# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome



Guidelines Breast
Version 2025.1D

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## Adjuvante Strahlentherapie

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# Adjuvante Radiotherapie (RT)

- **Versionen 2002 – 2024:**
  **Blohmer / Budach / Friedrich / Friedrichs / Göhring / Huober / Janni / Krug / Kühn / Möbus / Rody / Scharl / Schmidt / Seegenschmiedt / Solbach / Souchon / Thomssen / Untch / Wenz**

- **Version 2025:**
  **Budach / Krug / Thomssen**

Search Strategy
Search Terms: Radiotherapy Breast Cancer
Source: Pubmed 1/2010 – 1/2024

Radiotherapy to regional nodes in early breast cancer: an individual patient data meta-analysis of 14 324 women in 16 trials.
1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group). Lancet. 2023 Nov 25;402(10416):1991-2003.

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
1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al. Lancet. 2014 Jun 21;383(9935):2127-35.

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
1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, Correa C, et al. Lancet. 2011 Nov 12;378(9804):1707-16.

Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Correa C, McGale P, Taylor C, et al. Natl Cancer Inst Monogr. 2010;2010(41):162-77.

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# 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.**

1. Sedlmayer F, Sautter-Bihl ML, Budach W, et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines: radiotherapy of breast cancer I: radiotherapy following breast conserving therapy for invasive breast cancer. Strahlenther Onkol. 2013 Oct;189(10):825-33.
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3. Wenz F, Sperk E, Budach W et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer. Strahlenther Onkol. 2014 Aug;190(8):705-14.
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9. Piroth MD, Krug D, Sedlmayer F et al. Post-neoadjuvant treatment with capecitabine and trastuzumab emtansine in breast cancer patients-sequentially, or better simultaneously? Strahlenther Onkol. 2021 Jan;197(1):1-7.
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11. Strnad V, Krug D, Sedlmayer F, et al (2020) DEGRO practical guideline for partial-breast irradiation. Strahlenther Onkol 196:749–763.
12. Piroth MD, Krug D, Baumann R, et al. Strahlenther Onkol. 2025 Jan 9. doi: 10.1007/s00066-024-02334-3. Online ahead of print.

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

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Bestrahlung der operierten Brust** | 1a | A | ++ |
| ▪ **Moderat hypofraktionierte RT (Gesamtdosis ca. 40 Gy in ca. 15-16 Fraktionen in ca. 3 bis 5 Wochen)** | 1a | A | ++ |
| ▪ **Ultra-hypofraktionierte RT (Gesamtdosis 26 Gy, d.h. 5 Fraktionen in einer Woche = 1 Fraktion/Tag bzw. 28,5 Gy, d.h. 5 Fraktionen in 5 Wochen = 1 Fraktion/Woche)** | 1b | B | +/- |
| ▪ **Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25-28 Fraktionen in ca. 5-6 Wochen)** | 1a | B | +/- |
| ▪ **Bei Lebenserwartung < 10 Jahre und pT1, pN0, R0, ER / PR positiv, HER2-negativ, endokriner adjuvanter Therapie (alle Faktoren) kann unter Inkaufnahme eines erhöhten Risikos eines intramammären Rezidivs ohne Überlebensnachteil nach individueller Beratung auf die RT verzichtet werden.** | 1a | B | + |

Moderate Hypofractionation

1. Haviland JS, Owen JR, Dewar JA, et al; START Trialists' Group. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol. 2013 Oct;14(11):1086-94.
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3. Haviland JS, Bentzen SM, Bliss JM et al On behalf of the START Trial Management Group. Prolongation of overall treatment time as a cause of treatment failure in early breast cancer: An analysis of the UK START (Standardisation of Breast Radiotherapy) trials of radiotherapy fractionation. Radiotherapy and Oncology 121 (2016) 420–423
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7. Wang SL, Fang H, Hu C et al., Hypofractionated Versus Conventional Fractionated Radiotherapy After Breast-Conserving Surgery in the Modern Treatment Era: A Multicenter, Randomized Controlled Trial From China. J Clin Oncol. 2021;38:3604–3614.
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10. Purswani JM, Oh C, Jaros B et al. Breast Conservation in Women with Autoimmune Disease: The Role of Active Autoimmune Disease and Hypofractionation on Acute and Late Toxicity in a Case-Controlled Series. Int J Radiat Oncol Biol Phys. 2021;110(3):783-791.
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12. Meattini I, Becherini C, Boersma L et al. European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer. Lancet Oncol. 2022;23(1):e21-e31.

Ultra-Hypofractionation

1. Brunt AM, Haviland JS, Sydenham M et al. Ten-Year Results of FAST: A Randomized Controlled Trial of 5-Fraction Whole-Breast Radiotherapy for Early Breast Cancer. J Clin Oncol. 2020 Oct 1;38(28):3261-3272.
2. Brunt AM, Haviland JS, Wheatley DA et al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet. 2020 May 23;395(10237):1613-1626.
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5. Meattini I, Becherini C, Boersma L et al. European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer. Lancet Oncol. 2022;23(1):e21-e31.

Elderly patients with low-risk features

1. Fyles A, McCready DR, Manchul MA et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med. 2004 Sep 2;351(10):963-70.
2. Blamey RW, Bates T, Chetty U et al. Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial. Eur J Cancer. 2013 Jul;49(10):2294-302.
3. Hughes KS, Schnaper LA, Bellon J et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013 Jul 1;31(19):2382-7.
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9. Jagsi R, Griffith KA, Harris EE et al. Omission of Radiotherapy After Breast-Conserving Surgery for Women With Breast Cancer With Low Clinical and Genomic Risk: 5-Year Outcomes of IDEA. J Clin Oncol. 2023 Dec 7:JCO2302270. doi: 10.1200/JCO.23.02270.
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## Randomized controlled trials of radiotherapy omission after breast-conserving surgery in early breast cancer

| Trial | N | Time-frame | Inclusion criteria | Follow up | Local recurrence (no RT) | Local recurrence (RT) | Hazard ratio |
|---|---|---|---|---|---|---|---|
| Toronto-British Columbia | 769 | 1992-2000 | ≥ 50 years, T1/2 N0 R0 (ink) 80% HR+ | 5 y<br>8 y | 7.7%<br>17.6% | 0.6%<br>3.5% | 8.3 |
| BASO-II | 204 | 1992-2000 | < 70 J., T1, G1 L0 | 5 y | 0.8% p.a. | 0.2% p.a. | 7.34 |
| CALGB 9343 | 636 | 1994-1999 | ≥ 70 years, T1 (98%) cN0 ER+ (97%), R0 (ink) | 5 y<br>10 y | 4%<br>8% | 1%<br>2% | 5.55 |
| ABCSG-8A | 831 | 1996-2004 | Postmenopausal T ≤ 3 cm N0, G1/2, ER+ and/or PR+ | 5 y<br>10 y | 5.1%<br>7.5% | 0.4%<br>2.5% | 10.2 |
| PRIME II | 1326 | 2003-2009 | ≥ 65 years, T ≤ 3 cm N0, ER+ and/or PR+, R0 (≥1 mm) | 5 y<br>10 y | 4.3%<br>9.8% | 1.3%<br>0.9% | 10.4 |

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1. Fyles A, McCready DR, Manchul MA et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med. 2004 Sep 2;351(10):963-70.
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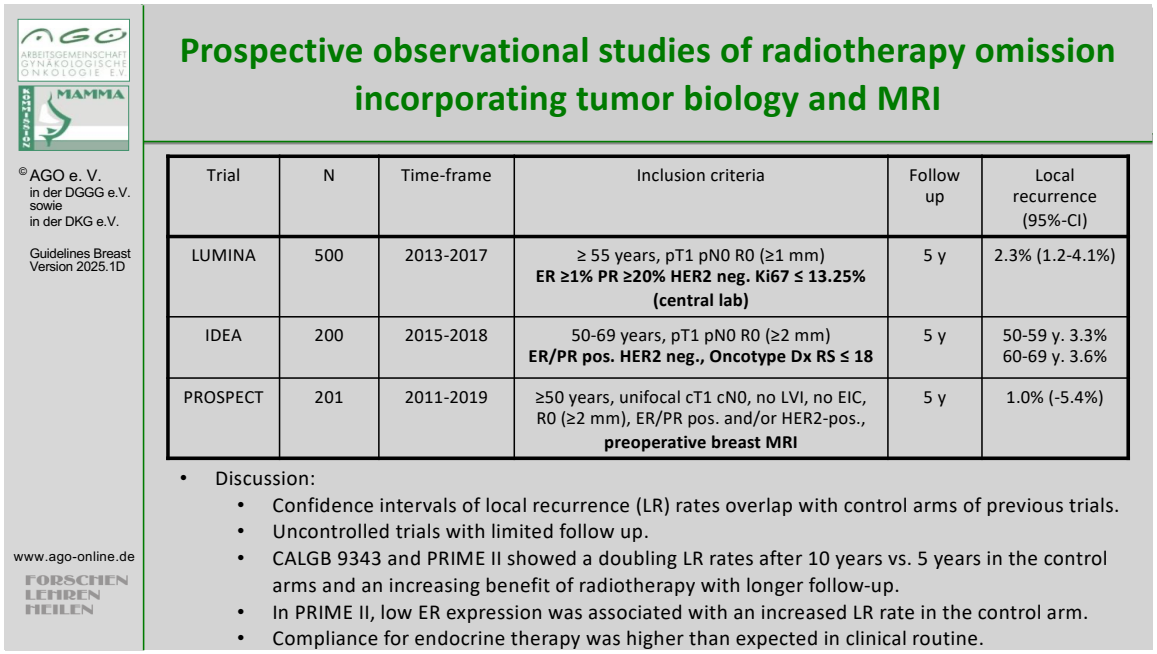



1. Whelan TJ, Smith S, Parpia S et al. Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer. N Engl J Med. 2023 Aug 17;389(7):612-619.
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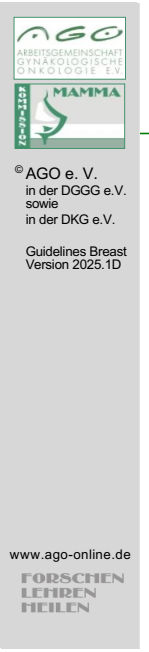


# Boostbestrahlung nach BEO beim invasiven Karzinom

| | Oxford LoE | GR | AGO |
|---|---|---|---|
| **Boost-RT des Tumorbettes (verbesserte lokale Kontrolle, kein Überlebensvorteil)** | | | |
| Prämenopausal | 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 konventionell fraktionierter RT) | 1b | B | + |
| Perkutan als simultan integrierter Boost (bei hypofraktionierter RT) | 1b | B | ++ |
| Intraoperative Radiotherapie (als vorgezogener Boost) | 2b | B | + |
| **Intraoperative Clipmarkierung des Tumorbetts bei Indikation für Boostbestrahlung** | 2b | B | + |

*kontinuierliche Variable bzgl. Rezidiv


Boost in general (EBRT/Brachytherapy, sequential)

1. Bartelink H, Maingon P, Poortmans P, et al: European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol. 2015 Jan;16(1):47-56.
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Boost-RT in premenopausal p.

Boost-RT in postmenopausal p.

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Simultaneous-integrated boost (conventionally fractionated RT)

1. Hörner-Rieber J, Forster T, Hommertgen A et al. Intensity-modulated radiotherapy (IMRT) with simultaneously integrated boost shortens treatment time and is non-inferior to conventional radiotherapy followed by sequential boost in adjuvant breast cancer treatment: results of a large randomized phase III trial (IMRT-MC2 trial). Int J Radiat Oncol Biol Phys. 2020 Dec 12:S0360-3016(20)34651-4.
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4. Bantema-Joppe EJ, Vredeveld EJ, de Bock GH, et al (2013) Five year outcomes of hypofractionated simultaneous integrated boost irradiation in breast conserving therapy; patterns of recurrence. Radiother Oncol 108:269–272.
5. Bantema-Joppe EJ, Schilstra C, de Bock GH, et al (2012) Simultaneous integrated boost irradiation after breast-conserving surgery: physician-rated toxicity and cosmetic outcome at 30 months' follow-up. Int J Radiat Oncol Biol Phys 83:e471–7.

Simultaneous-integrated boost (hypofractionated RT)

1. Paelinck L, Gulyban A, Lakosi F, et al (2017) Does an integrated boost increase acute toxicity in prone hypofractionated breast irradiation? A randomized controlled trial. Radiother Oncol 122:30–36.
2. Van Parijs H, Miedema G, Vinh-Hung V, et al (2012) Short course radiotherapy with simultaneous integrated boost for stage I-II breast

cancer, early toxicities of a randomized clinical trial. Radiat Oncol 7:80–10.

