

Precancerous Breast Pathology and Breast Cancer

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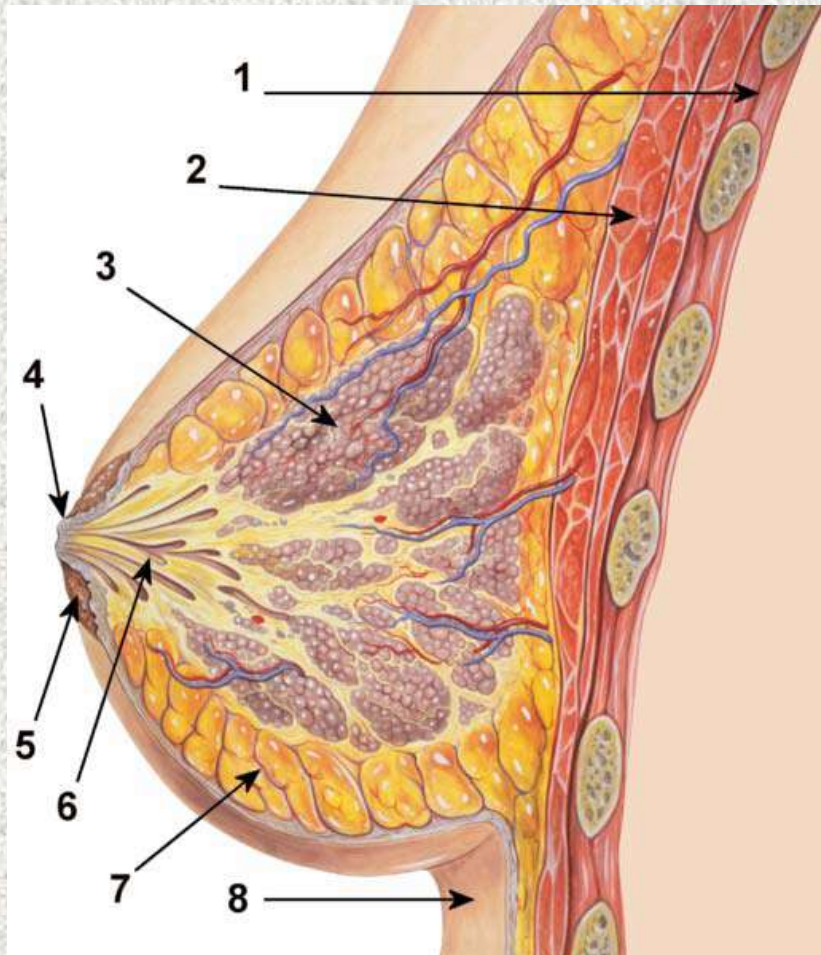
**Mammary gland is a paired organ,
which in its origin is a modified sweat
glands**

The mammary gland consists of:

- Glandular tissue,
- Connective (fibrous) tissue,
- Adipose tissue

**Their ratio depends on the age, the presence
of pathological processes in breast and
individual characteristics.**

Breast Anatomy



- 1. chest wall;
- 2. pectoral muscles;
- 3. lobules;
- 4. nipple;
- 5. areola;
- 6. duct;
- 7. adipose tissue;
- 8. skin.

Breast cancer occurs 3-5 times more frequently in patients with benign breast disease and in 30-40 times more common in patients with some forms of nodular mastopathy.

Risk factors for breast cancer

High-risk factors

- Mutations in BRCA1, BRCA2 gene
- Increasing age
- *Western culture*
- *Family history of breast or ovarian cancer in first-degree relatives (in mother, daughter or sisters)*
- Benign breast disease with atypical hyperplasia
- Exposure to ionizing radiation
- Prior diagnosis of breast cancer.
- Nulliparity or delayed first full-term pregnancy (above age 30)
- Lobular carcinoma *in situ* carries a 30% risk of *invasive cancer*.

Risk factors for breast cancer

Intermediate risk factors

- Early menarche
- Late menopause
- Prior diagnosis of uterine, ovarian, or colon cancer
- Diabetes mellitus
- Alcohol intake
- High socioeconomic status
- Obesity (*postmenopausal women only*)
- Unfavorable mammographic parenchymal pattern
- Benign breast disease with hyperplasia but without atypia
- Oral contraceptives (*for longer than 10 years*)
- Postmenopausal estrogen replacement therapy

Risk factors for breast cancer

Questionable risk factors

- Interrupted first pregnancy
- Psychosomatic factors
- High-fat diet
- Complex fibroadenoma
- Exposure to low-frequency electromagnetic fields

Factors known to decrease risk

- Full-term pregnancy before age 20
- Multiple pregnancies (?)
- Ovariectomy before age 45
- Regular exercise, especially during adolescence and early adulthood
- Breast feeding (?)

Factors having no effect on risk

Multiparity, lactation, breast feeding, breast size, fibrocystic disease without proliferative changes, smoking

Mutations in BRCA1 and BRCA2 genes

About 4 to 9% have hereditary breast cancer.

Mutations in BRCA1

- The probability of breast cancer is up to 75% under the age of 50 years and 85 - 90% in the age of 70 years
- are associated with early-onset breast cancer
- often observed bilateral and multiple primary cancers
- have lower diploidy rate, higher proliferative rate and higher mitotic counts
- are associated with ovarian cancer
- From 50 to 88% BRCA1-positive patients have a triple negative breast cancer, compared with 14-34% in the absence of the mutations indicated.

Mutations in BRCA2

- are associated with early-onset breast cancer
- are associated with male breast cancer
- are not associated with ovarian cancer.

Features in the history of a patient that increase the likelihood of having BRCA mutations

- ❖ Multiple cases of early onset breast cancer in the family
- ❖ Ovarian cancer with family history of breast or ovarian cancer
- ❖ Breast and ovarian cancer in the same woman
- ❖ Bilateral breast cancer
- ❖ Ashkenazi Jewish heritage
- ❖ Male breast cancer

Benign Breast Disease

No increased risk (no proliferative disease)

Adenosis

Apocrine change

Duct ectasia

Mild epithelial hyperplasia of usual type

Slightly increased risk (1.5–2 times) (proliferative disease without atypia)

- Hyperplasia of usual type, moderate or florid
- Papilloma (probably)
- Sclerosing adenosis

Moderately increased risk (4–5 times) (atypical hyperplasia or borderline lesion)

- Atypical ductal hyperplasia
- Atypical lobular hyperplasia

High risk (8–10 times) (carcinoma in situ)†

- Lobular carcinoma in situ—Both breasts
- Ductal carcinoma in situ (noncomedo)—unilateral, local

