Imaging of Male Breast Cancer

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ISBN 978-3-319-06049-1 ISBN 978-3-319-06050-7 (eBook)
DOI 10.1007/978-3-319-06050-7
Springer Cham Heidelberg New York Dordrecht London

Library of Congress Control Number: 2014952028

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Breast cancer in men is a rare disease, with an incidence of less than 1 % of all breast tumors. Although the incidence in men has increased during the last 30 years, patients almost always think of breast carcinoma as an exclusively "female" condition. Men are less aware of breast cancer and other breast pathology than women. The signs of the disease at early stages are indistinct, so male patients are usually late in consulting a doctor. Low awareness of the male population and doctors of a breast tumor results in late treatment. More than 30 % of patients with breast carcinoma begin treatment when the tumor is nonresectable.

The successful treatment of breast cancer (as well as other diseases) in men depends on early diagnosis. Diagnostic principles, including imaging modalities and treatment strategies, are based on the knowledge obtained from identifying and treating tumors in women. This problem is not well addressed because the low incidence of the disease precludes large randomized studies. Almost all data are based on small studies, and therefore, there is no uniform view regarding early and differential diagnosis of breast cancer in men. There is no standard approach to treatment that would permit to avoid unnecessary surgery and provide predictable and stable results. Modern means of examination for breast cancer in men are often criticized, and state guidelines are not developed. The screening for breast cancer within the limits of national programs involves only women. Screening programs with mammography and/or ultrasound for men (similar to programs for women) are unreasonable and are not cost-effective because of the low incidence of the disease. In general, men also tend to have an attitude of avoiding examinations. During routine health checkups of men, general practitioners also do not pay enough attention to this problem. Only the combination of efforts of patients and doctors can change the current situation.

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Abbreviations

3D	Three-dimensional image reconstruction
3DPD	Three-dimensional power Doppler vascular image reconstruction
ARFI	Acoustic radiation force impulse
CDI	Color Doppler imaging
CT	Computed tomography
EDV	End-diastolic blood flow velocity
FNAB	Fine needle aspiration biopsy
FSH	Follicle-stimulating hormone
ICD-10	International statistical classification of diseases and related health problems, 10th revision
LH	Luteinizing hormone
MRI	Magnetic resonance imaging
PDI	Power Doppler imaging
PET	Positron emission tomography
PI	Pulsatility index
PSV	Peak systolic blood flow velocity
PW	Pulsed wave
RI	Resistive index
T4	Thyroxine
TPO	Thyroid peroxidase
TSH	Thyroid-stimulating hormone
US	Ultrasound
VOCAL	Virtual organ computer-aided analysis
VTQ	Virtual Touch™ tissue quantification
WHO	World Health Organization

Contents

Modern Approaches to the Diagnosis of Breast Cancer: Diagnostic Methods of Breast Pathology in the Male Population

1

Alexander N. Sencha, Elena V. Evseeva, Irina A. Ozerskaya, Elena P. Fisenko, Yury N. Patrunov, Mikhail S. Mogutov, Elena D. Sergeeva, and Anastasia V. Kashmanova

The terms “male breast” and “male mammary gland” are both used in medical literature. Experimental and clinical studies demonstrate a similar origin and development of hyperplastic processes in breast in men and women, as well as common etiology and pathogenetic mechanisms of development of breast carcinoma in male and female organisms. The international standard for anatomical terminology (Terminologia Anatomica 1998) omitted the separate term “mamma masculine” because the male breast contains no unique elements but those of the female breast developed to a lesser extent. In the European and North American literature, several terms are used for breast carcinoma both in women and in men along with the Latin term “cancer mammae.” The common term in English is “breast cancer,” but with reference to men, the additional word “male” is applied.

The success in the treatment of breast diseases, including malignancies, substantially depends on timely diagnosis. Early diagnosis of breast diseases in men remains a problem, along with an increasing incidence of male breast carcinoma, and leads to corresponding mortality despite significant achievements in the study of cancer biology and modern approaches to treatment.

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_1

Cases of late-stage breast carcinoma in men are most often the consequence of insufficient attention of patients to their own health, which results in them seeking medical treatment late. Sometimes, the low oncologic awareness of general practitioners may lead to unreasonable or insufficient medical actions, which may worsen the clinical course. Because of the typical late presentation to the doctor, 60 % of patients have complications, including regional or remote metastases, by the time of the diagnosis (Svyatuhina 1979). Breast carcinoma in 20 % of patients remains undiagnosed (Letyagin and Makarenko 1983). The mortality among men with breast carcinoma is up to 0.3 % of the mortality from other malignancies.

Early detection of breast carcinoma is the principal diagnostic aim. The equipment of medical institutions permits the so-called secondary preventive maintenance (screening) of breast carcinoma in healthy women without palpable breast masses. Screening is an initial, preliminary, but effective enough stage of examination of a certain population. Its main objective is to detect the disease at such an early stage that the following treatment results in a change in the clinical flow and forecast of the disease. Screening provides the elements of a differential diagnosis that helps to optimally choose further examination methods, apply early treatment, and increase life expectancy. Optimal screening is safe for a patient, easily reproduced, and almost independent of the operator's skills and quality of equipment. It is comparatively cheap and not time-consuming. Its cost is definitely less than the expenses of preventive maintenance and treatment of corresponding pathology. One expected disadvantage of screening is low diagnostic accuracy. Early detection enables curing breast cancer completely. In addition to revealing latent cancers, for men, screening involves a psychological aspect.

Patients with breast pathology are subject to further examination, first with X-ray mammography or complex ultrasound (US) with all available diagnostic options. Such an examination leads to differential diagnoses with subsequent choices of therapeutic tactics or – in cases of suspected malignancy – a biopsy with morphological verification, operative treatment, and dynamic observation.

However, these questions are not yet answered for the male population. Current examinations of men with breast changes are criticized because common guidelines are absent and not all clinics apply to men the generally accepted algorithm of examination of women with the same pathology. Examination reports vary from ordinary clinical examination with biopsy to mammography without a biopsy, or US alone with or without biopsy, depending on the results of the scan.

A unified diagnostic algorithm for the diagnosis of breast diseases and carcinoma particularly in men does not yet exist. In the case of precise preoperative diagnosis in early stages of breast cancer, a highly effective complex of medical actions, such as breast-conserving operations in combination with modern optimized programs of radiotherapy and chemotherapy, can be applied. The list of such procedures is similar to those in early and differential diagnosis of breast pathology in women. However, the indications, technologies, and order of their application may be different.

Diagnostic Methods of Breast Carcinoma

1. Preoperative
   Principal
   (a) Noninvasive
      - Clinical examination (anamnesis, survey, palpation)
      - X-ray mammography
      - US of the breast and regional lymph nodes
      - Analysis of steroid hormone receptors of tumors

   (b) Invasive
      - Stereotactic core needle biopsy with histology
      - US-guided fine needle aspiration biopsy (FNAB) with cytology
      - Vacuum aspiration biopsy with US or X-ray guidance
      - Nipple discharge cytology
      - Preoperative marking of impalpable tumors with barbed needles

      Additional (if indicated on the basis of individual features of breast development)

      - Ductography
      - MRI
      - CT of the breast and thorax
      - Scintigraphy
      - Others (electrical impedance tomography, radiothermometry, etc.)

2. Intraoperative
   - Urgent histology

3. Postoperative
   - Histology of the specimen

1.1 Clinical Data

Clinical examination in upright and supine positions permits assessment of the breast size and symmetry, the shape of the nipples and areola, deformation, lesions, and the state of axillary lymph nodes. Positioning the patient with the arms raised facilitates detection of tumors, skin infiltration, and deformation of the nipple, areola, or nearby regions (Fig. 1.1). Comparison with the contralateral breast is always necessary.

Diagnostic accuracy of clinical examination in revealing benign breast changes in men and women does not exceed 65 %, and in the detection of breast cancer, 50–60 %. The sensitivity of clinical examination for breast carcinoma in women is

Fig. 1.1 Clinical survey. (**a**) (1, 2) Skin deformation (**b**) Nipple retraction

40–69 %, with a specificity of 88–95 % (Todua 1980; Korzhenkova 2004; Sencha et al. 2010a, b).

The experience of our clinic and literature analysis demonstrated that mistakes in the diagnosis of breast cancer arose in approximately 30 % of patients who saw the doctor for the first time for this purpose. Being aware of breast oncology often prevents incorrect medical decisions. It is necessary to remember this during routine examinations of men, especially for men older than 50–60 years.

Palpation of abnormal breast tissue is capable of revealing lesions (often of cartilaginous density) with rough contours that are located centrally behind the nipple or areola, or near to them. A detected lesion requires a more careful palpation of this area to determine the size, shape, consistency, motility of the mass, and status of the skin over the mass. The relatively thin layer of subcutaneous fat in men, as compared with women, and the affinity of the gland to the skin and underlying tissues mean that the tumor attaches early to the anterior thoracic wall and the skin, and the skin becomes wrinkled. However, palpation of a small breast tumor at early stages is often difficult, and the revelation of such tumors is often incidental.

The study of the status of *steroid hormone receptors* shows that receptors to estrogen and progesterone are often observed in men. The incidence of estrogen-positive malignant breast tumors in men is 65–100 %. Clinically significant levels can be registered in greater than 85 % of cases. Nevertheless, the expression of receptor-positive tumors in men does not increase with age, as compared with women. There is a correlation between clinically significant levels of estrogen receptors and the effects of hormone therapy.

1.2 Mammography

X-ray mammography is one of the most informative methods for the diagnosis of breast diseases, breast cancer in particular, in men and women (Khazov 1969; Todua 1980; Ostrovskaya and Yefimova 1985; Rozhkova 1993; Lindenbraten et al. 1997; Semiglazov 2002; Kharchenko and Rozhkova 2005; Komarova 2006).

Mammography is the technology of acquisition of negative images (digital or analog), which characterize the penetration of X-rays through tissue. A mammogram is a two-dimensional image of the breast. It permits the analysis of the density of the glandular tissue and the detection and assessment of the location, shape, margins, and dimensions of lesions. The spatial relationships of abnormal foci can be analyzed through obtaining images in several projections. Mammography can be performed as mammography screening, targeted mammography, axillography, pneumocystography, and ductography.

Mammography has the following advantages:

- Detection of impalpable breast lesions
- High diagnostic value
- Possibility of invasive and noninvasive diagnostic procedures
- Objective documented data accessible for dynamic analysis

The disadvantages of mammography are as follows:

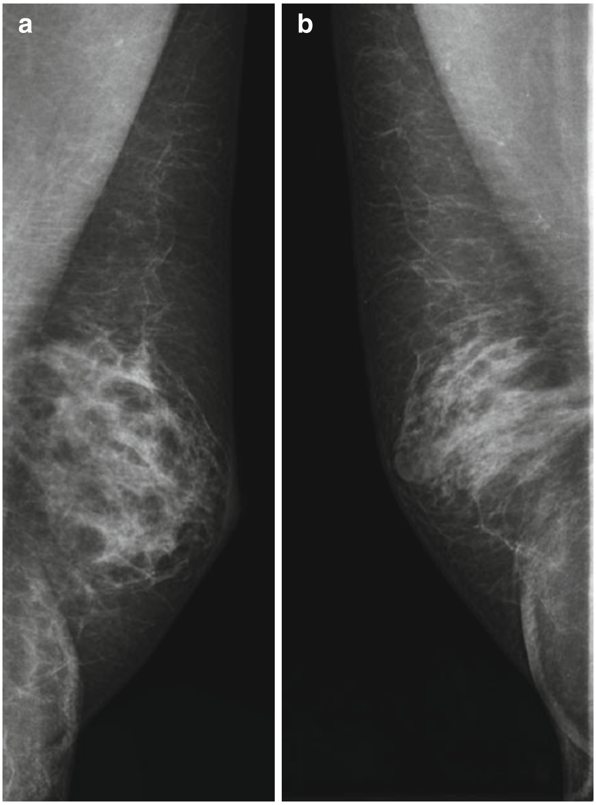
- Ionizing radiation
- Low value in dense and irregular structures of the breast, including X-ray-negative carcinoma, infiltration, inflammation, and fibrous changes

The indications for mammography in men are as follows:

- Age older than 60 years
- Suspicion or clinical features of breast cancer in any age group
- Other chronic breast diseases, especially nodular types (e.g., nodular type of chronic gynecomastia)

The criteria of mammographic diagnosis of breast carcinoma in men do not differ from the criteria in women (Khazov 1969; Todua 1980; Ostrovskaya and Yefimova 1985; Semiglazov 2002; Kharchenko and Rozhkova 2005). The characteristic features of breast cancer in men are lesions of increased density with radiant, spiky, indistinct margins, irregular structure with hyperdense linear patterns, and, often, microcalcifications. Dense spots are located eccentrically, which differentiates them from areas of gynecomastia (Fig. 1.2). Diagnostic mistakes are caused basically by difficulties in the definition of the mass against the increased density of the breast parenchyma. Mammography often permits the differentiation of gynecomastia and breast carcinoma on the basis of the characteristic location of gynecomastia (the retropapillary area and the relative symmetry of structures) and the status of the regional lymph nodes.

Fig. 1.2 Mammography. (**a**) Gynecomastia. (**b**) Breast cancer



The small thickness of the breast tissue layer in men often significantly complicates the performance of mammography, sometimes making it impossible, in comparison with women. Our experience shows that mammography in men is not always technically possible; however, it can be a beneficial addition to prophylactic medical examination with US. Some authors consider mammography a method of choice for the diagnosis of breast cancer in men and beneficial for the differential diagnosis of gynecomastia and breast carcinoma; others consider the efficacy of this method doubtful (Giordano 2005; Chen et al. 2006; Contractor et al. 2008; Khazov 1969; Todua 1980; Ostrovskaya and Yefimova 1985; Semiglazov 2002; Kharchenko and Rozhkova 2005; Dickson 2011).

The sensitivity of mammography for breast cancer in women is 50–93 %, with a specificity of up to 90 % and diagnostic accuracy up to 90 %. Impalpable carcinomas can be detected with mammography in 76–92 % of cases (Rozhkova et al. 1995; Chang et al. 1997; Korzhenkova 2004; Kharchenko and Rozhkova 2005; Letyagin 2006; Giordano 2005; Korde et al. 2010; Todua 1980). Ostrovskaya et al. (1988) consider that the optimal complex for the early diagnosis of breast carcinoma in men, as in women, is a classic triad of procedures: clinical observation, mammography, and cytology. This facilitates not only the correct diagnosis but also permits determination of the disease stage.

New technologies of mammography, a combination of analog, digital, and 3D-mammography with the introduction of digital tomosynthesis, open new prospects for radiology in the diagnosis of malignant breast pathology.

Ductography is seldom used in men. It is an X-ray modality that uses artificial contrasting of lactiferous ducts. It supplies information about the anatomy of lactiferous ducts: the type of branching, dilation, contours, and lumen condition. It permits assessment of intraductal lesions, their location, size, shape, and invasion.

1.3 Computed Tomography, Magnetic Resonance Imaging, and Positron Emission Tomography

Magnetic resonance imaging (MRI) is a valuable tool in the diagnosis of breast tumors in men and women (Pavic et al. 2004; Korzhenkova 2004; Mann et al. 2008; Serebryakova et al. 2011). Breast MRI enables T1- and T2-weighted imaging with complete acquisition sequences in all projections (axial, sagittal, and coronal). The technology of MRI analyzes data on the behavior of protons in hydrogen atoms. The motion of protons in one plane in a high-energy magnetic field is detected and analyzed to reconstruct an image. MRI enables the assessment of breast structure, including detection of abnormal foci and characterization of their capsules along with signs of invasion into surrounding tissues and visualization of lymph nodes. Dynamic MRI is a modality that is based on a series of variables, including different image characteristics (contrast, signal-to-noise ratio, resolution, time interval) and a series of other parameters. It allows the detection and interpretation of minimal changes in breast tissue (Fig. 1.3). Two important technical requirements of breast MRI are special magnetic coils and contrast agents.

MRI is considered in individual cases. It is not a screening test. Nevertheless, it is applicable for the detection of pathological processes and dynamic observation in women in groups with a high risk of breast carcinoma, for example, with mutations of the *BRCA 1* and *2* genes.

Contrast agents significantly increase the diagnostic value of breast MRI. The sensitivity of MRI with contrast enhancement in the diagnosis of breast tumors in men and women is 83–100 %, with a specificity of 29–97 % (Maryasheva 2003; Haylenko et al. 2005; Korzhenkova 2004).

MRI has the following advantages (Ternovoy et al. 1996; Kachanova 2000; Lukyanchenko and Gaurova 2001; Serebryakova et al. 2011):

- High resolution and contrast of soft tissues of the breast
- Possibility of acquisition of images in any plane without moving the patient
- Noninvasiveness
- Absence of ionizing radiation

Impressive possibilities of MRI in the detection of multifocal breast carcinoma were reported by Berg (2009). However, the high sensitivity of MRI in the diagnosis of breast pathology is accompanied by a low specificity and accuracy in revealing

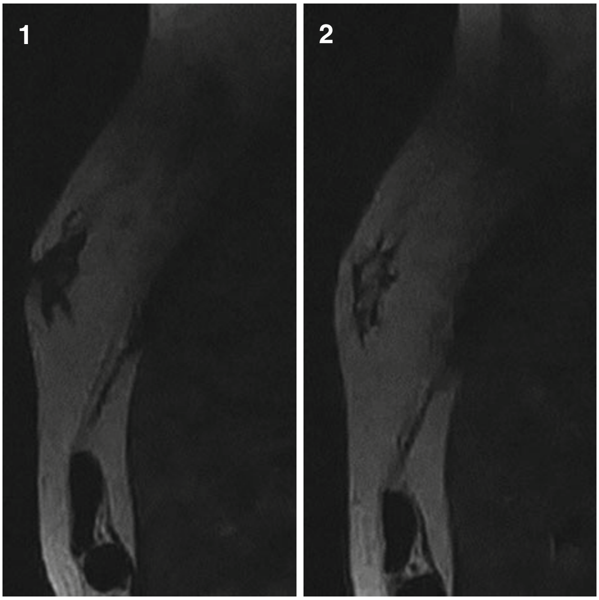


Fig. 1.3 (1, 2) MRI. T2-weighted fast relaxation, fast spin echo (T2FRFSE) sequence. Nodular gynecomastia

breast cancer. The high cost of the equipment forces the use of the technology only in difficult diagnostic cases (Haylenko et al. 2005).

Computed tomography (CT) is another modern radiological technology (Fig. 1.4). However, CT technology is not a screening modality for breast carcinoma because of significant radiation, high cost of examination, and low throughput. CT practically has no advantages in the early recognition of breast carcinoma as compared with mammography. However, the method is of great importance in the assessment of cancer invasion and is indicated to detect spreading of tumors into the retromammary space, metastases in lymph nodes, and remote metastases. The diagnostic value of CT in the detection of breast cancer is 60–62 %, the sensitivity is 100 %, and the specificity is 84 % (Dixon et al. 1993; Shevchenko 1997; Shishmareva 1997; Haylenko et al. 2005).

Mammoscintigraphy is a method used for the functional diagnosis of breast pathology and is based on the assessment of the distribution of radiopharmaceuticals in breast tissues. ^{99m}Tc-MIBI, ^{99m}Tc-tehnetril, ^{99m}Tc-teoksim, ^{99m}Tc-tetrofosmin, and others can be used for the examination. Mammoscintigraphy, along with examinations of the breast, permits the assessment of isotope distribution in other chest structures, including axillary areas and other regions of possible metastases. The technology can be performed in two varieties: with a gamma chamber (planar scanning, emission gamma tomography) or positron emission tomography (PET). In those cases, it can be performed as an isolated breast scintigraphy, a polypositional scintigraphy of the chest, or as a single-photon emission CT scan of the breast area and thorax.

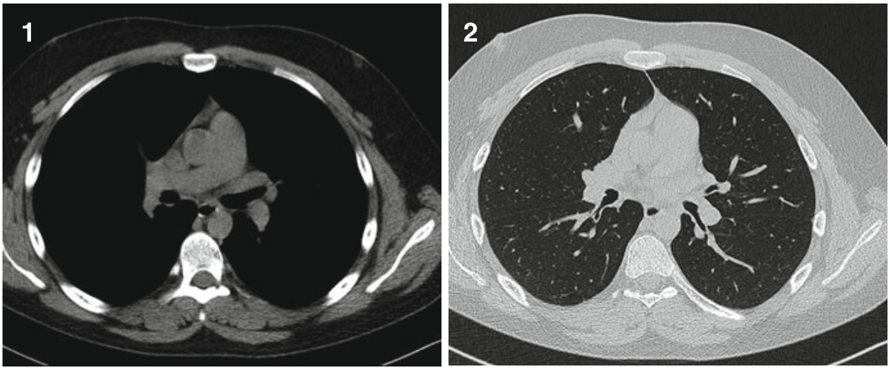


Fig. 1.4 (1, 2) CT. Breast carcinoma

The sensitivity of mammoscintigraphy with ^{99m}Tc-tehnetril in primary breast tumors in men and women ranges from 62 to 96.7 %, with a specificity of 71–100 % (Svensson et al. 2000; Haylenko et al. 2005). Mammoscintigraphy with ^{99m}Tc-MIBI is not of great value in revealing primary breast carcinoma. Its sensitivity depends on the size of the lesion (Usov et al. 1997). The sensitivity of scintigraphy in the detection of metastases of breast carcinoma in axillary lymph nodes is 51–85 %, the specificity is 91–93 %, and the diagnostic accuracy is 76–93 % (Perre et al. 1997; Svensson et al. 2000).

Positron emission tomography (PET) is a nuclear medicine technology using various agents (monosaccharides, fatty acids, antibodies, peptides, etc.) marked with positron-emitting radionuclides. A modified gamma chamber is applied. It permits the detection of gamma photons, which result from the annihilation of positrons with electrons. Since gamma photons are emitted in opposite directions, it is possible to localize the place of their formation. Short-lived radioactive tracer isotopes, which are chemically incorporated into a biologically active molecule (frequently 18F-fluordeoxyglucose), allow the detection of areas with increased metabolic activity, which is often characteristic of malignant cells.

PET is not yet widely applied for the diagnosis of breast carcinoma. Nevertheless, it is quite a promising technology (Tyutin and Stanzhevsky 2003; Shiryaev et al. 2005). Indications for PET are limited because of its low diagnostic value in small cancers (smaller than 1 cm). However, PET surpasses all known anatomical imaging methods for the localization of centers of breast carcinoma in soft tissues. Its possibilities should be applied for individualization of therapy and monitoring, because tumor metabolism decreases much more rapidly than tumor size with effective treatment. Alternatively, an absence of changes in tumor metabolism after treatment may predict the inefficiency of the treatment.

A number of examinations on the preoperative staging of breast cancer demonstrated that the sensitivity of PET for the diagnosis of multifocal lesions was twice as high, the same as the combination of mammography and US. The sensitivity and specificity of PET in the detection of metastases in axillary lymph nodes were 79 and 92 %, respectively (Kesler 2012). However, there are some limitations in the diagnosis of breast carcinoma with PET. They include highly differentiated tumors and specific locations (Valliant 2010).

For the diagnosis of breast carcinoma (in men as well as women), PET is developed in two basic ways: technological improvements (creation of detectors, hybrid systems, and software that are more effective) and development of new radiopharmaceuticals for the diagnosis of specific tumors at the molecular level at an early stage and for the prediction of the exact effects of different types of therapy (Kesler 2012).

Combined methods (hybrid PET technologies) are of great demand in modern medicine. They permit simultaneous visualization of morphological and metabolic abnormalities. Combined methods significantly increase the accuracy of the localization and definition of breast tumor structure and extension. Scanners that combine PET and CT or MRI (PET/CT, PET/MRI) are used most effectively (Rosen et al. 2007; Kesler 2012). PET/CT now is especially valuable in certain cases, such as local recurrence of breast carcinoma and detection of regional and remote metastases (Rosen et al. 2007; Kumar and Alavi 2008; Kesler 2012).

PET/MRI is a new achievement in hybrid radiology and is still developing. The manufacturers of such scanners expect that this combined technology will be more sensitive for the diagnosis of several types of cancer and metastases, as compared with PET/CT (Freiherr 2011). One large advantage of PET/MRI is the reduction in radiation dose in comparison with PET/CT, along with high contrast resolution and differentiation of soft tissues.

Electrical impedance tomography is a method of scanning the electrical impedance (full resistance) of breast tissues (Korzhenevsky 2003). It permits the quantitative assessment of the breast structure for the differential diagnosis of various physiological conditions and changes that accompany breast cancer. It analyzes the distribution of the electrical conductivity of breast tissues in several cross sections and detects the pathological focus with the abnormal value of electrical conductivity (Fig. 1.5).

According to Trohanova (2010), electrical impedance mammography is a simple and efficient method of screening for focal breast pathology in women of different ages. The sensitivity, specificity, and positive and negative prognostic values account for the following figures: for cysts, 91, 99, 93, and 99 %; for diffuse cystic mastopathy, 98, 97, 95, and 99 %; and, for breast carcinoma, 92, 98, 92, and 98 % (Trohanova 2010).

Radiothermometry is a modality that permits noninvasive measurement of the temperature in deep tissues. It is based on the remote registration of infrared radiation by means of special devices. The results of the examination are presented as a thermogram (temperature plot). The areas with increased temperature are suspicious for breast malignancy because of higher metabolism and vascularity. The character of breast thermograms depends on the age of the patient. Additionally, there are individual features of location of “cold” and “hot” areas that sometimes complicate the correct interpretation of the results. Radiothermometry is not often

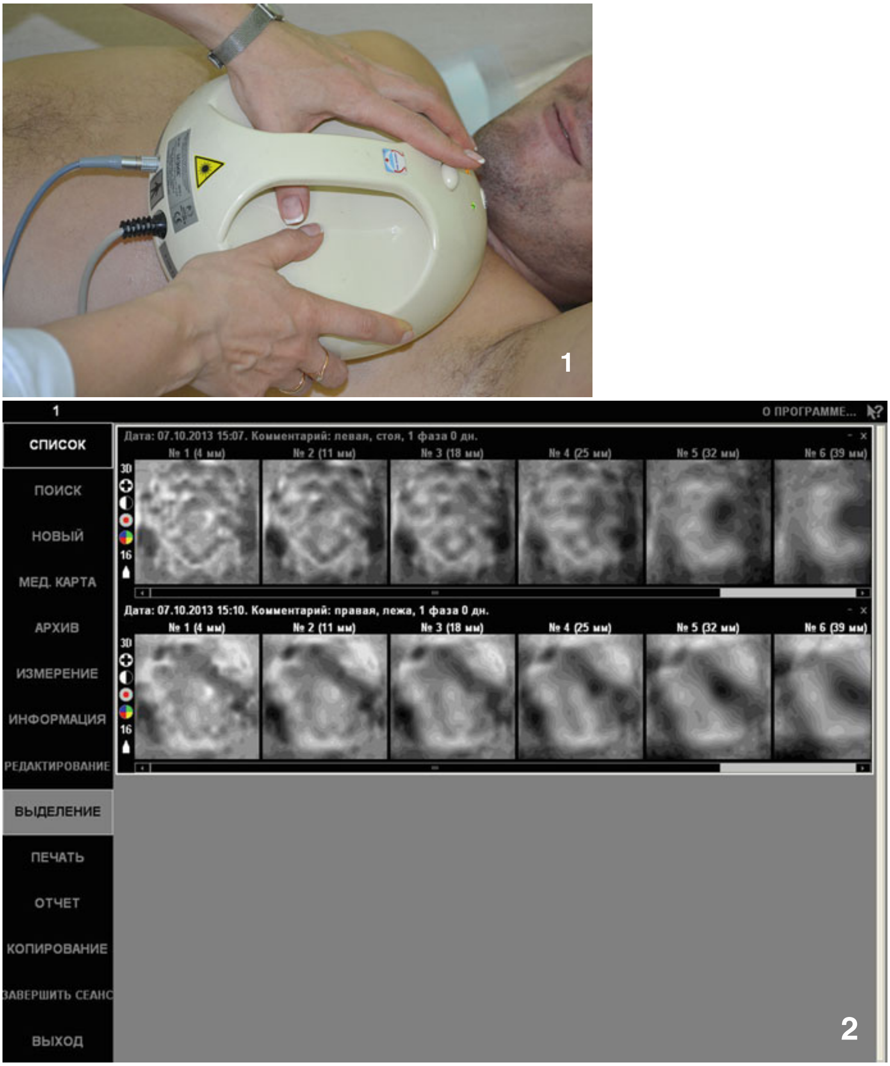


Fig. 1.5 (1, 2) Electrical impedance tomography

used nowadays in the diagnosis of breast cancer because of the large number of false-positive tests, which can exceed 25 %. The specificity of radiothermometry in the diagnosis of breast carcinoma is reported to be 85 %; the sensitivity is 84 %, and, in combination with US, 91 % (Yemelyanov et al. 2011).

MRI, CT, radiothermometry, electrical impedance tomography, radioisotope tests, laser mammography, microwave spectroscopy, and other sophisticated modalities have a limited number of indications and are not often used in daily practice.

1.4 Interventional Diagnostic Modalities: Fine Needle Aspiration Cytology and Core Biopsy

Morphological verification of breast tumors is possible with invasive diagnostic procedures. *Puncture biopsy* is an obligatory part of any diagnostic algorithm for breast carcinoma in men. Its efficacy is 50–90 % (Chen et al. 2006; Korde et al. 2010; Letyagin 2006; Dickson 2011; Sencha et al. 2011a, b). Puncture biopsy is a safe and efficient procedure. Several methods, with different diagnostic accuracies, are available. The diagnostic accuracy of fine needle breast biopsy is approximately 32 %; core biopsy, 57 %; and vacuum biopsy, 98 % (Ponedelnikov et al. 2011).

Core needle biopsy of the breast can be performed in several different ways. Stereotactic X-ray-guided breast biopsy is used more often. Special instruments, such as a biopsy gun and Tru-Cut needles, are necessary. The procedure aims to obtain material from the tumor for histological examination (Fig. 1.6).

The indications for core needle biopsy of the breast in men are as follows:

- Suspicion for malignant lesion
- Undetermined or doubtful breast masses
- Impalpable tumors
- Calcifications in breast structure (pathological, doubtful, uncertain)
- Asymmetric breast fibrosis

Stereotactic biopsy is the final stage in the modern complex diagnostics of impalpable breast cancer. Its sensitivity in the diagnosis of breast carcinoma in women is 97.6 %, its specificity is 100 %, and its diagnostic accuracy is 98 % (Kuplevatskaya 2004).

The wide application of US as a navigation method permits targeted *fine needle aspiration biopsy* (FNAB), which is highly efficient in obtaining samples from pathological foci (Fig. 1.7). FNAB with cytology started to be widely applied in oncologic practice after the absolute harmlessness of a malignant tumor puncture was proven. It is often used when the technical application of stereotactic biopsy is limited because of the clinical features of the pathological process. US is used for guidance in the majority of cases. The material for cytology from breast lesions in men is, as a rule, easily obtained. Subsequent cytology allows the definition of cellular structures in the sample and the differentiation of lesions of various natures. In addition to benign processes being differentiated from malignant processes, the degree of differentiation of carcinoma cells, if any are detected, can be specified (Joshi et al. 1999). The specification of the degree of differentiation of the tumor is only possible if well-preserved cells are present in the sample. According to Ostrovskaya et al. (1988), this is possible in 73.8–98 % of cases. According to Sinyukova et al. (2007), US-guided FNAB of breast lesions in combination with mammography and routine breast US improves the early detection of breast cancer (up to 95–98 %).