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Intraoperative irradiation (IORT/IOERT)

As boost-irradiation followed by WBI

1. Ciabattoni A, Gregucci F, Fastner G et al. IOERT versus external beam electrons for boost radiotherapy in stage I/II breast cancer: 10-year results of a phase III randomized study. Breast Cancer Res. 2021;23(1):46.
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IOERT in early stage breast cancer (HIOB): First results of a prospective multicenter trial (NCT01343459). Radiother Oncol. 2020 May;146:136-142.

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Clip placement

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radiotherapy in the presence of guidelines. Radiother Oncol 94:286–291.
5. Major T, Gutiérrez C, Guix B, et al (2015) Interobserver variations of target volume delineation in multicatheter partial breast brachytherapy after open cavity surgery. Brachytherapy 14:925–932.
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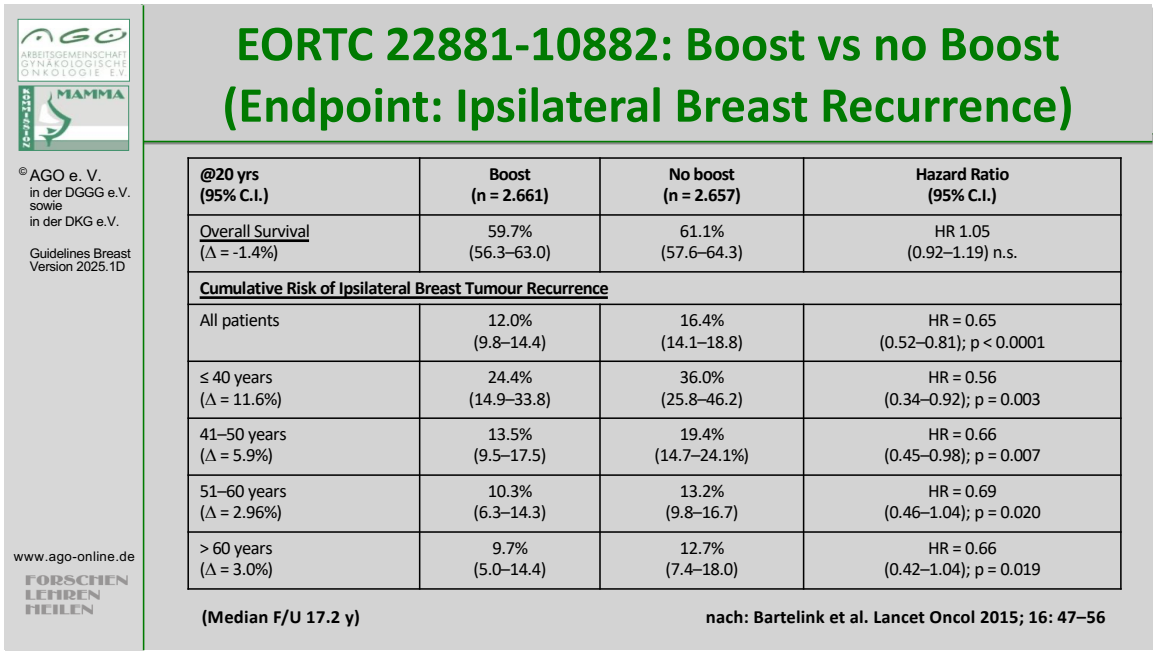



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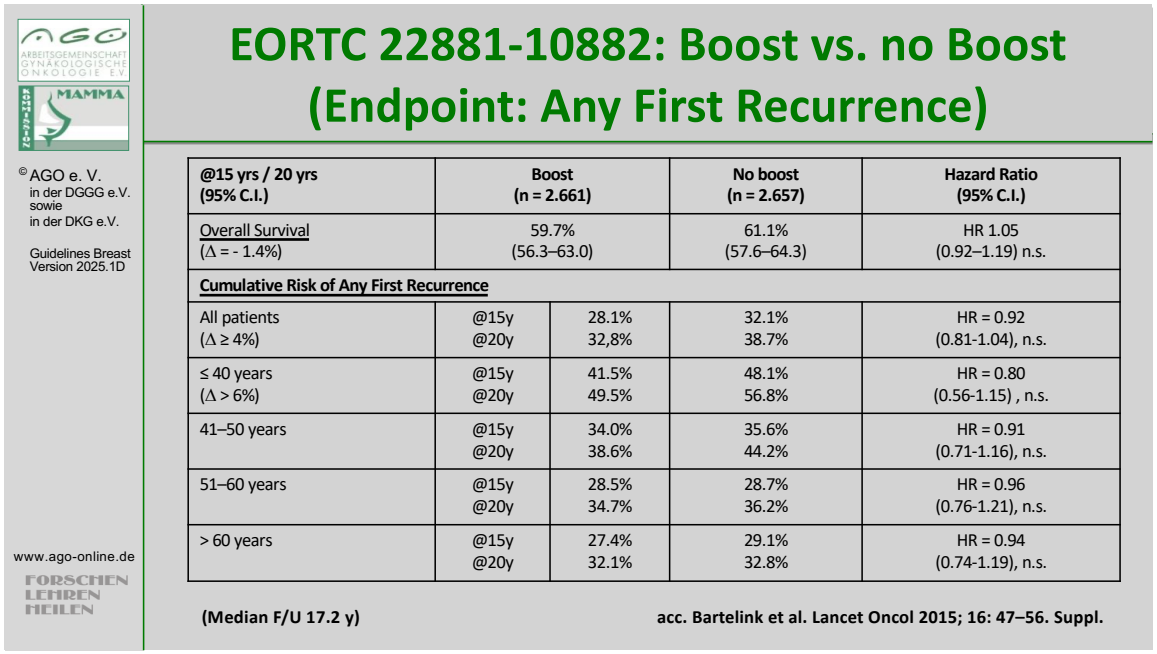



1. Bartelink H, Maingon P, Poortmans P, et al; European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol. 2015 Jan;16(1):47-56.
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# Moderate hypofractionation with simultaneous-integrated boost



Guidelines Breast
Version 2025.1D



| | RTOG 1005 (ASTRO 2022) | IMPORT-HIGH (Lancet 2023) | HYPOSIB (ASTRO 2024) |
|---|---|---|---|
| Patient number | 2262 | 2617 | 2179 |
| Schedule Breast | 40 Gy in 15 fx | 36 Gy in 15 fx<br>40 Gy in 15 fx | 40 Gy in 16 fx |
| Schedule Boost | 48 Gy in 15 fx | 48 Gy in 15 fx | 48 Gy in 16 fx |
| Primary endpoint | Ipsilateral in-breast recurrence<br>HR 1.32 (0.8-2.1)<br>→ Non-inferiority for SIB | Ipsilateral in-breast recurrence<br>HR 1.04 (0.56-1.92)<br>→ Non-inferiority for SIB | Disease-free survival<br>HR 1.10 (0.78-1.54)<br>→ Non-inferiority for SIB |
| Toxicity | Toxicity grade ≥3 (ROTG)<br><br>p = 0.79 | Any moderate / marked breast AE<br>p = 0.041 for SIB 48 Gy vs. sequential boost (less toxicity with SIB) | No significant difference for grade ≥2 skin toxicity, fibrosis, teleangiectasia, nausea, hot flashes, pain |

1. Vicini FA, Winter K, Freedman GM, et al. NRG RTOG 1005: A Phase III Trial of Hypo Fractionated Whole Breast Irradiation with Concurrent Boost vs. Conventional Whole Breast Irradiation Plus Sequential Boost Following Lumpectomy for High Risk Early-Stage Breast Cancer. Int J Radiat Oncol Biology Phys 2022. 114:S1.
2. Coles CE, Haviland JS, Kirby AM et al. Dose-escalated simultaneous integrated boost radiotherapy in early breast cancer (IMPORT HIGH): a multicentre, phase 3, non-inferiority, open-label, randomised controlled trial. Lancet. 2023 Jun 24;401(10394):2124-2137.
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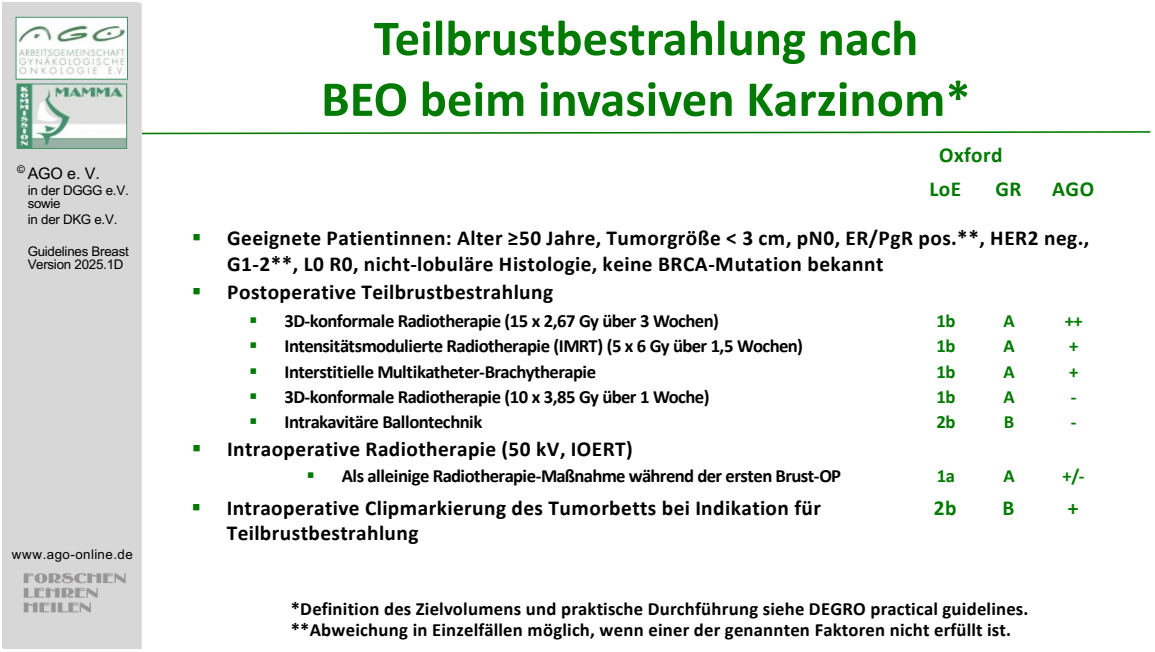



General guidelines

1. Shaitelman SF, Anderson BM, Arthur DW et al. Partial Breast Irradiation for Patients With Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ: An ASTRO Clinical Practice Guideline. Pract Radiat Oncol. 2023 Nov 14:S1879-8500(23)00296-5. doi: 10.1016/j.prro.2023.11.001.
2. Anderson B, Arthur D, Hannoun-Levi JM et al. Partial breast irradiation: An updated consensus statement from the American brachytherapy society. Brachytherapy. 2022 Nov-Dec;21(6):726-747.
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5. Strnad V, Hannoun-Levi J-M, Guinot J-L, et al (2015) Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery. Radiother Oncol 115:342–348.

Postoperative partial breast irradiation as sole radiotherapy modality (ABPI)

Interstitial brachytherapy


1. Aristei C, Palumbo I, Capezzali G, et al. Outcome of a phase II prospective study on partial breast irradiation with interstitial multi-catheter highdose rate brachytherapy. Radiother Oncol 2013;108:236-241.
2. Strnad V, Ott OJ, Hildebrandt G, et al: Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO). 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet. 2016 Jan 16;387(10015):229-38.
3. Schäfer R, Strnad V, Polgár C et al. Quality-of-life results for accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation in early breast cancer after breast-conserving surgery (GEC-ESTRO): 5-year results of a randomised, phase 3 trial. Lancet Oncol. 2018 Jun;19(6):834-844.
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6. Polgár C, Major T, Takácsi-Nagy Z et al. Breast-Conserving Surgery Followed by Partial or Whole Breast Irradiation: Twenty-Year Results of a Phase 3 Clinical Study. Int J Radiat Oncol Biol Phys. 2020 Nov 10;S0360-3016(20)34492-8.
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Intracavity balloon technique


1. Benitez PR, Keisch ME, Vicini F, et al:. Five-year results: the initial clinical trial of MammoSite balloon brachytherapy for partial breast irradiation in early-stage breast cancer. Am J Surg. 2007 Oct;194(4):456-62.

