Breast Cancer: Specific Situations
Brustkrebs:
Spezielle Situationen

- **Versions 2005-2017:**
  - Dall / Fehm / Fersis / Friedrich / Gerber / Göhring /
  - Harbeck / Huober / Janni / Loibl / Lück / Lux / Maass /
  - Mundhenke / Oberhoff / Rody / Scharl / Schütz / Schneeweiß / Sinn /
  - Solomayer / Thomssen

- **Versions 2018:**
  - Harbeck / Rody

Update January 2017 – Schütz / Sinn
Update January 2016 – Thomssen / Harbeck
Update January 2015 – Solomayer / Harbeck
Update January 2014 – Fehm/Schneeweiß
Update January 2013 – Fersis/Friedrich
Update January 2012 – Lux/Lück
Update Februar 2011 – Janni/Huober
Update Januar 2010 – Mundhenke/Rody

**Screened data bases:**

**Screened for:** Clinical Trials, Meta-Analysis, Practice Guideline, Randomized Controlled Trial, Reviews

**Screened guidelines:**
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 ≤ 35 Years

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### Aggressive biological behavior with worse prognosis
- Surgery like patients ≥ 35 y
- Guidelines adapted (neo-)adjuvant systemic treatment (see chapters there)
- GnRHa as ovarian protection (see chapter gyn. problems)
- Genetic and fertility counseling
- Contraception counseling

### Prognosis in young women

3. Gonzalez-Angulo AM et al., Women age < or = 35 years with primary breast carcinoma: Disease features at presentation. Cancer 2005;103: 2466-2472


Chemotherapy in young women
1. Aebi S. Special issues related to the adjuvant therapy in very young women. Breast 2005, 14: 594-599 (Review)


Endocrine therapy in young women

2. C. Davies et al. Long-term effects of continuing adjuvant tamoxifen to 10 years
versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381,805–816


**Benefit from trastuzumab**


**Benefit from temporary amenorrhoea after adjuvant chemotherapy (chemotherapy induced or GnRHa-related)**


9. Moore HCF, Unger JM, Phillips KA, et al Phase III trial (Prevention of Early Menopause Study [POEMS]-SWOG S0230) of LHRH analog during chemotherapy (CT) to reduce ovarian failure in early-stage, hormone receptor-negative breast cancer: An international Intergroup trial of SWOG, IBCSG, ECOG, and CALGB (Alliance). J Clin Oncol 32:5s, 2014 (suppl; abstr LBA505)

**Surgery in young women (Surgery like ≥ 35y - in particular BCT)**


Genetic and fertility counselling


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

<table>
<thead>
<tr>
<th>Procedure</th>
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<tbody>
<tr>
<td>Breast imaging &amp; biopsy like in non-pregnant</td>
<td>4</td>
<td>C</td>
<td>++</td>
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<tr>
<td>Staging if indicated (Bone scan after delivery)</td>
<td>5</td>
<td>D</td>
<td>+</td>
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<tr>
<td>Full body MRI (without contrast agent)</td>
<td>4</td>
<td>C</td>
<td>+/-</td>
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<tr>
<td>Surgery like in non-pregnant patients</td>
<td>4</td>
<td>C</td>
<td>++</td>
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<tr>
<td>Sentinel node excision (technetium only)</td>
<td>4</td>
<td>C</td>
<td>+</td>
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<tr>
<td>SLNE during 1st trimester</td>
<td>5</td>
<td>D</td>
<td>+/-</td>
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<tr>
<td>Sensitivity and specificity not established (during lactation); breast feeding should be avoided for 24 hrs</td>
<td>4</td>
<td>C</td>
<td>++</td>
</tr>
<tr>
<td>Blue dye (has not been tested in pregnant animals or humans)</td>
<td>4</td>
<td>C</td>
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</table>

* Participation in register study recommended

Study link: http://germanbreastgroup.de/studien/adjuvant/brustkrebs-in-der-schwangerschaft.html


Outcome information (e.g. GBG registry):
Statement: Breast imaging & biopsy like in non-pregnant

Statement: Staging: ultrasound, chest X-ray if indicated

Statement: Whole Body MRI

Statement: Surgery like in non-pregnant patients
Statement: „Sentinel node biopsy“ during pregnancy