FNAB with US guidance offers advantages in the following cases:

- Impalpable X-ray-negative breast lesions
- Puncture of cysts

Fig. 1.6 (1, 2) Core needle breast biopsy

Fig. 1.7 (1, 2) US-guided fine needle aspiration biopsy of the breast

- Lesions within a scar
- Lesions on the margin of the thoracic wall (retromammary space)
- Irregular breast lesions (for the exact choice of the most suspicious area)
- Enlargement of regional lymph nodes

FNAB of breast lesions is often performed with the free-hand method. Guidance and puncture can be performed by one or two specialists (specialists in US teamed with the surgeon, oncologist, or mammologist). FNAB is the least traumatic and most affordable modality among the invasive manipulations. Nevertheless, one of its disadvantages is the possibility of incorrect targeting of the needle to the lesion, which may result in an incorrect cytologic conclusion. The amount of cells obtained with breast FNAB does not allow the differentiation of the lesion in 13.4–25 % of cases (Semiglazov et al. 2001). This fact is often the result of poor guidance, a small number of cells or total absence of cellular substrate in the obtained material, or complications during the procedure.

Vacuum-assisted breast biopsy with stereotactic mammography or US guidance is an ergonomic and highly effective method of obtaining cellular material for verification. It permits to obtain multiple samples of tissue with a single needle. The procedure can be performed for both diagnostic and treatment purposes. High levels of qualification and experience of the US specialist, who guides the biopsy, affect the precision of targeting and obtaining the material.

Histology is the most informative method for the verification of breast carcinoma. When the cytology or core biopsy fails to specify the tumor for any reason, an excisional biopsy is necessary. In women, this may mean that a sector resection is indicated; in men, typically, the whole breast is removed for ablastic reasons.

1.5 Ultrasound

Ultrasound (US) is now one of the most widespread and affordable imaging methods for the diagnosis of breast pathology, early and differential diagnosis of breast masses, and guidance of minimally invasive modalities.

US has the following advantages in the diagnosis of breast pathology:

- Modern US equipment has high resolution and yields high diagnostic value.
- It is relatively simple to perform, fast, and cost-effective.
- It is noninvasive and painlessness.
- It can be performed without any patient preparation.
- It has no contraindications.
- It is harmless and safe for the patient, hence can be used for children and patients with serious accompanying pathology, and for repeated examinations.
- It permits accurate differentiation of several diseases based on a complex analysis of grayscale, Doppler modes, and three-dimensional image reconstruction (3D).
- Reconstruction, elastography, and other options are available.
- It supports objective follow-up by means of digital archiving.

- It permits computer processing and archiving of data in an objective form that is suitable for delayed analysis.
- Analysis and digital transfer with virtual consultations via telemedicine systems and the internet are possible.
- It supplies precise guidance for minimally invasive manipulations.

US is one of the leading modalities for imaging impalpable cancer lesions at the preclinical stage. It requires certain skills in performing the examination, detailed knowledge of the anatomy of and physiological changes in the breast, and correlations with clinical and mammographic data and the results of other diagnostic methods. Modern US equipment, in the majority of cases, helps to prove the mammographic finding of breast carcinoma and additionally permits the diagnosis of X-ray-negative tumors. According to Sencha et al. (2013a, b), the high efficacy of US in the diagnosis of breast carcinoma in men is the result of its high sensitivity (86.9 %) and specificity (85.3 %). US allows to examine the areas that are inaccessible to mammography (e.g. retromammary space and regions of lymph drainage) and precisely characterize the relation of a tumor to the skin and nipple.

US has the following advantages compared with mammography (Weinstein et al. 2003; Ivanov et al. 2013):

- Examination of breasts in ectomorphic patients is possible.
- Examination of breasts in cases of dense background in young men is possible.
- Breasts with acute trauma or inflammation can be assessed.
- Postoperative scars can be assessed, as well as early and late complications and early recurrence of the disease.
- It is relatively simple and fast.
- No radiation dose is applied.
- It is ideal for repeated examinations to assess dynamic changes.
- There is unlimited access to examine regional lymph nodes.
- It provides easy guidance for puncture biopsies.

The role of US is large in the definition of breast masses in areas that are technically difficult to examine with other imaging methods (e.g., on the margin of medial quadrants near the breastbone, and in aberrant mammary lobes). US is unique in terms of the analysis of the whole breast vascularity and vascular pattern of breast lesions. Additionally, US can be used to precisely characterize abnormal lymph nodes.

Epidermal cysts, lipomas, stromal hyperplasia, or intraductal papillomas in retroareolar regions in small breasts practically always result in hyperdiagnosis of malignant lesions with mammography. Therefore, US allows to avoid unnecessary puncture biopsies and surgery in men (Fisenko 1999; Ivanov et al. 2013).

According to Bazhenova et al. (1985), Ostrovskaya et al. (1988), and Makarenko et al. (1986), a diagnostic complex based on clinical data and additional methods (US, mammography and other radiological modalities, cytology, etc.) provides a correct diagnosis, including in cases of impalpable masses, in 95.5–99 % of men.

Anatomy, Physiology, and Development of the Male Breast

2

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2.1 Anatomical Features of the Male Breast

The normal anatomy and individual features of the breast and regional lymph nodes in men should be considered during the examination. Each breast is located on the anterior surface of the chest, on the pectoral fascia and pectoralis major muscle between the parasternal and anterior axillary lines, with the nipple on the midclavicular line (Fig. 2.1). The breast level typically corresponds to the second through sixth ribs.

Breasts in men and women have the same origin and development until puberty. They originate from the fourth pair of lactiferous points. Development starts during the fourth week of gestation with the growth of a basic milk streak. Milk lines, "ventral epidermal ridges," are seen by the sixth week of the embryo's life. Glands and their ducts develop separately. The development progresses in women, whereas in men, the progress stops. Some people have several pairs of breast germs within the milk lines, although not all of them develop completely after birth.

The nipple and areola in men are small in size. The nipples are located on the midclavicular lines; their heights are 2–5 mm. The lobules and ducts are short and

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DOI 10.1007/978-3-319-06050-7_2

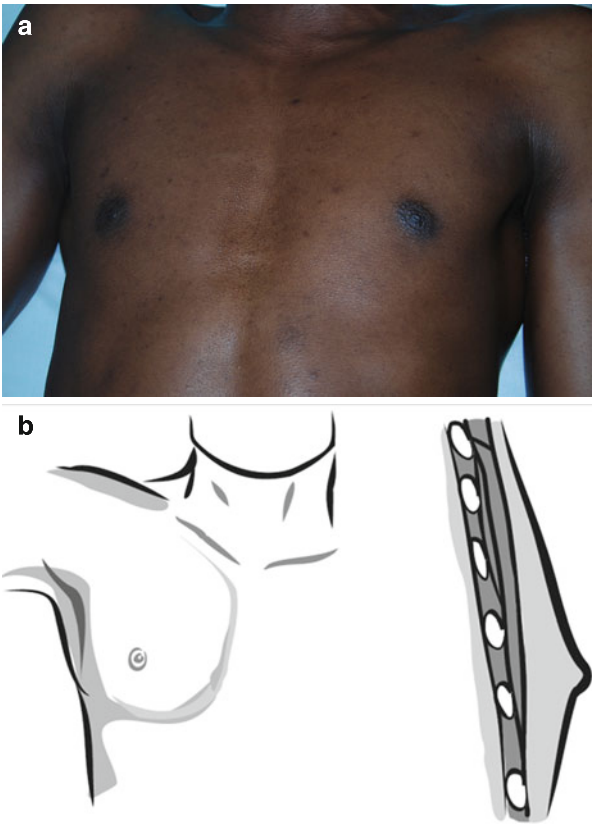

Fig. 2.1 Typical breast anatomy. (**a**) Photo. (**b**) Scheme

not developed. The size and shape of the breasts are variable and depend on the age, development of subcutaneous fat, and constitutional features. The nipple is located in the center of the breast and consists of muscular and epithelial tissues. It is surrounded by the areola, a pigmented skin area with multiple sweat glands. The breast is bordered by the anterior and posterior leaf of the superficial fascia of the thorax. Adipose tissue can be observed as subcutaneous fat and fatty lobes, which are surrounded with connective tissue fibers. The breast capsule is formed by connective tissue and fixed to the pectoral fascia.

The breast is highly vascular and is supplied by the branches of the internal thoracic, subclavian, axillary, and intercostal arteries that form the rete of anastomoses, predominantly in the subareolar area (Fig. 2.2). The venous rete accompanies the corresponding arteries and arterioles.

The lymphatic system is comprised of intramammary and abducent lymph ducts and regional lymph nodes, the latter conferring axillary, subclavian, supraclavicular, pectoral, and substernal groups. Intramammary lymph ducts form a complex rete with anastomoses and plexuses. Breast innervation is provided by the branches of thoracic, humeral, and intercostal nerves (Bazhenova et al. 1985).

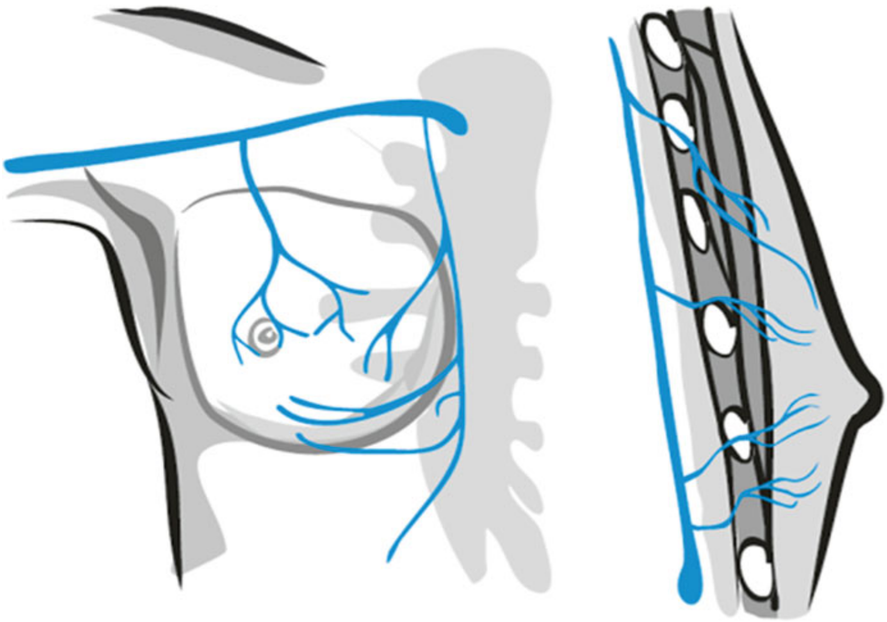

Fig. 2.2 Male breast vessels

2.2 Development and Physiology of the Breast in Boys

Breast tissue at birth is identical in boys and girls. Breasts in girls and boys from birth to puberty are represented by matrix (fragments of glandular tissue and ducts in germinal status) surrounded with adipose and connective tissue. Breast of both genders are identical until 7–8 years of age (Figs. 2.3 and 2.4).

At puberty, the breasts in boys remain rudimentary, whereas in girls, they start rapid development, differentiating under hormonal influence. Estrogens stimulate the proliferation of glandular tissue, whereas androgens counteract this effect. The majority of boys have a 30 times increase in the level of testosterone and a 3 times increase in the level of estrogen at puberty. At the age of 12–16 years, in the retroareolar area of healthy boys, ultrasound (US) may reveal images identical to those in girls at thelarche (Fig. 2.5). This reflects natural physiological changes in teenagers.

During fast puberty, the transitive proliferation of ducts and stroma finally results in the atrophy of ducts and involution of the breast. US usually fails to differentiate any elements of glandular tissue in boys younger than 18 years of age (Fig. 2.6). As a result, the breast of an adult man mainly consists of adipose tissue (subcutaneous fat) with insignificant subareolar residual ducts and fibrous tissue. The development of breast lobules requires estrogens and progesterone, which are detected in extremely low quantities in men. Cooper's ligaments, which are present in the female breast, are absent in men. Interstitial lymph nodes can be found in some cases.

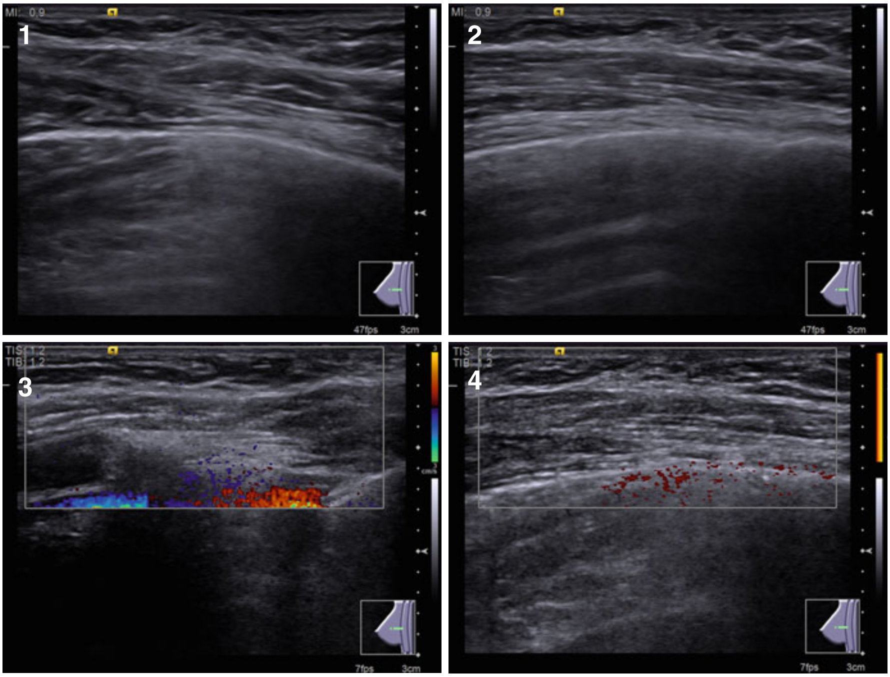

Fig. 2.3 (1–4) Healthy breast, 8-year-old boy. Grayscale US, color Doppler imaging (CDI), and power Doppler imaging (PDI)

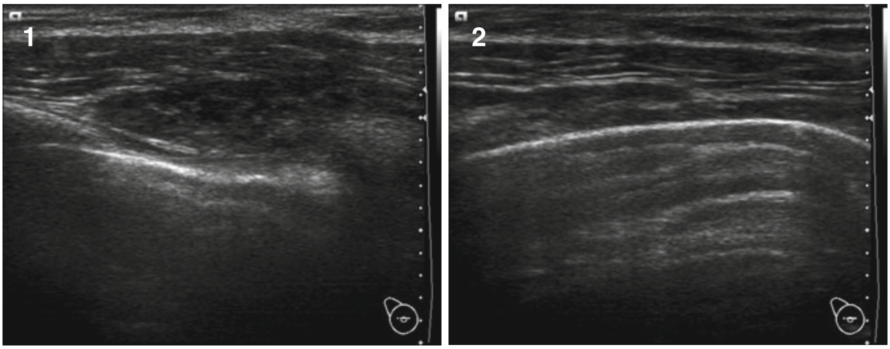

Fig. 2.4 (1, 2) Healthy breast, 8-year-old girl. Grayscale US

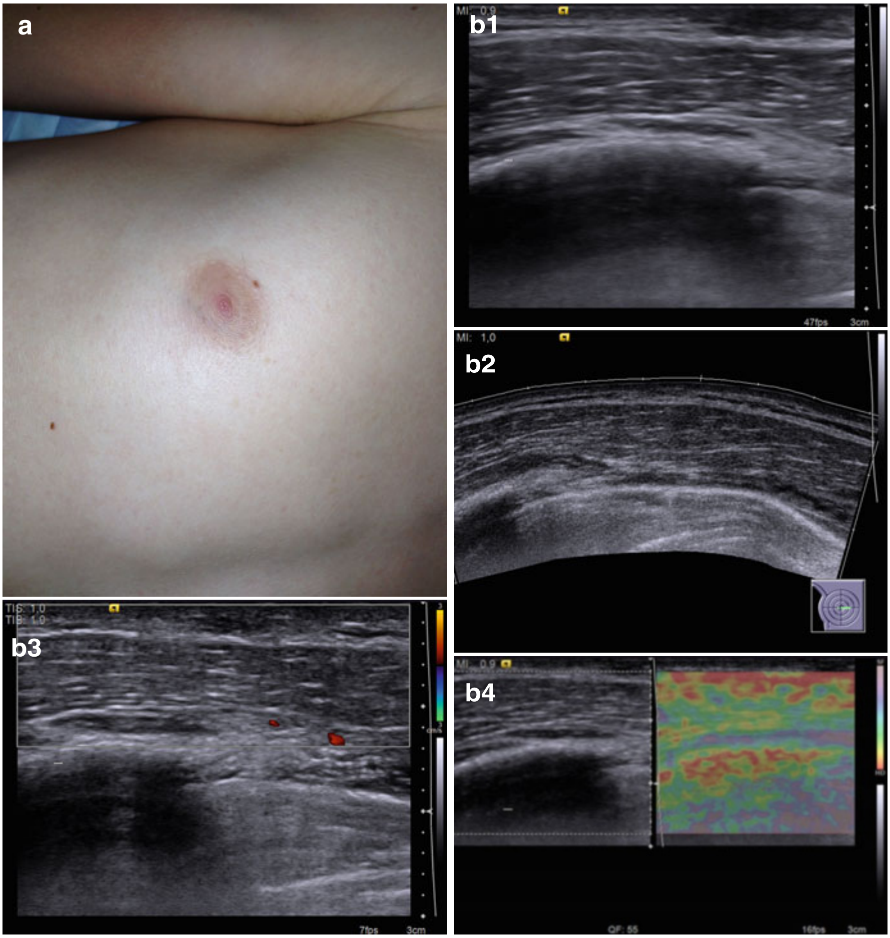

Fig. 2.5 Healthy breast, 14-year-old boy. (**a**) Photo (**b**) (1–4) Grayscale US, CDI, and ultrasound elastography

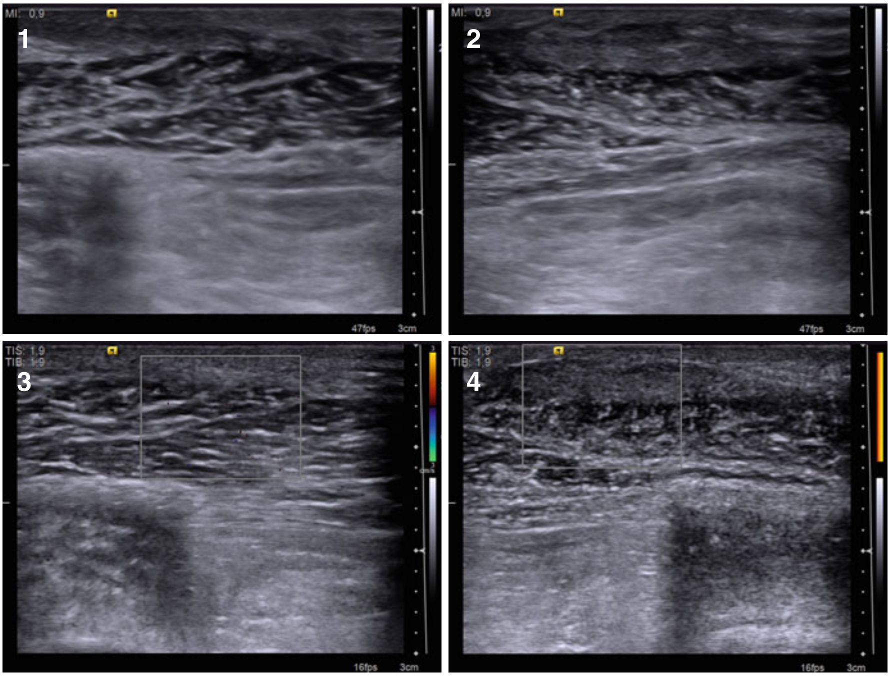

Fig. 2.6 (1–4) Healthy breast, 18-year-old boy. Grayscale US, CDI, and PDI

2.3 Congenital Abnormalities of the Male Breast

All breast anomalies that are present in men (as well as in women) can be divided into the following groups:

- Anomalies of the number of breasts, nipples, and areola
- Anomalies of the shape and size

Unilateral or bilateral anomalies are possible in both groups.

Amastia is the total absence of the breast, including the nipple and areola. It is an extremely rare condition and can be unilateral or bilateral. It is usually diagnosed at birth on the basis of the absence of the nipple and areola.

Aplasia of the breast is characterized by the presence of a small areola with an abortive nipple on the skin.

Athelia is the absence of nipples with normal development of the breast. It is also observed extremely rarely in men.

Polymastia is the excessive number of breasts. A condition with extra nipples, called *polythelia*, is observed more often. Accessory breasts and nipples are located, as a rule, along the milk lines. Rare cases of additional breasts in locations other than milk points, such as the face, ear, neck, hip, and back, have been described. The most frequent locations in men (as well as in women) are axillary and submammary areas.

Ectopia is a congenital breast displacement. The dislocated breast may be morphologically and functionally normal or abortive.

Asymmetry of the breasts is much more rarely registered in men than in women. However, this anomaly in men (as compared with women) causes prominent cosmetic defect or significant physical discomfort only in cases of significant disproportion.

Among the developmental anomalies of the nipple–areolar complex in men, *invaginated nipple* and *enlarged areola* can be rarely observed. Congenital and acquired invagination of the nipple should be differentiated, the latter resulting from breast hypertrophy.

Healthy Breast with Ultrasound

3

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3.1 Ultrasound Examination of the Male Breast

For breast ultrasound (US) of women, it is preferable that the examination be performed during certain periods of the menstrual cycle, whereas breast US examination in men does not require any special preparation or timing. The indications for breast US in men are as follows:

- Discomfort or pain in the breast area regardless of the detection of any palpable mass
- Breast enlargement
- Palpable lesions within the breast
- Changes of the skin of the breast, nipple, or areola
- Contralateral breast cancer
- Palpable masses in axillary areas
- Follow-up for patients treated for breast diseases
- Postoperative period
- Preventive examination in the cases of breast pathology in anamnesis or in close relatives of the patient

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_3

Fig. 3.1 (1, 2) Breast US in a man

The results of breast US, which often supplement data from X-ray mammography, especially in ambiguous cases, are valuable for:

- Differential diagnosis of lesions first detected with palpation or mammography
- Examination of the breast in children and teenagers
- Examination during the acute period of breast trauma or inflammation
- US guidance of puncture biopsy of breast lesions
- Assessment of breast infiltrations of obscure etiology

Breast US is performed with linear probes with frequencies of 7.5–12 MHz, currently more often 9–13 MHz. The patient is placed in the supine position with their hands under their head (Fig. 3.1). It is possible to perform the examination in the sitting or standing position, because the position does not influence the scanning access, the image quality, or the location of lesions.

According to the standard procedure recommended for women, in describing the location of pathological process in men, the breast is conventionally divided into four quadrants: upper (superior)–outer (lateral), upper (superior)–inner (medial), lower (inferior)–inner (medial), and lower (inferior)–outer (lateral). The subareolar area (central portion) and the nipple are described separately. The terminology of

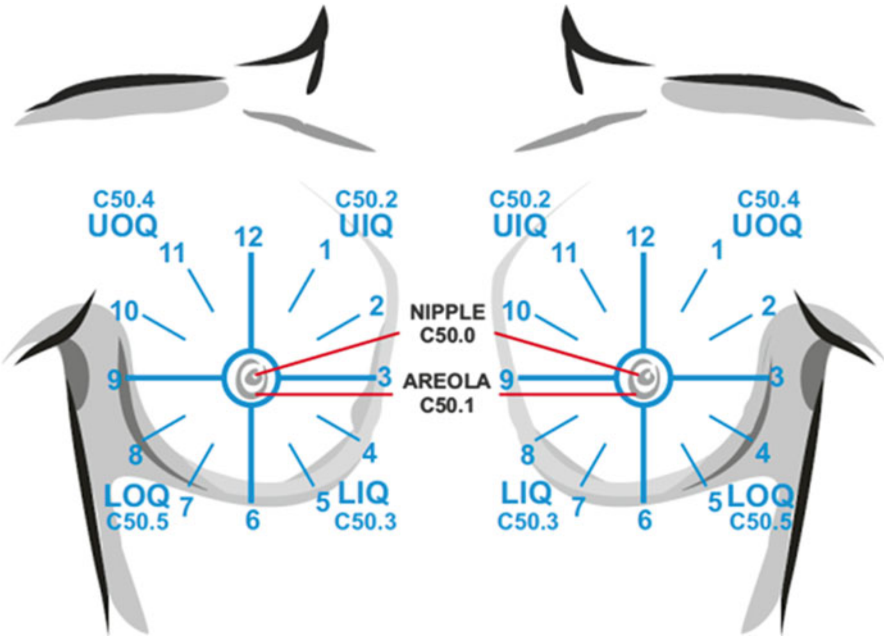

Fig. 3.2 Clock positions and quadrants of breasts

"clock positions" is appropriate as an additional subsite descriptor to indicate the exact location of an abnormality (Fig. 3.2).

The examination generally begins with the intact/healthy breast, or with either the right or left breast in cases of no complaints. The US specialist should understand that the breast region in men is not limited to the area of the nipple, areola, and retroareolar space. A roundish region approximately 7–10 cm in diameter should be scanned from periphery to the nipple, analogous to the female breast.

The direction of scanning does not matter. Breast US often begins with the upper–outer quadrant of the right breast and follows clockwise with the probe movements in a radial direction from the periphery to the nipple area along the course of lactiferous ducts. The examination of the left breast often starts with the upper–inner quadrant and proceeding clockwise. For a more detailed examination, the scans are repeated in a clockwise circular direction from the periphery to the nipple area. Special attention is paid to the subareolar and nipple areas, because the acoustic shadow from the nipple can hide various pathological processes.

If an area suspicious for pathological process is detected within the breast, other US options should be applied. They may be time-consuming and may require additional software. Moderate compression with the probe is applied to assess the mobility of the lesion against the surrounding tissues and its density (deformation) and to decrease US artifacts resulting from connective tissue elements (e.g., lateral acoustic shadows). It is necessary to assess the status of regional lymph nodes (axillary, supraclavicular, subclavial, and parasternal) during breast US.

The absence of clinical signs and masses in the breast and axillary areas, accompanied by normal oncomarkers, requires no further US follow-up. In cases of doubt, the doctor can recommend repeated US in a specific period of time to analyze changes in the pathological process or differentiate it from physiological features (typically, one to two times a year; rarely, two to four times a year).

3.2 Healthy Male Breast with Ultrasound Examination and Reporting

The US image of a healthy male breast, unlike in women, is usually constant and often does not depend on the age and cyclic physiological features of the patient. A variability in US images is quite small and can be caused by the patient's constitutional features (the development of subcutaneous fat) or could also depend on the class of US scanner or the US regimens and options.

US typically shows the status of the following male breast structures (Fig. 3.3):

- Subcutaneous adipose layer
- Superficial leaf of the fascia
- Presence and degree of development of the lactiferous ducts (if any are imaged)
- Back leaf of the fascia
- Retromammary space
- Regional lymph nodes

Whether the breast *skin* is assessed depends on the frequency of the US probe and the class of the US scanner. Healthy skin is imaged as a homogeneous echogenic layer of 0.5- to 7-mm thickness. Before puberty, the thickness of the skin usually ranges from 0.5 to 2 mm. It reaches 2–4 mm after puberty (Zabolotskaya and Zabolotsky 2010). Inflammatory process, condition after radiation therapy, and postoperative edema are accompanied with thickening and a rough echostructure of the skin. The echodensity typically decreases. Irregular anechoic fluid collections

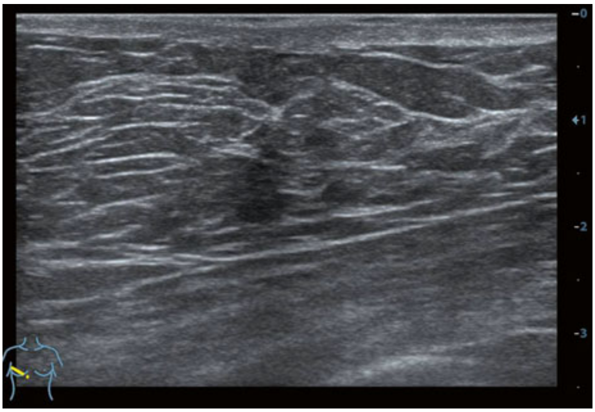

Fig. 3.3 Normal ultrasound anatomy of the breast

may be observed in some cases. The margin between the skin and subcutaneous fat is not always possible to differentiate with a 5–7.5-MHz probe.

Subcutaneous Fat. Adipose tissue is characterized by a decreased or normal echodensity and a fairly homogeneous structure with linear echogenic incorporations that often exhibit vague acoustic shadows (small amounts of elongated structures of decreased echodensity with rare hyperechoic connective tissue septa). Adipose tissue often looks like roundish hypoechoic structures located in rows. Each side of an adipose lobe is very often bordered by symmetric lateral acoustic shadows. Willson (2007) considered any constitutional corpus adiposum as a false gynecomastia. Superfluous adipose tissue with repeated lateral acoustic shadows prevents accurate differentiation of the breast echostructure. Compression of the breast with the US probe typically permits reduction of this artifact.

The *anterior (superficial) leaf of the fascia* is often distinctly observed as an echogenic line that separates subcutaneous fat from the underlying structures. Imaging of *lactiferous ducts* depends on male breast development. Typically, lactiferous ducts in men are abortive and short. In the overwhelming majority of cases, they are not observed with US. In rare cases of their detection, they are quite fragmentary. The ducts should be differentiated from blood and lymphatic vessels. Polypositional, polyprojective scanning, and Doppler imaging could be of benefit. *Cooper's ligaments and glandular tissue* in men's breasts are absent and are naturally not detected with US. The *back leaf of the fascia* borders the breast from the retromammary space and is imaged as a thin (~0.1 cm) homogeneous echogenic linear structure.

The *retromammary space* contains retromammary adipose tissue, the pectoralis major and minor muscles, intercostal muscles, and pleura. Retromammary fat consists of hypoechoic lobes between echogenic lines of the back leaf of the fascia and the anterior margin of the pectoralis major muscle. The pectoralis (major and minor) and intercostal muscles are defined as hypoechoic structures isolated with septa. The identification of these muscles guarantees that the breast layer is examined completely.

The echostructure of the ribs depends on the amounts of osteal and cartilaginous components. Each part of a rib has a different US image. Transverse US scans reveal the osteal part of a rib as an oval structure with increased echodensity on the periphery and acoustic shadowing. The cartilaginous part is hypoechoic with distinct anterior and posterior margins and some posterior shadowing. However, some inner structures can be observed in the cartilaginous parts. Intercostal muscles are defined in intercostal spaces as hypoechoic structures with a typical fibrillar pattern. The pleura can be detected as an echogenic line that changes with breathing. It is the deepest structure that can be distinguished during breast US. Imaging of the structures of the retromammary space is not always possible and depends on the frequency of the US probe and the class of the US scanner.

