Breast Cancer Surgery
Oncological Aspects
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- **Versions 2002–2013:**
  Bauerfeind / Böhme / Blohmer / Costa / Fersis / Gerber / Hanf / Janni / Junkermann / Kaufmann / Kümmel / Nitz / Rezai / Simon / Solomayer / Thomssen / Untch

- **Version 2014:**
  Kühn / Kümmel
## Pretherapeutic Assessment

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Oxford / AGO LoE / GR</th>
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</thead>
<tbody>
<tr>
<td>Palpation</td>
<td>5 D ++</td>
</tr>
<tr>
<td>Mammography</td>
<td>2b B ++</td>
</tr>
<tr>
<td>Ultrasound (breast &amp; axilla)</td>
<td>2b B ++</td>
</tr>
<tr>
<td>Minimalinvasive biopsy**</td>
<td>1c A +</td>
</tr>
<tr>
<td>MRI*</td>
<td>1c B +/-</td>
</tr>
</tbody>
</table>

*No reduction of re-excision rate.

The possibility of MRI guided biopsy is the precondition of breast MRI (e.g. dense breast tissue and invasive lobular cancer, suspicion of multifocal or multicentric disease).

**If clinical examination, mammography, ultrasound and in some cases MRI are not able to determine the extension of lesion.
Perioperative Staging

- History and physical examination
  - Oxford / AGO LoE / GR: 5 D ++

High metastatic potential and / or symptoms:

- Chest X-ray
  - 5 D +
- Liver ultrasound
  - 5 D +
- CT-scan
  - 5 D +
- Bone-scan
  - 5 D +
- FDG-PET or FDG-PET / CT
  - 4 C -
- Whole body MRI
  - 4 C -
Evidence of Surgical Procedure

- Survival rates after lumpectomy + XRT are equivalent to those after (modified) radical mastectomy
  - 1a A

- Survival rates after modified radical mastectomy are equivalent to those after radical mastectomy
  - 1b A

- Local recurrence rates after skin sparing mastectomy are equivalent to those after mastectomy
  - 2b B

- Conservation of the NAC (nipple areola complex) is an adequate surgical procedure in tumors of the periphery of the gland and after tumor-free section of retroareolar tissue
  - 4b C
# Breast Conservation: Surgical Technical Aspects

<table>
<thead>
<tr>
<th>Oxford / AGO LoE / GR</th>
<th>2b</th>
<th>B</th>
<th>++</th>
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<tbody>
<tr>
<td></td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
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<tr>
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<td>2b</td>
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<td>3b</td>
<td>C</td>
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<td></td>
<td>4</td>
<td>D</td>
<td>-  -</td>
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<tr>
<td></td>
<td>1a</td>
<td>A</td>
<td>+/-</td>
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</table>

- **Non-palpable lesion**
  - Wire guided localisation
  - Radionuclide guided localisation
  - Specimen radiography or ultrasound

- **Tumor-free margins required**

- **Immediate intraoperative re-excision for close margins (specimen radiography and/or intra-operative pathology)**

- **Re-excision required for involved margins (paraffin section)**

- **Therapeutic stereotactic excision alone**

- **Ultrasound guided surgery to prevent re-excision**
Breast Conservation Surgery (BCS)

- Multicentricity
- Positive microscopic margins after repeated excision
- Inflammatory breast cancer
- pCR after neoadjuvant chemotherapy

Oxford / AGO LoE / GR

- Multicentricity: 2b B +/-
- Positive microscopic margins after repeated excision: 2b B - -
- Inflammatory breast cancer: 2b B - -
- pCR after neoadjuvant chemotherapy: +/-
Axillary Lymph Node Dissection I

Axillary lymph node dissection (>=10 LN)
- To improve survival
- For staging
- For local control

Axillary lymph node dissection:
- DCIS
- cT1/2 cN0 (without prior sentinel)
- SN+ (cT1/2 cN0; < 3 SN+, BCS + tangential radiation field, no subsequent axillary radiation, adequate systemic therapy)
- SN+ (mic)
- SN (i+)
- SN+ mastectomy

