Radiotherapy of Breast Cancer

Overview and Take Home Messages

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AIIMS, Rishikesh.

ICRO Puducherry
5th August, 2017
Tumor Biology

Doubling

Tumor Doubling Time

Doubling

Doubling

Doubling
30 Doublings
Median Tumor Doubling Time 100 days

30 x 100 = 3000 days = 8 years

1. Primary Gross
2. Microscopic Distant Metastasis
Persistent Primary Disease

Source of Distant Metastasis

Microscopic Met

Systemic Therapy

Surgery and RT
Recurrence Risk

• Positive Axillary Nodes
  - ↑ with more LN involvement
  - 1-3 LN+: 5-15% at 10yrs
  - ≥4 LN+: 15-50%
  - Ratio of LN+ (>20%) = LRR >20%

• Tumour Size
  - Increases with Size

Truong IJRBP. 68(1):59-65. 2007
Recurrence Risk

- High Risk Features

  - Grade III Tumors
  - LVSI
  - TNBC
  - ER/PR Negative Tumours
Where are the recurrences?

- >50% chest wall (mastectomy scar/skin)
- 20-40% supraclavav or infraclavicular
- <5% post ALND (I/II)
- Internal mammary LN
  - 1/3 path involvement in high risk
  - Few clinical recurrences
Indication of PMRT

• **Definitive**
  - Tm size >5cm
  - 4 or >4 axillary nodes metastasis
  - Positive Surgical Margins
  - Pectoralis muscle involvement

• **Debatable**
  - 1 to 3 axillary nodes metastasis
  - 2 to 5 cm primary tumor

**Early Breast Cancer**
Evidences

• Controlled Randomized Trials.

• Meta analysis
82 b  Premenopausal Women
T1 & T2 (85%)
1-3 +ve Node (62%)

The New England Journal of Medicine
Danish 82b Trial

N=1708

CMF + PMRT

CMF

Disease Free Survival

Overall Survival

Median Follow Up 10 Years

The New England Journal of Medicine

Volume 337 Number 14 October 2, 1997
Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial

Marie Overgaard, Maj-Britt Jensen, Jens Overgaard, Per S Hansen, Carsten Rose, Michael Andersson, Claus Kamby, Mogens Kjær, Carl C Gadeberg, Birgitte Bruun Rasmussen, Mogens Blichert-Toft, Henning T Mouridsen
Danish 82c Trial

N=1375

Disease Free Survival

- TMX + PMRT
  - 36% 24%

- TMX
  - 45% 36%

Overall Survival

- Median Follow Up 10 Years

THE LANCET • Vol 353 • May 15, 1999
**Limitation of these Results**

**ECOG: 10 Year Cumulative Incidence of Loco-Regional Failure without XRT**

<table>
<thead>
<tr>
<th>Tumor Size, No. of Nodes</th>
<th>No. of Patients</th>
<th>Isolated LRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1, 1-3</td>
<td>407</td>
<td>9.1</td>
</tr>
<tr>
<td>T2, 1-3</td>
<td>576</td>
<td>7.0</td>
</tr>
<tr>
<td>T3, 1-3</td>
<td>35</td>
<td>22.9</td>
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</tbody>
</table>

Danish trial 82b^6: 30  
Danish trial 82c^7: 31

Recht et al, JCO, 1999
### Limitation of these Results

#### NSABP

<table>
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<tr>
<th></th>
<th>1-3 LN+</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>≤ 2</td>
<td>2.1-5</td>
<td>&gt; 5</td>
</tr>
<tr>
<td>No. of patients</td>
<td>1,045</td>
<td>1,489</td>
<td>229</td>
</tr>
<tr>
<td>Isolated LF, %</td>
<td>4.3</td>
<td>7.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Isolated RF, %</td>
<td>2.4</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Isolated LRF, %</td>
<td>6.0</td>
<td>9.7</td>
<td>7.5</td>
</tr>
<tr>
<td>LRF with or without DF, %</td>
<td>10.6</td>
<td>15.3</td>
<td>11.4</td>
</tr>
<tr>
<td>DF, %</td>
<td>24.6</td>
<td>35.7</td>
<td>40.5</td>
</tr>
</tbody>
</table>

**NOTE.** Subcolumn headings indicate tumor size (in centimeters).

Abbreviations: LN+, positive lymph nodes; LF, local failure; RF, regional failure.

