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Guidelines Breast
Version 2021.10

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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Adjuvante Strahlentherapie



Adjuvante Radiotherapie (RT)

- **Versionen 2002 – 2020:**
Blohmer / Budach / Friedrichs / Göhring / Huober / Janni / Kühn / Möbus / Rody / Scharl / Seegenschmiedt / Souchon / Thomssen / Untch / Wenz
- **Version 2021:**
Budach / Friedrich / Krug

Search Strategy

Search Terms: Radiotherapy Breast Cancer

Source: Pubmed 1/2010 – 1/2021

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.

Vorbemerkung



- **Diese Empfehlungen zur adjuvanten Strahlentherapie bei Brustkrebs basieren auf einer Konsensdiskussion 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.
2. Sautter-Bihl ML, Sedlmayer F, Budach W, et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines: radiotherapy of breast cancer III--radiotherapy of the lymphatic pathways. *Strahlenther Onkol.* 2014 Apr;190(4):342-51.
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.
4. Budach W, Matuschek C, Bölke E et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer V: Therapy for locally advanced and inflammatory breast cancer, as well as local therapy in cases with synchronous distant metastases. *Strahlenther Onkol.* 2015 Aug;191(8):623-33.
5. Harms W, Budach W, Dunst J, et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guidelines for radiotherapy of breast cancer VI: therapy of locoregional breast cancer recurrences. *Strahlenther Onkol.* 2016;192(4):199-208

6. Krug D, Baumann R, Budach W et al.: Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). Neoadjuvant chemotherapy for breast cancer-background for the indication of locoregional treatment. *Strahlenther Onkol.* 2018 Sep;194(9):797-805.
7. Duma MN, Baumann R, Budach W, et al; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). Heart-sparing radiotherapy techniques in breast cancer patients: a recommendation of the breast cancer expert panel of the German society of radiation oncology (DEGRO). *Strahlenther Onkol.* 2019 Oct;195(10):861-871.
8. Hehr T, Baumann R, Budach W, et al. 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.
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.
10. Krug D, Baumann R, Combs SE et al. Moderate hypofractionation remains the standard of care for whole-breast radiotherapy in breast cancer: Considerations regarding FAST and FAST-Forward. *Strahlenther Onkol* 2021 <https://doi.org/10.1007/s00066-020-01744-3>

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

	Oxford		
	LoE	GR	AGO
• Bestrahlung der operierten Brust	1a	A	++
• Hypofraktionierung RT (Gesamtdosis ca. 40 Gy in ca. 15-16 Fraktionen in ca. 3 bis 5 Wochen)	1a	A	++
• Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25-28 Fraktionen in ca. 5-6 Wochen)	1a	B	+
• Ultra-hypofraktionierte RT (Gesamtdosis 26 bzw. 28,5 Gy in 5 Fraktionen über 1 oder 5 Wochen)	1b	B	+/-
• Bei Lebenserwartung <10 Jahre und pT1, pN0, R0, ER/PR positiv, HER2-negativ, endokriner adjuvanter Therapie (alle Faktoren) kann unter Inkaufnahme eines erhöhten Lokalrezidivrisikos nach individueller Beratung auf die RT verzichtet werden.	1a	B	+

Hypofraktionation

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. Whelan TJ, Pignol JP, Levine M et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med.* 2010 Feb 11;362(6):513-20.
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4. Bane AL, Whelan TJ, Pond GR, et al. Tumor factors predictive of response to hypofractionated radiotherapy in a randomized trial following breast conserving therapy. *Ann Oncol.* 2014 May;25(5):992-8.
5. Budach W, Bölke E, Matuschek C. Hypofractionated Radiotherapy as Adjuvant Treatment in Early Breast Cancer. A Review and Meta-Analysis of Randomized Controlled Trials. *Breast Care (Basel).* 2015 Aug;10(4):240-5.
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7. Shaitelman SF, Lei X, Thompson A et al. Three-Year Outcomes With Hypofractionated Versus Conventionally Fractionated Whole-Breast Irradiation: Results of a Randomized, Noninferiority Clinical Trial. *J Clin Oncol*. 2018 Oct 31;JCO1800317.
8. 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.
9. Offersen BV, Alsner J, Nielsen HM et al. Hypofractionated Versus Standard Fractionated Radiotherapy in Patients With Early Breast Cancer or Ductal Carcinoma In Situ in a Randomized Phase III Trial: The DBCG HYPO Trial. *J Clin Oncol*. 2020 Nov 1;38(31):3615-3625.

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.
3. Whelan T, Levine M, Sussman J. Hypofractionated Breast Irradiation: What's Next? *J Clin Oncol*. 2020 Oct 1;38(28):3245-3247.
4. Krug D, Baumann R, Combs SE et al. Moderate hypofractionation remains the standard of care for whole-breast radiotherapy in breast cancer: Considerations regarding FAST and FAST-Forward. *Strahlenther Onkol* 2021 <https://doi.org/10.1007/s00066-020-01744-3>

Elderly patients with low-risk features

1. 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.
2. Kunkler IH, Williams LJ, Jack WJ, et al: On behalf of the PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. *Lancet Oncol*. 2015.
3. Hughes KS, Schnaper LA. Can older women with early breast cancer avoid radiation? *The Lancet Oncology* 2015
4. Fastner G, Sedlmayer F, Widder J et al. Endocrine therapy with or without whole breast irradiation in low-risk breast cancer patients after breast-conserving surgery: 10-year results of the Austrian Breast and Colorectal Cancer Study Group 8A trial. *Eur J Cancer*. 2020

Jan 18;127:12-20.

5. Kunkler et al. GS2-03. Prime 2 randomised trial (postoperative radiotherapy in minimum-risk elderly): Wide local excision and adjuvant hormonal therapy +/- whole breast irradiation in women \geq 65 years with early invasive breast cancer: 10 year results. SABCS 2020



	FAST	FAST Forward
Timeframe	2004-2007	2011-2014
Sample size	915	4096
Dosse/Fractionation	50 Gy/2 Gy/5 weeks 30 Gy/6 Gy/5 weeks 28,5 Gy/5,7 Gy/5 weeks	40 Gy/2,67 Gy/3 weeks 27 Gy/5,4 Gy/1 weeks 26 Gy/5,2 Gy/1 weeks
Median follow-up	119.8 months	71.5 months
Primary endpoint	change in photographic breast appearance	Ipsilateral breast tumor recurrence (non-inferiority margin 1,6%)
Inclusion criteria	pT1-2 (< 3 cm) pN0 Age ≥50 years Breast conserving surgery No chemotherapy	pT1-3 pN0-1 Age ≥18 years Breast-conserving surgery or mastectomy Approx. 25% adj. chemotherapy
Boost	No	Approx. 25%, 5-Bx 2 Gy

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Brunt AM et al. J Clin Oncol. 2020 Oct 1;38(28):3261-3272. Brunt AM et al. Lancet. 2020 May 23;395(10237):1613-1626.

