Specific Sites of Metastases
Specific Sites Of Metastases

Local Approaches to Metastatic Disease

- **Versions 2002–2020:**
  Albert / Bauerfeind / Bischoff / Böhme / Brunnert / Dall / Diel / Fehm / Fersis / Friedrich / Friedrichs / Gerber / Hanf / Janni / Kolberg-Liedtke / Kreipe / Loibl / Lück / Lux / Maass / Oberhoff / Rezai / Rody / Schaller / Schütz / Seegenschmiedt / Solomayer / Souchon / Thomssen

- **Version 2021:**
  Mundhenke / Park-Simon / Thomssen
Specific Sites of Metastases

- Liver and lung metastases
- Malignant pleural and pericardial effusions
- Ascites
- Bone marrow involvement
- Soft tissue metastases
- Any other organs

See also chapters „CNS Metastases“ and „Locoregional Recurrence (Loco-Regional Recurrence Treatment Options in Non Curative Cases)“
General Treatment Aspects of Metastases

- **Histological / cytological verification**
  - Oxford: 3 B +

- **Systemic therapy preferred**
  - Oxford: 2a B ++*

- **Consider surgery only in case of good response to palliative treatment, oligometastases**
  - Oxford: 2b C +

- **Radiation for patients in good physical condition with late onset of oligometastases**
  - Oxford: 3a B +

- **Local treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression**
  - Oxford: 5 D +/-

- **Systemic treatment after surgery**
  - Oxford: 5 D ++

* See chapters with systemic treatment recommendations
Local Therapy in Primary Metastatic Disease

- **Surgery (R0) of the primary tumor (no OS Benefit)**
  - In case of symptoms by primary tumor
  - In case of bone metastases only
  - In case of visceral metastases

- **Axillary surgery for cN1**
  - In case of symptoms by primary tumor

- **Sentinel if cN0**

- **Radiotherapy of the primary tumor**
  - Alone (without surgery)
  - After local surgical treatment with BCS or mastectomy (according to adjuvant indication)

* Individualized procedure in case of oligometastatic disease

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (R0) of the primary tumor (no OS Benefit) in case of symptoms by primary tumor</td>
<td>1b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td>Surgery (R0) of the primary tumor (no OS Benefit) in case of bone metastases only</td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Surgery (R0) of the primary tumor (no OS Benefit) in case of visceral metastases</td>
<td>2b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td>Axillary surgery for cN1</td>
<td>5</td>
<td>D</td>
<td>+/-</td>
</tr>
<tr>
<td>Sentinel if cN0</td>
<td>5</td>
<td>D</td>
<td>-</td>
</tr>
</tbody>
</table>

Specific Sites of Metastases

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Guidelines Breast Version 2021.1E
## Randomized Phase III Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Prior to Randomization</th>
<th>Local Control</th>
<th>Improved OS Primary Endpoint</th>
<th>QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG-Acrin 2108</td>
<td>256</td>
<td>4-8 months systemic therapy</td>
<td>yes</td>
<td>no</td>
<td>ns</td>
</tr>
<tr>
<td>Tata Memorial Hospital</td>
<td>350</td>
<td>chemotherapy</td>
<td>yes</td>
<td>no</td>
<td>-</td>
</tr>
<tr>
<td>MF07-01</td>
<td>278</td>
<td>no systemic therapy</td>
<td>yes</td>
<td>no in post analysis evaluation improved OS (notably in solitary bone mets.)</td>
<td>-</td>
</tr>
<tr>
<td>ABCSG-28*</td>
<td>90</td>
<td>no systemic therapy</td>
<td>yes</td>
<td>no</td>
<td>ns</td>
</tr>
<tr>
<td>JCOG 1017</td>
<td>410</td>
<td>completed, results not reported so far</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ns not significant  *trial terminated due to poor recruitment
Liver Metastases

Local Therapy

- Resection of liver metastases (R0)
  - HR-positive: chemotherapy-sensitive, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases
  - HER2-positive: age < 50y, metastasis < 5 cm, no further metastasis

- Regional chemotherapy

- Regional radiotherapy
  [SIRT, stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT), radiochemo-embolization, other modalities]

- Thermoablation (RFA, LITT, cryotherapy)

<table>
<thead>
<tr>
<th>Oxford</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection of liver metastases (R0)</td>
<td>3a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Regional chemotherapy</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Regional radiotherapy</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Thermoablation (RFA, LITT, cryotherapy)</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
</tbody>
</table>
### Pulmonary Metastases

#### Local Therapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oxford</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LoE</td>
</tr>
<tr>
<td>Before any surgery: staging and biopsy (CT-guided FNA / CNB or transbronchial FNA, EBUS)</td>
<td>3a</td>
</tr>
<tr>
<td>Resection of pulmonary metastases by VATS or conventional resection</td>
<td>3a</td>
</tr>
<tr>
<td>- In case of multi-locular metastatic disease</td>
<td>3a</td>
</tr>
<tr>
<td>- In case of single / few unilateral metastasis with curative intent</td>
<td>3a</td>
</tr>
<tr>
<td>Thermoablation (CT-guided RFA, LITT)</td>
<td>3b</td>
</tr>
<tr>
<td>Regional radiotherapy (e.g. stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT))</td>
<td>3a</td>
</tr>
</tbody>
</table>