Taghian et al, JCO, 2004
Limitation of these Results

- Surgery was not adequate specially the axillary dissection as compare to other trials.
- Median no of lymph nodes removed
  - Danish Trials 7
Danish Trial 82b & 82c
Sub-group Analysis

• Only select patients with no of nodes removed 8 or more.

• Further grouped based on 1-3 nodes or $\geq$ 4 nodes

• N=1152
Danish Trial 82b & 82c
Sub-group Analysis

Loco regional Recurrence

Median Follow Up  15 Years

M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253
Danish Trial 82b & 82c Sub-group Analysis

Loco regional Recurrence

Median Follow Up 15 Years

M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253
Danish Trial 82b & 82c
Sub-group Analysis

Loco regional Recurrence

Median Follow Up 15 Years

M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253
Danish Trial 82b & 82c
Sub-group Analysis (Hypothesis)

Larger Proportion of patients will have survival benefit

23% improvement in local control translate into 9% OS improvement

PMRT → Local Control → OS gain

1-3 positive nodes

Local RT

Systemic Treatment

M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253
Danish Trial 82b & 82c
Sub-group Analysis

Limited Proportion of patients will have survival benefit

41% improvement in local control translate into 9% OS improvement
PMRT → High Local Control → No OS gain
4 or >4 positive nodes

Local RT
Systemic Treatment

M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253
Hypothetical benefit of Local Tumor Control on Survival with increasing Metastatic Risk of Primary.

- Pts with 1-3 positive nodes
- Pts with 4 and more than 4 positive nodes

Adapted from *NEJM* 2007;356:2399-2405.
Postmastectomy irradiation

High local recurrence risk is not associated with large survival reduction after postmastectomy radiotherapy in high-risk breast cancer: A subgroup analysis of DBCG 82 b&c

Marianne Kyndi a,b,*, Marie Overgaard c, Hanne M. Nielsen a, Flemming B. Sørensen b, Helle Knudsen d, Jens Overgaard a

a Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark
b Department of Pathology, Aarhus University Hospital, Denmark
c Department of Oncology, Aarhus University Hospital, Denmark
d Department of Pathology, Herlev Hospital, Denmark
Danish Trial 82b & 82c Sub-group Analysis

- Among patients in 82b and 82c randomized to no radiation, 3 risk groups were identified

- **Good:** 4 of 5 favorable features
  - \( \leq 3 \) nodes
  - Size < 2 cm
  - Grade 1
  - ER or PR positive, her2 negative

- **Poor:** 2 of 3
  - Grade 3, \( >3 \) nodes, size > 5 cm

*Radiother Oncol 2009 Jan;90(1):74-9*
Danish Trial 82b & 82c
Sub-group Analysis

LRR by Risk Group

No Radiotherapy

\[ p < 0.001 \]

Local recurrence probability (%)

Years after mastectomy

- **Poor**: 50%
- **Intermediate**: 26%
- **Good**: 11%

Radiother Oncol 2009 Jan;90(1):74-9
Danish Trial 82b & 82c
Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group

Improvement in local control translate excellently into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9
Danish Trial 82b & 82c
Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group

- no RT Local rec. (5-year)
- + RT
- no RT Breast cancer mortality
- + RT (15-year)

Improvement in local control translate reasonable into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9
Danish Trial 82b & 82c
Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group

- no RT Local rec. (5-year)
- + RT
- no RT Breast cancer mortality
- + RT (15-year) 61%

Improvement in local control does not translate into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9
Hypothetical benefit of Local Tumor Control on Survival with increasing Metastatic Risk of Primary.

Adapted from

Take Home

All reports related with Danish trial 82b & c make strong case of PMRT in patients with 1-3 positive axillary nodes
Criticisms

- Local recurrence was still high in subgroup analysis of patients with > 8 nodes removed (27%) surgery alone arm
- Suboptimal Chemotherapy used (CMF).
- Tamoxifen was given for 1 year only.

