Adjuvant Radiotherapy
Search Strategy
Search Terms: Radiotherapy Breast Cancer
Source: Pubmed 1/2010 – 1/2020

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

Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 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 AGO and DEGRO experts.
- For technical radiotherapy details, we refer to the corresponding updated DEGRO practical guidelines.


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

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>1a</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>1a</td>
<td>B</td>
<td>+</td>
</tr>
</tbody>
</table>

### Hypofraktionierung


Ältere Patientin mit Niedrig-Risiko-Karzinom


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

<table>
<thead>
<tr>
<th>Boost-RT (improves local control, no survival benefit)</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>1b B</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal, if &gt;T1+ G3, HER2-positive, triple negative, EIC (at least 1 factor)</td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Techniques</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percutaneous boost (photons, electrons) as sequential boost</td>
<td>1a A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Multicatheter brachytherapy-boost</td>
<td>1a A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Percutaneous boost as simultaneous integrated boost (with normofractionated whole-breast irradiation)</td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Percutaneous boost as simultaneous integrated boost (with hypofractionated whole-breast irradiation)</td>
<td>2b B</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>Intraoperative boost irradiation (followed by whole-breast irradiation)</td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

* continuous parameter with regard to risk of relapse

**Boost allgemein (perkutan/Brachytherapie, sequentiell)**


**Boost-RT in premenopausal p.**


Simultan-integrierter Boost (normofraktionierte RT)


Simultan-integrierter Boost (hypofraktionierte RT)


Intraoperative irradiation (IORT/IOERT)

As boost-irradiation followed by WBI


### Intraoperative Radiotherapy (low-risk)*

- As sole radiotherapy, during first breast surgery (IORT 50 kV, IOERT)
  - >50 years: 1b A +/−
  - >70 years: 1b A +

### Postoperative partial breast irradiation (low-risk)*

- Interstitial Multicatheter-Brachytherapy: 1b A +
- Intracavitary balloon-technique: 2b B −
- Intensity-modulated radiotherapy (IMRT) (5x6 Gy in 2 weeks): 1b A +
- 3D-conformal radiotherapy (15x2.67 Gy in 3 weeks): 1b A +
- 3D-conformal radiotherapy (10x3.8 Gy in 2 weeks): 2b B +/−
- 3D-conformal radiotherapy (10x3.85 Gy in 1 week): 1b A +/−

For definition of target volume and practical conduct see DEGRO practical guidelines

* only for pT1 pN0 R0 G1-2, HR+, non-lobular, >50 years, no extensive DCIS

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**Intraoperative irradiation (IORT/IOERT)**

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


Intracavity balloon technique

IMRT (5x6 Gy)


3D-konformale Radiotherapie (15x2,57 Gy über zwei Wochen)


3D-konformale Radiotherapie (10x3,85 Gy über zwei Wochen)


3D-konformale Radiotherapie (10x3,85 Gy über eine Woche)


RAPID (Whelan TJ et al. Lancet. 2019 Dec 14;394(10215):2165-2172.)
- Randomised phase III non-inferiority trial, 2135 pat., 2006-2011, DCIS or invasive carcinoma ≤ 3 cm, pN0, age ≥40 y., no ILC
- 42.56/16 fr. or 50 Gy/25 fr. +/- Boost vs. APBI 38.5 Gy/10 fr. in one week (external beam irradiation)
- “In patients treated with APBI, the 5 year cumulative rate of IBTR was 2.3% (95% CI 1.4–3.2) and the 8 year cumulative rate was 3.0% (1.9–4.0). In patients treated with whole breast irradiation, the 5 year cumulative rate of IBTR was 1.7% (0.9–2.5) and the 8 year cumulative rate was 2.8% (1.8–3.9; figure 2). The HR for APBI versus whole breast irradiation was 1.27 (90% CI 0.84–1.91). Thus, the upper bound of the estimated 90% CI did not exceed the non-inferiority margin of 2.02.”
- “Late radiation toxicity [grade ≥2 [...] was more common in patients treated with APBI (346 [32%] of 1070 patients) than whole breast irradiation (142 [13%] of 1065 patients; p<0.0001). Adverse cosmesis [...] was more common in patients treated with APBI than in those treated by whole breast irradiation at 3 years (absolute difference, 11.3%; 95% CI 7.5–15.0), 5 years (16.5%, 12.5–20.4), and 7 years (17.7%, 12.9–22.3).”


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) 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


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: radiotherapy following mastectomy for invasive breast cancer.