IMRT (5x6 Gy)


1. Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. Eur J Cancer. 2015 Jan 17. pii: S0959-8049(15)00002-7.
2. Meattini I, Saieva C, Miccinesi G et al. Accelerated partial breast irradiation using intensity modulated radiotherapy versus whole breast irradiation: Health-related quality of life final analysis from the Florence phase 3 trial. Eur J Cancer. 2017 May;76:17-26.
3. Meattini I, Marrazzo L, Saieva C et al. Accelerated Partial-Breast Irradiation Compared With Whole-Breast Irradiation for Early Breast Cancer: Long-Term Results of the Randomized Phase III APBI-IMRT-Florence Trial. J Clin Oncol. 2020 Dec 10;38(35):4175-4183.


3D-conformal RT (15x2.67 Gy over two weeks)


1. Coles CE, Griffin CL, Kirby AM et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. Lancet. 2017 Sep 9;390(10099):1048-1060.
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3D-conformal RT (10x3.85 Gy over one week)


1. Olivotto IA, Whelan TJ, Parpia S, et al. Interim cosmetic and toxicity results from RAPID: a randomized trial of accelerated partial breast irradiation using three-dimensional conformal external beam radiation therapy. J Clin Oncol. 2013 Nov 10;31(32):4038-45.

2. Whelan TJ, Julian JA, Berrang TS et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial. Lancet. 2019 Dec 14;394(10215):2165-2172.
3. Vicini FA, Cecchini RS, White JR et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. Lancet. 2019 Dec 14;394(10215):2155-2164.
4. Ganz PA, Cecchini RS, White JR et al. Patient-reported outcomes (PROs) in NRG oncology/NSABP B-39/RTOG 0413: A randomized phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) in stage 0, I, or II breast cancer. Journal of Clinical Oncology 37, no. 15_suppl (May 20, 2019) 508-508. Presented at ASCO Annual Meeting 2019.
5. Meduri B, Baldissera A, Iotti C et al. Cosmetic Results and Side Effects of Accelerated Partial-Breast Irradiation Versus Whole-Breast Irradiation for Low-Risk Invasive Carcinoma of the Breast: The Randomized Phase III IRMA Trial. J Clin Oncol. 2023 Apr 20;41(12):2201-2210.

Intraoperative irradiation (IORT/IOERT)

1. Vaidya JS, Bulsara M, Baum M et al. Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGIT-IORT) for early breast cancer: TARGIT-A randomised clinical trial. BMJ. 2020 Aug 19;370:m2836.
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4. Orecchia R, Veronesi U, Maisonneuve P et al., Intraoperative irradiation for early breast cancer (ELIOT): long-term recurrence and survival outcomes from a single-centre, randomised, phase 3 equivalence trial. Lancet Oncol. 2021. 22:597–608.
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Conserving Therapy: A Large Mature Single Institution Matched-Pair Evaluation of True Local Relapse, Progression Free Survival, and Overall Survival. Int J Radiat OncolBiolPhys 116:757–769.

Clip placement

1. Freitas TB de, Lima KML de B, Carvalho H de A, et al (2018) What a difference a clip makes! Analysis of boost volume definition in radiation therapy for conservative breast surgery. Eur J Surg Oncol 44:1312–1317.
2. Dzhugashvili M, Tournay E, Pichenot C, et al (2009) 3D-conformal Accelerated Partial Breast Irradiation treatment planning: the value of surgical clips in the delineation of the lumpectomy cavity. Radiat Oncol 4:70.
3. Aldosary G, Caudrelier J-M, Arnaout A, et al (2021) Can we rely on surgical clips placed during oncoplastic breast surgery to accurately delineate the tumor bed for targeted breast radiotherapy? Breast Cancer Res Tr 186:343–352.
4. Mourik AM van, Elkhuizen PHM, Minkema D, et al (2010) Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines. Radiother Oncol 94:286–291.
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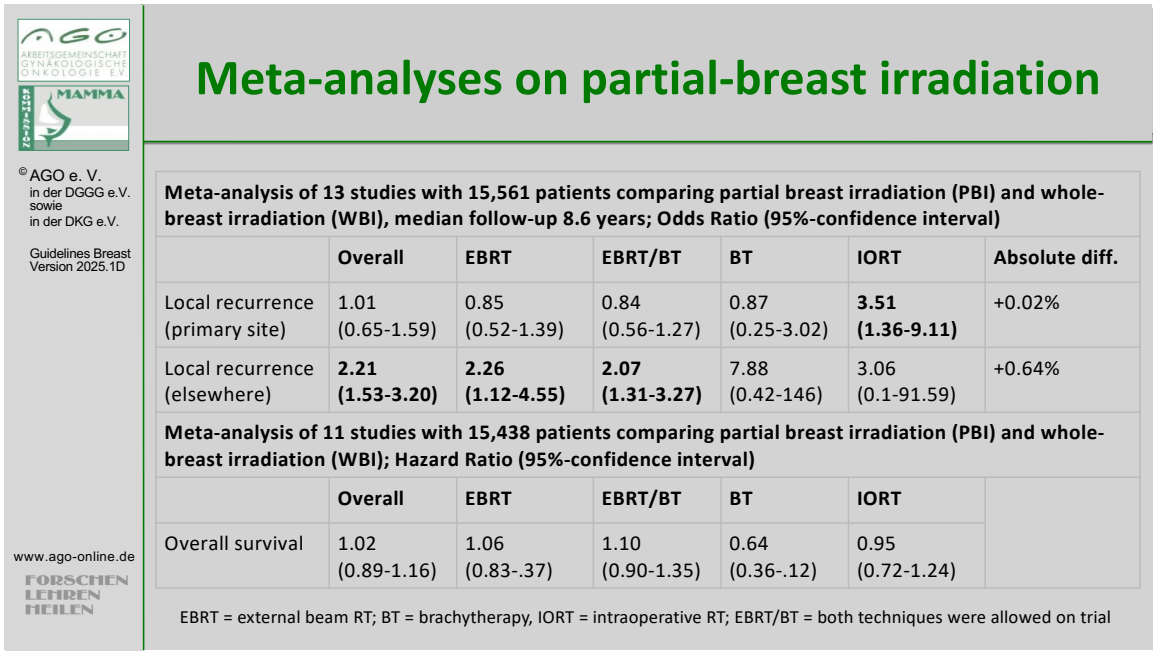



**Meta-analysis of 13 studies with 15,561 patients comparing partial breast irradiation (PBI) and whole-breast irradiation (WBI), median follow-up 8.6 years; Odds Ratio (95%-confidence interval)**

| | Overall | EBRT | EBRT/BT | BT | IORT | Absolute diff. |
|---|---|---|---|---|---|---|
| Local recurrence (primary site) | 1.01 (0.65-1.59) | 0.85 (0.52-1.39) | 0.84 (0.56-1.27) | 0.87 (0.25-3.02) | **3.51 (1.36-9.11)** | +0.02% |
| Local recurrence (elsewhere) | **2.21 (1.53-3.20)** | **2.26 (1.12-4.55)** | **2.07 (1.31-3.27)** | 7.88 (0.42-146) | 3.06 (0.1-91.59) | +0.64% |

**Meta-analysis of 11 studies with 15,438 patients comparing partial breast irradiation (PBI) and whole-breast irradiation (WBI); Hazard Ratio (95%-confidence interval)**

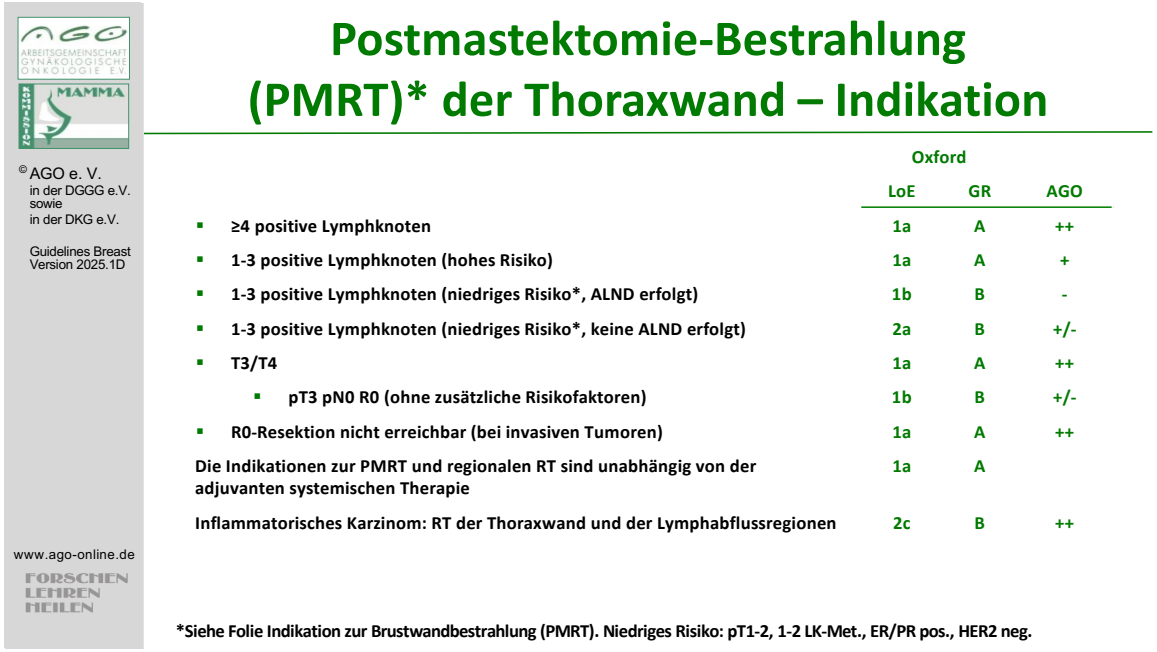
| | Overall | EBRT | EBRT/BT | BT | IORT |
|---|---|---|---|---|---|
| Overall survival | 1.02 (0.89-1.16) | 1.06 (0.83-.37) | 1.10 (0.90-1.35) | 0.64 (0.36-.12) | 0.95 (0.72-1.24) |

EBRT = external beam RT; BT = brachytherapy, IORT = intraoperative RT; EBRT/BT = both techniques were allowed on trial


1. Haussmann J, Budach W, Strnad V et al. Comparing Local and Systemic Control between Partial- and Whole-Breast Radiotherapy in Low-Risk Breast Cancer-A Meta-Analysis of Randomized Trials. Cancers (Basel). 2021 Jun 13;13(12):2967.
2. Haussmann J, Budach W, Corradini S et al. No Difference in Overall Survival and Non-Breast Cancer Deaths after Partial Breast Radiotherapy Compared to Whole Breast Radiotherapy-A Meta-Analysis of Randomized Trials. Cancers (Basel). 2020 Aug 17;12(8):2309.

# Comparison of different techniques for partial breast irradiation

| | Intraoperative radiotherapy | Multicatheter interstitial brachytherapy | External-beam radiotherapy |
|---|---|---|---|
| Advantages | • Shortest possible treatment time<br>• Direct visualization of the tumor bed | • High conformality<br>• Longest available follow-up data | • Broad availability<br>• Reproducibility |
| Disadvantages | • Lack of complete knowledge of risk factors (e.g. margin status, lympho-vascular invasion)<br>• Potentially increased risk of fibrosis with additional whole-breast irradiation<br>• Availability limited to specialized centers<br>• Prolongation of anesthesia | • Availability limited to specialized centers<br>• Additional invasive procedure<br>• Additional hospital stay<br>• Risk of target miss due to lack of visibility of the tumor bed | • Risk of target miss due to lack of visibility of the tumor bed<br>• Larger irradiated volume due to intra- and interfractional motion |




# Postmastektomie-Bestrahlung (PMRT)* der Thoraxwand – Indikation

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ ≥4 positive Lymphknoten | 1a | A | ++ |
| ▪ 1-3 positive Lymphknoten (hohes Risiko) | 1a | A | + |
| ▪ 1-3 positive Lymphknoten (niedriges Risiko*, ALND erfolgt) | 1b | B | - |
| ▪ 1-3 positive Lymphknoten (niedriges Risiko*, keine ALND erfolgt) | 2a | B | +/- |
| ▪ T3/T4 | 1a | A | ++ |
| ▪ ▪ pT3 pN0 R0 (ohne zusätzliche Risikofaktoren) | 1b | B | +/- |
| ▪ R0-Resektion nicht erreichbar (bei invasiven Tumoren) | 1a | A | ++ |
| Die Indikationen zur PMRT und regionalen RT sind unabhängig von der adjuvanten systemischen Therapie | 1a | A | |
| Inflammatorisches Karzinom: RT der Thoraxwand und der Lymphabflussregionen | 2c | B | ++ |

*Siehe Folie Indikation zur Brustwandbestrahlung (PMRT). Niedriges Risiko: pT1-2, 1-2 LK-Met., ER/PR pos., HER2 neg.