The *nipple and areola* are usually defined as a roundish structure of average or decreased echodensity with comparatively homogeneous structure and distinct even contours. Sometimes, the nipple is accompanied by a posterior acoustic shadow arising from muscular and connective tissue structures. The skin of the areola exhibits lower echodensity as compared with other breast areas. Subareolar structures are always more echogenic because of the low amount of fat. Thus, it is necessary to examine the subareolar area polypositionally to exclude abnormalities in this area, especially in cases of inverted or retracted nipples.

There are certain US features of the breast in men of different age groups. In boys before puberty, the breast is composed of adipose tissue and fibrous stromal components without any glandular tissue. The ductal system, which is undeveloped, is represented by merging hypoechoic structures in the retroareolar space. Adipose tissue has decreased echodensity, and a relatively homogeneous structure with fine echogenic linear incorporations without acoustic shadow. The thickness of the adipose layer is approximately 0.5–1 cm and depends on the patient's constitution, but generally increases with age.

In early puberty, adipose tissue can be defined with US as a thin layer between the skin and glandular tissue. With age, the thickness of the adipose layer increases, with a slight increase in its echodensity. It also becomes more heterogeneous. The connective tissue structures of the breast have increased echodensity and are often accompanied by an acoustic shadow. This fact is necessary to consider during breast US to avoid mistaking artifacts for pathological changes. In such a case, it is beneficial to compare symmetric areas of both breasts. Further changes in adipose tissue are characterized with an increase in the heterogeneity of connective tissue, defined as echogenic linear structures.

In young men, adipose tissue presents as a thin layer under the skin. With age, the thickness of this adipose layer increases, accompanied by a slight increase in echodensity. In adult men, the adipose tissue becomes more irregular due to the development of connective tissue, which is defined as echogenic linear structures with acoustic shadows. Fibrous changes in the breast with large numbers of acoustic shadows negatively affect the quality of imaging of deep structures and the detection of abnormalities, especially of small-sized lesions.

Normal US images of the breast in age-matched men may differ depending on several aspects associated with individual features (anatomical and constitutional features, injuries or surgical operations, hormonal treatment, etc.). During breast US, it is necessary to compare the structures of the right and left breasts and assess dynamic changes in US images during a certain time interval (3–6 months). Complete and correct information about the breast condition can be obtained taking into account all features, such as the complaints, clinical data, age, accompanying pathology, endocrine status, and others.

The breast of adult men consists mainly of adipose tissue and can normally contain insignificant amounts of residual ducts and fibrous tissue in the subareolar area. The skin is imaged as a 0.5- to 1.5-mm-thick echogenic line. Subcutaneous fat lies under the skin and is defined as a relatively uniform hypoechoic layer, 2 to 3 cm thick. Healthy breast does not contain any cystic or solid lesions on US or mammographic images (Figs. 3.4 and 3.5).

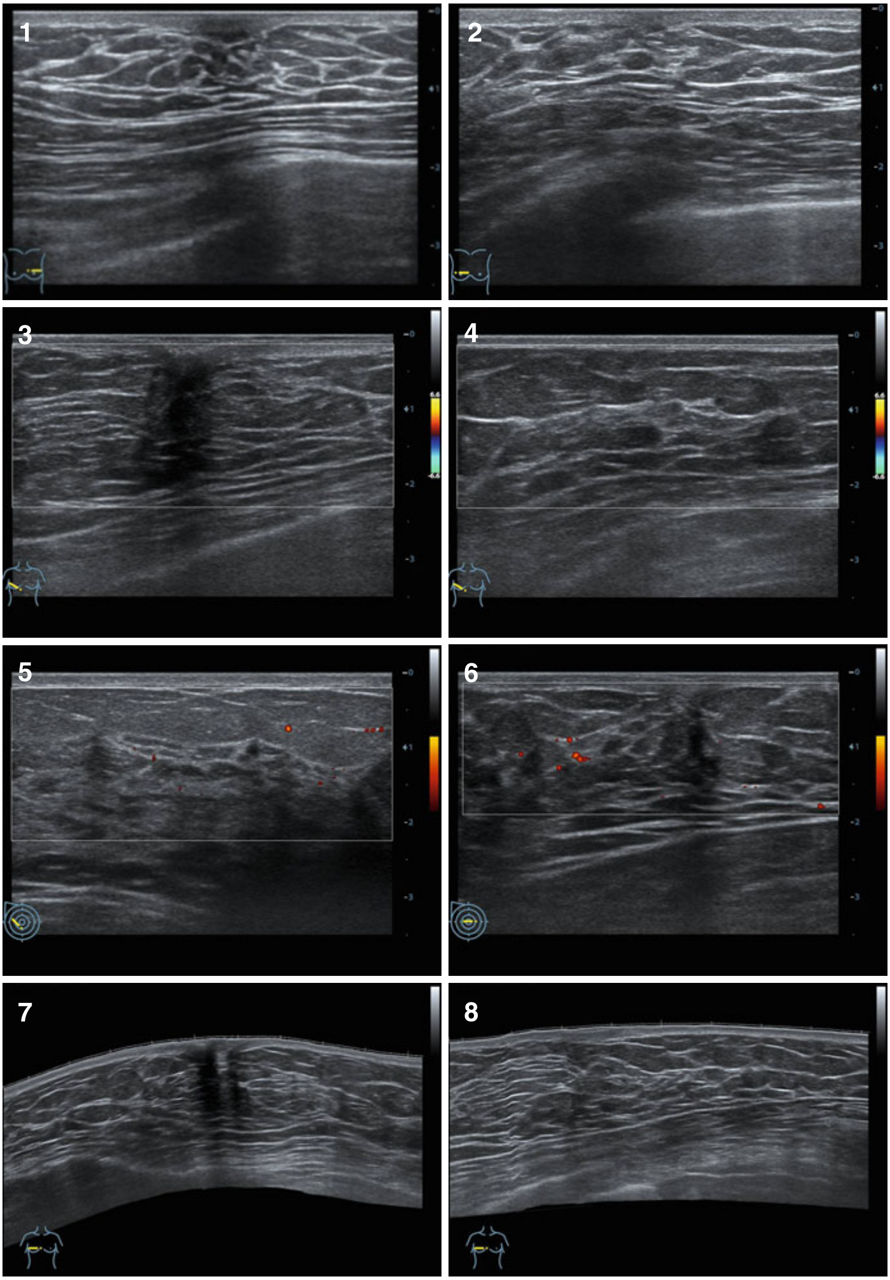

Fig. 3.4 (1–14) Healthy male breast. Grayscale US, color Doppler imaging (CDI), power Doppler imaging (PDI), panoramic scan, compression elastography, and strain ratio

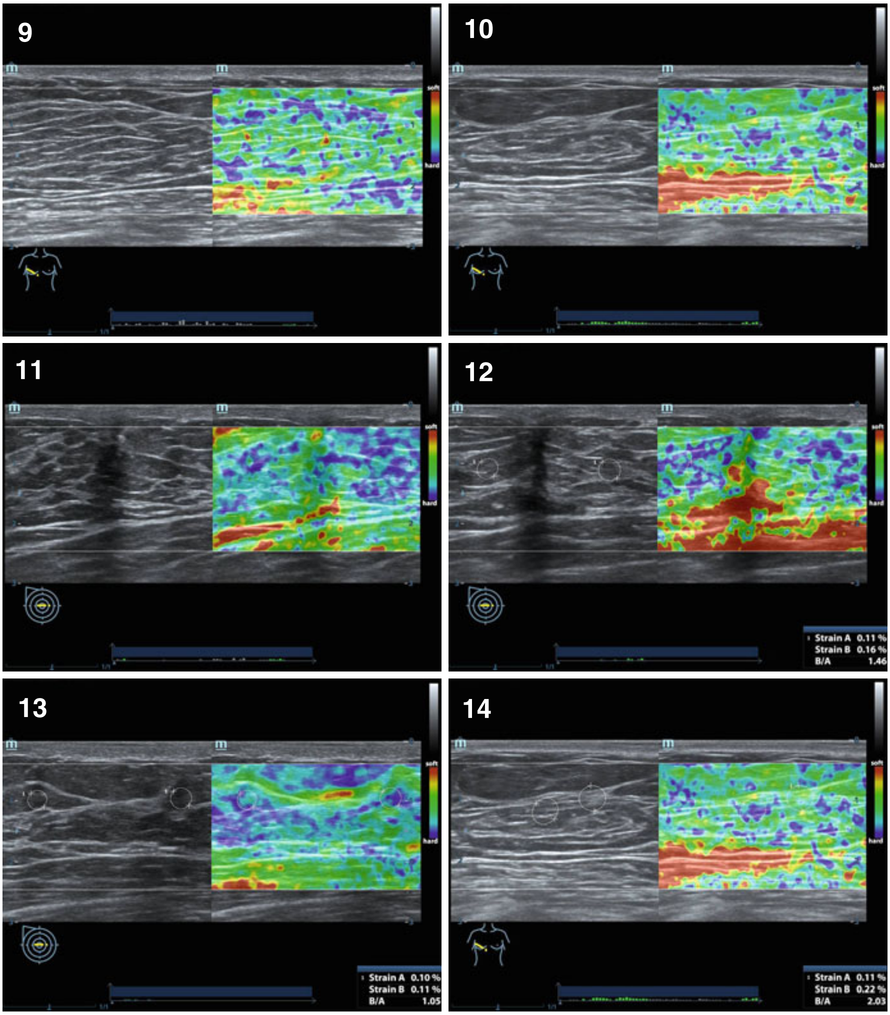

Fig. 3.4 (continued)

The standard report of breast US results should describe the presence of lesions or fields (areas) with abnormal structures, their location, and precise description in different US regimens. The examination of regional lymph nodes is also necessary.

An US report example in healthy breast is:

First name, middle initial, last name
Age
Date
The breasts are of masculine type, mainly consisting of adipose tissue. Fibrous tissue is insignificantly present in all regions. Lactiferous ducts are not shown. Cystic and solid lesions are not detected. Axillary, supraclavicular, and subclavian lymph nodes are not enlarged.
CONCLUSION: Healthy breast US

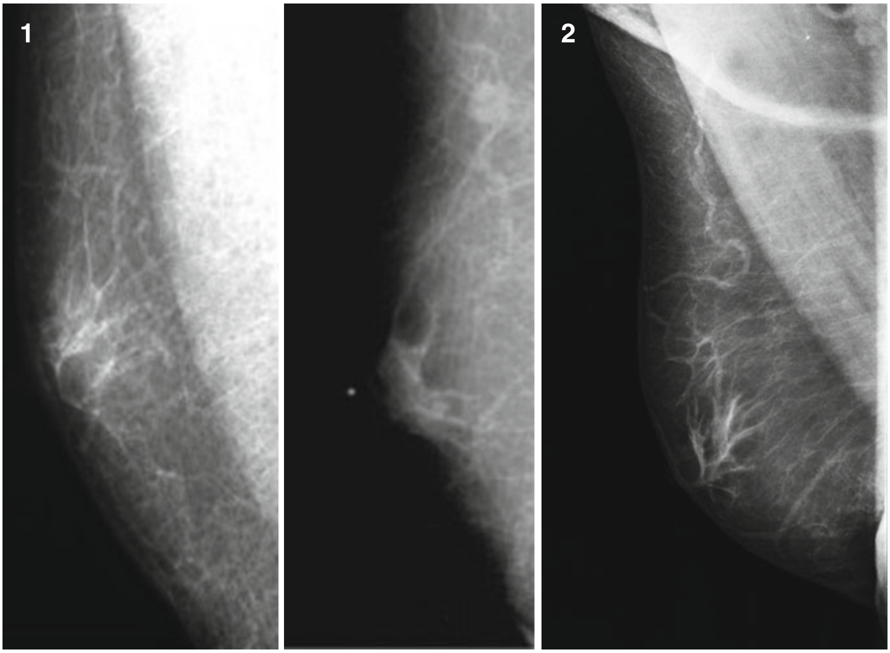

Fig. 3.5 (1, 2) X-ray mammograms. Healthy male breast

Ultrasound of Male Breast Cancer

4

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4.1 Epidemiology, Etiology, Development, and Prognosis

Breast carcinoma in men is a rare disease, with an incidence of 1:100,000. It is found approximately 100 times more rarely in men than in women. Breast carcinoma represents 0.2–1.5 % of all malignant tumors in men (Crichlow 1972; Ostrovskaya et al. 1988). Studies demonstrate that black men are affected more often than white men, regardless of age. The incidence of breast cancer in black men is 1.8:100,000, compared with 1.1:100,000 in white men (Anderson et al. 2004).

The majority of publications on breast carcinoma in men are based on rather small clinical groups. Few authors have published surveys with more than 100 cases. Scientific works with a large number of patients analyze the data of several medical institutions or review the literature. This substantially complicates the analysis because of the heterogeneity of the data. The first large works were published by Yamamoto in 1911 (167 cases) and Wainwright in 1927 (418 cases). Later, meta-analyses of large numbers of cases appeared in 1959 from Treves et al. (146 cases), in 1964 from Moss (507 cases), in 1968 from Holleb et al. (198 cases), in 1969 from Norris et al. (113 cases), in 1972 from Crichlow (2,217 cases), in 1975 from Scheike

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_4

(257 cases), in 1977 from Brunei et al. (537 cases), in 1977 from Falsati (114 cases), in 1977 from Ribeiro (200 cases), in 1980 from Todua et al. (125 cases), in 1981 from Steiniz et al. (187 cases), in 1983 from Letyagin et al. (103 cases), in 1983 from Kantarjian et al. (140 cases), and in 1986 from Makarenko et al. (125 cases).

The etiology and pathogenesis of male breast cancer are unclear. There are some opinions on factors that influence the development of male breast cancer, but the results have been inconsistent across studies. Nevertheless, the following *risk factors* can be taken into account:

- Age – the sixth and seventh decades of life
- Hormonal disturbances that result in true or relative increase in estrogens in a male body, diseases of male reproductive system of tumoral and nontumoral nature, adrenal tumors
- Hypogonadism or Klinefelter syndrome
- Hermaphroditism
- Gynecomastia
- Detection of sex chromatin of the female type and 47 chromosomes, instead of the typical 46 chromosomes, because of an extra X chromosome
- Extended treatment with medicines that contain female hormones
- Chronic diseases of the liver
- Familial history of male breast cancer
- Radiation exposure of the breast at a young age
- Breast trauma
- Erosion or eczema of the nipple

Between 6 and 30 % of patients connect the beginning of breast cancer (discovering the tumor) with trauma (Letyagin 2006). Some researchers consider breast trauma as a factor that contributes to the development of cancer, whereas others deny the possibility of such a connection. Sachs (1941) reported that 29.3 % of men with breast carcinoma had a preceding breast trauma in their history. Crichlow (1972) analyzed the data of 14 publications (523 patients) and reported breast trauma in 6 % of men. A single or repeated trauma can induce hemorrhage, leading to the enlargement of the breast. Adipose necrosis and an area of fibrosis, which are sometimes difficult to distinguish from a true tumor, appear in certain cases after trauma. Treves (1959) and Sinner (1961) reported breast trauma in the history of 12–14 % of men with breast carcinoma. They considered that the trauma itself might not induce cancer but attracts the attention of patients to a preexisting breast mass that they had not noticed before. In the data of Ostrovskaya et al. (1988), 8.2 % of patients (from a group of 61 men with breast carcinoma) report bruises of the breast in the preceding 6 months to 3 years.

Familial anamnesis (presence of a malignant breast tumor in the direct relatives of the first or second generation) was reported in 7–27 % of cases. Ten percent of men with breast carcinoma exhibit a genetic predisposition (Everson et al. 1980; Korde et al. 2010). True hermaphroditism may be one possible cause. Similar cases were observed by Moriarty (1944) and Decker et al. (1982). The panel of chromosomes in these cases corresponded to the male and female karyotype XX/XY.

Some genetic studies investigated correlations of *BRCA* genes with the incidence of breast carcinoma in men. Publications by Basham et al. (2002) and Ottini et al. (2003) demonstrated that the frequency of mutations in *BRCA1* ranges from 0 to 16 % and *BRCA2* from 8 to 14 %. Assessments of population-based studies suggest that approximately 15–30 % of men have a familial anamnesis of breast carcinoma. Mutations in *BRCA* genes influence the development of breast cancer in men and increase the risk 80 times in comparison with the general population.

The incidence of *BRCA* gene mutation carriers ranges from 4 to 40 %. Men with a mutation in *BRCA2* exhibit a higher risk of breast carcinoma throughout life. This risk is approximately 6 % and is 150–200 times higher than in the general population (Brose et al. 2002). One multicenter study in Italy assessed the correlation of clinical and pathological features of male breast carcinoma with mutations in genes *BRCA1* and/or *BRCA2* (Ottini et al. 2012). An important factor in male breast cancer is the overexpression of the oncoprotein Her2–neu and the indicator of proliferative activity, Ki-67, because the disease in men demonstrates similar characteristics as in women but is more aggressive and has a more unfavorable prognosis.

According to Akimov (1992), breast carcinoma in men in most cases (81 %) appears on a normal background. Much more rarely (9 %), residual elements of gynecomastia can be observed along with carcinoma. Bykova et al. (2011) reported that approximately 30 % of breast cancers arise on preexisting gynecomastia, in particular the nodular type.

As in women, the risk of developing breast carcinoma increases with age. However, the disease can begin at any age. Some researchers consider that young men (up to 40 years) have an increased incidence of breast cancer (Makarenko et al. 1986). Other researchers (the majority) note that breast cancer is most often reported in men in their sixth and seventh decades of life.

The mean age of men with breast cancer is 55–65 years (Davidov and Letyagin 2006) and 62–67 years (Dickson 2011), which is, on average, 10 years later than reported in women with this disease (Contractor et al. 2008). Bässler (1978), based on 698 autopsies, noted that the highest mortality of men with breast cancer was reported in the seventh decade of life (65–70 years of age).

Male breast cancer is usually unilateral. Only 5 % of cases develop bilateral, synchronous, or metachronous lesions. The analysis of the publications from 1927 to 1971 demonstrated that bilateral cancer was reported in 1.4 % of men (Crichlow 1972). Later publications reported higher incidences, even up to 12 % (Dana et al. 1978).

Malignant breast neoplasms exhibit eccentric locations, often round the areola, that distinguish them from benign lesions (Sencha et al. 2013a, b). The location of the tumor behind the nipple results in nipple retraction. Fixed skin over the tumor is observed in one third of cases of breast carcinoma in men. If the tumor invades the retromammary space, it affixes to the pectoralis major muscle. There is a popular belief that breast carcinoma in men generally develops eccentrically, as compared with the locus of nodular gynecomastia, the latter locating centrally. In particular, D. Oulmet-Oliva et al. (1978) consider the eccentric location of the lesion as the differential feature of breast cancer in men. The data of I. M. Ostrovskaya et al.

(1988) deny this point of view. Authors note that the majority of abnormalities in men's breasts initially develop from rudimentary lactiferous ducts, which are mainly located behind the nipple. Hence, the pathological process, whatever it is, a cancer or nodular gynecomastia, is more often expected in the retroareolar area. Nevertheless, the authors mention that an eccentric location is possible in both diseases; however, it is more often observed in cancer than in gynecomastia, with a ratio of 4:1.

Breast carcinoma in men usually has no clinical signs and most often is detected as a palpable mass. According to O. V. Akimov (1992), 44 % of patients found the lesion themselves. Because of the fast growth of the tumor and the small breast size in men, the disease anamnesis is usually short. Its duration in men with breast carcinoma ranged from 1 month to 5 years and longer, 7.4 months on average. Twelve percent of patients saw a doctor more than a year after the first symptoms of the disease. Late stages of cancer generally were diagnosed in such cases. Some publications report that the most often reported sign of cancer is the retraction of the nipple (64.3 % of cases according to the data of I. M. Ostrovskaya et al., 1988), whereas O. V. Akimov (1992) reported it in 17.8 % of patients.

Pain or discomfort in the breast is not typical for cancer, but it attracts the attention of the patient to the breast. Thirty percent of cancers are accompanied with a thickening and/or dimpling of the skin with possible ulceration. Discharge from the nipple may be observed in 10 % of cases. The small size and flat shape of the breast in men facilitates early detection of malignancies (Fig. 4.1). Approximately 47 % of men have significant local spreading of breast carcinoma when they are first seen by a doctor for the disease (Letyagin 2006).

Despite characteristic features, only one third of men with breast cancer visit their doctor within 1 month after detection of the disease. The other two thirds of men with breast lesions do not seek medical care for months and sometimes years. According to V. P. Letyagin (2006), the primary reason for consulting a doctor in 21 % of cases was long-lasting breast skin ulceration. However, late stages of breast carcinoma at diagnosis in men are not only caused by men not seeking medical consultation promptly. Sometimes, it is a consequence of inefficient primary medical care because of low oncologic awareness. Breast cancer was not suspected in approximately 20 % of men at the first referral to a doctor (Letyagin 2006).

Poor development of subcutaneous fat and affinity to the skin and underlying tissues mean that the tumor becomes immobile very early in relation to the anterior thoracic wall, and the skin over the tumor fixes and dimples. Even superficial palpation permits identification of an irregular lesion of cartilaginous density near the nipple and areola. While examining the status of the nipples and areolas, it is necessary to pay attention to thickening of the skin, retraction or dimpling, and discharge from the nipples. Skin ulceration over the tumor in men appears significantly earlier than in women.

The average size of a diagnosed tumor is usually 2–4 cm and may vary from 0.5 to 12.5 cm. Breast cancer is more often observed in the left breast, with a ratio of 1.07–1.63:1 (Ostrovskaya et al. 1988; Akimov 1992; Contractor et al. 2008). The reason for that is unclear, but a similar observation is noted in women.

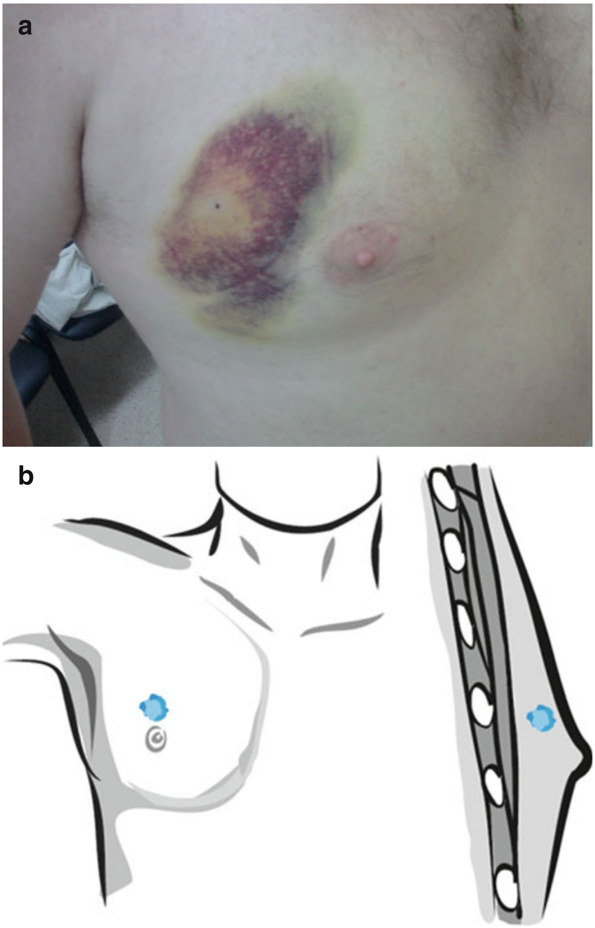


Fig. 4.1 Breast carcinoma in a man. (**a**) Photo. (**b**) Scheme

The same histological types of breast carcinoma (preinvasive ductal and lobular, infiltrative ductal) are observed in men as are seen in women. Some additional breast malignancies described in men were inflammatory, lobular, papillary, ductal cancer in situ, and atypical hyperplasia of ductal epithelium (Giordano et al. 2004). Some observations of tubular cancer characterized with high differentiation and good prognosis were published (Scheike 1975). Single instances of breast sarcomas in men were described. Their histological types were quite different: fibrosarcomas, leiomyosarcomas, neurosarcomas, reticulosarcomas, lymphosarcomas, and carcinosarcomas. In most cases, histology of the cancer reveals typical ductal cancer with the structures of cribrous, papillary, and solid types, and, rarely, lobular, comedocarcinoma, and adenocarcinoma. Cystic transformation is typical, whereas invasive growth is reported less often (Paltsev and Anichkov 2005).

According to O. V. Akimov (1992), there is no significant difference in the incidence of intraductal, invasive ductal, and other (mucous, medullary, and papillary) carcinoma types. The most frequent finding in men, as well as in women, is invasive ductal cancer (80.2 and 82.0 %, respectively). Intraductal carcinoma in men and women also exhibits practically identical incidence (1.3 and 2.3 %, respectively). Special histological types of cancer were detected in 20.0 % of cases in men and 13.0 % of cases in women. The comparison of the degree of differentiation of invasive ductal breast cancers in men and women revealed that carcinoma in men is usually less differentiated than in women. Highly differentiated carcinoma in men was not reported at all, as compared with 5.9 % in women. In the group of special histological types, tubular adenocarcinoma in men was not observed, whereas its incidence in women was 3.6 %. Clinical signs of Paget disease of the breast are described in detail in women and are practically the same in men. It is an extremely rare condition that accounts for less than 1 % of all male breast cancers. Inflammatory breast carcinoma in men is rare and extremely aggressive. It is likely that not all researchers include this type of cancer in the description of their own observations. N. Treves (1959) specifies that the frequency of inflammatory cancer in men is slightly less than 2 %.

Male breast cancer has a bad prognosis. It develops quickly and metastasizes early. The 5-year survival rate is 20–30 % (Ostrovskaya et al. 1988).

4.2 Ultrasound Signs of Breast Cancer in Men

The first publications devoted to the differential diagnosis of breast pathology with ultrasound (US) technologies in A-mode belong to J. J. Wild and D. Neil (1951) and in B-mode to J. J. Wild and J. M. Reid (1952). Before the mid-1970s, subcentimetric breast lesions could be successfully detected only in 8 % of cases. In the 1980s, echography was considered an additional diagnostic procedure to clinical survey and mammography. US today is a highly effective and obligatory method of examination, which is used in men along with mammography, clinical survey, and palpation in the diagnosis of breast pathology, including early and differential diagnosis of malignancies (Zabolotskaya and Zabolotsky 1997; Trofimova 2000a, b; Korzhenkova 2004; Komarova 2006).

US examination is based on the ability of tissues with different acoustic resistances to reflect US (cyclic sound pressure waves with a frequency greater than 20,000 Hz). Modern US scanners work in real time, which provides an opportunity to observe the locomotion of organs in a natural time course. The development of new diagnostic equipment, the introduction of digital US scanners, the use of modern high-frequency probes of 7.5–18 MHz, and the complex use of modern options and technologies significantly increased the diagnostic possibilities of sonography.

The complex of modern US technologies for the diagnosis of breast cancer confers the following options:

1. Grayscale regimen
2. Tissue harmonics
3. Adaptive coloring
4. Color Doppler imaging
5. Power Doppler mapping
6. Three-dimensional reconstruction of grayscale images, real-time 3D
7. Three-dimensional vascular reconstruction
8. Panoramic scan
9. Spectral pulse Doppler
10. US elastography (compression and shear wave)
11. Other options (multislice view, volume computed tomography (CT), contrast US, etc.)

Our own experience is based on the analysis of examinations of 14,827 men and treatment of 4,847 patients with various breast pathologies (Fig. 4.2). The majority of cases of gynecomastia (4,500 men) were patients with diabetic gynecomastia who were treated in the endocrinology center of the Yaroslavl Railway Clinic of JSC “Russian Railways.” There were 180 patients with benign breast diseases and 225 men with breast trauma. More than 10,000 US examinations were performed in our clinic and the Yaroslavl Regional Oncologic Center.

Our experience is based on retrospective and prospective analysis of 122 cases of men with breast cancer treated in the Yaroslavl Regional Clinical Oncologic Center from 1993 to 2013. The mean age of the patients was 65.8 ± 8.6 years. Morphological examination of breast carcinoma in men demonstrated that all histological types observed in women were seen at practically the same incidence in men. Pathology of the material obtained from biopsies and after surgeries revealed the following types of breast carcinoma: ductal invasive carcinoma in 40.2 %, lobular invasive carcinoma in 9.9 %, tubular adenocarcinoma in 4.1 %, solid adenocarcinoma in 4.1 %, moderately differentiated adenocarcinoma in 3.3 %, serous adenocarcinoma in 1.6 %, squamous carcinoma in 1.6 %, leiomyosarcoma in 0.8 %, and unspecified carcinoma in 34.4 % of cases (Fig. 4.3).

More than half of the patients were diagnosed with locally spread cancer. Metastases in lymph nodes were observed in 59 patients (48.3 %). More than four lymph nodes were affected in 16.4 % of patients. According to the TNM classification, the T1 stage of breast cancer was reported in 18.9 %, T2 in 44.3 %, T3 in 25.4 %, and T4 in 11.4 % of cases.

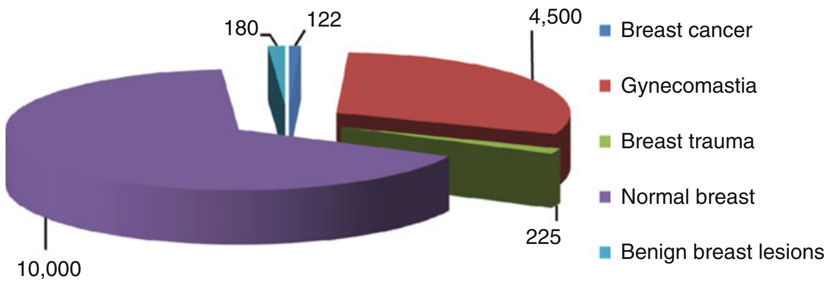


Fig. 4.2 Distribution of patients examined for breast abnormalities

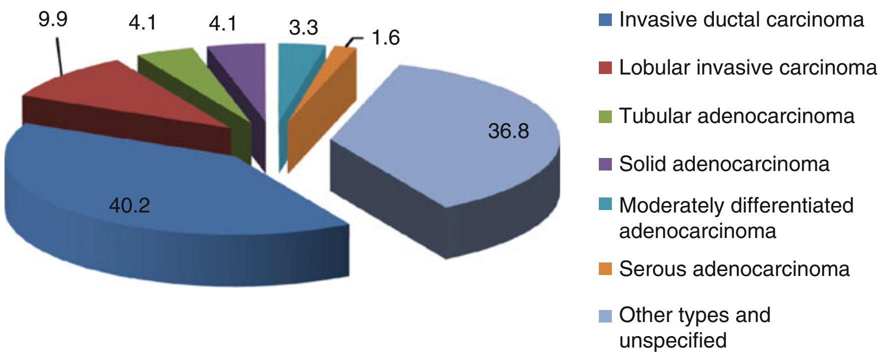


Fig. 4.3 Types of breast carcinoma

The majority of tumors had the second degree of malignancy (122 cases). Immunohistochemical study of samples for estrogen and progesterone receptors was performed in 85 % of patients, expression of Her2/neu in 65 %, and Ki-67 proliferation index in 57 % of patients. Seventy-seven percent of tumors appeared positive for both estrogen and progesterone receptors, whereas 3.3 % of tumors were negative.

