

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Breast Cancer: Specific Situations

Breast Cancer: Specific Situations

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- **Versions 2005–2019:**

**Dall / Fehm / Fersis / Friedrich / Gerber / Göhring /
Harbeck / Huober / Janni / Loibl / Lück / Lux / Maass /
Mundhenke / Müller / Oberhoff / Rody / Scharl / Schneeweiss / Schütz /
Sinn / Solomayer / Stickeler / Thomssen**

- **Version 2020:**

Ditsch / Kolberg-Liedtke

Breast Cancer: Specific Situations

- **Young patients**
- **Pregnancy- and breast-feeding-associated BC**
- **Elderly patients**
- **Male patients**
- **Inflammatory BC**
- **Occult Breast Cancer (Cancer of unknown primary – axillary CUP)**
- **Paget's disease**
- **Malignant and Borderline Phyllodes Tumor**
- **Angiosarcoma**
- **Breast Implant-Associated Anaplastic Large-Cell Lymphoma (BIA-ALCL)**
- **Metaplastic breast cancer**

Breast Cancer in Young Women ≤ 40 Years

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	Oxford		
	LoE	GR	AGO
■ Aggressive biological behavior with worse prognosis	2a	B	
■ Local therapy independent of young age	2b	B	+
■ Guidelines adapted (neo-)adjuvant systemic treatment (see respective chapters)	1b	A	++
■ GnRHa as ovarian protection (see chapter gynecological problems)	1a	B	+
■ Genetic and fertility counseling	2b	B	++
■ Contraception counseling	2b	B	++

Breast Cancer During Pregnancy* or Breast Feeding – Diagnostics and Surgery

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- Breast imaging and biopsy like in non-pregnant
- Staging if indicated (bone scan after delivery)
- Full body MRI (without contrast agent)
- Surgery like in non-pregnant patients
- Sentinel node excision (technetium only)
- SLNE during 1st trimester
 - Sensitivity and specificity not established (during lactation);
breast feeding should be avoided for 24 hrs
 - Blue dye (not tested in pregnant animals or humans)

Oxford		
LoE	GR	AGO
4	C	++
5	D	+
4	C	+/-
4	C	++
4	C	+
5	D	+/-
4	C	++
4	C	--

Breast Cancer During Pregnancy

- (Neo-)adjuvant Therapy -

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- Radiation therapy during pregnancy
- (Neo-)adjuvant chemotherapy only after first trimester (indication as in non-pregnant)
 - Anthracyclines: AC, EC
 - Taxanes
 - Platinum salts (carboplatin, cisplatin)
 - MTX (e.g. CMF)
- Endocrine treatment
- HER2-targeted treatment
- Bisphosphonates, denosumab

Oxford		
LoE	GR	AGO
4	C	-
		++
2b	B	++
2b	B	+
4	C	+/-
4	D	--
4	D	--
3a	C	--
4	D	-

Breast Cancer During Pregnancy*

– Delivery and Breast-Feeding –

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- **Delivery should be postponed until sufficient fetal maturation (avoid iatrogenic prematurity)**
- **Termination of pregnancy does not improve maternal outcome**
- **Delivery mode like in healthy women; avoid delivery during chemotherapy-induced leucocyte nadir**
- **If further systemic therapy is needed after delivery, breast feeding may be contra-indicated depending on drug toxicities**

	Oxford		
	LoE	GR	AGO
	2b	C	++
	3b	C	
	4	C	++
	5	D	++

* Participation in register study recommended

Breast Cancer and Pregnancy

– Family Planning –

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- After breast cancer diagnosis, reproductive techniques can be used to induce pregnancy
- Success rates for getting pregnant and for delivering a child lower in breast cancer patients compared to non-cancer patients
- Breast cancer patients of reproductive age should be offered fertility counseling before starting any kind of treatment
- Breast cancer patients should not be advised against getting pregnant independent of their tumor's hormone receptor status

Oxford		
LoE	GR	AGO
5	D	++
5	D	++
5	D	++
5	D	++

Pregnancy Associated Breast Cancer*: Outcome

**Oxford
LoE**

- **BC during pregnancy / lactation**
 - Adequate treatment is essential
- **Pregnancy and lactation after BC**
 - Outcome not compromised

