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Adjuvant Radiotherapy

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Adjuvant Radiotherapy (RT)

- **Versions 2002 – 2020:**
  Blohmer / Budach / Friedrichs / Göhring / Huober/ Janni / Kühn / Möbus / Rody / Scharl / Seegenschmiedt / Souchon / Thomssen / Untch / Wenz

- **Version 2021:**
  Budach / Friedrich / Krug

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Preliminary Note

- **The recommendations on adjuvant radiotherapy for breast cancer are based on a consensus discussion between AGO and DEGRO experts**
- **For technical radiotherapy details, we refer to the corresponding updated DEGRO practice guidelines**

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

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	Oxford		
	LoE	GR	AGO
▪ Radiotherapy of the affected breast	1a	A	++
▪ Hypofractionated radiotherapy (total dose approx. 40 Gy in 15-16 fractions within 3-5 weeks	1a	A	++
▪ Conventionally fractionated radiotherapy (total dose about 50 Gy in approx. 25-28 fractions in 5-6 weeks)	1a	B	+
▪ Ultra-hypofractionated RT (total dose 26 or 28,5 Gy in 5 fractions in 1 or 5 weeks)	1b	B	+/-
▪ In case of life expectancy <10 years and pT1, pN0, R0, ER/PR-positive, HER2-negative, endocrine therapy (all criteria), radiotherapy can be omitted after individual counseling, resulting in an increased risk for in-breast recurrence	1a	B	+

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FAST / FAST-Forward

	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%, 5-8x 2 Gy

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.

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FAST / FAST-Forward

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	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.

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BCS >=70y <4cm 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 (Δ=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

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

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

* continuous parameter with regard to risk of relapse

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

@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)	61.1% (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 (0.52–0.81); p<0.0001
≤40 years (Δ=11.6%)	24.4% (14.9–33.8)	36.0% (25.8–46.2)	HR=0.56 (0.34–0.92); p=0.003
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% (6.3–14.3)	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)

acc. to: Bartelink et al. Lancet Oncol 2015; 16: 47–56

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EORTC 22881-10882: Boost vs no Boost (Endpoint: Any First Recurrence)

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@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)		61.1% (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%	48.1% 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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Radiotherapy (RT) after Breast Conserving Surgery (Invasive Cancer) – Partial Breast Irradiation (PBI)

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	Oxford		
	LoE	GR	AGO
Intraoperative Radiotherapy (low-risk)*			
As sole radiotherapy, during first breast surgery (IORT 50 kV, IOERT)			
>50 years	1b	A	+/-
>70 years	1b	A	+
Postoperative partial breast irradiation (low-risk)*			
Interstitial Multicatheter-Brachytherapy	1b	A	+
Intracavitary balloon-technique	2b	B	-
Intensity-modulated radiotherapy (IMRT) (5x6 Gy in 2 weeks)	1b	A	+
3D-conformal radiotherapy (15x2.67 Gy in 3 weeks)	1b	A	+
3D-conformal radiotherapy (10x3.8 Gy in 2 weeks)	2b	B	+/-
3D-conformal radiotherapy (10x3.85 Gy in 1 week)	1b	A	+/-

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

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

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Data on partial breast irradiation

NSABP B-39/RTOG 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**. "

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Data on partial breast irradiation

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

- Randomised phase III non-inferiority trial, 2135 pat., 2006-2011, DCIS or invasive carcinoma ≤ 3 cm, pN0, age ≥40 y., no ILC
- 42.56/16 fr. or 50 Gy/25 fr. +/- Boost vs. APBI 38.5 Gy/10 fr. in one week (external beam irradiation)
- "In patients treated with **APBI, the 5 year cumulative rate of IBTR was 2·3%** (95% CI 1·4–3·2) and the **8 year cumulative rate was 3·0%** (1·9–4·0). In patients treated with **whole breast irradiation, the 5 year cumulative rate of IBTR was 1·7%** (0·9–2·5) and the **8 year cumulative rate was 2·8%** (1·8–3·9; figure 2). The HR for APBI versus whole breast irradiation was 1·27 (90% CI 0·84–1·91). Thus, **the upper bound of the estimated 90% CI did not exceed the non-inferiority margin** of 2·02."
- "**Late radiation toxicity (grade ≥2 […]) was more common in patients treated with APBI** (346 [32%] of 1070 patients) than whole breast irradiation (142 [13%] of 1065 patients; p<0·0001). **Adverse cosmesis […] was more common in patients treated with APBI** than in those treated by whole breast irradiation at 3 years (absolute difference, 11·3%, 95% CI 7·5–15·0), 5 years (16·5%, 12·5–20·4), and 7 years (17·7%, 12·9–22·3)."