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.
3. Whelan T, Levine M, Sussman J. Hypofractionated Breast Irradiation: What's Next? J Clin Oncol. 2020 Oct 1;38(28):3245-3247.
4. Krug D, Baumann R, Combs SE et al. Moderate hypofractionation remains the standard of care for whole-breast radiotherapy in breast cancer: Considerations regarding FAST and FAST-Forward. Strahlenther Onkol (in press).


FAST / FAST-Forward

	FAST (10 year-data)			FAST Forward (5 year-data)		
	Dose	Frequency	Hazard ratio (95%-CI)	Dose	Frequency	Hazard ratio (95%-CI)
Ipsilateral in-breast recurrence	50 Gy	0.7%	-	40 Gy	2.1%	-
	30 Gy	1.4%	HR 1.36 (0.3-6.06)	27 Gy	1.7%	HR 0.86 (0.51-1.44)
	28.5 Gy	1.7%	HR 1.35 (0.3-6.05)	26 Gy	1.4%	HR 0.67 (0.38-1.16)
Moderate/marked normal tissue effects breast/chestwall	50 Gy	33.6%	-	40 Gy	26.8%	-
	30 Gy	50.4%	HR 1.79 (1.37-2.34)	27 Gy	35.1%	HR 1.41 (1.23-1.61)
	28.5 Gy	47.6%	HR 1.45 (1.10-1.91)	26 Gy	28.5%	HR 1.09 (0.95-1.27)

Brunt AM et al. J Clin Oncol. 2020 Oct 1;38(28):3261-3272. Brunt AM et al. Lancet. 2020 May 23;395(10237):1613-1626.

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.
3. Whelan T, Levine M, Sussman J. Hypofractionated Breast Irradiation: What's Next? J Clin Oncol. 2020 Oct 1;38(28):3245-3247.
4. Krug D, Baumann R, Combs SE et al. Moderate hypofractionation remains the standard of care for whole-breast radiotherapy in breast cancer: Considerations regarding FAST and FAST-Forward. Strahlenther Onkol (in press).



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BCS ≥ 70 y < 4 cm cN0 : Tamoxifen vs. Tamoxifen + RT

Time: 1994-1999, since 8/1996 only pT1cN0 ER/PR+ or unknown allowed

@10 yrs (95% C.I.)	Tamoxifen	Tamoxifen plus Radiotherapy	Hazard Ratio
Local recurrence-free ($\Delta=8\%$)	90% (85%-93%)	98% (96%-99%)	HR=0.18 (95% CI, 0.07 to 0.42; P < .001)
Mastectomy-free	96% (93% - 98%)	98% (96% - 99%)	HR=0.50 (95% CI, 0.17 to 1.48; n.s.)
Distant metastasis-free	95% (91% - 97%)	95% (92% - 97%)	HR=1.20 (95% CI, 0.63 to 2.32; n.s.)
Overall survival	66% (61% - 71%)	67% (62% - 72%)	HR=0.95 (95% CI, 0.77 to 1.18; n.s.)

Hughes KE et al J Clin Oncol 2013; 31:2382-2387

1. 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.

Boostbestrahlung nach BEO beim invasiven Karzinom

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> • Boost-RT des Tumorbettes (verbesserte lokale Kontrolle, kein Überlebensvorteil) <ul style="list-style-type: none"> • Prämenopausal • Postmenopausal, sofern >T1*, G3, HER2-positiv, triple-negativ, EIC (mindestens 1 Faktor) 	1b	B	++
<ul style="list-style-type: none"> • Techniken <ul style="list-style-type: none"> • Perkutan (Photonen, Elektronen) als sequentieller Boost • Multikatheter-Brachytherapie • Perkutan als simultan integrierter Boost (bei konventionell fraktionierter RT) • Perkutan als simultan integrierter Boost (bei hypofraktionierter RT) • Intraoperative Radiotherapie (als vorgezogener Boost) 	1a	A	++
	1a	A	++
	1b	B	+
	2b	B	+/-
	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.
2. Jones HA, Antonini N, Hart AA et al. Impact of pathological characteristics on local relapse after breast-conserving therapy: a subgroup analysis of the EORTC boost versus no boost trial. *J Clin Oncol.* 2009 Oct 20;27(30):4939-47.
3. Romestaing P, Lehingue Y, Carrie C et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. *J Clin Oncol.* 1997 Mar;15(3):963-8.
4. Polgár C, Fodor J, Orosz Z et al. Electron and high-dose-rate brachytherapy boost in the conservative treatment of stage I-II breast cancer first results of the randomized Budapest boost trial. *Strahlenther Onkol.* 2002 Nov;178(11):615-23.
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Boost-RT in premenopausal p.

Boost-RT in postmenopausal p.

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. Including Supplementary appendix.
2. Livi L, Borghesi S, Saieva C et al. Benefit of radiation boost after whole-breast radiotherapy. *Int J Radiat Oncol Biol Phys.* 2009 Nov 15;75(4):1029-34.
3. Antonini et al. Effect of age and radiation dose on local control after breast conserving treatment: EORTC trial 22881-10882. *Radiotherapy and Oncology* 82 (2007) 265–271

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.
2. Choi KH, Ahn SJ, Jeong JU et al. Postoperative radiotherapy with intensity-modulated radiation therapy versus 3-dimensional conformal radiotherapy in early breast cancer: A randomized clinical trial of KROG 15-03. *Radiother Oncol.* 2020 Sep 24;154:179-186.
3. Krug D, Köder C, Häfner MF et al. Acute toxicity of normofractionated intensity modulated radiotherapy with simultaneous integrated boost compared to three-dimensional conformal radiotherapy with sequential boost in the adjuvant treatment of breast cancer. *Radiat Oncol.* 2020 Oct 13;15(1):235.
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.