3a

3a

* Participation in register study recommended

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Geriatric Assessment

- **No specific algorithm is available**
- **Ability to tolerate treatment varies greatly („functional reserve“)**
- **Comprehensive geriatric assessment (CGA) describes a multidisciplinary evaluation of independent predictors of morbidity and mortality for older individuals**
 - Physical, mental, and psycho-social health
 - Basic activities of daily living (dressing, bathing, meal preparation, medication management, etc.)
 - Living arrangements, social network, access to support services
- **Assessment tools:**
 - Charlson Comorbidity Index (widely used; good predictor over a 10-year period)
 - 12 prognostic indicators to estimate 4-year mortality risk
 - Short screening tests (more qualitative evaluation)
 - IADL (IADL = The Lawton Instrumental Activities of Daily Living Scale with 8 domains of function, that are measured), G8
 - Geriatric Prognostic Index (GPI), 3 parameters in oncological patients (psychological distress or acute disease, >3 prescribed drugs, neuropsychological problems)

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Treatment for Fit Elderly Patients

(Life Expectancy > 5 yrs. and Acceptable Comorbidities)

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- **Clinical geriatric assessment**
- **Treatment according to guidelines**
 - Surgery similar to „younger“ age
 - Endocrine treatment (endocrine responsive)
 - Chemotherapy (standard regimens)
 - < 70 years
 - > 70 years (especially N+, ER/PgR-)
 - Radiotherapy
 - Omit radiotherapy after BCS if low-risk and endocrine treatment
 - Trastuzumab

Oxford		
LoE	GR	AGO
2b	B	++
2a	C	++
2b	B	++
1a	A	++
1a	A	+
2a	C	+*
1a	A	+
1b	B	+
2b	C	+

* Study participation recommended

Treatment for Frail Patients

(Life Expectancy <5 yrs, Substantial Comorbidities)

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- **Reduced standard treatment**
- **Options extrapolated from trials in elderly:**
 - No breast surgery (consider endocrine options)
 - No axillary clearing (≥ 60 y, cN0, HR-pos)
 - No radiotherapy (≥ 65 y, pT1, pN0, HR-pos)
 - Hypofractionated radiotherapy
 - No chemotherapy if >70y and negative risk-benefit analysis

Oxford		
LoE	GR	AGO
2b	C	++
2b	C	+
2b	B	+
1b	B	++
2b	B	+
2b	C	+

Male Breast Cancer: Diagnostic Work-Up and Loco-Regional Therapy

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- **Diagnostic work-up as in women**
 - Mammography
 - Ultrasound
- **Standard-surgery: Mastectomy**
 - BCT is an option (tumor/breast relation)
 - Sentinel-node excision (SNE)
- **Radiotherapy as in women**
(consider tumor/breast relation!)
- **Genetic counseling if one additional relative affected**
(breast/ovarian cancer)
- **Screening for 2nd malignancies according to guidelines**

Oxford		
LoE	GR	AGO
4	C	+
3b	C	+/-
2b	B	++
4	C	++*
4	C	++*
2b	B	+
4	C	+
2b	B	++
GCP		++

* Participation in register study recommended

Male Breast Cancer: Systemic Therapy

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- **Adjuvant chemotherapy as in women**
- **HER2-targeted therapy (if HER2-positive)**
- **Endocrine therapy**
 - Tamoxifen
 - Aromatase inhibitors (adjuvant)
 - Aromatase inhibitors (metastatic BC)
 - GnRHa and AI (metastatic BC)
 - Fulvestrant (metastatic BC)
 - CDK4/6i (in combination) *
- **Palliative chemotherapy as in women**

Oxford		
LoE	GR	AGO
2a	B	++
5	D	++
4	D	++
2b	B	++
2b	B	.*
4	C	+/-
4	C	+*
4	C	+/-
2b	B	+
4	C	++

* Study participation recommended

Benefit from Trimodal Treatment in Inflammatory Breast Cancer

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Median survival probability		
Trimodal therapy	72 months	p<0.05
Surgery alone	26 months	

Overall survival-probability (OS)	10 years-OS	5 years-OS
Trimodal therapy	55.4%	37.3%
Surgery & chemotherapy	42.9%	28.5%
Surgery & radiotherapy	40.7%	23.5%
Surgery alone		16.5%

Multivariate analysis of OS	Hazard Ratio	95% CI
Surgery & chemotherapy & RT (trimodal therapy)	1.00	-
Surgery & chemotherapy	1.64	1.46 to 1.84
Surgery & radiotherapy	1.47	0.96 to 2.24
Surgery alone	2.28	1.80 to 2.89

