Adjuvant Radiotherapy
Search Strategy

Search Terms: Radiotherapy Breast Cancer
Source: Pubmed 1/2010 – 1/2017

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.


Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast.
Preliminary Note

- The recommendations on adjuvant radiotherapy for breast cancer are based on a consensus discussion between experts of the AGO and DEGRO
- For technical details of radiotherapy we recommend to refer to the corresponding updated DEGRO practical guidelines 2014-2016

DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer.

DEGRO practical guidelines: radiotherapy of breast cancer III--radiotherapy of the lymphatic pathways.


Radiotherapy (RT) after Breast Conserving Surgery (Invasive Cancer): Whole Breast Irradiation

- Radiotherapy of the affected breast
- Hypofractionated radiotherapy (total dose approximately 40 Gy in 15-16 fractions within 3-5 weeks)
- Conventionally fractionated radiotherapy (total dose about 50 Gy in approx. 25-28 fractions in about 5-6 weeks)
- In case of life expectancy <10 years and pT1, pN0, R0, ER/PR positive, HER2 negative, endocrine therapy (all criteria) radiotherapy can be omitted after individual counseling accepting an increased risk of in breast recurrence

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Additional Information with Regard to Effects of Breast Radiotherapy (BCT)

- **Hypofractionation:**
  - “Some normal tissue effects were less common after the 15 fraction regimen than the control schedule (breast shrinkage, telangiectasia, and breast oedema).”
  - In 1 of 5 trials: “There were significantly fewer distant relapses up to 10 years in the 40 Gy group (HR 0.74, 95% CI 0.59–0.94), which contributed to the significantly higher rates of disease-free survival and overall survival in the 40 Gy group compared with the 50 Gy group.” (HR<sub>0.8</sub>; p=0.042)
  

- **Elderly patients should be advised about the following:**
  - In older patients with pT1-2 (=<3 cm) pN0 hormone receptor-positive breast cancer, breast irradiation for breast conserving therapy is able to reduce the risk of a local recurrence by about 8% over 10 years. A benefit with regard to metastasis-free survival and overall survival has not been found yet.

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<table>
<thead>
<tr>
<th>@10 yrs (95% C.I.)</th>
<th>Tamoxifen</th>
<th>Tamoxifen plus Radiotherapy</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence-free (Δ=8%)</td>
<td>90% (85%-93%)</td>
<td>98% (96%-99%)</td>
<td>HR=0.18 (95% CI, 0.07 to 0.42; P &lt; .001)</td>
</tr>
<tr>
<td>Mastectomy-free</td>
<td>96% (93% - 98%)</td>
<td>98% (96% - 99%)</td>
<td>HR=0.50 (95% CI, 0.17 to 1.48; n.s.)</td>
</tr>
<tr>
<td>Distant metastasis-free</td>
<td>95% (91% - 97%)</td>
<td>95% (92% - 97%)</td>
<td>HR=1.20 (95% CI, 0.63 to 2.32; n.s)</td>
</tr>
<tr>
<td>Overall survival</td>
<td>66% (61% - 71%)</td>
<td>67% (62% - 72%)</td>
<td>HR=0.95 (95% CI, 0.77 to 1.18; n.s.)</td>
</tr>
</tbody>
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Hughes KE et al J Clin Oncol 2013; 31:2382-2387

Radiotherapy (RT) after Breast Conserving Surgery (Invasive Cancer) – Partial Breast Irradiation

- Boost-RT (improves local control, no survival benefit)
  - Premenopausal
  - Postmenopausal, if >T1<sup>+</sup> G3, HER2-positive, triple negative, EIC (at least 1 factor)

- Intraoperative irradiation (intraop. APBI)
  - As boost-irradiation followed by WBI
  - As sole radiotherapy modality (IORT 50 kV, IOERT)**
    - >50 years**
    - >70 years**

- Postoperative partial breast irradiation as sole radiotherapy modality (APBI)
  - Interstitial brachytherapy
    - >70 years**
  - Intracavity balloon technique
  - IMRT***

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1a A +
1b B +/-
1b B +
2b B *
2b B *

Study participation recommended;
** only for pT1 pN0 R0 G1-2, HR+, non-lobular, no extensive DCIS, IORT during first surgery;
*** no long term data
# continuous parameter with regard to risk of relapse


Radiotherapy (RT) after Breast Conserving Surgery (Invasive Cancer) - Partial Breast Irradiation -

Boost-RT (improves local control, no survival benefit)


Boost-RT in premenopausal p.

