Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

Breast Cancer Surgery

Oncological Aspects
Breast Cancer Surgery
Oncological Aspects

Versions 2002–2016:
Bauerfeind / Blohmer / Böhme / Brunnert / Costa / Fersis / Gerber / Hanf / Janni / Junkermann / Kaufmann / Kühn / Kümmel / Nitz / Rezai / Simon / Solomayer / Thill / Thomssen / Untch

Version 2017:
Kühn / Rezai
Surgery is one sub-step out of multiple steps in breast cancer treatment. Thus, both a diagnostic and an oncological expertise are indispensable and a definite requirement.
Pretherapeutic Assessment

- Palpation
- Mammography
- Ultrasound (breast & axilla)
- Minimal invasive biopsy*
- MRI**

<table>
<thead>
<tr>
<th>Oxford / AGO</th>
<th>LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>1c</td>
<td>A</td>
</tr>
<tr>
<td>1c</td>
<td>B</td>
</tr>
</tbody>
</table>

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

** No significant reduction of re-excision rate.

The possibility of MRI guided biopsy is the precondition of breast MRI (e.g. dense breast tissue 3-4, C, D and invasive lobular cancer, suspicion of multifocal or multicentric disease)
Perioperative Staging

- History and physical examination

Only recommended in high metastatic potential and / or with symptoms:

- Chest X-ray
- Liver ultrasound
- CT-scan
- Bone-scan
- FDG-PET or FDG-PET / CT
- Whole body MRI

Oxford / AGO LoE / GR

<table>
<thead>
<tr>
<th>Procedure</th>
<th>LoE</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examination</td>
<td>5</td>
<td>D++</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>5</td>
<td>D+</td>
</tr>
<tr>
<td>Liver ultrasound</td>
<td>5</td>
<td>D+</td>
</tr>
<tr>
<td>CT-scan</td>
<td>5</td>
<td>D+</td>
</tr>
<tr>
<td>Bone-scan</td>
<td>5</td>
<td>D+</td>
</tr>
<tr>
<td>FDG-PET or FDG-PET / CT</td>
<td>4</td>
<td>C-</td>
</tr>
<tr>
<td>Whole body MRI</td>
<td>4</td>
<td>C-</td>
</tr>
</tbody>
</table>
Evidence of Surgical Procedure

- Survival rates after lumpectomy + XRT are equivalent to those after (modified) radical mastectomy
- Survival rates after modified radical mastectomy are equivalent to those after radical mastectomy
- Local recurrence rates after skin sparing mastectomy are equivalent to those after mastectomy
- 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

Oxford / AGO LoE / GR

1a A
1b A
2b B
2b C
Breast Conservation: Surgical Technical Aspects

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

- **Tumor-free margins required**
  - (also in unfavorable biology „no cells on ink“ are enough)

- **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**

- **Intraop. margin evaluation with margin probe**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Oxford/AGO LoE</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wire guided localisation</td>
<td>2b B ++</td>
<td></td>
</tr>
<tr>
<td>Radionuclide guided localisation</td>
<td>2b B +/-</td>
<td></td>
</tr>
<tr>
<td>Specimen radiography or ultrasound</td>
<td>2b B ++</td>
<td></td>
</tr>
<tr>
<td>Tumor-free margins required</td>
<td>2a A ++</td>
<td></td>
</tr>
<tr>
<td>Immediate intraoperative re-excision for close margins</td>
<td>1c B ++</td>
<td></td>
</tr>
<tr>
<td>Re-excision required for involved margins</td>
<td>3b C +</td>
<td></td>
</tr>
<tr>
<td>Therapeutic stereotactic excision alone</td>
<td>4 D - -</td>
<td></td>
</tr>
<tr>
<td>Ultrasound guided surgery to prevent re-excision</td>
<td>1a A +/-</td>
<td></td>
</tr>
<tr>
<td>Intraop. margin evaluation with margin probe</td>
<td>1b A +/-</td>
<td></td>
</tr>
</tbody>
</table>
Breast Conservation Surgery (BCS)

- Multicentricity
- Positive microscopic margins after repeated excision
- Inflammatory breast cancer

Surgery after neoadjuvant chemotherapy go to chapter „neoadjuvant chemotherapy“
Axillary Lymph Node Dissection I

<table>
<thead>
<tr>
<th>Axillary lymph node dissection (&gt;=10 LN)</th>
<th>Oxford / AGO LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>To improve survival</td>
<td>3  D  -</td>
</tr>
<tr>
<td>For staging</td>
<td>3  A  -</td>
</tr>
<tr>
<td>For local control</td>
<td>2a  A  +/-</td>
</tr>
</tbody>
</table>

Axillary lymph node dissection

- DCIS
- If SLNB is possible
- SN + (cT1/2 cN*0; < 3 SN +, BCS + tangential radiation field, no subsequent axillary radiation, adequate systemic therapy)
- SN + (mic)
- SN (i+)
- SN + mastectomy (no radiotherapy of the chestwall)
- SN+ mastectomy (radiotherapy of the chestwall)
  - Only if T1, T2 and 1-2 pos. SLN