Rueth et al. J Clin Oncol 2014; 32:2018–2024

Primary inflammatory breast cancer

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	5yr- OS	
pCR	77%	p<0.0001
Non-pCR	54%	
TN-IBC	37%	p<0.0001
other biologic subtypes (HR+/HER2–, HR+/HER2+, HR–/HER2+)	60%	

- N=8.550
- On multivariable analysis, TNBC, positive margins, and not receiving either chemotherapy, hormonal therapy or radiotherapy were independently associated with poor 5-year survival (p < 0.0001).

Inflammatory Breast Cancer (IBC, cT4d)

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- Invasive BC and clinical signs of inflammation (e.g. $\geq 1/3$ of the breast affected) determine stage cT4d
- Staging
- Skin punch biopsy (at least 2; detection rate < 75%)
- Treatment according to guidelines (neoadjuvant or adjuvant – as in non-IBC)
- Mastectomy after chemotherapy
 - Breast conserving therapy in case of pCR (individual)
 - Sentinel excision only
- Radiotherapy (PMRT)

Oxford		
LoE	GR	AGO
		++
2c	B	++
2c	B	+
2c	B	++
2c	B	+
2b	C	+/-
3b	C	-
2c	B	++

Axillary Metastasis in Occult Breast Cancer (Cancer of Unknown Primary – Axillary CUP)

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- **Incidence: < 1% of metastatic axillary disease**
- **In > 95% occult breast cancer, < 5% other primary**
- **Immunohistology**
 - ER-positive: 55%**
 - HER2 3+: 35%**
 - Triple-negative: 38%**
- **Nodal status:**
- **1 - 3 Ln-Met. in 48%**
> 3 Ln-Met in 52%
- **Outcome similar or better than in breast cancer with similar tumor biology and tumor stage**

Axillary Metastasis in Occult Breast Cancer (Axillary CUP) Imaging Diagnostics

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- **Mammography, Breast-ultrasound, Breast-MRI**
- **Exclude contralateral cancer**
- **Exclude non-breast malignancy, especially in case of TNBC** (e.g. skin, female genital tract, lung, thyroid gland, stomach)
- **Staging** (CT thorax / abdomen, thyroid scintigraphy, HNT-exam)
- **PET / PET-CT**

Oxford		
LoE	GR	AGO
3	B	++
3	B	++
5	D	++
3	B	++
3b	B	+

Axillary Metastasis in Occult Breast Cancer (ex. CUP)

Pathology, molecular pathology

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- ER, PgR, HER2, GATA3
- Exclusion of other primary malignancies in case of triple-negative phenotype or unusual histology, e.g. lung, female genital tract, HNT tumors, neuroendocrine ca.
- Gene expression profiling for determination or primary site (e.g. CUPprint, Pathwork, TOT, Theros CTID)
- NGS, epigenetics for determination of primary site (Panel-Sequencing, e.g. EPICup)
- Prognostic gene expression tests

Oxford		
LoE	GR	AGO
5	D	++
5	D	++
2c	B	+/-
2c	B	+/-
5	D	--

Axillary Metastasis in Occult Breast Cancer (Axillary CUP): Therapy

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- **Axillary dissection**
- **Mastectomy if breast MRI is negative**
- **(Neo-) adjuvant systemic therapy according to breast cancer guidelines (AGO)**
- **Breast irradiation if breast MRI is negative**
- **Irradiation of regional lymph nodes according to breast cancer guidelines (AGO)**

Oxford		
LoE	GR	AGO
3a	C	++
3a	C	-
5	D	++
2c	B	+
3b	B	+

Paget's Disease of the Breast

- **Definition:** Paget's disease of the breast is characterized by an intraepidermal tumor manifestation originating in intraductal or invasive breast cancer.
- **Clinical presentation:** skin eczema of the nipple, areola and surrounding skin; thickening, pigmentation and scaly skin

Feature

Frequency

Presentation

Paget's disease with invasive Ca. (37 - 58%)
 Paget's disease mit DCIS (30 - 63%)
 Isolated Paget's disease (4 - 7%)
 Isolated Paget's disease with invasion (rare)

IHC

HER2-positive (83 - 97%)
 ER-positive (10 - 14%)
 AR-positive (71 - 88%)