The clinical signs listed in the Table 4.1 were analyzed in men with breast tumors. Their expression substantially depended on the stage of malignancy. The US features of male breast lesions that are suspicious for cancer are decreased echodensity, eccentric location, heterogeneous structure, avascularity, and enlarged axillary lymph nodes (Table 4.2, Fig. 4.4). Our study proved that breast carcinoma in men has similar US signs as those observed in women (Sencha et al. 2011a, b, 2013a, b) (Fig. 4.5).

The wide choice of US technologies and options with different frequencies of US scanning provide detailed images of breast structures and facilitate daily practice. High contrast and spatial resolution, and complex analysis of various US technologies permits easier and more effective data collection. Algorithms

Table 4.1 Basic complaints and clinical signs in men with breast cancer

Clinical feature	Incidence (%)
Palpable breast mass	81.5
Eccentric location	69.7
Discomfort in breast	69.7
Deformation of the breast (especially in nipple and areola)	65.6
Nipple retraction	64.7
Pain	34.4
Thickening and/or ulceration of the skin	34.4
Breast edema	34.4
Discharge from the nipple	19.7
Lesions in the axillary area	48.3
Absence of complaints	3.3

Table 4.2 Basic US features of breast carcinoma in men

US regimen	US feature	Incidence (%)
Grayscale US	Solid lesion in the breast	98.4
Grayscale US	Eccentric location of a mass	69.7
Grayscale US	Irregular shape of breast lesion	60.65
Grayscale US	Rough margins	69.7
Grayscale US	Indistinct contours	56.55
Grayscale US	Decreased echodensity	95.1
Grayscale US	Heterogeneous structure	70.5
Grayscale US	Echogenic incorporations, microcalcifications	15.6
Grayscale US	Anechoic component	11.5
Grayscale US	Acoustic shadowing	36.1
CDI, PDI, 3DPD	Avascularity	55.7
	Hypovascularity (1 color pixel)	24.6
	Hypervascularity (2 and more color pixels)	19.7
CDI, PDI, 3DPD	Irregular distribution of vessels within the lesion, chaotic and disorganized vascular pattern, pathological transformation of vessels	13.1
Compression US elastography	Intensive staining (red or blue), clearly distinct from the surrounding structures	84.6
	Uniform color of the mass	88.5
ARFI (VTQ)	Average shear-wave velocity within the lesion	4.2 ± 0.032 m/s
Strain ratio	Average value within lesion in relation to normal tissue	2.8 ± 0.013 U
Lymph node metastases	Axillary lymph nodes	75.4
	One sided	59.0
	In combination with subclavial lymph nodes on the affected side	10.65
	Remote metastases in organs and lymph nodes	13.1

of automatic image optimization based on signal preprocessing allows balancing of the effects of tissue heterogeneity, to differentiate and suppress noise and artifacts.

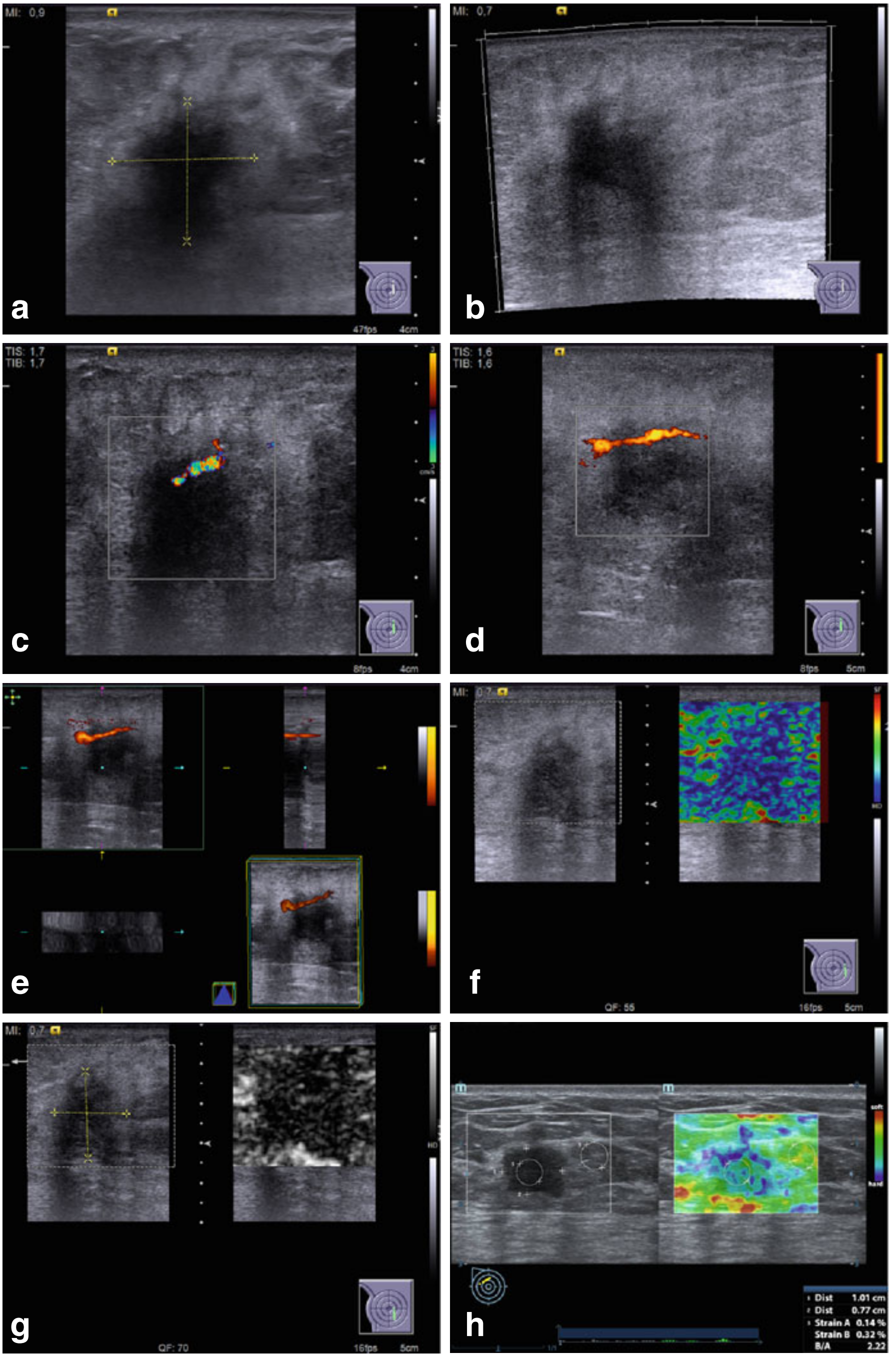


Fig. 4.4 US of breast carcinoma in a man. (**a**, **b**) Gray scale. (**c**) CDI. (**d**) PDI. (**e**) 3DPD. (**f**, **g**) US elastography. (**h**) Strain ratio

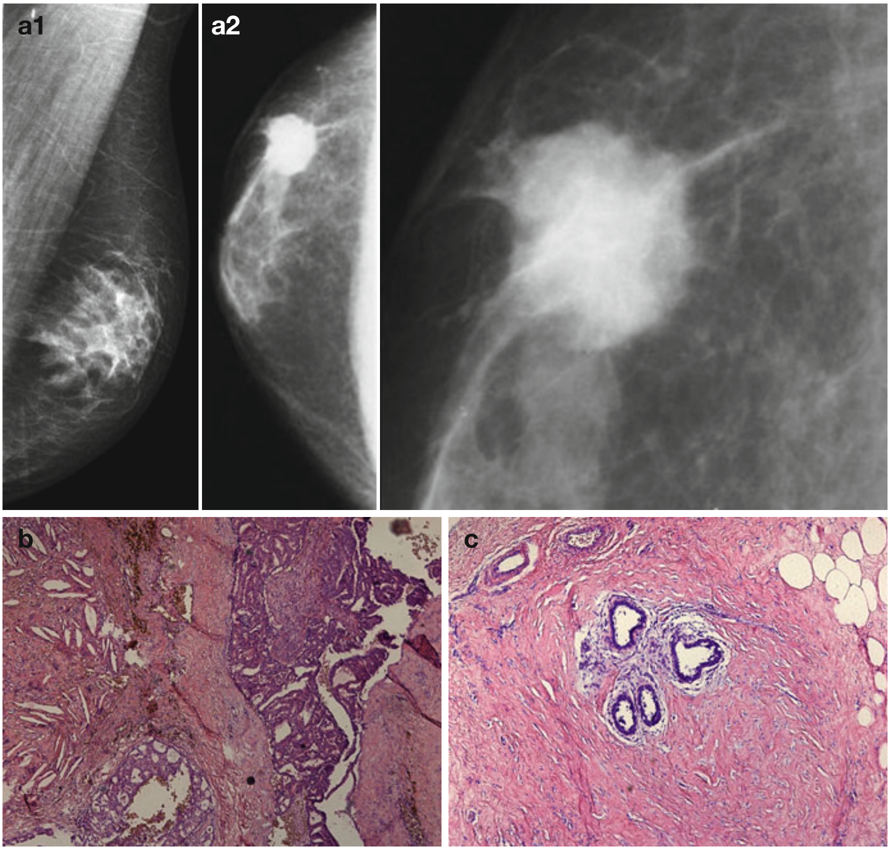


Fig. 4.5 Breast carcinoma in a man. (**a**) (1, 2) X-ray. (**b**) Photomicrograph of a histopathologic specimen (hematoxylin–eosin stain, original magnification, ×20). (**c**) ×100

4.3 Grayscale US

Grayscale (2D, B-mode) US is the principal US imaging modality for the diagnosis of breast diseases and breast cancer, in particular (Fig. 4.6). B-mode scanning permits assessment of the following US parameters of breast structure:

- Disturbance in the differentiation of tissues of the breast
- Presence of one or several areas of local disturbance of the breast structure with clear or indistinct margins
- Skin thickening
- Indistinct border between the deep layer of derma and underlying structures
- Presence and the expression of transverse and/or vertical hypoechoic tubular structures in the subcutaneous area
- Rough connective tissue components of the breast
- Presence of dilated lactiferous ducts

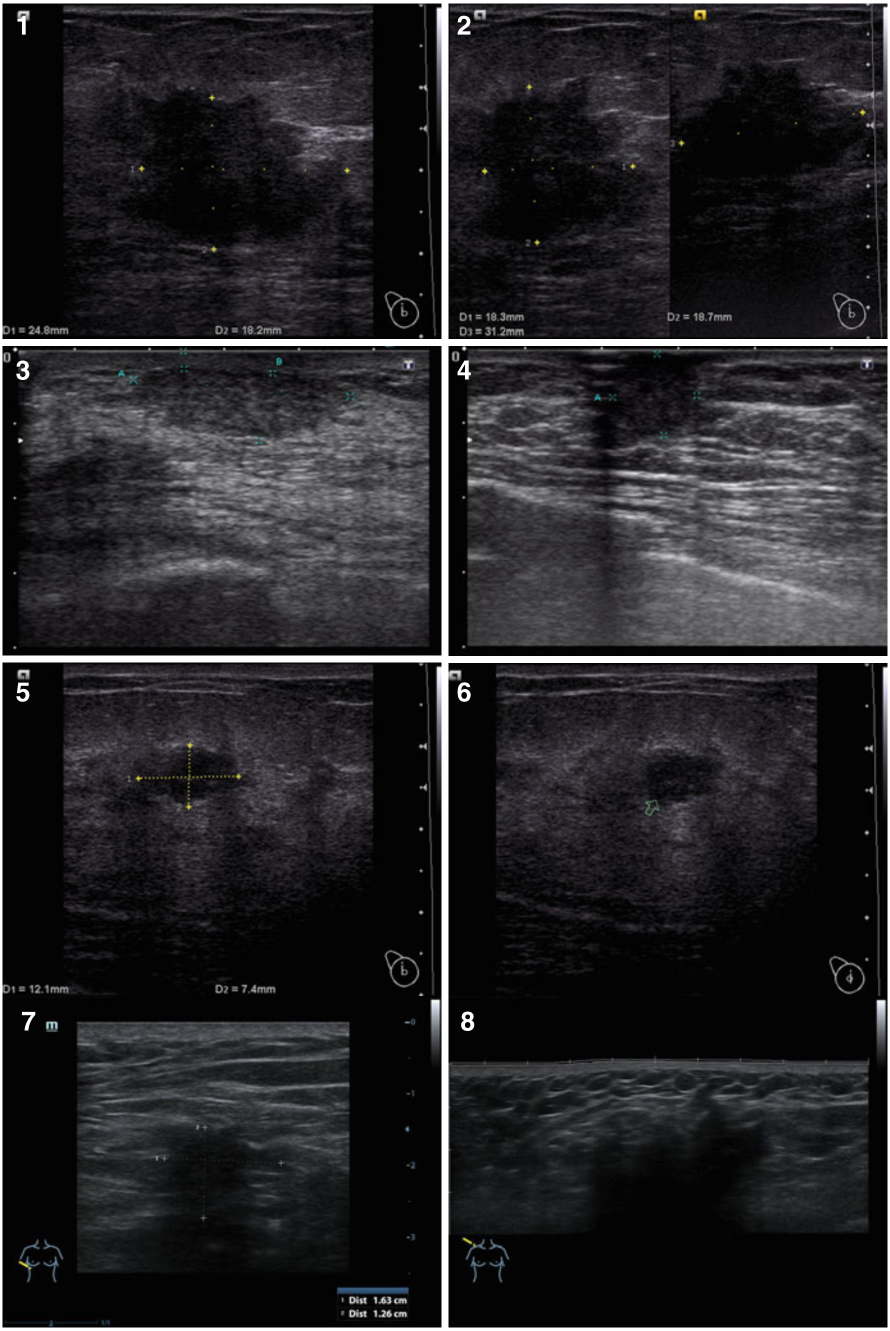


Fig. 4.6 (1–8) Nodular breast carcinoma. Grayscale US

Grayscale imaging supplies basic information on the character of pathological process, thus decreasing the number of unspecified diagnoses. The wide range of histological types of tumoral growth invoke interest in searching for correlations between morphological and US structures.

Breast carcinoma in men, as well as in women, may exhibit nodular or diffuse (infiltrative) growth. The *nodular type* of breast cancer is primarily characterized by the presence of a lesion within the breast structure that can be revealed in grayscale mode or other US regimens. In our study, the nodular type of breast cancer was observed in 98.4 % of men (120 of 122 men). Sixty percent of tumors were located in the left breast. Tumors in the upper–outer quadrant were reported in 19.7 % of cases, in the upper–inner in 5.7 %, in the lower–inner in 3.3 %, and in the lower–outer in 1.6 %. Because of the small size of the male breast, the tumor, located in different quadrants of the breast, adjoined the areola edge in most cases. The tumor was bilateral in 3.3 % of men.

Nodular breast carcinoma has the following US features (Table 4.2):

- Eccentric location of a mass in relation to the nipple
- Decreased echodensity
- Heterogeneity of the structure
- Irregular shape
- Rough and indistinct margins
- Less often – calcifications within the lesion, fluid component, posterior changes in acoustic signal (Fig. 4.7)

The location of a palpable breast tumor in men differs from the same in women. According to Zabolotskaya (2006), up to 50 % of all cancers in women originate from the upper–outer quadrant of the breast, 15 % are located in the upper–inner, 10 % in the lower–outer, 5 % in the lower–inner, and up to 17 % in the central area. In men, the central subareolar area is affected most often (59.7 %).

Considering that invasive lesions usually disorganize the normal location of layers of fat and connective tissue, malignant tumors can be slightly hypoechoic and have distinct contours. In the case of detection of calcifications and a heterogeneous echostructure with a spotted posterior shadow, the probability of a malignant tumor is very high.

Anatomical features of the male breast cause the most frequent location of cancer to be in the subareolar area. Tumors can be located under the nipple and merge into the skin. However, more often they have a slightly eccentric location. The last variant can be accompanied with an umbrella-shaped extrusion on the skin surface. It is very important to carefully examine the back edge of the lesion to assess its relation to the pectoral muscle because this influences the choice of treatment.

The lesion can demonstrate infiltrating or expansive growth. According to Ciatto et al. (1994), Marquet et al. (1995), Vetshev et al. (1997), and Trofimova (2002), US images of breast carcinomas are quite variable. The basic criteria of breast cancer with grayscale US are the following: irregular shape of the lesion, heterogeneity of

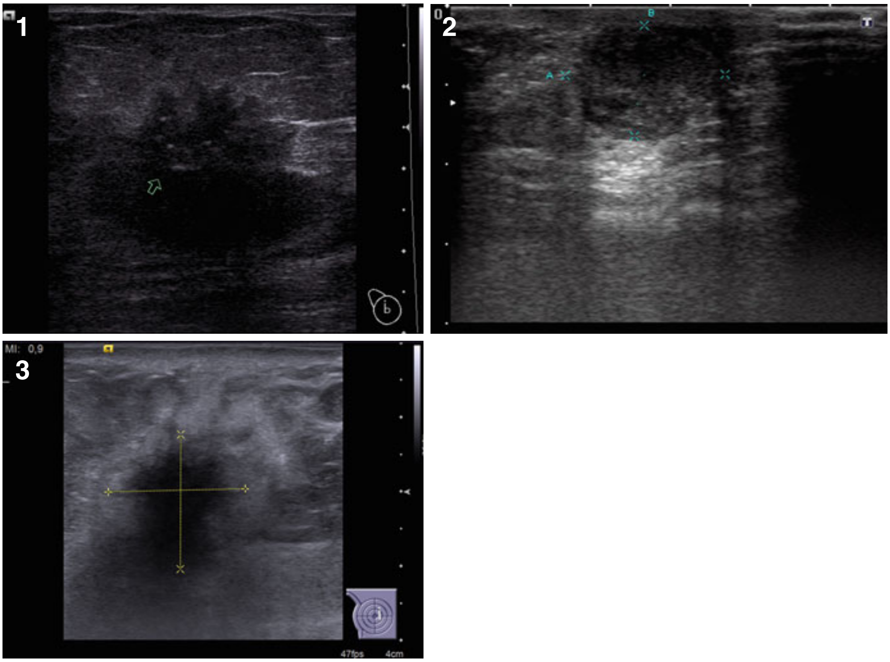


Fig. 4.7 (1–3) Nodular breast carcinoma. Calcifications within the tumor. Grayscale US

the echostructure, rough indistinct contours, and posterior acoustic shadows of various intensities often emerging from the posterior or lateral aspects of the tumor. While analyzing the shape of a lesion in grayscale mode, attention should be paid to the orientation of the long axis of a malignant breast lesion toward the skin with the prevalence of anteroposterior size.

There is no common opinion in the literature regarding microcalcifications in male breast cancer and their value for diagnosis I. Rosen and H. Nadel (1966) described microcalcifications on mammograms of a man with breast carcinoma. The analysis of publications at that time allowed the authors to say that it was the first case of a preoperative radiological diagnosis of microcalcifications in breast cancer in men. L. Kalisher and R. Peyster (1975) considered that the absence of microcalcifications was a typical feature of breast carcinoma in men. Other researchers also observed this sign in men, however, at an extremely rare incidence of 3–5 %. Some authors diagnosed calcifications in 15 % of men with breast cancer, but pointed out their specific feature. Patients had not only multiple microcalcifications in groups but also large coarse calcifications similar to those observed in fibroadenoma in women (Ostrovskaya et al. 1988). In males, as opposed to women, there are no cyclic hormonal processes that define breast status. This may explain the fact that men's breasts in benign conditions do not contain calcifications of vessels, ducts, foci of gynecomastia, or benign tumors. The detection of calcifications of any character on a male mammogram is a bad sign. It is necessary to note that calcifications in men, unlike in women, are always observed in the tumoral mass. Haylenko et al. (2005) reported microcalcifications in 33 % of cases of breast cancer and note that this sign has a high specificity in women. According to Zabolotskaya (2006), microcalcifications are reported in 65 % of intraductal breast carcinomas in women.

Breast carcinoma can be bilateral in 3–15 % of cases. The cancer within the second breast can arise simultaneously with the tumor of the first breast (Rozhkova 1993). Multicentric cancer is observed in 18 % of women, and synchronous affection of the second breast is detected in 43 % of cases. Male breast cancer exhibits similar figures.

In some cases, grayscale US images of breast carcinoma in men can look like gynecomastia without typical malignant features (Dickson 2011; Sencha et al. 2011a, b). Other authors consider that tumoral diseases of the male breast can be hardly differentiated with US from true gynecomastia (Zabolotskaya and Zabolotsky 2010). Any doubt about the benign character of a lesion should be followed by puncture biopsy.

Breast US has some limitations in the detection of lesions against adipose infiltration and in the assessment of ductal extension of the tumor. This is of particular concern for men who have had surgery for gynecomastia. Retromammary tumors and lesions smaller than 1 cm in size may be left undetected. One significant disadvantage of US is a high dependency on the operator.

In our study, the *infiltrative type of breast carcinoma* was observed in 1.6 % of men (2 of 122 men). Infiltrative breast cancer is often characterized with grayscale US by the following features:

- Thickening of the skin
- Increase in echodensity of the subcutaneous adipose layer
- Disorganization of its structure
- Asymmetric dilation of lactiferous ducts and lymph vessels
- Enlargement of regional lymph nodes
- Grainy irregular color pattern with US elastography

The absence of a lesion within the breast often creates difficulties in the differential diagnosis of the infiltrative type of breast carcinoma in men (as well as in women).

4.4 Tissue Harmonic US

Tissue harmonic US is based on an algorithm to detect the harmonic components of US waves induced in tissues with basic US impulses (Fig. 4.8). The option is usually incorporated into ordinary scanners and uses conventional US probes. It permits the detection of US signs of breast carcinoma that are more exact (the quality of imaging subjectively improves in 18.7 % of cases), mainly at the expense of accurate definition of the contours and heterogeneity of the lesion with specification of the presence and location of calcifications. The option is especially effective in the assessment of large (>30 mm) or small (<5 mm) lesions; however, it does not have a high value in the differential diagnosis of breast carcinoma in men.

4.5 Adaptive Coloring

The technology of adaptive coloring uses a color scale in place of the gray scale used in conventional US. The intensity of color depends on the power of the obtained US signal (Fig. 4.9). Inversion of the color of the image is possible. Adaptive coloring is applied as a software option for color US systems and does not require

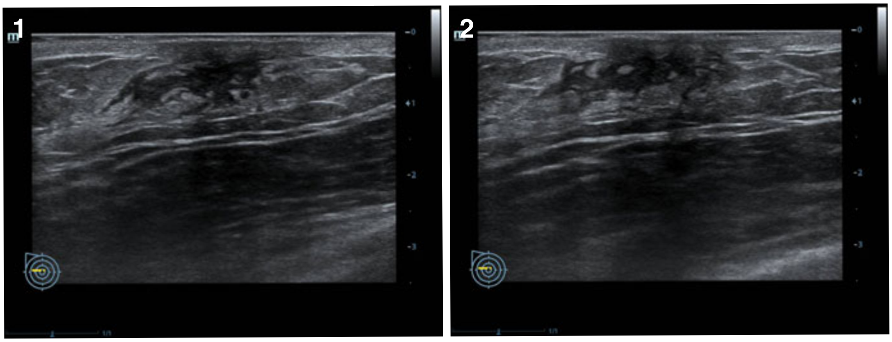


Fig. 4.8 (1, 2) Breast carcinoma. Tissue harmonic imaging

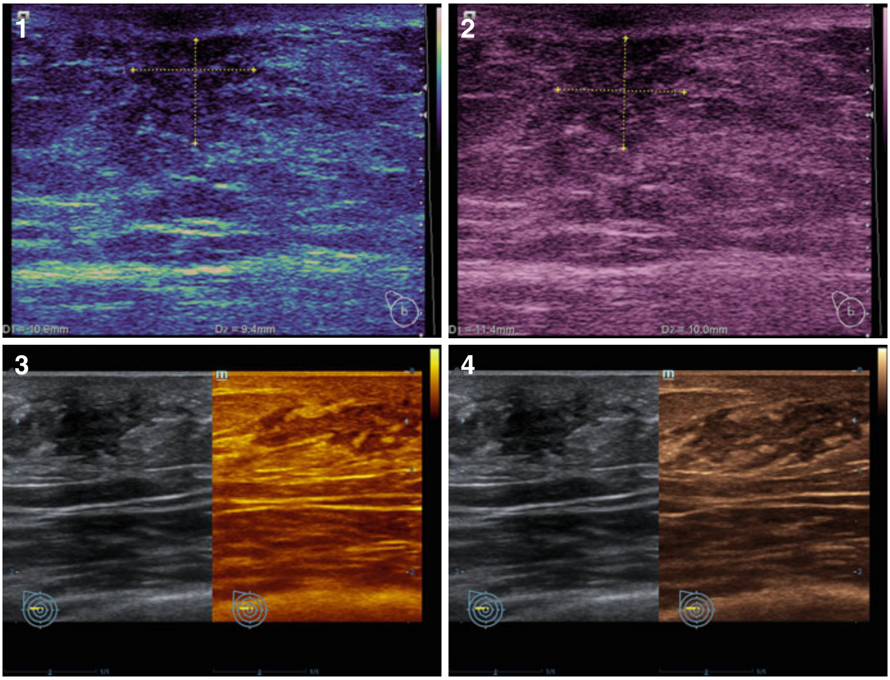


Fig. 4.9 (1–4) Breast cancer. Adaptive coloring

hardware modifications. The option is effective in combination with the grayscale mode for the detection of breast abnormalities (often isoechoic), characterization of its contours, and effects of posterior artifacts, especially in small-sized lesions (<0.5 cm). This technology is seldom used to diagnose breast abnormalities.

4.6 Color and Power Doppler Imaging

Color Doppler imaging (CDI) is an US technology of blood flow imaging based on registration of velocities of blood flow in the area of interest with further coding with different colors and superimposition on a 2D grayscale image. The modality is available on all modern scanners and uses the same probes as conventional grayscale US. Modern US equipment with Doppler imaging permits imaging of blood flow in arteries and veins of calibers greater than 2 mm. The majority of researchers and practitioners agree about the great value of CDI for the diagnosis of malignant breast lesions.

CDI normally detects poor vascular patterns in breast tissue. The color pattern generally is represented by individual color points, which are distributed in a relatively regular way among all quadrants of the breast (Kharchenko et al. 1993a, b; Sandrikov and Fisenko 1998). Several methods to make color and power Doppler imaging more objective were suggested, such as calculation of color pixel density. According to Folkman (1995), one significant feature of breast carcinoma is vascular asymmetry.

Tumor growth is often accompanied with neovascularization and development of an independent pathological vascular rete. Neoangiogenesis of a malignant tumor results in vascular architectonics that differ from benign lesions and physiological breast changes. According to Holcombe et al. (1995), a large number of vessels within a malignant breast lesion suggests a higher stage and possible metastases in axillary lymph nodes.

Our study revealed that the nodular type of breast carcinoma in men is predominantly avascular with CDI (55.7 % cases), with no vessels within the tumor. One vascular pixel was interpreted as a hypovascularization and was reported in 24.6 % of men with breast carcinoma. Two and more color pixels (hypervascularization) were defined in 19.7 % of patients. Vascular pattern and neoangiogenesis in men with breast malignancies was significantly poorer than in women with the same pathology. We consider one and more vascular pixels within the lesion suspicious for cancer (Fig. 4.10).

Madjar et al. (1995) suggested counting all vessels detected within the nodule for quantitative assessment of the vascularity of breast lesions. According to their data, benign lesions demonstrated 2 arteries on the average, whereas malignant lesions demonstrated up to 11 arteries. Sohn et al. (1997) report correlation between vascularization and size of the tumor. Fiedler et al. (1996) consider that CDI is effective only in tumors larger than 1–2 cm in size (blood flow was identified in 90 % of cases, whereas in tumors <1 cm, in only 41.7 %). According to Chao (1999), the average size of avascular breast neoplasms was 1.9 ± 0.1 cm, and vascularized

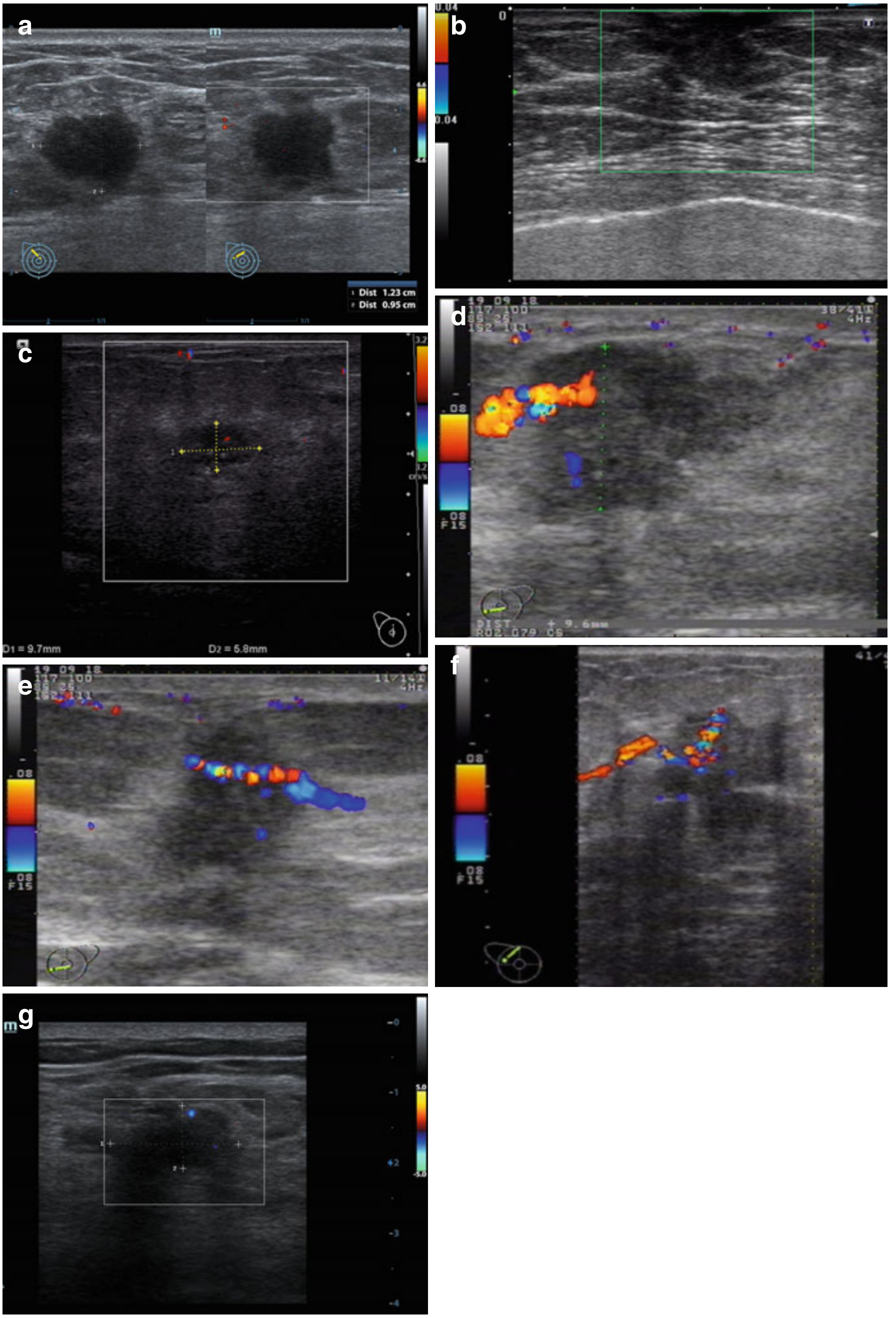


Fig. 4.10 Breast carcinoma. Sonograms. (**a**–**c**) CDI. (**d**) Radial course of the vessel. (**e**–**g**) Penetrating vessels in a tumor

tumors had an average size of 2.7 ± 0.1 cm. Sohn et al. (1997) consider that the mentioned methods of scoring are too labor intensive and are not reliable in practice because of high operator and scanner dependency.