3. Freedman GM, White JR, Arthur DW, et al. Accelerated fractionation with a concurrent boost for early stage breast cancer. *Radiother Oncol*. 2013 Jan;106(1):15-20.
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5. Krug D, Baumann R, Krockenberger K et al. Adjuvant hypofractionated radiotherapy with simultaneous integrated boost after breast-conserving surgery: results of a prospective trial. *Strahlenther Onkol*. 2020 Oct 1. doi: 10.1007/s00066-020-01689-7.
6. Dellas K, Vonthein R, Zimmer J, et al (2014) Hypofractionation with simultaneous integrated boost for early breast cancer: results of the German multicenter phase II trial (ARO-2010-01). *Strahlenther Onkol* 190:646–653.
7. De Rose F, Fogliata A, Franceschini D, et al (2016) Phase II trial of hypofractionated VMAT-based treatment for early stage breast cancer: 2-year toxicity and clinical results. *Radiat Oncol* 11:120–9.

Intraoperative irradiation (IORT/IOERT)

As boost-irradiation followed by WBI

1. Fastner G, Reitsamer R, Urbański B et al. Toxicity and cosmetic outcome after hypofractionated whole breast irradiation and boost-IOERT in early stage breast cancer (HIOB): First results of a prospective multicenter trial (NCT01343459). *Radiother Oncol*. 2020 May;146:136-142.
2. Fastner G, Sedlmayer F, Merz F et al. IORT with electrons as boost strategy during breast conserving therapy in limited stage breast cancer: long term results of an ISIORT pooled analysis. 2013 Aug;108(2):279-86.
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Boost vs no Boost: EORTC 22881-10882 Trial

@20 yrs (95% C.I.)	Boost (n=2.662)	No boost (n=2.657)	Hazard Ratio (95% C.I.)
Overall Survival (Δ=1.4%)	59.7% (56.3-63.0)	61.1% (57.6-64.3)	HR 1.05 (0.92-1.19) n.s.
Cumulative Risk of Ipsilateral Breast Tumour Recurrence			
All patients	12.0% (9.8-14.4)	16.4% (14.1-18.8)	HR=0.65 (0.51-0.83); p<0.0001
≤40 years (Δ=11.8%)	24.4% (14.9-33.8)	36.0% (25.8-46.2)	HR=0.56 (0.34-0.93); p=0.029
41-50 years (Δ=5.9%)	13.5% (9.5-17.5)	19.4% (14.7-24.1%)	HR=0.66 (0.45-0.98); p=0.007
51-60 years (Δ=2.96%)	10.3% (8.3-14.3)	13.2% (9.8-16.7)	HR=0.69 (0.46-1.04); p=0.020
>60 years (Δ=3.0%)	9.7% (5.0-14.4)	12.7% (7.4-18.0)	HR=0.66 (0.42-1.04); p=0.019

(Median F/U 17.2 y) nach: Bartelink et al. Lancet Oncol 2015; 16: 47-56

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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.
2. Vrieling C et al. European Organisation for Research and Treatment of Cancer, Radiation Oncology and Breast Cancer Groups. Prognostic Factors for Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial: A Randomized Clinical Trial. JAMA Oncol. 2017 Jan 1;3(1):42-48

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

@15 yrs/20 yrs (95% C.I.)	Boost (n=2.661)		No boost (n=2.657)		Hazard Ratio (95% C.I.)
Overall Survival (Δ= -1.4%)	59.7% (56.3-63.0)		61.5% (57.6-64.3)		HR 1.05 (0.92-1.19) n.s.
Cumulative Risk of Any First Recurrence					
All patients (Δ=4%)	@15y @20y	28.1% 32.8%	32.1% 38.7%		HR=0.92 (0.81-1.04) n.s.
≤40 years (Δ=6%)	@15y @20y	41.5% 49.5%	48.5% 56.8%		HR=0.80 (0.56-1.15) n.s.
41-50 years	@15y @20y	34.0% 38.6%	35.6% 44.2%		HR=0.91 (0.71-1.16) n.s.
51-60 years	@15y @20y	28.5% 34.7%	28.7% 36.2%		HR=0.96 (0.76-1.21) n.s.
>60 years	@15y @20y	27.4% 32.1%	29.1% 32.8%		HR=0.94 (0.74-1.19) n.s.

(Median F/U 17.2 y) acc. Bartelink et al. Lancet Oncol 2015; 16: 47-56. Suppl.

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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.
2. Vrieling C et al. European Organisation for Research and Treatment of Cancer, Radiation Oncology and Breast Cancer Groups. Prognostic Factors for Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial: A Randomized Clinical Trial. *JAMA Oncol.* 2017 Jan 1;3(1):42-48

Teilbrustbestrahlung nach BEO beim invasiven Karzinom

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> • Intraoperative Radiotherapie (niedriges Risiko)* <ul style="list-style-type: none"> • Als alleinige Radiotherapie-Maßnahme während der ersten Brust-OP (IORT 50 kV, IOERT) <ul style="list-style-type: none"> + >50 Jahre + >70 Jahre 	1b	A	+/-
<ul style="list-style-type: none"> • Postoperative Teilbrustbestrahlung (niedriges Risiko)* <ul style="list-style-type: none"> • Interstitielle Multikatheter-Brachytherapie • Intrakavitäre Ballontechnik • Intensitätsmodulierte Radiotherapie (IMRT) (5x2 Gy über 2 Wochen) • 3D-konformale Radiotherapie (15x2,67 Gy über 3 Wochen) • 3D-konformale Radiotherapie (10x3,8 Gy über 2 Wochen) • 3D-konformale Radiotherapie (10x3,85 Gy über 1 Woche) 	1b	A	+
<ul style="list-style-type: none"> • 2b • 2b • 1b • 1b • 2b • 1b 	B	B	-
	1b	A	+
	1b	A	+
	2b	B	+/-
	1b	A	+/-

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

Intraoperative irradiation (IORT/IOERT)

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

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.
2. Vaidya JS, Bulsara M, Saunders C et al. Effect of Delayed Targeted Intraoperative Radiotherapy vs Whole-Breast Radiotherapy on Local Recurrence and Survival: Long-term Results From the TARGIT-A Randomized Clinical Trial in Early Breast Cancer. JAMA Oncol. 2020 Jul 1;6(7):e200249.
3. Vaidya JS, Joseph DJ, Tobias JS, et al. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. Lancet. 2010 Jul 10;376(9735):91-102.
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5. Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. Lancet Oncol. 2013 Dec;14(13):1269-77. #
6. Vaidya JS , Bulsar M, Wenz F, et al.: Reduced Mortality With Partial-Breast Irradiation for Early Breast Cancer:

A Meta-Analysis of Randomized Trials. *Int J Radiation Oncol Biol Phys*, Vol. 96, No. 2, pp. 259e265, 2016

