95% CI)  | 353        | 355        |              |        |                                          |


- Partial Breast Still Remains Experimental
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>IORT technique</th>
<th>IORT dose</th>
<th>EBRT Whole breast dose</th>
<th>Median follow-up (Years)</th>
<th>IBTR for IORT Group (%)</th>
<th>IBTR for EBRT Group (%)</th>
<th>IBTR Hazard ratio in favour of IORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eliot [14]</td>
<td>1305</td>
<td>Intra-operative Electrons</td>
<td>21 Gy</td>
<td>50 Gy / 25 Fx, whole breast, followed by 10 Gy / 5 Fx tumour bed boost</td>
<td>5.8</td>
<td>4.4</td>
<td>0.4</td>
<td>9.3 (95% CI 3.3–26.3).</td>
</tr>
<tr>
<td>TARGIT-A [42]</td>
<td>3451</td>
<td>Intrabeam</td>
<td>20 Gy</td>
<td>40–56 Gy with or without a boost of 10–16 Gy</td>
<td>2.4</td>
<td>3.3</td>
<td>1.3</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>IORT technique</th>
<th>IORT dose</th>
<th>EBRT Whole breast dose</th>
<th>Median follow-up (Years)</th>
<th>IBTR for IORT Group (%)</th>
<th>IBTR for EBRT Group (%)</th>
<th>IBTR Hazard ratio in favour of IORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eliot [14]</td>
<td>1305</td>
<td>Intra-operative Electrons</td>
<td>21 Gy</td>
<td>50 Gy / 25 Fx, whole breast, followed by 10 Gy / 5 Fx tumour bed boost</td>
<td>5.8</td>
<td>4.4</td>
<td>0.4</td>
<td>9·3 (95% CI 3·3–26·3).</td>
</tr>
<tr>
<td>TARGIT-A [42]</td>
<td>3451</td>
<td>Intrabeam</td>
<td>20 Gy</td>
<td>40–56 Gy with or without a boost of 10–16 Gy</td>
<td>2.4</td>
<td>3.3</td>
<td>1.3</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Cardiac Irradiation and DIBH
RT induced heart disease

Fig 1. Combined survival curves according to allocated treatment for trials using radical mastectomy.

Radiation induced heart disease

Radiation-induced heart disease manifest as three distinct diseases:

1. Radiation-induced pericarditis may occur if a large proportion of the heart (>30%) receives a dose of ≥50Gy. The mean latency is approximately 1 year.

2. Radiation-induced myocardial damage may be diagnosed at lower mean doses to the heart. The mean latency is > 5 years.

3. The risk of radiation-induced cardiovascular disease begins to increase 10 years after irradiation and is progressive with time.

A significant increase of risk of cardiovascular disease has been observed after mean heart doses lower than 10% of the generally accepted tolerance dose to the heart of 40-50 Gy.
Modern Left breast irradiation

Left anterior descending coronary artery

Right coronary artery

Circumflex coronary artery

Is a RT dose response present?

Methods of reducing cardiac dose

• Change wedge angle
• MLC cardiac shielding
• Use direct electrons (post-mastectomy only)
• Prone planning
• IORT / Brachytherapy
• DIBH
• Protons
MLC Cardiac Shielding


<table>
<thead>
<tr>
<th>Tumour quadrant</th>
<th>WBCTV V95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central $n = 9$</td>
<td>89 (9)</td>
</tr>
<tr>
<td>Lower inner $n = 4$</td>
<td>86 (8)</td>
</tr>
<tr>
<td>Lower outer $n = 6$</td>
<td>91 (6)</td>
</tr>
<tr>
<td>Upper inner $n = 3$</td>
<td>85 (2)</td>
</tr>
<tr>
<td>Upper outer $n = 26$</td>
<td>90 (5)</td>
</tr>
<tr>
<td>$P$</td>
<td>0.46</td>
</tr>
</tbody>
</table>
Prone Breast Planning

Prone versus DIBH

Prone versus DIBH

DIBH visual display system
Deep inspiration breath hold

IMC / Nodal Irradiation
INTERNAL Mammary and Medial Supraclavicular Irradiation in Breast Cancer

Study Design

pN+ axillary nodes
or pN- central
or medial tumour

RANDOM

CW/ breast RT only (50Gy)

CW/ breast & IM-MS RT (50Gy)

ENDPOINTS

Primary: Overall survival

Secondary: Disease -free survival
Metastases-free survival
Cause of death
After adjustment for stratification factors $p=0.04$

OS at 5 years:
91.5 (95% CI: 90.2, 92.7)
90.3 (95% CI: 88.9, 91.5)

OS at 10 years:
82.3 (95% CI: 80.4, 83.9)
80.7 (95% CI: 78.8, 82.5)

HR = 0.87 (95% CI: 0.76, 1.00)

Logrank test: $p=0.056$

After adjustment for stratification factors $p=0.04$
Regional Nodal Irradiation in Early-Stage Breast Cancer

**Study Design**

- **pN+ axillary LN (90%)**
- **or pN- “high-risk” (mainly T3N0) (10%)**

**Randomization**

- **Breast RT only (50Gy)**
- **Breast, level III-IV axilla & IMC RT (50Gy)**

**Endpoints**

- **Primary:** Overall survival
- **Secondary:** Disease-free survival, Locoregional & distant DFS, Toxicity
Locoregional RT fields in MA-20 test arm

Diagram 1a: Technique 1: Modified Wide Tangent Technique

Diagram: Modified Wide Tangent Technique for locoregional RT fields in MA-20 test arm. The diagram illustrates the placement of radiation fields around the chest and upper abdomen, highlighting the midsternum, intercostal spaces, and lateral tangent fields. The medial tangent field is noted as being 3 cm from the midsternum with lower cardiac/lung shield. Wire markers are indicated for specific anatomical landmarks, such as the 3rd intercostal space and lower half of breast circumference.
MA-20 Results

Nodal Irradiation

- Appears to improve both local control
- Additional toxicity is limited
- Uncertainty regarding late cardiac effects

**Possible Criteria for IMC RT**

- N2-3 disease
- Medial central tumours with N1 and other adverse features
- ??? T3NO with adverse features
Safe omission of radiotherapy
PRIME II: Design

1326

WBI*, N=658
* 40 - 50Gy in 15 - 25 #

No WBI, n=668

≥ 65, ≤3cm, NO ER+ or PR+
PRIME II: 5 Year LRR

CI: Charlotte Coles
Tumour bed clips are essential for accurate breast RT

Hypofractionation is now standard of care for breast RT

IMRT reduces inhomogeneity and reduces toxicity

APBI and IORT remain experimental techniques

DIBH permits cardiac sparing

IMC / Nodal RT should be considered in node positive patients