

Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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Breast Cancer Surgery Oncological Aspects

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Breast Cancer Surgery

Oncological Aspects

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- **Version 2021:**
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AGO: ++

Surgery is one sub-step out of multiple steps in breast cancer treatment. Thus, both diagnostic and oncological expertise are an essential requirement for every breast surgeon.

AGO: +

Avoidance of a significant delay in cancer treatment

Pre-therapeutic Assessment of Breast and Axilla

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	Oxford		
	LoE	GR	AGO
■ Clinical examination	5	D	++
■ Mammography	2b	B	++
■ Tomosynthesis (DBT)***	2b	B	+
■ Contrast-enhanced mammography (alone or as adjunct)	2a	B	+
■ Sonography (breast and axilla)	2b	B	++
■ MRI*	1b	B	+
■ Minimally invasive biopsy**	1b	A	++
■ Axilla CNB, if lymph node is suspect	2b	B	++
■ Breast-CT	5	D	-

* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions (in house or with cooperations). Individual decision for patients at high familiar risk, with dense breast (density C/D), lobular invasive tumors, suspicion of multilocular disease. No reduction in re-excision rate.

** Histopathology of additional lesions if relevant for treatment

*** replacement of FFDM with SM

Pre-therapeutic Staging

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	Oxford		
	LoE	GR	AGO
History and clinical examination	5	D	++
CT scan of thorax/abdomen	2a	B	+
Bone scan	2b	B	+
Chest X-ray	5	C	+/-
Liver ultrasound	5	D	+/-
In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)	2a	B	+
FDG-PET or FDG-PET /CT**	2b	B	+/-
Whole body MRI	4	C	+/-

- History and clinical examination

Additional diagnosis for patients with tumors of high metastatic potential and/or symptoms and/or indication for (neo-)adjuvant chemotherapy and/or antibody-therapy):

- CT scan of thorax/abdomen
- Bone scan
- Chest X-ray
- Liver ultrasound
- In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)
- FDG-PET or FDG-PET /CT**
- Whole body MRI

* Contrast enhanced ultrasound

** especially in patients with high tumor stage (III) if available

Evidence of Surgical Procedure

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	Oxford	
	LoE	GR
<ul style="list-style-type: none"> Survival rates after lumpectomy + RT are equivalent to those after (modified) radical mastectomy 	1a	A
<ul style="list-style-type: none"> Local recurrence rates after skin sparing mastectomy are equivalent to those after mastectomy 	2b	B
<ul style="list-style-type: none"> Conservation of the NAC (nipple areola complex) is an adequate surgical procedure if R0 resection is achieved 	2b	C

Breast Conservation: Surgical Technical Aspects

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- **Wire guided localization**
- **Wireless intraoperative ultrasound localization***
- **Other procedures (Radionuclide guided localization/RADAR reflection, Magnetic Seeds**, RFID)**

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

***The lesion must be visualized by the same examiner pre- and intraoperatively in its whole extension. Adequate equipment and training of the surgeon are mandatory**

****not adequate for MRI-FU under NACT**

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	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ▪ Tumor-free margins required (also in unfavorable biology, „no ink on tumor“ is sufficient) 	2a	A	++
<ul style="list-style-type: none"> ▪ Re-excision required for involved margins (paraffin section) 	3b	C	+
<ul style="list-style-type: none"> ▪ Therapeutic stereotactic excision alone 	4	D	--
<ul style="list-style-type: none"> ▪ Ultrasound guided surgery to prevent re-excision 	2a	B	+
<ul style="list-style-type: none"> ▪ Intraoperative margin evaluation (with Margin Probe®) 	1b	A	+/-
<ul style="list-style-type: none"> ▪ Specimen radiography or ultrasound 	2b	B	++

Breast Conservation Surgery (BCS)

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- **Multicentric disease (MF/MZ)
(R0-resection of all lesions)**
- **Positive microscopic margins after repeated
excision**
- **Inflammatory breast cancer**

Oxford		
LoE	GR	AGO
2b	B	+
2b	B	--
2b	B	--

**For surgery after neoadjuvant chemotherapy
see chapter „neoadjuvant chemotherapy“**

Primary Axillary Lymph Node Dissection (ALND) I



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	Oxford		
	LoE	GR	AGO
▪ Endpoint: Survival	3	D	-
▪ Endpoint Staging	3	A	-
▪ Endpoint: Locoregional control	2a	A	+/-
▪ pN+ (pre-surgery) without neoadjuvant systemic therapy	2a	B	+
▪ cN0 pN0(sn)(i+)	1b	A	--
▪ cN0 pN1(mi)	2b	B	--
▪ cN0 pN 1(sn) (cT1/2 , < 3 SN +, BCS + tangential radiation field, adequate systemic therapy)	1b	A	-
▪ cN0 pN1 (sn) and mastectomy (no chestwall radiotherapy)	1b	B	+*
▪ cN0 pN1(sn) and mastectomy (T1/2, <3SN+) (chestwall radiotherapy)	5	D	+/-*
▪ ALND indicated, but not feasible			
▪ Radiotherapy according to AMAROS-trial (validated for cN0 pN1sn)	1b	B	+