7. Vaidya JS, Wenz F, Bulsara M, et al. An international randomised controlled trial to compare TARGeted Intraoperative radioTherapy (TARGIT) with conventional postoperative radiotherapy after breast-conserving surgery for women with early-stage breast cancer (the TARGIT-A trial). *Health Technol Assess* 2016;20(73).
8. Gentilini O, Botteri E, Leonardi MC, et al. Ipsilateral axillary recurrence after breast conservative surgery: The protective effect of whole breast radiotherapy. *Radiother Oncol*. 2017 Jan 4. pii: S0167-8140(16)34462-0. doi: 10.1016/j.radonc.2016.12.021. [Epub ahead of print]

>70 yrs

1. Abbott AM, Dossett LA, Loftus L, et al: Intraoperative radiotherapy for early breast cancer and age: clinical characteristics and outcomes. *Am J Surg*. 2015 Oct;210(4):624-8.
2. Vaidya JS, Wenz F, Bulsara M, et al: TARGIT trialists' group. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. *Lancet*. 2014 Feb 15;383(9917):603-13.
3. Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. *Lancet Oncol*. 2013 Dec;14(13):1269-77.
4. Vaidya JS, Wenz F, Bulsara M et al. An international randomised controlled trial to compare TARGeted Intraoperative radioTherapy (TARGIT) with conventional postoperative radiotherapy after breast-conserving surgery for women with early-stage breast cancer (the TARGIT-A trial). *Health Technol Assess* 2016;20(73).

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 multicatheter high-dose 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.
4. Polgár C, Ott OJ, Hildebrandt G et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. *Lancet Oncol.* 2017 Feb;18(2):259-268.
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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

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.


2. Bhattacharya IS, Haviland JS, Kirby AM et al. Patient-Reported Outcomes Over 5 Years After Whole- or Partial-Breast Radiotherapy: Longitudinal Analysis of the IMPORT LOW (CRUK/06/003) Phase III Randomized Controlled Trial. J Clin Oncol. 2019 Feb 1;37(4):305-317.

3D-conformal RT (10x3.85 Gy over two weeks)

1. Ott OJ, Strnad V, Stillkrieger W et al. Accelerated partial breast irradiation with external beam radiotherapy : First results of the German phase 2 trial. Strahlenther Onkol. 2017 Jan;193(1):55-61.

3D-conformal RT (10x3.85 Gy over one week)

1. Olivetto 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



Daten zur Teilbrustbestrahlung

*AGO e. V.
 in der DGOO e. V.
 in der DKG e. V.
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 FÜR GYNAKOLOGIE
 UND GYNÄKOLOGIE

NSABP B-39/RT0G 0413 (Vicini FA et al. Lancet. 2019 Dec 14;394(10215):2155-2164.)

- Randomised phase III equivalence trial, 4216 pat., 2005-2013, DCIS or invasive carcinoma ≤ 3 cm, 0-3 involved lymph nodes, age >18 y
- 50 Gy/25 fr. +/- boost vs. APBI with
 - 38.5 Gy/10 fr. in one week (external beam irradiation)
 - 34 Gy/10 fr. in one week (Multicatheter- or Single lumen-Brachytherapy)
- **"We observed an HR of 1.22 with a 90% CI of 0.94-1.58, which did not meet the equivalence criteria and favoured whole-breast irradiation. The 10-year cumulative incidence of IBTR was 3.9% (95% CI 3.1-5.0) in the whole-breast irradiation group and 4.6% (3.7-5.7) in the APBI group for an absolute difference of 0.7%."**
- **"Significantly more evaluable patients in the APBI group had recurrence-free interval events than patients in the whole-breast irradiation group (figure 3). The 10-year point estimate of recurrence-free interval for the whole breast irradiation group was 93.4% (95% CI 92.1-94.6), and in the APBI group it was 91.8% (90.4-93.0; figure 3)."**
- **"Our findings support whole-breast irradiation but the absolute outcome difference compared with APBI is small, so partial breast irradiation might also be an acceptable treatment for some patients."**

1. 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.



Daten zur Teilbrustbestrahlung

RAPID (Whelan TJ et al. Lancet. 2019 Dec 14;394(10215):2165-2172.)

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

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 FÜR DEN DEUTSCHEN
 KREBSKRANKEN

1. 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.

Postmastektomie-Bestrahlung (PMRT)* der Thoraxwand

	Oxford		
	LoE	GR	AGO
• >3 positive Lymphknoten	1a	A	++
• 1-3 positive Lymphknoten (hohes Risiko)	1a	A	+
• 1-3 positive Lymphknoten (niedriges Risiko*)	5	D	+/-
• T3 / T4	1a	A	++
• pT3 pN0 R0 (ohne zusätzliche Risikofaktoren)	2b	B	+/-
• R0-Resektion nicht erreichbar (bei invasiven Tumoren)	1a	A	++
• Bei jungen Patientinnen mit hohem Rückfallrisiko	2b	B	++
Die Indikationen zur PMRT und regionalen RT sind unabhängig von der adjuvanten systemischen Therapie	1a	A	

* Zur Definition „niedriges Risiko“ siehe nächste Folie Indikation zur Brustwandbestrahlung (PMRT)

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.
6. 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.
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]

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.
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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]

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*.

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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.

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

1. Garg AK, Oh JL, Oswald MJ, et al. Effect 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.
3. Dragan AE, Huang B, Gupta S, et al: One decade later: trends and disparities in the application of post-mastectomy radiotherapy since the release of the American Society of Clinical Oncology clinical practice guidelines. *Int J Radiat Oncol Biol Phys* 2012;83:e591-6.
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5. van der Sangen MJ, van de Wiel FM, Poortmans PM, et al. Are breast conservation and mastectomy equally effective in the treatment of young women with early breast cancer? Long-term results of a population-based cohort of 1,451 patients aged ≤ 40 years. *Breast Cancer Res Treat* 2011;127:207-15.

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

1. Wright JL, Takita C, Reis IM, et al: Predictors of locoregional outcome in patients receiving neoadjuvant therapy and postmastectomy radiation. *Cancer*. 2013 Jan 1;119(1):16-25.
2. Huang EH, Tucker SL, Strom E et al.: Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol*. 2004 Dec 1;22(23):4691-9.
3. Hoffman KE, Mittendorf EA, Buchholz TA. Optimising radiation treatment decisions for patients who receive neoadjuvant chemotherapy and mastectomy. *Lancet Oncol*. 2012 Jun;13(6):e270-6.

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

1. Wright JL, Takita C, Reis IM et al: Predictors of locoregional outcome in patients receiving neoadjuvant therapy and postmastectomy radiation. *Cancer*. 2013 Jan 1;119(1):16-25.
2. Huang EH, Tucker SL, Strom EA et al. Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol*. 2004 Dec 1;22(23):4691-9.
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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 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.
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.