1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al. 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. N Engl J Med. 1997 Oct 2;337(14):949-55.
3. Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet. 1999 May 15;353(9165):1641-8.
4. Truong PT, Olivotto IA, Kader HA, et al. Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
5. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. ISRN Surg. 2013 Sep 11;2013:212979.
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7. Shen H, Zhao L, Wang L, et al. Postmastectomy radiotherapy benefit in Chinese breast cancer patients with T1-T2 tumor and 1-3 positive axillary lymph nodes by molecular subtypes: an analysis of 1369 cases. Tumour Biol. 2015 Dec 2. [Epub ahead of print]
8. Kunkler et al. GS2-03: Does postmastectomy radiotherapy in 'intermediate-risk' breast cancer impact overall survival? 10 year results of the BIG 2-04 MRC SUPREMO randomised trial: on behalf of the SUPREMO trial investigators. San Antonio Breast Cancer

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9. Piroth MD, Krug D, Baumann R, et al. Strahlenther Onkol. 2025 Jan 9. doi: 10.1007/s00066-024-02334-3. Online ahead of print.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al.: 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. Lancet. 2014 Jun 21;383(9935):2127-35.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.
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3. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. N Engl J Med. 1997 Oct 2;337(14):949-55.
4. Overgaard M, Jensen MB, Overgaard J, et al: Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet. 1999 May 15;353(9165):1641-8.
5. Truong PT, Olivotto IA, Kader HA, et al: Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
6. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. ISRN Surg. 2013 Sep 11;2013:212979.
7. Kyndi M, Overgaard M, Nielsen HM, et al: High local recurrence risk is not associated with large survival reduction after postmastectomy radiotherapy in high-risk breast cancer: a subgroup analysis of DBCG 82 b&c. Radiother Oncol. 2009 Jan;90(1):74-9.
8. Shen H, Zhao L, Wang L et al. Postmastectomy radiotherapy benefit in Chinese breast cancer patients with T1-T2 tumor and 1-3 positive axillary lymph nodes by molecular subtypes: an analysis of 1369 cases. Tumour Biol. 2015 Dec 2. [Epub ahead of print]
9. Kunkler et al. GS2-03: Does postmastectomy radiotherapy in 'intermediate-risk' breast cancer impact overall survival? 10 year results of the BIG 2-04 MRC SUPREMO randomised trial: on behalf of the SUPREMO trial investigators. San Antonio Breast Cancer

Symposium 2024.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Wenz F, Sperk E, Budach W, et al: Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer. Strahlenther Onkol. 2014 Aug;190(8):705-14.
3. Truong PT, Olivotto IA, Kader HA, et al: Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
4. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. ISRN Surg. 2013 Sep 11;2013:212979.
5. Kyndi M, Overgaard M, Nielsen H et al. High local recurrence risk is not associated with large survival reduction after postmastectomy radiotherapy in high-risk breast cancer: a subgroup analysis of DBCG 82 b&c. Radiother Oncol. 2009 Jan;90(1):74-9.
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Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with T3 / T4 breast cancer

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Valli MC; Association of Radiotherapy and Oncology of the Mediterranean arEa (AROME). Controversies in loco-regional treatment: post-mastectomy radiation for pT2-pT3N0 breast cancer arguments in favour. Crit Rev Oncol Hematol. 2012 Dec;84 Suppl 1:e70-4.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al. 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Boutrus R, Taghian AG; Association of Radiotherapy and Oncology of the Mediterranean arEa (AROME). Post mastectomy radiation for large node negative breast cancer: time for a second look. Crit Rev Oncol Hematol. 2012 Dec;84 Suppl 1:e75-8.
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4. Kunkler et al. GS2-03: Does postmastectomy radiotherapy in 'intermediate-risk' breast cancer impact overall survival? 10 year results of the BIG 2-04 MRC SUPREMO randomised trial: on behalf of the SUPREMO trial investigators. San Antonio Breast Cancer Symposium 2024.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Freedman GM, Fowble BL, Hanlon AL, et al. A close or positive margin after mastectomy is not an indication for chest wall irradiation except in women aged fifty or younger. Int J Radiat Oncol Biol Phys. 1998 Jun 1;41(3):599-605.
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5. Rowell NP. Are mastectomy resection margins of clinical relevance? A systematic review. Breast. 2010 Feb;19(1):14-22.
6. Rowell NP. Radiotherapy to the chest wall following mastectomy for node-negative breast cancer: a systematic review. Radiother Oncol. 2009 Apr;91(1):23-32.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: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. Lancet. 2014 Jun 21;383(9935):2127-35.

Post-mastectomy radiotherapy (PMRT) and regional nodal irradiation for patients with inflammatory breast cancer

1. Cardoso F, Paluch-Shimon S, Senkus E et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Ann Oncol. 2020;31(12):1623-1649.
2. Ueno NT, Fernandez JRE, Cristofanilli M et al. International Consensus on the Clinical Management of Inflammatory Breast Cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference. J Cancer. 2018; 9(8): 1437–1447.
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4. Dawood S, Lei X, Dent R et al. Survival of women with inflammatory breast cancer: a large population-based study. Ann Oncol. 2014;25(6):1143-51.
5. Dawood S, Merajver SD, Viens P et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. Ann Oncol. 2011;22(3):515-523.

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

1. Wenz F, Sperk E, Budach W, et al: Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). Strahlenther Onkol. 2014 Aug;190(8):705-14.
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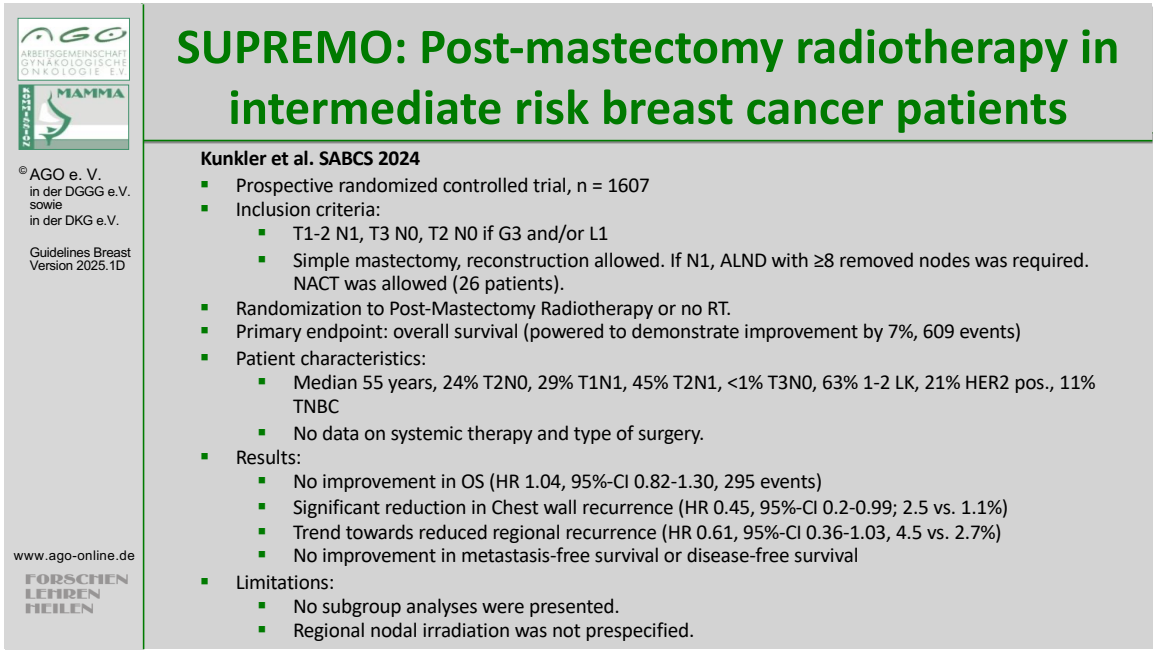


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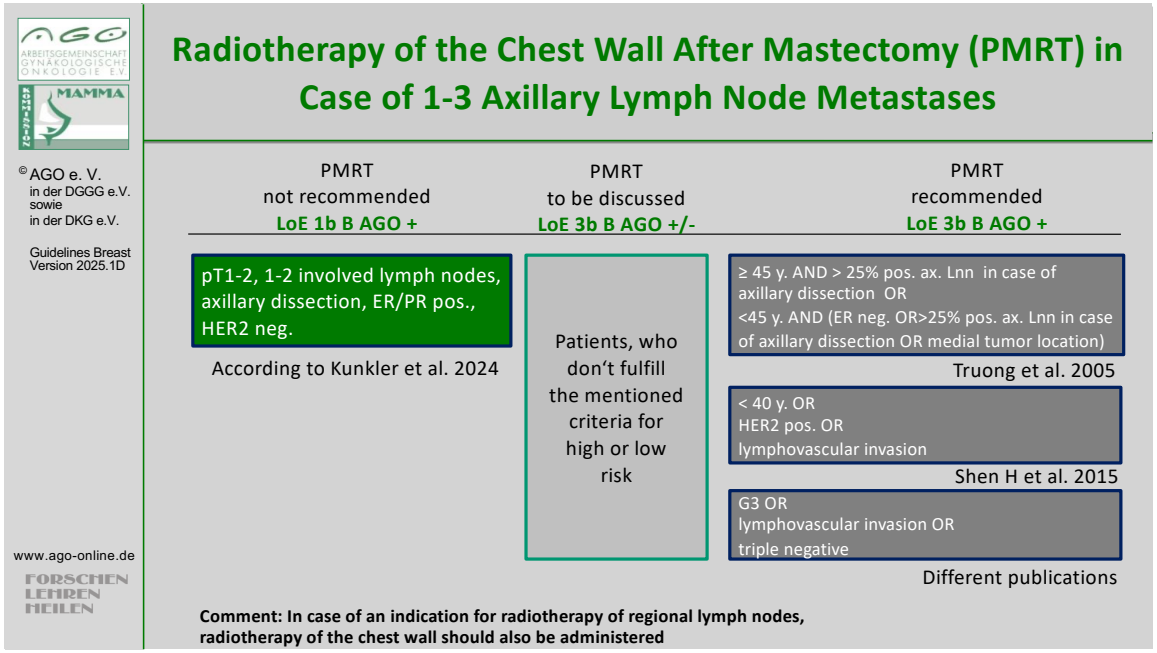



1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014 Jun 21;383(9935):2127-35.
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3. Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet. 1999 May 15;353(9165):1641-8.
4. Truong PT, Olivotto IA, Kader HA, et al: Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
5. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. ISRN Surg. 2013 Sep 11;2013:212979.
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9. Kunkler et al. GS2-03: Does postmastectomy radiotherapy in 'intermediate-risk' breast cancer impact overall survival? 10 year results of the BIG 2-04 MRC SUPREMO randomised trial: on behalf of the SUPREMO trial investigators. San Antonio Breast Cancer Symposium 2024

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.

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

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al. 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. Lancet. 2014 Jun 21;383(9935):2127-35.
2. Wenz F, Sperk E, Budach W, et al. Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer. Strahlenther Onkol. 2014 Aug;190(8):705-14.
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5. Truong PT, Olivotto IA, Kader HA, et al. Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
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Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with 1–3 tumor infiltrated lymph nodes (Lnn.) low risk

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2. Wenz F, Sperk E, Budach W, et al: Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer IV: radiotherapy following mastectomy for invasive breast cancer. Strahlenther Onkol. 2014 Aug;190(8):705-14.
3. Truong PT, Olivotto IA, Kader HA et al. Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high postmastectomy locoregional recurrence risk for adjuvant radiotherapy. Int J Radiat Oncol Biol Phys. 2005 Apr 1;61(5):1337-47.
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5. Kyndi M, Overgaard M, Nielsen HM, et al. High local recurrence risk is not associated with large survival reduction after postmastectomy radiotherapy in high-risk breast cancer: a subgroup analysis of DBCG 82 b&c. Radiother Oncol. 2009 Jan;90(1):74-9.
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Postmastectomy Radiotherapy (PMRT) to the Chest Wall in pts. with  pT3 pN0 R0 breast cancer (and no additional risk factors)


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2. Freedman GM, Fowble BL, Hanlon AL, et al: A close or positive margin after mastectomy is not an indication for chest wall irradiation except in women aged fifty or younger. Int J Radiat Oncol Biol Phys. 1998 Jun 1;41(3):599-605.
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5. Rowell NP. Are mastectomy resection margins of clinical relevance? A systematic review. Breast. 2010 Feb;19(1):14-22.
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Postmastectomy Radiotherapy (PMRT) to the Chest Wall in young pts with high risk features


1. Garg AK, Oh JL, Oswald MJ, et al. Eff ect of postmastectomy radiotherapy in patients <35 years old with stage II-III breast cancer treated with doxorubicin-based neoadjuvant chemotherapy and mastectomy. Int J Radiat Oncol Biol Phys 2007; 69: 1478–83.