Axillary lymph node dissection indicated, but not feasible
- Radiation according to AMAROS-Trial

<table>
<thead>
<tr>
<th>Oxford / AGO</th>
<th>LoE / GR</th>
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<tbody>
<tr>
<td>3</td>
<td>D -</td>
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<tr>
<td>3</td>
<td>A ++</td>
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<td>2a</td>
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<td>2b</td>
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<tr>
<td>1b</td>
<td>B +</td>
</tr>
<tr>
<td>1b^a</td>
<td>B +/-</td>
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</tbody>
</table>
Surgical Treatment of Axillary Lymph Nodes pre and post NACT (Neoadjuvant Chemotherapy)

<table>
<thead>
<tr>
<th>SLNB pre or post NACT - cN0</th>
<th>Oxford / AGO LoE / GR</th>
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<tbody>
<tr>
<td>SLNB pre NACT</td>
<td>SLNB post NACT</td>
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</table>

**Surgical Procedure according to lymph node status**

<table>
<thead>
<tr>
<th>cN-Status (prior Therapy)</th>
<th>pN-Status (prior Therapy)</th>
<th>cN-Status (after Therapy)</th>
<th>Surgical Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>cN0</td>
<td>pN0(sn)</td>
<td>-</td>
<td>nihil</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1a      A  +</td>
</tr>
<tr>
<td>cN0</td>
<td>pN+(sn) according ACOSOG Z11* criteria</td>
<td>ycN0</td>
<td>ALND</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3      B  +/-</td>
</tr>
<tr>
<td>cN0</td>
<td>pN+(sn) not according to ACOSOG* criteria</td>
<td>ycN0</td>
<td>ALND</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2b      B  +</td>
</tr>
<tr>
<td>cN+</td>
<td>cN+ (CNB/FNA)</td>
<td>ycN0</td>
<td>SNB ALND</td>
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<td></td>
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<td></td>
<td>3      2b  B  +/-</td>
</tr>
<tr>
<td>cN+</td>
<td>ycN+ (CNB/FNA)</td>
<td>ycN+ (CNB/FNA)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2b      B  ++</td>
</tr>
</tbody>
</table>

* T1/T2, BCT, 1-2 SLN pos, Breast radiation
Sentinel Lymph Node Excision (SNE): Indications I

- Clinically (cN0) / sonographically neg. axilla
- T 1-2
- T 3, 4a-c
- Multifocal / multicentric lesions
- DCIS
  - ≥ 5 cm or 2,5 cm + high grade (see DCIS) if mastectomy is required
- Male breast cancer
- In the elderly
- Add. FNA/CNB of LN (clinical/sonogr. suspicious) in order to enable SNE

Oxford / AGO LoE / GR

<table>
<thead>
<tr>
<th>Indication</th>
<th>LoE</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically (cN0) / sonographically neg. axilla</td>
<td>1b</td>
<td>A ++</td>
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<td>T 1-2</td>
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<tr>
<td>DCIS</td>
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<tr>
<td>Male breast cancer</td>
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<td>B +</td>
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<tr>
<td>In the elderly</td>
<td>3b</td>
<td>B +</td>
</tr>
<tr>
<td>Add. FNA/CNB of LN (clinical/sonogr. suspicious) in order to enable SNE</td>
<td>2b</td>
<td>C +</td>
</tr>
</tbody>
</table>
Sentinel Lymph Node Excision (SNE): Indications II

- During pregnancy and/or breast feeding (No blue duy)
  - Oxford / AGO LoE / GR: 3 C +

- After previous tumor excision
  - Oxford / AGO LoE / GR: 2b B +

- Previous major breast surgery (e.g. reduction mammoplasty, mastectomy)
  - Oxford / AGO LoE / GR: 3b C +/−

- Ipsilateral breast recurrence after prior BCS and prior SNE
  - Oxford / AGO LoE / GR: 4 D +/−*