Reviews

1. Sophie E. McGrath Chemotherapy for breast cancer in pregnancy: evidence and guidance for oncologists


**Breast Cancer During Pregnancy**

- **(Neo-)adjuvant Therapy**

<table>
<thead>
<tr>
<th>Radiation therapy during pregnancy</th>
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<tr>
<td>(Neo-)adjuvant chemotherapy only after first trimester (indication as in non-pregnant)</td>
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<tr>
<td>Anthracyclines: AC, EC</td>
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<tr>
<td>Taxanes</td>
<td>2b</td>
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<tr>
<td>Platin salts (carboplatin, cisplatin)</td>
<td>4</td>
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<td>+/-</td>
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<tr>
<td>MTX (e.g. CMF)</td>
<td>4</td>
<td>D</td>
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<tr>
<td>Endocrine treatment</td>
<td>4</td>
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<tr>
<td>HER2-neu targeted treatment</td>
<td>3a</td>
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<tr>
<td>Bisphosphonates, denosumab</td>
<td>4</td>
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</table>

**General principles**


**Statement: Radiotherapy during pregnancy**


**Statement: (Neo-)adjuvant chemotherapy only after first trimester (indication as in non-pregnant):**

Statement: Anthracyclines: AC, EC


Omission of 5FU based on the same evidence as in non-pregnant patients (GIM2 study) - see also chapter on adjuvant chemotherapy:


Statement: Taxanes


Statement: Platinum salts


**Statement: MTX (e.g. CMF)**


**Statement: Endocrine treatment**


**Statement Trastuzumab during pregnancy**


Statement Bisphosphonate during pregnancy

General information: Chemotherapy during pregnancy
### Breast Cancer During Pregnancy*  
– Delivery and Breast-Feeding –

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<tr>
<td>Delivery should be postponed until sufficient fetal maturation (avoid iatrogenic prematurity)</td>
<td>2b</td>
<td>C</td>
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<tr>
<td>Termination of pregnancy does not improve maternal outcome</td>
<td>3b</td>
<td>C</td>
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<tr>
<td>Delivery mode like in healthy women, avoid delivery ≤3 weeks from last cycle of chemotherapy</td>
<td>4</td>
<td>C</td>
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<tr>
<td>If further systemic therapy is needed after delivery, breast feeding may be contraindicated depending on drug toxicities</td>
<td>5</td>
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* Participation in register study recommended

### General principles


### Statements

**Delivery should be postponed until sufficient fetal maturation since termination of pregnancy does not improve maternal outcome**


**Delivery mode like in non-pregnant; Avoid delivery ≤ 3 weeks from prior chemotherapy**

Statements: If further systemic therapy is needed after delivery, breast feeding may be contraindicated depending on drug toxicities

1. Williams Obstetrics lecture book
**Breast Cancer and Pregnancy**

- **Family Planning**

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<th>Oxford</th>
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<tr>
<td>After breast cancer diagnosis reproductive techniques can be used to induce pregnancy</td>
<td>5</td>
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<tr>
<td>Success rates for getting pregnant and for deliver a child are lower in breast cancer patients in comparison to non-cancer patients</td>
<td>5</td>
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<tr>
<td>Breast cancer patients of reproductive age should be offered a fertility counseling before starting any kind of treatment</td>
<td>5</td>
<td>D</td>
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<tr>
<td>Breast cancer patients should not be advised against getting pregnant regardless of tumor’s hormone receptor status</td>
<td>5</td>
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</tbody>
</table>
Pregnancy Associated Breast Cancer*: Outcome

General principles

Statement: Breast cancer during pregnancy / lactation: Outcome not compromised, if treated adequately


Statement: Pregnancy and lactation after breast cancer: Outcome not compromised

1. Gelber S et al. Effect of pregnancy on overall survival after diagnosis of early stage breast cancer. JCO 2001; 19: 1671-5: IBCSG-participants - matched pair analysis: 94 patients pregnant after treatment (RR 0.44 – 0.96; p=0.04).


Review articles


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)


Statement: Treatment according to standard


Statement: Surgery similar to „younger“ age


Statement: Endocrine treatment (endocrine resp.)