Clinical classification of the benign breast disease

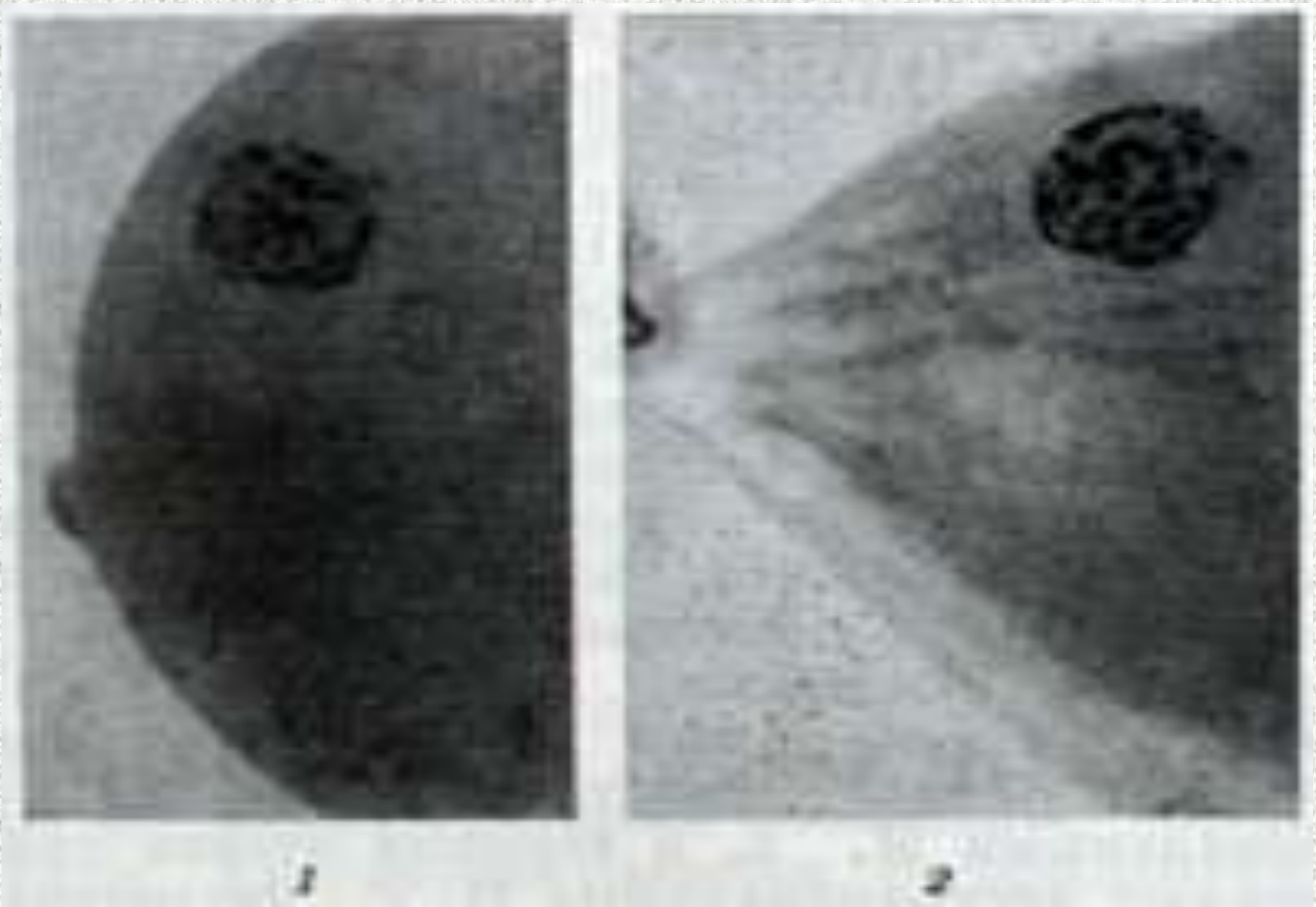
- dysplastic disease (fibrocystic breast disease)
- benign tumors (fibroadenoma, intraductal papilloma)
- chronic mastitis

Local symptoms are often associated with the menstrual cycle

- Pain
- Sense of breast engorgement
- Swelling of mammary gland (localized or diffuse) or the presence of a tumor with clear smooth contours (fibroadenoma)
- Discharge from the nipple (bleeding are associated with the intraductal papilloma)

Common symptoms

- Headache
- Swelling
- Increased nervous irritability
- Anxiety, fear in the premenstrual period



Mammogram of patients with breast fibroadenoma



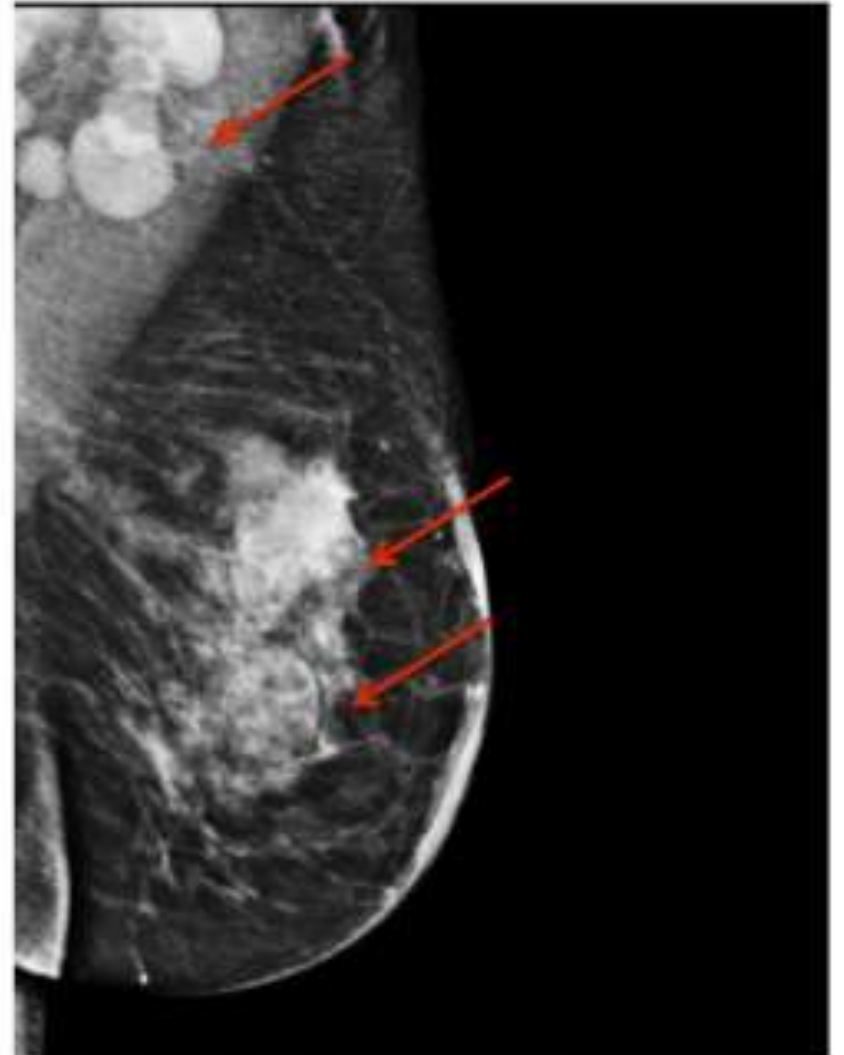
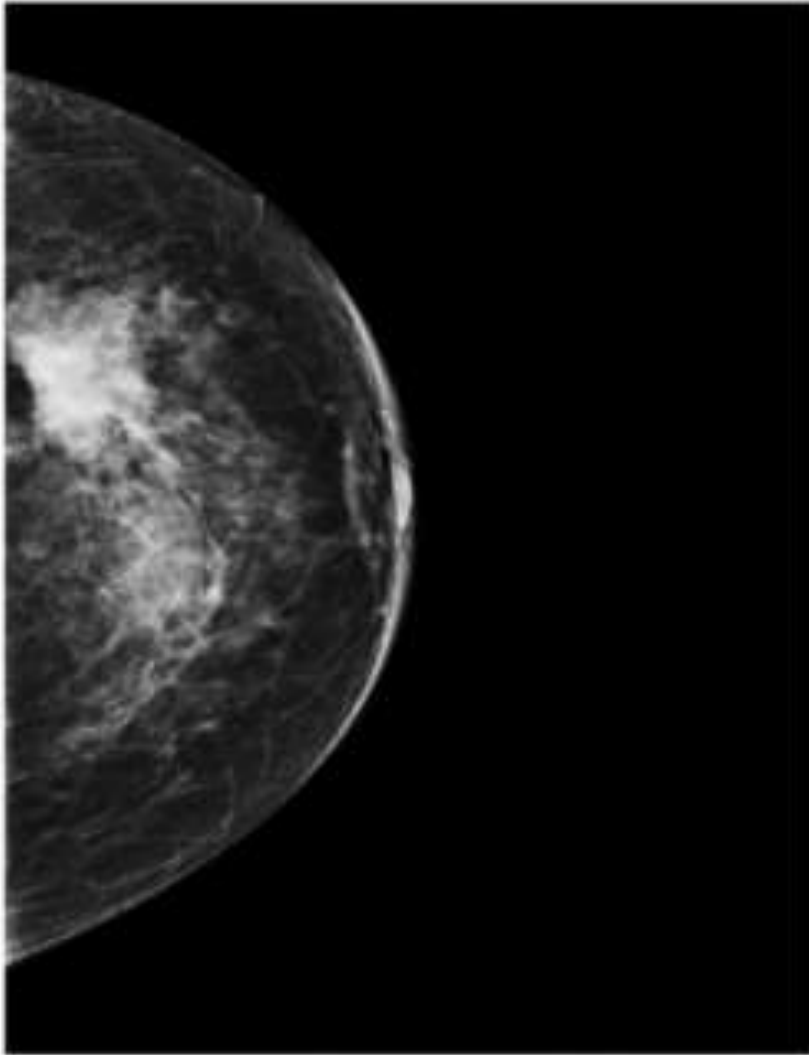
Image of fibroadenoma on
ultrasonography