- SN in the mammarian internal chain
  - Oxford / AGO LoE / GR: 2b B −

- After axillary surgery
  - Oxford / AGO LoE / GR: 3b B +/−*

- Prophylactic bilateral/contralateral mastectomy
  - Oxford / AGO LoE / GR: 3b B − −

- Inflammatory breast cancer
  - Oxford / AGO LoE / GR: 3b C +/−

* Lymph node scintigraphy is necessary
Procedure after Neoadjuvant Therapy

- Marking of tumor
- Surgery
- Microscopically clear margins
- Tumor resection in the new margins

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<tr>
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<tr>
<td>Marking of tumor</td>
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<td>2b C ++</td>
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<tr>
<td>Microscopically clear margins</td>
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<tr>
<td>Tumor resection in the new margins</td>
<td>3b C +</td>
</tr>
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</table>
Surgery and Irradiation after Neoadjuvant Therapy

Breast surgery:

After the nadir of the leucocyte count
(2 to 4 weeks after the last chemotherapy)

If irradiation after Mastectomy is recommended
< 6 weeks after surgery
Indication based on the initial stage prior NT (cN+, cT3/4a-d)

Oxford / AGO
LoE / GR

4 C ++
2b B ++
Surgery after Neoadjuvant Therapy

**Guidelines Breast**

**Version 2014.1**

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### Surgery after Neoadjuvant Therapy

#### Breast conservation after clinical response possible:

- **Multicentric lesion**
- **cT4a-c**
- **Inflammatory breast cancer (in case of pCR)**

#### Mastectomy is recommended:

- **If after re-excision no clear margins are achieved**
- **Extensive DCIS**
- **If irradiation is not feasible**

<table>
<thead>
<tr>
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<tr>
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</tr>
<tr>
<td><strong>cT4a-c</strong></td>
</tr>
<tr>
<td><strong>Inflammatory breast cancer (in case of pCR)</strong></td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td><strong>Extensive DCIS</strong></td>
</tr>
<tr>
<td><strong>If irradiation is not feasible</strong></td>
</tr>
</tbody>
</table>

* Study participation recommended
### Adjuvant Therapy after Primary Surgery

- **Start adjuvant systemic therapy and RT as soon as possible (a.s.a.p.) after surgery**
  - Oxford / AGO LoE / GR: 1b A ++

- **Start of adjuvant chemotherapy after surgery a.s.a.p., and prior to RT**
  - Oxford / AGO LoE / GR: 1b A ++

**Without cytotoxic therapy:**

- **Start irradiation 6-8 weeks after surgery**
  - Oxford / AGO LoE / GR: 2b B ++

- **Start endocrine therapy after surgery and a.s.a.p.**
  - Oxford / AGO LoE / GR: 5 D ++

- **Tamoxifen concurrent with radiotherapy**
  - Oxford / AGO LoE / GR: 3b C +

- **AI concurrent with radiotherapy**
  - Oxford / AGO LoE / GR: 2a B +/-
Further information and references: Kühn T., Kümmel S.

Update Januar 2014
Screened consensus conference:
Cochrane library:
Pretherapeutic Assessment (3/15)

Further information:

Preoperative breast diagnosis is required for planing breast surgery and avoiding surgery in benign conditions. Breast palpation, actual mammography and breast ultrasound are mandatory. Breast imaging diagnostic is avoidable in LABC (e.g. bleedings, ulceration). Malignancy and tumor size can best be evaluated by using both imaging procedures. Suspicious microcalcifications can be further characterized by magnification views. MRI staging causes more extensive breast surgery in an important proportion of women by identifying additional cancer, however there is a need to reduce FP MRI detection. Randomized trials are needed to determine the clinical value of detecting additional disease which changes surgical treatment in women with apparently localized breast cancer. MRI could be an option in patients with ambiguous mammographic and/or ultrasound findings to further characterize the lesions and in young women at high risk of breast cancer. Histological examination of every suspicious breast lesion should be carried out preoperatively by (image-directed) percutaneous needle biopsy to warrant one-session definitive surgery. The relationship between benign and malignant lesions should not exceed 1:2 after open biopsy. FDG PET is not recommended for axillary staging of patients with newly diagnosed breast cancer because of it fails to detect axillae with small and few nodal metastases.