Statement: Chemotherapy in pts. < 70 years


3. Fargeot P: Disease-free survival advantage of weekly epirubicin plus tamoxifen versus tamoxifen alone as adjuvant treatment of operable, node-positive, elderly breast cancer patients: 6-year follow-up results of the French adjuvant study group 08 trial. J Clin Oncol. 2004 Dec 1;22(23):4622-30


Statement: Chemotherapy in pts. > 70 years:


**Statement: Radiotherapy**


2. Sautter M.L et al When are breast cancer patients old enough for the quitclaim of local control Strahlenther Onkol 2012 :1-5


Statement: Trastuzumab


### Treatment for Frail Patients

*(Life Expectancy <5 yrs, Substantial Comorbidities)*

**Reduced standard treatment**

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

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1. Walzer DE Measuring the value of radiotherapy in older women with breast cancer J Clin Oncol 2012 30 (23) 2809-2811
2. Audisio RA et al When reporting on older patients with cancer, frailty information is needed Ann Surg Oncol 2011; 18: 4-5
3. Smith BD et al Improvement in breast cancer outcomes over time: are older missing out? J Clin Oncol 2011 29 (35) 4647-4653
4. Hughes KS et al Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer 2010 J Clin Oncol 28:69s (suppl 15, abstr 507).

**Statement:** Reduced standard treatment:

**Statement:** No breast surgery (consider endocrine options):


Statement: No axillary clearing (≥ 60 y, cN0, ER+)


Statement: No radiotherapy (≥ 70 y, pT1, pN0, ER+)


Statement: Hypofractionated radiotherapy

Statement: No chemotherapy > 70 years and negative risk benefit analysis
Male Breast Cancer: Diagnostic Work-Up and Loco-Regional Therapy

- 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 relaion!)
- Genetic counselling if one additional relative affected (breast/ovarian cancer)
- Screening for 2nd malignancies according to guidelines

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* Participation in register study recommended

International registry:

General:

Statement: Diagnostic work up as in women
**Statement: Mammography**


**Statement: Ultrasound**


**Statement: Standard-surgery: Mastectomy – men**


**Statement: Sentinel-node excision (SNE)**


Statement: Radiotherapy as in women (consider tumor breast relation!)

Statement: Genetic counselling if 1 additional relative affected (breast/ovarian cancer)
1. Ottini L et al. BRCA1/BRCA2 mutation status and clinical-pathologic features of 108 male breast cancer cases from Tuscany: a population-based study in central Italy. Breast Cancer Res Treat. 2008 Sep 26

Statement: Screening for 2nd malignancies according guidelines

Statement: Systemic therapy
5. Zagouri F et al. Aromatase inhibitors with or without gonadotropin-releasing

Review articles
Male Breast Cancer: Systemic Therapy

- **Adjuvant chemotherapy as in women**
  - HER2-targeted therapy
  - Endocrine therapy
    - Tamoxifen
    - Aromatase inhibitors (adjuvant)
    - Aromatase inhibitors (metastatic BC)
    - GnRHα and AI (metastatic BC)
    - Fulvestrant (metastatic BC)
- **Palliative chemotherapy as in women**

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* Participation in register study recommended

**Statement: Adjuvant Chemotherapy**


**Statement Trastuzumab**


**Statement endocrine therapy**


Statement palliative chemotherapy

Survival benefit by trimodal treatment (NACT, MRM, RT)

In case of invasive BC and clinical signs of inflammation (e.g. ≥ 1/3 of the breast affected) determine stage cT4d


Survival benefit by trimodal treatment (NACT, MRM, RT)


Statement: Staging


Statement: Preoperative chemotherapy


Statement: Regimens as in non-inflammatory BC


Statement: in HER2 positive disease addition of trastuzumab


Statement: in HER2 positive disease addition of trastuzumab and pertuzumab


Statement: in HER2 negative disease addition of bevacizumab

Statement: Mastectomy after chemotherapy


Statement: Sentinel lymph node


Statement: Radiotherapy


Statement: Postoperative systemic therapy as in non-inflammatory BC


Reviews


4. Brouwers B et al. Clinicopathological features of inflammatory versus noninflammatory locally advanced nonmetastatic breast cancer


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

- 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

Guidelines:

Reviews:

Pathology


Outcome

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

- 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

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Statement: Mammography / Breast ultrasound/ Breast MRI


Statement: Staging


Statement: PET


Axillary Metastasis in Occult Breast Cancer (ex. CUP)
Pathology, molecular pathology