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.
6. 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.
7. NCCN Guidelines for Treatment of Cancer by Site
["http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf"](http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf) download 2016
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]

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.
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. NCCN Guidelines for Treatment of Cancer by Site
“http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf” download 2016
9. 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]

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, Olivetto 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 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.
6. NCCN Guidelines for Treatment of Cancer by Site
“http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf” download 2016

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.
3. 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 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.
3. Truong PT, Olivetto IA, Speers CH, et al. A positive margin is not always an indication for radiotherapy after mastectomy in early breast cancer. *Int J Radiat Oncol Biol Phys*. 2004 Mar 1;58(3):797-804.
4. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. *ISRN Surg*. 2013 Sep 11;2013:212979.
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.

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

1. Garg AK, Oh JL, Oswald MJ, et al. Effect 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.
3. Dragun AE, Huang B, Gupta S, et al. One decade later: trends and disparities in the application of post-mastectomy radiotherapy since the release of the American Society of Clinical Oncology clinical practice guidelines. *Int J Radiat Oncol Biol Phys* 2012;83:e591-6.
4. Mallon PT, McIntosh SA. Post mastectomy radiotherapy in breast cancer: a survey of current United Kingdom practice. *J BUON* 2012;17:245-8.
5. van der Sangen MJ, van de Wiel FM, Poortmans PM, et al. Are breast conservation and mastectomy equally effective in the treatment of young women with early breast cancer? Long-term results of a population-based cohort of 1,451 patients aged ≤ 40 years. *Breast Cancer Res Treat* 2011;127:207-15.

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)

1. Wright JL, Takita C, Reis IM, et al. Predictors of locoregional outcome in patients receiving neoadjuvant therapy and postmastectomy radiation. *Cancer*. 2013 Jan 1;119(1):16-25.
2. Huang EH, Tucker SL, Strom EA et al. Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol*. 2004 Dec 1;22(23):4691-9.
3. Hoffman KE, Mittendorf EA, Buchholz TA. Optimising radiation treatment decisions for patients who receive neoadjuvant chemotherapy and mastectomy. *Lancet Oncol*. 2012 Jun;13(6):e270-6.
4. Rusthoven CG, Rabinovitch RA, Jones BL et al: The Impact of Postmastectomy and Regional Nodal Radiation after Neoadjuvant Chemotherapy for Clinically Lymph Node Positive Breast Cancer: A National Cancer Database (NCDB) Analysis. *Ann Oncol*. 2016 Feb 9. pii: mdw046. [Epub ahead of print]

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

1. Wright JL, Takita C, Reis IM et al. Predictors of locoregional outcome in patients receiving neoadjuvant therapy and postmastectomy radiation. *Cancer*. 2013 Jan 1;119(1):16-25.
2. Huang EH, Tucker SL, Strom EA, et al: Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol*. 2004 Dec 1;22(23):4691-9.
3. Hoffman KE, Mittendorf EA, Buchholz TA. Optimising radiation treatment decisions for patients who receive neoadjuvant chemotherapy and mastectomy. *Lancet Oncol*. 2012 Jun;13(6):e270-6.
4. Rusthoven CG, Rabinovitch RA, Jones BL, et al: The Impact of Postmastectomy and Regional Nodal Radiation after Neoadjuvant Chemotherapy for Clinically Lymph Node Positive Breast Cancer: A National Cancer Database (NCDB) Analysis. *Ann Oncol*. 2016 Feb 9. pii: mdw046. [Epub ahead of print]

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.

Boost bei PMRT

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



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

	Oxford		
	LoE	GR	AGO
BET und ACOSOG Z0011-Kriterien* erfüllt * Radiotherapie der Brust unter Einschluss von Level 1 + 2 bis 5 mm unterhalb der Vena axillaris (PTV)	2b	B	+*
BET und ACOSOG Z0011-Kriterien* nicht erfüllt * Radiotherapie der Axilla (analog AMAROS)	1b	B	++*
Nach ME, RT der Thoraxwand indiziert und ACOSOG Z0011-Kriterien* nicht erfüllt oder ME und RT der Thoraxwand nicht geplant * Radiotherapie der Axilla (analog AMAROS)	1b	B	++
>=3 pos. SLN * Radiotherapie der Axilla (analog AMAROS)	1b	B	+

* Studienteilnahme empfohlen
** Makrometastasen
* -T3, keine palpablen LK, RD, 1-2 befallene SLN, kein extrakapsuläres Wachstum, keine NACT

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

1. Giuliano AE, Hunt KK, Ballmann KV, et al Axillary dissection vs no axillary dissection in women with breast invasive cancer and sentinel node metastasis. A randomised clinical trial. JAMA 2011;305(6):569-575.
2. Galimberti V, Cole BF, Zurrada 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.
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

1-2 pos SLN: BCT: Axillary dissection

1. Giuliano AE, Hunt KK, Ballmann KV, et al. Axillary dissection vs no axillary dissection in women with breast invasive cancer and sentinel node metastasis. A randomised clinical trial. JAMA 2011;305(6):569-575.
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

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

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

2. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.

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

1. Donker M, Tienhoven G, Straver ME et al: Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS) a randomised, multicenter open label, phase 3 non inferiority trial. Lancet Oncol 2014;15:1333-10.
2. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.

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

EXPERT OPINION, extrapolated from:

1. Giuliano AE, Hunt KK, Ballmann KV, et al. Axillary dissection vs no axillary dissection in women with breast invasive cancer and sentinel node metastasis. A randomised clinical trial. JAMA 2011;305(6):569-5753.
2. Galimberti V, Cole BF, Zurrada 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.

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 (EORTC 10981-22023 AMAROS) a randomised, multicenter open label, phase 3 non inferiority trial. Lancet Oncol 2014;15:1333-10.
2. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.

>=3 positive SLN: Axillary LN dissection

1. Giuliano AE, Hunt KK, Ballmann KV, et al. Axillary dissection vs no axillary dissection in women with breast invasive cancer and sentinel node metastasis. A randomised clinical trial. JAMA 2011;305(6):569-575.
2. 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.

3. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.
4. 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.

>=3 positive SLN: Radiotherapy of the axilla

1. Giuliano AE, Hunt KK, Ballmann KV, et al: Axillary dissection vs no axillary dissection in women with breast invasive cancer and sentinel node metastasis. A randomised clinical trial. JAMA 2011;305(6):569-575.
2. 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.
3. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.
4. 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.