7. NCCN Guidelines for Treatment of Cancer by Site


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

8. NCCN Guidelines for Treatment of Cancer by Site


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


6. NCCN Guidelines for Treatment of Cancer by Site

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)**


6. Rowell NP. Radiotherapy to the chest wall following mastectomy for node-negative breast cancer: a systematic review. Radiother
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**


**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: radiotherapy following mastectomy.


Thoracic wall boost irradiation


Tumor residuals after axillary dissection

1. Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms, Aktualisierung 2017 Version 4.2. Herausgeber: Leitlinienprogramm Onkologie der AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V.

Sentinel node negative


2. Helms G, Kuhn T, Moser L, et al. Shoulder-arm morbidity in patients with sentinel node biopsy and complete axillary dissection:


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


Radiotherapy of axillary lymph nodes in patients with positive sentinel-lymph nodes**, who did not undergo axillary dissection

<table>
<thead>
<tr>
<th>BCS and ACOSOG Z0011-criteria* met</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy of the breast including LN level 1 + 2 to 5 mm below the axillary vein (PTV)</td>
<td>2b</td>
<td>B</td>
<td>+*</td>
</tr>
<tr>
<td>BCS and ACOSOG Z0011-criteria* not met</td>
<td>1b</td>
<td>B</td>
<td>++*</td>
</tr>
<tr>
<td>Radiotherapy of the axillary lymph nodes (analog AMAROS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ME and chest wall RT indicated and ACOSOG Z011-criteria* not met or ME and chest wall RT not planned</td>
<td>1b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>Radiotherapy of the axillary lymph nodes (analog AMAROS) &gt;=3 pos. SLN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy of the axillary lymph nodes (analog AMAROS)</td>
<td>1b</td>
<td>B</td>
<td>+</td>
</tr>
</tbody>
</table>

* = Study participation recommended
** = Macrometastases
+* = >T3, no palpable LN, R0, 1-2 positive SN, no extracapsular extension, no NACT

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


1-2 pos SLN: BCT: Axillary dissection


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


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:

1. Donker M, Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer...


>=3 positive SLN: Axillary LN dissection


>=3 positive SLN: Radiotherapy of the axilla


Dose in the axillary LN-levels I + II using different RT-techniques

<table>
<thead>
<tr>
<th></th>
<th>LN level 1</th>
<th>mean dose*</th>
<th>encompassed volume**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMAROS</td>
<td>&gt;95%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>high tangent</td>
<td>86%</td>
<td>79%</td>
<td></td>
</tr>
<tr>
<td>standard tangent</td>
<td>66%</td>
<td>51%</td>
<td></td>
</tr>
<tr>
<td>IMRT*</td>
<td>29%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AMAROS</td>
<td>&gt;95%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>high tangent</td>
<td>71%</td>
<td>51%</td>
<td></td>
</tr>
<tr>
<td>standard tangent</td>
<td>44%</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>IMRT*</td>
<td>7%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

* in relation to the prescribed dose in the breast  
** % volume receiving the prescribed dose  
* Lee et al. Medicine 2016 (3)

Data from 228/856 pat.


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

RT to supra-/infraclavicular lymphatic regions

- ≥ 4 positive axillary lymph nodes (LN) or involved LN in level III or in supra-/infraclavicular LN
  - 1b A ++

- 1–3 positive axillary lymph nodes\(^1\) in case of
  - central or medial tumor and G2-3 or ER/PgR-negative
  - premenopausal patient and G2-3 or ER/PgR-negative
  - pN0 with central or medial tumors, if premenopausal and G2-3 and ER/PgR-negative
  - 2a B +/−

\(^1\) not applicable for micrometastases

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


Supra-/infraclavicular lymphatic regions

RT to Supra-/infraclavicular lymphatic regions if ≥ pN2a

2. Poortmans et al. Fifteen-year results of the randomised EORTC trial 22922/10925 investigating internal mammary and medial supraclavicular (IM-MS) lymph node irradiation in stage I-III breast cancer. Journal of Clinical Oncology 36, no. 15_suppl (May 20,


8. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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


6. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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


6. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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


5. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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


4. Budach W, Bölke E, Kammers K et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of


6. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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

1. Please check slide on radiotherapy after NACT
## Radiotherapy (RT) of Other Locoregional Lymph Node Areas (IMN)

### Internal mammary lymph node region (IMN)

1. **pN0 high-risk with central or medial tumor and premenopausal and G2-3 and ER/PgR-negative**
   - LoE 1b, GR B, AGO +/-

