Partial breast radiotherapy

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Overview

• Background

• Partial breast radiotherapy (PBI)
  • Intraoperative radiotherapy (IORT)
  • Postoperative radiotherapy

• Patient selection

• Conclusions & Questions
Partial breast irradiation

Background
Radiotherapy reduces recurrence rates after breast conserving surgery.................

**Any first recurrence**
- 10-year gain 15.7% (SE 1.0)
- RR 0.52 (95% CI 0.48–0.56)
- Log-rank 2p < 0.00001

**Breast cancer death**
- 15-year gain 3.8% (SE 1.1)
- RR 0.82 (95% CI 0.75–0.90)
- Log-rank 2p = 0.00005
......but increases non-breast cancer mortality......
.....and affects cosmesis
Recurrence rates are falling

\begin{table}
\centering
\caption{Ipsilateral local relapse (LR) rates in randomised trials testing radiotherapy (RT) versus no radiotherapy after breast conservation surgery for early breast cancer, ranked by earliest year of treatment.}
\begin{tabular}{lcc}
\hline
Trials & 5-year LR rate (%) & \\
 & No-RT arm & RT arm \\
\hline
NSABP B-06 (1976–1984) [78] & 39.2$^a$ & 14.3$^a$ \\
Uppsala-Örebro (1981–1988) [34] & 24$^b$ & 8.5$^b$ \\
CRC, UK (1981–1990) [79] & 40.6$^c$ & 19.7$^c$ \\
SCTBG (1985–1991) [81] & 24.5$^e$ & 5.8$^e$ \\
West Midlands, UK (1985–?)$^f$ & & \\
INT Milan 3 (1987–1989) [82] & 23.5$^b$ & 5.8$^b$ \\
NSABP B-21 (1989–1998) [83] & 16.5$^e$ & 2.8$^e$ \\
Holli et al. (1990–1995) [85] & 14.1 & 6.3 \\
Fyles et al. (1992–2000) [7] & 7.7 & 0.6 \\
Planned subgroup analysis & 5.9 & 0.4 \\
ABCStudy 8 (1996–2004) [9] & 5.1$^b$ & 0.4$^b$ \\
BASO II [10] & 1.2 pa$^1$ & 0.4 pa$^1$ \\
Boston Prospective study (1986–1992) [89] & 10$^f$ & \\
\hline
\end{tabular}
\end{table}

- Most recurrences in region of tumour bed

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Mannino et al., Radiother Oncol, 2009
Partial breast irradiation

Intraoperative radiotherapy
Intraoperative radiotherapy (IORT)

Intrabeam

Electrons

Intrabeam Floor Stand

X-ray tube

Internal Radiation Monitor
Cathode Gun
Accelerator Section
Beam deflector
Electron beam
Gold target

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Intrabeam

- Miniature X-ray source
- 50 kV
- Spherical applicators
- RT delivered over ~ 30 mins
Intraoperative electrons

- Mobile linac
- Single dose
- Collimator size selected
- Shielding to pectoralis fascia
- Setup/delivery ~ 15 mins
Potential benefits of IORT

- Tumour bed site known exactly
- RT delivered during surgery
- Likely reduction in normal tissue toxicity
TARGIT-A

• Non-inferiority trial
• Randomised
• 3,451 patients
• 1<sup>o</sup> endpoint: local recurrence
• Median follow-up 29 months
TARGIT-A

Study criticism:

• Short duration of follow-up

• Non-standard statistical methods
Intrabeam radiotherapy system for early breast cancer

1 Recommendations

1.1 The Intrabeam radiotherapy system is not recommended for routine commissioning for adjuvant treatment of early invasive breast cancer during breast-conserving surgical removal of the tumour.

1.2 Use of the Intrabeam radiotherapy system is recommended only using machines that are already available and in conjunction with NHS England specified clinical governance, data collection and submission arrangements.

1.3 The procedure should only be carried out by clinicians with specific training in the use of the Intrabeam radiotherapy system.

1.4 Patient selection for Intrabeam radiotherapy should be done by a multidisciplinary team experienced in the management of early invasive breast cancer, which includes both breast surgeons and clinical oncologists.

1.5 Clinicians wishing to undertake Intrabeam radiotherapy should take the following actions:
   - Inform the clinical governance leads in their NHS trusts.
   - Ensure that patients understand the uncertainties about the procedure and inform them about alternative treatment options.
   - Provide patients with NICE’s written information on the evidence of the risks and benefits of the range of treatment options available as an aid to shared decision-making.
ELIOT

- Randomised
- Equivalence trial
- 1,305 women
- 1st endpoint: ipsilateral breast recurrence
- Median follow-up 5.8 years
ELIOT

![Graph showing survival rates and overall survival](image)

<table>
<thead>
<tr>
<th></th>
<th>External radiotherapy</th>
<th>Intraoperative radiotherapy with electrons</th>
<th>p value†</th>
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<tr>
<td><strong>Any skin toxicity</strong></td>
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<td></td>
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</tr>
<tr>
<td>No</td>
<td>427</td>
<td>401</td>
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<td>Yes, acute</td>
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<tr>
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<td>Grade 5</td>
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<td>&lt;0.0001</td>
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</table>
Partial breast irradiation

Postoperative radiotherapy
Postoperative PBI

Two main types:
1. Brachytherapy
2. External beam radiotherapy

Advantage:
• Final pathology known

Challenge:
• Accurately defining tumour bed
Brachytherapy

Multicatheter

Applicator (MammoSite)
Multicatheter brachytherapy
MammoSite

- Balloon placed at surgery
- Balloon inflated
- Twice daily for 10 fractions
- FDA approval 2002
- No randomised trial data
GEC-ESTRO Trial

- Phase 3
- Median follow-up 6.6 years
- Randomised
- Non-inferiority
  LR rates: 1.44% vs 0.92%
- Brachy vs EBRT
- Late effects similar
- Up to Stage II A
- Improved early skin toxicity
- 1,184 patients
External beam PBI

• ‘Standard RT’
• Trials often ‘accelerated’ and ‘hypofractionated’
• Still waiting for 4 Phase 3 trials
• Require accurate TB definition
Marker-based tumour bed localisation
IMPORT LOW

• Randomised
• Phase 3
• 2,018 women
• 30 UK centres
IMPORT LOW RT Planning
1° endpoint: local recurrence

HR_{Reduced} = 0.33 (95% CI 0.09-1.20), p-value for non-inferiority: whole breast vs reduced dose = 0.003

HR_{Partial} = 0.65 (95% CI 0.23-1.84), p-value for non-inferiority: whole breast vs partial breast = 0.016

2° endpoint: late normal tissue toxicity

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Partial breast irradiation

Patient selection
Patient Selection

- Inconsistent trial eligibility

- Guidelines now published by:
  - ASTRO
  - GEC-ESTRO
  - ABS
  - RCR
RCR UK Consensus Statement

7. Partial breast radiotherapy after breast-conserving surgery

Discussion statement

Partial breast radiotherapy can be considered for patients ≥50 years, Grade 1–2, ≤3 centimetres (cm), oestrogen receptor positive (ER+), human epidermal growth factor receptor negative (HER2-), N0 using either (i) external beam radiotherapy with 40 Gray (Gy) in 15 fractions over three weeks or (ii) multicatheter brachytherapy using fractionation within Groupe Européen de Curiethérapie and European Society for Radiotherapy and Oncology (GEC-ESTRO) trial.
Conclusions

• PBI not a single entity

• Advantages mean its use likely to increase

• Longer term follow-up of Phase 3 clinical trials required

• Increasing adoption across the UK
Questions?