* VATS = video-assisted thoracic surgery

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### Specific Sites of Metastases

- Before any surgery: staging and biopsy
- Resection of pulmonary metastases by VATS or conventional resection
- Thermoablation (CT-guided RFA, LITT)
- Regional radiotherapy
Malignant Pleural Effusions (MPE)

Incidence:
- ~ 10% of patients with metastatic breast cancer
- ~ 17-30% of all MPE are caused by breast cancer

Clinical presentation:
- Extensive MPE are mostly due to malignancy
- The majority of MPE are symptomatic [dyspnea (80%), dull chest pain (30%), nonproductive cough (10%)]
- Survival is related to the presence of additional metastases, age, ECOG PS and extent of involving the pleural surface

Diagnostic procedures:
- Clinical examination
- Imaging techniques (chest X-Ray, US, CT-Scan)
- Proven malignant effusion [cytology (→ 50% false negative), histology by thoracoscopy]
Malignant Pleural Effusion (MPE)

Local Therapy

- If short life expectancy, less invasive procedures should be considered

- VATS and Talcum-pleurodesis*  
  - Talcum powder
  - Bleomycin, Doxycycline, Mitoxantrone
  - Povidone-iodine (20 ml of 10% solution)

- Chemical pleurodesis*  
  - VATS: video-assisted thoracoscopic surgery

- Continous pleural drainage

- Systemic treatment after pleurodesis

- Serial thoracocentesis

* Adequate pain-relief

Oxford

<table>
<thead>
<tr>
<th>Procedure</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>VATS and Talcum-pleurodesis*</td>
<td>1b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>Chemical pleurodesis*</td>
<td>1a</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Talcum powder</td>
<td>2b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Bleomycin, Doxycycline, Mitoxantrone</td>
<td>1b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Povidone-iodine (20 ml of 10% solution)</td>
<td>2a</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>Continous pleural drainage</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Systemic treatment after pleurodesis</td>
<td>4</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Serial thoracocentesis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Specific Sites of Metastases
# Malignant Ascites

## Local Therapy

### Ascites:

- Puncture, drainage in symptomatic patients  
  - **Oxford LoE**: 4  
  - **Oxford GR**: D  
  - **AGO**: ++

- Continuous drainage of ascites  
  - **Oxford LoE**: 3b  
  - **Oxford GR**: D  
  - **AGO**: +

- Systemic therapy  
  - **Oxford LoE**: 3b  
  - **Oxford GR**: D  
  - **AGO**: ++

- Local chemotherapy  
  - **Oxford LoE**: 3b  
  - **Oxford GR**: D  
  - **AGO**: +/−
## Malignant Pericardial Effusion

### Local Therapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oxford LoE</th>
<th>Oxford GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drainage, fenestration</td>
<td>3b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>Combination with optimized systemic therapy</td>
<td>4</td>
<td>C</td>
<td>++</td>
</tr>
<tr>
<td>VATS (video-assisted thoracic surgery)</td>
<td>4</td>
<td>C</td>
<td>+</td>
</tr>
<tr>
<td>Ultrasound-guided puncture and instillation of cytotoxic compounds</td>
<td>4</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>- Bleomycin, cisplatinum, mitomycin C, mitoxantrone etc.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Bevacizumab</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Symptomatic pericardial effusion:

- Drainage, fenestration
- Combination with optimized systemic therapy
- VATS (video-assisted thoracic surgery)
- Ultrasound-guided puncture and instillation of cytotoxic compounds
  - Bleomycin, cisplatinum, mitomycin C, mitoxantrone etc.
  - Bevacizumab
Bone Marrow Infiltration Associated with Pancytopenia

- **Weekly chemotherapy with***:
  - Epirubicin, Doxorubicin, Paclitaxel
  - Capecitabine

- **HER2-positive**:
  - Add anti-HER2-treatment

- **Hormone receptor-positive**:
  - Endocrine-based therapy

* Consider pre-treatment

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Oxford

<table>
<thead>
<tr>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>4</td>
<td>C</td>
<td>+</td>
</tr>
</tbody>
</table>

Specific Sites of Metastases
## Soft Tissue Metastasis

### Local Therapy

- **Surgery of limited locoregional metastasis (skin, muscular, nodal) with complete resection (R0) after exclusion of further metastasis**

- **Radiotherapy (after surgery or, if immediate surgery is not indicated):**
  - Soft tissue metastasis
  - Paresis, spinal cord compression
  - Plexus infiltration

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Oxford</th>
<th>AGO</th>
<th>LoE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue metastasis</td>
<td>3b</td>
<td>C</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Paresis, spinal cord compression</td>
<td>2b</td>
<td>C</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Plexus infiltration</td>
<td>3b</td>
<td>C</td>
<td>++</td>
<td></td>
</tr>
</tbody>
</table>