Breast Cancer Follow-Up
Aktualisierung der Therapieempfehlungen nach Durchsicht der ASCO, NCCN und ACS Guidelines*, sowie der S3 Leitlinie
(2019/01-2023/01)
*Runowicz CD et al., American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care
Guideline, JCO 34:611-635,
Breast Cancer Follow-Up Objectives

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early detection of curable events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-breast recurrence</td>
<td>1a</td>
<td>B</td>
</tr>
<tr>
<td>Loco-regional recurrence*</td>
<td>1a</td>
<td>B</td>
</tr>
<tr>
<td><strong>Early detection of contralateral cancers</strong></td>
<td>1a</td>
<td>B</td>
</tr>
<tr>
<td><strong>Early detection of metastasis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early detection of symptomatic metastases</td>
<td>3b</td>
<td>C</td>
</tr>
<tr>
<td>Early detection of asymptomatic metastases</td>
<td>1a</td>
<td>A</td>
</tr>
</tbody>
</table>

* Loco-regional recurrence is associated with a higher risk of mortality in node-positive, PR-negative, younger patients and in patients with a short time between primary diagnosis and recurrence

of Regular Postoperative Surveillance for Patients with Early Breast Cancer

Statement: risk factors of mortality after loco-regional recurrence
Breast Cancer Follow-Up Objectives

- Improve quality of life
- Improve physical performance
- Reduction and/or early detection of therapy-related side effects (such as osteoporosis, cardiac failure, fatigue, neurotoxicity, lymphedema, web axillary pain syndrome (abacterial lymphangitis), sexual disorders, cognitive impairment, sterility, and secondary tumors) and start of necessary therapies
- Participation in interventional programs during follow-up for breast cancer survivors in order to maximize therapy adherence, assess life-style interventions, and improve quality of life

Oxford LoE GR AGO
2b B +
2a B +
2b B +
3b B +

Statement: Outcome measurements


Statement: Obesity, physical activity and quality of life


Statement: Obesity and breast cancer prognosis

Statement: Lymphedema

Statement: Neurotoxicity:
1. Jordan B, Margulies A, Cardoso F et al. Systemic anticancer therapy-induced peripheral and central neurotoxicity:

Statement: web axillary pain syndrome (Morbus Mondor):

Statement: sexual disorders and cognitive impairment:

Statement kognitive Einschränkungen

Statement: Secondary tumors:
Monitoring after Cardiotoxic Therapy (e.g. Anthracyclins, anti-HER2)

After anthracyclines / Trastuzumab:
- ECG and echocardiography:
  - 6, 12, 24 months and yearly up to 5 years after therapy
  - after 5th year, every 5 years and if patient is symptomatic
- If cardiovascular risk factors:
  - blood pressure at least yearly
  - lipids and HbA1c in serum yearly
- Modify risk factors if possible:
  - nicotine, body weight, bmi
- Education about individual risk profile and lifestyle

Risk factors:
radiotherapy of left breast, nicotine, hypertonus, diabetes mell., dyslipidaemia, adiposity, age ≥ 60, cardiac diseases: reduced ejection fraction, post-myocardial infarction status, ≥ moderate heart defects

Evaluation of current adjuvant therapy

2. Lueck H-J, Hadji P, Harbeck N et al. 24 Months Follow-Up Results from PACT (Patient’s Anastrozole Compliance to Therapy Programme), a Non-Interventional Study Evaluating the Influence of a Standardized Information Service on Compliance in Postmenopausal Women with Early Breast Cancer. SABCS 2011 [P5-17-05].

Adhärenz erhöhen durch Verhaltenstherapie/-training
Statement: Psycho-social aspects

Psychooncology 19:573–582, 2010 Crossref, Medline, Google Scholar
9. Y Kim, RL Spillers, DL Hall: Quality of life of family caregivers 5 years after a relative’s cancer diagnosis: Follow-up of the
10. BA Given, CW Given, PR Sherwood: Family and caregiver needs over the course of the cancer trajectory J Support Oncol
10:57–64, 2012 Crossref, Medline, Google Scholar
11. Tran TXM, Jung S, Lee EG et al., Fear of Cancer Recurrence and Its Negative Impact on Health-Related Quality of Life in
12. Knerr S, Guo B, Wernli KJ et al. (2023) Longitudinal adherence to breast cancer surveillance following cancer genetic

Statement: prophylactic surgery
1. Rhiem K, Engel C, Graeser M et al.. The risk of contralateral breast cancer in patients from BRCA ½ negative high risk
families as compared to patients from BRCA1 or BRCA2 positive families: a retrospective cohort study. Breast Cancer

Statement zur Analgesie
1. Lu YC, Chen PT, Lin MC et al., Nonsteroidal Anti-Inflammatory Drugs Reduce Second Cancer Risk in Patients With Breast
Cancer: A Nationwide Population-Based Propensity Score-Matched Cohort Study in Taiwan. Front Oncol. 2021 Nov
### Interventions regarding lifestyle risks and comorbidity in order to reduce an unfavorable impact on disease outcome

