

# Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Version 2023.1E

## Loco-Regional Recurrence

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# Loco-regional Recurrence Incidence and Prognosis

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Localization	10-y. incidence (%)	5-y. Overall Survival (%)
<b>Ipsilateral recurrence<sup>1</sup> (post BEO + irradiation)</b>	<b>10 (2–20)</b>	<b>65 (45–79)</b>
<b>Chest wall<sup>1</sup> (post mastectomy)</b>	<b>4 (2–20)</b>	<b>50 (24–78)</b>
<b>As above plus supraclavicular fossa<sup>2</sup> Axilla:</b>	<b>34</b>	<b>49 (3-y. OS)</b>
<b>After ALND<sup>1</sup></b>	<b>1 (0.1–8)</b>	<b>55 (31–77)</b>
<b>After SLNE<sup>4</sup></b>	<b>1</b>	<b>93</b>
<b>Multiple localizations<sup>2</sup></b>	<b>16 (8–19)</b>	<b>21 (18–23)</b>

<sup>1</sup> Haffty et al. Int J Radiat Oncol Biol Phys 21(2):293-298, 1991;

<sup>2</sup> Reddy JP. Int J Radiat Oncol Biol Phys 80(5):1453-7, 201;

<sup>3</sup> Karabali-Dalamaga S et al. Br Med J 2(6139):730-733,1978;

<sup>4</sup> Andersson Y, et al. Br J Surg 99(2):226-31,2012

# Loco-regional Recurrence Staging

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## Examinations before treatment

- Tissue biopsy
- Re-assessment of ER, PR, HER2
- Complete re-staging (slice imaging\*)
- „Liquid biopsy“

Oxford		
LoE	GR	AGO

3b	B	++
3b	B	++
2b	B	++
5	D	-

\* Standard: CT thorax / abdomen and bone scan, in certain cases whole body MRI or <sup>18</sup>F FDG PET-CT may be used

# Risk Factors for another Relapse\*

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	Oxford		
	LoE	GR	AGO
▪ <b>Tumor size</b>	2a	B	
▪ <b>Multifocality</b>	2a	B	
▪ <b>Localisation</b>	2b	B	
▪ <b>Negative progesterone receptor</b>	3b	B	
▪ <b>High grade</b>	3b	C	
▪ <b>Omitted radiotherapy at first recurrence</b>	3b	C	
▪ <b>Omitted chemotherapy at first recurrence</b>	3b	C	
<b><u>Parameters of the locally recurrent tumor to define the risk for distant metastasis / survival</u></b>			
▪ <b>Early (&lt; 2-3 yrs.) vs. late recurrence</b>	2b	B	
▪ <b>LVSI / Grade / ER-neg / positive margins (if ≥ 2 factors positive)</b>	3b	B	
<b><u>Predictive factors for treatment considerations</u></b>			
▪ <b>HER2</b>	2b	B	++
▪ <b>ER and PR</b>	2b	B	++

\* Risk factors for local relapse see chapter “prognostic factors”

# Ipsilateral Locoregional Recurrence Surgical Treatment

## Oxford

LoE GR AGO

	LoE	GR	AGO
▪ <b>After mastectomy: wide exzision (aim R0)</b>	3b	B	++
▪ <b>After BCS:</b>			
▪ <b>Mastectomy (aim: R0)</b>	3b	B	++
▪ <b>Re-BCS with tumor-free margins (R0) +partial breast irradiation*</b>	2b	B	+
▪ <b>Re-BCS with tumor-free margins (R0)</b>	2b	B	+/-
▪ <b>rcN0:</b>			
▪ <b>Axillary intervention after prior AxDis</b>	4	C	-
▪ <b>Re-SLNE after prior SLNE</b>	2a	B	-
▪ <b>rfnN+: (Re-)Axillary dissection (R0)</b>	5	C	+
▪ <b>Palliative surgery in M1-situation or R0 not achievable (e.g. pain, ulceration, psychosocial indication)</b>	5	D	+

\* After consideration of risk factors for repeated relapse (time from primary diagnosis, tumor size)

# Mastectomy vs. BCS + Partial Breast Irradiation

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- **1327 pts. from 7 European countries with first local recurrence 01/1995 - 06/2017**
- **ME vs. BCS + Brachytherapy**
- **Propensity Score matched control (1:1): clinical and histopathological factors**
- **Primary endpoint: 5-y OS; secondary endpoints: e.g. 5-y-DFS, complications**
- **Median follow-up 75.4 months**
- **No differences in 5-y OS and sec. Endpoints: 5-y -OS: 88 vs. 87%**
- **cumulative incidence 2. recurrence: 2.3 vs. 2.8%**
- **5-y incidence of mastectomy after 1. recurrence 3.1%**

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# Loco-regional Recurrence after R0-Resection Systemic Treatment

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**According to pathohistological re-evaluation of the recurrent tumor (ER, PR, HER2) and in consideration of time from primary diagnosis, pre-treatment, co-morbidities and patient's preference**