Less Effective Systemic Therapy
British Columbia Trial

Pre menopausal Early Breast Cancer Majority T1 & T2 with pN+ve
N=318 (60% 1-3 nodes +)

CMF + PMRT
CMF

Median Follow Up 15 Years

Disease Free Survival

Overall Survival

The New England Journal of Medicine  Volume 337  Number 14  October 2, 1997
Updated Result of British Columbia

Median Follow Up 20 Years

Breast ca Specific Survival

Overall Survival

p-value = 0.001  RR: 0.63 (0.47, 0.83)

p-value = 0.03  RR: 0.73 (0.55, 0.98)

Journal of the National Cancer Institute, Vol. 97, No. 2, January 19, 2005
Evidences

• Controlled Randomized Trials.

• Meta analysis
Oxford 2005 Meta-analysis
LN + patients → +/- Postmastectomy Radiation

Total No of Patients 8500

Local Recurrence
local control
at 5 years

Overall Survival
MRM
MRM + RT

Absolute gain 17%
Absolute gain 4.4%

Every 4 LR avoided, 1 death is avoided over the following 15 years.

EBCTCG, Lancet, 2005
Oxford 2005 Meta-analysis
LN + patients → +/- Postmastectomy Radiation

Total No of Patients 8500

Breast ca Mortality

Overall Survival

Non Cancerous Deaths are taking place
Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials

EBCTCG (Early Breast Cancer Trialists’ Collaborative Group) *

www.thelancet.com  Published online March 19, 2014  http://dx.doi.org/10.1016/S0140-6736(14)60488-8

- Negative Axilla
- Positive Axilla
- 1-3 +ve Nodes

Axillary Dissection  Level I & II or Min 10 nodes

Axillary Sampling
Negative Axilla

<table>
<thead>
<tr>
<th>Dissection (700)</th>
<th>No effect of RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling (870)</td>
<td>RT reduces overall and LR recurrences No effect on Survival</td>
</tr>
</tbody>
</table>

Take Home In inadequately dissected Axilla, RT may be considered in patients with negative axilla
Patients with 1-3 Positive Nodes

Total No of Patients  1314

Every 2 LR avoided, 1 death is avoided over the following 20 years.

10 years Local Recurrence

Absolute gain 16.5%

20 years Breast ca Mortality

Absolute gain 7.9%

EBCTCG, Lancet, 2014
Effect of PMRT Based on Systemic Therapy

EBCTCG, Lancet, 2014
Oxford 2014 Meta-analysis

PMRT in 1-3 Positive Nodes Who received Systemic Treatment

Total No of Patients 1133

Every 2 LR avoided, 1 death is avoided over the following 20 years.

10 years Local Recurrence

Absolute gain 16.7%

20 years Breast ca Mortality

Absolute gain 7.9%

EBCTCG, Lancet, 2014
Effect of PMRT Based on No of Nodes

### A. Any first recurrence (years 0-9)

<table>
<thead>
<tr>
<th>Category</th>
<th>Events/women</th>
<th>RT events</th>
<th>Ratio of annual event rates</th>
<th>Rate ratio (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Allocated RT</td>
<td>Allocated no RT</td>
<td>Log-rank O-E</td>
<td>Variance of O-E</td>
</tr>
<tr>
<td>1 positive node</td>
<td>35/145</td>
<td>63/173</td>
<td>-10.6</td>
<td>21.1</td>
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<tr>
<td></td>
<td>(24.1%)</td>
<td>(36.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 positive nodes</td>
<td>69/178</td>
<td>92/187</td>
<td>-8.5</td>
<td>32.7</td>
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<tr>
<td></td>
<td>(38.8%)</td>
<td>(49.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown but pN1-3</td>
<td>73/216</td>
<td>107/234</td>
<td>-18.3</td>
<td>38.3</td>
</tr>
<tr>
<td></td>
<td>(33.8%)</td>
<td>(45.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>177/539</strong></td>
<td><strong>262/594</strong></td>
<td><strong>-37.5</strong></td>
<td><strong>92.1</strong></td>
</tr>
<tr>
<td></td>
<td><strong>(32.8%)</strong></td>
<td><strong>(44.1%)</strong></td>
<td></td>
<td></td>
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</tbody>
</table>