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment of type II-diabetes</strong></td>
<td>2a B</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>(&gt; 25% undetected DM in postmenopausal BC patients, endocrine therapy improves risk for DM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight/lifestyle intervention</strong> (if BMI &lt; 18.5 and &gt; 30)</td>
<td>2a B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td><strong>Nightly fasting &gt; 13h</strong></td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td><strong>Reduction of dietary intake (at least 15 % calories from fat)</strong></td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>in HR-negative BC is associated with improved overall survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stop smoking</strong> (smoking causes 2-fold increase in BC-specific and 4-fold increase in not directly BC-associated mortality)</td>
<td>2b B</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol consumption reduction (below 6g/d)</strong></td>
<td>2b B</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate sport</strong> (in patients with reduced physical activity prior to diagnosis) (at least 150 minutes/w, 2x/w)</td>
<td>1b A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td><strong>Distress reduction</strong></td>
<td>3b B</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>


AHT erhöht Diabetes mellitus


Statement: for all statements see most recent literature see at Survivorship care guidelines of ASC and ASCO


Weight intervention.


6. Roberts SA, Gillespie TC, Shui AM et al., Weight loss does not decrease risk of breast cancer-related arm lymphedema.
Moderate sport intervention when physical activity was reduced

Das Essen von Nüssen erhöht OS und DFS

Bariatrische Operationen
Nightly Fasting

Prolonged nightly fasting improves prognosis in breast cancer patients

retrospective cohort study:

2413 BC-pat. (no diabetes), nightly fasting more or less than 13 hrs

Fasting < 13 hrs:  HR 1.36, 36% increase of risk for recurrence
HR 1.21, n.s. increase of risk for mortality

every 2-hrs-prolonged fasting was correlated with a 20% increase
of sleeping duration


Statement: Physical examination

Statement: Mammography

Statement: Sonography of the breast
5. Song SE, Cho N, Chang JM et al. Diagnostic performances of supplemental breast ultrasound screening in women with

**Statement: MRI of the breast**


**Statement: Pelvic examination, Expert Opinion**


Statement: Dext scan Expert Opinion
Routine Follow-Up Examinations in Asymptomatic Patients

<table>
<thead>
<tr>
<th>Test</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine biochemistry (incl. tumor markers)</td>
<td>1a</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td>Blood tests for monitoring of acute and late toxicities</td>
<td>5</td>
<td>D</td>
<td>+</td>
</tr>
<tr>
<td>Ultrasound of the liver / Bone scan / Chest X-ray</td>
<td>1a</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td>CT of chest, abdomen, and pelvis</td>
<td>2a</td>
<td>D</td>
<td>-</td>
</tr>
<tr>
<td>Detection of isolated / circulating tumor cells</td>
<td>2a</td>
<td>D</td>
<td>-</td>
</tr>
<tr>
<td>ctDNA</td>
<td>2a</td>
<td>D</td>
<td>-</td>
</tr>
<tr>
<td>PET / Whole body MRI</td>
<td>2b</td>
<td>B</td>
<td>-</td>
</tr>
</tbody>
</table>


**Statement: Magnetic resonance imaging (MRI) of the breast**


**Statement: Routine biochemistry (incl. tumor markers)**


**Statement: Ultrasound of the liver**
**Statement: Bone scan**
**Statement: Chest X-ray**
**Statement: CT of chest, abdomen and pelvis**


**Statement: Detection of isolated/circulating tumor cells/ctDNA**

**Statement: PET / WB-MRI**

## Background for Toxicity Management

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Laboratory Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen:</td>
<td>Cholesterol, Triglycerides, Bilirubin, ALAT, ASAT, gamma-GT, Glucose</td>
</tr>
<tr>
<td>Aromatase inhibitors:</td>
<td>Cholesterol, Triglycerides, Bilirubin, ALAT, ASAT, gamma-GT</td>
</tr>
<tr>
<td>Anthracyclines:</td>
<td>pro-BNP, possibly Troponin</td>
</tr>
<tr>
<td>Trastuzumab:</td>
<td>pro-BNP, possibly Troponin</td>
</tr>
<tr>
<td>Checkpoint inhibitors:</td>
<td>Bilirubin, ALAT, ASAT, gamma-GT, Creatinine, TSH, fT3/fT4, Myoglobin</td>
</tr>
</tbody>
</table>
Statement incidence

Statement breast self examination

Early Detection of Potentially Curable Events

Locoregional recurrence (chest wall, in-breast):