2. Cardoso F, Loibl S, Pagani O, et al.; European Society of Breast Cancer Specialists. The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer. Eur J Cancer 2012;48:3355-77.
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Indications for Postmastectomy Radiotherapy (PMRT) to the Chest Wall and regional RT are independent of adjuvant systemic treatment

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.

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.

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C et al: Lancet. 2014 Jun 21;383(9935):2127-35.

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

1. Wenz F, Sperk E, Budach W, et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). Strahlenther Onkol. 2014 Aug;190(8):705-14.
2. Hehr T, Baumann R, Budach W et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). Radiotherapy after skin-sparing mastectomy with immediate breast reconstruction in intermediate-risk breast cancer : Indication and technical considerations. Strahlenther Onkol. 2019 Nov;195(11):949-963.
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# Postmastektomie-Bestrahlung (PMRT) der Thoraxwand* – Fraktionierung

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Moderat hypofraktionierte RT (Gesamtdosis ca. 40 Gy in ca. 15-16 Fraktionen in ca. 3 bis 5 Wochen)** | 1a | A | ++ |
| ▪ **Nach Brustrekonstruktion** | 1b | B | ++ |
| ▪ **Ultra-hypofraktionierte RT (Gesamtdosis 26 Gy, d.h. 5 Fraktionen in einer Woche = 1 Fraktion/Tag bzw. 28,5 Gy, d.h. 5 Fraktionen in 5 Wochen = 1 Fraktion/Woche)** | 1b | B | +/- |
| ▪ **Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25-28 Fraktionen in ca. 5-6 Wochen)** | 1a | B | + |

* **Zur Fraktionierung bei Bestrahlung der Lymphabflusswege siehe Folie „Fraktionierung der Radiotherapie lokoregionärer Lymphabflussregionen“.**

Moderate Hypofractionation

1. Haviland JS, Owen JR, Dewar JA, et al; START Trialists' Group. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol. 2013 Oct;14(11):1086-94.
2. Hickey BE, James ML, Lehman M et al. Fraction size in radiation therapy for breast conservation in early breast cancer. Cochrane Database Syst Rev. 2016 Jul 18;7:CD003860.
3. Wang SL, Fang H, Song YW et al.
Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. Lancet Oncol. 2019 Mar;20(3):352-360.
4. Meattini I, Becherini C, Boersma L et al. European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer. Lancet Oncol. 2022;23(1):e21-e31.
5. Wong JS, Uno H, Tramontano A et al. Hypofractionated vs Conventionally Fractionated Postmastectomy Radiation After Implant-Based Reconstruction. JAMA Oncol. 2024, 10:1370-1378.
6. Poppe et al. A Randomized Trial of Hypofractionated Post-Mastectomy Radiation Therapy (PMRT) in Women with Breast

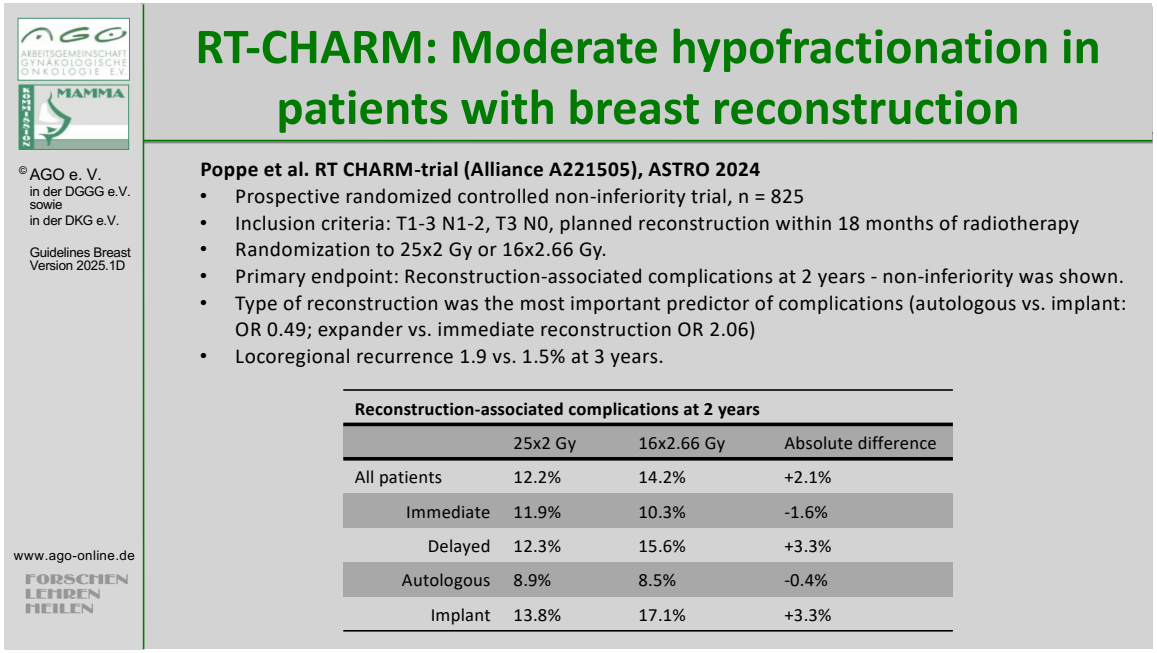
Reconstruction (RT CHARM, Alliance A221505). ASTRO Annual Meeting 2024. 10.1016/j.ijrobp.2024.07.002

Moderate hypofractionation and breast reconstruction

1. Kim D-Y, Park E, Heo CY, et al (2022) Influence of Hypofractionated Versus Conventional Fractionated Postmastectomy Radiation Therapy in Breast Cancer Patients With Reconstruction. Int J Radiat Oncol Biology Phys 112:445–456.
2. Kim D-Y, Park E, Heo CY, et al (2021) Hypofractionated versus conventional fractionated radiotherapy for breast cancer in patients with reconstructed breast: Toxicity analysis. Breast 55:37–44.
3. Rojas DP, Leonardi MC, Frassoni S, et al (2021) Implant risk failure in patients undergoing postmastectomy 3-week hypofractionated radiotherapy after immediate reconstruction. Radiother Oncol 163:105–113.
4. Wong JS, Uno H, Tramontano A et al. Patient-Reported and Toxicity Results from the FABREC Study: A Multicenter Randomized Trial of Hypofractionated vs. Conventionally-Fractionated Postmastectomy Radiation Therapy after Implant-Based Reconstruction. Presented at ASTRO Annual Meeting 2023 (LBA 5) https://doi.org/10.1016/j.ijrobp.2023.08.029
5. Ryu H, Shin KH, Chang JH et al. (2024) A nationwide study of breast reconstruction after mastectomy in patients with breast cancer receiving postmastectomy radiotherapy: comparison of complications according to radiotherapy fractionation and reconstruction procedures. Br J Cancer 131:290–298.
6. Poppe et al. A Randomized Trial of Hypofractionated Post-Mastectomy Radiation Therapy (PMRT) in Women with Breast Reconstruction (RT CHARM, Alliance A221505). ASTRO Annual Meeting 2024. 10.1016/j.ijrobp.2024.07.002

Ultra-Hypofractionation

1. Brunt AM, Haviland JS, Wheatley DA et al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet. 2020 May 23;395(10237):1613-1626.
2. Meattini I, Becherini C, Boersma L et al. European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer. Lancet Oncol. 2022;23(1):e21-e31.




Poppe et al. A Randomized Trial of Hypofractionated Post-Mastectomy Radiation Therapy (PMRT) in Women with Breast Reconstruction (RT CHARM, Alliance A221505). ASTRO Annual Meeting 2024. 10.1016/j.ijrobp.2024.07.002

# Boost bei PMRT

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ Eine Boost-Bestrahlung der Thoraxwand hat keinen Einfluss auf das brustkrebsspezifische und Gesamtüberleben | 2a | B | |
| ▪ Eine Boost-Bestrahlung der Thoraxwand sollte nur bei nachgewiesener R1 / R2-Situation ohne Möglichkeit einer Nachresektion erfolgen | 5 | D | ++ |
| ▪ Reicht der Tumor nach Mastektomie (unter Mitnahme der Pectoralisfaszie) an den pectoralen Absetzungsrand heran und ist ein faszienüberschreitendes Tumorwachstum klinisch nicht zu erkennen, ist von einer R0-Situation auszugehen. Eine Boostbestrahlung ist nicht erforderlich | 5 | D | ++ |

Thoracic wall boost irradiation

1. Mayadev J, Fish K, Valicenti R et al. Utilization and impact of a postmastectomy radiation boost for invasive breast cancer, Pract Radiat Oncol. 2014 Nov-Dec;4(6):e269-78

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Guidelines Breast
Version 2025.1D

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LEHREN
HEILEN

## Radiotherapie der Axilla bei Patientinnen mit positiven Sentinel-Lymphknoten* ohne axilläre Dissektion

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| **BEO oder Mastektomie und SENOMAC-Kriterien** erfüllt** | | | |
| ▪ Radiotherapie der Brust/Thoraxwand und Axilla (Level I-IV) | 1b | B | + |
| ▪ Radiotherapie der Brust/Thoraxwand unter Einschluss von Level 1 + 2 bis 5 mm unterhalb der Vena axillaris (PTV)*** | 2b | B | + |
| **BEO oder Mastektomie und SENOMAC-Kriterien** nicht erfüllt** | 5 | D | ++ |
| ▪ Radiotherapie der Brust/Thoraxwand und Axilla (Level I-IV) | | | |
| **Mastektomie und SENOMAC-Kriterien erfüllt, Radiotherapie der Thoraxwand nicht geplant** | | | |
| ▪ Alleinige Radiotherapie der Axilla | 5 | D | +/- |
| **≥ 3 pos. SLN** | | | |
| ▪ Radiotherapie der Axilla (Level I-IV analog AMAROS) | 1b | B | + |

*Makrometastasen **T1-T3, keine sonographisch suspekten LK (oder FNP/CNB neg.), 1-2 befallene SN, keine NACT
***nur wenn ansonsten keine Indikation zur Bestrahlung des Lymphabflusses besteht (siehe Folie „RT der lokoregionären Lymphabflussregionen“)


1-2 pos SLN: BCT:

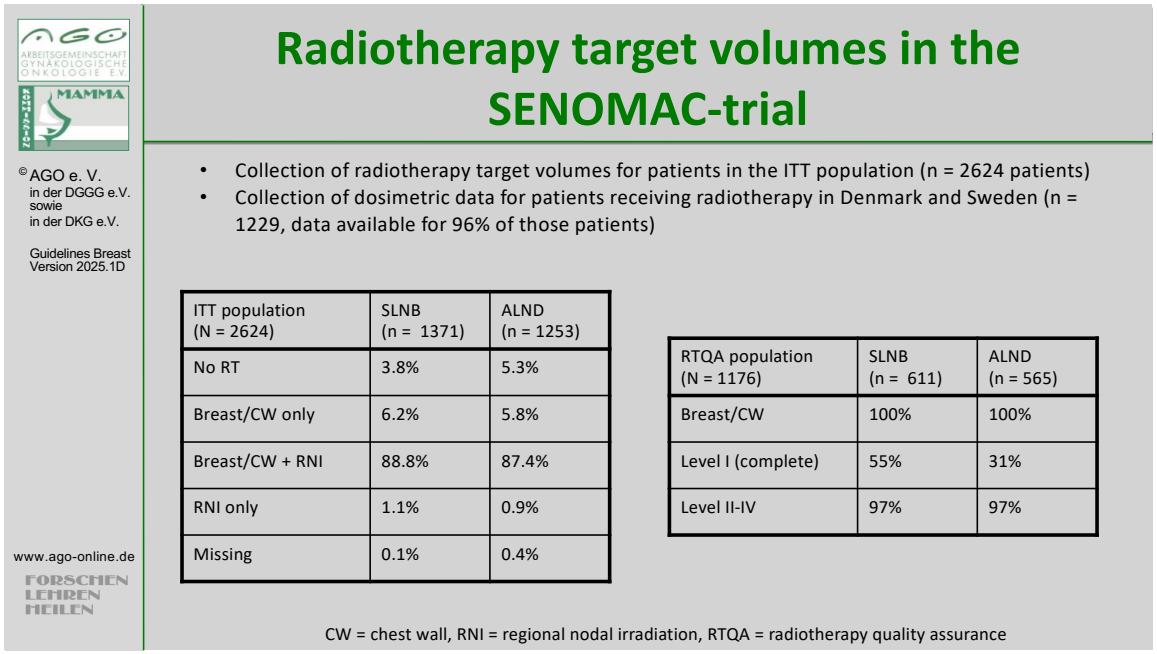
1. Giuliano AE, Ballman KV, McCall L, et al (2017) Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA 318:918–926.
2. Jagsi R, Manjoet C, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) trial. J Clin Oncol 2014;Nov 10;32(32): 3600-6
3. Sávolt Á, Péley G, Polgár C, et al (2017) Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla – Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer A randomized, single centre, phase III, non-inferiority trial. European J Surg Oncol Ejso 43:672–679.
4. Tinterri C, Gentile D, Gatzemeier W, et al (2022) Preservation of Axillary Lymph Nodes Compared with Complete Dissection in T1–2 Breast Cancer Patients Presenting One or Two Metastatic Sentinel Lymph Nodes: The SINODAR-ONE Multicenter Randomized Clinical Trial. Ann Surg Oncol 1–13
5. Algara M, Rodríguez E, Martínez-Arcelus FJ, et al (2022) OPTimizing Irradiation through Molecular Assessment of Lymph node (OPTIMAL): a randomized clinical trial. Radiother Oncol 176:76–82.
6. de Boniface J, Filtenborg Tvedskov T et al. Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases. N Engl J Med. 2024 Apr 4;390(13):1163-1175.