	Oxford		
	LoE	GR	AGO
■ Endocrine therapy in endocrine responsive tumors	2b	B	++
■ Chemotherapy (consider preoperative) in particular in case of first HR-negative relapse	2b	B	+
■ In case of HER2-positive disease, chemotherapy + HER2-targeted therapy	5	D	+



# Locoregional Recurrence Chemotherapy

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## ■ CALOR Trial update

- **n = 163 (2003–2010), median follow-up of 4.9 years, all R0 resection**
- **5-y DFS: 69% (95% CI 56–79) with chemotherapy vs. 57% (44–67) without chemotherapy (hazard ratio 0.59 [95% CI 0.35–0.99]; p = 0.046): 24 (28%) patients vs. 34 (44%).**
- **Adjuvant chemotherapy was significantly more effective in ER negative disease ( $p_{\text{interaction}} = 0.046$ ).**
- **Multivariate analysis: predictors of survival**
- **chemotherapy for primary cancer (HR 3.55, p = 0.03)**
- **interval from primary surgery (HR 0.87, p = 0.05)**

# Loco-regional Recurrence Chemotherapy

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## ■ CALOR Trial update

	ER-positive			ER-negative		
Endpoint	CT	No-CT	HR (95% CI)	CT	No-CT	HR (95% CI)
10-yr DFS	50%	59%	1.07 (0.57 – 2.00)	70%	34%	0.29 (0.13 – 0.67)
	Interaction P-Value =0.013					
10-yr OS	76%	66%	0.70 (0.32 – 1.55)	73%	53%	0.48 (0.19 – 1.20)
	Interaction P-value =0.53					
10-yr BCFI	58%	62%	0.94 (0.47 – 0.85)	70%	34%	0.29 (0.13 – 0.67)
	Interaction P-value = 0.034					

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# Locoregional Recurrence in Case of R1-Resection / Inoperability – Systemic Treatment

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**According to pathohistological re-evaluation of the recurrent tumor (ER, PR, HER2)**

- **Endocrine based therapy in endocrine responsive tumors corresponding to metastatic disease**
- **Chemotherapy and targeted therapy (pre- or postoperative) corresponding to metastatic disease**

Oxford		
LoE	GR	AGO

2b	B	++
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2b	B	++
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# Ipsilateral breast tumor recurrence after BCT – Radiotherapy

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	Oxford		
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<b><u>After Re-BCS</u></b>			
▪ Whole breast irradiation (in case of no prior adjuvant radiotherapy)	3b	C	++
▪ Repeated (2.)-breast irradiation (Partial breast irradiation, brachytherapy/ external beam RT, in case of prior adjuvant radiotherapy) *	2b	B	+
<b><u>After mastectomy</u></b>			
▪ Radiation of chest wall +/- regional lymph nodes (in case of no prior adjuvant radiotherapy, according to risk factors)	2b	B	+
▪ Radiation dose escalation	3b	C	-
▪ Repeated (2.) irradiation			
▪ in case of R0 resection (according to risk factors)	3b	B	+/-
▪ in case of R1/R2 resection (e.g. as brachytherapy)	3b	B	+
▪ Additional regional hyperthermia (especially for R1/2-resections)	1a	B	+/-

\* Preoperative consultation with Radiation Oncology to determine if re-irradiation is possible.

# Thoracic wall recurrence after mastectomy and axillary recurrence – Radiotherapy

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	Oxford		
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<b><u>Thoracic wall recurrence after mastectomy</u></b>			
▪ <b>No prior radiotherapy</b>			
▪ Curative situation: Radiotherapy to the thoracic wall +/- regional nodal irradiation	2b	B	+
▪ <b>Re-irradiation of the thoracic wall</b>	3b	B	+/-
▪ R0-resection	3b	B	+/-
▪ R1/2-resection (e.g. brachytherapy)	3b	B	+
▪ Additional regional hyperthermia (especially for R1/2-resections)	1a	B	+
<b><u>Axillary recurrence</u></b>			
▪ <b>Radiotherapy to the axilla (R0-resection)</b>			
▪ No prior radiotherapy to the axilla	3b	C	+
▪ Prior radiotherapy to the axilla	5	D	+/-

# Loco-Regional Recurrence

## Treatment Options in Non-Curative Cases

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■ <b>Concomitant radio-chemotherapy</b>	<b>3b</b>	<b>C</b>	<b>+</b>
■ <b>Hyperthermia (in centers listed on DKG website)</b>			
■ In combination with radiotherapy	<b>1b</b>	<b>B</b>	<b>+</b>
■ In combination with chemotherapy	<b>4</b>	<b>C</b>	<b>+/-</b>
■ <b>Intra-arterial chemotherapy</b>	<b>4</b>	<b>C</b>	<b>+/-</b>
■ <b>Photodynamic therapy</b>	<b>4</b>	<b>C</b>	<b>+/-</b>
■ <b>Electrochemotherapy</b>	<b>3b</b>	<b>C</b>	<b>+/-</b>