Postmastectomy Radiotherapy (PMRT)* to the Chest Wall

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	Oxford		
	LoE	GR	AGO
▪ > 3 tumor infiltrated lymph nodes (LN)	1a	A	++
▪ 1–3 tumor infiltrated LN (high-risk)	1a	A	+
▪ 1–3 tumor infiltrated LN (low-risk*)	5	D	+/-
▪ T3 / T4	1a	A	++
▪ pT3 pN0 R0 (and no additional risk factors)	2b	B	+/-
▪ If R0 is impossible to reach (for invasive tumor)	1a	A	++
▪ In young pts with high-risk features	2b	B	++
The indications for PMRT and regional RT are independent of adjuvant systemic treatment	1a	A	

* For definition of low-risk, see next slide Radiotherapy of the Chest Wall After Mastectomy (PMRT)

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Radiotherapy of the Chest Wall After Mastectomy (PMRT) in Case of 1-3 Axillary Lymph Node Metastases

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PMRT can be omitted **LoE 3b B AGO +**	PMRT to be discussed **LoE 3b B AGO +/-**	PMRT recommended **LoE 3b B AGO +**
ER pos, G1, HER2 neg, pT1 (at least 3 criteria present)	Patients, who don't fulfill the mentioned criteria for high or low risk	≥45 y. AND >25% pos. ax. Lnn in case of axillary dissection OR <45 y. AND (ER neg. OR>25% pos. ax. Lnn in case of axillary dissection OR medial tumor location)
Kyndi et al. 2009		Truong et al. 2005
		<40 y. OR HER2 pos. OR lymphovascular invasion
		Shen H et al. 2015
		G3 OR lymphovascular invasion OR triple negative
		Different publications

Comment: In case of an indication for radiotherapy of regional lymph nodes, radiotherapy of the chest wall should also be administered

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Boost in PMRT

	Oxford		
	LoE	GR	AGO
▪ An additional boost irradiation to a part of the chest wall has not been shown to improve DSS and overall survival	2a	B	
▪ An additional boost irradiation to a part of the chest wall should be given in case of of R1/R2-resection, if secondary resection is not feasible	5	D	++
▪ In case of tumor extention to the pectoral resection margin, but no clinical signs of extention beyond the fascia, the resection margin should be regarded as R0 (provided, that the pectoral fascia was resected). A boost radiotherapy is not required in this situation	5	D	++

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

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

* Study participation recommended

** Macrometastases

+ <T3, no palpable LN, R0, 1-2 positive SN, no extracapsular extention, no NACT

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Additional RT of the axilla after primary surgery

(in case of an indication for RT of the breast/chest wall[1] +/- supra-/infraclavicular and internal mammary node RT[2])

Expansion of the PTV (planning target volume) to level I-II[3]

	Oxford		
	LoE	GR	AGO
pN-status			
pN0(sn)/pN1mic(sn)	1b	B	--
pN0/+ after ALND	1a	A	--
pN+(sn) in analogy to ACOSOG Z0011 (no ALND)	2b	B	+
pN+(sn) not fitting ACOSOG Z0011-criteria → RT in analogy to AMAROS[4] (no ALND)	1b	B	++
R2-situation in the axilla	5	D	++

[1]Incidental dose to parts of level i/II is inevitable. [2]The indication for supra-/infraclavicular and internal mammary node RT has to be assessed separately. [3]Cranial border 5 mm below the axillary vein. [4] ≤ T3, cN0, no NACT, always in conjunction with supra-/infraclavicular RT