	Oxford		
	LoE	GR	AGO
Zusätzliche RT der Axilla nach primärer Operation (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			
pN-Status			
pN0(sn)/pN1mic(sn)	1b	B	--
pN0/+ nach ALND	1a	A	--
pN+(sn) analog ACOSOG Z0011 (keine ALND)	2b	B	+
pN+(sn) nicht analog ACOSOG Z0011 → gemäß AMAROS-Studie ⁴ (ALND nicht erfolgt)	1b	B	++
R2-Situation Axilla	S	D	++

¹AGO e. V.
 in der DGOG e. V.
 in der SGO e. V.
 in der DRG e. V.
 Guidelines Breast
 Version 2021.10
 www.ago-online.de
 FÜR DEN
 1. STUFE
 2. STUFE
 3. STUFE

¹Eine inzidentelle Dosisbelastung in Teilen von Level I/II ist technisch nicht zu umgehen. ²Die Indikation für eine RT der SOG/ICG und der IMC ist separat zu prüfen. ³Bis 5 mm unterhalb der Vena axillaris. ⁴± cT3, cN0, keine NACT, RT immer in Kombination mit supra- und infraklavikulärer RT

Sentinel node negative

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 findings 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.

Complete Axillary lymph node dissection after positive sentinel lymph node may be omitted in certain cases due to lack of benefit in prospectively randomized studies

1. Galimberti V, Cole BF, Zurrada 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

Regional nodal irradiation without ALND in non-Z0011-eligible patients

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. Rutgers et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients – 10-year results of the EORTC AMAROS trial. Presented at SABCS 2018.

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.

		Orford		
		LoE	GR	AGO
<p>Zusätzliche RT der Axilla nach neoadjuvanter Chemotherapie (bei Indikation zur Radiotherapie der Mamma/Brustwand¹ +/- supra-/infraklavikulärer und parasternaler RT²) Erweiterung des PTV (planning target volume) zur Erfassung von Level I-II³</p>				
N-Status prä/post NACT	pN-Status			
cN0 / ycN0	ypN0(sn)	S	D	-
cN0 / ycN0	ypN1mic(sn)/ypN+(sn) (keine ALND erfolgt)	S	D	+ ⁴
pN ^{low} / ycN0	ypN0(sn/TAD)	S	D	+/ ⁴
pN ^{low} / ycN0	ypN1mic(sn/TAD)/ypN+(sn/TAD) (keine ALND erfolgt)	S	D	+ ⁴
cN0/cN+	ypN0/+ nach ALND	2b	B	-
	R2-Situation Axilla	S	D	++

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

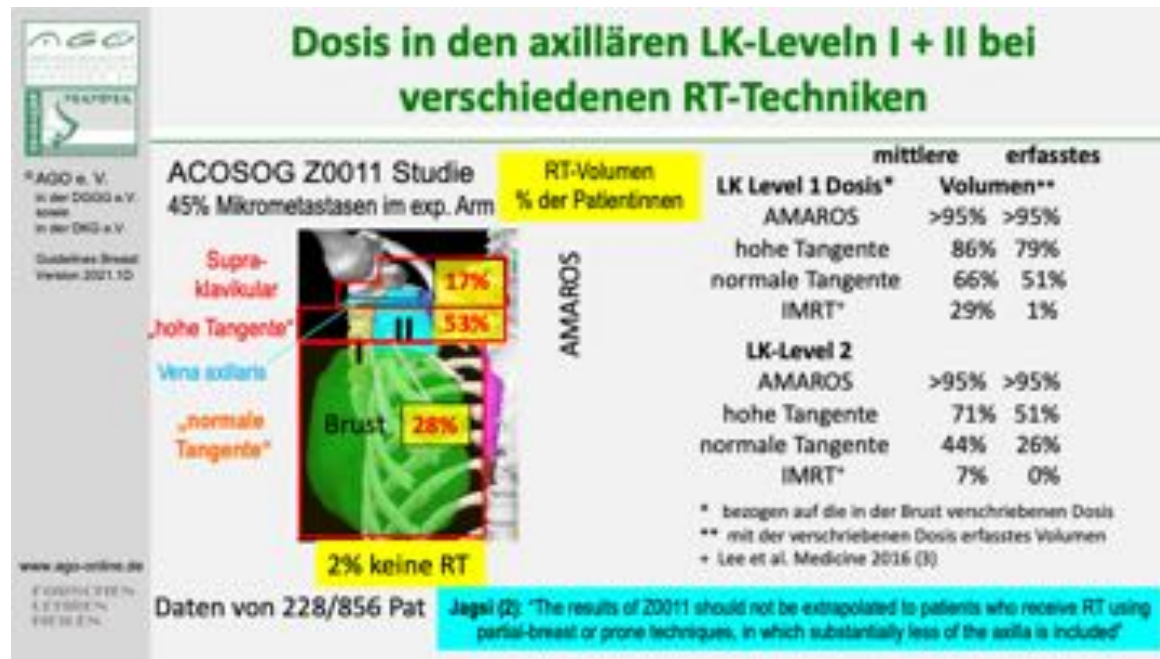
Axillary intervention after PST

1. 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.
2. 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.

3. 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.
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5. 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.

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.



1. Giuliano 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
2. Jagsi R et al. Radiation field design in the ACOSOG Z0011 (Alliance) Trial. J Clin Oncol. 2014 Nov 10;32(32):3600-6
3. Lee J et al.. Dosimetric evaluation of incidental irradiation to the axilla during whole breast radiotherapy for patients with left-sided early breast cancer in the IMRT era. Medicine (Baltimore). 2016 Jun;95(26):e403

Radiotherapie (RT) anderer lokoregionärer Lymphabflussregionen (SCG/ICG)

	Oxford		
	LoE	GR	AGO
<u>RT der supra-/infraklavikulären Lymphregion</u>			
• ≥ 4 befallene axilläre Lymphknoten oder Befall im Level III oder der supra-/infraklavikulären Lymphknoten	1b	A	++
• 1–3 befallene axilläre Lymphknoten ¹ bei - zentralem oder medialem Sitz und G2-3 oder ER/PR-negativ - prämenopausale Patientin und G2-3 oder ER/PR-negativ	2a	B	+
• pN0 und prämenopausal bei zentralen oder medialen Sitz und G2-3 und ER/PR-negativ	2a	B	+/-

¹ = gilt nicht für Mikrometastasen

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

1. Yates L, Kirby A, Crichton S, et al. Risk factors for regional nodal relapse in breast cancer patients with one to three positive axillary nodes. *Int J Radiat Oncol Biol Phys.* 2012 Apr 1;82(5):2093-103.
2. Viani GA, Godoi da Silva LB, Viana BS. Patients with N1 breast cancer: who could benefit from supraclavicular fossa radiotherapy? *Breast.* 2014 Dec;23(6):749-53.