<table>
<thead>
<tr>
<th>Incidence 7–20% (depending on time of F/U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast self-examination</td>
</tr>
<tr>
<td>5 D</td>
</tr>
<tr>
<td>Physical examination, mammography &amp; US</td>
</tr>
<tr>
<td>1a A ++</td>
</tr>
<tr>
<td>Magnetic resonance imaging (MRI)*</td>
</tr>
<tr>
<td>3a B +/-</td>
</tr>
</tbody>
</table>

* Consider in case of increased risk (age < 50 y, HR neg., diagnostic assessability C/D in mammography + ultrasound)
## Early Detection of Potentially Curable Events

**Contralateral breast cancer:**

<table>
<thead>
<tr>
<th>Relative risk: 2.5 - 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence: 0.5 - 1.0 %/year</td>
</tr>
<tr>
<td>Breast self-examination</td>
</tr>
<tr>
<td>Physical examination, mammography &amp; US</td>
</tr>
<tr>
<td>Routine breast MRI*</td>
</tr>
<tr>
<td><strong>Male breast cancer: analogous to BC in women</strong></td>
</tr>
</tbody>
</table>

* Consider in case of increased risk: age < 50 y, HR-neg., diagnostic assessability C/D in mammography + ultrasound.

**See chapter “Breast Cancer Specific Situations”**

### Statement risk and incidence


### Statement breast self examination

2. Montgomery DA, Krupa K, Cooke TG et al. Follow-up in breast cancer: does routine clinical examination improve...

Statement physical examination, mammography & US&MRI

Statement surveillance of male breast cancer
## Early Detection of Potentially Curable Events

**Unrelated site carcinoma:**
- MDS (RR 10.9), AML (RR 2.6–5.3), Colon RR 3.0;
- endometrium RR 1.6; ovary RR 1.5; lymphoma RR 7

### Screening for secondary malignancies according to current guidelines

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>UK GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>D</td>
<td>++</td>
</tr>
</tbody>
</table>

### Pelvic examination and PAP smear

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>UK GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>D</td>
<td>++</td>
</tr>
</tbody>
</table>

### Routine endometrial ultrasound / biopsy

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>UK GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>B</td>
<td>-</td>
</tr>
</tbody>
</table>

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**Statement: Risk**

7. Kaplan HG, Malmgren JA, Atwood MK. Increased incidence of myelodysplastic syndrome and acute myeloid leukemia following breast cancer treatment with radiation alone or combined with chemotherapy: a registry cohort analysis 1990-

Statement: Screening for secondary malignancies according to current guidelines

Statement: Pelvic examination and PAP smear
Statement: Endometrial ultrasound / biopsy

Statement: Marrow neoplasms after adjuvant breast cancer therapy

Statement: Secondary lung tumors:
Follow-Up Care for invasive / non-invasive Breast Cancer

Recommendations for asymptomatic pts.
(mod. according to ASCO-ACS recommendations 2016, NCCN 2021, ESMO 2019 and S3-guidelines 2017)

<table>
<thead>
<tr>
<th>Clinical follow-up</th>
<th>Follow-up*</th>
<th>Screening/ Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years after primary therapy</td>
<td>1 2 3 4 5 &gt; 5</td>
<td></td>
</tr>
<tr>
<td>History, physical examination, counseling</td>
<td>every 3 months, DCIS every 6 months</td>
<td>every 6 months inv.: every 12 months</td>
</tr>
<tr>
<td>Self-examination</td>
<td>monthly</td>
<td></td>
</tr>
<tr>
<td>Imaging modalities and biochemistry</td>
<td>indicated only if complaints, clinical findings, or suspicion of recurrence</td>
<td>Monitoring of side effects of therapy</td>
</tr>
<tr>
<td>Mammography and additional sonography</td>
<td>BCT**</td>
<td>both sides: every 12 months</td>
</tr>
<tr>
<td>Mastectomy</td>
<td></td>
<td>contralateral every 12 months</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>6,12,24 months and yearly up to 5 years after completion of cardiotoxic therapy, after 5th year, every 5 years and if patient is symptomatic.</td>
<td></td>
</tr>
</tbody>
</table>

* Continued follow-up visits if still on adjuvant treatment
** In pts after breast-conserving therapy (BCT): First mammography 1 year after initial mammography or at least 6 months after completion of radiotherapy


# Breast Cancer Follow-up
## Duration and Breast Nurses

<table>
<thead>
<tr>
<th>Duration of follow-up</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>up to 5 years</td>
<td>1c</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>up to 10 years</td>
<td>1c</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>Surveillance by specialized breast nurses</td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
</tbody>
</table>

* Studies recommended

Luminal-like, HER2-positive and Triple-negative Breast Cancer Patients

- Intrinsic typing of breast cancer leads to subgroups with different course of disease. Thus, postoperative surveillance should be adapted to specific time-dependent hazards of recurrence.
- ER-positive patients have stable risk over many years requiring long term surveillance.
- However, patients with HER2-positive disease and TNBC have more risk in the early phase of follow-up and should therefore receive more intense surveillance in the first years of follow-up.