1-2 pos SLN: Mastectomy:


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.
2. Bartels SAL, Donker M, Poncet C, et al (2022) Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node in Breast Cancer: 10-Year Results of the Randomized Controlled EORTC 10981-22023 AMAROS Trial. J Clin Oncol JCO2201565. https://doi.org/10.1200/jco.22.01565
3. Sávolt Á, Péley G, Polgár C, et al (2017) Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla – Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer A randomized, single centre, phase III, non-inferiority trial. European J Surg Oncol Ejso 43:672–679.
4. de Boniface J, Filtenborg Tvedskov T et al. Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases. N Engl J Med. 2024 Apr 4;390(13):1163-1175


>=3 positive SLN: Radiotherapy of the axilla


1. Bartels SAL, Donker M, Poncet C, et al (2022) Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node in Breast Cancer: 10-Year Results of the Randomized Controlled EORTC 10981-22023 AMAROS Trial. J Clin Oncol JCO2201565. https://doi.org/10.1200/jco.22.01565
2. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al: 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. Lancet. 2014 Jun 21;383(9935):2127-35.




# Radiotherapy target volumes in the SENOMAC-trial

- Collection of radiotherapy target volumes for patients in the ITT population (n = 2624 patients)
- Collection of dosimetric data for patients receiving radiotherapy in Denmark and Sweden (n = 1229, data available for 96% of those patients)

| ITT population (N = 2624) | SLNB (n = 1371) | ALND (n = 1253) |
|---|---|---|
| No RT | 3.8% | 5.3% |
| Breast/CW only | 6.2% | 5.8% |
| Breast/CW + RNI | 88.8% | 87.4% |
| RNI only | 1.1% | 0.9% |
| Missing | 0.1% | 0.4% |

| RTQA population (N = 1176) | SLNB (n = 611) | ALND (n = 565) |
|---|---|---|
| Breast/CW | 100% | 100% |
| Level I (complete) | 55% | 31% |
| Level II-IV | 97% | 97% |

CW = chest wall, RNI = regional nodal irradiation, RTQA = radiotherapy quality assurance


1. Alkner S, Wieslander E, Lundstedt D et al. Quality assessment of radiotherapy in the prospective randomized SENOMAC trial. Radiother Oncol. 2024 Aug;197:110372.
2. de Boniface J, Filtenborg Tvedskov T et al. Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases. N Engl J Med. 2024 Apr 4;390(13):1163-1175.

Guidelines Breast
Version 2025.1D

## Zusätzliche RT der Axilla nach primärer Operation

**(bei Indikation zur Radiotherapie der Mamma/Brustwand[1] +/- supra- / infraklavikulärer und parasternaler RT[2])**

| pN-Status | | Oxford LoE | Oxford GR | AGO |
|---|---|---|---|---|
| cN0 / pNx analog SOUND/INSEMA | Keine intentionelle RT der Axilla[1] | 1b | B | - |
| pN0(sn) / pN1mic(sn) | Keine intentionelle RT der Axilla[1] | 1b | B | -- |
| pN0/+ nach ALND | Keine intentionelle RT der Axilla[1] | 1a | A | -- |
| pN+(sn) analog SENOMAC/AMAROS[3] (keine ALND) | Level I-IV | 1b | B | + |
| pN+(sn) analog SENOMAC/AMAROS[3] (keine ALND) | Level I-II[4] | 2b | B | + |
| pN+(sn) nicht analog SENOMAC/AMAROS[3] (keine ALND) | Level I-IV | 5 | D | ++ |
| Ausgedehnte perinodale Fettgewebsinfiltration in der Axilla | Level I-IV | 2b | B | + |
| Axillärer Resttumor nach ALND | Level I-IV | 5 | D | ++ |

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FORSCHEN LEHREN HEILEN

[1]Eine inzidentelle Dosisbelastung in Teilen von Level I/II ist technisch nicht zu umgehen. [2]Die Indikation für eine RT der SCG/ICG und der IMC ist separat zu prüfen. [3] T1-T3, keine sonographisch suspekten LK (oder FNP/CNB neg.), 1-2 befallene SN, keine NACT [4]Bis 5 mm unterhalb der Vena axillaris. Nur wenn ansonsten keine Indikation zur Bestrahlung des Lymphabflusses besteht, siehe Folie „RT der lokoregionären Lymphabflussregionen“

Clinically node negative without sentinel lymph node biopsy

1. Gentilini OD, Botteri E, Sangalli C et al. Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes. JAMA Oncol 2023. 9: 1557-1564.
2. Reimer T, Stachs A, Veselinovic K, et al (2024) Axillary Surgery in Breast Cancer — Primary Results of the INSEMA Trial. N Engl J Med. 2024 https://doi.org/10.1056/nejmoa2412063

Sentinel node negative or micrometastases in case of primary surgery

1. Krag DN, Anderson SJ, Julian TB, et al: Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival fi ndings from the NSABPB-32 randomised phase 3 trial. Lancet Oncol 2010; 11: 927–33.
2. Galimberti V, Manika A, Maisonneuve P, et al. Long-term follow-up of 5262 breast cancer patients with negative sentinel node and no axillary dissection confirms low rate of axillary disease. Eur J Surg Oncol. 2014 Oct;40(10):1203-8.
3. Galimberti V, Cole BF, Viale G, et al (2018) Axillary dissection versus no axillary dissection in patients with breast cancer and sentinel-node micrometastases (IBCSG 23-01): 10-year follow-up of a randomised, controlled phase 3 trial. The Lancet Oncology 19:1385–1393.

Radiotherapy to the axilla instead of completion axillary lymph node dissection in case of sentinel lymph node involvement

1. Galimberti V, Cole BF, Zurrida S, et al. International Breast Cancer Study Group Trial 23-01 investigators. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. 2013 Apr;14(4):297-305.
2. Giuliano AE, Ballman KV, McCall L, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017 Sep 12;318(10):918-926.
3. Jagsi R, Manjoet C, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) trial. J Clin Oncol 2014;Nov 10;32(32): 3600-6
4. Alkner S, Wieslander E, Lundstedt D et al. Quality assessment of radiotherapy in the prospective randomized SENOMAC trial. Radiother Oncol. 2024 Aug;197:110372.
5. de Boniface J, Filtenborg Tvedskov T et al. Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases. N Engl J Med. 2024 Apr 4;390(13):1163-1175.
6. 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
7. Bartels SAL, Donker M, Poncet C, et al (2022) Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node in Breast Cancer: 10-Year Results of the Randomized Controlled EORTC 10981-22023 AMAROS Trial. J Clin Oncol JCO2201565. https://doi.org/10.1200/jco.22.01565

Axillary soft tissue involvement

1. Naoum GE, Oladeru O, Ababneh H, et al (2024) Pathologic Exploration of the Axillary Soft Tissue Microenvironment and Its Impact on Axillary Management and Breast Cancer Outcomes. J Clin Oncol 42:157–169.

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.

## Zusätzliche RT der Axilla nach neoadjuvanter Chemotherapie

**(bei Indikation zur Radiotherapie der Mamma/Brustwand[1] +/- supra- / infraklavikulärer und parasternaler RT[2])**

**Erweiterung des PTV (planning target volume) zur Erfassung von Level I-II[3]**

| N-Status prä/post NACT | pN-Status | Oxford LoE | Oxford GR | AGO |
|---|---|---|---|---|
| cN0 / ycN0 | ypN0(sn) | 5 | D | - |
| cN0 / ycN0 | ypN1mi(sn) / ypN+(sn) (keine ALND erfolgt) | 5 | D | +[4] |
| $cN+_{CNB}$ / ycN0 | ypN0 / ypN0(i+) (sn/TAD) | 5 | D | +/-[4] |
| $cN+_{CNB}$/ ycN0 | ypN1mi(sn/TAD) / ypN+(sn/TAD) (keine ALND erfolgt) | 5 | D | +[4] |
| cN0/cN+ | ypN0/+ nach ALND | 2b | B | - |
| cN0/cN+ | ypN+ mit ausgedehnter perinodaler Fettgewebsinfiltration in der Axilla | 2b | B | + |
| cN0/cN+ | ypN+ mit axillärem Resttumor nach ALND | 5 | D | ++ |

[1] Eine inzidentelle Dosisbelastung in Teilen von Level I/II ist technisch nicht zu umgehen. [2]Die Indikation für eine RT der SCG/ICG und der IMC ist separat zu prüfen. [3]Bis 5 mm unterhalb der Vena axillaris. [4] Studienteilnahme empfohlen.

Statement surgical intervention in the axilla before or after neoadjuvant chemotherapy

1. Ryu JM, Lee SK, Kim JY, et al. Predictive Factors for Nonsentinel Lymph Node Metastasis in Patients With Positive Sentinel Lymph Nodes After Neoadjuvant Chemotherapy: Nomogram for Predicting Nonsentinel Lymph Node Metastasis. Clin Breast Cancer. 2017 Nov;17(7):550-55
2. Galimberti V, Ribeiro Fontana SK, Maisonneuve P. Sentinel node biopsy after neoadjuvant treatment in breast cancer: five-year follow-up of patients with clinically node-negative or node-positive disease before treatment. Eur J Surg Oncol 2016;42(3) 361-8
3. Martelli G, Miceli R, Folli S, et al. Sentinel node biopsy after primary chemotherapy in cT2 N0/1 breast cancer patients: Long-term results of a retrospective study. Eur J Surg Oncol. 2017 Nov;43(11):2012-2020.
4. Kahler-Ribeiro-Fontana S, Pagan E, Magnoni F, et al.: Long-term standard sentinel node biopsy after neoadjuvant treatment in breast cancer: a single institution ten-year follow-up, Eur J Surg Oncol. 2020 Oct 15;S0748-7983(20)30846-5.
5. Tee SR, Devane LA, Evoy D et al. Meta-analysis of sentinel lymph node biopsy after neoadjuvant chemotherapy in patients with initial biopsy-proven node-positive breast cancer. Br J Surg. 2018 Nov;105(12):1541-1552.
6. Balic M, Thomssen C, Würstlein R, Gnant M, Harbeck N. St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment. Breast Care (Basel). 2019 Apr;14(2):103-110.
7. Classe JM, Loaec C, Gimbergues P et al. Sentinel lymph node biopsy without axillary lymphadenectomy after neoadjuvant chemotherapy is accurate and safe for selected patients: the GANEA 2 study. Breast Cancer Res Treat. 2019 Jan;173(2):343-352.