Prognosis and tumor biology

Better in isolated Paget's disease
 Worse if in combination with invasive breast cancer or DCIS compared to isolated Paget's disease

Paget's Disease of the Breast Diagnosis

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- **Histological verification by skin biopsy**
- **Mammography, sonography**
- **MRI of the breast if other imaging negative**
- **Immunohistochemistry (ER, PgR, HER2, Ck7)
to detect benign and HER2-negative cases**

Oxford		
LoE	GR	AGO
		++
4	D	++
4	C	+
5	D	++

Paget's Disease of the Breast - Therapy

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■ Paget's disease with underlying disease (invasive breast cancer, DCIS)

- Therapy according to standard of underlying disease
- Surgery must achieve R0

■ Isolated Paget's disease of the NAC:

- Surgery must achieve R0
- Surgical resection only, no adjuvant radiotherapy
- Sentinel-node excision (SNE)

Oxford		
LoE	GR	AGO
5	D	++
1c	B	++
1c	B	++
4	D	++
2b	B	--

Borderline and Malignant Phyllodes Tumor

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- Name derived from greek term of “Phyllon” (leaf) due to its lobulated histological aspect
- Differential diagnosis may be problematic on core biopsy
- Resection margin is independent prognostic parameter
- Comparable rates of recurrence in association with BCT or mastectomy
- In-Breast recurrence relatively frequently seen (10 - 30%)
- Distant metastasis relatively rare (< 10%) and almost exclusively seen in malignant phyllodes tumor.
- Adverse pathological criteria: marked stromal cellularity and overgrowth, increased nuclear atypia, presence of large necrohemorrhagic areas, and high mitotic activity associated with increased risk of distant recurrence

Phyllodes tumor

- **Fibroepithelial tumors of the breast: frequency 0.3 – 1% of all primary breast tumors**

parameter	frequencies
Grading (3-STEP histological grading system)	Benign (75%) Borderline (16%) Malignant (9%)
Median age at time of diagnosis	Benign PT: 39 y Borderline PT: 45 y Malignant PT: 47 y
Local recurrence	Benign PT: 4 – 17% Borderline PT: 14 – 25% Malignant PT: 23 – 30%
Metastasis	Benign PT: <1% Borderline PT: 1.6% Malignant PT: 16-22%

10y OS: 86–90% (range: 57–100%) depending on subtype and unfavorable histological criteria

Borderline and Malignant Phyllodes Tumor

Diagnosis

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- **Mammography, sonography**
- **Diagnosis on core biopsy, grade determination on resection specimen**
- **Breast MRI**
- **Staging only malignant PT (CT thorax, skeletal system)**

Oxford		
LoE	GR	AGO
3	C	++
3	C	++
3	C	+/-
5	D	++

Borderline and Malignant Phyllodes Tumor Surgery

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	Oxford		
	LoE	GR	AGO
■ Benign phyllodes tumor: complete resection	2b	B	++
■ Borderline /malignant phyllodes tumor: resection margin $\geq 1\text{mm}$	2b	B	++
■ Borderline /malignant phyllodes tumor: resection margin $>10\text{mm}$ (local control)	2b	B	+
■ SNE / Axillary dissection when cN0	4	C	--
■ Treatment of local recurrence			
■ R0 resection or simple mastectomy	4	C	++

Borderline and Malignant Phyllodes Tumor

Adjuvant Therapy

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	Oxford		
	LoE	GR	AGO
■ Adjuvant radiotherapy (younger age, increased tumor volume > 5 cm, close resection margin)	2b	B	+/-
■ Systemic adjuvant therapy (chemo, endocrine)	4	C	--
■ Treatment of local recurrence			
■ R0 resection or simple mastectomy	4	C	+
■ Radiotherapy, chemotherapy after R1 resection	4	C	+/-
■ Distant metastasis (very rare)			
■ Treatment like soft tissue sarcomas	4	C	++

Sarcomas of the Breast

- **Not infrequently associated with familial syndromes (Li-Fraumeni, familial adenomatous polyposis, neurofibromatosis type 1)**
- **Primary sarcomas: angiosarcoma, undifferentiated sarcoma, leiomyosarcoma, liposarcoma, osteosarcoma**
- **Secondary malignancies of the breast:**
 - Radiotherapy-Associated Angiosarcoma
 - Breast Implant Associated Large-Cell Anaplastic Lymphoma (BI-ALCL)
- **Rare: intramammary sarcoma metastases**
- **Staging: TNM (UICC) or AJCC scheme of the soft tissue sarcoma analogous to sarcoma of the breast**
- **Grading: Analogous to the FNCLCC system for sarcoma or according to Rosen (1988) for angiosarcomas**

