Supplementary Material

Volume matters: Breast induration is associated with irradiated breast volume in the Danish Breast Cancer Group phase III randomized Partial Breast Irradiation trial

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Supplementary Figure 1

Distribution of breast volume (CTVp_breast) [mL], n=865, partial breast volume (CTVp_PB) [mL], n=842, and tumour bed volume [mL], n=808.
Supplementary Figure 2

A. Distribution of breast volumes irradiated to ≥38Gy [%], ≥40Gy [%], and ≥42Gy [mL], n=864.
**Supplementary Figure 2 (continued)**

**B.** Distribution of dose to the 1% of the breast covered with highest doses (D01) [Gy] and the maximum breast dose (D_{max}) [Gy], n=864

**C.** Distribution of V_{17Gy,lung} [%], n=864
Supplementary Figure 2 (continued)

D. Distribution in left-sided patients of $V_{17\text{Gy,heart}}$ [%], $V_{35\text{Gy,heart}}$ [%], mean heart dose (MHD) [Gy], n=437, and $D_{\text{max, LADCA}}$ [Gy], n=434
Supplementary Figure 3

Sensitivity analysis comparing the model based on crude incidence rates of grade 2-3 breast induration at 3 years after RT (A) with models based on crude incidence rates at 5 years after RT (B) and on cumulative incidence at 3 years after RT (C), including model parameters (D).

**A**

Main model: Frequency @ year 3

- **Volume @ 5% risk:** 177 (95% CI 94-260)
- **Volume @ 10% risk:** 426 (95% CI 286-567)

**D**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>β (95% CI)</th>
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<tbody>
<tr>
<td>Frequency @ year 3 after RT</td>
<td>7.359 (-9.753, -4.965)</td>
</tr>
<tr>
<td>Frequency @ year 5 after RT</td>
<td>6.493 (-8.854, -4.132)</td>
</tr>
<tr>
<td>Cumulative incidence @ year 3 after RT</td>
<td>7.443 (-9.806, -5.080)</td>
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**B**

Frequency @ year 5

- **Volume @ 5% risk:** 135 (95% CI 47-223)
- **Volume @ 10% risk:** 379 (95% CI 230-528)

Comparison with model @ 3 year

Test of coefficients: p=0.53

**C**

Cumulative incidence @ year 3

- **Volume @ 5% risk:** 190 (95% CI 107-273)
- **Volume @ 10% risk:** 454 (95% CI 303-604)

Comparison with model @ 3 year

Test of coefficients: p=0.97
**Supplementary Figure 4**

A. Correlations between breast volume and irradiated volume. B. Comparison of models based on irradiated volume vs. breast volume with either WBI, PBI, or combined (C: C-statistics). C. Model parameters.

### A

- Volume of breast irradiated to 20-60 Gy [mL]
  - Breast volume [mL]

### B

- Breast volume
  - WBI: \( C = 0.58 \, (0.49-0.66) \)
  - PBI: \( C = 0.57 \, (0.44-0.70) \)
  - Combined: \( C = 0.57 \, (0.50-0.64) \)

- Frequency of induration grade 2/3 (95% CI)
  - Breast volume [mL]

- Volume of breast irradiated
  - WBI: \( C = 0.59 \, (0.51-0.68) \)
  - PBI: \( C = 0.59 \, (0.51-0.68) \)
  - Combined: \( C = 0.68 \, (0.61-0.74) \)

### C

<table>
<thead>
<tr>
<th>Model</th>
<th>( \beta_0 ) (95% CI)</th>
<th>( \beta_1 ) (95% CI)</th>
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<tbody>
<tr>
<td>Breast volume, WBI</td>
<td>-5.203 (-9.063, -1.344)</td>
<td>0.467 (-0.116, 1.050)</td>
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<tr>
<td>Breast volume, PBI</td>
<td>-5.886 (-11.601, -0.172)</td>
<td>0.447 (-0.416, 1.310)</td>
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<tr>
<td>Breast volume, Combined</td>
<td>-5.507 (-8.708, -2.305)</td>
<td>0.462 (-0.021, 0.945)</td>
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<tr>
<td>Irradiated volume, WBI</td>
<td>-6.025 (-9.784, -2.266)</td>
<td>0.640 (0.029, 1.250)</td>
</tr>
<tr>
<td>Irradiated volume, PBI</td>
<td>-8.739 (-13.255, -4.223)</td>
<td>1.100 (0.273, 1.928)</td>
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<tr>
<td>Irradiated volume, Combined</td>
<td>-7.359 (-9.753, -4.965)</td>
<td>0.853 (0.449, 1.256)</td>
</tr>
</tbody>
</table>
Supplementary Figure 5

Comparison of models based on V95 (percentage of breast volume receiving 95% of the dose, 38 Gy) and volume of breast irradiated to D=40 Gy. The distributions of V95 are shown in Supplementary Figure 2A. For PBI the two models based on relative and absolute irradiated volume are comparable (A) whereas only the absolute irradiated volume is relevant with WBI (B).