Boost-RT in postmenopausal p.

1. Bartelink H, Maingon P, Poortmans P et al; European Organisation for Research and


Intraoperative irradiation (IORT/IOERT)

As boost-irradiation followed by WBI


As sole radiotherapy modality

IORT using 50 kV (pT1 pN0 R0 G1-2, non-lobular, age >50 y, no extensive DCIS, IORT during first surgery, HR+)


>70 yrs


Postoperative partial breast irradiation as sole radiotherapy modality (ABPI)

Interstitial brachytherapy


Interstitial brachytherapy >70 yrs

Intracavity balloon technique

IMRT

### EORTC 22881-10882: Boost vs no Boost (Endpoint: Ipsilateral Breast Recurrence)

<table>
<thead>
<tr>
<th>@20 yrs (95% C.I.)</th>
<th>Boost (n=2,661)</th>
<th>No boost (n=2,657)</th>
<th>Hazard Ratio (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival (Δ=-1.4%)</td>
<td>59.7% (56.3–63.0)</td>
<td>61.1% (57.6–64.3)</td>
<td>HR 1.05 (0.92–1.19) n.s.</td>
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#### Cumulative Risk of Ipsilateral Breast Tumour Recurrence

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<th>All patients</th>
<th>41–50 years (Δ=5.9%)</th>
<th>51–60 years (Δ=2.96%)</th>
<th>&gt;60 years (Δ=3.0%)</th>
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<tr>
<td>≤40 years (Δ=11.6%)</td>
<td>12.0% (9.8–14.4)</td>
<td>24.4% (14.9–33.8)</td>
<td>13.5% (9.5–17.5)</td>
<td>9.7% (5.0–14.4)</td>
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<tr>
<td>(Δ=11.6%)</td>
<td>16.4% (14.1–18.8)</td>
<td>36.0% (25.8–46.2)</td>
<td>19.4% (14.7–24.1%)</td>
<td>12.7% (7.4–18.0)</td>
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<td>≥40 years</td>
<td>HR=0.65 (0.52–0.81); p&lt;0.0001</td>
<td>HR=0.56 (0.34–0.92); p=0.003</td>
<td>HR=0.66 (0.45–0.98); p=0.007</td>
<td>HR=0.66 (0.42–1.04); p=0.019</td>
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Postmastectomy Radiotherapy (PMRT)* to the Chest Wall

- > 3 tumor infiltrated lymph nodes (Lnn.)
- 1–3 tumor infiltrated Lnn. (high risk)
- 1–3 tumor infiltrated Lnn. (low risk*)
- T3 / T4
  - pT3 pN0 R0 (and no additional risk factors)
- If R0 is impossible to reach (for invasive tumor)
- In young pts with high risk features

The indications for PMRT and regional RT are independent of adjuvant systemic treatment

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* For definition of risk, go to next slide Radiotherapy of the Chest Wall After Mastectomy (PMRT)


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with > 3 tumor infiltrated lymph nodes (Lnn.)


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with 1–3 tumor infiltrated lymph nodes (Lnn.) high risk


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with 1–3 tumor infiltrated lymph nodes (Lnn.) low risk


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with T3 / T4 breast cancer

Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with pT3 pN0 R0 breast cancer (and no additional risk factors)


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with if R0 is impossible to reach (for invasive tumor)


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in young pts with high risk features


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. after neoadjuvant chemotherapy (NACT) based on the initial stage prior to NACT (cN+, cT3/4a-d)


Omission of Postmastectomy Radiotherapy (PMRT) to the Chest Wall after NACT in case of ypT0 ypN0 after NACT

1. Wright JL, Takita C, Reis IM et al: Predictors of locoregional outcome in patients


**Indications for Postmastectomy Radiotherapy (PMRT) to the Chest Wall and regional RT are independent of adjuvant systemic treatment**


**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.**


**DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer.**


**Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with > 3 tumor infiltrated lymph nodes (Lnn.)**


**Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with 1–3 tumor infiltrated lymph nodes (Lnn.) high risk**


7. Kyndi M, Overgaard M, Nielsen HM et al. High local recurrence risk is not


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with 1–3 tumor infiltrated lymph nodes (Lnn.) low risk


Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with T3 / T4 breast cancer

21;383(9935):2127-35.


**Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with pT3 pN0 R0 breast cancer (and no additional risk factors)**


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### Radiotherapy of the Axilla

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- **Tumor residuals after axillary dissection**
- **Sentinel node negative**
- **Axillary dissection not indicated**
  - e.g. cN0, SLN pos. (see chapter surgery)
- **Extracapsular tumor spread (ECS)**
- **Axillary micrometastases or isolated cells found in regional lymph nodes**


#### Tumor residuals after axillary dissection

1. Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms Langversion 3.0, Aktualisierung 2012 AWMF-Register-Nummer: 032 – 045OL Leitlinie. Herausgeber: Leitlinienprogramm Onkologie der AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V.

#### Sentinel node negative


Axillary dissection not indicated e.g. cN0, SLN positive (see surgical chapter)


Extracapsular tumor spread (ECS)


Axillary micrometastases or isolated cells found in regional lymph nodes


# Axillary Interventions in Patients with Positive Sentinel Lymph Nodes

**1-2 pos. SLN: Axillary dissection or RT of the axilla**

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- **Axillary dissection**
- **Radiotherapy of the axilla**

* Study participation recommended

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1-2 pos SLN: BCT: No further treatment to the axilla neither axillary dissection nor RT of the axilla (criteria according ACOSOG Z011)


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1-2 pos SLN: BCT: Axillary dissection


---

1-2 pos SLN: BCT: radiotherapy of the axilla

1. Donker M, Tienhoven G, Straver ME et al. Radiotherapy or surgery of the axilla after a
positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS) a randomised, multicenter open label, phase 3 non inferiority trial. Lancet Oncol 2014;15:1333-10

1-2 pos SLN: Mastectomy: If RT of chestwall is indicated, axillary dissection or radiotherapy of the axilla


1-2 pos SLN: Mastectomy: If RT of chestwall is indicated, no axillary treatment (criteria ACOSOG Z011)

EXPERT OPINION, extrapolated from:


1-2 pos SLN: Mastectomy: If RT of chestwall is not planned, axillary dissection or radiotherapy of the axilla

EXPERT OPINION, extrapolated from:


>=3 positive SLN: Axillary LN dissection


>=3 positive SLN: Radiotherapy of the axilla


Radiotherapy (RT) of Other Locoregional Lymph Node Areas (SCG/ICG)

**RT to supra-/infraclavicular lymphatic regions**
- ≥ pN2a or level III involved
- pN1a high risk*
  *tumor central or medial and (G2-3 or ER/PgR-negative)
  *tumor lateral and premenopausal and (G2-3 or ER/PgR-negative)
- pN0 high risk** with central or medial tumors
  **premenopausal and G2-3 and ER/PgR-negative

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**Internal mamma lymph node region (IMN)**

RT to Internal mamma lymph node region (IMC) if pN0 high risk with central/medial tumors


RT to Internal mammary lymph node region (IMN) if pN1-pN2 and HR positive in patients who had systemic chemotherapy


### Supra-/infraclavicular lymphatic regions

**RT to Supra-/infraclavicular lymphatic regions if ≥ pN2a**


RT to Supra-/infraclavicular lymphatic regions if Level III involved

RT to Supra-/infraclavicular lymphatic regions if pN1a high risk


RT to Supra-/infraclavicular lymphatic regions if pN1a low risk


RT to Supra-/infraclavicular lymphatic regions if pN0 high risk, if radiotherapy of the internal mammaria ln chain is indicated (see below)


RT to Supra-/infraclavicular lymphatic regions after NACT/NAT (indications as for PMRT)