Primary Angiosarcoma of the Breast

- **Most common primary sarcoma of the breast**
- **Young age (median: 24–46 years)**
- **Indistinct tumor borders**
- **Large tumor (median: 5–7 cm)**
- **Uncharacteristic findings on mammography and sonography**
- **High local recurrence risk, even after mastectomy**
- **More unfavorable prognosis than other primary sarcoma of the breast**

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Primary Angiosarcoma of the Breast*

Diagnosis

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	Oxford		
	LoE	GR	AGO
■ Mammography, sonography to determine extent of disease	3a	C	--
■ Preoperative MRI to determine the extent of disease	3a	C	++
■ Diagnosis by core biopsy	3a	C	++
■ Diagnosis by FNB	3a	C	--
■ Staging (CT thorax & abd.; angiosarcoma: MRI brain)	4	D	++
■ Prognostic factors: size, grade, margins	3a	C	++

Primary Angiosarcoma of the Breast*

Therapy

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- **Surgery with wide clear margins, mostly as mastectomy**
 - Breast-conserving therapy
- **SNB or axillary dissection if cN0**
- **Adjuvant chemotherapy (anthracycline/taxane-based)**
- **Adjuvant radiotherapy if high risk (size > 5 cm, R1)**

Oxford		
LoE	GR	AGO
2b	C	++
3a	C	-
3a	C	--
4	C	+/-
4	C	+/-

Secondary (Radiotherapy-associated) Angiosarcoma of the Breast

- **Cumulative incidence of radiotherapy-associated sarcoma: 3.2 per 1,000 after 15 years**
- **Clinical presentation**
 - > 5 years after BCT or mastectomy with irradiation
 - usually intracutaneously or subcutaneously in the irradiation area with livid discoloration
 - multiple foci
 - most often in advanced stages (II–III)
 - metastasis mostly pulmonary
 - lymph node metastasis possible
- **Prognosis is more unfavorable than in non-radiotherapy-associated sarcoma**
- **Survival: after 5 yrs up to 50.5%, after 10 yrs up to 25.2%**

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Secondary Angiosarcoma of the Breast Therapy

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- **Secondary mastectomy**
- **Adjuvant chemotherapy
(anthracycline/taxane-based)**
- **Adjuvant radiotherapy if high risk
(size > 5 cm, R1)**
- **Regional hyperthermia (to improve local control)
plus chemotherapy and/or radiotherapy**

Oxford		
LoE	GR	AGO
3a	C	++
2b	B	+/-
2b	B	+/-
2b	B	+/-

Angiosarcoma of the Breast

Treatment of Local Recurrence and Metastases

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Treatment of Local Recurrence:

- R0 resection
- Adjuvant radiotherapy for high-risk patients
(tumor size > 5 cm, R1)

Distant Metastases / Unresectable Tumors:

- Treatment like soft tissue sarcomas
- Paclitaxel weekly / liposomal doxorubicin (as in angiosarcoma)
- Antiangiogenic treatment (e.g. in angiosarcoma)

Oxford		
LoE	GR	AGO
4	C	++
4	C	+/-
4	C	++
2b	B	+
4	C	+/-

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

- Rare disease, 3 % of Non-Hodgkin Lymphomas, 0.04-0.5 % of all malignant breast diseases
- Estimated incidence 0.6-1.2 / 100.000 women with implants (median age: 54 y)
- Mainly associated with textured implants
- Interval to diagnosis: 8 years (median)
- Clinical symptoms
 - Swelling and seroma. (60 %)
 - Solid tumor (17 %)
 - Seroma and solid tumor (20 %)
- Histology: CD30+ / ALK-T-Cell Lymphoma
- Compulsory registration as SAE (§ 3 MPSV to BfArM)

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BIA-ALCL - Surfaces of Breast Implants

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- The cause of BIA-ALCL is not established; however, it has been proposed that lymphomagenesis may be driven by a chronic inflammatory reaction induced by capsule contents or surface. **The risk for BIA-ALCL has been shown to be significantly higher for implants with grade 3 and 4 surfaces.**