References:

Statement: Palpation
GCP
Statement: All Methods:

Statement: Mammography / Ultrasound

**Statement MRI**

and meta-analysis of incremental cancer detection and impact on surgical management. JCO 2009; 27(33):5640-5649

17. Houssami N, Hayes DF Review of preoperative magnetic resonance imaging (MRI) in breast cancer: Should MRI be performed on all women with newly diagnosed early stage breast cancer. CA Cancer J Clin 2009; 59:290-302


Statement Minimal invasive biopsy

Further information:

A history and physical examination are good clinical practice and an obligation in every patient. Chest X-ray, liver ultrasound and bone scan have been used for initial staging of breast cancer. Patients with early, low risk breast cancer do not benefit from routine staging procedures. The routinously examination of serum liver enzymes, chest X-ray, liver ultrasound and bone scans in patients with high risk disease (clinically N1 and/or G3, cT3) could be helpful to avoid an overtreatment in cases with distant metastases. FDG-PET / PET-CT are valuable tools for detecting breast cancer recurrence and occult metastases, however a survival benefit due to early detection has not been proven yet. Moreover the technique is expensive and not everywhere available.

References:

Statement: history and physical examination
GCP

Statement: high metastatic potential / symptoms

Evidence of Surgical Procedure (5/15)

Further information:

The standard surgical procedure for early breast cancer is breast conservation followed by radiation therapy. Ipsilateral breast tumor relapse rates should be lower than 10% after 10 years of follow-up. Randomised trials and clinical series of breast conservation report conflicting evidence relating to tumour size as a risk factor for local recurrence, although most studies report no association. There is little evidence to justify the use of tumour size alone as an exclusion criterion for breast-conservation therapy. Survival rates after modified radical mastectomy are equivalent to those after radical mastectomy. The skin sparing mastectomy with or without conservation of the nipple-areola complex and autologous reconstruction is a oncological safe treatment option in selected patients. Survival rates after modified radical mastectomy are equivalent to those after radical mastectomy according to Rotter-Halstedt.

References:

Statement: lumpectomy - mastectomy

Statement skin sparing mastectomy


**Statement: Nipple sparing mastectomy**


Statement radical mastectomy vs. simple mastectomy
Breast Conservation (6/15)

Further information:

Excisional biopsy should be wire guided if the lesion is not palpable and specimen radiography should be performed. Radioguided occult lesion localisation' (ROLL) is a possible alternative to the commonly used 'wire-guided localisation' (WGL) of non-palpable breast lesions. Intratumoural injection of a radiotracer identifies both the primary tumour and the sentinel lymph nodes for intraoperative gamma probe guided dissection. The intraoperative radiography or ultrasound is in all cases of non-palpable lesions indicated (GCP). In breast conserving surgery the margins of the specimen have to be tumor free. There is no universal agreement on the width of the tumor free margin. Re-excision is required for a close margin $< 1$ mm in paraffin section. The re-excision is recommended in a period of $< 4$ weeks. Patients with involved margins, large tumour size and/or a DCIS component are more likely to have residual disease on re-excision. The rate of re-excision even in experienced and large breast centers is about 20% (up to 25% in case of DCIS).

References:

Statement: Wire guided ...


Statement: Specimen radiography

Statement: specimen radiography ...
Statement: tumor free margins ...

Statement: ... re-excision ...
Statement: stereotactic excision alone ...


Breast Conservation Surgery (7/15)

Further information:

There are no randomized trials concerning BCS vs mastectomy in patients with multicentric breast cancer or inflammatory breast cancer. Multicentricity is defined as at least two separate lesions with a distance of > 4 cm. All indications for mastectomy in these patients are driven from the fact that local recurrence rate is significantly elevated in these patient groups. If there are no free margins after repeated excisions the option of mastectomy should discussed with the patient.