surgery specimen of fibroadenoma of



Image of the intraductal papilloma on
ultrasonography



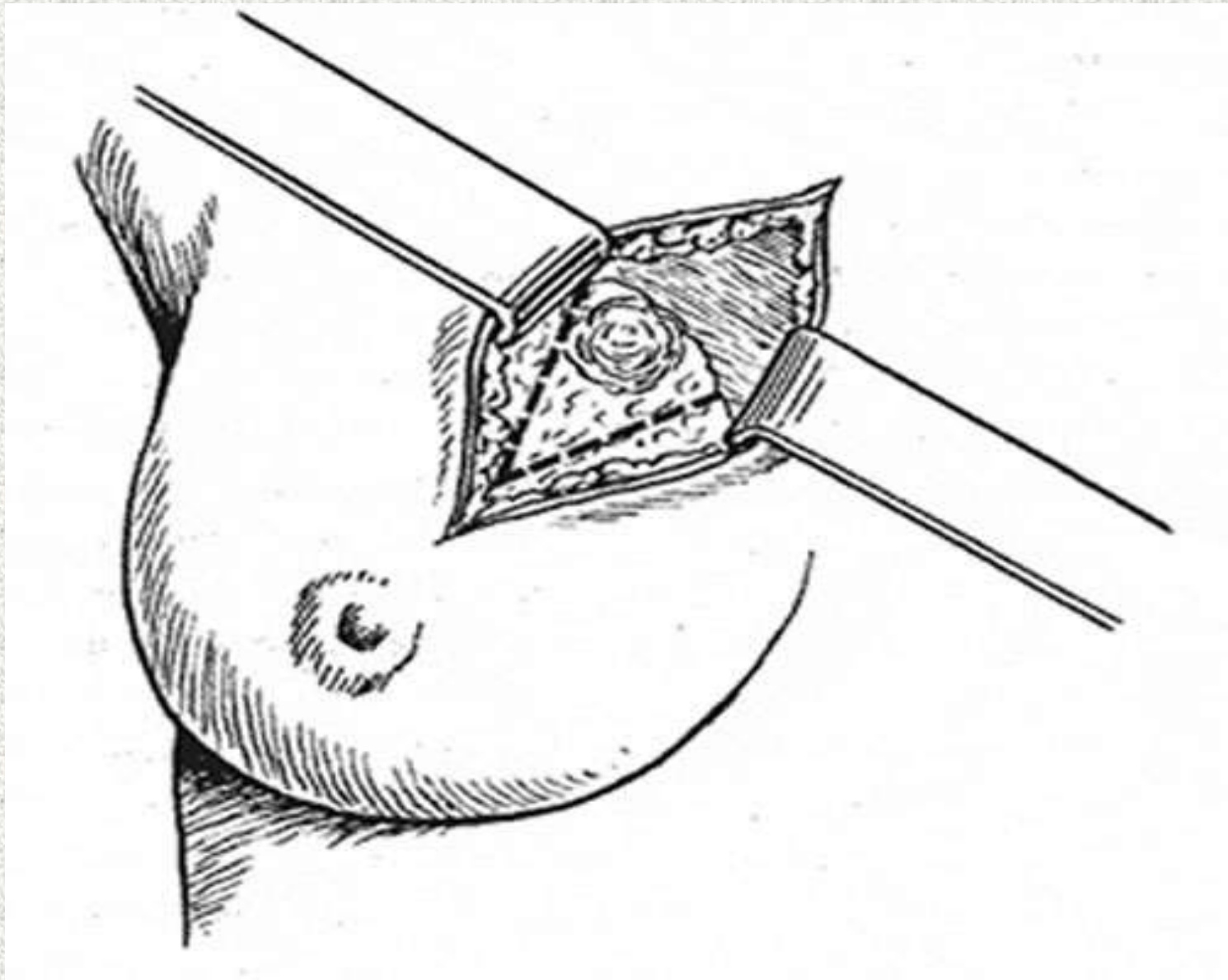
Mammogram of patients with the diffuse form of mastopathy

Treatment of the diffuse forms of fibrocystic breast disease

- Herbal drugs
- Vitamin therapy
- Enzymotherapy
- Antipsychotics
- Antihistamines and antiprostaglandine drugs
- Homeopathic medicines
- Iodine-containing drugs
- Immunomodulators
- Antioxidants
- Psychotherapy
- Refusal of bad habits

Operative treatment in the volume of breast sectoral resection is required at

- nodal mastopathy
- intraductal papilloma
- fibroadenoma



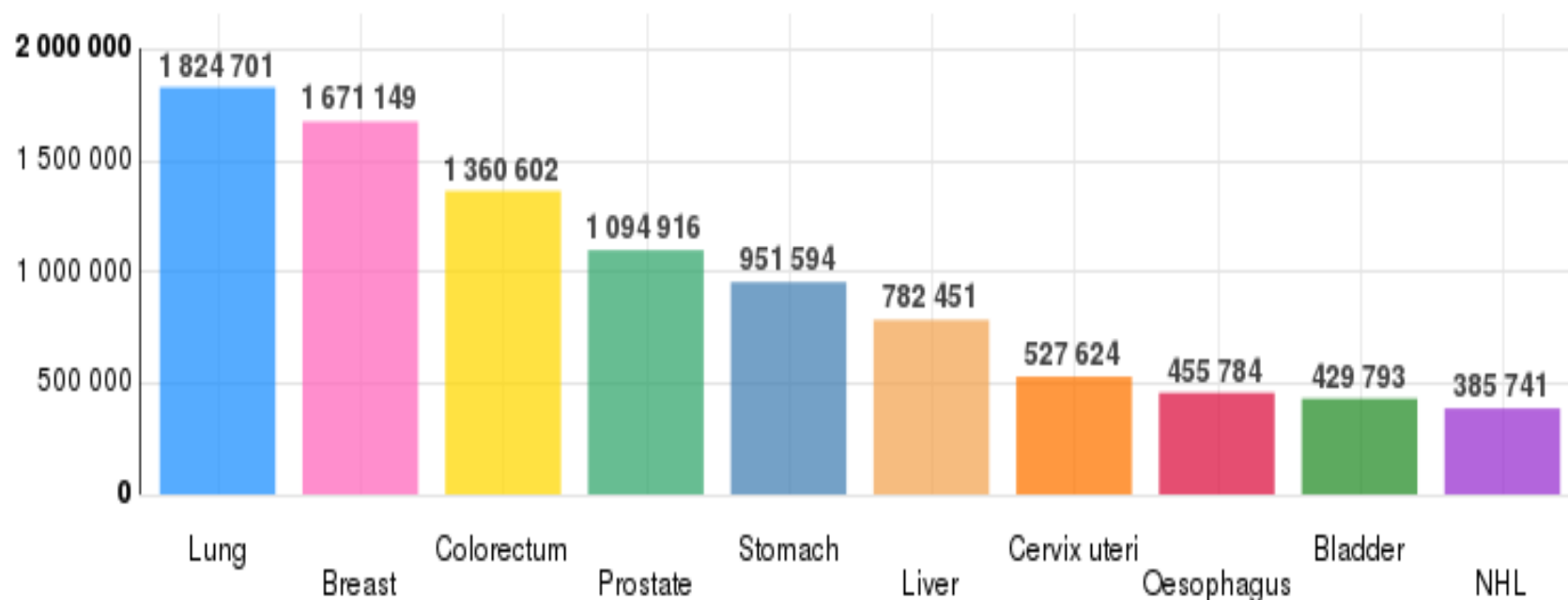
Sectoral resection of the breast - is the removal of the part gland