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Additional RT of the axilla after neoadjuvant therapy

(in case of an indication for RT of the breast/chest wall[1] +/- supra-/infraclavicular and internal mammary node RT[2])

Expansion of the PTV (planning target volume) to level I-II[3]

N-status pre/post NACT	pN-status	Oxford LoE	Oxford GR	AGO
cN0 / ycN0	ypN0(sn)	5	D	-
cN0 / ycN0	ypN1mic(sn)/ypN+(sn) (no ALND)	5	D	+[4]
$pN+_{CNB}$ / ycN0	ypN0(sn/TAD)	5	D	+/-[4]
$pN+_{CNB}$/ ycN0	ypN1mic(sn/TAD)/ypN+(sn/TAD) (no ALND)	5	D	+[4]
cN0/cN+	ypN0/+ after ALND	2b	B	-
	R2-situation in the axilla	5	D	++

[1]Incidental dose to parts of level i/II is inevitable. [2]The indication for supra-/infraclavicular and internal mammary node RT has to be assessed separately. [3]Cranial border 5 mm below the axillary vein. [4]Study participation recommended.

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

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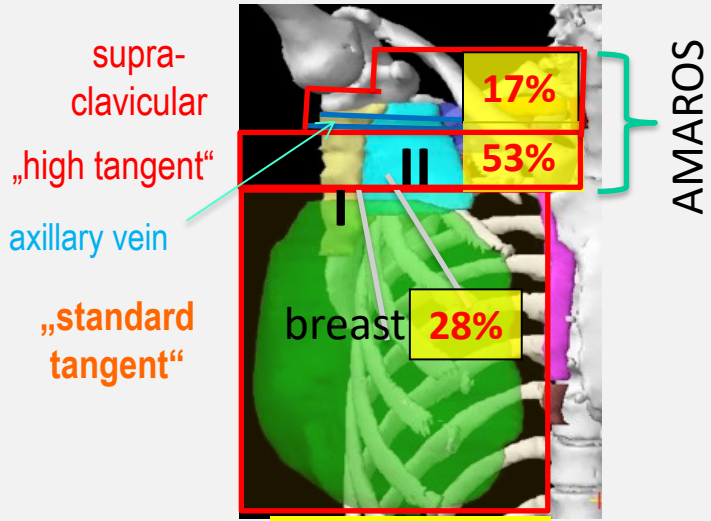
ACOSOG Z0011 Trial

45% micrometast. in the exp. arm

RT-volume
% of patientis



	mean dose*	encompassed volume**
LN level 1		
AMAROS	>95%	>95%
high tangent	86%	79%
standard tangent	66%	51%
IMRT+	29%	1%
LN-level 2		
AMAROS	>95%	>95%
high tangent	71%	51%
standard tangent	44%	26%
IMRT+	7%	0%

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

Data from 228/856 pat.

Jagsi (2): “The results of Z0011 should not be extrapolated to patients who receive RT using partial-breast or prone techniques, in which substantially less of the axilla is included”

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

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	Oxford		
	LoE	GR	AGO
RT to supra-/infraclavicular lymphatic regions			
▪ ≥ 4 positive axillary lymph nodes (LN) or involved LN in level III or in supra-/infraclavicular LN	1b	A	++
▪ 1–3 positive axillary lymph nodes[1] in case of - central or medial tumor and G2-3 or ER/PR-negative - premenopausal patient and G2-3 or ER/PR-negative	2a	B	+
▪ pN0 with central or medial tumors, if premenopausal and G2-3 and ER/PR-negative	2a	B	+/-

[1] not applicable for micrometastases

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

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	Oxford		
	LoE	GR	AGO
Internal mammary lymph node region (IMN)			
▪ pN0 high-risk with central or medial tumor and premenopausal and G2-3 and ER/PR-negative	1b	B	+/-
▪ 1–3 positive axillary lymph nodes[1] in case of - central or medial tumor and G2-3 or ER/PR-negative - premenopausal patient and G2-3 or ER/PR-negative	2a	B	+
▪ ≥ 4 positive axillary lymph nodes	2a	B	+
▪ involved internal mammary lymph nodes	2a	B	+
▪ In case of cardiac risk factors or if trastuzumab is given	2b	A	--