Difference between treatment effects in two categories: χ² = 0.8; 2p = 0.1, NS

### B. Breast cancer mortality

<table>
<thead>
<tr>
<th>Category</th>
<th>Deaths/women</th>
<th>RT deaths</th>
<th>Ratio of annual death rates</th>
<th>Rate ratio (SE)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Allocated RT</td>
<td>Allocated no RT</td>
<td>Log-rank O-E</td>
<td>Variance of O-E</td>
</tr>
<tr>
<td>1 positive node</td>
<td>46/145</td>
<td>66/173</td>
<td>-5.7</td>
<td>23.8</td>
</tr>
<tr>
<td></td>
<td>(31.7%)</td>
<td>(38.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 positive nodes</td>
<td>76/178</td>
<td>96/187</td>
<td>-7.0</td>
<td>37.1</td>
</tr>
<tr>
<td></td>
<td>(42.7%)</td>
<td>(51.3%)</td>
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</tr>
<tr>
<td>Unknown but pN1-3</td>
<td>80/216</td>
<td>111/234</td>
<td>-14.4</td>
<td>41.4</td>
</tr>
<tr>
<td></td>
<td>(37.0%)</td>
<td>(47.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>202/539</strong></td>
<td><strong>273/594</strong></td>
<td><strong>-24.1</strong></td>
<td><strong>102.3</strong></td>
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<tr>
<td></td>
<td><strong>(37.5%)</strong></td>
<td><strong>(46.0%)</strong></td>
<td></td>
<td></td>
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</table>

Difference between treatment effects in two categories: χ² = 0.0; 2p = 0.1, NS

EBCTCG, Lancet, 2014
Limitation of Oxford Meta-analysis

- All trials since 1960 onwards.
- Radiotherapy technique was old.
- Usually radiation was given to all regional lymphatic (Axilla, S/C and IM)

More Long term side effects

With Modern radiotherapy the impact in improving the outcome may be much higher
Limitation of Oxford Meta-analysis

• With Modern Systemic Chemotherapy
• Much improved Surgical Technique

5 years Local Recurrence may be much less than in these trial

The impact of Radiotherapy in improving the outcome likely to be smaller
Oxford Meta-analysis

- This also support the use of PMRT in patients with early breast ca with 1-3 positive nodes
Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update


Clinical Question 1
Is PMRT indicated in patients with T1-2 tumors with one to three positive axillary lymph nodes who undergo ALND?

Recommendations
Recommendation 1a. The panel unanimously agreed that the available evidence shows that PMRT reduces the risks of locoregional failure (LRF), any recurrence, and breast cancer mortality for patients with T1-2 breast cancer and one to three positive lymph nodes.
START TRIALS
Q1. Hypo fraction is Effective?

A 1. YES as effective as conventional
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80+</th>
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<tbody>
<tr>
<td></td>
<td>5 (0.7)</td>
<td>4 (0.5)</td>
<td>3 (0.4)</td>
<td>12 (0.5)</td>
<td>116 (15.5)</td>
<td>136 (18.1)</td>
<td>129 (17.5)</td>
</tr>
<tr>
<td></td>
<td>38 (5.1)</td>
<td>40 (5.3)</td>
<td>38 (5.2)</td>
<td>116 (5.2)</td>
<td>215 (28.7)</td>
<td>192 (25.6)</td>
<td>194 (26.3)</td>
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<tr>
<td></td>
<td>87 (11.6)</td>
<td>85 (11.3)</td>
<td>78 (10.6)</td>
<td>250 (11.2)</td>
<td>8 (1.1)</td>
<td>10 (1.3)</td>
<td>9 (1.2)</td>
</tr>
</tbody>
</table>