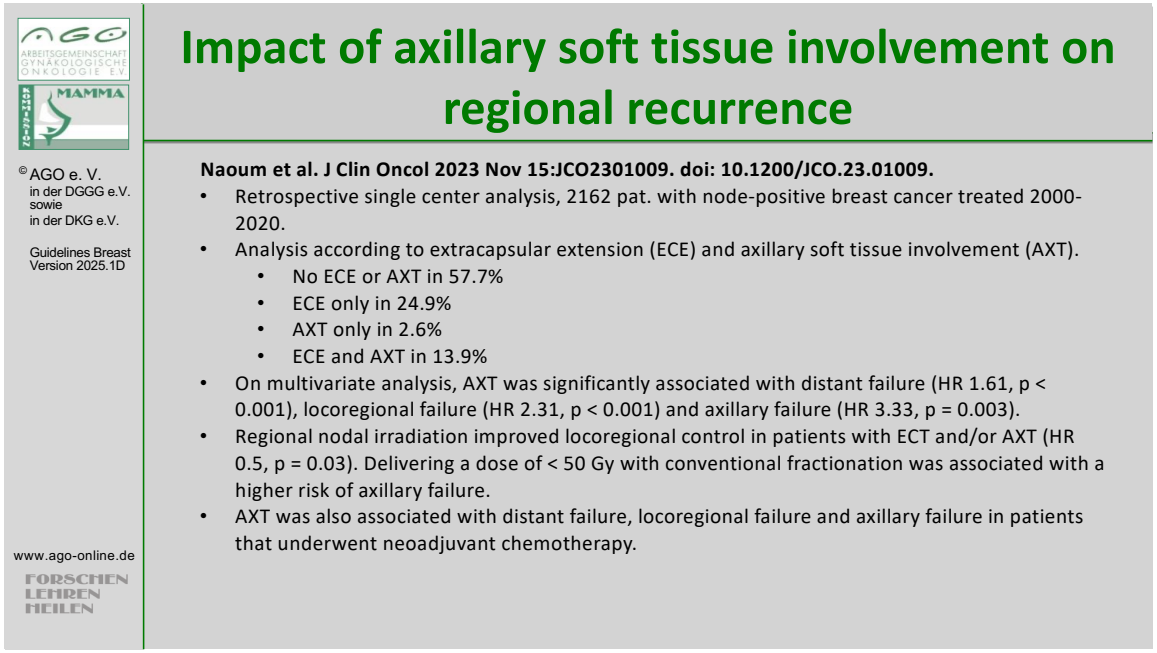
8. Moo TA, Edelweiss M, Hajiyeva S, et al. Is Low-Volume Disease in the Sentinel Node After Neoadjuvant Chemotherapy an Indication for Axillary Dissection? [published correction appears in Ann Surg Oncol. 2020 Feb 21;:]. *Ann Surg Oncol*. 2018;25(6):1488–1494.
9. Wong SM , Almana N , Choi J et al: Prognostic Significance of Residual Axillary Nodal Micrometastases and Isolated Tumor Cells After Neoadjuvant Chemotherapy for Breast Cancer, Ann Surg Oncol. 2019 Oct;26(11):3502-3509.
10. Montagna G, Mrdutt MM, Sun SX, et al (2024) Omission of Axillary Dissection Following Nodal Downstaging With Neoadjuvant Chemotherapy. JAMA Oncol 10:793–798.
11. Cabıoğlu N, Koçer HB, Karanlık H, et al (2025) De-Escalation of Nodal Surgery in Clinically Node-Positive Breast Cancer. JAMA Surg 160:. https://doi.org/10.1001/jamasurg.2024.5913

Axillary soft tissue involvement

1. Naoum GE, Oladeru O, Ababneh H et al. Pathological Exploration of the Axillary Soft Tissue Microenvironment and Its Impact on Axillary Management and Breast Cancer Outcomes. J Clin Oncol 2023 Nov 15:JCO2301009. doi: 10.1200/JCO.23.01009.

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.




Naoum GE, Oladeru O, Ababneh H, et al (2024) Pathologic Exploration of the Axillary Soft Tissue Microenvironment and Its Impact on Axillary Management and Breast Cancer Outcomes. J Clin Oncol 42:157–169.

# Radiotherapie (RT) der lokoregionären Lymphabflussregionen

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| **RT der supra- / infraklavikulären und Mammaria interna Lymphabflussregion** | | | |
| ▪ ≥ 4 befallene axilläre Lymphknoten[1] | 1a | A | ++ |
| ▪ 1–3 befallene axilläre Lymphknoten[1]<br>- zentralem oder medialem Sitz oder<br>- HR-negativ | 1a | A | + |
| ▪ pN0 und prämenopausal bei zentralem oder medialem Sitz und G3 und HR-negativ | 1a | B | + |
| ▪ klinischer Befall in den oben genannten Regionen | 2b | B | + |
| ▪ Für Mammaria interna: Bei linksseitigem Tumorsitz und erhöhtem kardialem Risiko oder simultaner Gabe von HER2-zielgerichteter Therapie | 2b | A | - |

[1] gilt nicht für Mikrometastasen

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Radiotherapy to regional nodes in early breast cancer: an individual patient data meta-analysis of 14 324 women in 16 trials. Lancet. 2023 Nov 25;402(10416):1991-2003.
2. Poortmans PM, Collette S, Kirkove C et al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):317-27.
3. Poortmans PM, Weltens C, Fortpied C, et al. Internal mammary and medial supraclavicular lymph node chain irradiation in stage I-III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial. Lancet Oncol. 2020 Dec;21(12):1602-1610.
4. Poortmans PM, Struikmans H, De Brouwer P et al., Side Effects 15 Years After Lymph Node Irradiation in Breast Cancer: Randomized EORTC Trial 22922/10925. J Nat Cancer Inst. 2021;113:1360-1368.
5. Whelan TJ, Olivotto IA, Parulekar WR et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):307-16.
6. Kim YB, Byun HK, Kim DY et al. Effect of Elective Internal Mammary Node Irradiation on Disease-Free Survival in Women With Node-Positive Breast Cancer: A Randomized Phase 3 Clinical Trial. JAMA Oncol. 2021;e216036. doi: 10.1001/jamaoncol.2021.6036.
7. Thorsen LBJ, Overgaard J, Matthiessen LW, et al (2022) Internal Mammary Node Irradiation in Patients With Node-Positive Early Breast Cancer: Fifteen-Year Results From the Danish Breast Cancer Group Internal Mammary Node Study. J Clin Oncol JCO2200044. https://doi.org/10.1200/jco.22.00044

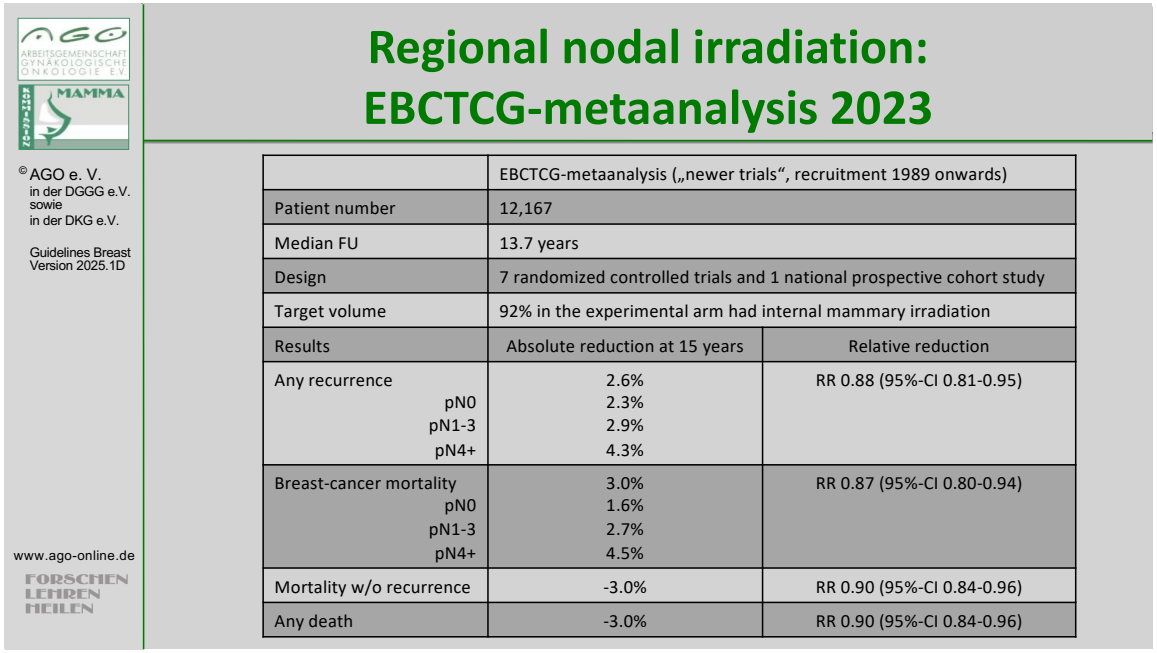
8. Hennequin C, Bossard N, Servagi-Vernat S, et al. Ten-Year Survival Results of a Randomized Trial of Irradiation of Internal Mammary Nodes After Mastectomy. Int J Radiation Oncol Biol Phys 2013; 86 (5): 860-866.

RT plus concurrent Trastuzumab +/- Pertuzumab

1. Bachir B, Anouti S, Jaoude JA et al. Evaluation of Cardiotoxicity in HER-2 Positive Breast Cancer Patients Treated with Radiation Therapy and Trastuzumab. Int J Radiat Oncol Biol Phys. 2022;S0360-3016(21)03432-5.
2. Belkacemi and J. Gligorov, Concurrent trastuzumab — internal mammary irradiation for HER2 positive breast cancer: “It hurts to be on the cutting edge”. Radiother Oncol 2010;94:119-20 (Letter to the editor).
3. Belkacémi Y, Gligorov J, Ozsahin M, et al. Concurrent trastuzumab with adjuvant radiotherapy in HER2-positive breast cancer patients: acute toxicity analyses from the French multicentric study. Ann Oncol 2008;19:1110-6.
4. Halyard MY, Pisansky TM, Dueck AC, et al. Radiotherapy and adjuvant trastuzumab in operable breast cancer: tolerability and adverse event data from the NCCTG Phase III Trial N9831. J Clin Oncol 2009;27:2638-44.
5. Jacob J, Belin L, Pierga JY, et al: Concurrent administration of trastuzumab with locoregional breast radiotherapy: long-term results of a prospective study. Breast Cancer Res Treat. 2014 Nov;148(2):345-53.
6. 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 Radiother 2009;13:276-80.
7. Shaffer R, Tyldesley S, Rolles M, et al. Acute cardiotoxicity with concurrent trastuzumab and radiotherapy including internal mammary chain nodes: A retrospective single-institution study. Radiother Oncol 2009;90:122-126
8. Aboudaram A, Loap P, Loirat D, et al (2021) Pertuzumab and Trastuzumab Combination with Concomitant Locoregional Radiotherapy for the Treatment of Breast Cancers with HER2 Receptor Overexpression. Cancers 13:4790.

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

1. Please check slide on radiotherapy after NACT




## Regional nodal irradiation: EBCTCG-metaanalysis 2023

| | EBCTCG-metaanalysis („newer trials“, recruitment 1989 onwards) | |
|---|---|---|
| Patient number | 12,167 | |
| Median FU | 13.7 years | |
| Design | 7 randomized controlled trials and 1 national prospective cohort study | |
| Target volume | 92% in the experimental arm had internal mammary irradiation | |
| Results | Absolute reduction at 15 years | Relative reduction |
| Any recurrence<br>pN0<br>pN1-3<br>pN4+ | 2.6%<br>2.3%<br>2.9%<br>4.3% | RR 0.88 (95%-CI 0.81-0.95) |
| Breast-cancer mortality<br>pN0<br>pN1-3<br>pN4+ | 3.0%<br>1.6%<br>2.7%<br>4.5% | RR 0.87 (95%-CI 0.80-0.94) |
| Mortality w/o recurrence | -3.0% | RR 0.90 (95%-CI 0.84-0.96) |
| Any death | -3.0% | RR 0.90 (95%-CI 0.84-0.96) |

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Radiotherapy to regional nodes in early breast cancer: an individual patient data meta-analysis of 14 324 women in 16 trials. Lancet. 2023 Nov 25;402(10416):1991-2003.

# Fraktionierung der Radiotherapie lokoregionärer Lymphabflussregionen

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Moderat hypofraktionierte RT (Gesamtdosis ca. 40–43,5 Gy in ca. 15–16 Fraktionen in ca. 3 bis 5 Wochen)** | 1b | B | ++ |
| ▪ **Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25–28 Fraktionen in ca. 5–6 Wochen)** | 1a | A | + |
| ▪ **Ultra-hypofraktionierte RT (Gesamtdosis 26 Gy, d.h. 5 Fraktionen in einer Woche = 1 Fraktion/Tag)** | 2b | B | - |

1. Poortmans PM, Collette S, Kirkove C et al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):317-27.
2. Whelan TJ, Olivotto IA, Parulekar WR et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):307-16.
3. Wang SL, Fang H, Song YW et al. Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. Lancet Oncol. 2019 Mar;20(3):352-360.
4. Bellefqih S, Elmajjaoui S, Aarab J et al. Hypofractionated Regional Nodal Irradiation for Women With Node-Positive Breast Cancer. Int J Radiat Oncol Biol Phys. 2017 Mar 1;97(3):563-570.
5. Badiyan SN, Shah C, Arthur D et al. Hypofractionated regional nodal irradiation for breast cancer: examining the data and potential for future studies. Radiother Oncol. 2014 Jan;110(1):39-44.
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.
7. Meattini I, Becherini C, Boersma L et al. European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast

cancer. Lancet Oncol. 2022;23(1):e21-e31.