According to Madjar et al. (1995), the vessels in a malignant breast neoplasm can be detected in 43–100 % of instances with 5–14 arteries (8–11 arteries on average) identified within the tumor. Madjar et al. (1995) report that the presence of two and more vessels within a tumor is a typical sign of cancer. According to Ivanova (2006), only infiltrative cancer is vascularized in 100 % of cases. It has specific characteristics with pulsed-wave Doppler, such as the absence of a diastolic component and arteriovenous shunts. Trufanov et al. (2009) report that the majority of malignant breast tumors are well vascularized and exhibit intranodular (72.6 %) or mixed (13.8 %) types of vascular patterns.

Cosgrove et al. (1993) differentiate three types of blood flow within a lesion: perinodular, intranodular, and mixed. Lesions are often divided into hypervascular (with multiple arterial and venous vessels), hypovascular (with two–three color pixels), and avascular (without color pixels) (Kharchenko et al. 1999). Nadareishvili (2002) suggested dividing Doppler signals in lesion structures into four types according to their shape: individual, linear, chaotic, and branching. Depending on the localization, the tumoral blood flow is divided into three groups: central (up to 6.4 %), peripheral (25.9 %), and mixed (67.7 %).

The vessels within malignant breast lesions are often located chaotically with multiple anastomoses and arteriovenous shunts. They often have irregular calibers (narrow and wide parts) and looped or spiral shapes (Madjar et al. 1995). Dilation of vessels within breast carcinomas can result from several factors, such as local increase in the temperature and the influence of an oxide of nitrogen caused by the malignant process. These aspects explain the increase in local vascularity of breast carcinoma with CDI and PDI (Fisenko 1999).

Trofimova (2000a, b) reports that vascularization can be detected in 90.5 % of malignant lesions (in 100 % of tumors >4 cm in size and in 76 % of tumors <2 cm). The vessels in malignant neoplasms were characterized with irregular calibers (narrow and dilated segments), collaterals, and branching. Smirnova (1995) and Trofimova (2000a, b) observed an absence of vascularity in 85–95 % of lesions and consider that blood vessels can be detected only within tumors >2 cm and are associated with expressed cellular proliferation.

According to Shevchenko (1999), the absence of neovascularization in a solid breast lesion, which is highly suspicious for cancer, does not permit exclusion of a malignant nature. Almost 31 % of cancers appear avascular. Alternatively, CDI can detect vessels in healthy breast tissue. Some authors report a "twinkling" artifact with CDI caused by microcalcifications within the cancer structure (Gromov and Kubova 2004; Trufanov et al. 2009).

CDI has some disadvantages, such as aliasing in cases of high velocities, background noise, and dependence on the angle between the US beam and the blood flow.

Power Doppler imaging (PDI) permits obtaining angle-independent images of smaller vessels with contours that are more distinct that increase the diagnostic value of Doppler mapping (Fig. 4.11). PDI quality is characterized by a low dependence on the angle between the blood flow and the US beam and no aliasing effect.

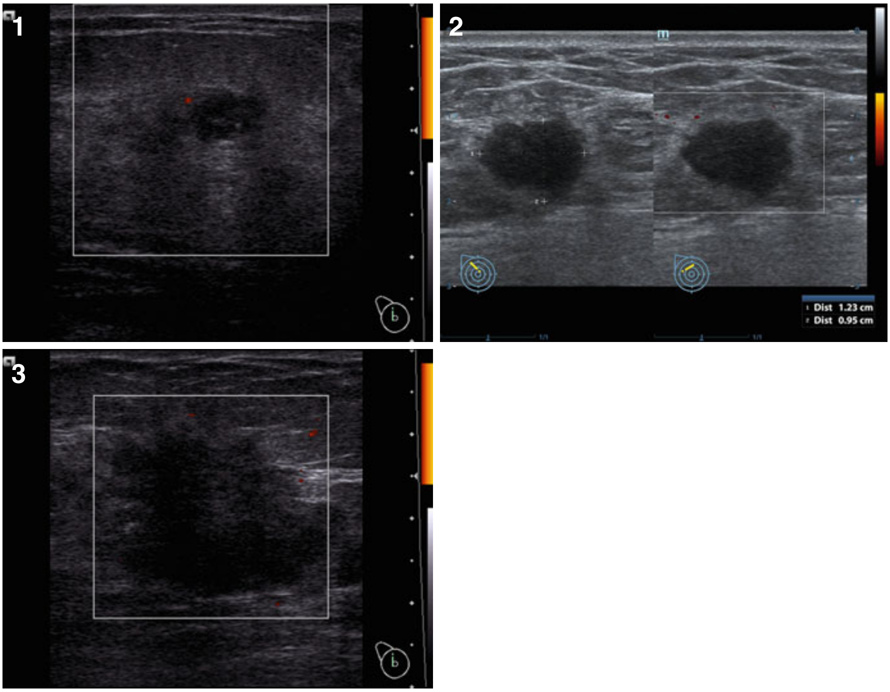


Fig. 4.11 (1–3) Breast carcinoma. PDI

Noise is efficiently reduced because the noise energy is constantly low, and blood flow exhibits a significantly higher energy. Therefore, PDI is three to five times more sensitive than CDI. PDI is capable of defining a larger number of vessels (as compared with CDI) in all breast malignancies, especially in infiltrative carcinoma. The disadvantages of PDI are its high dependence on the motion of the surrounding structures with movement artifacts and coloring of perivascular areas.

The combination of grayscale US with spectral and color Doppler permits additional information to be obtained and increases the sensitivity of US in the diagnosis of cancer from 82–97 % to 93–99 % and the specificity from 59 to 97 % (Possover et al. 1994; Sohn et al. 1997; Sandrikov and Fisenko 1998; Sencha et al. 2011a, b).

4.7 Pulsed Doppler Imaging

Pulsed-wave Doppler mode displays the obtained data as a curve, which permits the analysis of velocities and spectral parameters of blood flow and the calculation of several indexes, such as the peak systolic velocity (PSV), end-diastolic velocity (EDV), resistive index (RI), and pulsatility index (PI) (Fig. 4.12). Pulsed-wave Doppler is used to measure blood flow indexes in large afferent breast arteries, vessels of the breast parenchyma, and vessels within breast lesions. Trofimova (2002) considers that assessment of blood flow only within the breast lesion is sufficient.

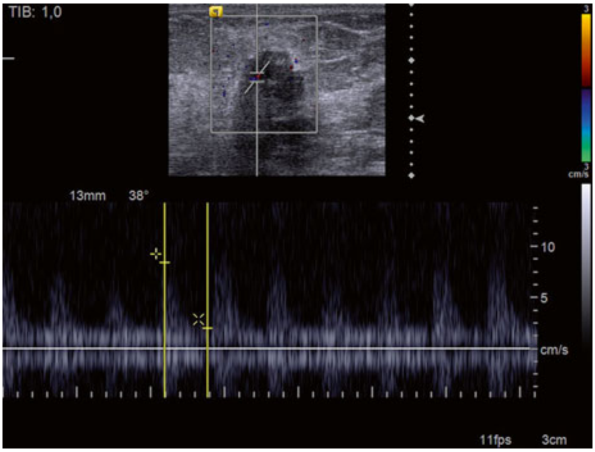


Fig. 4.12 Breast cancer. Pulsed-wave Doppler

Nevertheless, in cases of infiltrative cancer, it appears necessary to compare the vascular pattern with the contralateral area in the other breast. Sohn et al. (1997) report the value of pulsed Doppler data of blood flow in branches of the lateral thoracic artery, the pectoral branch of the thoracoacromial trunk, and the medial mammary branches of the internal thoracic (internal mammary) artery of affected and healthy breast.

Our study revealed no patterns in the pulsed Doppler data that could facilitate differential diagnosis of breast lesions in men. The wide range of figures obtained with pulsed Doppler does not add any diagnostic information; in the majority of cases, pulsed Doppler imaging cannot be used as a reliable differential criterion and can be considered only as an accessory feature. According to Sohn et al. (1997), the methods for quantitative assessments of imaged vessels are labor intensive and unreliable.

Pulsed Doppler imaging can confirm blood flow enhancement within a lesion in comparison with that in healthy parenchyma; in rare cases, vascularization is identical. The intensity of blood flow of the lesion is often related not so much to its morphological structure but to its size (Lelyuk and Lelyuk 2007). According to Svensson (1997), the indexes of blood flow in the vessels of a malignant tumor directly depend on its volume, and enlargement in tumor size results in the increase of spectral characteristics. Haylenko et al. (2005) reported that the indicators of blood flow in malignancies with CDI and PDI also exhibit direct correlations with the lesion volume.

In the opinion of De Albertis et al. (1995), breast carcinoma is characterized by the presence of several (more than two) vascular areas, high PSV, and high PI. The detection of a vessel that courses radially to the center of the tumor or penetrates the tumor is considered characteristic of malignant tumors (Trofimova 2000a, b; Fisenko 1999).

Many researchers analyzed different parameters of vascularization and suggest the following Doppler criteria of malignancy: high PSV of intranodular blood flow (Teh and Wilson 1998), high RI (Sohn et al. 1997), and high PI (Zabolotskaya 2006).

According to Kharchenko et al. (1993a, b), PSV in the vessels of healthy breast tissue is 0.06 ± 0.02 m/s, whereas the average PSV within cancer is 0.3 m/s. Pulsed Doppler imaging in breast carcinoma is thought to exhibit the following characteristics: PSV, 0.05–0.47 m/s; EDV, 0.07–0.09 m/s; RI, 0.67–0.81; and PI, 1.47–1.76 (Trofimova 2000a, b; Fisenko and Sandrikov 1998; Madjar et al. 1995; Youssefzadeh et al. 1996). According to Lee et al. (1995), PSV in 67 % of breast carcinomas exceeds 0.15 m/s. According to Shevchenko (1999), the velocities of arterial blood flow in malignant tumors are as follows: PSV, 4.6–56.6 cm/s (average value, 18.98 cm/s); EDV, 0.3–9.8 cm/s (average value, 2.99 cm/s); and RI, 0.56–1.34 (average value, 0.82). Higher blood velocities and RI are reported when the number of vessels in a tumor is larger. Trofimova (2000b) reported the following blood flow parameters within breast carcinoma: PSV, 0.27 (0.06–0.91) m/s; EDV, 0.07 (0.01–0.33) m/s; RI, 0.76 (0.31–1.42); and PI, 1.71 (0.46–8.09). She noted that blood flow parameters in the vessels around the tumor are close to the data obtained in the areas of mastopathy. Lee et al. (1995) did not observe any differences between the vascular pattern around benign breast tumors and healthy tissue of the contralateral breast. According to Trufanov et al. (2009), the increase in RI, PSV, and EDV is characteristic for malignant breast lesions. The authors also noted that the same parameters are often observed in men with only diffuse breast changes. Authors also report asymmetric blood flow in thoracic arteries.

Sandrikov and Fisenko (1998) report that vessels within the tumor exhibit a pathological spectrum of blood flow characterized by an absence of a late diastolic component and an appearance of retrograde flow in 20–25 % of cases. This may be the consequence of microthrombosis and shunts in neoangiogenesis. Spectral characteristics of blood flow in the vessels of infiltrative breast carcinoma are very variable, starting from an almost normal curve with pulsed Doppler imaging and ending with shunts and low-resistive pathological vessels, irregular dilations, disorganization of vascular pattern, and different calibers of detected vessels (Zabolotskaya and Zabolotsky 2010).

The majority of authors note the following criteria for the differential diagnosis of breast carcinoma: arteriovenous shunts, change in PSV and EDV, absence of an end-diastolic component, increased RI, detection of more than three vessels, and irregular courses and calibers of vessels within the lesion (Yang et al. 1996; Trofimova 2000a, b). The sensitivity of Doppler imaging in the diagnosis of breast carcinoma is 81–99 %, the specificity is 71–98 %, and the diagnostic accuracy is 82–93 % (Fisenko and Sandrikov 1998; Trofimova 2000b).

4.8 3D Imaging

Computer processing of US images permits three-dimensional (3D) reconstruction of breast structure and its lesions to facilitate assessment of borders and topographic interrelation with the surrounding tissues (Figs. 4.13 and 4.14). The technology can be performed with special volume (3D) probes or by means of application of conventional linear US probes with subsequent computer processing of the obtained data. 3D imaging allows sectioning of the lesion in any plane (frontal, axial, and sagittal) at all depths. It opens up certain prospects in terms of postprocessing of the obtained US volume and its archiving for delayed analysis.

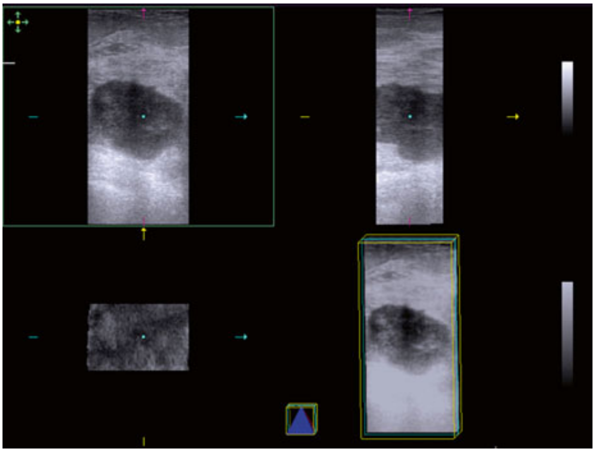


Fig. 4.13 Breast carcinoma. 3D US

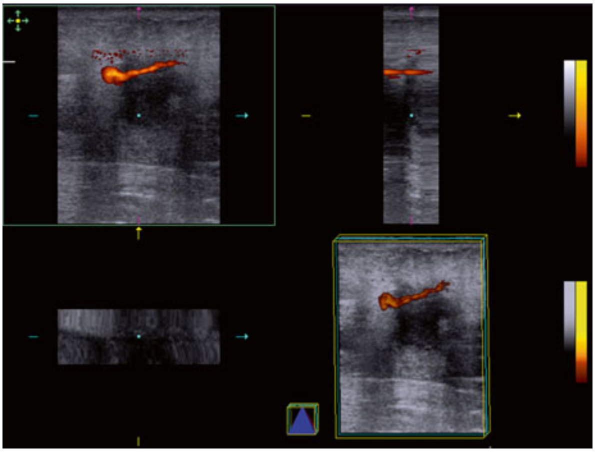


Fig. 4.14 Breast carcinoma. 3DPD

3D image reconstruction of US breast structure is advantageous over other imaging methods that supply only plane (2D) images. 3D US of breast carcinoma permits assessment of the number and structure of lesions within the breast and also allows specification of lesion location in relation to the capsule, detailed information regarding the signs of invasion (such as indistinct tuberous margins, discontinuous capsule, and spreading of the tumor out of the breast to adjacent organs), identification of calcifications and multinodosity, and calculation of the volume of affected and intact breast tissue. 3D imaging often allows the objective analysis of lesion dynamics, such as the change in shape and inner structure, especially against fibrous changes in recurrent tumors. The possibility of rotation and obtaining multislice images facilitates the subjective perception of abnormalities. Sometimes, it enables a reduction in diagnostic terms and improvement in the early diagnosis of breast malignancies.

3D reconstruction of US images using a vascular regimen (3D power Doppler imaging (3DPD)) permits a more precise assessment of the pathological transformation of vessels within a malignant lesion, their density, and their disorganized course. The symmetry and regularity of the vascular pattern and the presence of dilated and narrowed segments are often assessed. The character of perinodular and intranodular vascularization and the disorganized vascular pattern (Fig. 4.14) are accurately defined. Volume reconstruction is valuable not only for the confirmation of the degree of vascularity but also for guidance of puncture biopsy. 3D scanning allows the generation of a model of the lesion or the area of gynecomastia and facilitates the procedure (Ivanov et al. 2013).

The real-time 3D mode (4D) uses special US probes and high-quality scanners. Constantly repeating 3D scanning and displaying the object of examination is performed in real time. This significantly reduces examination time. The fast acquisition of volume data allows a precise definition of the breast structure and spatial features of its vascularity with less noise and artifacts, especially in cases of breast lesions. This enables the performance of detailed and more confident differential diagnoses of mixed or incomplete types of vascular patterns within breast lesions. Numerous methods of optimization of US images in gray scale, Doppler mapping, 3D reconstruction, and the technology of enhanced filtration depending on regions of interest significantly improve the contrast of US images and reduce artifacts and noise. A wide choice of postprocessing options significantly reduces the time of the examination and improves its quality.

4.9 Ultrasound Elastography

J. Ophir et al. were the first to introduce elastography for diagnostics in the early 1990s. The technology has constantly improved. Attempts were made to use elastography in the early diagnosis of mammary cancer (Garra et al. 1997; Zubarev 2009), prostate cancer, ovarian carcinoma, uterine cancer (Mitkov et al. 2011), inflammatory changes, liver metastases, thyroid gland (Sencha et al. 2009, 2010a, b), metastatic neck lymph nodes, parathyroid cancer, tumors of the salivary glands, etc.

Depending on the technique of elastography, the following varieties are specified (Zubarev 2009):

1. Elastography with manual compression of tissues. The sonographer pushes the US probe to achieve a tissue shift or deformation.
2. Elastography based on the pulsation of large vessels.
3. Sonoelastography based on outer vibration (vibroelastography).
4. Elastometry, where the velocity of shear-wave propagation through the tissue is analyzed to calculate the elastic modulus, strain ratio.

4.9.1 Compression Elastography

Compression elastography (US elastography) is a unique modality that permits visualization of organs and tissues based on elasticity features (elasticity and stiffness). It is available in modern US equipment. It analyzes tissue stiffness on the basis of the deformation that takes place when the structures are exposed to external dosed compression and permits visualization of the obtained data.

The mechanical properties of biological tissues depend on macromolecular components (parenchyma, fat, collagen, etc.). Tissue elasticity is characterized by tissue shift or distortion in response to external compression. Differences in the elasticity of different tissues after compression result in changes in the reflection of US. Elastography is based on an expanded combined autocorrelative method that processes traditional echographic images of distortable tissues. Special mathematically based algorithms are used to correct possible lateral shifts of a lesion out of the two-dimensional scanning range. Some scanners incorporate a feature of obtaining data regarding tissue elasticity based on mechanical wave distribution from pulsing large vessels, the heart, or the chest. No additional external compression with an US probe or very limited compression is required in such cases (Dighe et al. 2008).

The mode of elastography depends on a scanner and can be conducted in real time or by means of data postprocessing. The breast tissue is exposed to external compression with an US probe (Fig. 4.15). The US probe is positioned perpendicularly to the skin over the lesion. Compression time varies from 2 to 5 s. Periodic compression is performed to obtain several images with minor artifacts. The analyzed area should contain some healthy breast tissue for accurate comparison with the stiffness of the lesion. The time needed for the examination is usually 1–5 min.

Tissues under the US probe are deformed with compression (strain). Abnormal tissues exhibit unique features. Malignant tumors are "hard" as compared with the surrounding healthy tissues (Fig. 4.16). The elastogram is an image that results from overlaying the "compressive" image onto the grayscale image. Tissue elasticity image is coded with shades of gray or color palettes. Hard structures are usually colored with dark gray or blue. Soft areas are usually marked with light gray or red. Intermediate colors are applied, respectively. Scanners usually offer several color maps, such as "blue–green–red," shades of gray, or customized maps with shades of red or other colors (Fig. 4.17).

Lesions are usually classified with elastography into groups according to the following features (Sencha et al. 2009):

1. Presence or absence of color pattern within the lesion and its intensity
2. Character of staining (hard, mixed, other)
3. Regularity of staining (homogeneous, heterogeneous)
4. Dimensions of the stained area in comparison with the dimensions of the same lesion in grayscale US
5. Degree of differentiation of the staining with the surrounding tissues

Uniform compression of the whole breast is impossible because of the comparatively small size of US probes. Healthy breast parenchyma with moderate compression exhibits a relatively regular, homogeneous, and symmetric fine-grained pattern. Compression of individual breast segments or lesions is performed more effectively.

Ei Ueno (1996) suggests a classification for differentiating benign and malignant lesions based on color pattern with elastography (Table 4.3). Zubarev (2009) reports five types of stiffness of lesions depending on color pattern with US elastography.

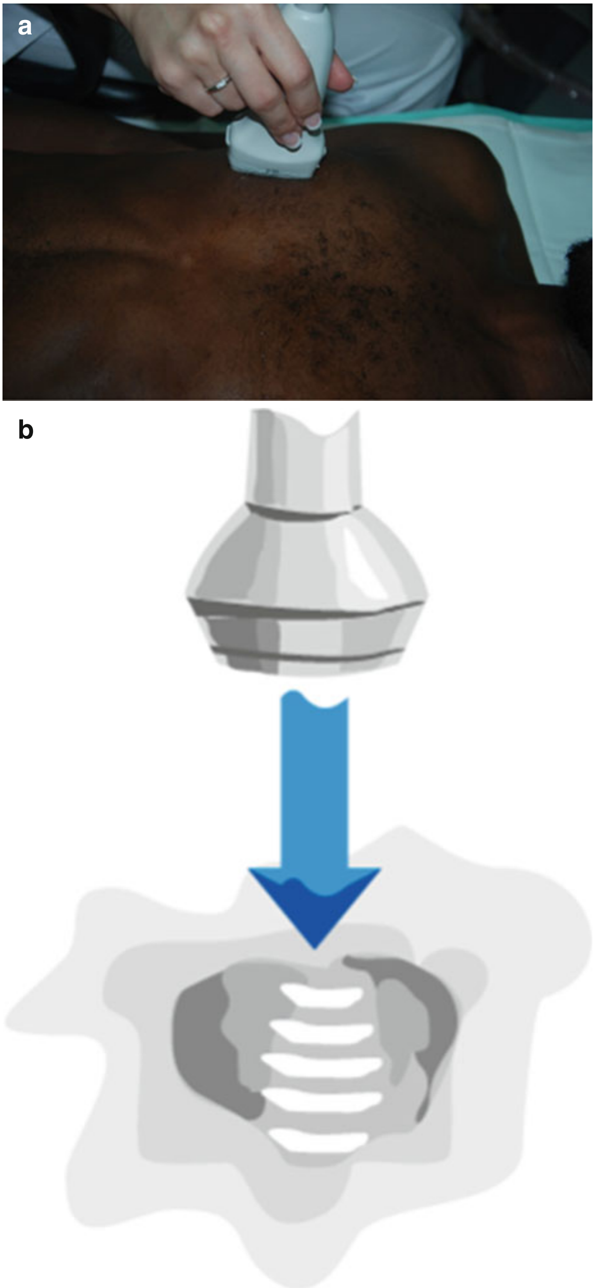


Fig. 4.15 Compression of the area of interest with an US probe. (**a**) Image. (**b**) Graphic

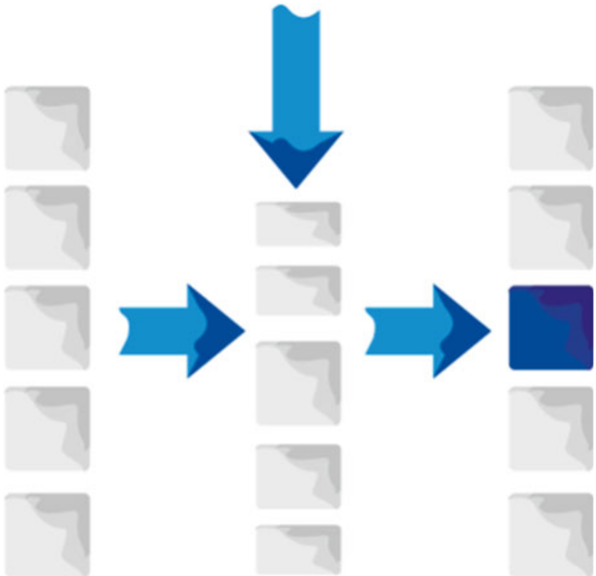


Fig. 4.16 Scheme of elastography imaging

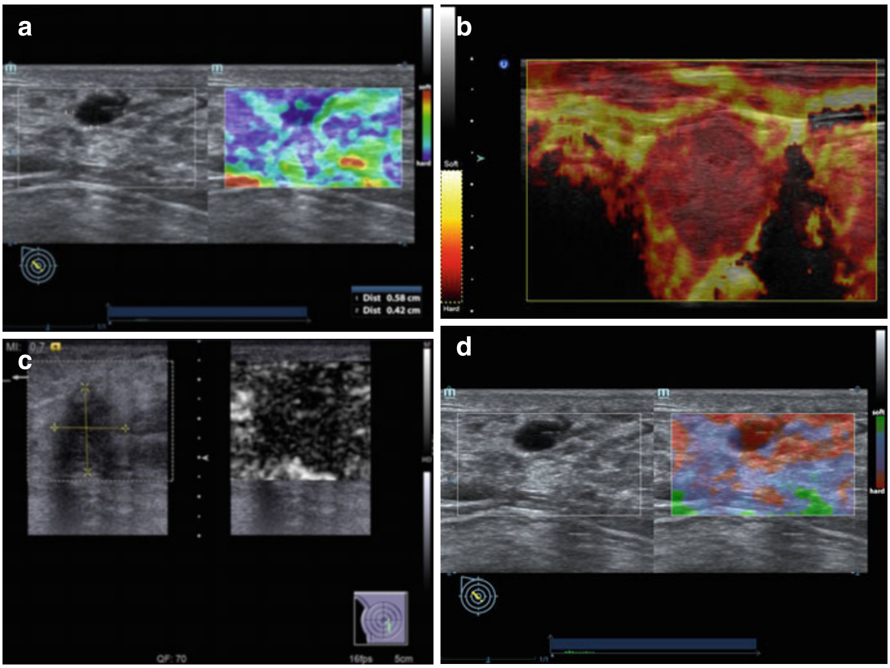
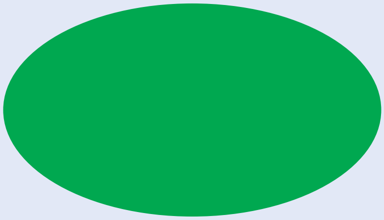
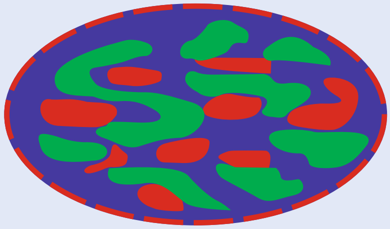
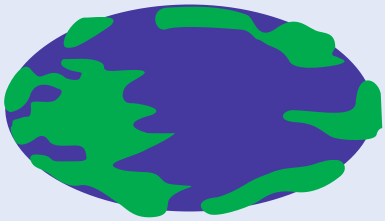
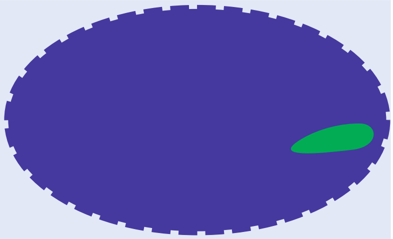
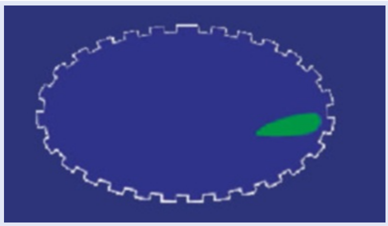


Fig. 4.17 US elastography. Coloration examples. (**a**) Blue–green–red scale. (**b**) Yellow–red scale. (**c**) Shades of gray. (**d**) Others

Table 4.3 Classification after Ueno (1996)

Benign		
Score 1	Entire area is evenly shaded green, as is the surrounding tissue	
Score 2	Lesion area shows a mosaic pattern of green, blue, and red	
Intermediate		
Score 3	Central part of the area is blue (stiff), and peripheral part is green (soft)	
Malignant		
Score 4	Entire area is blue (stiff)	
Score 5	Entire area and its surrounding area are blue (stiff)	

Dark blue (stiff) staining that corresponds to the fifth type of color pattern is characteristic of breast carcinoma. The data obtained with sonoelastography facilitate the differential diagnosis of breast lesions of a tumoral nature in complex and doubtful cases.

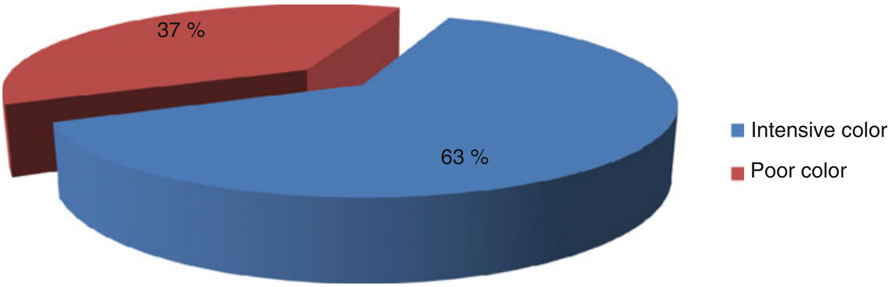


Fig. 4.18 Intensity of staining of malignant breast lesions with US elastography

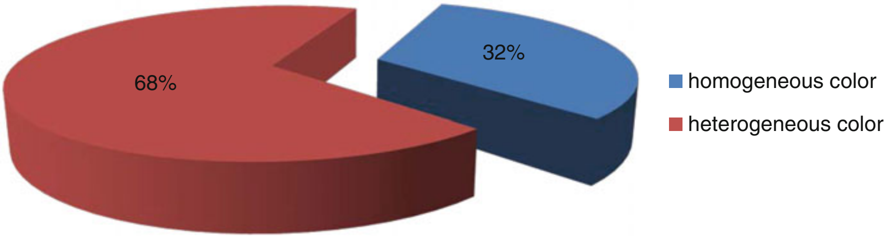


Fig. 4.19 Homogeneity of staining of malignant breast lesions with US elastography

US elastography based on color pattern is quite subjective and operator dependent. Park et al. (2009) reported a very high interobserver variability for free-hand compression sonoelastography. To achieve better reproducibility of compression sonoelastography, the manufacturers of US scanners introduced quality factors that reflect the quality of the obtained data in real time and the possibility of its interpretation. The higher the quality factor, the more reliable the obtained data are for assessment. Some data that lie below 60 % cannot be interpreted at all because of major artifacts. This approach allows both the introduction of quality standards for interpreting elastograms and also skill development for effective work with sonoelastography for US specialists.