References:

Statement: all

Statement: positive microscopic ...

Statement: Inflammatory Carcinoma

1. Jennifer A. Low, Arlene W. Berman, Seth M. Steinberg: Long-Term Follow-Up for Locally Advanced and Inflammatory Breast Cancer Patients Treated With Multimodality Therapy. JCO 2004: 4067-4074
**Axillary Lymph Node Dissection I (8/15)**

*Further information:*

Axillary lymph node dissection improves clinical outcome only in patients with lymph node metastases. Axillary dissection is mainly a diagnostic procedure. Removal of tumor-free lymph nodes increases morbidity and has no prognostic impact. Available evidence suggests that quality assured sentinel lymph node biopsy (SLNB) is a reliable predictor of axillary lymph node status with high levels of sensitivity (90-95%), specificity (100%), negative predictive value (95%) and accuracy (97%).

In case of adequate multimodal treatment axillary dissection axillary dissection is not associated with improved overall survival

*References:*

**Statement: Axillary lymph node dissection**

   Complete Axillary lymph node dissection after positive sentinel lymph node may be ommitted in certain cases due to lack of benefit in pospectively randomized studies.

Statement AMAROS trial
Axillary dissection and radiotherapy are both associated with excellent regional control rates in clinically node-negative patients with a positive sentinel lymph node as has been shown in the AMAROS trial. Patients who received radiotherapy had significant less arm morbidity compared to patients who underwent axillary dissection. However some questions remain regarding this study such as the necessity of internal and supra-infra node irradiation. Due to many open questions the publication of the full paper of the AMAROS trial should be awaited before radiotherapy is used routinely to replace axillary surgery in patients, who require axillary dissection
1. Rutgers E, Donker M Straver ME et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients: Final analysis of the EORTC AMAROS trial (10981/22023). J Clin Oncol 31,2013 (suppl;abstr LBA 1001)
Further information:

Statement surgical intervention in the axilla before or after Neoadjuvant Chemotherapy
Axillary surgery is a diagnostic procedure with the primary goal to provide prognostic information for the planning of treatment decisions. In the adjuvant setting the axillary status may tailor systemic (in luminal B) and regional treatment. The systemic treatment in patients, who undergo neoadjuvant therapy is (in general) predefined. In these patients the histopathologic response to chemotherapy (that includes response in the breast and the lymph nodes) is an important prognostic factor with a high potential to tailor future systemic and regional treatment decisions. Therefore it would be more reasonable to perform SLNB after NACT in order to provide this important prognostic factor.

SLNB after neoadjuvant chemotherapy is, however, associated with less favourable success rates (detection rate, false negative rate) compared to SLNB in primary surgery (as shown in the SENTINA trial). This relates especially to patients, who present initially with positive lymph nodes and convert to a negative axillary status under NACT. For patients with initially negative lymph nodes the success rates for SLNB after NACT appear more favourable although evidence from sufficiently powered prospective trials is lacking. Furthermore no data regarding oncologic endpoints (disease free survival, overall survival) are yet available for the SLN procedure after NACT.

In conclusion SLNB prior to NACT is a safe procedure, that can spare many patients with advanced tumors from axillary dissection. SLNB after NACT is an important future perspective, that should, however, be performed within clinical trials to provide the urgently awaited data on clinical outcome.

No references
Sentinel Lymph Node Excision: Indications I (10/15)

Further information:

Sentinel lymph node excision (SLN) has become a standard surgical procedure in patients with clinically and sonographically negative axilla (cN0). Sonographically critria for the definition of „negative lymph node“ has to be precised. Indication for SNE is not only focused on small tumours but nowadays possible and proven in many indications (cT3, Multicentricity). In large DCIS or if a mastectomy is required - SNE should be offered to the patient. Although male breast cancer patients presented with older age and larger tumors than female breast cancer patients - SLN procedure in clinically node-negative men is feasible and accurate. Preoperative ultrasound guided needle biopsy is accurate for initial staging of the axilla and should be used for women with invasive breast cancer and clinical suspect axillary lymph nodes, as has been shown in a recently published metaanalysis