2. **1–3 positive axillary lymph nodes in case of**
   - central or medial tumor and G2-3 or ER/PgR-negative
   - premenopausal patient and G2-3 or ER/PgR-negative
   - LoE 2a, GR B, AGO +

3. **≥ 4 positive axillary lymph nodes**
   - LoE 2a, GR B, AGO +

4. **involved internal mammary lymph nodes**
   - LoE 2a, GR B, AGO +

5. **In case of cardiac risk factors or if trastuzumab is given**
   - LoE 2b, GR A, AGO --

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### Radiotherapy (RT) of Other Locoregional Lymph Node Areas (IMN)

Internal mammary lymph node region (IMN)

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

4. Poortmans et al. Fifteen-year results of the randomised EORTC trial 22922/10925 investigating internal mammary and medial...


8. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018

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


8. Dodwell et al. Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials. Presented at SABCS 2018


6. Haviland JS, Mannino M, Griffin C et al. Late normal tissue effects in the arm and shoulder following lymphatic radiotherapy: Results from the UK START (Standardisation of Breast Radiotherapy) trials. Radiother Oncol. 2018 Jan;126(1):155-162.

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**Fractionation of Radiotherapy in Case of Regional Nodal Irradiation**

<table>
<thead>
<tr>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
</tbody>
</table>

- **Conventionally fractionated radiotherapy** (total dose about 50 Gy in approx. 25-28 fractions within 5–6 weeks)
- **Hypofractionated radiotherapy** (total dose approx. 40–43.5 Gy in 15-16 fractions within 3–5 weeks)
Radiotherapy following NACT

<table>
<thead>
<tr>
<th>Retreatment</th>
<th>Posttreatment</th>
<th>RT-BCS</th>
<th>PMRT</th>
<th>RT-RN</th>
<th>Oxford</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<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>
</tr>
<tr>
<td>cT1/2 cN1a*</td>
<td>ypT0 / ypN0 + [in 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 cN1a*</td>
<td>ypT0 / ypN0</td>
<td>yes</td>
<td>Increased risk of relapse*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cT1/2 cN0</td>
<td>ypT0 / ypN0</td>
<td>Ja</td>
<td>nein</td>
<td>nein</td>
<td>2b/2b/2b</td>
<td>B/B/B</td>
<td>+/-/+</td>
</tr>
</tbody>
</table>

Locally advanced: T3-4 or cN2-N3,

BCS: Breast conserving surgery, PMRT: Post mastectomy radiotherapy, RN: Regional nodes

* Criteria for increased risk of relapse:
  * pN0 premenopausal high risk: central or medium tumor localization, and (G2-3 and ER/Pgr-negative)
  * pretreatment pN1a cN0 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


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


**Tamoxifen concurrent with radiotherapy**


**AI (letrozole, anastrozole) concurrent with radiotherapy**


Pertuzumab concurrent with radiotherapy

T-DM1 concurrent with radiotherapy

Checkpoint inhibitors concurrent with radiotherapy
Extrapolated from trial results in other tumor entities and from current clinical trial in breast cancer

Capecitabine and radiotherapy

Simultaneous Capecitabine with Locoregional Radiotherapy

- Prospective phase trial, 32 pat. with LABC, sim. def./neoadj. chemoradiotherapy, median total dose 66 Gy
- “The first 9 patients analyzed [...] received CAP 825 mg/m² twice daily continuously beginning on the first day of RT. Because of observed excess grade 3 toxicity the protocol was amended, and subsequent patients received CAP only on RT days (5 days per week).”
- “Noncontinuous CAP dosing was much better tolerated than continuous dosing. Thirteen of 26 patients (50%) had grade ≥3 and higher treatment-related dermatologic toxicity.”

Alhanafy et al. Menoufia Medical Journal 2015, 28:325-332
- Randomised phase II-trial, 100 pat., adj. Radiotherapy 40 Gy/15 fr. +/- CAP 825 mg/m2 Mo-Fr, LABC
- “[…] concurrent capecitabine was feasible with a high percent of patients (96%), […] only two out of 50 (4%) patients had capecitabine dose modification ….”
- “All early toxicities were GI/GII. Radiation dermatitis had a peak incidence in the last few fractions of the radiation therapy and the week after radiotherapy; no treatment interruption was needed and the incidence was close in both groups”.
- Radiation dermatitis grade I 14% vs. 18%; grade 2 4% vs. 4%