Axillary lymph node dissection indicated, but not feasible

- Radiation according to AMAROS-trial
  - 1b<sub>a</sub>  B  +

* Study participation recommended
# Axillary Intervention Before or After NACT

<table>
<thead>
<tr>
<th>SLNB before or after NACT in cN0</th>
<th>SLNB before NACT</th>
<th>SLNB after NACT</th>
<th>Oxford / AGO LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td><strong>SLNB before NACT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SLNB after NACT</strong></td>
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</tbody>
</table>

**Further surgical procedures depending on SLNB status**

<table>
<thead>
<tr>
<th>cN-Status (before NST)</th>
<th>pN-Status (before NST)</th>
<th>cN-Status (after NST)</th>
<th>Surgical Procedure (after NST)</th>
<th>Oxford / AGO LoE / GR</th>
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</thead>
<tbody>
<tr>
<td>cN0</td>
<td>pN0(sn)</td>
<td>-</td>
<td>nihil</td>
<td>1a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>cN0</td>
<td>pN+(sn)</td>
<td>ycN0</td>
<td>nilhil Re-SLNB alone ALND</td>
<td>5</td>
</tr>
<tr>
<td>(analog ACOSOG Z0011)</td>
<td></td>
<td></td>
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<td>D</td>
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<td></td>
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<td></td>
<td>+</td>
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<tr>
<td></td>
<td></td>
<td>ycN0</td>
<td>Re-SLNB alone ALND Axilla XRT</td>
<td>2b</td>
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<tr>
<td>(not analog ACOSOG Z0011)</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td>cN0</td>
<td>pN+(sn)</td>
<td>ycN0</td>
<td>SLNB alone ALND</td>
<td>2b</td>
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<tr>
<td>not done</td>
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<td>B</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>cN0</td>
<td>not done</td>
<td>ycN0</td>
<td>SLNB alone ALND</td>
<td>2b</td>
</tr>
<tr>
<td>ypN0 (sn)</td>
<td></td>
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<td></td>
<td>B</td>
</tr>
<tr>
<td>ypN+ (sn)</td>
<td></td>
<td></td>
<td></td>
<td>B</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td>cN+</td>
<td>cN+ (CNB/FNA)</td>
<td>ycN0</td>
<td>SLNB alone* ALND ALND</td>
<td>2b</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+/-</td>
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</tbody>
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Guidelines Breast
Version 2017.1

www.ago-online.de
Improvement of the False-Negative Rate of SLNB after NACT in Patients with (cN+) (FNA/CNB)

- Removal of > 2 SLNs
- Combined tracer
- IHC and serial sections
- LN localisation

Oxford / AGO LoE / GR

<table>
<thead>
<tr>
<th></th>
<th>LoE</th>
<th>Evid.</th>
<th>Grade</th>
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</thead>
<tbody>
<tr>
<td>Removal of &gt; 2 SLNs</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Combined tracer</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>IHC and serial sections</td>
<td>2b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>LN localisation</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Sentinel Lymph Node Biopsy (SLNB): Indications I

- Clinically (cN0) / sonographically neg. axilla
- Add. FNA/CNB of LN (clinical/sonogr. suspicious) in order to enable SLNB
- T 1-2
- T 3, 4a-c
- Multifocal / multicentric lesions
- DCIS
  - Mastectomy
  - DCIS in male
- BCT
- Male breast cancer
- In the elderly

Oxford / AGO LoE / GR

<table>
<thead>
<tr>
<th>Indication</th>
<th>LoE</th>
<th>Grade</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically (cN0) / sonographically neg. axilla</td>
<td>1b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Add. FNA/CNB of LN (clinical/sonogr. suspicious) in order to enable SLNB</td>
<td>2a</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>T 1-2</td>
<td>2b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>T 3, 4a-c</td>
<td>3b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Multifocal / multicentric lesions</td>
<td>2b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>DCIS</td>
<td>3b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>3b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>DCIS in male</td>
<td>5</td>
<td>D</td>
<td>+</td>
</tr>
<tr>
<td>BCT</td>
<td>3b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>2b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>In the elderly</td>
<td>3b</td>
<td>B</td>
<td>+</td>
</tr>
</tbody>
</table>
Sentinel Lymph Node Excision (SNE): Indications II

- During pregnancy and / or breast feeding
  (no blue dye)
- After previous tumor excision
- Previous major breast surgery
  (e.g. reduction mammoplasty, mastectomy)
- Ipsilateral breast recurrence after prior BCS
  and prior SNE
- SN in the mammarian internal chain
- After axillary surgery
- Prophylactic bilateral / contralateral mastectomy
- Inflammatory breast cancer

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

* Lymph node scintigraphy is necessary
Sentinel Lymph Node Excision (SNE): Marking

- $^{99m}$Tc Kolloid
- Blue dye
- Methylene blue
- Indocyanin green (ICG)*
- SPIO#

<table>
<thead>
<tr>
<th>Oxford / AGO LoE / GR</th>
<th>1a</th>
<th>A</th>
<th>++</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>B</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>D</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>B</td>
<td>+/-</td>
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# SPIO: Superparamagnetic Iron Oxide