Supra-/infraclavicular lymphatic regions

RT to Supra-/infraclavicular lymphatic regions if \geq pN2a

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. 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.
3. Whelan TJ, Olivetto IA, Parulekar WR et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):307-16.
4. Budach W, Kammers K, Boelke E, et al. Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of

randomized trials. Radiat Oncol. 2013 Nov 14 ;8:267.

5. P. F. Nguyen-Tan, L. Vincent, F. Methot et al., "The incidence of supraclavicular failure in patients with T1-2 breast cancer an four or more positive nodes treated by conservative surgery and tangential breast irradiation without regional nodal irradiation," International Journal of Radiation Oncology Biology Physics, vol. 42, supplement 1, p. 249, 1998.
6. Whelan TJ, Olivotto IA, Parulekar WR, et al. MA.20 Study Investigators. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):307-16.
7. Budach W, Bölke E, Kammers K, et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. Radiat Oncol. 2015 Dec 21;10(1):258.
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

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. 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.
3. 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.
4. Budach W, Bölke E, Kammers K, et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. Radiat Oncol. 2015 Dec 21;10(1):258.
5. Budach W, Kammers K, Boelke E, et al. Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials. Radiat Oncol. 2013 Nov 14 ;8:267.
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

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. 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.
3. Whelan TJ, Olivetto IA, Parulekar WR et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):307-16.
4. Budach W, Bölke E, Kammers K et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. *Radiat Oncol.* 2015 Dec 21;10(1):258.
5. Whelan TJOI, Ackerman I, Chapman JW, et al: NCIC-CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer. *J Clin Oncol ASCO Annual Meeting Proceed (Post-Meeting Edition)* 2011:29.
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

1. Poortmans PM, Collette S, Kirkove C, et al; EORTC Radiation Oncology and Breast Cancer Groups. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):317-27.
2. 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.
3. Whelan TJ, Olivetto IA, Parulekar WR, et al. MA.20 Study Investigators. Regional Nodal Irradiation in Early-Stage Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):307-16.
4. Budach W, Bölke E, Kammers K, et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. *Radiat Oncol.* 2015 Dec 21;10(1):258.
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)

1. Poortmans PM, Collette S, Kirkove C, et al; EORTC Radiation Oncology and Breast Cancer Groups. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):317-27.

2. 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.
3. Whelan TJ, Olivetto IA, Parulekar WR, et al; MA.20 Study Investigators. Regional Nodal Irradiation in Early-Stage Breast Cancer. *N Engl J Med.* 2015 Jul 23;373(4):307-16.
4. Budach W, Bölke E, Kammers K et al. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. *Radiat Oncol.* 2015 Dec 21;10(1):258.
5. Budach W, Kammers K, Boelke E, et al. Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials. *Radiat Oncol.* 2013 Nov 14 ;8:267.
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

Radiotherapie (RT) anderer lokoregionärer Lymphabflussregionen (IMC)

	Oxford		
	LoE	GR	AGO
Mammaria interna Lymphknotenregion (IMC)			
• pN0 und prämenopausal und zentraler oder medialer Sitz und G2-3 und ER/PR-negativ	1b	B	+/-
• 1-3 befallene axilläre Lymphknoten ¹ bei - zentralem oder medialem Sitz und G2-3 oder ER/PR-negativ - prämenopausale Patientin und G2-3 oder ER/PR-negativ	2a	B	+
• > = 4 befallene axilläre Lymphknoten bei G2-3 oder ER/PR-negativ	2a	B	+
• befallene Mammaria interna Lymphknoten	2a	B	+
• bei kardialem Risiko oder bei Gabe von Trastuzumab	2b	A	-

¹ = gilt nicht für Mikrometastasen

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

Internal mammaria lymph node region (IMN)

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

1. 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.
2. Chang JS, Park W, YB Kim, et al. Long-term Survival Outcomes Following Internal Mammary Node Irradiation in Stage II-III Breast Cancer: Results of a Large Retrospective Study With 12-Year Follow-up. *Int J Radiation Oncol Biol Phys*, 2013; 86 (5): 867-872.
3. 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.
4. 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.
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.
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7. Budach W, Kammers K, Boelke E, et al. Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of

randomized trials. Radiat Oncol. 2013 Nov 14 ;8:267.

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

1. 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.
2. Chang JS, Park W, YB Kim, et al. Long-term Survival Outcomes Following Internal Mammary Node Irradiation in Stage II-III Breast Cancer: Results of a Large Retrospective Study With 12-Year Follow-up. Int J Radiation Oncol Biol Phys, 2013; 86 (5): 867-872.
3. 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.
4. 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.
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. Jagsi R. Postmastectomy radiation therapy: an overview for the practicing surgeon. ISRN Surg. 2013 Sep 11;2013:212979.
7. Budach W, Kammers K, Boelke E, et al. Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials. Radiat Oncol. 2013 Nov 14 ;8:267.
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




Fraktionierung der Radiotherapie lokoregionärer Lymphabflussregionen

- Konventionell fraktionierte RT (Gesamtdosis ca. 50 Gy in ca. 25–28 Fraktionen in ca. 5–6 Wochen)
- Hypofraktionierung RT (Gesamtdosis ca. 40–43,5 Gy in ca. 15–16 Fraktionen in ca. 3 bis 5 Wochen)

Oxford		
LoE	GR	AGO
1a	A	++
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, Olivetto 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.




Hypofraktionierte Radiotherapie der Thoraxwand und Lymphabflusswege

Wang et al. *Lancet Oncol.* 2019 Mar;20(3):352-360.

- Randomised phase III non-inferiority trial, 820 pat., 2008-2016, T3/4 and/or ≥4 involved lymph nodes, 50 Gy/25 fr. vs. 43.5 Gy/15 fr.
- 98% 2D-planned radiotherapy, no treatment of the internal mammary lymph nodes
- "The 5-year cumulative incidence of locoregional recurrence was 8.3% (90% CI 5.8–10.7) in the hypo-fractionated radiotherapy group compared with 8.1% (90% CI 5.4–10.6) in the conventional fractionated radiotherapy group (absolute difference 0.2%, 90% CI –3.0 to 2.6; HR 1.10, 90% CI 0.72 to 1.69; figure 2).
- "In conclusion, this study provides high-level evidence for the clinical use of hypofractionated postmastectomy radiotherapy for patients with high-risk breast cancer. It can be recommended in clinical practice to patients who do not plan breast reconstruction and will not receive internal mammary node irradiation."