BREAST CANCER

Incidence

- ❖ Breast cancer is the most common lethal neoplasm in women
- ❖ More than 1,5 mln. of new cases of breast cancer are detected in the world annually
- ❖ In North America, Northern Europe, Australia and New Zealand breast cancer is about five times more common than in women of most Asian or African countries
- ❖ The average age for women first presenting with breast cancer is about 60 years, but this disease may be seen in women in their 20s or even rarely in teenagers
- ❖ Fewer than 1% of all breast cancer cases occur in men.

Estimated number of incidence cases, both sexes, worldwide (top 10 cancer sites) in 2012



Data source: GLOBOCAN 2012

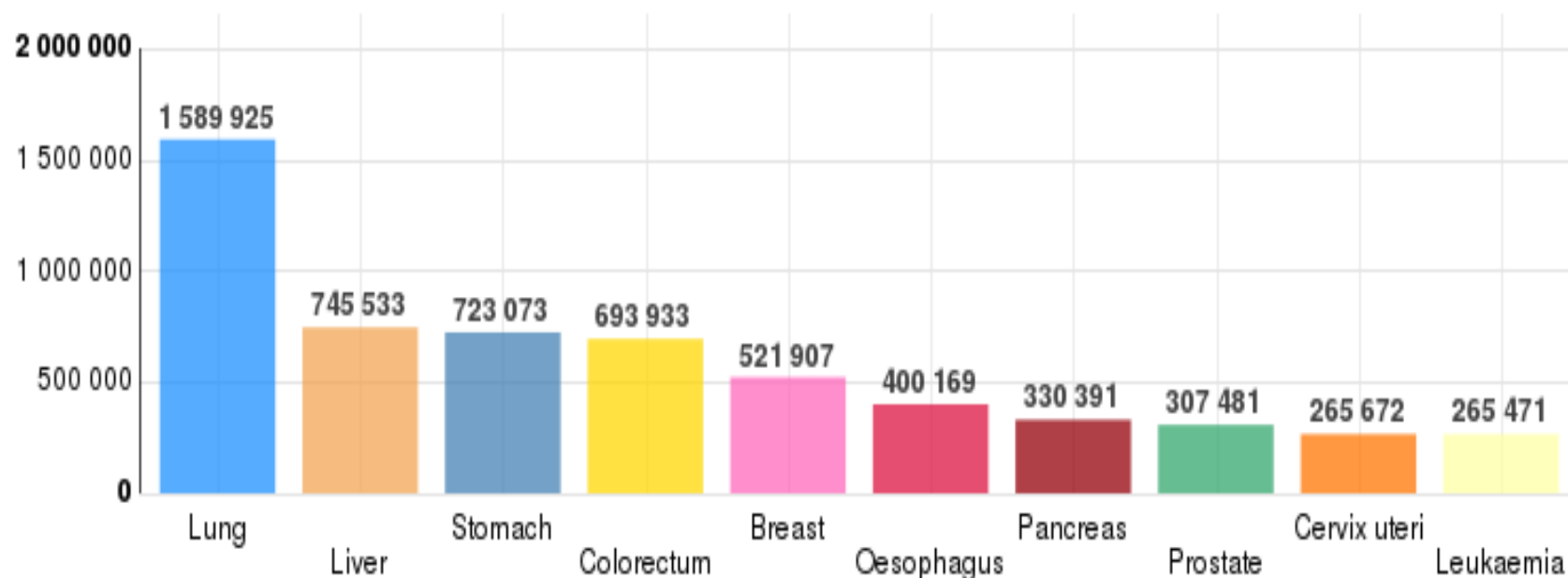
Graph production: Cancer Today (<http://gco.iarc.fr/today>)

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Estimated number of deaths, both sexes, worldwide (top 10 cancer sites) in 2012



Data source: GLOBOCAN 2012

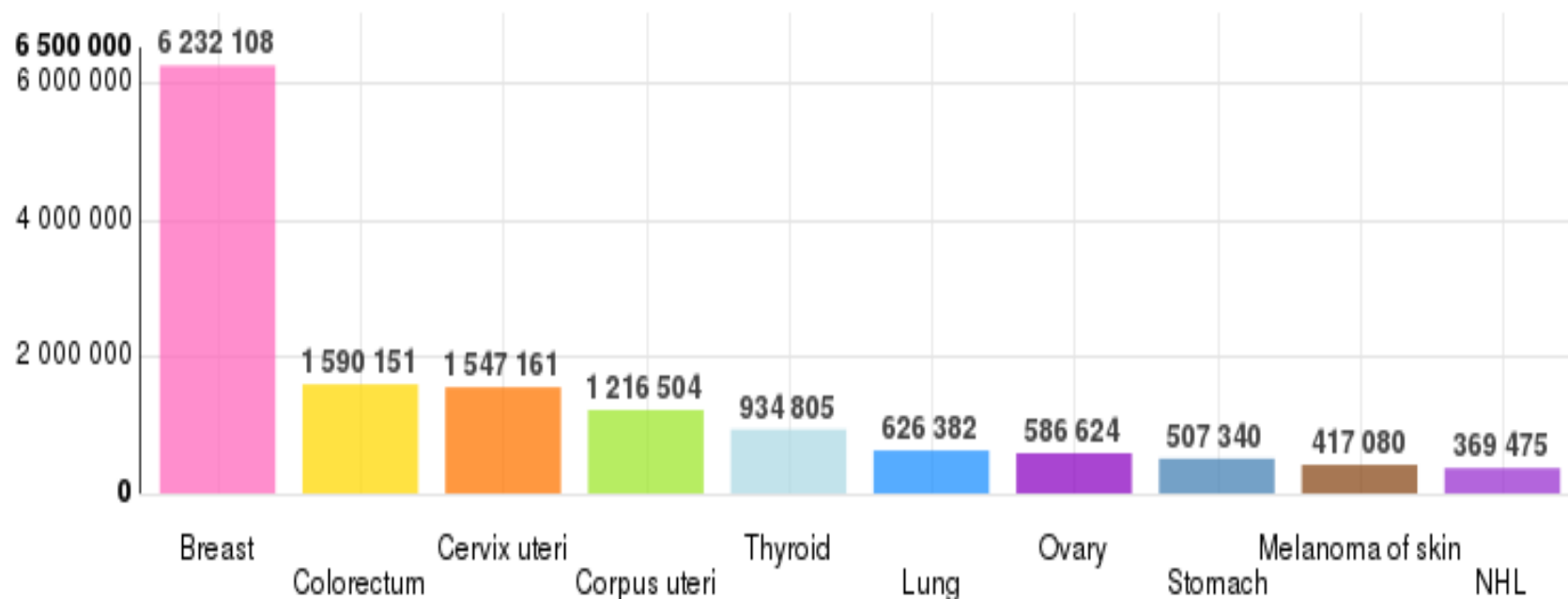
Graph production: Cancer Today (<http://gco.iarc.fr/today>)