* Study participation recommended

Axillary Surgery and NACT

Oxford
LoE GR AGO

SLNE after NACT
SLNE before NACT

2b B ++
2b B -

cN-Status (before NACT)	pN-Status (before NACT)	cN-Status (after NACT)	Surgical procedure (after NACT)	pN-Status (after NACT and Surgery)	Surgical consequence from histology**			
cN0	—	ycN0	SLNE alone	ypN0 (sn)	—	2b	B	++***
				ypN0 (i+) ypN1 _{mic} (sn)	ALND	2b	C	+ (+/- at i+)
					none **	5	D	+/-
				ypN1 (sn)	ALND	2b	C	++
none **	5	D	+/-					
cN+	pN _{CNB}	ycN0	SLNE alone* TAD (TLNE + SLNE)* ALND*	ypN0 ypN0 ypN0	—	2b 2b 2b	B B B	+/-*** +*** +***
			SLNE alone* TAD (TLNE + SLNE)*	ypN+ incl. ypN0 (i+)	ALND	2b	B	+ (+/- at i+)
			ALND	ypN+	—	2b	B	++
			none	n.d.	none**	5	D	-
cN+	pN _{CNB}	ycN+	ALND	ypN+ incl. ypN0 (i+)	—	2b	B	++
			none	n.d.	none**	5	D	-

*Study participation (Axsana) recommended; ** s. Recommendations chapter Radiotherapy, irradiation alone is not recommended in case of pN1(sn) and pN+ ; ***recommendation grade concerning to staging at cN0 and cN+ ypN0

Improvement of the False-Negative Rate of SLNE in Patients with pN+_{CNB} before NACT and ycN0 after NACT

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	Oxford		
	LoE	GR	AGO
▪ Removal of > 2 SLNs (SLNE, no untargeted axillary sampling)	2a	B	+
▪ Combined tracer	2a	B	+/-
▪ IHC and serial sections to detect ITC or micrometastases	2b	B	+
▪ Localization of pos. LN before NACT	2b	B	+*
▪ Targeted Axillary Dissection (TAD = TLNE + SLNE)	2b	B	+*
▪ TLNE only	2b	B	+/-*

* Study participation recommended

Reduction of individual failures for SLNB in pN1 ypN0

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- **Predictive factors for axillary remission
pN1 (before NACT) to ypN0_{sn/TAD} (after NACT)**
 - Young age
 - Intrinsic Subtype (ER neg, HER 2 pos)
 - Grade 3
 - N1 (vs N2)
 - pCR (breast)

Sentinel Lymph Node Excision (SLNE)

Indications I

	Oxford		
	LoE	GR	AGO
■ Clinically / sonographically negative axilla (cN0)	1b	A	++
■ Add CNB in cN1 (clinically/sonographically suspicious) in order to enable SLNB	2a	B	+
■ cT 1–2	2b	A	++
■ cT 3–4c	3b	B	+
■ Multifocal / multicentric lesions	2b	B	+
■ DCIS			
■ Mastectomy	3b	B	+
■ BCT	3b	B	-
■ DCIS in male	5	D	+/-
■ Male breast cancer	2b	B	+
■ In elderly patients	3b	B	+

- Clinically / sonographically negative axilla (cN0)
 - Add CNB in cN1 (clinically/sonographically suspicious) in order to enable SLNB
- cT 1–2
- cT 3–4c
- Multifocal / multicentric lesions
- DCIS
 - Mastectomy
 - BCT
 - DCIS in male
- Male breast cancer
- In elderly patients

Sentinel Lymph Node Excision (SNLE)

Indications II

Oxford

	LoE	GR	AGO
▪ During pregnancy and / or breast feeding (only ^{99m}Tc-colloid, no blue dye)	3	C	++
▪ After prior tumor excision	2b	B	+
▪ After prior major breast surgery (e.g. reduction mammoplasty)	3b	C	+/-
▪ Ipsilateral breast recurrence after prior BCS and prior SNLE	4	D	-
▪ SLNE in the mammary internal chain	2b	B	-
▪ After axillary surgery	3b	B	+/-
▪ Prophylactic bilateral / contralateral mastectomy	3b	B	--
▪ Inflammatory breast cancer	3b	C	-

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Sentinel Lymph Node Excision (SLNE) Marking

Oxford

- **^{99m}Tc colloid**
- **Preoperative lymphoscintigraphy (added information limited, but mandatory by legal regulations)***
- **Patent blue dye**
- **Methylen blue**
- **Indocyanin green (ICG)**
- **SPIO#**

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

* In Germany required for quality assurance of nuclear medicine

SPIO: Superparamagnetic Iron Oxide

Procedure after Neoadjuvant Therapy

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- **Early marking of tumor (incl. detailed topographic documentation)**
- **Surgical removal of tumor / representative excision of post-therapeutic, marked tumor area**
- **Tumor resection in new margins**
- **Microscopically clear margins**

Oxford		
LoE	GR	AGO
5	D	++
2b	C	++
2b	C	++
2a	B	++

**For „Surgery after neoadjuvant chemotherapy“
see chapter „Neoadjuvant chemotherapy“**

Adjuvant Therapy after Primary Surgery

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	LoE	GR	AGO
<ul style="list-style-type: none"> Start adjuvant systemic therapy and radiotherapy (RT) as soon as possible (asap) after surgery 	1b	A	++
<ul style="list-style-type: none"> Start of adjuvant chemotherapy +/- HER2 therapy asap after surgery, prior to RT 	1b	A	++
<ul style="list-style-type: none"> Without cytotoxic therapy +/- anti-HER2 therapy: <ul style="list-style-type: none"> Start RT 6–8 weeks after surgery Start endocrine therapy asap after surgery Endocrine therapy concurrent with radiotherapy 	2b	B	++
	5	D	++
	3b	C	+