**Pathological node status**

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
<th>No known (no axillary surgery)</th>
<th>Not known (missing data)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>722 (29.6)</td>
<td>514 (68.6)</td>
<td>12 (1.5)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td></td>
<td>197 (26.3)</td>
<td>536 (71.5)</td>
<td>17 (2.2)</td>
<td>0 (0.0)</td>
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<tr>
<td></td>
<td>224 (20.4)</td>
<td>497 (67.4)</td>
<td>13 (2.2)</td>
<td>1 (0.2)</td>
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<td></td>
<td>642 (28.8)</td>
<td>1547 (69.2)</td>
<td>4 (0.2)</td>
<td>2 (0.1)</td>
</tr>
</tbody>
</table>

**Tumour size (cm)**

<table>
<thead>
<tr>
<th></th>
<th>&lt;1</th>
<th>1-</th>
<th>2-</th>
<th>3-</th>
<th>Not known</th>
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<tbody>
<tr>
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<td>24 (3.2)</td>
<td>26 (3.5)</td>
<td>24 (3.3)</td>
<td>74 (3.3)</td>
<td></td>
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<tr>
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<td>362 (48.3)</td>
<td>347 (46.3)</td>
<td>355 (48.2)</td>
<td>1064 (47.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>202 (27.0)</td>
<td>203 (27.1)</td>
<td>198 (26.9)</td>
<td>603 (27.0)</td>
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<tr>
<td></td>
<td>156 (20.8)</td>
<td>169 (22.5)</td>
<td>157 (21.3)</td>
<td>482 (21.6)</td>
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<tr>
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<td>5 (0.7)</td>
<td>5 (0.7)</td>
<td>3 (0.3)</td>
<td>13 (0.6)</td>
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</table>

**Tumour grade**

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<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Not known (not applicable)*</th>
<th>Not known</th>
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<tr>
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<td>157 (21.0)</td>
<td>150 (20.0)</td>
<td>149 (20.2)</td>
<td>456 (20.4)</td>
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<tr>
<td></td>
<td>369 (49.3)</td>
<td>379 (50.5)</td>
<td>368 (49.9)</td>
<td>1116 (49.9)</td>
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<tr>
<td></td>
<td>212 (26.3)</td>
<td>207 (26.3)</td>
<td>210 (26.5)</td>
<td>629 (28.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 (1.5)</td>
<td>10 (1.3)</td>
<td>6 (0.8)</td>
<td>27 (1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 (0.0)</td>
<td>4 (0.6)</td>
<td>4 (0.5)</td>
<td>8 (0.4)</td>
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</table>

**Adjuvant therapy**

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<tr>
<th></th>
<th>None</th>
<th>Tamoxifen/no chemotherapy</th>
<th>Chemotherapy/no tamoxifen</th>
<th>Tamoxifen+chemotherapy</th>
<th>Other endocrine therapy†</th>
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<tbody>
<tr>
<td></td>
<td>52 (6.9)</td>
<td>53 (7.1)</td>
<td>86 (11.5)</td>
<td>173 (23.1)</td>
<td>17 (2.3)</td>
<td>5 (0.7)</td>
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<tr>
<td></td>
<td>555 (55.5)</td>
<td>557 (55.7)</td>
<td>557 (51.0)</td>
<td>548 (24.5)</td>
<td>21 (2.1)</td>
<td>0 (0.0)</td>
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<tr>
<td></td>
<td>12 (11.5)</td>
<td>10 (10.3)</td>
<td>11 (11.1)</td>
<td>245 (11.0)</td>
<td>7 (0.9)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td></td>
<td>173 (23.1)</td>
<td>187 (25.0)</td>
<td>188 (25.5)</td>
<td>548 (24.5)</td>
<td>17 (2.3)</td>
<td>14 (0.6)</td>
</tr>
</tbody>
</table>