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Estimated number of prevalence cases (5-year), females, worldwide (top 10 cancer sites) in 2012



Data source: GLOBOCAN 2012

Graph production: Cancer Today (<http://gco.iarc.fr/today>)

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The incidence of Breast Cancer per 100 000 people

Africa	29.8
America, Central and South	74.7
Canada	77.7
USA	89.2
China	35.5
India	36,6
Russian Federation	47.4

Histology types of breast cancer

I. Noninvasive tumors (carcinoma in situ):

- intraductal carcinoma
- intralobular carcinoma

II. Invasive cancer:

- Ductal adenocarcinoma (78%).
- Lobular carcinoma (9%). Lobular carcinoma is associated with an increased risk for bilateral breast cancer (about one third of cases).
- Special types with a good prognosis (10%). Pure papillary, tubular, mucinous, and typical medullary carcinomas.
- Comedocarcinoma (5%).
- Colloid carcinoma (3%).
- Inflammatory carcinoma (1%). Poorest prognosis. Lymphatics become packed with tumor, leading to breast and skin changes that mimic infection.

III. Paget's disease of the breast. Unilateral eczema of the nipple; always associated with ductal carcinoma in women. Prognosis is good if detected before a mass is present.

Spread of breast cancer

Breast cancers spread by contiguity (skin metastases), lymphatic channels, and blood-borne metastases.

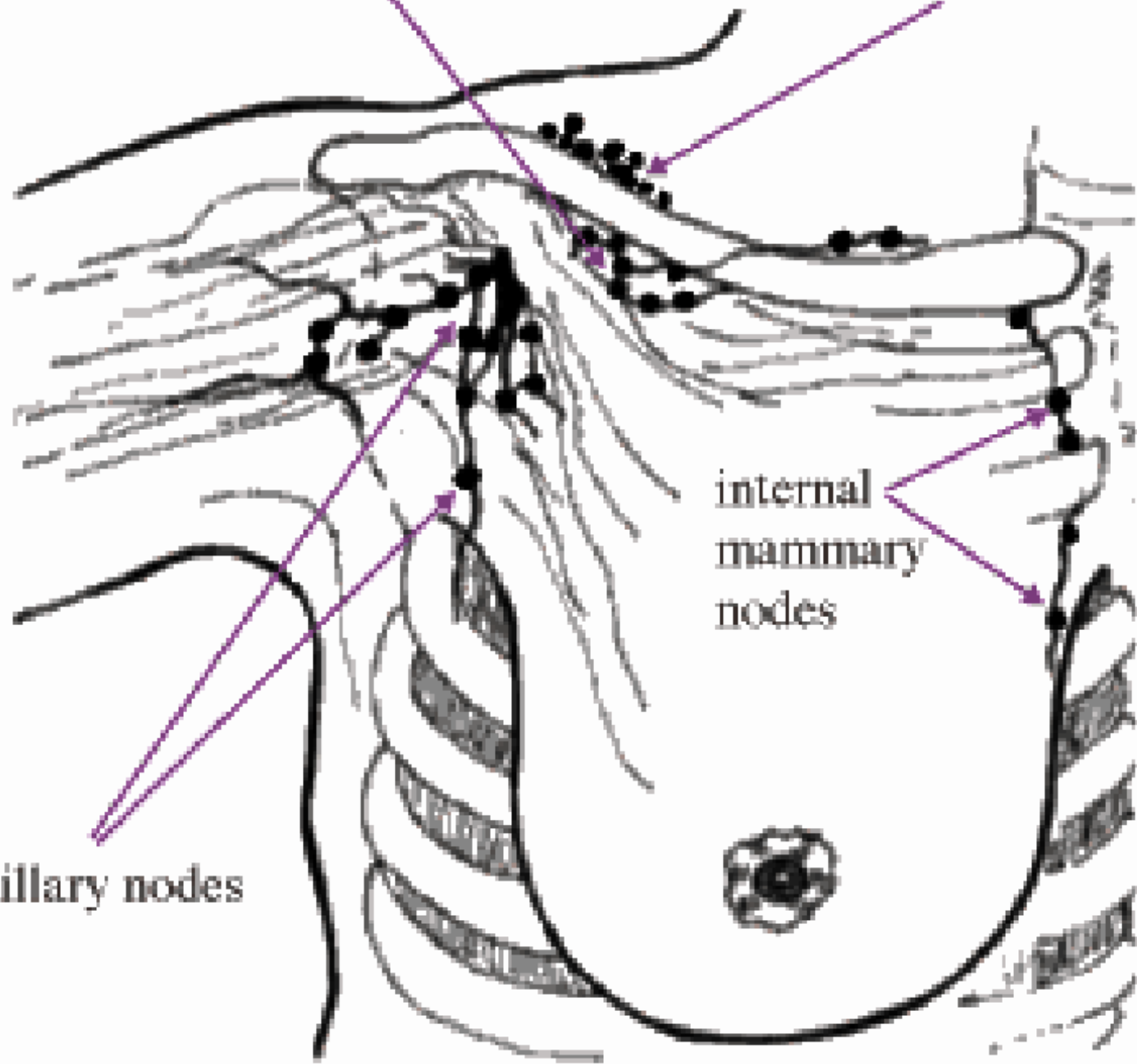
The most common organs involved with symptomatic metastases are regional lymph nodes, skin, bone, liver, lung, and brain.

infraclavicular nodes

supraclavicular nodes

internal
mammary
nodes

axillary nodes





Skin metastases

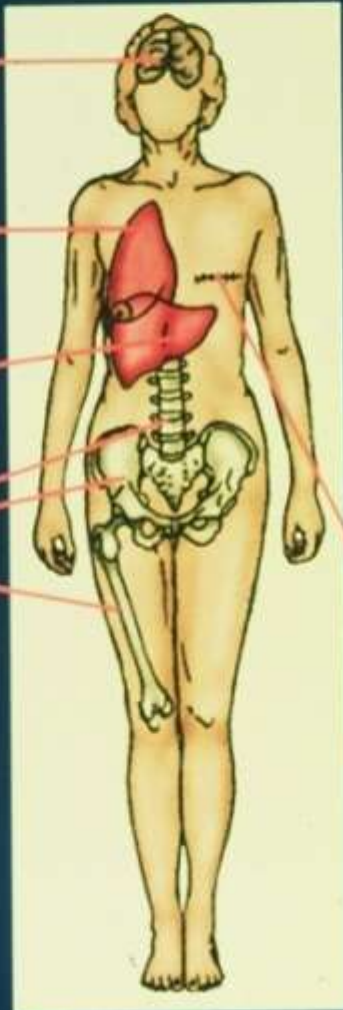
Metastatic breast cancer

brain
(5–10%)

lung / pleura
(15–25%)

liver
(5–15%)

bone
(20–60%)

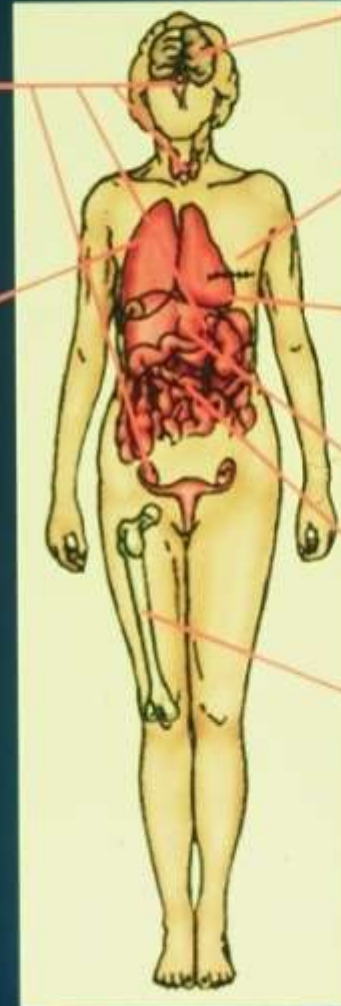


At first recurrence

endocrine
(40–60%)

lung / pleura
(50–75%)

local = regional
(20–40%)



At autopsy

CNS (30–50%)

local (30–50%)

**pericardium,
heart** (25–40%)

liver (50–75%)

gastrointestinal
(30–40%)

bone (60–90%)

CLINIC AND DIAGNOSIS OF BREAST CANCER

Factors affecting the clinical manifestations of breast cancer

- Clinical form
- Stage of disease
- Age of the patient

Clinical forms of breast cancer

- **Nodal form**
- **Diffuse form**
- **Atypical form**
 - Paget's cancer
 - Occult breast cancer
 - Ulcerative form of breast cancer

The nodal form of breast cancer

Presence of breast lumps

- usually solid, hard, irregular, non-mobile, and painless
- often has indistinct contours
- may cause deformation and asymmetry of breast
- ulceration of skin
- nipple discharge (serous, serosanguineous or bloody)

Skin symptoms

- nipple retraction
- umbilicatsii
- invasion into the skin

The increase in regional lymph nodes







Diffuse forms of breast cancer

- The increase in breast size (rarely decrease)
- Edema
- No tumor node
- Diffuse induration of breast tissue, or portion thereof
- Symptom "lemon peel"
- Skin color change (pastosity, cyanosis, erythema)
- The increase in regional lymph nodes
- Changes in the nipple
- Pain and heaviness in the breast

These forms of breast cancer are aggressive form with high-rate progression





Symptom "lemon peel"



Paget's carcinoma appears as unilateral
eczema of the nipple.



The main diagnostic methods

1. Palpation of the breast, regional lymph nodes, liver
2. Mammography. Ductography with contrast in patients with suspected intraductal cancer
3. Ultrasonography
4. Thermography
5. Magnetic resonance imaging (MRI)
6. Cytological methods or trephine biopsy
7. Immune histochemical study (IHC)
8. Bone scan
9. Chest X-ray
10. Liver ultrasound or KT
11. Consultation of gynecologist
12. Consultation of other specialists
13. Direct color lymphography
14. Method radionuclide lymphoscintigraphy
15. Trans-sternal venography

Mammography

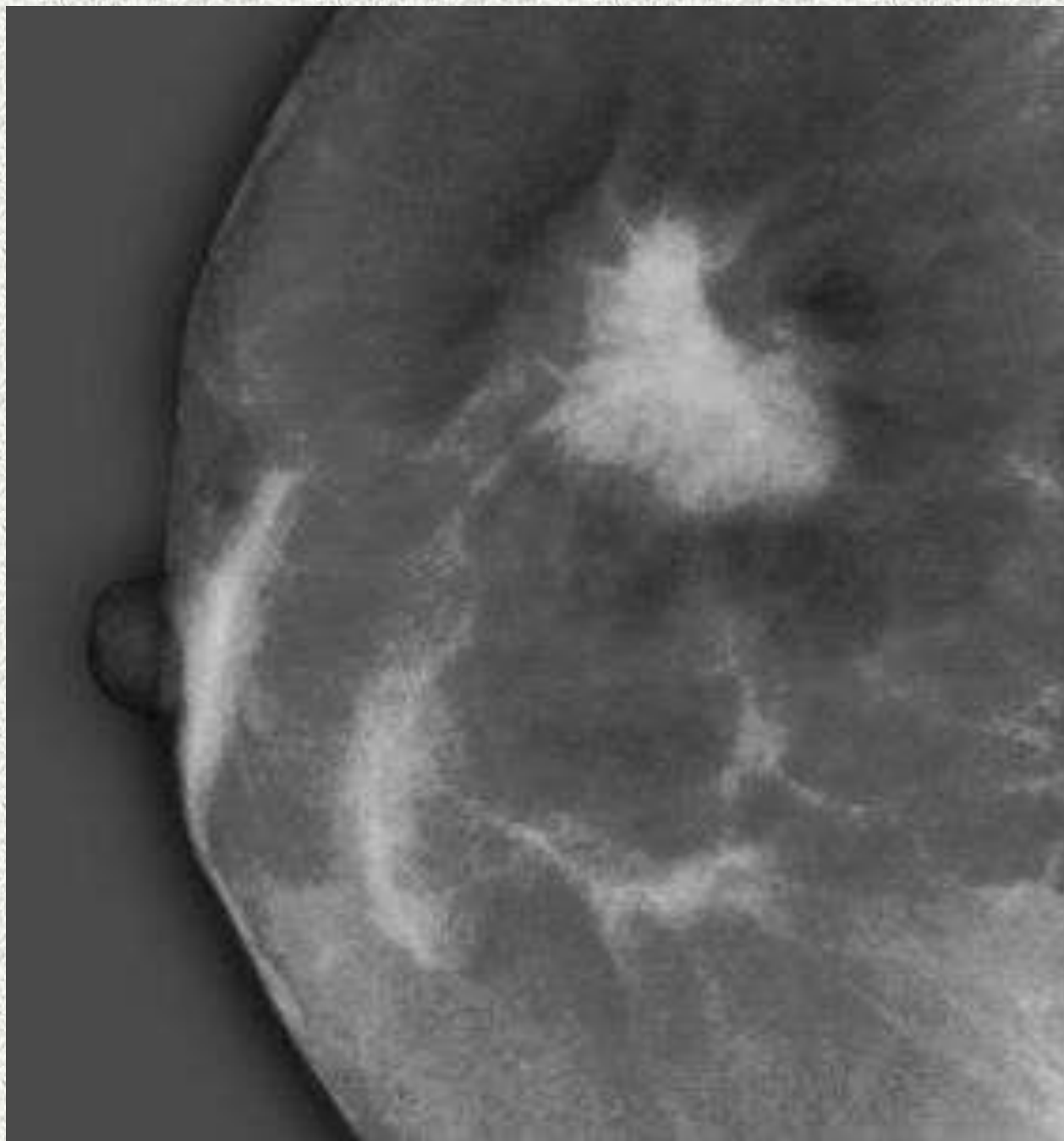
- Mammography detects 85% of breast cancers.
- 15% of breast cancers cannot be visualized with mammography.
- 45% of breast cancers can be seen on mammography before they are palpable.

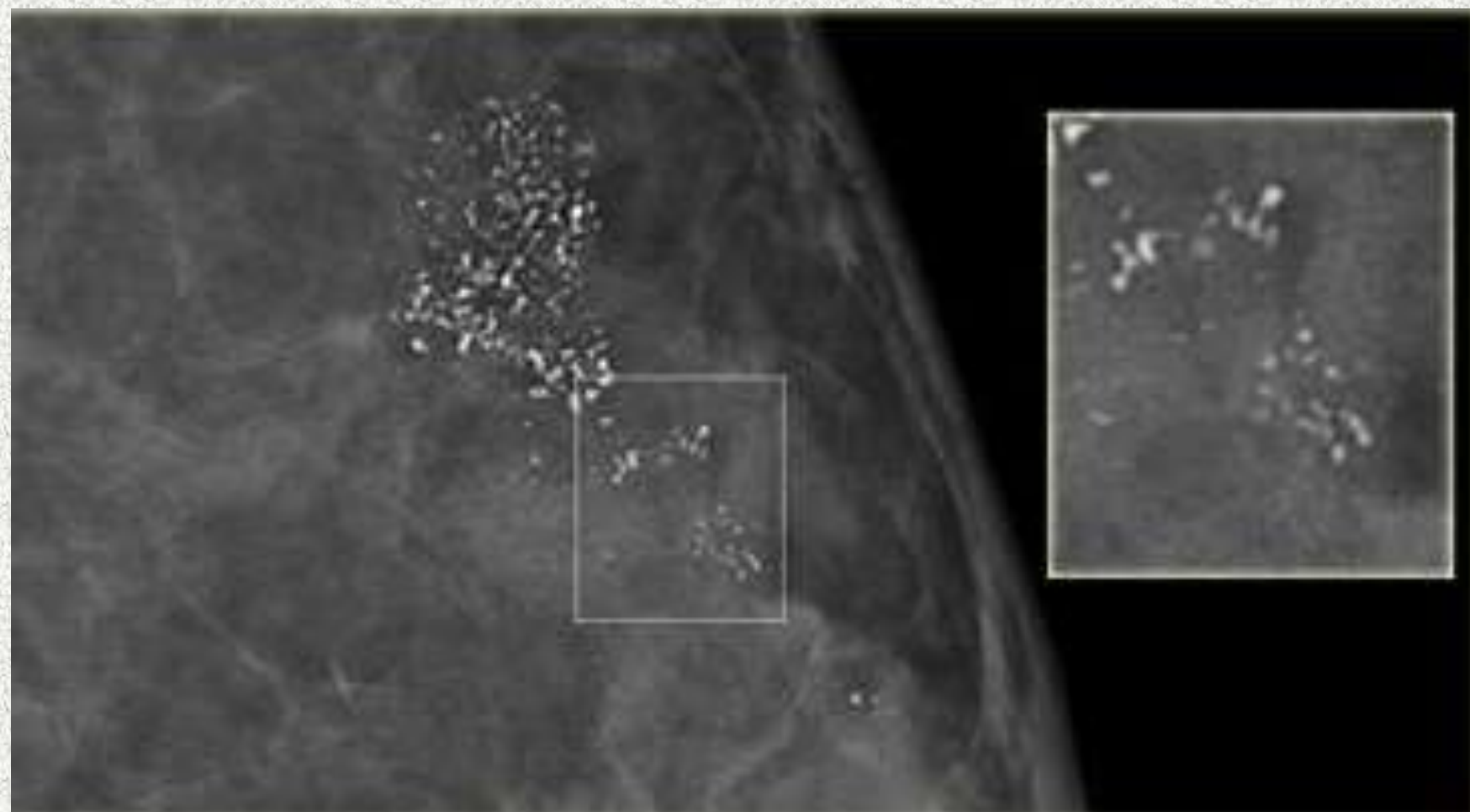
Indications for mammography

1. Evaluation of suspected benign or malignant breast disease.
2. Evaluation of the contralateral breast in patients with documented breast cancer
3. Follow-up of patients with prior breast cancer
4. Follow-up of patients with premalignant breast disease (gross cystic disease, multiple papillomatosis, lobular neoplasia, and severe atypia)
5. Evaluation of breasts that are difficult to examine
6. Workup of metastatic adenocarcinoma from an unknown primary
7. Evaluation of patients at high risk for breast cancer (especially patients with prior breast augmentation with silicone and patients with a strong family history of breast cancer)
8. Screening for breast cancer

Mammographic signs of malignancy (sensitivity is about 75% and specificity almost 90%)

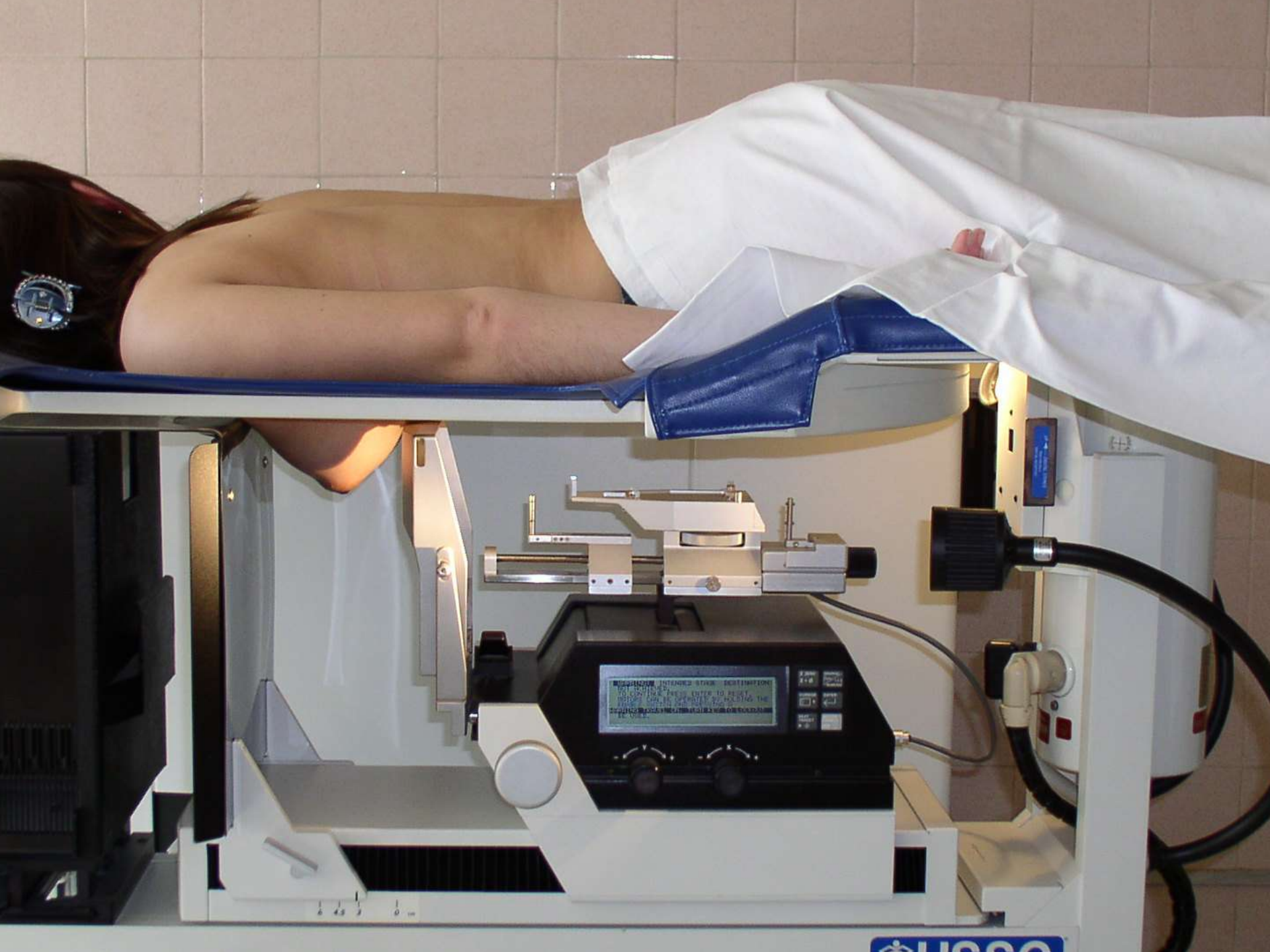
1. Calcium deposits, unless in a mulberry (fibroadenoma) or curvilinear (cystic disease) pattern
2. Mammary duct distortion or asymmetry
3. Skin or nipple thickening
4. Breast mass
5. Microcalcifications







Photograph and illustration of mammography. Small-dose X-rays are taken with the breast held firmly between two plates