Figures 4.18 and 4.19 illustrate color patterns, intensity, and homogeneity of breast neoplasms with elastography that were obtained in our research. Breast carcinoma more often (in 76.1 %) exhibits intense, well-circumscribed hard (stiff) staining. Irregular color distribution within the lesion was reported in 81.8 % of breast cancers. The efficacy of elastography in male breast malignancy is demonstrated in Table 4.4, which demonstrates that the combined use of elastography and B-mode scanning significantly increases the accuracy of the diagnosis of breast cancer. US elastography in 15.9 % of cases of breast carcinoma supplied additional diagnostic information to other US modalities. The increase in diagnostic value was a consequence of the following factors:

- Specification of the size of the lesion (due to precise differentiation of invasion margins and the expression of perifocal induration). Differences in size of 0.5–10 mm between grayscale and elastographic images of the lesion were

Table 4.4 Diagnostic value of US elastography in the diagnosis of breast carcinoma

Breast carcinoma	Positive cancer with histology	Negative cancer with histology
US +	1,093	57
US –	174	5,376
Sensitivity 86 %		
Specificity 99 %		
Prognostic value of positive result 95 %		
Prognostic value of negative result 97 %		

Breast carcinoma	Positive cancer with histology	Negative cancer with histology
US and elastography +	88	3
US and elastography –	4	1,134
Sensitivity 96 %		
Specificity 99 %		
Prognostic value of positive result 97 %		
Prognostic value of negative result 99 %		

observed in 22.7 % of cases. The difference of the dimensions of coloration is explained by merging of malignant tumors into the surrounding tissues. This permits differentiation from benign lesions, the latter usually having a capsule. The region of malignant invasion exhibits abnormal strain characteristics as compared with intact tissue that is observed on the monitor of the US scanner and corresponds to Score 5 in the Ueno classification. The dimensions of malignant lesions with sonoelastography can be 60 % larger than the corresponding dimensions in B-mode scanning.

- Analysis of the uniformity of the inner structure of the lesion (variation of elasticity).
- Specification of the interrelation of the lesion with the surrounding tissues (specification of invasion).
- Determination of the mass origin.

According to our data, elastography fails to differentiate breast lesions in 11.4 % of patients. This is a consequence of an absence of color pattern within the lesion, no difference between the color patterns of the tumor and surrounding structures. The sensitivity and specificity of elastography are limited by a number of factors (Sencha et al. 2010a, b):

1. Objective
   - No general consensus regarding the elastographic appearance of healthy breast and different types of focal and diffuse pathology
   - Elastographic options in different manufacturers of US equipment not standardized
2. Subjective
   - Imperfect technique (absence of standardization of the compression force, some disputable principles of data estimation)

- High operator dependency and intraobserver and interobserver variability
- Certain limits of compression of the breast (discomfort), especially in patients with anatomical, constitutional, psychological, emotional, or physiological constraints
- Noise and artifacts

US elastography is capable of assessing only focal changes, which could be identified with standard US. It is not suitable for screening, for diffuse changes, or for dense structures of the organ. The development of traditional modalities and the appearance of new technologies are a continuous process that aims to improve the accuracy and efficacy of diagnostics.

4.9.2 Shear-Wave Elastography

Quantitative assessment of elasticity is much more objective. Thus, numerical representation is preferable to precisely interpret tissue elasticity. A "strain ratio," which is calculated as a ratio of the strain index of the lesion to the strain index of healthy tissue (Ning et al. 2012) (Fig.4.20), an elasticity modulus, and others have been proposed. A lesion-to-muscle strain ratio is used in some publications (Kagoya et al. 2010). The authors consider an index exceeding 1.5 to be a criterion of malignancy, with a sensitivity of 90 % and a specificity of 50 %. We failed to find publications devoted to elastometry with elasticity indexes or shear-wave velocities in the differential diagnosis of breast pathology in men. According to our data, the average strain ratio for a breast malignancy in men was 2.8 ± 0.013 relative to healthy surrounding tissue.

Recently, a technology based on the measurement of shear-wave velocity was introduced to evaluate tissue stiffness. One example of the technology of shear-wave elastography is acoustic radiation force impulse (ARFI), which forms the basis of virtual touch tissue quantification® (VTQ) technology. The method uses a

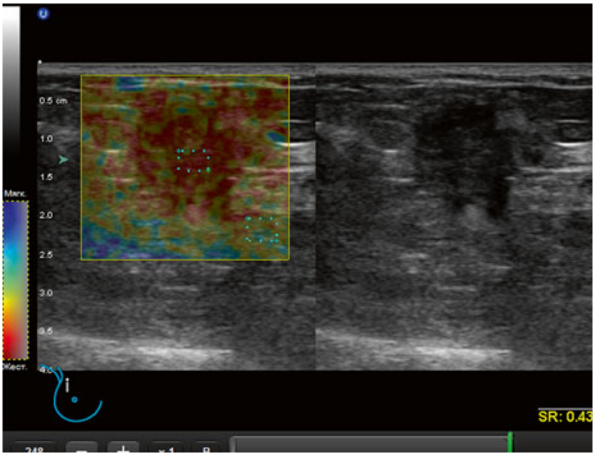


Fig. 4.20 Strain ratio in breast cancer

focused US beam to induce an acoustic shear wave and works in real time. It uses an acoustic impulse of high power to induce the deformation of a lesion within the region of interest. This results in the generation of shear waves. The velocity of these waves depends on tissue stiffness. The velocity can be measured and correlated with the stiffness of structures in the area of interrogation. Tissue elasticity is in an inverse relationship with the velocity of the shear wave generated with the high-power acoustic impulse. The measurement of this velocity, which is done automatically and displayed in meters per second, enables an objective opinion regarding the rigidity of examined structures (e.g., breast lesions) (Zubarev 2009). According to our data, the average shear-wave velocity with ARFI (VTQ) within breast malignancies in men was 4.2 ± 0.032 m/s.

This technique is completely quantitative and does not depend on the sonographer. Harder tissue (which is more characteristic for malignant tumors) generates higher shear-wave velocities (Piscaglia et al. 2011). The calculated shear-wave velocity is the indicator and is a constant feature of the tissue stiffness. Manufacturers of US equipment report the values in kilopascals or meters per second. In any case, the higher the value, the stiffer the tissue in the zone of interest is. This technology aims not only to create objective data but also to evaluate the stiffness of deeply located masses, which are inaccessible for compressive elastography. According to Zubarev (2009), intraductal breast carcinoma in situ is characterized by a strain ratio of 5.2; infiltrative lobular cancer, 16.58; fibroadenoma, 1.02 ± 0.21; and benign intraductal papilloma, 1.37. He reported that the sensitivity of this method in the diagnosis of breast lesions in women is 78.9 %, the specificity is 95.2 %, and the diagnostic accuracy is 90.1 %.

Elastography is an innovative technique of US examination for the early diagnosis and follow-up in patients with breast diseases. It is expected to be of great practical use (Sencha et al. 2010a, b). Many studies have demonstrated that elastography is a powerful tool for excluding breast malignancies. Further multicenter studies can significantly improve its accuracy.

4.10 Other Ultrasound Technologies

Panoramic scan enables reconstruction of extended images that include several adjacent fields of view and are larger than a conventional scan. This facilitates precise measurements of long objects. The method of presentation of the obtained data in panoramic scan often helps to characterize pathological foci in cases of multicenter growth, to assess invasion, and to plan the surgery.

The sensitivity of CDI and PDI for the assessment of vascularity of breast lesions may be significantly increased by intravenous administration of *US contrast* agents similar to contrast enhancement in CT and MRI. Contrast agents significantly improve imaging of abnormal vessels. The number of detected vessels increases up to 36–95 % (Moon et al. 2000).

Multislice view (US tomography) is a software algorithm that transforms 3D US images in a series of consecutive thin sections in any plane, similar to CT. It permits a more objective and reliable method of analysis of the breast image and is associated with better accuracy.

The diagnostic accuracy of US in breast carcinoma in men and women ranges from 78 to 94 %. Its sensitivity is 58–100 % and its specificity is 65–97 % (Gracey et al. 2009; Sencha et al. 2013a, b). The diagnostic accuracy increases as the size of the lesion increases. The diagnostic accuracy is 87.3 % in tumors smaller than 10 mm; 87.2 % in tumors of 1–2 cm; 88.0 % in tumors of 2–5 cm, and 100 % in tumors larger than 5 cm.

High qualification and cooperation of doctors of different specialties, following the principles of continuity of diagnostic process, and the use of all available technologies enable rational planning of diagnostic and medical tactics with improvements in the diagnosis of breast tumors and significant increases in the efficacy of their treatment.

Example US report in a man with breast cancer:

Date:
Name: C.
Age: 67

Breasts are of male type and consist of adipose tissue. Fibrous tissue is moderately developed in all regions. Lactiferous ducts are not detected.	
Right breast	**Left breast**
A heterogeneous hypoechoic lesion of 1.7 × 1.9 × 1.2 cm in size of irregular star shape with indistinct, rough boundaries is located in the lower–outer quadrant (8 o'clock position) of the right breast. The lesion is hypervascular with CDI and PDI. It is moderately painful with limited mobility. It demonstrates intense irregular hard (blue) staining with sonoelastography. The average shear-wave velocity is 3.9 m/s. The strain ratio is 2.9 as compared with healthy areas	No lesions detected

Enlarged axillary lymph nodes are detected on the right side up to 1.0–2.3 cm in size and are hypoechoic with irregular structure and disorganized blood flow pattern. Other regional lymph nodes are not enlarged.

CONCLUSION*:* Right breast lesion suspicious for carcinoma. Sonographic signs of metastasis in the right axillary lymph nodes. Biopsy of the lesion and right axillary lymph nodes is recommended.

5 Classification of Breast Masses

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The classification of breast tumors and differentiation of stages in men, as well as in women, is necessary for defining tactics, methods of treatment, duration of therapy, volume of surgery, follow-up strategy, and prognosis. Male breast cancer is not separately classified as an independent nosology. Existing classifications accepted for breast carcinoma in women are most often used. Some classifications of breast cancer are based on clinical and etiological features, imaging methods, and pathology to characterize the primary breast tumor, its spreading, and local and remote metastases. Some examples of clinical classifications that have been used in different countries are those proposed by Holdin in Russia and the countries of former USSR, by Holsted and Manchester in Great Britain, by Colombian in the United States, and by Steinthal in European countries. The international clinical classification based on the TNM system is now the most appropriate for breast cancer staging.

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_5

5.1 World Health Organization (WHO) Histological Classification of Tumors of the Breast
(Tavassoéli and Devilee 2003)

Epithelial Tumors

- Invasive ductal carcinoma, not otherwise specified (NOS) – 8500/3
  - Mixed-type carcinoma
  - Pleomorphic carcinoma – 8022/3
  - Carcinoma with osteoclastic giant cells – 8035/3
  - Carcinoma with choriocarcinomatous features
  - Carcinoma with melanotic features
- Invasive lobular carcinoma – 8520/3
- Tubular carcinoma – 8211/3
- Invasive cribriform carcinoma – 8201/3
- Medullary carcinoma – 8510/3
- Mucinous carcinoma and other tumors with abundant mucin
  - Mucinous carcinoma – 8480/3
  - Cystadenocarcinoma and columnar cell mucinous carcinoma – 8480/3
  - Signet ring cell carcinoma – 8490/3
- Neuroendocrine tumors
  - Solid neuroendocrine carcinoma
  - Atypical carcinoid tumor – 8249/3
  - Small cell/oat cell carcinoma – 8041/3
  - Large cell neuroendocrine carcinoma – 8013/3
- Invasive papillary carcinoma – 8503/3
- Invasive micropapillary carcinoma – 8507/3
- Apocrine carcinoma – 8401/3
- Metaplastic carcinomas – 8575/3
  - Pure epithelial metaplastic carcinomas – 8575/3
  - Squamous cell carcinoma – 8070/3
  - Adenocarcinoma with spindle cell metaplasia – 8572/3
  - Adenosquamous carcinoma – 8560/3
  - Mucoepidermoid carcinoma – 8430/3
  - Mixed epithelial/mesenchymal metaplastic carcinomas – 8575/3
- Lipid-rich carcinoma – 8314/3
- Secretory carcinoma – 8502/3
- Oncocytic carcinoma – 8290/3
- Adenoid cystic carcinoma – 8200/3
- Acinic cell carcinoma – 8550/3
- Glycogen-rich clear cell carcinoma – 8315/3
- Sebaceous carcinoma – 8410/3
- Inflammatory carcinoma – 8530/3
- Lobular neoplasia
  - Lobular carcinoma in situ – 8520/2
- Intraductal proliferative lesions
  - Usual ductal hyperplasia
  - Flat epithelial atypia

  - Atypical ductal hyperplasia
  - Ductal carcinoma in situ – 8500/2
- Microinvasive carcinoma
- Intraductal papillary neoplasms
  - Central papilloma – 8503/0
  - Peripheral papilloma – 8503/0
  - Atypical papilloma
  - Intraductal papillary carcinoma – 8503/2
  - Intracystic papillary carcinoma – 8504/2
- Benign epithelial proliferations
  - Adenosis including variants: sclerosing adenosis, apocrine adenosis, blunt duct adenosis, microglandular adenosis, adenomyoepithelial adenosis
  - Radial scar/complex sclerosing lesion
  - Adenomas
    Tubular adenoma – 8211/0
    Lactating adenoma – 8204/0
    Apocrine adenoma – 8401/0
    Pleomorphic adenoma – 8940/0
    Ductal adenoma – 8503/0

Myoepithelial Lesions

- Myoepitheliosis
- Adenomyoepithelial adenosis
- Adenomyoepithelioma – 8983/0
- Malignant myoepithelioma – 8982/3

Mesenchymal Tumors

- Hemangioma – 9120/0
- Angiomatosis
- Hemangiopericytoma – 9150/1
- Pseudoangiomatous stromal hyperplasia
- Myofibroblastoma – 8825/0
- Fibromatosis (aggressive) – 8821/1
- Inflammatory myofibroblastic tumor – 8825/1
- Lipoma – 8850/0
  - Angiolipoma – 8861/0
- Granular cell tumor – 9580/0
- Neurofibroma – 9540/0
- Schwannoma – 9560/0
- Angiosarcoma – 9120/3
- Liposarcoma – 8850/3
- Rhabdomyosarcoma – 8900/3
- Osteosarcoma – 9180/3
- Leiomyoma – 8890/0
- Leiomyosarcoma – 8890/3

Fibroepithelial Tumors

- Fibroadenoma – 9010/0
- Phyllodes tumor – 9020/1
  - Benign – 9020/0
  - Borderline – 9020/1
  - Malignant – 9020/3
- Periductal stromal sarcoma, low grade – 9020/3
- Mammary hamartoma

Tumors of the Nipple

- Nipple adenoma – 8506/0
- Syringomatous adenoma – 8407/0
- Paget disease of the nipple – 8540/3

Malignant Lymphoma

- Diffuse large B-cell lymphoma – 9680/3
- Burkitt lymphoma – 9687/3
- Extranodal marginal-zone B-cell lymphoma of MALT type – 9699/3
- Follicular lymphoma – 9690/3

Metastatic Tumors – Tumors of the Male Breast

- Gynecomastia
- Carcinoma
  - Invasive – 8500/3
  - In situ – 8500/2

5.2 Anatomical Subsites of Malignant Neoplasms of the Breast according to International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10, 2010) C50

Including: connective tissue of the breast
Excluding: skin of the breast (C43.5, C44.5)

C50.0 – Nipple and areola
C50.1 – Central portion of the breast
C50.2 – Upper–inner quadrant of the breast
C50.3 – Lower–inner quadrant of the breast
C50.4 – Upper–outer quadrant of the breast
C50.5 – Lower–outer quadrant of the breast
C50.6 – Axillary tail of the breast
C50.8 – Overlapping lesion of the breast
C50.9 – Breast, unspecified

5.3 TNM 7 Clinical Classification (2010)

T – Primary Tumor

- TX – Primary tumor can0not be assessed
- T0 – No evidence of primary tumor
- Tis – Carcinoma in situ
  - Tis (DCIS) – Ductal carcinoma in situ
  - Tis (LCIS) – Lobular carcinoma in situ
  - Tis (Paget) – Paget disease of the nipple with no tumor
  - Note: Paget disease associated with a tumor is classified according to the size of the tumor.
- T1 – Tumor 2 cm or less in greatest dimension
  - T1mic – Microinvasion 0.1 cm or less in greatest dimension
  - Note: Microinvasion is the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1 cm in greatest dimension. When there are multiple foci of microinvasion, the size of only the largest focus is used to classify the microinvasion. (Do not use the sum of all individual foci.) The presence of multiple foci of microinvasion should be noted, as it is with multiple larger invasive carcinomas.
  - T1a – More than 0.1 cm but not more than 0.5 cm in greatest dimension
  - T1b – More than 0.5 cm but not more than 1 cm in greatest dimension
  - T1c – More than 1 cm but not more than 2 cm in greatest dimension
- T2 – Tumor more than 2 cm but not more than 5 cm in greatest dimension
- T3 – Tumor more than 5 cm in greatest dimension
- T4 – Tumor of any size with direct extension to the chest wall or skin only as described in T4a to T4d

  Note: The chest wall includes ribs, intercostal muscles, and the serratus anterior muscle but not the pectoral muscle.
  - T4a – Extension to the chest wall
  - T4b – Edema (including *peau d'orange*), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
  - T4c – Both 4a and 4b, above
- T4d – Inflammatory carcinoma

  Note: Inflammatory carcinoma of the breast is characterized by diffuse, brawny induration of the skin with an erysipeloid edge, usually with no underlying mass. If the skin biopsy is negative and there is no localized measurable primary cancer, the T category is pTX when pathologically staging a clinical inflammatory carcinoma (T4d). Dimpling of the skin, nipple retraction, or other skin changes, except those in T4b and T4d, may occur in T1, T2, or T3 without affecting the classification.

N – Regional Lymph Nodes

- NX – Regional lymph nodes cannot be assessed (e.g., previously removed)
- N0 – No regional lymph node metastasis
- N1 – Metastasis in movable ipsilateral axillary lymph node(s)

- N2 – Metastasis in fixed ipsilateral axillary lymph node(s) or in clinically apparent* ipsilateral internal mammary lymph node(s) in the absence of clinically evident axillary lymph node metastasis
  - N2a – Metastasis in axillary lymph node(s) fixed to one another or to other structures
  - N2b – Metastasis only in clinically apparent* internal mammary lymph node(s) and in the absence of clinically evident axillary lymph node metastasis
- N3 – Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement; or in clinically apparent* ipsilateral internal mammary lymph node(s) in the presence of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
  - N3a – Metastasis in infraclavicular lymph node(s)
  - N3b – Metastasis in internal mammary and axillary lymph nodes
  - N3c – Metastasis in supraclavicular lymph node(s)

    *Note: Clinically apparent is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.

M – Distant Metastasis

- MX – Distant metastasis cannot be assessed.
- M0 – No distant metastasis.
- M1 – Distant metastasis.

5.4 Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1[a]	N0	M0
Stage IIA	T0	N1	M0
	T1[a]	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	T4	N0, N1, N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

[a]T1 includes T1mic

5.5 Summary

Breast			
Tis	In situ		
T1	≤2 cm		
T1mic	≤0.1 cm		
T1a	>0.1–0.5 cm		
T1b	>0.5–1 cm		
T1c	>1–2 cm		
T2	>2–5 cm		
T3	>5 cm		
T4	Chest wall/skin		
T4a	Chest wall		
T4b	Skin edema/ulceration, satellite skin nodules		
T4c	Both 4a and 4b		
T4d	Inflammatory carcinoma		
N1	Movable axillary	pN1mi	Micrometastasis, >0.2 mm, ≤2 mm
		pN1a	1–3 axillary nodes
		pN1b	Internal mammary nodes with microscopic metastasis by sentinel node biopsy but not clinically apparent
		pN1c	1–3 axillary nodes and internal mammary nodes with microscopic metastasis by sentinel node biopsy but not clinically apparent
N2a	Fixed axillary	pN2a	4–9 axillary nodes
N2b	Internal mammary clinically apparent	pN2b	Internal mammary nodes, clinically apparent, without axillary nodes
N3a	Infraclavicular	pN3a	≥10 axillary nodes or infraclavicular node(s)
N3b	Internal mammary and axillary	pN3b	Internal mammary nodes, clinically apparent, with axillary node(s) or >3 axillary nodes and internal mammary nodes with microscopic metastasis by sentinel node biopsy but not clinically apparent
N3c	Supraclavicular	pN3c	Supraclavicular

The breast imaging–reporting and data system (BI-RADS) categorization recommended by the American College of Radiology is an essential stage of assessment of breast imaging (mammography, ultrasound (US), and magnetic resonance imaging (MRI)) and arriving at conclusions in major clinics of the United States and Europe. It enables improved interpretation of breast pathology and standardized diagnostic and treatment algorithms. BI-RADS categorization has been introduced into practice for the assessment of pathology detected with US. As soon as US and X-ray characteristics differ in various pathological processes, the direct application of radiological BI-RADS for the assessment of US images is impossible. However, the general principles of categorization of US images correspond to classic categories.

5.6 BI-RADS Mammography Assessment Categories

5.6.1 Mammographic Assessment Is Incomplete

Category 0

Need additional imaging evaluation and/or prior mammograms for comparison:

Finding for which additional imaging evaluation is needed. This is almost always used in a screening situation. Under certain circumstances, this category may be used after a full mammographic workup. A recommendation for additional imaging evaluation may include, but is not limited to, the use of spot compression, magnification, special mammographic views, and ultrasound. Whenever possible, if the study is not negative and does not contain a typically benign finding, the current examination should be compared with previous studies. The radiologist should use judgment on how vigorously to attempt to obtain previous studies. Category 0 should only be used for old film comparison when such comparison is required to make a final assessment.

5.6.2 Mammographic Assessment Is Complete: Final Categories

Category 1

Negative:

There is nothing on which to comment. The breasts are symmetric and no masses, architectural distortion, or suspicious calcifications are present.

Category 2

Benign finding(s):

Like Category 1, Category 2 is a "normal" assessment, but, in this instance, the interpreter chooses to describe a benign finding in the mammography report. Involuting; calcified fibroadenomas; multiple secretory calcifications; fat-containing lesions such as oil cysts, lipomas, and galactoceles; and mixed-density hamartomas all have characteristically benign appearances and may be labeled with confidence. The interpreter may also choose to describe intramammary lymph nodes, vascular calcifications, implants, or architectural distortion clearly related to prior surgery while still concluding that there is no mammographic evidence of malignancy. Note that both Category 1 and Category 2 assessments indicate that there is no mammographic evidence of malignancy. The difference is that Category 2 should be used when describing one or more specific benign mammographic findings in the report, whereas Category 1 should be used when no such findings are described.

Category 3

Probably benign finding – initial short-interval follow-up suggested:

A finding placed in this category should have less than a 2 % risk of malignancy. It is not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability. There are several prospective clinical studies demonstrating the safety and efficacy of initial short-term follow-up for specific mammographic findings. Three specific findings are described as being probably benign (a noncalcified circumscribed solid mass, a focal asymmetry, and a cluster of round (punctate) calcifications; the latter is anecdotally considered by some radiologists to be an absolutely benign feature). All of the published studies emphasize the need to conduct a complete diagnostic imaging evaluation before making a probably benign (Category 3) assessment; hence, it is inadvisable to render such an assessment when interpreting a screening examination. Additionally, all of the published studies exclude palpable lesions; therefore, the use of a probably benign assessment for a palpable lesion is not supported by scientific data. Finally, evidence from all of the published studies indicates the need for biopsy rather than continued follow-up when most probably benign findings increase in size or extent. Although the vast majority of findings in this category will be managed with an initial short-term follow-up (6 months) examination followed by additional examinations until longer-term (2 years or longer) stability is demonstrated, there may be occasions where biopsy is performed (patient wishes or clinical concerns).

Category 4
Suspicious abnormality – biopsy should be considered:
This category is reserved for findings that do not have the classic appearance of malignancy but have a wide range of probability of malignancy that is greater than those in Category 3. Thus, most recommendations of breast interventional procedures will be placed within this category. By subdividing Category 4 into 4A, 4B, and 4C, as suggested in the guidance chapter, it is encouraged that relevant probabilities for malignancy be indicated within this category, so the patient and the physician can make an informed decision regarding the ultimate course of action.

Category 5
Highly suggestive of malignancy – appropriate action should be taken (almost certainly malignant):
These lesions have a high probability (≥95 %) of being cancer. This category contains lesions for which one-stage surgical treatment could be considered without preliminary biopsy. However, current oncologic management may require percutaneous tissue sampling as, for example, when sentinel node imaging is included in surgical treatment or when neoadjuvant chemotherapy is administered at the outset.

Category 6
Known biopsy-proven malignancy – appropriate action should be taken:
This category is reserved for lesions identified on the imaging study with biopsy proof of malignancy before definitive therapy.

BI-RADS categories predict potential risks for detected pathology based on diagnostic possibilities of mammography and US in every individual case.

The BI-RADS categorization of US results significantly differs from the traditional assessment of obtained images. The examination along with the statement of nosological diagnosis (fibroadenoma, cyst, cancer, etc.) aims to provide an accurate definition of the character of observed changes and further tactics in the form of scheduled follow-up and appointment of various kinds of biopsies and treatments. It provides continuity of optimum medical activities in cases of follow-up by different experts, in different clinics, or in different countries, and decreases the operator dependency of US imaging.

Breast US is often performed to assess abnormalities that were detected with mammography or clinical inspection. Standardization of terminology used to describe breast structures and a uniform system of reports facilitate the work of doctors of different specialties. The general assessment of findings becomes possible if the conclusion about the character of a lesion results not from separate symptoms but from their complex. The system of description of breast examinations developed for mammography permitted improvement in the assessment of lesions and calcifications. Recommendations on further examinations of patients were included in the Mammography Quality Standards Act (MQSA), which was enacted by the United States Congress to regulate the quality of care in mammography. Nevertheless, the most exact assessment of detected lesions and determination of further tactics is based on a combined analysis of US and mammography results.

Unification of terminology for the description of breast US implicated the following aspects: US screening of breast carcinoma, differential diagnosis of benign and malignant solid lesions, possible application of US for excision of the detected lesions, and the use of US for interventions. Based on the principles of the BI-RADS atlas for mammography, the terminology and categories of assessment of breast US have been developed. The accuracy of the terminology of this system is proven by the fact that the same terms are equally applied by both skilled and beginning experts and correctly understood by all specialists. Conclusions of complex examinations with mammography and US are based on the features that specify malignant processes with the greatest probability. The use of standard terms in the examination report allows a decrease in operator dependency in US.

5.7 BI-RADS US Assessment Categories

5.7.1 Assessment Is Incomplete

Category 0

Need additional imaging evaluation:

In many instances, the US examination completes the evaluation of the patient. If US is the initial study, other examinations may be indicated. An example would be the need for mammography if US were the initial study for a patient in their late 20s evaluated with US for a palpable mass that had suspicious sonographic features. Another example might be if mammography and US results are nonspecific, such as differentiating between scarring and recurrence in a patient with breast cancer treated with lumpectomy and radiation therapy. Here, MRI might be the recommendation. A need for previous studies to determine appropriate management might also defer a final assessment.

5.7.2 Assessment Is Complete: Final Categories

Category 1
Negative:
This category is for sonograms with no abnormality, such as a mass, architectural distortion, thickening of the skin, or microcalcifications. For greater confidence in rendering a negative interpretation, an attempt should be made to correlate the US and mammographic patterns of breast tissue in the area of concern.

Category 2
Benign finding(s):
Essentially a report that is negative for malignancy. Simple cysts would be placed in this category, along with intramammary lymph nodes (also possible to include in Category 1), breast implants, stable postsurgical changes, and probable fibroadenomas noted to be unchanged on successive US studies.

Category 3
Probably benign finding – short-interval follow-up suggested:
With accumulating clinical experience and by extension from mammography, a solid mass with circumscribed margins, oval shape, and horizontal orientation, most likely a fibroadenoma, should have a less than 2 % risk of malignancy. Although additional multicenter data may confirm safety of follow-up rather than biopsy based on US findings, short-interval follow-up is currently increasing as a management strategy. Impalpable complicated cysts and clustered microcysts might also be placed in this category for short-interval follow-up.

Category 4
Suspicious abnormality – biopsy should be considered:
Lesions in this category would have an intermediate probability of cancer, ranging from 3 % to 94 %. An option would be to stratify these lesions, giving them a low, intermediate, or moderate likelihood of malignancy. In general, Category 4 lesions require tissue sampling. Needle biopsy can provide a cytologic or histological diagnosis. Included in this group are sonographic findings of a solid mass without all of the criteria for a fibroadenoma and other probably benign lesions.

Category 5
Highly suggestive of malignancy – appropriate action should be taken (almost certainly malignant):

The abnormality identified sonographically and placed in this category should have a 95 % or higher risk of malignancy so that definitive treatment might be considered at the outset. With the increasing use of sentinel node imaging as a way of assessing nodal metastases and also with the increasing use of neoadjuvant chemotherapy for large malignant masses or those that are poorly differentiated, percutaneous sampling, most often with imaging-guided core needle biopsy, can provide the histopathologic diagnosis.

Category 6
Known biopsy-proven malignancy – appropriate action should be taken:
This category is reserved for lesions with biopsy proof of malignancy before institution of therapy, including neoadjuvant chemotherapy, surgical excision, or mastectomy.

5.7.3 Basics of the US Lexicon Classification Form

(a) Masses: a mass occupies space and should be seen in two different projections. The shape, margin, lesion boundary, echo pattern, posterior acoustic features, and surrounding tissue should be recorded.
(b) Calcifications: calcifications are poorly characterized with ultrasound but can be recognized, particularly in a mass.
(c) Special cases: special cases are those with a unique diagnosis or finding. Clustered microcysts, complicated cysts, mass in or on skin, foreign body, intramammary lymph nodes, and axillary lymph nodes should be recorded.
(d) Vascularity should be recorded as not present or not assessed, present in lesion, present immediately adjacent to lesion, and diffusely increased vascularity in surrounding tissue.
(e) Assessment category (Category 0 - Icomplete; Categories 1–6 - Final assessment from negative to known cancer).

6 Ultrasound Imaging of Breast Cancer Metastases

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About 47 % of men with breast cancer have significant local spreading of the process by the time of first reference to the doctor (Letyagin 2006). Because of the more aggressive development of breast carcinoma in men compared with women, metastases in regional lymph nodes are expected earlier, first in the axillary region.

Early metastases in regional lymph nodes are a consequence of the anatomical features of the male breast, with frequent and strong contractions of the muscles of the anterior thoracic wall and enhancement of local lymphatic and blood circulation. Therefore, the enlargement of the axillary lymph nodes may be the first sign of the disease. According to Letyagin (2006), approximately half of patients at the first reference to the doctor have enlarged axillary lymph nodes. However, the reliability of the clinical assessment of the status of the axillary area is quite low. False-positive results range from 8 to 50 %.

Ultrasound (US) features of metastases of breast cancer in lymph nodes in men are similar to those in women. The severity of changes depends on the character and stage of the primary malignancy. During complex examination of a patient, it is necessary to keep in mind the possibility of secondary breast malignancies – metastases of lung, stomach, kidney, and bladder cancer.

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_6

6.1 Healthy Lymph Nodes with Ultrasound

The examination of regional lymph nodes, especially of the axillary area, is an obligatory part of breast US because the basic lymph outflow flows through the axillary collector. The clinical method of revealing abnormal axillary lymph nodes has low sensitivity (50–88 %) and often fails to detect deep lymph nodes (Frolov 1996; Kharchenko et al. 1996; Chissov 2003).

The first use of US probes with a frequency of 5.0 MHz for the assessment of lymph nodes was reported in 1975. US was considered unable to determine the structure of healthy lymph nodes until the middle of the 1990s. US often failed to differentiate healthy lymph nodes from the surrounding adipose tissue, especially lymph nodes smaller than 5 mm (Trofimova 2008). Limited US data was the consequence of low capabilities of the equipment used at that time. Modern US scanners can detect not only abnormal lymph nodes that are smaller than 5 mm in size but also metastatic foci of 2–3 mm within their structure.