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 FÜR DEN FACHBEREICH
 STRAHLENTHERAPIE

1. 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.



Multivariate Analysis of Overall Survival: Effect of Radiotherapy of the Internal Mammaria Lymph Nodes


(median follow-up 10.9 yrs)

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

* missing data on 40 patients

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 ESTRO
 POORTMANS ET AL. ECCO AMSTERDAM 2013

1. Poortmans P, Struikmans H, Kirkove C, et al: Irradiation of the internal mammary and medial supraclavicular lymph nodes in stage I to III breast cancer: 10 years results of the EORTC Radiation Oncology and Breast Cancer Groups phase III trial 22922/10925. Eur J Cancer, 2013; 49 (Suppl. 3): abstr. #2BA.



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Radiotherapie nach NACT

Prätherapeutisch	Posttherapeutisch	RT-BET	PMRT	RT-LAN*	Oxford		
					LoE	GR	AGO
Lokal fortgeschritten	pCR / keine pCR	ja	ja	ja	1a/1a/1a	A/A/A	++/+/++
cT1/2 cN1>**	ypT1+ s. ypN0 + (keine pCR)	ja	ja	ja	1a/2b/2b	A/B/B	++/+/+
cT1/2 cN1>**	ypT0/s ypN0	ja	Risikofälle ¹		2b/2b/2b	B/B/B	+/-/+
cT1/2 cN0 (Sonogr. obligat)	ypT0/s ypN0	ja	nein	nein	2b/2b/2b	A/B/B	+/-/-

Lokal fortgeschritten: T3-4 oder cN2-N3

¹ Kriterien für hohes Rezidivrisiko:

- * pN0 prämenopausal hohes Risiko: zentraler oder medialer Sitz, und (G2-3 und ER/PR-negativ)
- * prätherapeutisch pN1a/ cN+* hohes Risiko: zentraler oder medialer Sitz und (G2-3 oder ER/PR-negativ) oder prämenopausal, lateraler Sitz und (G2-3 oder ER/PR-negativ)
- * = bzgl. Erfassung von Axilla-Level 1/2 s. Folien „Zusätzliche RT der Axilla nach primärer Operation“/„Zusätzliche RT der Axilla nach neoadjuvanter Chemotherapie“. ** = durch Stadienanalyse gesichert

1. Cortazar P, Zhang L, Untch M, et al (2014) Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet* 384:164–172. doi: 10.1016/S0140-6736(13)62422-8
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5. Poortmans PM, Collette S, Kirkove C, et al (2015) Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. *N Engl J Med* 373:317–327. doi: 10.1056/NEJMoa1415369
6. Whelan TJ, Olivetto IA, Parulekar WR, et al (2015) Regional Nodal Irradiation in Early-Stage Breast Cancer. *N Engl J Med* 373:307–316. doi: 10.1056/NEJMoa1415340
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- Patients With One to Three Positive Axillary Lymph Nodes. *J Clin Oncol* 35:1256-1258. doi: 10.1200/JCO.2016.71.0764
9. Poortmans P (2014) Postmastectomy radiation in breast cancer with one to three involved lymph nodes: ending the debate. *Lancet* 383:2104–2106. doi: 10.1016/S0140-6736(14)60192-6
 10. Fowble BL, Einck JP, Kim DN, et al (2012) Role of postmastectomy radiation after neoadjuvant chemotherapy in stage II-III breast cancer. *Int J Radiat Oncol Biol Phys* 83:494–503. doi: 10.1016/j.ijrobp.2012.01.068
 11. White J, Mamounas E (2014) Locoregional Radiotherapy in Patients With Breast Cancer Responding to Neoadjuvant Chemotherapy: A Paradigm for Treatment Individualization. *J Clin Oncol* 32:494–495. doi: 10.1200/JCO.2013.53.4974
 12. Rusthoven CG, Rabinovitch RA, Jones BL, et al (2016) The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis. *Ann Oncol* 27:818–827. doi: 10.1093/annonc/mdw046
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- II-III breast cancer patients with pN0: a multicenter, retrospective study (KROG 12-05). *Int J Radiat Oncol Biol Phys* 88:65–72. doi: 10.1016/j.ijrobp.2013.09.021
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Molekulare Prädiktion für die Radiotherapie

- Ergebnisse von Genexpressionsprofilen sollen nicht für die Indikationsstellung der Radiotherapie herangezogen werden

Oxford		
LoE	GR	AGO
2b	B	++

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Simultane Kombination systemischer 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	+/.***

- * Bei HER2-positiven Tumoren sollte eine simultane parasternale RT generell vermieden werden; keine simultane Trastuzumab-/Pertuzumabtherapie bei parasternaler RT.
- ** bei hypo-fraktionierter RT bis ca. 40 Gy, Dosisreduktion von Capecitabin erwägen, Pat. mit hohem Rezidivrisiko
- *** In bisherigen Phase III-Studien (monarchie, PALLAS, Penelope-B) Gabe erst nach Abschluss der RT, in der Palliativsituation bisher kein Anhalt für deutlich erhöhte Toxizität

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

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Tamoxifen concurrent with radiotherapy

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AI (letrozole, anastrozole) concurrent with radiotherapy

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Checkpointinhibitors concurrent with radiotherapy

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

Capecitabine and radiotherapy

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Simultane Gabe von Capecitabin zur lokoregionären Radiotherapie

Woodward et al. *Int J Radiat Oncol Biol Phys.* 2017 Nov 15;99(4):777-783

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

Alhanafy et al. *Menoufia Medical Journal* 2015, 28:325-332

- Randomised phase II-trial, 100 pat., adj. radiotherapy 40 Gy/15 fr. +/- CAP 825 mg/m² Mo-Fr, LABC
- "[...] concurrent capecitabine was feasible with a high percent of patients (96%), [...] only two out of 50 (4%) patients had capecitabine dose modification ..."
- "All early toxicities were GI/GII. Radiation dermatitis had a peak incidence in the last few fractions of the radiation therapy and the week after radiotherapy; no treatment interruption was needed and the incidence was close in both groups".
- Radiation dermatitis grade 1 14% vs. 18%; grade 2 4% vs. 4%

Interaktion zwischen Strahlentherapie und Rauchen

- Nach einer Strahlentherapie wegen Brustkrebs ist das Risiko für ein Lungenkarzinom für Raucher erhöht
- Patientinnen sollten über dieses Risiko informiert werden
- Es sollte empfohlen werden, nicht mehr zu rauchen

Oxford		
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1a	A	

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