- **77% > 50 yrs**
- **70% N0**
- **78% T1**
- **70% Low Grade**
- **64% No CCT**
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>70-79</th>
<th>80-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>7 (0.6)</td>
<td>0 (0.0)</td>
<td>7 (0.3)</td>
</tr>
<tr>
<td>30-39</td>
<td>62 (5.6)</td>
<td>39 (3.5)</td>
<td>101 (4.6)</td>
</tr>
<tr>
<td>40-49</td>
<td>179 (16.2)</td>
<td>170 (15.3)</td>
<td>349 (15.8)</td>
</tr>
<tr>
<td>50-59</td>
<td>427 (38.6)</td>
<td>447 (40.3)</td>
<td>874 (39.5)</td>
</tr>
<tr>
<td>60-69</td>
<td>304 (27.5)</td>
<td>327 (29.5)</td>
<td>631 (28.5)</td>
</tr>
<tr>
<td>70-79</td>
<td>117 (10.6)</td>
<td>119 (10.7)</td>
<td>236 (10.7)</td>
</tr>
<tr>
<td>80-</td>
<td>9 (0.8)</td>
<td>8 (0.7)</td>
<td>17 (0.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathological node status</th>
<th>70-79</th>
<th>80-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>238 (21.5)</td>
<td>266 (24.0)</td>
<td>504 (22.8)</td>
</tr>
<tr>
<td>Negative</td>
<td>831 (75.2)</td>
<td>804 (72.4)</td>
<td>1635 (73.8)</td>
</tr>
<tr>
<td>Not known (no axillary surgery)</td>
<td>36 (3.3)</td>
<td>39 (3.5)</td>
<td>75 (3.4)</td>
</tr>
<tr>
<td>Not known (missing data)</td>
<td>0 (0.0)</td>
<td>1 (0.1)</td>
<td>1 (0.04)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumour size (cm)</th>
<th>70-79</th>
<th>80-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>151 (13.7)</td>
<td>167 (15.0)</td>
<td>318 (14.4)</td>
</tr>
<tr>
<td>1-</td>
<td>552 (50.0)</td>
<td>542 (48.8)</td>
<td>1094 (49.4)</td>
</tr>
<tr>
<td>2-</td>
<td>287 (26.0)</td>
<td>288 (25.9)</td>
<td>575 (26.0)</td>
</tr>
<tr>
<td>3-</td>
<td>113 (10.2)</td>
<td>107 (9.6)</td>
<td>220 (9.9)</td>
</tr>
<tr>
<td>Not known</td>
<td>2 (0.2)</td>
<td>6 (0.5)</td>
<td>8 (0.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumour grade</th>
<th>70-79</th>
<th>80-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>306 (27.7)</td>
<td>311 (28.0)</td>
<td>617 (27.9)</td>
</tr>
<tr>
<td>2</td>
<td>518 (46.9)</td>
<td>532 (47.9)</td>
<td>1050 (47.4)</td>
</tr>
<tr>
<td>3</td>
<td>261 (23.6)</td>
<td>248 (22.3)</td>
<td>509 (23.0)</td>
</tr>
<tr>
<td>Not known (not applicable)*</td>
<td>15 (1.4)</td>
<td>15 (1.3)</td>
<td>30 (1.3)</td>
</tr>
<tr>
<td>Not known</td>
<td>5 (0.4)</td>
<td>4 (0.4)</td>
<td>9 (0.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjuvant therapy</th>
<th>70-79</th>
<th>80-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>37 (3.3)</td>
<td>47 (4.2)</td>
<td>84 (3.3)</td>
</tr>
<tr>
<td>Tamoxifen/no chemotherapy</td>
<td>782 (70.8)</td>
<td>810 (73.0)</td>
<td>1592 (71.9)</td>
</tr>
<tr>
<td>Chemotherapy/no tamoxifen</td>
<td>77 (7.0)</td>
<td>78 (7.0)</td>
<td>155 (7.0)</td>
</tr>
<tr>
<td>Tamoxifen+chemotherapy</td>
<td>181 (16.4)</td>
<td>155 (14.0)</td>
<td>336 (15.2)</td>
</tr>
<tr>
<td>Other endocrine therapy†</td>
<td>16 (1.4)</td>
<td>11 (1.0)</td>
<td>27 (1.2)</td>
</tr>
<tr>
<td>Not known</td>
<td>12 (1.1)</td>
<td>9 (0.8)</td>
<td>21 (0.9)</td>
</tr>
</tbody>
</table>
Evidences generated are for

- Age > 50 years
- T1
- N0
- Low or Intermediate Grade
- Good prognostic factors where Chemotherapy is not indicated

- ASTRO Guidelines

1. Patient is 50 years or older at diagnosis.
2. Pathologic stage is T1–2 N0 and patient has been treated with breast-conserving surgery.
3. Patient has not been treated with systemic chemotherapy.
Q2. Role of Tumor bed boost?