Process	Poly-urethane foam	Salt Loss (Biocell/ Euro-silicone)	Gas Diffusion	Salt Loss (Nagotex)	Imprinting	Smooth/ Nano
Surface Area	high	intermediate	intermediate	low	low	minimal
Roughness	high	intermediate	low	low	low	minimal
SURFACE TYPE	4	3	3	2	2	1

BIA-ALCL– Diagnosis

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	Oxford		
	LoE	GR	AGO
▪ Breast US (assessment of new seromas > 1 year after implant insert, solid lesion)	3a	D	++
▪ Mamma-MRT in confirmed cases	3a	D	++
▪ Staging (Imaging, e.g. CT, PET-CT)	3a	D	++
▪ Cytology of late seromas			
- > 50 ml			
- Complete assessment	3a	D	++
- flow-cytology (T-cell clone)			
- BIA-ALCL specific cytologic diagnostic (CD 30+)			
▪ Core needle biopsy in solid lesions	3a	D	++
▪ Lymphoma assessment of resected tissue and histologic staging			
▪ Documentation of the implant (manufacturer, size, volume, surface, Batch-number) and enter in registry	5	D	++

BIA-ALCL – Therapy

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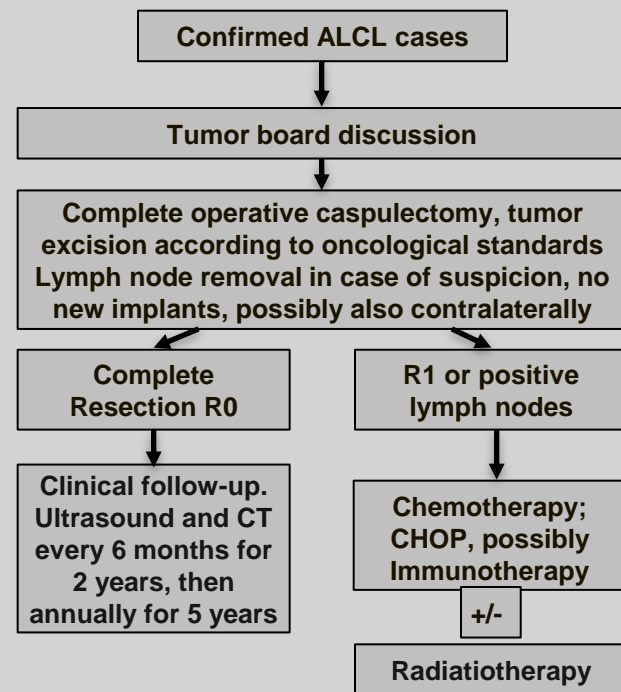
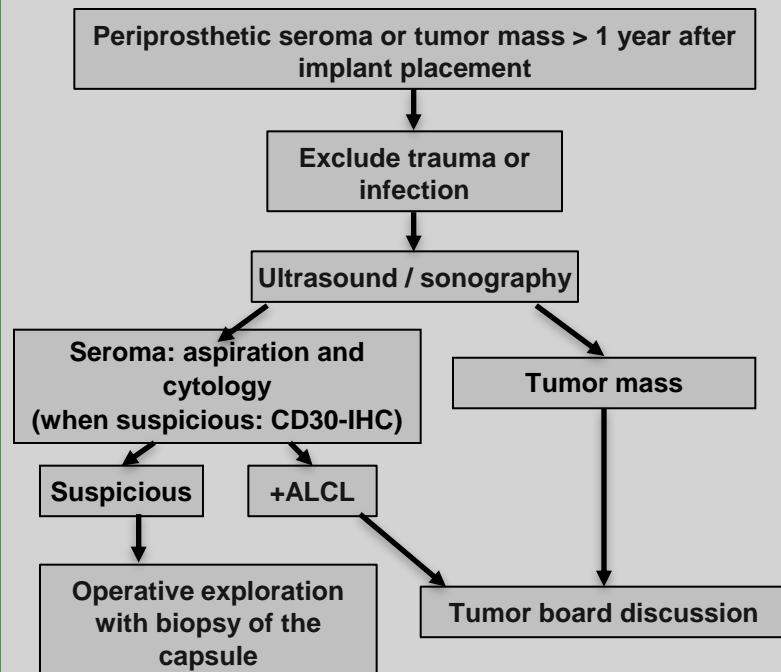
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- **Implant resection and complete capsulectomy including tumorectomy**
- **Resection of suspicious lymph nodes, no routine use of Sentinel-Node-Biopsy, no axillary dissection**
- **Polychemotherapie (z.B. CHOP) bei extrakapsulärer Tumorausbreitung**
- **Radiotherapy in unresectable tumors**
- **Case discussion in an interdisciplinary tumor board in the presence of a specialist for lymphomas**