References:

Statements


   Sentinel lymph node biopsy at the time of mastectomy does not increase the risk of lymphedema: implications for prophylactic surgery.
**Sentinel Lymph Node Excision: Indications I (11/15)**

*Further information:*

There are only few experiences reported about SNE during pregnancy. The radioactive dosage of the applied radiocolloid is estimated very low and therefore not harmful for the unborn. Nothing is known about altered lymphdrainage during pregnancy. The Bundesamt für Strahlenschutz has stated in a letter to the author that no fetal harm will be expected after application of 11 MB at the day of surgery and that therefore is no indication for termination of pregnancy. By performing a SLN biopsy, a large proportion of patients with PABC may be spared the risk of a complete axillary lymph node dissection. Therefore the commission decided a + for the procedure during pregancy. The management of internal mammary nodes (IMNs) in breast cancer is still controversial. RCT are in progress. Data from small series have shown that second SLNB after previous SLNB is technically feasible and likely effective in selected breast cancer patients. A SLNE is not recommended in patients with prior surgery and large disturbing the lymphatic vessels in the breast or axillar or between these regions. In Inflammatory BC the feasibilty of SNE is of limited data. Suspected clinical lymph node involvement should be clarified with FNA/CNB to avoid overtreatment in case of axillary lymph node dissection with negative involvement after clinically suspicious lymph nodes.

For patients, who undergo repeat SLNB after previous axillary surgery lymphoscintigraphy should be performed because a high rate of extraaxillary SLN has been described in this setting.

*References:*

**Statement: pregnancy**


Statement: mammarian internal

Statement: all others

Statement 10
**Procedure after Neoadjuvant Therapy (12/15)**

*Further information:*

Precise documentation of tumor location before – e.g. with intratumoral clip implantation -, during and at the end of primary systemic therapy (PST) is necessary. Surgery is an integral part of primary breast cancer treatment following PST. The aim of surgery is to completely remove invasive and non invasive breast cancer residues after PST and to obtain clear margins of at least 1 mm at pathology examination. No compromise should be made in surgical margins to obtain better cosmetic results. Under these circumstances excision within new tumor margins might be feasible according to current data.

**References**

Surgery and Irradiation after Neoadjuvant Therapy (13/15)

Further information:

It is unknown whether preoperative radiotherapy following primary systemic therapy (PST) achieved similar results as radiotherapy following PST and surgery. Preoperative radiotherapy might result in higher rates of breast conservation without compromising cosmetic result.\(^1\) However, preoperative external beam and brachytherapy are not established as modes of treatment in conjunction with PST\(^2\) and do not replace adequate surgery\(^3\)–\(^6\) which should be performed after leucocyte nadir around 2 to 4 weeks following last cycle of chemotherapy.\(^7\) Adjuvant radiotherapy after PST should be administered according to the same recommendations made for those patients who do not receive PST.\(^8\)–\(^10\) Even in patients with pathological complete response following PST whole breast irradiation is indicated after breast-conserving surgery.\(^3\)\(^,\)^\(^4\) According to retrospective analyses the addition of radiation to PST and mastectomy reduces local regional recurrence and increases breast cancer specific survival for patients presenting with clinical T3 tumors or stage III and IV (ipsilateral supraclavicular nodal) disease and for patients with \(\geq\) four positive axillary nodes regardless of their response to PST.\(^11\)

References:

**Surgery after Neoadjuvant Therapy (14/15)**

*Further information:*

Primary systemic therapy (PST) to achieve breast conserving surgery is not indicated in multicentric cancer, if extensive DCIS is present or if radiotherapy is not feasible.\(^{1-3}\)

*References:*

3. Osteen RT. Cancer 74, 366, 1994
Adjuvant Therapy after Primary Surgery (15/15)

No further information

References:

Concurrent use of endocrine therapy:

Timing of radiation and chemotherapy:
