As mammary carcinoma is the most frequent malignant disease in women, early detection is important. There are numerous diagnostic tools available, the mammogram being the gold standard. The next step would be developing a treatment plan that is individualized for the patient and the type of carcinoma. The following article will teach you to accurately diagnose mammary carcinoma and to initiate the appropriate therapy.
Diagnosis of Breast Cancer (Mammary carcinoma)

Patient history and clinical examinations in cases of breast cancer

History and physical examination are the cornerstone in every disease, including breast cancer. Though patients with breast cancer are often asymptomatic, it is important to ask targeted questions regarding the aforementioned symptoms (changes in the size of the breast, differences between both sides, skin retraction, etc.), as well as individual risk factors.

The physical examination should be done with the patient’s upper body unclothed and her arms down, as well as with her arms raised up. Palpation should be done after the end of menstruation. It is important to palpate the supraclavicular and axillary lymph nodes.

Diagnostic tools for mammary carcinoma

Breast Exam

Traditionally, women were encouraged to regularly perform breast self-exams and palpation but the current United States Preventive Services Task Force (USPSTF) recommends against breast self-examination as it does not reduce breast cancer-related mortality and leads to excessive anxiety.

Therefore a regular breast exam, self-exam or by the medical expert, is not recommended. Still, all women should be familiar with the look and feel of their breasts and must consult a medical expert if any changes are noticed.

Mammography
Mammography is the gold standard of the instrument-based examination of the breast for the early detection of mammary carcinoma.

**The USPSTF recommends biennial (every two years) screening mammography for women between the ages of 50 and 74 years.**

In women younger than 50 years, the decision to start screening mammography should be an individualized one depending upon patient’s risk factors.

Mammography is a specific type of low-dose x-ray imaging in which radiopaque structures such as carcinoma, calcifications or fibroadenomas create shadows but appear light on the scan, whereas fatty tissue appears dark.

While benign tumors mostly appear homogenous, smoothly outlined and dense, the following criteria are signs of malignant findings:

- Asymmetric focal findings with unsharp delineation
- Inhomogeneous band- and mesh-like shadows
- Star-shaped thickening with spicules
- Polymorphic clustered microcalcifications (pointing toward DCIS!)
- Surrounding tissue: retraction phenomenon
- Outlined thickening/retraction (skin, mammillary gland)

![Image: “Typical mammogram in MLO view from clinical dataset. In the ROI demonstrated, there are micro-calcifications in the upper quadrant of the left breast.” by Openi. License: CC BY 2.0]

**Note:** Polymorphic, clustered microcalcifications are suspicious and are to 80 or 90% a sign of in situ or early-stage carcinoma, respectively! Mammography has a sensitivity of between 85 to 90%, depending on the tissue density: The fatter the tissue, the better the sensitivity. The specificity, however, is very limited.

Mammography findings are classified according to BI-RADS (Breast Imaging-Reporting and Data System):

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>Diagnosis/Findings</th>
<th>Procedure</th>
<th>Risk of carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Imaging has not been concluded</td>
<td>Further clarification is necessary</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>Unremarkable findings</td>
<td>Normal care</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>Benign findings</td>
<td>Normal care</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>Unclear, probably benign findings</td>
<td>Requiring follow-up (after six months)</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>4</td>
<td>Suspect findings</td>
<td>Histological clarification</td>
<td>2 - 90%</td>
</tr>
<tr>
<td></td>
<td>Suspecting carcinoma</td>
<td>Histological clarification</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----------------------</td>
<td>-----------------------------</td>
<td>---</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>6</td>
<td>Histologically confirmed carcinoma</td>
<td>-</td>
<td>100%</td>
</tr>
</tbody>
</table>

Other imaging diagnostic tools

In addition to the aforementioned methods, the following tests may be done:

1. **Sonography**
   - Most important complementary test in addition to mammography.
   - Benefit: no radiation exposure, differentiates solid (such as a benign fibroadenoma or cancer) from fluid-filled cystic (such as a benign cyst) lesions.
   - Disadvantage: highly operator-dependent, not suited for screening.

   ![Image: “Breast Cancer Ultrasound Images.” by Openi. License: CC BY 4.0](image)

2. **Galactography**
   - Imaging of the milk-producing ducts using contrast agent injections, followed by x-rays with mammillary gland secretion.
   - Pathological findings: caliber fluctuations in the milk ducts, discontinue contrast agent.

   ![Image: “Galactography suggestive of breast papillary lesions. A. Galactography with ductal tree display from the affected duct, showing a small retroareolar filling defect (in a circle). B. Galactography with filling defect (in a circle) in a magnified mammographic plate.” by Openi. License: CC BY 3.0](image)

3. **Magnetic Resonance Tomography (MRT)**
   - Conclusive findings are only possible with contrast agents.
   - Benefit: high soft-tissue contrast, very high sensitivity.
   - Disadvantage: low specificity, no detection of microcalcifications.
If metastases are suspected, pre-therapeutic staging to include chest x-rays, liver sonography, as well as skeletal scintigraphy, should be pursued.

**Biopsy and Histology**

The histological examination of the suspected breast cancer is important to confirm the diagnosis of breast cancer, its type, grade, the presence of certain receptors and genes, and to further plan therapy. For this purpose, breast tissue samples are collected from the suspicious area via minimally invasive procedures and subsequently examined microscopically.

Immunohistochemical staining of tumor cells is used in the diagnosis of tumors and may determine therapy. Hereby, the **hormone receptors** (estrogen, progesterone and steroid hormones), as well as the growth factor receptors (**HER2/neu**), play a role:

If more than 10% of the tumor cells stain positive for estrogen and/or progesterone receptors (**ER/PR**), the mammary carcinoma is hormone-receptor-positive. This means that it is suitable for endocrine therapy and has, in addition, a **better prognosis**.

In cases of an invasive mammary carcinoma, **HER2/neu** is overexpressed, which is referred to as **HER2-positive**. This status of over-expression indicates the direction of therapy: In cases of **HER2/neu** positive, patients are treated with **trastuzumab**, an **HER2 antibody**.
Differential Diagnosis

The breast cancer has to be differentiated from the benign breast lesions, such as:

- Fibroadenomas
- Lipomas
- Cystic changes
- Papillomas
- Mastitis

Therapy of Breast Cancer

Neoadjuvant therapy

The neoadjuvant therapy is the therapy that is given before surgery in order to shrink large tumors.

Surgery

Breast Cancer

Surgery is the main treatment for breast cancer. It includes either radical mastectomy or breast-conserving surgery with the same goal of removing the tumor, as well as affected regional lymph nodes.

Breast-conserving surgery

The breast-conserving treatment (BCT) followed by radiation therapy is the standard surgical treatment of care. The prerequisite is that the tumor has not yet infiltrated the surrounding tissue and that there is a favorable ratio between the size of the tumor and the volume of the breast.

- **Lumpectomy**: The lump (tumor) is removed along with the removal of one centimeter of healthy tissue on all sides. In some cases, the removal of the nipple may be necessary as well. The removal of the axillary lymph nodes is done with a second incision.
- **Quadrantectomy**: Removal of the quadrant of the breast where the tumor is located, as well as the axillary lymph nodes.
Mastectomy

If the tumor is large, multicentric, or if the patient is contraindicated for post-surgery radiation, BCT will not be an option. In these situations, a modified radical mastectomy is performed.

During this procedure, the breast, the axillary lymph nodes, as well as the pectoral fascia, are removed, while the pectoral musculature (as opposed to a Halsted radical mastectomy) is preserved. In cases of inflammatory mammary carcinomas, there is an indication for a mastectomy as well.

Breast Reconstruction

The female patients must be educated on the option of breast reconstruction, which may take place simultaneously or after a latent period of at least six months. Suitable materials include heterologous implants or autologous tissue. Autologous tissue allows for the following flap technique reconstructions:

- Thoraco-epigastric flap reconstruction
- Latissimus dorsi flap reconstruction
- (Transverse) Rectus abdominis (myocutaneous) flap reconstruction (TRAM)

Note: Both, mastectomy and BCT are to be regarded as equal with regard to survival rates, whereby the risk for a local recurrence is elevated for patients who have
undergone BCT.

**Lymphonodectomy**

In order to determine a patient’s nodal status, it is necessary to perform a lymphonodectomy. When the lymph nodes are removed, there is an increased risk of lymphedema.

If the tumor is less than three centimeters in size, the axillary lymph nodes have not been affected and, if there are no contraindications (i.e. a multifocal, multicentric, metastasizing or inflammatory mammary carcinoma, Paget disease), the *sentinel lymph node* should be removed.

During this procedure, the lymph node that is attacked by the tumor cells first because of the lymph flow (*sentinel/guardian lymph node*) is marked via injection of peritumoral subdermal dye or radionuclide.

[Image: “blau gefärbter Wächterlymphknoten (Axilla)” by Will Blake. License: CC BY-SA 3.0]

If this lymph node is free of tumor (sentinel negative), the removal of the axillary lymph node is not necessary resulting in reduced shoulder-arm morbidity.

If the sentinel lymph node is positive, axillary dissection with removal of a minimum of ten lymph nodes is indicated.

**Adjuvant therapy of mammary carcinoma**

Adjuvant therapy takes place after the resection of the tumor with the goal to reduce the risk of a local recurrence and to eliminate potential tumor cells in the body. This can be systemically achieved via local radiation, chemotherapy, or via endocrine or monoclonal antibody therapy, respectively.

**Radiation**

Adjuvant postoperative radiation following BCT is an obligatory measure in order to reduce the risk of local recurrence. Following a mastectomy involving large tumors (pT3, pT4), in cases of skin infiltration or extensive lymphangiosis and if more than three axillary lymph nodes are affected, adjuvant radiation therapy is indicated.

**Chemotherapy**

Chemotherapy is indicated if there is an increased risk of recurrence and it should begin
one to two weeks following surgery. The most frequent medications used are a combination of cytostatic drugs for which regular recommendations are established in guidelines.

**Monoclonal Antibodies**

In cases of HER2/neu-positive cancers, it is imperative to administer the monoclonal antibody **trastuzumab** for one year in addition to chemotherapy (see above).

**Endocrine Therapy**

For ER-/PR-positive female patients (see above), endocrine therapy is indicated. The goal is estrogen deprivation in order to decrease the growth of carcinoma cells. The standard medication being used is tamoxifen. Another option for premenopausal patients is the administration of GnRH analogs in order to suppress ovarian function. Aromatase inhibitors are indicated for postmenopausal patients.

**Follow-up, Prognosis, and Prevention of Mammary Carcinoma**

**Follow-up care in cases of mammary carcinoma**

After locoregional primary therapy, regular follow-ups are recommended, usually every three months during the first three years, every six months during the fourth and fifth year, and annually after the sixth year. After a mammary carcinoma, the risk of contralateral breast cancer is two to five times higher which is why there should be an annual instrument-based check-up in that area as well.

**Prognosis**

The prognosis of breast cancer depends on the multiple factors, including tumor stage, grade, HER2/neu and hormone receptor status. The earlier it is detected and treated, the better the prognosis. In early breast cancers, the therapy is curative. This underlines the importance of breast cancer screening in women.

**Note:** The most important prognosis factor with regard to remote metastases is if the axillary lymph nodes are affected!

In cases of remote metastases (in 5% of female patients when they are first diagnosed and in 30% of patients during the progression of the disease), therapy will take a palliative course as healing is no longer possible. The median survival time is approximately two years, the five-year survival rate is between 5 and 10% approximately.

**Prevention**

In order to prevent mammary carcinoma (primary prevention), the following options are available:

- In cases of hereditary mammary carcinoma, a bilateral mastectomy with a risk reduction of 90% and/or a bilateral adnexectomy with a risk reduction of 50% should be considered.
- In cases where the patient is at increased risk, drug therapy with tamoxifen, strictly according to the indication, may be an option.
Early detection screenings serve as secondary prevention (see above).

Review Questions

The answers are below the references.

1. During a breast self-exam, a 53-year-old female patient noticed a palpable resistance in the left mamma. She presents at her gynecologist’s office who, during the clinical examination, detects a palpable tumor, 1.2 cm in size. The tumor also shows up in sonography imaging. Which diagnostic step should be next?

   A. MRT examination of the mamma
   B. Mammography
   C. Galactography
   D. Stereotactically controlled vacuum biopsy
   E. CT-examination of the mamma

2. Which of the following mammography findings is the least likely indicator for a malignant tumor?

   A. Asymmetrical focal findings
   B. Inhomogeneous, band-like shadows
   C. Star-shaped thickening with spicules
   D. Homogeneous, dense findings, smoothly outlined
   E. Polymorphous, clustered microcalcifications

3. Which of the aforementioned therapy options are not suitable for treating a mammary carcinoma?

   A. Lumpectomy
   B. Modified radical mastectomy
   C. Systemic chemotherapy
   D. Antibody therapy
   E. Cerclage

References


Correct answers: 1B, 2D, 3E

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