* Study participation recommended
### Procedure after Neoadjuvant Therapy

<table>
<thead>
<tr>
<th>Oxford / AGO</th>
<th>LoE / GR</th>
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<tbody>
<tr>
<td>5 D ++</td>
<td></td>
</tr>
<tr>
<td>2b C ++</td>
<td></td>
</tr>
<tr>
<td>5 D ++</td>
<td></td>
</tr>
<tr>
<td>3b C +</td>
<td></td>
</tr>
</tbody>
</table>

1. Marking of tumor in a timely manner
2. Surgery
3. Microscopically clear margins
4. Tumor resection in the new margins

For „Surgery after neoadjuvant chemotherapy“ see chapter „Neoadjuvant chemotherapy“
Adjuvant Therapy after Primary Surgery

- Start adjuvant systemic therapy and RT as soon as possible (a.s.a.p.) after surgery
  - 1b A ++

- Start of adjuvant chemotherapy after surgery a.s.a.p., and prior to RT
  - 1b A ++

Without cytotoxic therapy:

- Start irradiation 6-8 weeks after surgery
  - 2b B ++

- Start endocrine therapy after surgery and a.s.a.p.
  - 5 D ++

- Tamoxifen concurrent with radiotherapy
  - 3b C +

- AI concurrent with radiotherapy
  - 3b C +
Breast Cancer Surgery Oncologic Aspects (2/16)

Further information and references:

Update Januar 2017

Screened consensus conference:
Cochrane library:
Breast Cancer Surgery Oncologic Aspects (3/16)

No further information

No references
Pretherapeutic assessment (4/16)

No further information

References:

Statement: Palpation

1. GCP

Statement: General


Statement: Mammography / Ultrasound


Statement minimal invasive biopsy

Statement MRI

6. 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


Pre-operative staging (5/16)

No further information

References:

Statement: history and physical examination

1. GCP

Statement: high metastatic potential / symptoms

Evidence of surgical procedure (6/16)

No further information

References:

Statement: lumpectomy – mastectomy


Statement: skin sparing mastectomy


Statement: Nipple sparing mastectomy


Breast Conservation, Surgical Technical Aspects (7/16)

No further information

References:

Statement: Wire guided ...


Statement: Radioguided ...

Statement: specimen radiography


Statement: tumor free margins ...


Statement: tumor free margins in intrinsic subtypes


Statement: ... re-excision ...

Statement: stereotactic excision alone ...


Statement: Intraoperative ultrasound...


Statement: Margine probe

1. Freya Schnabel, Susan K. Boolbol, Mark Gittleman, Tami Karni, Lorraine Tafra, Sheldon Feldman, Alice Police, Neil B. Friedman, Scott Karlan, Dennis Holmes, Shawna C. Willey, Moshe Carmon, Kristen Fernandez, Stephanie Akbari, Jay Harness, Lisa Guerra, Thomas Frazier, Karen Lane, Rache M. Simmons, Alison Estabrook, and Tanir Allweiss. A Randomized Prospective Study of Lumpectomy Margin Assessment with Use of MarginProbe in
Breast Conservation Surgery (8/16)

No further information

References:

Statement: Multicentricity


Statement: positive microscopic ...


Statement: Inflammatory Carcinoma


Statement: general

Axillary Lymph Node Dissection I (9/16)

No further information

References:

Statement: Axillary lymph node dissection


**Statement AMAROS-trial**

Surgical Treatment of Axillary Lymph Nodes Pre and Post Nact (10/16)

No further information

References:

Statement: Axillary lymph node dissection

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


Statement surgical intervention in the axilla before or after neoadjuvant chemotherapy


Axillary Intervention Before or After NACT (11/16)

No further information

References:

Sentinel Lymph Node Excision: Indications I (12/16)

No further information

References:

Statement: SLNB


Statement: DCIS


Statement: elderly


Statement: preoperative FNA / core biopsy of suspicious lymph nodes


Statement: Lymphedema

Sentinel Lymph Node Excision: Indications II (13/16)

No further information

References:

Statement: pregnancy


Statement: mammarian internal

Statement: prophylactic mastectomy


Statement: After previous tumor excision


Statement: previous major breast surgery

1. Intra et al. Sentinel lymph node biopsy is feasible even after total mastectomy. J Surg Oncol 2007 Feb 1;95(2):175-9

Statement: Ipsilateral breast recurrence after prior BCS and prior SLNB


Statement: inflammatory breast cancer


Statement: Others


Sentinel Lymph node excision: Marking (14/16)

No further information

References:

Statement radiotracer/blue dye:


Statement: methylene blue


Statement: ICG:


Statement: SPIO:


Statement: General


Statement: Comparisons

Procedure after Neoadjuvant Therapy (15/16)

No further information

References

Statement: clip marking


Statement: operation and: tumor resection in new margins


Statement: tumor free margins ...

Ajuvant Therapy after Primary Surgery (16/16)

No further information

References:

Statement: Timing of radiation and chemotherapy


Statement: Tamoxifen concurrent with chemotherapy


Statement AI concurrent with radiotherapy