Oxford		
LoE	GR	AGO
3a	C	++
4	D	++
4	D	+
5	D	+/-
5	D	++

Breast Implant-Associated Anaplastic Large-Cell Lymphoma (BIA-ALCL)

- Summary of the Management (acc. to Noah 2017) -



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Stage Adapted Therapy of BIA-ALCL

TNM	Description
T= tumor extent	
T1	Confined to effusion or a layer on luminal side of capsule
T2	Early capsule infiltration
T3	Cell aggregates or sheets infiltrating the capsule
T4	Lymphoma infiltrates beyond the capsule
N= lymph node	
N0	No lymph node involvement
N1	One regional lympho nodes positive
N2	Multiple regional lymph nodes positive
M= metastasis	
M0	No distant spread
M1	Spread to other organs /distant sides

IA-IC/(IIA): surgical **complete resection** of capsula, implant, suspected nodular lesions and, only if suspicious, regional lymph nodes
no indication for mastectomy, sentinel node extirpation or axillary dissection

IIA/IIB-IV: 2-18%

- surgical complet resection (see above)
- **CHO(E)P** (Cyclophosphamide, Vincristin, Doxorubicin, Prednison) +/- Etoposid
- **Brentuximab Vedotin** (Adcetris®) antibody-drug-conjugate (ADC) containing monoclonal antibody against human CD30 antigen and 3-5 molecules of cytostatic drug Monomethylauristatin E
- **CHT & stem cell transplantation** and **radiotherapy** only in for patients with incomplete resection and advanced stages

BIA-ALCL – EUSOMA-Recommendation

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- **Despite an increase of BIA-ALCL in association with texture implants the use of textured implants is still permitted!**

„For the moment, textured implants can safely continue to be used with patient's fully informed consent, and that women that have these type of implants already in place don't need to remove or substitute them, which would undoubtedly cause harm to many tens of thousands of women, to prevent an exceptionally rare, largely curable and currently poorly understood disease.“

Metaplastic Breast Cancer

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- **Imaging and histology for diagnosis according to standard**
- **Staging including chest and abdominal CT (hematogenous metastasis)**
- **Surgical treatment according to standard (more often MRM needed due to advanced tumor stage)**
 - **SNB**
- **Adjuvant chemotherapy (tumors more chemoresistant)**
- **Adjuvant endocrine standard therapy**
- **Adjuvant standard radiotherapy**

Oxford		
LoE	GR	AGO
5	D	++
4	C	++
4	C	++
4	C	+
4	C	+
4	C	+/-
4	C	+

Metaplastic Breast Cancer

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Incidence: 0,2–5 % of all breast cancers (1)

Histology: epithelial and mesenchymal components with two to three different components within a tumor;
high proliferation rate; subtypes: according to WHO (4)

Metaplastic carcinoma of no special type

Low-grade adenosquamous carcinoma

Fibromatosis-like carcinoma

Squamous cell carcinoma

Spindle cell carcinoma

Metaplastic carcinoma with mesenchymal differentiation

Chondroid differentiation

Osseous differentiation

Other types of mesenchymal differentiation

Mixed metaplastic carcinoma

Myoepithelial carcinoma

Molecular biology: > 90 % ER-, PR-, HER2-
~. 70 % overexpression of HER1, CK 5/6-expression (stem-cell-like and BRCA-like)(2)
molecular profile mostly basal-like (3)
frequent mutations in PIK3CA and PTEN (mTOR-overactivity)

Clinical features:

- Large tumors at diagnosis (> 5 cm)
- Frequent hematogenous metastases; nodal involvement in ~ 20 % (no nodal involvement in spindle cell carcinoma carcinosarcoma)
- Poor clinical course compared to TNBC
- Impaired prognosis in asian women (MRM more frequently, poor grading, more often squamous cell carcinoma, spindle cell carcinoma less frequent)
- Low response rated to (neoadjuvant) chemotherapy