8. Offersen B, Alsner J, Nielsen HM, et al (2022) OC-0102 DBCG phase III randomized trial of hypo- vs standard fractionated RT in 2879 pN+ breast cancer pts. Radiother Oncol 170:S76–S77.
9. Wheatley D, Haviland J, Patel J, et al (2022) OC-0101 First results of FAST-Forward phase 3 RCT nodal substudy: 3-year normal tissue effects. Radiother Oncol 170:S75–S76.
10. Rivera S, Karamouza E, Kirova Y et al. HypoG01:UNICANCER phase 3 trial of locoregional hypo vs normo fractionated RT in early breast cancer. Presented at ESTRO Annual Meeting 2023 (OC-0758) DOI: 10.1016/S0167-8140(23)08699-1 and ESMO Annual Meeting 2024

# Hypofractionated regional nodal irradiation

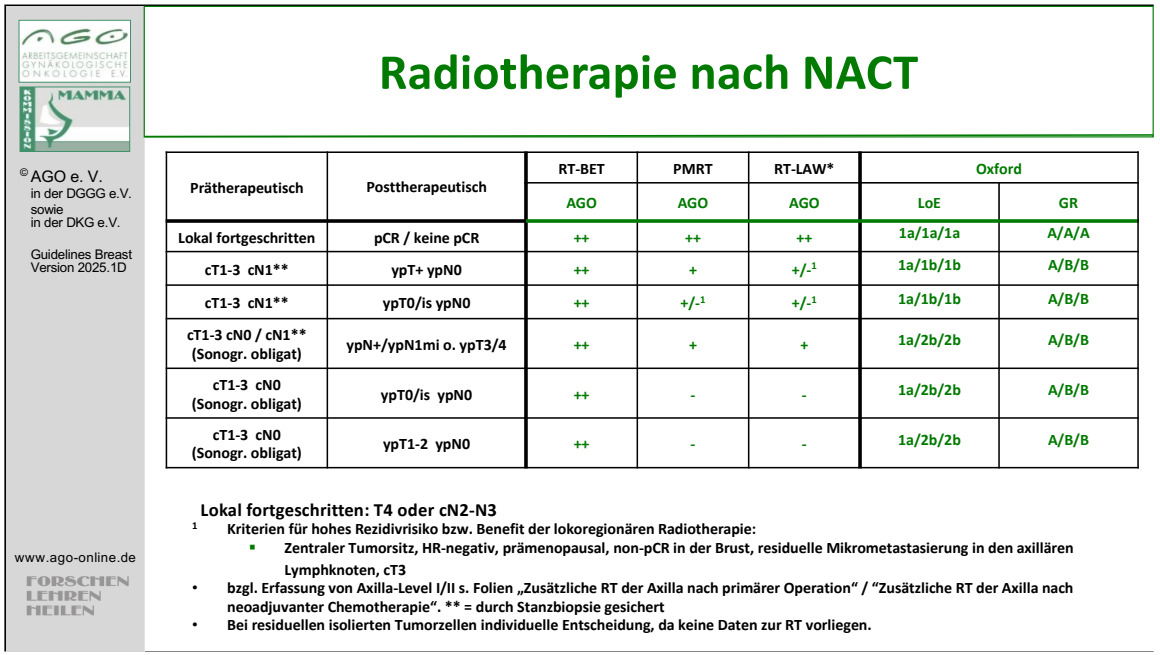


Guidelines Breast
Version 2025.1D

| | START-P/A/B subgroups | Wang et al. | DBCG Skagen 1 (Abstract) | HypoG-01 (Abstract) |
|---|---|---|---|---|
| Patient number | 864 | 820 | 2963 | 1265 |
| Fractionation | 39-42.9 Gy in 13-15 fx | 43.5 Gy in 15 Fx | 40 Gy in 15 Fx | 40 Gy in 15 Fx |
| Median FU | 10 years | 58.5 months | 3 years | 5 years |
| Primary endpoint | Late normal tissue effects | Locoregional recurrence | Lymphedema at 3 years | Lymphedema at 3 years |
| Statistical design | Retrospective analysis | Non-inferiority | Non-inferiority | Non-inferiority |
| Results | No statistically significant differences for LRR or late normal tissue effects | Non-inferiority for LRR (primary analysis) | No increased risk of lymphedema or LRR (primary analysis) | Non-inferiority for lymphedema<br>Superiority for LRR, DDFS, OS |



1. 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.
2. Wang SL, Fang H, Song YW et al.
Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. Lancet Oncol. 2019 Mar;20(3):352-360.
3. Offersen B, Alsner J, Nielsen HM, et al (2022) OC-0102 DBCG phase III randomized trial of hypo- vs standard fractionated RT in 2879 pN+ breast cancer pts. Radiother Oncol 170:S76–S77.
4. Rivera S, Karamouza E, Kirova Y et al. HypoG01:UNICANCER phase 3 trial of locoregional hypo vs normo fractionated RT in early breast cancer. Presented at ESTRO Annual Meeting 2023 (OC-0758). DOI: 10.1016/S0167-8140(23)08699-1 and ESMO Annual Meeting 2024




| Prätherapeutisch | Posttherapeutisch | RT-BET | PMRT | RT-LAW* | Oxford | |
|---|---|---|---|---|---|---|
| | | AGO | AGO | AGO | LoE | GR |
| Lokal fortgeschritten | pCR / keine pCR | ++ | ++ | ++ | 1a/1a/1a | A/A/A |
| cT1-3 cN1** | ypT+ ypN0 | ++ | + | +/-[1] | 1a/1b/1b | A/B/B |
| cT1-3 cN1** | ypT0/is ypN0 | ++ | +/-[1] | +/-[1] | 1a/1b/1b | A/B/B |
| cT1-3 cN0 / cN1** (Sonogr. obligat) | ypN+/ypN1mi o. ypT3/4 | ++ | + | + | 1a/2b/2b | A/B/B |
| cT1-3 cN0 (Sonogr. obligat) | ypT0/is ypN0 | ++ | - | - | 1a/2b/2b | A/B/B |
| cT1-3 cN0 (Sonogr. obligat) | ypT1-2 ypN0 | ++ | - | - | 1a/2b/2b | A/B/B |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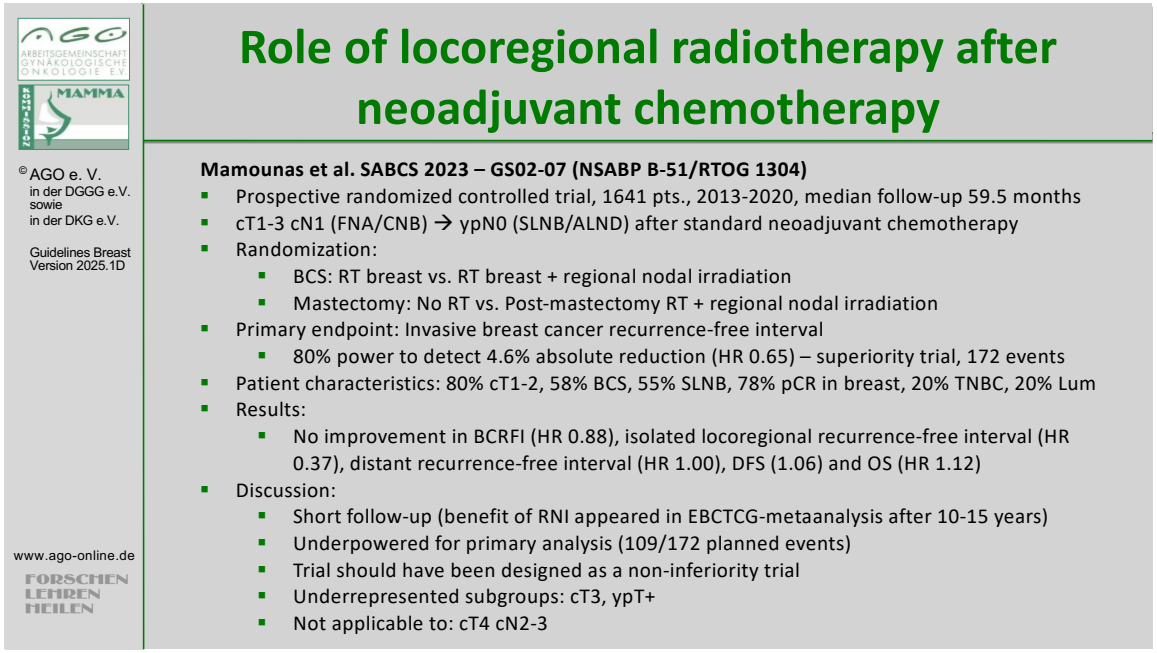


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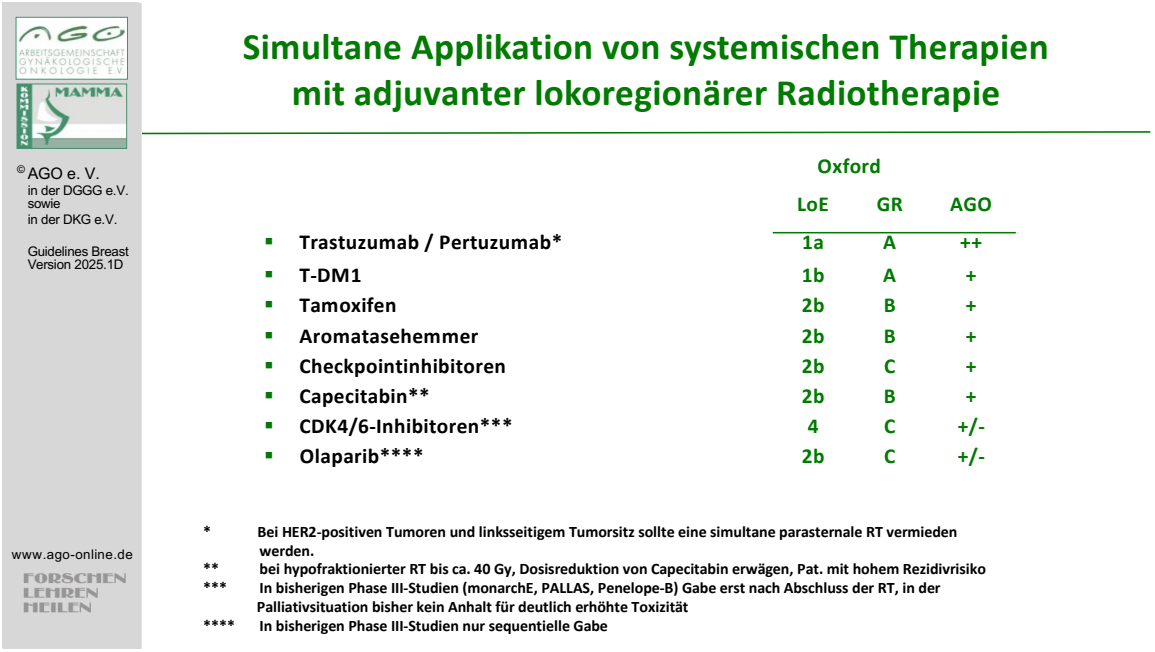


## Simultane Applikation von systemischen Therapien mit adjuvanter lokoregionärer Radiotherapie

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ Trastuzumab / Pertuzumab* | 1a | A | ++ |
| ▪ T-DM1 | 1b | A | + |
| ▪ Tamoxifen | 2b | B | + |
| ▪ Aromatasehemmer | 2b | B | + |
| ▪ Checkpointinhibitoren | 2b | C | + |
| ▪ Capecitabin** | 2b | B | + |
| ▪ CDK4/6-Inhibitoren*** | 4 | C | +/- |
| ▪ Olaparib**** | 2b | C | +/- |

* Bei HER2-positiven Tumoren und linksseitigem Tumorsitz sollte eine simultane parasternale RT vermieden werden.
** bei hypofraktionierter RT bis ca. 40 Gy, Dosisreduktion von Capecitabin erwägen, Pat. mit hohem Rezidivrisiko
*** In bisherigen Phase III-Studien (monarchE, PALLAS, Penelope-B) Gabe erst nach Abschluss der RT, in der Palliativsituation bisher kein Anhalt für deutlich erhöhte Toxizität
**** In bisherigen Phase III-Studien nur sequentielle Gabe


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# Interaktion zwischen Strahlentherapie und Rauchen

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Nach einer Strahlentherapie wegen Brustkrebs ist das Risiko für ein Lungenkarzinom für Raucher erhöht** | 1a | A | |
| ▪ **Patientinnen sollten über dieses Risiko informiert werden** | | | ++ |
| ▪ **Es sollte empfohlen werden, nicht mehr zu rauchen** | | | ++ |

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