Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Adjuvante Strahlentherapie
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

Vorbemerkung

- Diese Empfehlungen zur adjuvanten Strahlentherapie bei Brustkrebs basieren auf einer Konsensusdiskussion zwischen Experten der Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO) und der Deutschen Gesellschaft für Radioonkologie (DEGRO).
- Für technische Details zur Durchführung der Strahlentherapie verweisen wir auf die entsprechenden aktualisierten Leitlinien der DEGRO.


Radiotherapie (RT) nach brusterhaltenden Operationen (BEO; invasive Karzinome)

- Bestrahlung der operierten Brust
- Hypofraktionierung RT (Gesamtdosis ca. 40 Gy in ca. 15-16 Fraktionen in ca. 3 bis 5 Wochen)
- Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25-28 Fraktionen in ca. 5-6 Wochen)
- Bei Lebenserwartung <10 Jahre und pT1, pN0, R0, HR/PR positiv, HER2-negativ, endokriner adjuvanter Therapie (alle Faktoren) kann unter Inkaufnahme eines erhöhten Lokalrezidivrisikos nach individueller Beratung auf die RT verzichtet werden.

<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>
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Hypofraktionierung


Ältere Patientin mit Niedrig-Risiko-Karzinom


Boost allgemein (perkutan/Brachytherapie, sequentiell)


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**Boostbestrahlung nach BEO beim invasiven Karzinom**

- **Boost-RT des Tumorbettes (verbesserte lokale Kontrolle, kein Überlebensvorteil)**
  - Prämepopausal: 1b B ++
  - Postmenopausal, sofern >T1*, G3, HER2-positiv, tripel-negativ, EIC (mindestens 1 Faktor): 2b B +

- **Techniken**
  - Perkutan (Photonen, Elektronen) als sequentieller Boost: 1a A ++
  - Multikatheter-Brachytherapie: 1a A ++
  - Perkutan als simultan integrierter Boost (bei normofraktionierter RT): 2b B +
  - Perkutan als simultan integrierter Boost (bei hypofraktionierter RT): 2b B +/-
  - Intraoperative Radiotherapie (als vorgezogener Boost): 2b B +

* kontinuierliche Variable bzgl. Rezidiv
Boost-RT in postmenopausal p.


Simultan-integrierter Boost (normofraktionierte RT)


Simultan-integrierter Boost (hypofraktionierte RT)


Intraoperative irradiation (IORT/IOERT)
As boost-irradiation followed by WBI


Boost vs no Boost:  
EORTC 22881-10882 Trial

<table>
<thead>
<tr>
<th>10 yrs</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>
</tr>
</tbody>
</table>

**Cumulative Risk of Ipsilateral Breast Tumour Recurrence**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Boost (95% C.I.)</th>
<th>No boost (95% C.I.)</th>
<th>HR (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59 years</td>
<td>16.0% (14.1–18.8)</td>
<td>18.4% (15.7–21.3)</td>
<td>HR 0.85 (0.75–0.97)</td>
</tr>
<tr>
<td>60-69 years</td>
<td>18.3% (16.2–20.6)</td>
<td>22.1% (19.5–24.8)</td>
<td>HR 0.80 (0.71–0.89)</td>
</tr>
<tr>
<td>≥70 years</td>
<td>19.7% (17.5–22.1)</td>
<td>24.9% (22.0–28.1)</td>
<td>HR 0.78 (0.69–0.89)</td>
</tr>
</tbody>
</table>

(Median F/U 17.2 y)  


### EORTC 22881-10882: Boost vs no Boost (Endpoint: any first recurrence)

<table>
<thead>
<tr>
<th>@15 yrs/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>
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</tr>
</tbody>
</table>

**Cumulative Risk of Any First Recurrence**

<table>
<thead>
<tr>
<th>Category</th>
<th>@15y</th>
<th>@20y</th>
<th>@40y</th>
<th>@40+</th>
<th>@51-60y</th>
<th>@60+y</th>
<th>HR (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (Δ=0%)</td>
<td>28.1%</td>
<td>32.8%</td>
<td>32.1%</td>
<td>38.7%</td>
<td>HR=0.92 (0.81–1.04), n.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤40 years (Δ=6%)</td>
<td>41.5%</td>
<td>49.5%</td>
<td>48.1%</td>
<td>56.8%</td>
<td>HR=0.80 (0.56–1.15), n.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;41–50 years</td>
<td>34.0%</td>
<td>38.6%</td>
<td>35.6%</td>
<td>44.2%</td>
<td>HR=0.91 (0.71–1.16), n.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;51–60 years</td>
<td>28.5%</td>
<td>34.7%</td>
<td>28.7%</td>
<td>36.2%</td>
<td>HR=0.96 (0.76–1.21), n.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>27.4%</td>
<td>32.1%</td>
<td>29.1%</td>
<td>32.8%</td>
<td>HR=0.94 (0.74–1.19), n.s.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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+)


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<table>
<thead>
<tr>
<th>Intraoperative Radiotherapie (niedriges Risiko)*</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Als alleinige Radiotherapie-Maßnahme während der ersten Brust-OP (IORT 50 kV, IOERT)</td>
<td>1b</td>
<td>A</td>
<td>+/-</td>
</tr>
<tr>
<td>&gt;50 Jahre</td>
<td>1b</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>&gt;70 Jahre</td>
<td>1b</td>
<td>A</td>
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<table>
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<tr>
<th>Postoperative Teilbrustbestrahlung (niedriges Risiko)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitielle Multikatheter-Brachytherapie</td>
</tr>
<tr>
<td>Intrakavitäre Ballontherapie</td>
</tr>
<tr>
<td>Intensitätsmodulierte Radiotherapie (IMRT) (5×6 Gy über 2 Wochen)</td>
</tr>
<tr>
<td>3D-konformale Radiotherapie (15×2,67 Gy über 3 Wochen)</td>
</tr>
<tr>
<td>3D-konformale Radiotherapie (10×3,8 Gy über 2 Wochen)</td>
</tr>
<tr>
<td>3D-konformale Radiotherapie (10×3,85 Gy über 1 Woche)</td>
</tr>
</tbody>
</table>

Definition des Zielvolumens und praktische Durchführung siehe DEGRO practical guidelines

* nur bei pT1 pN0 R0 G1-2, HR+, nicht-lobulär, >50 J., kein extensives DCIS

>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)


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

4. 3D-konformale Radiotherapie (10x3,85 Gy über eine Woche)


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.


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


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**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

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**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)


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


Boost Thoraxwand und Gesamtüberleben


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 Krebgesellschaft 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


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


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

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 Inn. 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)**

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.


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


Checkpointinhibitors concurrent with radiotherapy

Extrapolated from trial results in other tumor entities and from current clinical trial in breast cancer

Capecitabine and radiotherapy


Simultane Gabe von Capecitabin zur lokoregionären Radiotherapie

- Prospektive Phase II-Studie, 32 Pat. mit LABC, sim. def./neoadj. Radiochemotherapie, mediane Dosis 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
- Randomisierte Phase II-Studie, 100 Pat., adj. Radiotherapie 40 Gy/15 Fraktionen +/- 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%