[1] not applicable for micrometastases

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Fractionation of Radiotherapy in Case of Regional Nodal Irradiation

	Oxford		
	LoE	GR	AGO
▪ Conventionally fractionated radiotherapy (total dose about 50 Gy in approx. 25-28 fractions within 5–6 weeks)	1a	A	++
▪ Hypofractionated radiotherapy (total dose approx. 40–43.5 Gy in 15-16 fractions within 3–5 weeks)	2b	B	+/-

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Hypofractionated post-mastectomy radiotherapy and regional nodal irradiation

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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."

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

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(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

Poortmans et al. ECCO Amsterdam 2013

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Radiotherapy following NACT

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Pretreatment	Posttreatment	RT-BCS	PMRT	RT-RN
Locally advanced	pCR / no pCR	yes	yes	yes
cT1/2 cN1+*	ypT1+ o. ypN1 + (no pCR)	yes	yes	yes
cT1/2 cN1+*	ypT0/is ypN0	yes	Increased risk of relapse[1]	
cT1/2 cN0 (Sonogr.bligat)	ypT0/is ypN0	Ja	nein	nein

Oxford		
LoE	GR	AGO
1a/1a/1a	A/A/A	++/++/++
1a/2b/2b	A/B/B	++/+/+
2b/2b/2b	B/B/B	+/+/+
2b/2b/2b	A/B/B	+/-/-

Locally advanced: T3-4 or cN2-N3,

[1] Criteria for increased risk of relapse:

- **pN0 premenopausal high risk: central or medium tumor localization, and (G2-3 and ER/PR-neg.)**
- **pretreatment pN1a/ cN+* high risk: central or medium tumor localization and (G2-3 or ER/PR-neg.) or premenopausal, lateral tumor localization and (G2-3 or ER/PR-neg.)**

*** Regarding coverage of axilla level I/II please also see slides „Additional RT of the axilla after primary surgery“ and „Additional RT of the axilla after neoadjuvant therapy“**

**** = confirmed by core biopsy**

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Molecular predictors and use of radiotherapy

	Oxford		
	LoE	GR	AGO
▪ Results of gene expression profiling should not be used for indication of radiotherapy	2b	B	++

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Use of concomitant systemic therapy with adjuvant locoregional radiotherapy

	Oxford		
	LoE	GR	AGO
▪ Trastuzumab/Pertuzumab*	1a	A	++
▪ T-DM1	1b	A	+
▪ Tamoxifen	2b	B	+
▪ Aromatase inhibitors	2b	B	+
▪ Checkpoint inhibitors	2b	C	+
▪ Capecitabine	2b	B	+**
▪ CDK4/6-inhibitors	4	C	+/-***

* concurrent Trastuzumab/Pertuzumab and parasternal radiotherapy should be avoided

** with hypofractionated RT approx. 40 Gy, consider dose reduction of Capecitabine, Pat. at high-risk for locoregional recurrence

*** In currently available phase III-trials (monarchE, PALLAS, Penelope-B) RT was given before initiation of CDK4/6-inhibitors. No definitive signs of significantly increased toxicity with concomitant RT in the palliative setting.

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Simultaneous Capecitabine with locoregional radiotherapy

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/m^2 twice daily continuously beginning on the first day of RT. **Because of observed excess grade 3 toxicity the protocol was amended,** and subsequent patients received CAP only on RT days (5 days per week)."
- "Noncontinuous CAP dosing was much better tolerated than continuous dosing. **Thirteen of 26 patients (50%) had grade ≥3 and higher treatment-related dermatologic toxicity**. "

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

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

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Smoking and Risk of secondary lung cancer

	Oxford		
	LoE	GR	AGO
▪ Increased risk of lung cancer secondary to breast cancer radiotherapy in smokers	1a	A	
▪ Inform patients about risk			++
▪ Recommend to stop smoking			++

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