The objective data on a breast lesion determine the patient's further management, including the individual approach to the choice of treatment, specification of indications, and adequate volume for surgery (Maryasheva 2003; Korzhenkova 2004; Kuplevatskaya 2004; Allahverdyan and Chekalova 2011). The evaluation of regional metastases of breast carcinoma is complicated by the large number of diseases that demonstrate lymph node enlargement and creates difficulties in their differential diagnosis. In patients younger than 30 years of age, approximately 80 % of enlarged lymph nodes are benign. Meanwhile, in patients older than 50 years, benign lymph nodes are found only in 40 % of cases.

US of lymph nodes is performed with the patient in the standard position for breast scanning (Fig. 6.1). Axillary lymph nodes are examined with the patient's arms under their head. US examination of axillary, supraclavicular, subclavian, substernal, and pectoral groups of lymph nodes (Fig. 6.2) demand high-frequency

Fig. 6.1 Patient's position for US of axillary lymph nodes

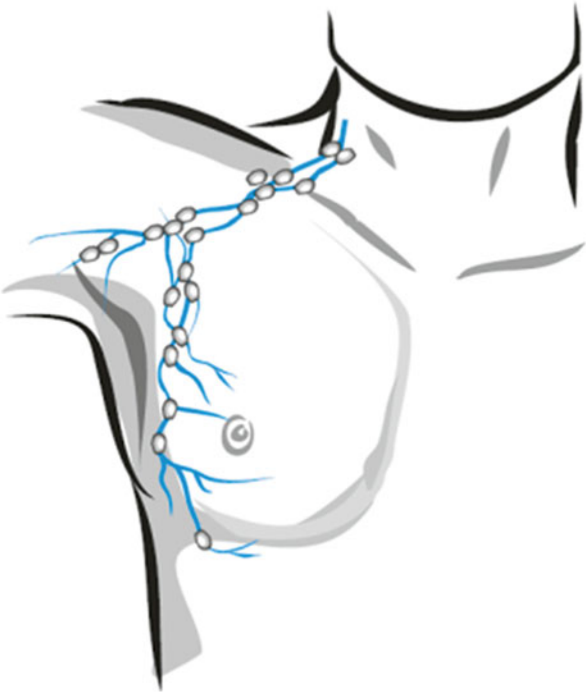


Fig. 6.2 Lymph nodes affected at breast pathology

US probes of 7.5–15 MHz. US analyzes conventional anatomical borders between areas to identify the groups of lymph nodes, such as supplied below. The lateral edges of the pectoralis minor and latissimus dorsi muscles form the axillary area; the upper edge of the clavicle and medial edge of the digastric muscle, the supraclavicular area; the projection of the subclavian vascular bundle and the surrounding fat, the subclavian area; and the intercostal spaces along the breast bone, the parasternal area. US also detects the subgroups of axillary lymph nodes located in the following areas:

- Medially from the pectoralis minor muscle
- Along axillary vessels
- Between the pectoralis major and minor muscles

Axillary lymph nodes can be classified into the following levels:

- Level 1 (inferior axillary) lymph nodes are located laterally from the lateral border of the pectoralis minor muscle.
- Level 2 (middle axillary) lymph nodes are located between medial and lateral edges of the pectoralis minor muscle and interpectoral (Rotter's) lymph nodes.
- Level 3 (apical axillary) lymph nodes are located medially from the medial edge of the pectoralis minor muscle including subclavian and apical.
- Intramammary lymph nodes are coded as axillary.

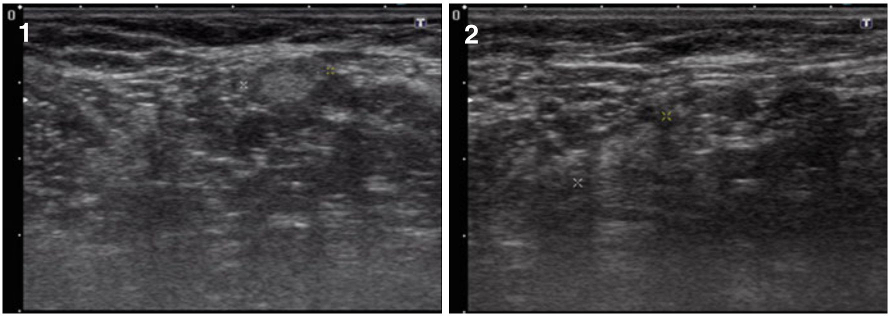


Fig. 6.3 (1, 2) Healthy axillary lymph nodes. Grayscale US

US characterization of the lymph nodes involves evaluating the following aspects:

- Site, according to anatomical area
- Number
- Dimensions (in three planes)
- Short/long axis ratio in transverse view
- Similarity of changes
- Shape (flat, oval, spherical, or irregular)
- Echodensity of the lymph node in general (increased, medium, or decreased)
- Differentiation of lymph node parts (present/absent)
- Differentiation of the hilum (present/absent)
- Core echodensity (high, low, or isoechoic)
- Status of the cortex of the lymph node (narrow/wide)
- Mobility upon compression with the probe
- Vascularity
- Features of stiffness evaluated with elastography

Healthy axillary lymph nodes demonstrate the following sonographic features (Fig. 6.3):

- Oval (or bean-like, tape-like) shape
- Length smaller than 10 mm
- Regular, well-defined contours
- Hypoechoic or isoechoic peripheral part and hyperechoic central part
- Painless, moderately mobile upon compression with the US probe
- Avascular or hypovascular in color Doppler imaging (CDI), power Doppler imaging (PDI), and vascular three-dimensional power Doppler imaging (3DPD), with predominant vascularity of the hilum (Fig. 6.4)
- Soft- or mixed-type color pattern with sonoelastography comparable with the pattern of the surrounding structures

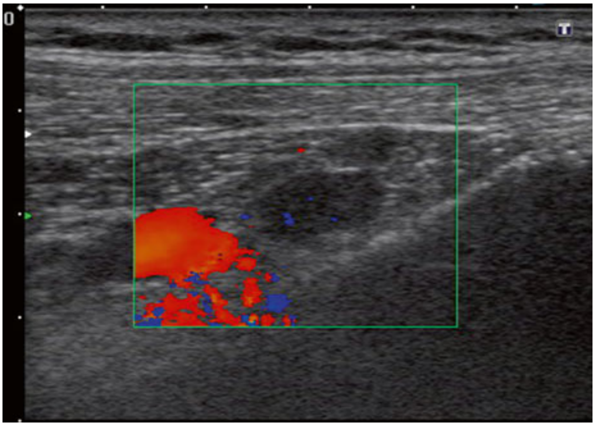


Fig. 6.4 Healthy axillary lymph nodes. CDI and PDI

A healthy lymph node has a width of up to 10 mm on transverse scan, although, according to a number of authors, the dimensions of healthy lymph nodes vary significantly. The Solbiati index (SI), which is the ratio of the largest to the smallest diameter of a lymph node, is normally 2.9 ± 0.13 in adults and 2.4 ± 0.05 or above in children (Solbiati and Rissato 1995).

The assessment of vascularity with CDI and PDI supplies additional data for the differential diagnosis of the origin of an enlarged lymph node. Vessels, if any are detected, are usually located within the hilum in healthy or reactive lymph nodes. Even in large benign hyperplastic lymph nodes, the vascular pattern remains regular. Vessels are normally observed along the capsule and radially from the hilum to the periphery.

Abbasova et al. (2005) classify the vascular pattern of lymph nodes into the following four categories:

1. Hilar: individual arterial and/or venous flow signals without diffusion to the parenchyma of the lymph node and without branching
2. Activated hilar (central) type: venous and arterial flow signals branching radially within the hilum and medulla
3. Peripheral: flow signals along the periphery of the lymph nodes without subcapsular branches arising from the hilar vessels
4. Mixed: presence of hilar and peripheral flow signals
   (a) One large artery in the hilum with individual dot-shaped color signals in the periphery
   (b) Fragments of afferent artery and chaotic flow signals within the solid component of the lymph node

According to Sinyukova et al. (2007), healthy lymph nodes exhibit single vessels in 58 % of cases. In the case of multiple vessels, their pattern is regular, with branching

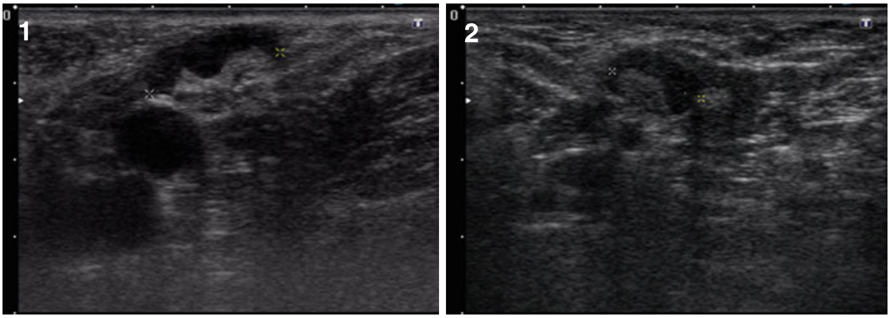


Fig. 6.5 (1, 2) Reactive axillary lymph nodes. Grayscale US

from the hilum to periphery. Doppler data, according to Abbasova et al. (2005), do not affect the differential diagnosis of enlarged lymph nodes. The enlargement of a lymph node may appear as a manifestation of a variety of diseases, such as specific or nonspecific inflammation of head and neck organs, metastases, and hemoblastoses (e.g., Hodgkin's disease).

Nonspecific types of lymphadenitis are divided into the following groups (Trofimova 2008):

1. According to disease severity
   - Acute
   - Subacute
   - Chronic
2. According to dispersion
   - Isolated
   - Regional (in groups)
   - Extended
   - Generalized

Individual and multiple lymph nodes as well as lymph node conglomerations can be also described. Reactive hyperplasia of lymph nodes may result from different pathological processes (an inflammatory process, vaccination, injections, etc.). Lymph nodes that are close to a tumor can also present a nonspecific reaction of an inflammatory character (Trofimova 2008).

Hyperplastic lymph nodes usually exhibit the following US features (Sinyukova et al. 2007) (Figs. 6.5, 6.6 and 6.7):

- Size of >10 mm
- Roundish shape
- Decreased or normal general echodensity
- Heterogeneous echostructure with thick regular cortex
- Regular distinct margins

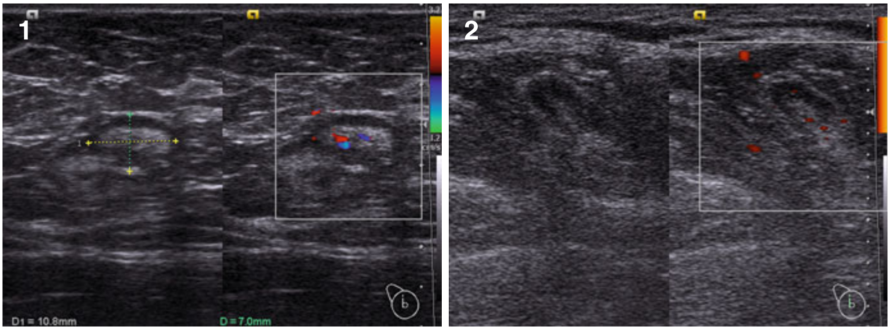
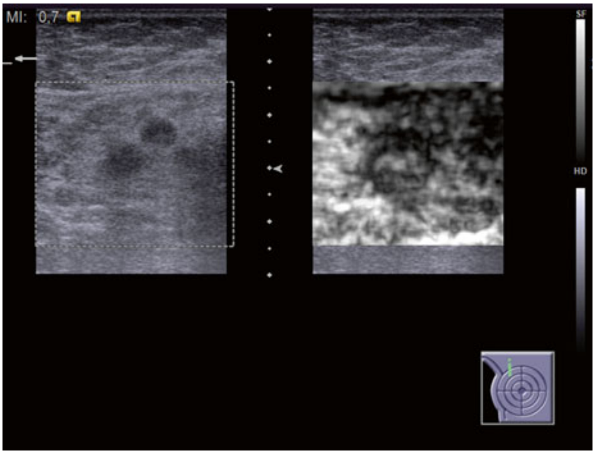


Fig. 6.6 (1, 2) Reactive axillary lymph nodes. CDI and PDI

Fig. 6.7 Reactive axillary lymph nodes. US elastography



- Avascularity or hypovascularity in CDI, PDI, and 3DPD
- Low values of peak systolic blood flow velocity (PSV), end-diastolic blood flow velocity (EDV), and resistive index (RI) in pulsed-wave (PW) Doppler imaging
- No difference in color pattern as compared with the surrounding tissues in US elastography

Inflammatory lymph nodes show fast dynamics. Even without therapy, they often sonographically disappear after 5–7 days. Treatment speeds up their involution, resulting in the restoration of the oval shape of the node and the sharpness of margins, an increase in the general echodensity with more accurate corticomedullary differentiation, and a decrease in blood flow intensity and morbidity upon compression.

6.2 Regional Lymph Node Metastases

Low differentiation with high malignant potential is the factor that promotes progression of breast carcinoma in men. The most unfavorable prognostic feature is invasion of tumor cells into lymphatic and blood vessels, which significantly increases the risk of remote metastases. Metastatic processes are detected in 62.5 % of men with such an invasion and only in 18.7 % of patients without it (Akimov 1992). The incidence of metastases of breast cancer in regional lymph nodes is 19–75 % (Chissov 2003; Sinyukova et al. 2007; Trufanov et al. 2009). The sensitivity of US in the detection and differentiation of malignant lymph nodes in patients with breast carcinoma ranges from 70 to 99 %, with a specificity of 83–97 % (Table 6.1). Both depend on the quality of equipment and the skills and experience of the operator (Cosgrove et al. 1990; Svensson et al. 2000; Drincovic 2002).

Palpable axillary lymph nodes sometimes can be both the first and the only sign of breast cancer. Such a cancer is termed as an occult type. According to the literature, this type is rare in women, from 0.97 to 2 %. Occult breast carcinoma in men is reported quite seldom (Crichlow 1972). Our own data based on 122 US examinations of patients with breast carcinoma revealed metastases in axillary lymph nodes in 55 patients (48.3 % of cases). More than 4 lymph nodes were affected in 16.9 % of cases.

Some US features that are suspicious for a malignant process in a lymph node are listed below (Figs. 6.8, 6.9, 6.10, 6.11, and 6.12):

- Size >10 mm (average size, 19 ± 2 cm)
- Oval (50 %) or irregular (46 %) shape
- Irregular margins (55 %), blurred (15 %) contours
- Decreased general echodensity (94 %)
- Heterogeneous echostructure (88 %)
- Pathological echogenic inclusions (5 %)
- Anechoic component (34 %)
- Dislocation or deformation of the hilum, indistinct image of the hilum of the lymph node up to its full disappearance (32 %)

Table 6.1 Diagnostic value of US in the diagnosis of metastases of breast carcinoma in axillary lymph nodes

Authors	Year	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
Kharchenko et al.	1996	88		80
Fiedler et al.	1996	87.5	56.9	
Stavros et al.	1995	91	72	57
Haylenko et al.	2005	91	72	57
Popli et al.	2006	86.3	41.6	73.3
Sinyukova et al.	2007	91	57	72

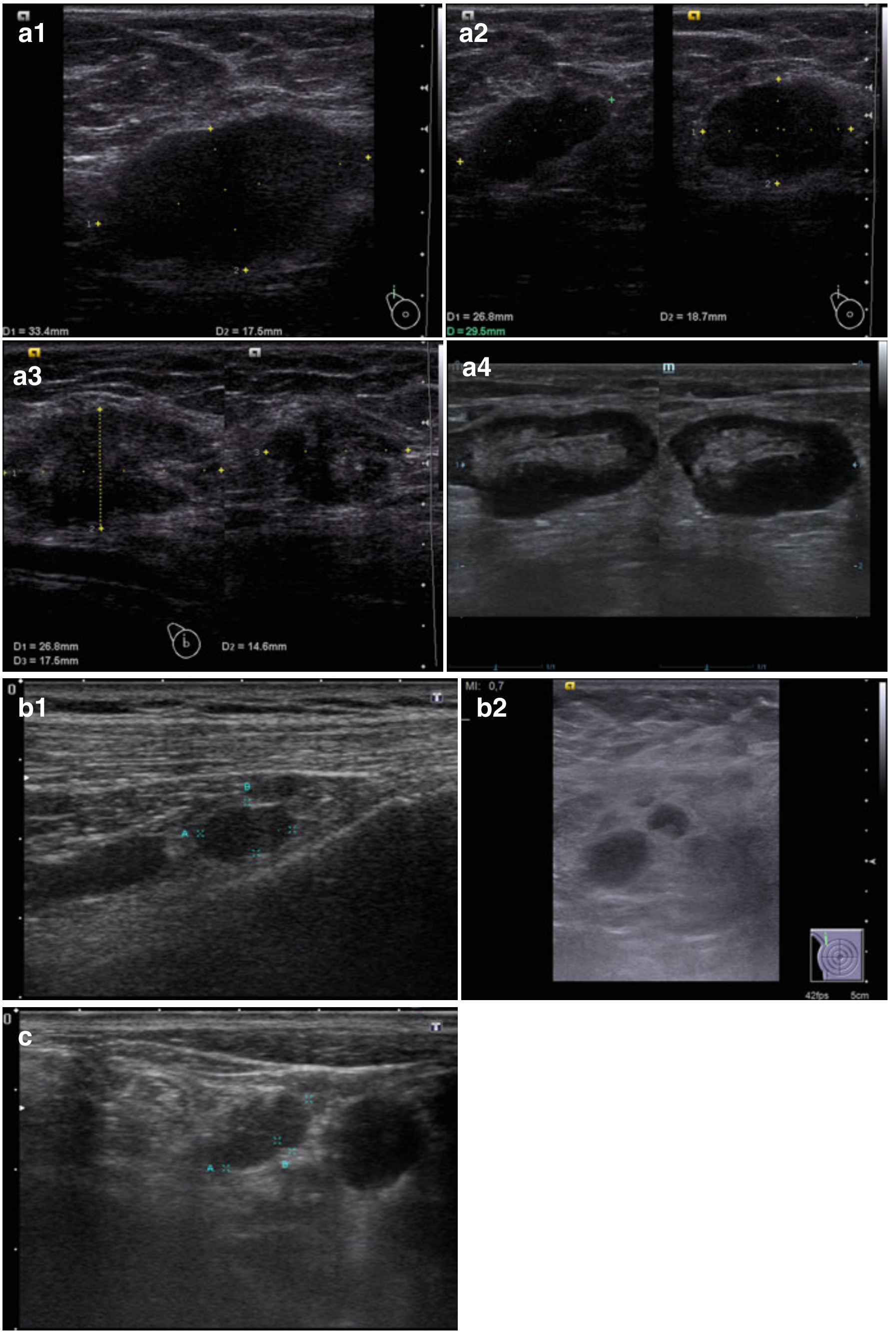


Fig. 6.8 Metastases of breast carcinoma. Grayscale US. (**a**) (1–4) Axillary lymph nodes. (**b**) (1–2) Subclavian lymph nodes. (**c**) Supraclavicular lymph nodes

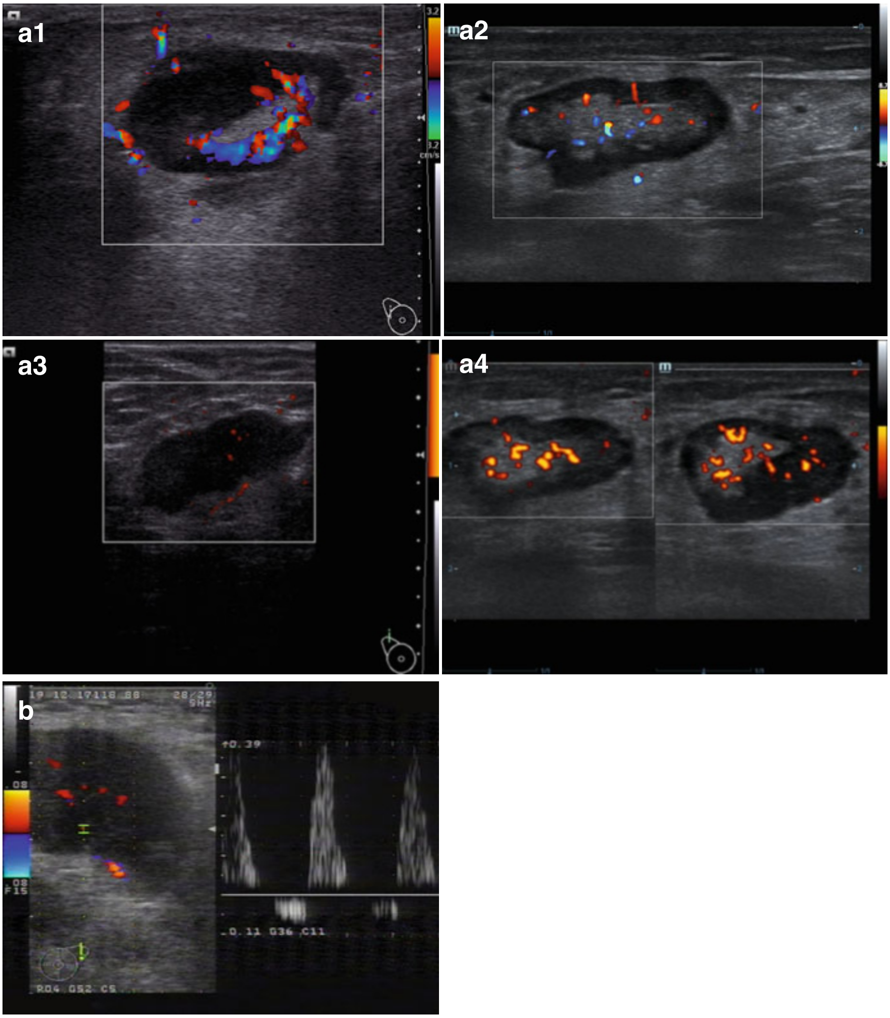


Fig. 6.9 Metastases of breast carcinoma in axillary lymph nodes. (**a**) (1–4) CDI and PDI. (**b**) Pulsed Doppler. Abnormal blood flow spectrum with retrograde flow in late diastole

- Local thickening of the cortex of the lymph node in combination with dislocation of the hilar vessels
- Conglomerations of lymph nodes
- Immobility or limited mobility against the surrounding tissues
- Pathological vascular patterns in CDI, PDI, and 3DPD with general hypovascularity (59 %) or hypervascularity (32 %)
- Abnormal types of blood flow in the arteries within the lymph node without late diastolic flow and inverse flow (32 %)

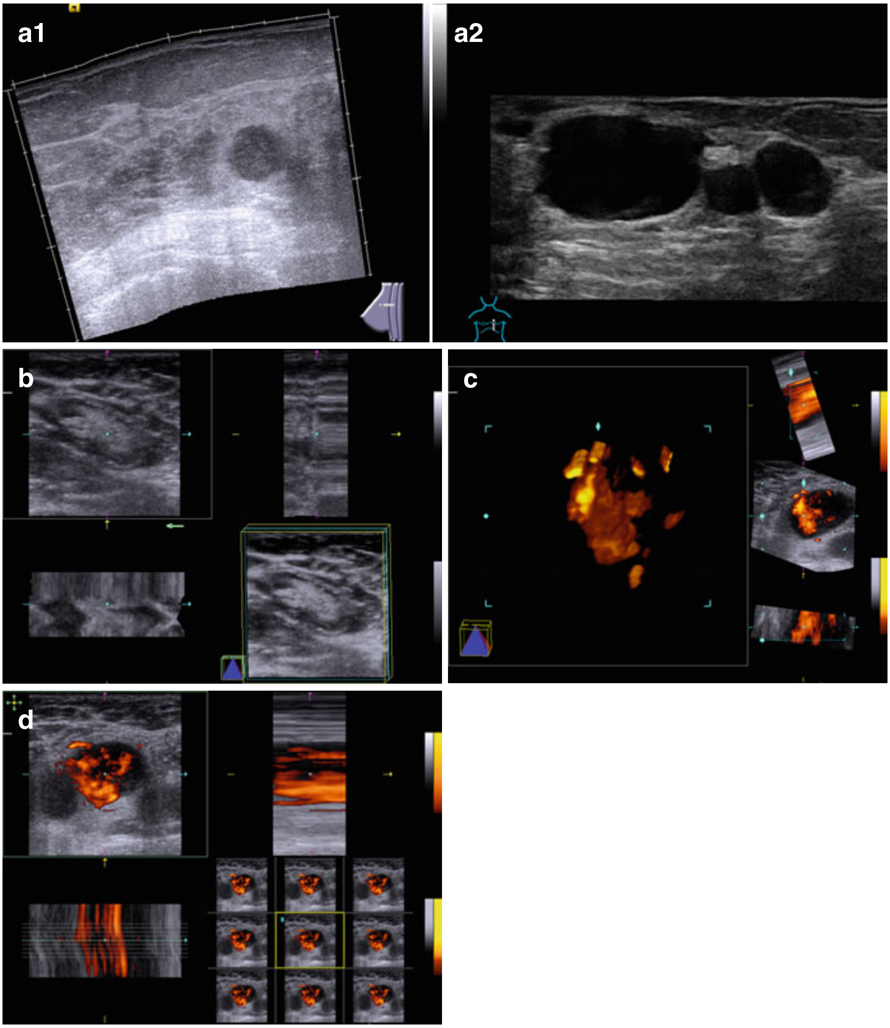


Fig. 6.10 Metastases of breast carcinoma in axillary lymph nodes. (**a**) (1, 2) Panoramic scan. (**b**) 3D. (**c**) 3DPD. (**d**) Multislice

- No difference from the surrounding tissues with compression elastography in 75 %. Only 15 % of cases exhibit intense hard (blue) heterogeneous color pattern
- Shear-wave velocity with acoustic radiation force impulse (ARFI) of 2 m/s
- Middle values of strain ratio (~1.8)

The sites of metastases do not always correspond to the locations of the primary breast tumor. The number of affected lymph nodes exceeds three in 40 % of cases

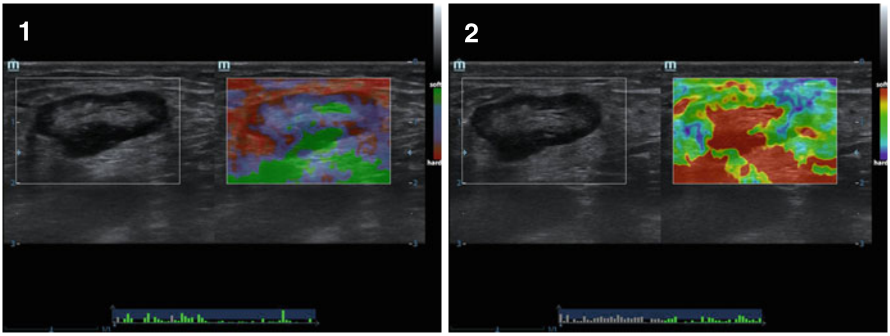


Fig. 6.11 (1, 2) Metastases of breast carcinoma in axillary lymph nodes. US elastography. Various color scales

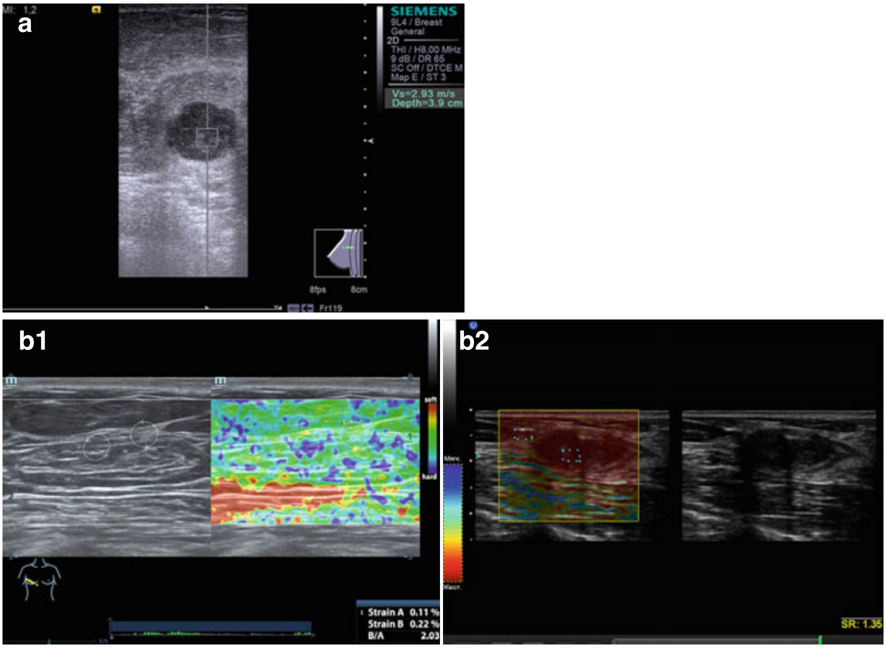


Fig. 6.12 Metastases of breast carcinoma in axillary lymph nodes. (**a**) ARFI. (**b**) Strain ratio

(Cuturi et al. 1995). Grayscale US remains the principal method for the diagnosis of the pathology in the axillary area. B-mode US significantly surpasses the possibilities of palpation and mammography in the definition of the nature of enlarged lymph nodes. Up to 55 % of sonographically detected abnormal lymph nodes are impalpable (Sencha et al. 2011a, b).

According to Trufanov et al. (2009), local metastases are characterized with multiple (>2) abnormal lymph nodes of roundish shape, heterogeneous echostructure, rough margins, and irregular cortical thickening located on the side of the breast carcinoma (Figs. 6.8, 6.9, and 6.10). Rough indistinct margins of a lymph node are generally a consequence of capsule invasion. Heterogeneity of echostructure, fluid collections, and calcifications characterize necrosis and fibrosis within the affected lymph node. The echodensity of a malignant lymph node is associated with the morphological structure of the primary tumor and the ratio of lymphoid and tumoral tissues. Along with the decrease of normal elements within a lymph node, its structure becomes more homogeneous and hypoechoic. Many authors consider a narrow or absent hilum in combination with a thickened cortex suspicious for malignant nature of a lymph node (Allahverdyan and Chekalova 2011).

The risk of regional metastases depends on the size of the primary tumor. Breast carcinomas of stages T1, T2, and T3 metastasize in axillary lymph nodes in 3, 7, and 15 % of cases, respectively. The growth of secondary tumors leads to extracapsular invasion and merging into the surrounding adipose tissue. This often results in shapeless conglomerations of lymph nodes with the involvement of surrounding organs and structures in the malignant process.

CDI is used in addition to grayscale US (Fig. 6.9a). It permits assessment of both vascular pattern and functional features of blood supply. Sinyukova and Sholokhov (2010) report that CDI permits detection of blood vessels in metastatic lymph nodes in 93 % of cases. The vascular pattern is usually disorganized with irregular distribution and nonuniform caliber and shape of vessels.

The average indexes of blood flow with PW Doppler are the following: PSV, 42.8 ± 2.5 cm/s; EDV, 10.5 ± 0.8 cm/s; RI, 0.75 ± 0.01; and PI, 1.6 ± 0.06. Some investigators consider the pulsed Doppler criterion of lymph node malignancy to be RI > 0.9; some, RI > 0.73; and others, decrease of RI (Fig. 6.9b). Difficulties in PW Doppler assessments of lymph nodes result from irregular wavy courses of vessels with wide ranges of velocities.