Issues:

1. May reduce the local recurrence as established in CF WBI.
2. May increase local toxicity thus cosmesis may be poor.

<table>
<thead>
<tr>
<th></th>
<th>START A (10)</th>
<th>START B (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>6 MV*</td>
<td>6 MV*</td>
</tr>
<tr>
<td>Wedges</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Inhomogeneity corrections</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Planning</td>
<td>2D or 3D</td>
<td>2D or 3D</td>
</tr>
<tr>
<td>Central Axis Dose Homogeneity Separation</td>
<td>-5% to +5%</td>
<td>-5% to +5%</td>
</tr>
<tr>
<td>Percent receiving boost</td>
<td>61%</td>
<td>39%</td>
</tr>
<tr>
<td>Boost dose</td>
<td>10 Gy, 5 fr</td>
<td>10 Gy, 5 fr</td>
</tr>
<tr>
<td>Boost modality</td>
<td>Electrons</td>
<td>Electrons</td>
</tr>
<tr>
<td>Percent receiving regional nodal irradiation</td>
<td>14%</td>
<td>7%</td>
</tr>
<tr>
<td>Target for nodal irradiation</td>
<td>SCV ± Ax</td>
<td>SCV ± Ax</td>
</tr>
<tr>
<td>Use of PAS</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Dose to regional nodes</td>
<td>Same as breast</td>
<td>Same as breast</td>
</tr>
</tbody>
</table>

Boost may be used with Hypo fraction RT
Q3. Regional Nodal Irradiation?

Issues:
1. May increase the axilllary toxicity like arm edema, brachial plexus injury etc.

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<th>START B (16)</th>
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<tr>
<td>Wedges</td>
<td>Yes</td>
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<td>Variable</td>
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</tr>
<tr>
<td>Planning</td>
<td>2D or 3D</td>
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</tr>
<tr>
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<td>Use of PAS</td>
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</tr>
<tr>
<td>Dose to regional nodes</td>
<td>Same as breast</td>
<td>Same as breast</td>
</tr>
</tbody>
</table>

Data scanty to draw firm conclusion but present evidence do not show increased toxicity.
Q4. Status of HF-WBI in Left sided breast?

Population Based data base from Canada

No difference in cardiac events at a median follow up of 13 years

Cumulative Probability of Cardiac Hospitalization

Years Since Radiotherapy

P = 0.98
Take Home from START

- Hypo fraction is equally effective in very early CA breast treated with BCS.
- Patients with poor prognostic features require conventional fraction RT.
- Boost may be given with HF-WBI.
- When nodal irradiation is required it is better to use conventional fractions.
- Safe for left sided breast as well.
BOOST VS. NO BOOST
EORTC

- No of Patients: 5318
- Follow Up: 20 years
- Overall Survival: No difference
Ipsilateral Local Recurrence

Statistical Significance difference

No difference

Local Recurrences

Overall Survival

Number of positive nodes

<table>
<thead>
<tr>
<th></th>
<th>No boost group (n=2657)</th>
<th>Boost group (n=2661)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>25 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>0</td>
<td>2078 (78%)</td>
<td>2090 (79%)</td>
</tr>
<tr>
<td>1-3</td>
<td>452 (17%)</td>
<td>449 (17%)</td>
</tr>
<tr>
<td>≥4</td>
<td>102 (4%)</td>
<td>102 (4%)</td>
</tr>
</tbody>
</table>

21% is node positive
Ipsilateral Local Recurrence

As Age increases the impact of Boost to reduce the LR decreases but remained significant.
Take Home for Boost

- Decreases Local Recurrences.
- Reduces mastectomy rate.
- Not improved overall survival.
- May improve survival in node positive patients.
- Impact is more in younger patients.
- More than 60 years of age, may be omitted as impact is less and no improvement in OS but more fibrosis.
Thanks

Greetings From Rishikesh