Trends in Fractionation for Breast-Conserving Therapy

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Enschede
Breast-Conserving Treatment:

• Lumpectomy

• SN or axillary dissection

• Radiotherapy breast
• Conventional fractionation ± boost

• Hypofractionation

• Accelerated partiel breast irradiation

• Preoperative partiel breast irradiation
Conventional fractionation
+ Boost

Radiotherapie borst
50.0 Gy / 2.0 Gy / 5x wk.
+ Boost primaire tumor bed
14.0 Gy / 2.0 Gy / 5x wk
Breast-Conserving Therapy

EBCTCG results

Local recurrence

\[
\begin{align*}
\text{RT (N0 / N+)} & \quad \text{no RT (N0 / N+)} \\
5\text{-year} & \\
6.7 / 11.0\% & 22.9 / 41.1\% \\
10\text{-year} & \\
10.0 / 13.1\% & 29.2 / 46.5\%
\end{align*}
\]
Results breast-conserving therapy Twente – Achterhoek 1983 - 2007

Local failure rate for 3372 breast-conserving therapies

0.00 0.10 0.20 0.30 0.40 0.50
0 12 24 36 48 60 72 84 96 108 120 132 144 156 168 180

months
local failure for 2915 breast-conserving treatments

negative margins

- agecat = <=40
- agecat = 41-50
- agecat = >50

months

0 12 24 36 48 60 72 84 96 108 120 132 144 156 168 180
local failure for 2915 breast-conserving treatments
negative margins

Number at risk
1983-1995 935 910 838 780 720 670 399
1996-2001 884 856 802 754 670 660 399
2002-2007 1096 1050 763 357 99 0
local failure for 194 breast-conserving treatments
negative margins and age <41-years

Number at risk

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>0 months</td>
<td>77</td>
<td>56</td>
<td>61</td>
</tr>
<tr>
<td>12 months</td>
<td>73</td>
<td>55</td>
<td>59</td>
</tr>
<tr>
<td>24 months</td>
<td>62</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>36 months</td>
<td>58</td>
<td>43</td>
<td>31</td>
</tr>
<tr>
<td>48 months</td>
<td>52</td>
<td>40</td>
<td>31</td>
</tr>
<tr>
<td>60 months</td>
<td>49</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>72 months</td>
<td>52</td>
<td>40</td>
<td>23</td>
</tr>
<tr>
<td>84 months</td>
<td>49</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>96 months</td>
<td>52</td>
<td>40</td>
<td>23</td>
</tr>
<tr>
<td>108 months</td>
<td>49</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>120 months</td>
<td>52</td>
<td>40</td>
<td>23</td>
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</tbody>
</table>
Conventional fractionation **no** boost

Radiotherapie borst

50.0 Gy / 2.0 Gy / 5x wk.
External Boost Volume in breast-conserving therapy
1983 – 1995
Twente - Achterhoek

Local failure rate for 967 breast-conserving treatments according to external boost volume

- <66 cm³
- 66-98 cm³
- >98 cm³

Cumulative incidence of recurrence of tumour as first event in the ipsilateral breast after 50 Gy whole-breast irradiation or 50 Gy whole-breast irradiation and a boost of 16 Gy

HR = 0.59
99% CI, 0.46 to 0.76
P < .0001

Cumulative incidence of ipsilateral breast cancer recurrence according to age

Géén boost bij borstsparend therapie in Twente / Achterhoek

2004

• Age >60:
  • Negatieve lymfklieren
  • Tumor < 1,1 cm (T1b)
  • Negatieve snijrand

• Age >70:
  • Negatieve lymfklieren
  • Tumor < 2.1 cm (T1)
  • Negatieve snijrand
Hypofractionation

Fraction size > 2.0 Gy

Less fractions

Short period
Long-term results of a randomized trial of accelerated hypofractionated whole breast irradiation following breast conserving surgery in women with node negative breast cancer

LOCAL RECURRENCE

<table>
<thead>
<tr>
<th></th>
<th>SWBI</th>
<th>AHWBI</th>
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<tbody>
<tr>
<td>5 years</td>
<td>3.2%</td>
<td>2.8%</td>
</tr>
<tr>
<td>10 years</td>
<td>6.7%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

No difference in Overall Survival
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 yr</th>
<th>5 yr</th>
<th>10 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWBI</td>
<td>83% (604)</td>
<td>77% (496)</td>
<td>79% (423)</td>
<td>71% (216)</td>
</tr>
<tr>
<td>AHWBI</td>
<td>84% (616)</td>
<td>77% (518)</td>
<td>78% (448)</td>
<td>70% (235)</td>
</tr>
</tbody>
</table>

% excellent or good (# evaluable)
CONCLUSIONS: Whelan

Accelerated Hypofractionated Whole Breast Irradiation:

- Demonstrated excellent local control
- Was not associated with long-term morbidity
  - Skin and soft tissue toxicity
  - Breast Cosmesis
  - Non-cancer deaths
### Resultaten hypofractionering trials

<table>
<thead>
<tr>
<th>Studie</th>
<th>Patienten</th>
<th>Schema</th>
<th>Follow-up</th>
<th>Lokaal recidief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yarnold/Owen</td>
<td>1410</td>
<td>42.9Gy/13 fract/5wk</td>
<td>10-jaar</td>
<td>9.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39Gy/13 fract/5wk</td>
<td>10-jaar</td>
<td>14.8%</td>
</tr>
<tr>
<td>START A</td>
<td>2236</td>
<td>41.6Gy/13 fract/5wk</td>
<td>5-jaar</td>
<td>3.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39Gy/13 fract/5wk</td>
<td>5-jaar</td>
<td>5.2%</td>
</tr>
<tr>
<td>START B</td>
<td>2215</td>
<td>40Gy/15 fract/5wk</td>
<td>5-jaar</td>
<td>2.2%</td>
</tr>
<tr>
<td>Whelan</td>
<td>1234</td>
<td>42.5Gy/16 fract/3wk</td>
<td>5-jaar</td>
<td>2.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10-jaar</td>
<td>6.2%</td>
</tr>
</tbody>
</table>
# Prognostic factors for local recurrence

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate</th>
<th>Multivariate</th>
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<tbody>
<tr>
<td>Age</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history: FDR characteristics</td>
<td>0.0221</td>
<td></td>
</tr>
<tr>
<td>Lymph vascular space invasion</td>
<td>0.0072</td>
<td></td>
</tr>
<tr>
<td>Presence carcinoma in situ</td>
<td>0.0007</td>
<td>0.001</td>
</tr>
<tr>
<td>Margin status</td>
<td>&lt;0.0001</td>
<td>0.007</td>
</tr>
<tr>
<td>Estrogen status</td>
<td>0.0595</td>
<td></td>
</tr>
<tr>
<td>Progesterone status</td>
<td>0.0546</td>
<td></td>
</tr>
<tr>
<td>Contra lateral breast cancer</td>
<td>0.0035</td>
<td>0.005</td>
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</tbody>
</table>
Important factors
Local recurrence

• Age
• Margin status
MST
Hypofractionering

TD 42.5 Gy /16 fracties, 5x per week

• pT1-2N0-1, tumor ≤ 3 cm
  • Unifocaal
  • Resectierandenvrij:
    Infiltrerend carcinoom > 2 mm
    Carcinoma in situ > 5 mm
  • Leeftijd > 50-jaar
MST
Hypofractionering

TD 42,5 Gy /16 fracties, 5x per week
+ boost 13,3 /5 fracties

• pT1-2N0-1, tumor ≤ 3 cm
  • Resectieranden vrij:
    Infiltrerend carcinoom ≤ 2 mm
    Carcinoma in situ ≤ 5 mm
  • Leeftijd ≤ 50-jaar
Accelerated Partial Breast Irradiation (APBI)

6 – 7 weeks of radiotherapy costs logistic access
no subset of women who do not benefit from radiotherapy shortest of radiotherapy facilities

Radiotherapy to only area at risk for recurrence
Short period
Same Local Control

Concept: APBI
Accelerated Partial Breast Irradiation (APBI)

• Limited volume of breast
  • High dose
  • 1-10 fractions
  • 5 days

4 methods:
Interstitial brachytherapy
Intracavitary brachytherapy
External beam radiotherapy
Intra-operative radiotherapy
Biological rationale for APBI

- No data: whole breast irradiation neccessary
- Studies: residual disease beyond tumor most likely DCIS
- Clinically occult multicentric foci beyond the quadrant is rare.

- Three prospective randomized trials (Fisher, Veronesi, and Liljegren):
  - Lumpectomy – lumpectomy + WBI
  - Primary location tumor failure adjacent site lumpectomy
  - 4% failed elsewhere
Accelerated Partial Breast Irradiation (APBI)

On going trials:
- GEC-ESTRO (MIB)
- NSABP B-39, USA (MIB / 3D EBCRT)
- IMPORT-LOW, UK (EBRT)
- IRMA, Italie (3D CRT)
- RAPID, Canada (3D CRT)
- TARGIT, UK (IORT)
- ELIOT, Italie (IORT)
IRMA

- **Trial arm:** 38.5 Gy / 3.85 Gy / 2x day / 1 wk

- **pT1-2, < 3cm**
- **Unifocal**
- **Margins ≥ 2mm negative**
- **Positioning 3 – 6 clips**
- **Start < 12 weeks after surgery**
- **Age ≥ 50-years**
- < pN2
Preoperative partiel breast irradiation

- Irradiation of exact tumor volume with tumor in situ
- Irradiated volume much smaller, less toxicity (breast, heart, lung)
- Hypofractionation; 1-2 weeks
- Low risk patients