- 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 (CUPprint, Pathwork, TOT, Theros CTID)
- NGS, epigenetics for determination of primary site (Panel-Sequencing, EPICup)
- Prognostic gene expression tests

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Immunohistochemistry


Gene expression profiling and other molecular approaches in CUP disease


gene expression signature for the identification of tumor tissue origin. Modern Pathology, 29(6), 546–556. http://doi.org/10.1038/modpathol.2016.60
## Axillary Metastasis in Occult Breast Cancer (Axillary CUP) Therapy

- **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)**

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### Guidelines:


### Reviews:

http://doi.org/10.1016/j.amjsurg.2005.06.026


Statement: Axillary dissection


Statement: Mastectomy without (in-)breast tumor:

References 1-4 (retrospective analysis, case reports)


Statement: Breast irradiation if breast MRI is negative


Statement: Systemic treatment according N+ tumor


Paget’s disease of the breast is characterized by an intraepidermal tumor manifestation originating in intraductal or invasive breast cancer. Isolated Paget’s disease of the nipple is more rarely seen, and less aggressive.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Presentation</td>
<td>Paget’s disease with invasive Ca. (37 - 58%)</td>
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<tr>
<td></td>
<td>Paget’s disease mit DCIS (30 - 63%)</td>
</tr>
<tr>
<td></td>
<td>Isolated Paget’s disease (4 - 7%)</td>
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<tr>
<td></td>
<td>Isolated Paget’s disease with invasion (rare)</td>
</tr>
<tr>
<td>IHC</td>
<td>HER2-positive (83 - 97%)</td>
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<td>ER-positive (10 - 14%)</td>
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<td>AR-positive (71 - 88%)</td>
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Clinical Presentation:


Pathology and Immunohistochemistry


Paget’s Disease of the Breast Diagnosis

Imaging:

Pathology:
Pathology, 67(11), 1010–1012. http://doi.org/10.1136/jclinpath-2014-202280

Surgical Treatment of Paget's disease associated with breast tumor (invasive carcinoma or DCIS):


**Treatment of isolated Paget’s disease**


**Statement: Sentinel-node excision (SNE)**

Borderline and Malignant Phyllodes Tumor

- Differential diagnosis may be problematic on core biopsy
- In-Breast recurrence relatively frequently seen (10 - 30%)
- Distant metastasis relatively rare (< 10%) and almost exclusively seen in malignant phyllodes tumor.

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<tr>
<th>Feature</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Grading</td>
<td>Benign PT (75%)</td>
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<tr>
<td></td>
<td>Borderline PT (16%)</td>
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<tr>
<td></td>
<td>Malignant PT (9%)</td>
</tr>
<tr>
<td>Median age on diagnosis</td>
<td>Benign PT: 39 J.</td>
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<td></td>
<td>Borderline PT: 45 J.</td>
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<tr>
<td></td>
<td>Malignant PT: 47 J.</td>
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<tr>
<td>Local recurrence</td>
<td>Benign PT: 10 - 17%</td>
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<td>Borderline PT: 14 - 25%</td>
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<td>Malignant PT: 23 - 30%</td>
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</tbody>
</table>

Review


Pathology and Outcome

Borderline and Malignant Phyllodes Tumor Diagnosis

### Imaging


### Core biopsy


Statement: Complete (wide) local excision or MRM

Surgical margins:


Operative management and prognosis of Phyllodes Tumors.


Statement: SNE / Axillary dissection in cN0


Statement: Staging


Statements: Systemic adjuvant therapy/Chemotherapy and Endocrine therapy


Statement: Adjuvant radiotherapy, if T ≥2cm (BCT) or T ≥10cm (mastectomy)


Statement: Treatment of local recurrence => R0 Resection: References (retrospective analysis, case reports)


Statement: Radiotherapy, chemotherapy after R1 resection

Statement: Distant metastases (very rare) => Treatment like soft tissue sarcomas


Borderline and Malignant Phyllodes Tumor
Adjuvant Therapy

- **Adjuvant radiotherapy**
  - If T ≥ 2 cm (BCT) or T ≥ 10 cm (mastectomy)
  - **Systemic adjuvant therapy (chemo, endocrine)**
  - **Treatment of local recurrence**
    - R0 resection or simple mastectomy
    - Radiotherapy, chemotherapy after R1 resection
  - **Distant metastasis (very rare)**
    - Treatment like soft tissue sarcomas