<table>
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<th>Conformation</th>
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<tr>
<td>Conventionally fractionated radiotherapy (total dose about 50 Gy in approx. 25-28 fractions in about 5-6 weeks)</td>
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<tr>
<td>Hypofractionated radiotherapy (total dose approximately 40 Gy in 15-16 fractions within 3-5 weeks)</td>
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**Multivariate Analysis of Overall Survival: Effect of Radiotherapy of the Internal Mammaria Lymph Nodes**

(median follow-up 10.9 yrs)

<table>
<thead>
<tr>
<th>Adjuvant treatment</th>
<th>n*</th>
<th>Hazard ratio (95%CI)</th>
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<tbody>
<tr>
<td>No adjuvant reported</td>
<td>625</td>
<td>0.91 (0.59 - 1.39)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>954</td>
<td>1.05 (0.84 - 1.32)</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>1185</td>
<td>0.82 (0.63 - 1.06)</td>
</tr>
<tr>
<td>Both (endocrine th. and chemotherapy)</td>
<td>1200</td>
<td>0.72 (0.55 – 0.94)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4004</strong></td>
<td><strong>0.88 (0.76 – 1.01)</strong></td>
</tr>
</tbody>
</table>

* missing data on 40 patients

Poortmans et al. ECCO Amsterdam 2013
Radiotherapy following NACT

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Posttreatment</th>
<th>RT-BCS</th>
<th>PMRT</th>
<th>RT-RN</th>
<th>Oxford LoE</th>
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<tbody>
<tr>
<td>Locally advanced</td>
<td>pCR / no pCR</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1a/1a/1a</td>
<td>A/A/A</td>
<td>++/++/+</td>
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<tr>
<td>cT1/2 cN1+</td>
<td>ypT1+ o. ypN1 + (no pCR)</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1a/2b/2b</td>
<td>A/B/B</td>
<td>++/+/+</td>
</tr>
<tr>
<td>cT1/2 cN1+</td>
<td>ypT0/is ypN0</td>
<td>yes</td>
<td>Increased risk of relapse</td>
<td></td>
<td>2b/2b/2b</td>
<td>B/B/B</td>
<td>+/+/+</td>
</tr>
<tr>
<td>cT1/2 cN0 (Sonogr. bligtat)</td>
<td>ypT0/is ypN0</td>
<td>Ja</td>
<td>nein</td>
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<td>2b/2b/2b</td>
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Locally advanced: T3-4 or cN2-N3, BCS: Breast conserving surgery, PMRT: Post mastectomy radiotherapy, RN: Regional nodes

1 Criteria for increased risk of relapse:
- pN0 premenopausal high risk: central or medium tumor localization, and (G2-3 and ER/PgR-negative)
- pretreatment pN1a/ cN+ high risk: central or medium tumor localization and (G2-3 or ER/PgR-negative) or premenopausal, lateral tumor localization and (G2-3 or ER/PgR-negative)

* = confirmed by core biopsy


Concomitant Use of Systemic Therapy with Radiotherapy

- Trastuzumab* concurrent with radiotherapy
- Tamoxifen concurrent with radiotherapy
- AI (letrozole, anastrozole) concurrent with radiotherapy

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* In HER2 pos. tumors parasternal RT should generally be avoided; no concurrent trastuzumab should be avoided in parasternal RT

Trastuzumab* concurrent with radiotherapy (*in HER2 pos tumors parasternal RT should generally be avoided no concurrent trastuzumab in parasternal RT)

7. Kirova YM, Caussa L, Granger B, et al. [Monocentric evaluation of the skin and cardiac toxicities of the concomitant administration of trastuzumab and radiotherapy]. Cancer

Tamoxifen concurrent with radiotherapy


AI (letrozole, anastrozole) concurrent with radiotherapy


6. Azria D, Betz M, Bourgier C et al. Identifying patients at risk for late radiation-


Other compounds (bevacizumab)

Interaction between Smoking and Risk of Irradiation-induced Side Effects

- Enhanced risk of lung cancer secondary to breast cancer radiotherapy in smokers
- Inform patients about the risk
- Recommend to stop smoking

Oxford

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