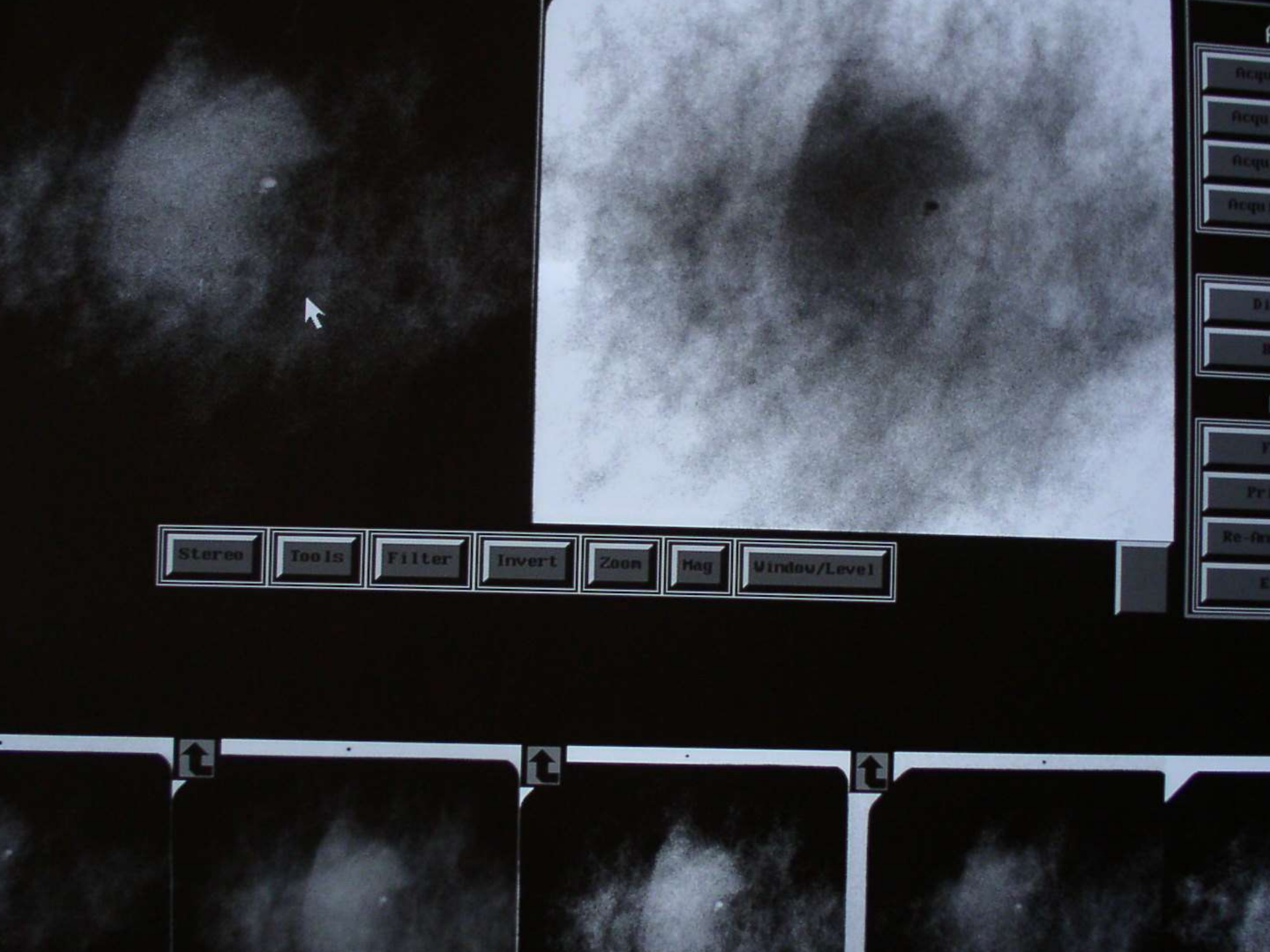


MEASUREMENT INTENSIVE SYSTEM (MIS)
TO MEASURE THE PRESSURE OF THE
TONGUE, THE PRESSURE OF THE
TONGUE IS MEASURED BY MEANS OF
A PRESSURE SENSITIVE FILM.

1. Press
2. Enter
3. Exit
4. Help







Stereo

Tools

Filter

Invert

Zoom

Mag

Window/Level

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Biopsy

- a. Fine-needle aspiration cytology
- b. Ultrasound or stereotactic core biopsy.
- c. Trepanobiopsy
- d: Excisional biopsy

After trepanobiopsy and excisional biopsy
fresh tissue should be sent for ER, PgR, and
histologic evaluation.

TNM Classification of Breast Cancer

- T0 No evidence of primary tumor
- Tis cancer in situ cancer
- T1 Tumor 2 cm or less in its greatest dimension
- T2 Tumor more than 2 cm but not more than 5 cm in its greatest dimension
- T3 Tumor more than 5 cm in its greatest dimension
- T4 Tumor of any size with direct extension to chest wall or skin (fixation to chest wall, edema, ulceration of the skin of the breast, or satellite skin nodules confined to the same breast)

Regional lymph nodes

- N0 Homolateral axillary nodes not considered to contain growth
- N1 Movable homolateral axillary nodes considered to contain growth
- N2 Homolateral axillary nodes containing growth and fixed to one another or to other structures
- N3 Homolateral supraclavicular or infraclavicular nodes containing growth, or edema of the arm

Distant metastasis

- M0 No evidence of distant metastasis
- M1 Distant metastasis present, including skin involvement beyond the breast area

Screening women for breast cancer

1. **Monthly self-examination** for all women older than 20 years of age. Premenopausal women should perform the examination 5 days after the end of the menstrual cycle; postmenopausal women should examine themselves on the same day each month.

2. **Physical examination** by a physician every 3 years for women between 20 and 40 years of age and annually for women older than 40 years of age.

3. **Mammography.**

a. Annual mammograms have been demonstrated to reduce breast cancer mortality in women older than 50 years of age.

b. The American Cancer Society (ACS) recommends a mammogram as a baseline for women 35 to 39 years old, mammograms every 1 to 2 years for women 40 to 49 years old, and mammograms yearly for women 50 years of age and older.

c. The National Cancer Institute makes no recommendations for mammographic screening before 50 years of age but does recommend annual mammography after 50 years of age.

TREATMENT OF BREAST CANCER

Surgery

Radical mastectomy:

Halstead

Pate

Madena

Radical resection of the breast (lumpectomy)

Simple mastectomy

Sectoral resection of the breast

Reconstructive plastic surgery

Primary Breast Implants

Delayed Breast Implants

There are two basic ways to simulate the shape and volume of the breast:

- endoprosthesis
- reconstructive surgery using autologous tissue



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Radiation treatment

Postoperative irradiation is used

- when the presence of adverse morphological factors and includes primary cancer zone and zones of regional metastasis
- after conservative surgery (radical resection of the breast or sectoral resection of the breast)

Time of radiation therapy will vary:

- immediately after surgery and followed by drug therapy;
- simultaneously with drug therapy
- after drug treatment, but no later than 6 months

Drug treatment. Neoadjuvant chemotherapy

- Neoadjuvant chemotherapy is the standard treatment for locally advanced cancer
- At the early stages neoadjuvant chemotherapy is used to perform the conservative surgery
- The best combination are taxanes with anthracyclines. The number of courses is 4.

Drug treatment. Adjuvant chemotherapy

- Adjuvant chemotherapy is used in most patients.
- The minimum number of courses is 6.
- The best combination is the use of anthracyclines with taxanes (AC + taxanes)
- Using CMF and AC with following administration of a kapetsetabina is possible for elderly patients

Adjuvant endocrine therapy and Targeted therapy of breast cancer

- The using of anti-estrogens (tamoxifen), and inhibitors of aromatase inactivators (aramideks) are advisable in the presence of ER +, PR +
- Antibodies to epidermal growth factor (Herceptin) are used at a high level of expression of Her - 2 - new –
- Blockers angiogenesis - in metastatic breast cancer (Avastin)
- Biofosfanaty - in breast cancer metastases in the bone (bonaftos).

**THANK YOU FOR
ATTENTION**