Guidelines Breast
Version 2009.1.0

Adjuvant Radiotherapy

START

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Adjuvant Radiotherapy (RT)

- **Version 2002:**
  Souchon / Seegenschmiedt
- **Version 2003–2008:**
  Blohmer / Souchon / Seegenschmiedt
- **Version 2009:**
  Souchon / Göhring

Further Information

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Postmastectomy Radiotherapy (PMRT)*

	Oxford / AGO LoE / GR		
➢ >3 tumor infiltrated lymph nodes (Lnn.)	1a	A	++
➢ ≥ pN1a (depending on patients' age)	1a	A	+
➢ pT 3	1a	A	++
➢ pT3 pN0	2c	C	+/-
➢ T 4	1a	A	++
➢ If R0 is impossible to reach	1a	A	++
➢ After primary systemic treatment (PST) based on the initial stage prior to PST (cN+, cT3/4a-d)	2a	A	++
➢ In young pts with high risk features	3b	C	++
➢ RT of supra-/infraclav. region in > 3 Lnn.	1a	A	++
* Indications for PMRT is independent of adjuvant systemic treatment	1a	A	++

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RT of the Breast after Breast Conserving Surgery (BCS)

	Oxford LoE	AGO GR	
➢ **Whole breast irradiation (WBI)**	1a	A	++
➢ **Consider hypofractionated WBI in selected pts**	2a	B	+/-
➢ **Partial breast irradiation (PBI)**	3	C	+/-*
No long term follow up! Only as part of prospective trials!			
➢ **Boost-irradiation (improves local control)**	1b	A	+
➢ **Absolute benefit depending on patient's age**	1b		
➢ **Dose-effect relationship independ't of pts.' age**	1b		
➢ **Boost-irradiation in node-negative, endocrine responsive tumors after complete resection**	3a	C	+/-

*Study participation recommended

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Boost RT after BCS in Invasive Carcinoma

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	Oxford / AGO LoE		
➢ **Improved local tumor control**	1b	A	+
➢ **All ages: LRR reduction (12 ≥ 7%)**	1b	A	+
➢ **< 40 years: LRR reduction (29 ≥ 10%)**	1b	A	++
➢ **Additional boost RT does not impact survival**			

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Side effects of radiotherapy

- **Independant prognostic factors (p< 0.01) of fibrosis with an increase of moderate/severe fibrosis rate from 13% to 28% (med. f/u: 10.7 yrs.):**
  - ✓ **Maximum irradiation dose: increasing risk with increasing maximum WBI dose**
  - ✓ **Boost (26.9%) vs no boost (12.6%): HR = 2.3, CI 95%: 1.97-2.69, p=0,0001**
  - ✓ **Boost technique, energy of electron boost (MeV)**
  - ✓ **Concomitant CTX: increased with concomitant CTX**
  - ✓ **Tamoxifen vs. no tamoxifen: increased in postmenopausal woman receiving adjuvant tamoxifen**
  - ✓ **Postsurgery complication: increased for pts with postoperative breast edema or haematoma**

Note: Side effects of radiotherapy are

- ✓ **Independent of age**
- ✓ **Decreased, if WBI was delivered with >6 MV photons**

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Fraction Size in RT for Breast Conservation in Early Breast Cancer

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Prospective randomised trials comparing different concepts of hypofractionation versus standard fractionated adjuvant radiotherapy following breast conserving surgery

			Standard	Hypofractionation	p (to standard)		p (to standard)		
Study	n	f/u yrs	Local relapse %	Local relapse	Local relapse	Survival	Late effects	Dose (Gy)	# of fractions
Canadian[a]	1234	10	6.7					50	25
Canadian[a]		10		6.2	n.s.	n.s.	n.s.	42.5	16
RMH/GOC[b]	1410	10	12.1					50	25
RMH/COG[b]		10		9.6	n.s.	n.s.	0.001 worse	42.9	13
RMH/COG[b]		10		14.8	n.s.	n.s.	n.s.	39	13
START A[c]	2236	5	3.5					50	25
START A[c]		5		3.4	n.s.	n.s.	n.s.	41.6	13
START A[c]		5		5.0	n.s	n.s.	0.01 better	39	13
START B[d]	2215	5	3.5					50	25
START B[d]		5		2.3	n.s.	0.03 better	n.s.	40	15
Total	7095								

a: Whelan T et al. J Natl Cancer Inst 2002; 94:1143-50; b: Owen JR et al. Lancet Oncol 2006;7:467-471; c: START Trialists' Group. Lancet Oncol 2008;9:331-41; : START Trialists' Group. Lancet 2008;371(9618):1098-107; James ML et al. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD003860

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Radiotherapy of the Axilla

	Oxford / AGO LoE / GR		
➢ No irradiation if sentinel node is negative	1	B	++
➢ Clinically involved (N1, N2a), SN+ and no or incomplete axillary clearing	3b	B	++
➢ Postoperative tumor residuals	2b	B	++
➢ In case of contraindication or patients withdrawal of sufficient axillary clearing	2b	C	+

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Radiotherapy (RT) of Other Locoregional Lymph Node Areas

	Oxford / AGO LoE	GR	
RT of supra-/infraclavicular lymph nodes:			
➢ Level III involved	3b	B	+
➢ In case of RT of the axilla	3b	B	+
➢ pN1a (1–3)	1b	B	+/-
➢ pN2a (> 3) (if only clearance of level I)	2a	B	+
➢ (p)N3a-c	3a	B	++
➢ Following axillary clearing of level I + II	3b	D	-
➢ SNB tumor-free	4	D	-
➢ In case of contraindication or patients withdrawal of sufficient axillary clearing	2b	C	+/-
➢ **RT of internal mammary lymph nodes**	4	D	-

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Radiotherapy of Other Locoregional Lymph Node Areas

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	Oxford / AGO LoE	GR
➢ Internal mammary lymph node irradiation*:	4	D -
Due to the lack of sufficient data individual decision in case of:		
➢ N2b, N3b		
➢ ≥pN1b (involvement of internal mammary lymph node detected by SNB)		
➢ pN1c–pN3	3b	D +/-

* The role of RT of internal mammary lymphatics is subject of ongoing clinical trials; study participation is recommended

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Key Points

- **The best results for all clinical endpoints can be obtained by an optimal combination of surgery, systemic treatment and radiotherapy. This might be considered as a plea for dedicated breast cancer centers.**
- **Adjuvant systemic treatment has a positive effect on survival (LoE 1a)**
- **The influence of adjuvant systemic treatment on locoregional control is existing but not large enough to obviate the use of radiation therapy (LoE 1a)**
- **Both, adjuvant systemic treatment and radiotherapy should be started as soon as possible after surgery (LoE 2a)**
- **Combined chemotherapy and radiotherapy leads to a higher risk of especially late toxicity: the sequential administration is therefore preferred (LoE 2b)**
- **The sequence can be discussed on a patient per patient base depending on type (especially the duration) of treatment and the individual patients‘ risk factors**

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Trastuzumab in Combination with Concurrent Radiotherapy

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	Oxford / AGO LoE / GR		
Trastuzumab concurrent with radiotherapy	2b	B	+

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Remaining Questions

- **The most appropriate sequence of radiation therapy, chemotherapy, endocrine treatment as well as trastuzumab treatment in HER-2 positive breast cancers might very well remain to stay unknown.**

Poortmans P. Evidence based radiation oncology: breast cancer. Radiother Oncol 2007;84:84-101

Further Information

References