Overview: Key innovations

1. 2D to 3D planning
2. Hypofractionation
3. Intensity modulated radiotherapy
4. Tumour bed localisation
5. Heart-sparing breast radiotherapy
6. Risk-adapted radiotherapy
7. Intra-operative radiotherapy
Overview: Key innovations

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Increasing efficacy
Reducing side-effects
2D to 3D planning
2D-planned radiotherapy
Potential for missing tumour bed
Potentially large normal tissue doses
2D vs 3D radiotherapy dose distributions
Full 3D optimisation
3D planning: the benefits

- Increases accuracy
- Allows optimisation of breast coverage vs normal tissue doses
- Reduces late side-effects including breast shrinkage, firmness, pain and rib fracture
- 80% of UK RT centres offer 3D dose optimisation (RCR audit 2012)
Hypofractionation
START Trial

Trial B
N= 2215

50Gy in 25 #
(2.0Gy) 5 wks
N=1105

40Gy in 15 #
(2.67Gy) 3 wks
N=1110
# Trial B: Local-regional (LR) tumour relapse

## % of patients with no LR relapse

<table>
<thead>
<tr>
<th>Years since randomisation</th>
<th>40 Gy (29 / 1110)</th>
<th>50 Gy (36 / 1105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
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</table>

## Cumulative hazard rate

<table>
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<th>Years since randomisation</th>
<th>40 Gy</th>
<th>50 Gy</th>
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<tbody>
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<td>4</td>
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<td>0.04</td>
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<tr>
<td>5</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>6</td>
<td>0.06</td>
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</tbody>
</table>

## Hazard Ratio (95%CI)

<table>
<thead>
<tr>
<th>40 Gy vs. 50 Gy</th>
<th>Hazard Ratio (95%CI)</th>
<th>Absolute difference at 5 yr (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Gy</td>
<td>0.79 (0.48 – 1.29)</td>
<td>-0.6% (-1.7% – 0.9%)</td>
</tr>
<tr>
<td>50 Gy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Trial B: Change in breast appearance

% of patients with no change in breast appearance

Years since randomisation

Hazard Ratios (95%CI) Absolute difference at 5 yr (95%CI)

40 Gy vs. 50 Gy 0.83 (0.66 – 1.04) -5.6% (-11.8% – 1.2%)

40 Gy/15F (145 / 462) 50 Gy/25F (167 / 461)
Trial B: Late normal tissue effects

PATIENT self-assessment
(moderate or marked)

40Gy vs. 50Gy

- Shrinkage
- Hardness
- Skin appearance
- Breast appearance
- Swelling

Hazard Ratio (95% CI)

40Gy

50Gy

0.15
0.5
1
2

PHYSICIAN assessment of
(moderate or marked)

40Gy vs. 50Gy

- Shrinkage
- Induration
- Telangiectasia
- Oedema

Hazard Ratio (95% CI)

40Gy

50Gy

0.15
0.5
1
2
## Standard RT Regimens are Changing

<table>
<thead>
<tr>
<th></th>
<th>Total dose (Gy)</th>
<th>Number fractions</th>
<th>Fraction size (Gy)</th>
<th>Time (weeks)</th>
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</thead>
<tbody>
<tr>
<td>International Standard</td>
<td>50</td>
<td>25</td>
<td>2.0</td>
<td>5</td>
</tr>
<tr>
<td>New UK Standard</td>
<td>40</td>
<td>15</td>
<td>2.67</td>
<td>3</td>
</tr>
</tbody>
</table>
Advantages of hypofractionated breast RT

- Reduced acute and late side-effects
- Trend towards greater efficacy
- Easier to integrate with surgery & systemic therapies
- More convenient for patients
Intensity modulated radiotherapy (IMRT)
Simple forward-planned IMRT: “step and shoot”
Simple forward-planned IMRT: “step and shoot”
Inverse-planned IMRT

- Pectus excavatum
- Internal mammary chain
- Bilateral breast RT
Volumetric modulated arc therapy
Tumour bed localisation
Tumour bed localisation

Landis et al, IJROBP, 2007
Oncoplastic surgery: scar ≠ tumour bed

X 4 ml blue dye

I as shown.

F/ 2 blue nodes
A = benign (HK)

2 white nodes
C

I 1 cm away from inframammary crease (to avoid underwiring)

F 1.8 cm tumour

F with

cavity marked double clips
(each suture separately)

C 2/0 Vicryl SC

N, S, W, E, bars, not
Marker-based tumour bed localisation
Boost planning based on markers

Skin entry point

Excision cavity

Clips

IMPORT High Trial, RMH Sutton
Heart-sparing radiotherapy
Addition of RT to BCS improves local control & survival

Early Breast Cancer Trialists’ Collaborative Group, Lancet, 2005
but increases non breast cancer mortality

15-y loss 1.3% (SE 0.6)
Logrank 2p = 0.001

Non-breast-cancer mortality

Radiotherapy 15.9%
Control 14.6%

The Royal Marsden
Standard tangents often result in high doses to cardiac tissues esp LAD
Heart-sparing breast RT techniques

Multileaf collimation (MLC)

IMRT

Prone

Breath-hold
UK HeartSpare Study (NIHR funded)

ABC_DIBH

~vs~

v_DIBH

Digital spirometer

- Good data
- Expensive

Monitoring

- Reproducibility
- Cost

Visual

- Data lacking
- Cheap
HeartSpare: Example of heart-sparing achieved in breath-hold

Free breathing
Risk-adapted radiotherapy
Risk-adapted radiotherapy

Diagram of the breast
Case Nr. 358
IMPORT HIGH dose escalation study

2.4Gy

2.7Gy

3.2Gy

15 Fractions
(3 weeks)
Brings together advances in planning, fractionation & localisation
Requires real time verification of position of tumour bed markers

RT beam

Cone beam imaging
Tumour bed clips make automated set-up possible
Partial breast radiotherapy
Partial breast irradiation techniques

• Intraoperative techniques
  • Intrabeam (TARGIT)
  • ELIOT (Italy)

• Post-operative techniques
  • Mammosite (US)
  • External beam RT (UK and US)
Intrabeam (TARGIT)

- Intra-operative RT
- 50kV photons via 3.2mm diam tube for 25-30mins
- >45yrs, eligible for BCT
- Mean FU 60mths,
- 5yr LRR 1.7%

Vaidya et al, IJROBP 2011
Mammosite

- Post-operative
- Balloon
- 30% seroma rate, 10% infection rate, 90% good cosmesis at median FU of 72 mths

Vicini IJROBP 2011
External beam partial breast irradiation

- Treats 25mm margin around tumour bed
- Full path report available
Partial breast irradiation

- Currently available in trial setting only
- Awaiting long-term follow-up of a number of studies
- Likely to be available to limited subgroups of women in the medium term
Advances in breast RT: what do these mean for your patients?

• Most women can be treated in 3-4 weeks with reduced risk of late-side effects due to
  • Homogeneous 3D-doses
  • Reduced total dose to normal tissues
  • Use of heart-sparing techniques
• Accuracy of treatment is within mm due to
  • 3D anatomical information
  • Tumour bed markers
The future of breast radiotherapy

- Ongoing studies in risk-adapted radiotherapy aim to individualise treatment further
- Improved imaging techniques will help guide use of nodal irradiation
- Likely to be delivering less RT in future
  - Either less tissue treated
  - Or no RT
- Indications for intra-operative radiotherapy likely to increase