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<tr>
<th>Treatment</th>
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<tr>
<td>Adjuvant radiotherapy</td>
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<td>C</td>
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<tr>
<td>Systemic adjuvant therapy (chemo, endocrine)</td>
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<tr>
<td>Treatment of local recurrence</td>
<td>4</td>
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<tr>
<td>Distant metastasis (very rare)</td>
<td>4</td>
<td>C</td>
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</table>
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

Reviews


Imaging


Pathology


Prognostic Factors


Primary Angiosarcoma of the Breast* Therapy

- 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)

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</table>

*Therapy in specialized centres recommended

**Surgery**

**Adjuvant Treatment (Chemotherapy, Radiotherapy)**


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 years**: 15%


Secondary Angiosarcoma of the Breast Therapy

- **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

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<td>2b</td>
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</tr>
</tbody>
</table>

**Surgery**


**Adjuvant Chemotherapy**

angiosarcoma. Tumori, 95(6), 828–831.


Adjuvant Radiotherapy


Adjuvant Hyperthermia


3. Huang J, Mackillop WJ. Increased risk of soft tissue sarcoma after radiotherapy in women with breast carcinoma. Cancer 2001; 92: 172-180
Treatment of local recurrences

Treatment of metastatic and non-resectable tumors
Breast Implant-Associated Anaplastic Large-Cell Lymphoma (BIA-ALCL)

- Rare, estimated annual incidence <1 per 100,000 women with implants (median age 54 years)
- Occurrence predominantly of textured implants
- 5-year OAS 89%
- Interval for lymphoma diagnosis: 8 years (median)
- Clinical presentation
  - Effusion only (60%)
  - Mass only (17%)
  - Effusion and mass (20%)
- Histological: CD30+ / ALK-T cell lymphoma
- Reporting obligation as SAE according to § 3 MPSV to the BfArM

Reviews


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


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

- Implant removal and complete capsulectomy including tumor removal
  
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</tr>
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<td>3a</td>
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</table>

- Removal of suspicious lymph nodes, no routine sentinel-node biopsy, no axillary dissection
  
  | 4         | D  | ++  |

- Polychemotherapy (e.g., CHOP) when extracapsular tumor infiltration
  
  | 4         | D  | +   |

- Radiation for unresectable tumors or R1
  
  | 5         | D  | +/- |

- Reconstruction after 1 year disease-free interval
  
  | 5         | D  | +   |


Breast Implant-Associated
Anaplastic Large-Cell Lymphoma (BIA-ALCL)
- Summary of the Management (acc. to Noah 2017) -

Periprosthetic seroma or tumor mass > 1 year after implant placement

- Exclude trauma or infection
- Ultrasound / sonography

Seroma: aspiration and cytology (when suspicious: CD30-IHC)

- Suspicious
- +ALCL

Operative exploration with biopsy of the capsule

Tumor mass

Confirmed ALCL cases

Tumor board discussion

Complete operative capsulectomy, tumor excision according to oncological standards; Lymph node removal in case of suspicion, no new implants, possibly also contralaterally

Complete Resection R0

R1 or positive lymph nodes

Clinical follow-up: Ultrasound and CT every 6 months for 2 years, then annually for 5 years

Chemotherapy; CHOP, possibly immunotherapy

+/-

Radiation therapy
Metaplastic Breast Cancer

**Imaging, Prognosis, Staging**


**Surgical Therapy**


Adjuvant chemotherapy

Adjuvant endocrine therapy

Adjuvant radiotherapy
# Metaplastic Breast Cancer

**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)

<table>
<thead>
<tr>
<th>Metaplastic carcinoma of no special type</th>
<th>Low-grade adenosquamous carcinoma</th>
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<tbody>
<tr>
<td>Fibromatosis-like carcinoma</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Spindle cell carcinoma</td>
<td>Metaplastic carcinoma with mesenchymal differentiation</td>
</tr>
<tr>
<td>Chondroid differentiation</td>
<td>Osseous differentiation</td>
</tr>
<tr>
<td>Other types of mesenchymal differentiation</td>
<td>Mixed metaplastic carcinoma</td>
</tr>
<tr>
<td>Myoepithelial carcinoma</td>
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</tbody>
</table>

**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)

## Background