Comparison of the vascular patterns of breasts and lymph nodes on the healthy and affected sides with CDI and PDI is also necessary. The status of incoming arteries and smaller vessels may be obviously assessed with 3D reconstruction in vascular mode. This permits the targeted study of maximally changed vessels with PW Doppler.

Visual parameters of vascular structures, which should be paid attention to in 3D reconstruction, are (Fig. 6.10):

- Spatial symmetry of large vessels and their branches
- Regularity of the vessels' calibers (asymmetric dilation and narrowing)

Metastatic lymph nodes are often characterized with moderate or high vascularity with diffuse chaotic pattern. Trufanov et al. (2009) classify lymph nodes according to the character of vascularity into avascular and lymph nodes with individual color spots in the central or peripheral parts. Metastatic axillary lymph nodes often exhibit high values of Doppler indicators in detected vessels (PSV >0.23 m/s). Many authors consider that the majority of lymph nodes that are totally substituted by tumoral tissue often appear avascular in CDI and PDI. Anyway, CDI and PDI are often useless in the differential diagnosis of enlarged lymph nodes. According to Trufanov et al. (2009), metastatic lymph nodes in supraclavicular, subclavian, and cervical areas are more often of roundish or irregular shape and hypoechoic, whereas in parasternal and intrathoracic areas, corticomedullary differentiation and color pattern are preserved (in 40 % of cases).

Most authors agree that, in many cases, sonography does not allow the ultimate definition of the nature of the lymph nodes, although it does detect indirect features that facilitate further diagnostics. US-guided fine needle aspiration biopsy (FNAB) with cytological examination is feasible. FNAB increases the sensitivity in the diagnosis of axillary lymphadenopathy up to 96 %, with a specificity of 94 % and a diagnostic accuracy of 88 %.

6.3 Distant Metastases

Twenty percent of men with breast carcinoma have remote metastases when they first see a doctor. Approximately 18–54 % of patients develop remote metastases after the treatment of local types of cancer (Scheike 1975; Ostrovskaya et al. 1988; Letyagin 2006; Contractor et al. 2008; Korde et al. 2010). Based on studies of invasion of breast carcinoma into blood vessels, Akimov (1992) reported that the incidence is less in men than in women (9.1 % vs. 15.3 %, respectively). The same ratio (1:1.7) was characteristic for remote metastases: men 6.1 % and women 10.5 % of cases.

Remote metastases are observed in 6–56 % of patients with breast carcinoma. The most frequent sites are the peripheral areas of the lungs (29–63 %), pleura, bones (5–31 %), mediastinal lymph nodes (8 %), liver, brain, ovaries, and neck lymph nodes (Rozhkova 1993; Zabolotskaya 2006). Much more rarely, there are metastases in the thyroid gland, pancreas, retroperitoneal or submandibular lymph nodes, anterior abdominal wall, and soft tissues of the extremities (Sinyukova et al. 2007).

Metastases of breast carcinoma in men often appear between 4 months and 9 years after primary treatment. The greatest incidence of metastases, 50 %, is detected within the first 3 years, 25 % in the next 2 years, and the remaining 25 % 6–9 years after primary treatment (Ostrovskaya et al. 1988). These data confirm the necessity of not only complex effective treatment at early stages but also the development of follow-up programs and effective therapy at the late stages of the disease.

Several imaging modalities, such as X-ray, CT, MRI, and scintigraphy, are used to detect remote metastases. Metastases in lungs at an early dissemination are usually multiple (62–78 % of cases) and bilateral (71 %), whereas late metastases are multiple only in 38 % of cases. However, imaging of the organs of the abdominal cavity (first of all, the liver), pelvis, retroperitoneal space, thyroid gland, soft tissues, pleura at the thoracic wall, and superficial lymph nodes is well examined with US (Figs. 6.13 and 6.14).

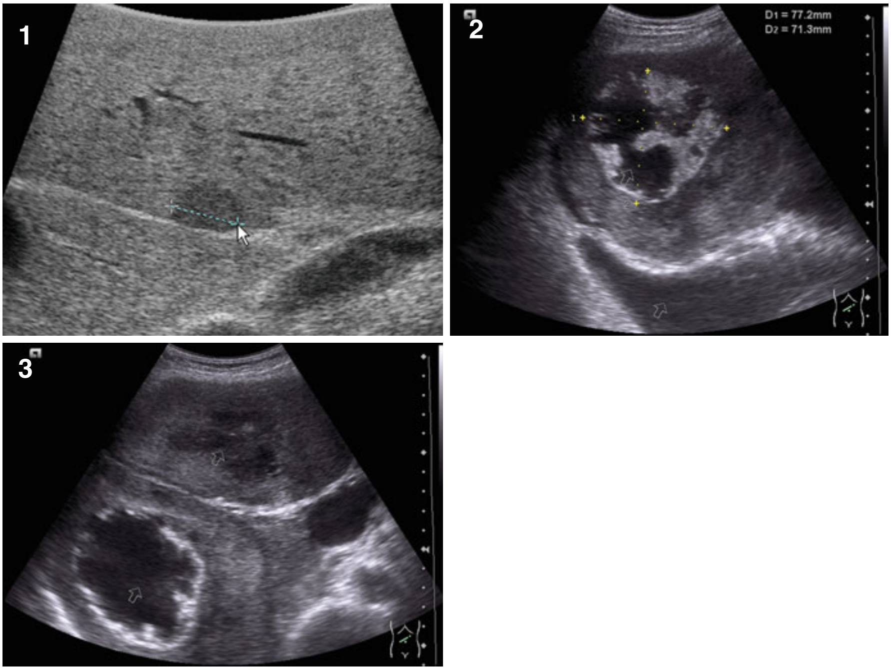


Fig. 6.13 (1–3) Metastases of breast carcinoma in the liver. Gray scale

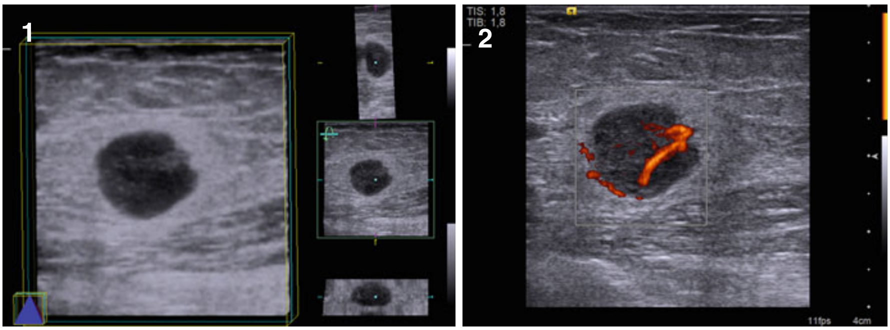


Fig. 6.14 (1, 2) Metastases of breast carcinoma in the liver. 3D and PDI

The breast itself is much more rarely affected by metastases of malignant neoplasms of other locations, for example, melanoma, colorectal, or kidney cancer. There are individual publications about metastatic breast lesion in men with prostate, pancreatic (Salyer 1973; Dretichman 1980), and thyroid cancers (Belous and Yefimova 1972; Ostrovskaya et al. 1988).

Differential Diagnosis of Male Breast Cancer

7

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The differential diagnosis of breast carcinoma with its large variety of types cannot be limited to one disease. It includes benign diseases (gynecomastia, benign tumors) and malignant processes (sarcoma, metastases of tumors of other localizations) and various inflammations. In this respect, differential imaging features of breast diseases, which indicate structure, vascularity, interrelation with surrounding tissues, and the status of regional lymph nodes, are beneficial.

7.1 Gynecomastia

One breast abnormality in men is gynecomastia. It requires complex examination and careful differentiation from a tumor. Gynecomastia is the enlargement of the breast in men caused by benign intraductal and stromal proliferation. It is a dishormonal hyperplastic process characterized by a wide spectrum of proliferative and regressive changes of breast tissue with an abnormal ratio of epithelial and connective tissue components.

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_7

According to Weitz (1950), gynecomastia was reported in 0.57 % of a group of 14,000 healthy men. Peter and Lobner (1967) examined 122,019 men and detected gynecomastia in 0.28 %. The incidence of the disease is approximately 280–570 in 100,000 men. According to Ostrovskaya et al. (1988), hormonal dysplasia is the most widespread breast disease in men. It constitutes 74 % of all male breast abnormalities.

The risk of malignant transformation of the nodular type of gynecomastia ranges from 3.9 % (Norris and Taylor 1969) to 17 % (Letyagin 2006) and even 40 % (Heller et al. 1978). Chronic gynecomastia may be similar to breast carcinoma, and malignant tumors can mimic gynecomastia. According to Letyagin (2006), urgent histology detected breast carcinoma in 7.9 % of men who underwent surgery for nodular gynecomastia. Gynecomastia arises as an independent disease in 19 % of cases, whereas in 81 % of cases, it appears with preexisting pathology.

Different breast changes that reflect functional features and hormonal disturbances are studied in detail in women. They are united by the term “fibroadenomatosis.” However, because of the high frequency of this abnormality, it is almost impossible to assess its influence on cancer development. There is a point of view that gynecomastia, which is obviously a dishormonal hyperplasia, is analogous to female fibroadenomatosis in the male breast. However, there are discordant opinions regarding the possibility of malignant transformation of gynecomastia. The majority of researchers deny such a possibility and do not consider gynecomastia a precancer (Kremer 1979). Some reports note a transition of gynecomastia into cancer (Cole and Qizilbash 1979). The incidence of breast cancer in men with gynecomastia is reported as three to five times higher than in the general population (Letyagin 2006).

According to Akimov (1992), the age of men with gynecomastia ranges from 14 to 75 years; however, gynecomastia is most often reported in the fifth to eighth decades of life, with the maximum in the fifth decade (27.8 %). These data indirectly indicate the dishormonal nature of gynecomastia because involution of the sexual glands begins after 50 years of age with a decrease in the secretion of androgens and a corresponding change in the androgen-to-estrogen ratio (Ostrovskaya et al. 1988). One report favors the dishormonal nature of gynecomastia. After surgical removal of gynecomastia, 17 of 159 men (10.6 %) developed similar changes in the contralateral breast between 3 months and 2.5 years (Akimov 1992).

Breast enlargement is diagnosed clinically (Fig. 7.1). The patient’s basic complaint is a palpable mass in the breast. Discomfort or pain is a variable sign; however, it is often the reason the patient seeks medical advice. Some retraction of the nipple may be observed. Other skin changes are not characteristic of gynecomastia. A typical feature of gynecomastia is its central location, which is symmetric under the nipple.

According to Akimov (1992), one third of men with gynecomastia had lesions diffusely distributed within the breast and presented with small fibrous areas in adipose tissue. Sometimes they contained cysts of 0.5 cm in size with transparent fluid. Approximately 9 % of patients exhibited bilateral changes. Two thirds of cases of gynecomastia were local. The areas were centrally located in the subareolar area, elastic with palpation, had a roundish shape, and ranged in size from 0.7 to 8 cm. All cases of focal gynecomastia were unilateral (Akimov 1992).

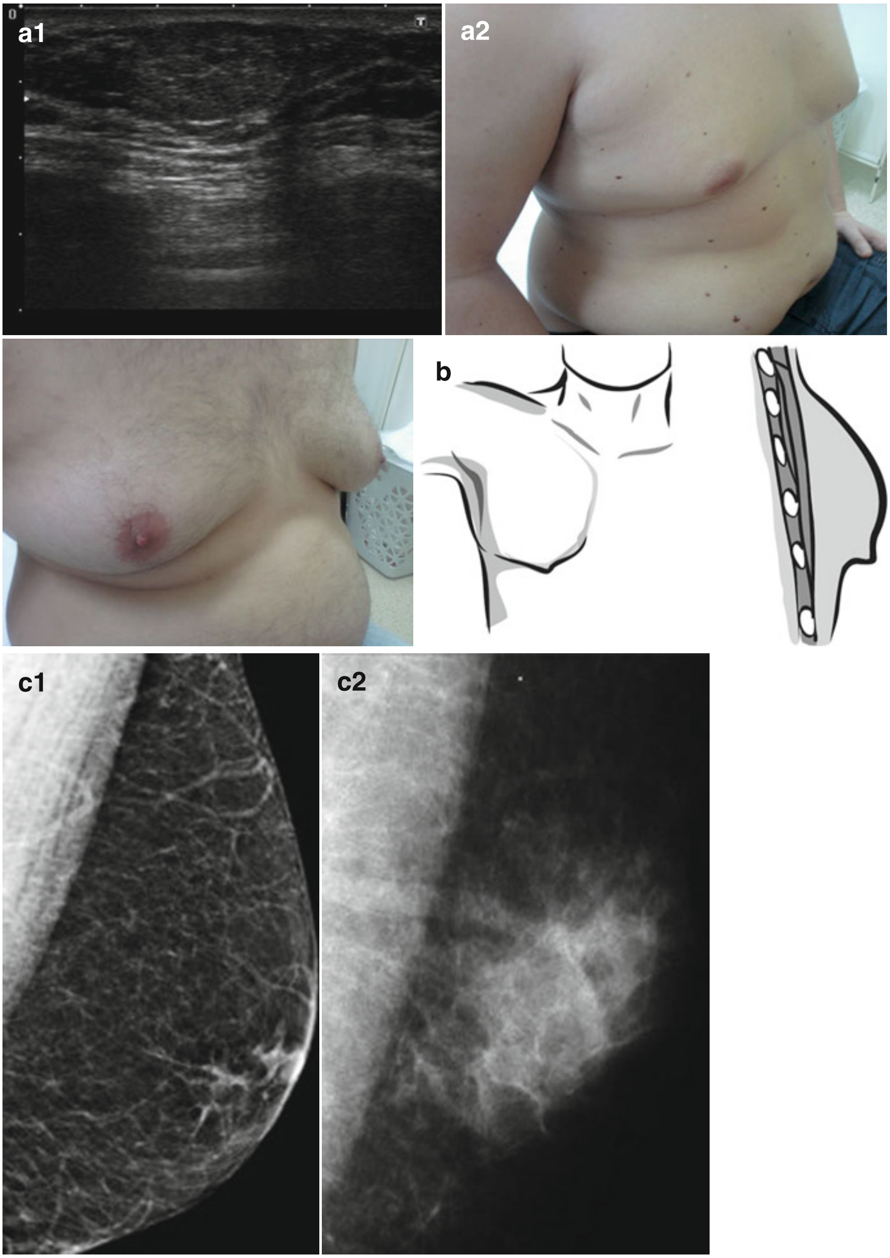

Fig. 7.1 Gynecomastia. (**a**) (1, 2) Photo. (**b**) Scheme. (**c**) (1, 2) Mammography

Classifications of gynecomastia are based mainly on etiological factors. Thus, Zhukovsky and Lebedev (1982) classify gynecomastia as drug-induced, symptomatic, familial, and false. Eulenburg et al. (1984), considering a principal cause of gynecomastia to be the disturbance in hormonal balance between estrogens and androgens, classify three physiological types of gynecomastia: gynecomastia of newborns, young men, and the elderly. Ostrovskaya et al. (1988) classify gynecomastia as true and false, the first being a breast dishormonal hyperplasia and the second characterized by enlargement of the breast because of excess subcutaneous fat.

Gynecomastia can be a consequence of hormonal imbalance, such as elevated level of estrogen, lowered level of androgen, defect of androgen receptors, and increased sensitivity of mammary tissue to estrogen. Gynecomastia can be physiological or can result from a disease. Of all cases, 25 % are of an idiopathic nature. Classifications of the syndrome of gynecomastia can be based on the causes of imbalance of male and female sex hormones.

One example of classification is:

I. Physiological gynecomastia
   - Newborns
   - Teenagers
   - In elderly people

II. True gynecomastia
   - Idiopathic
   - Persistent in teenagers
   - Familial

III. Symptomatic gynecomastia
   - Hormone-secreting tumors (e.g., tumors of testicles or various organs (lung, liver, intestine) that secrete chorionic gonadotropin)
   - Endocrine diseases, including genetic (e.g., true hermaphroditism, Klinefelter syndrome, congenital adrenal hyperplasia, Kennedy's disease, Graves' disease)
   - Primary hypoandrogenism (e.g., infectious, granulomatous orchitis, anorchism, castration)
   - Renal and/or hepatic failure
   - Medicinal (estrogen, human chorionic gonadotropin, spironolactone, flutamide, cardiac glycosides, tricyclic antidepressants, opiates, etc.)

IV. False gynecomastia
   - Adipose breast tissue hyperplasia

V. Breast tumors
   - Malignant (cancer or sarcoma)
   - Benign (adenoma, lipoma, fibroma, etc.)

Physiological gynecomastia exhibits three age peaks: in newborns, during puberty, and in the elderly.

A classification based on the stability of pathological hyperplasia (Serra-Diaz et al. 1999) is:

1. Neonatal.
2. Pubertal (transitional) gynecomastia as a physiological phenomenon is observed in 4–9 % of boys in puberty and disappears after puberty.
3. Persistent pubertal gynecomastia is considered abnormal and does not exhibit spontaneous regression.

Sotnikov and Baytinger (2006) suggest four degrees of severity of gynecomastia:

I. Minimum subareolar nodosity
II. Subareolar mass smaller than the diameter of the areola
III. Mass equal to the diameter of the areola
IV. Mass larger than the diameter of the areola

In surgical practice, gynecomastia division into nodular, diffuse, and mixed is considered most convenient.

Gynecomastia is also classified in accordance with its dimensions into the following groups: moderate, medium, and expressed. The formula, $C \times H \div 2$, where C is the circumference of the breast (in centimeters) and H is the height of the breast (in centimeters), is used to define the groups; moderate gynecomastia corresponds to <6 cm^2 (incidence ~10 %), medium is 6–10 cm^2 (incidence ~71 %), and expressed is >10 cm^2 (incidence ~18 %).

Gynecomastia of newborns is a secondary event related to transplacental transmission of hormones into the fetus. It is observed in 60–90 % of all newborns. It is characterized with infiltration in the subareolar region, sometimes accompanied with colostrum. It spontaneously passes within several days or weeks and does not require any medical influence.

Gynecomastia in puberty is reported in 4–6 % of adolescents. It is usually bilateral and asymptomatic. In most cases, it spontaneously passes within several months or years. In some cases, it can be significant and last for an extended period because of the sensitivity of the mammary tissue to estrogen stimulation.

During early puberty, the level of estrogens increases faster than testosterone, inducing an imbalance of the estrogen/androgen ratio. During the formation of the sexual system, the secretion of follicle-stimulating hormone (FSH) and the aromatase activity of testicular Sertoli cells increase against a low level of luteinizing hormone (LH), which should stimulate the hormonopoiesis of testosterone in Leydig cells. The latter reaches the level of adult men only some years later. Pubertal gynecomastia with histology shows the changes in the interstitial tissue with insignificant proliferation of ductal epithelium. It requires conservative or surgical treatment in severe cases. To exclude other than physiological causes of gynecomastia, the patient should consult a urologist and undergo examinations of the liver and intestines (the organs and systems participating in hormone metabolism). Pubertal gynecomastia usually spontaneously disappears in 6–18 months. A small enlargement of the breast does not require any treatment in the majority of teenagers.

Persistent gynecomastia is a pathological condition. After puberty, the remaining enlargement of the breast requires surgical treatment, if conservative treatment fails to improve the situation. Endocrinologic examination permits the classification of persistent gynecomastia into four variants: normopubertal, hypopubertal, hyperpubertal, and femininopubertal.

Gynecomastia of elderly people can be observed in men older than 60 years. The abnormality results from fading of testicular function leading to a change in the hormone ratio (a relative elevation of estrogen levels). The diagnosis is applicable if other causes of gynecomastia are excluded.

Iatrogenic gynecomastia in adult men is reported most often. More than 120 drug groups can induce gynecomastia, such as estrogen, steroids, glucocorticoids, and gonadotropins. This type of gynecomastia is reversible and regresses after drug cessation. Gynecomastia in endocrine and nonendocrine diseases can accompany liver or kidney pathology. It is a consequence of disturbance in metabolism and excretion of steroid hormones and prolactin.

Gynecomastia may periodically accompany diabetes (Sencha et al. 2013a, b). The main causes are considered disturbances in liver and kidney functions. Diffuse diabetic glomerulosclerosis usually appears 4–5 years after diabetes manifestation, and 15–20 years from the onset of the disease, these changes are observed practically in all patients with diabetes. The nodular affection of the renal glomulus is often observed. It starts almost from the very beginning of diabetes and quickly progresses, resulting in glomerulocapillary microaneurysms, which narrow or completely obstruct the capillaries. It leads to the accumulation of toxic products and disturbance in the destruction of peptide hormones. It subsequently results in their accumulation in the blood, with influence on sexual glands and directly on breast tissue, with the growth of the ductal tree and development of gynecomastia. There is an opinion that gynecomastia can be a sign of functional abnormalities of the pituitary–sexual gland system in diabetic men because of progressing insufficiency of the microcirculation.

Gynecomastia in men with prolactinoma may accompany galactorrhea and hyperprolactinemic hypogonadism. Treatment of a tumor of the pituitary gland, conservative (dopamine agonists) or adenomectomy, leads to involution of gynecomastia. Gynecomastia in subthalamic dysfunction is caused by a disturbance in the regulation of adenohypophysis with the change in production of prolactin, LH, or/and FSH. Gynecomastia can accompany hyperthyroidism in children and be the first sign of hyperthyroidism in adult men because thyroid hormones activate steroidogenesis. Hypothyroidism may also be accompanied by gynecomastia, when hyperstimulation of the pituitary gland arises under the influence of excess thyroliberin. This is characteristic for primary hypothyroidism. Correction of hypothyroidism leads to the regression of gynecomastia. In men with cryptorchism, anorchism, and ineffective spermatogenesis and synthesis of testosterone and after testicular trauma or autoimmune processes in testicles with their atrophy, hormone replacement therapy is a method of treatment and gynecomastia preventive maintenance. Gynecomastia appears in genetic diseases with endocrinopathies (hyperprolactinemia and hypersensitivity of breast tissues to estrogens in Klinefelter syndrome and increase in the production of estrogens in Reifenstein syndrome and testicular feminization syndrome).

Gynecomastia in nonendocrine diseases often accompanies severe pathology of the liver and kidneys, such as hepatitis, liver cirrhosis, and chronic renal insufficiency. The method of choice for treatment in such cases is surgical because drug administration can negatively affect the pathological processes.

Kidney diseases with so-called uremic hypogonadism are also associated with gynecomastia. Chronic renal insufficiency with suppression of glomerular filtration and increase in blood urea, creatinine, and other nitric slags leads to a decrease in the secretory activity of Leydig cells. At the same time, gynecomastia can be related to chronic renal insufficiency because the kidneys are the location of the degradation of peptide hormones (prolactin, gonadotropin). A disturbance in the process of their destruction results in their accumulation in blood and their influence on sex glands and breast tissue. Breast enlargement may be observed in men with chronic renal insufficiency on hemodialysis. The duration of hemodialysis does not always matter for the development of gynecomastia. However, gynecomastia often arises within the first weeks of hemodialysis and spontaneously disappears in most cases.

The understanding of the connection of gynecomastia with prostate diseases is enhanced by data regarding the increase in the conversion of testosterone to dihydrotestosterone by hypertrophied prostates. The close interrelation between the prostate and sexual glands in the development of gynecomastia is based on the interaction of secretory functions of these organs. Thus, a decrease in the function of the prostate is accompanied by testicular atrophy and abnormal spermatogenesis. An enhanced secretory activity of the prostate suppresses the activity of testicles, whereas the reduction of its secretion stimulates their function.

Gynecomastia as a paraneoplastic syndrome can arise in cases of hormone-secreting tumors. It is often the first and the single sign of a tumor (lung, pancreatic, liver, kidney, testicular cancer) for a long time. Breast enlargement is induced by ectopic secretion of estrogens or gonadotropins by the tumor and, hence, typically bilateral. Gynecomastia may be observed in cases of benign hormone-active tumors in any age (feminizing adrenal or testicular tumors).

Gynecomastia is idiopathic in 25 % of cases, and the cause is left undetermined. Gynecomastia can be unilateral or bilateral and symmetric or asymmetric. Obesity in men leads to breast enlargement caused by adipose tissue hyperplasia (pseudogynecomastia). True gynecomastia is defined with ultrasound (US) by the presence of subareolar infiltration, which can be of different density and structure. There are several types of gynecomastia, such as nodular (in the form of roundish intense homogeneous lesion), treelike (in the form of wide dense fibrous branches), and diffuse glandular (an appearance similar to mastopathy in women). Diffuse gynecomastia presents clinically with a painful swelling of one or both breasts, in some cases with nipple discharge, coarse lobularity, and multiple foci that have a changeable character. Nodular gynecomastia more often affects one breast and is constant with a tendency toward enlargement.

The risk of breast carcinoma depends on the expression of ductal, lobular, or intracystic proliferation. Based on the degree of proliferative activity of epithelium, the following types are specified (Letyagin 2006):

- Gynecomastia without proliferation (the risk of development of breast cancer is 1.5 times higher)
- Gynecomastia with epithelial proliferation (the risk of malignancy increases up to 1.9 times)

- Gynecomastia with atypical epithelial proliferation (3 times increase in risk, up to 25 times according to some publications)

US often detects the following features in all types of gynecomastia (Fig. 7.2):

- Hypoechoic area or lesion
- Central retroareolar location within the breast
- Irregular shape
- Accurate or indistinct contours, rough borders
- Various dimensions from 5–7 mm to 25–30 mm
- Hypovascular or avascular with color Doppler imaging (CDI), power Doppler imaging (PDI), and three-dimensional power Doppler vascular image reconstruction (3DPD)
- Heterogeneous medium-grained color pattern with US elastography similar to the surrounding tissues
- Average shear-wave velocity of 2.4 m/s with acoustic radiation force impulse (ARFI) (Virtual Touch™ tissue quantification (VTQ)) and average strain ratio in different aspects not differing from those in healthy breast tissues

Fourteen percent of men with gynecomastia in our study exhibited the nodular type with the following features (Fig. 7.3):

- A lesion of 1.2–3.8 cm in size against fibroadipose tissue in retropapillary area
- Irregular shape (74.6 %)
- Decreased echodensity
- Heterogeneous structure (anechoic component was observed in 59.7 % of cases)
- Indistinct, rough contours
- Hypovascularity with CDI, PDI, and 3DPD (68.4 %)
- Heterogeneous large/medium-grained color pattern with US elastography almost identical to the surrounding structures
- Average shear-wave velocity of 2.4 m/s with ARFI (VTQ) and average strain ratio in different aspects not differing from those in healthy breast tissues

The treelike type of gynecomastia was observed in 32.3 % of patients. US defined wide dense fibrous linear structures in some breast areas (most often retroareolar) with a heterogeneous echostructure (an anechoic component was observed in 11.5 % of cases), and avascular with CDI, PDI, and 3DPD (Fig. 7.4). The diffuse type was reported in 53.7 % of men with gynecomastia. It was characterized by diffuse changes of various degree of manifestation throughout the whole breast without solid or cystic lesions (Fig. 7.5).

False gynecomastia exhibits only excess fibroadipose tissue in the breast. Grayscale US reveals a hypoechoic breast structure with echogenic linear incorporations of connective tissue. The fat starts to form roundish hypoechoic spots organized in rows or layers, similar to involutive breast in women. As a result, echogenic capsules cover the spots of adipose tissue and form adipose lobes. Sometimes symmetric

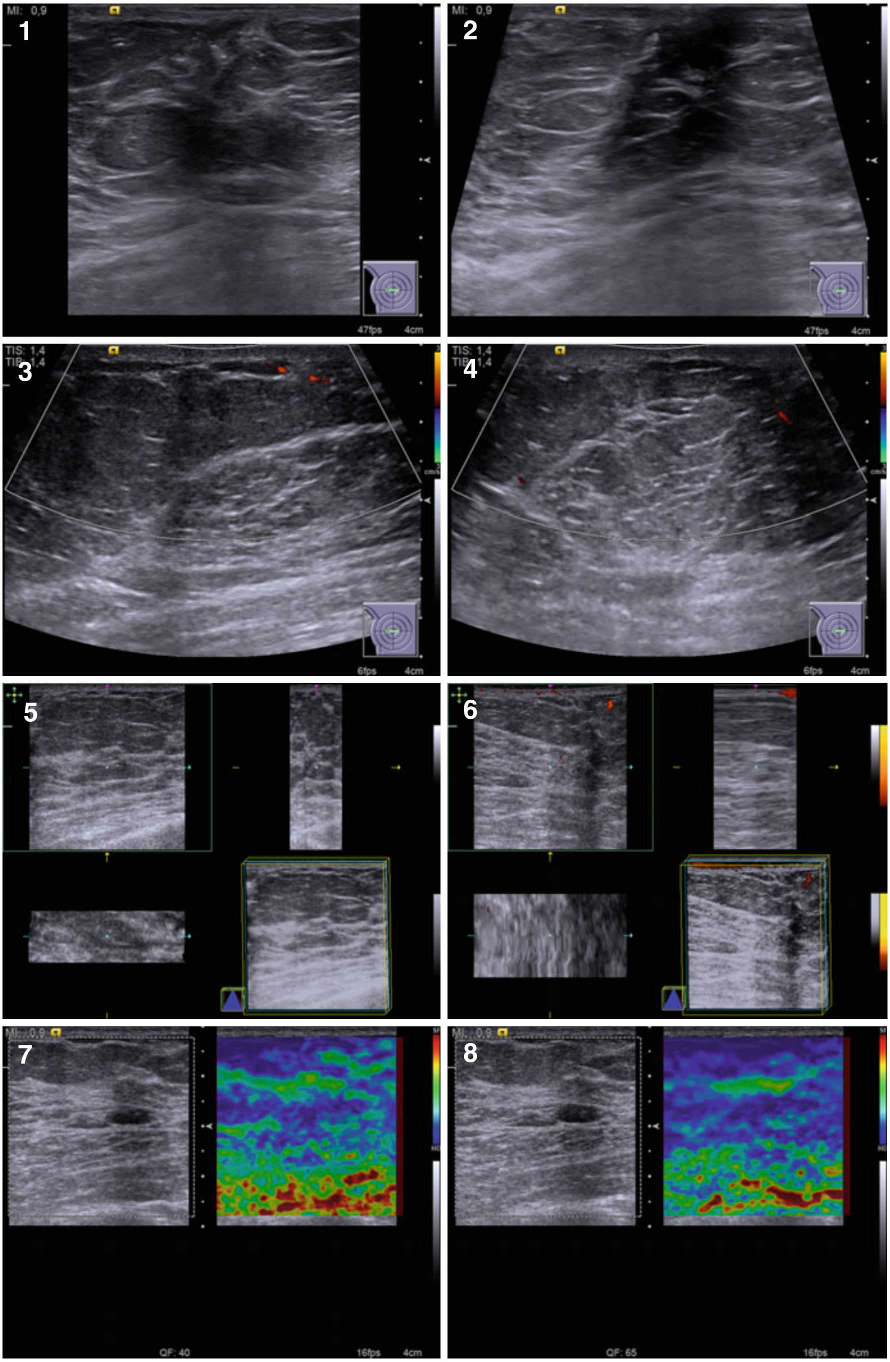

Fig. 7.2 (1–8) Gynecomastia. Grayscale US, CDI, 3D, and US elastography

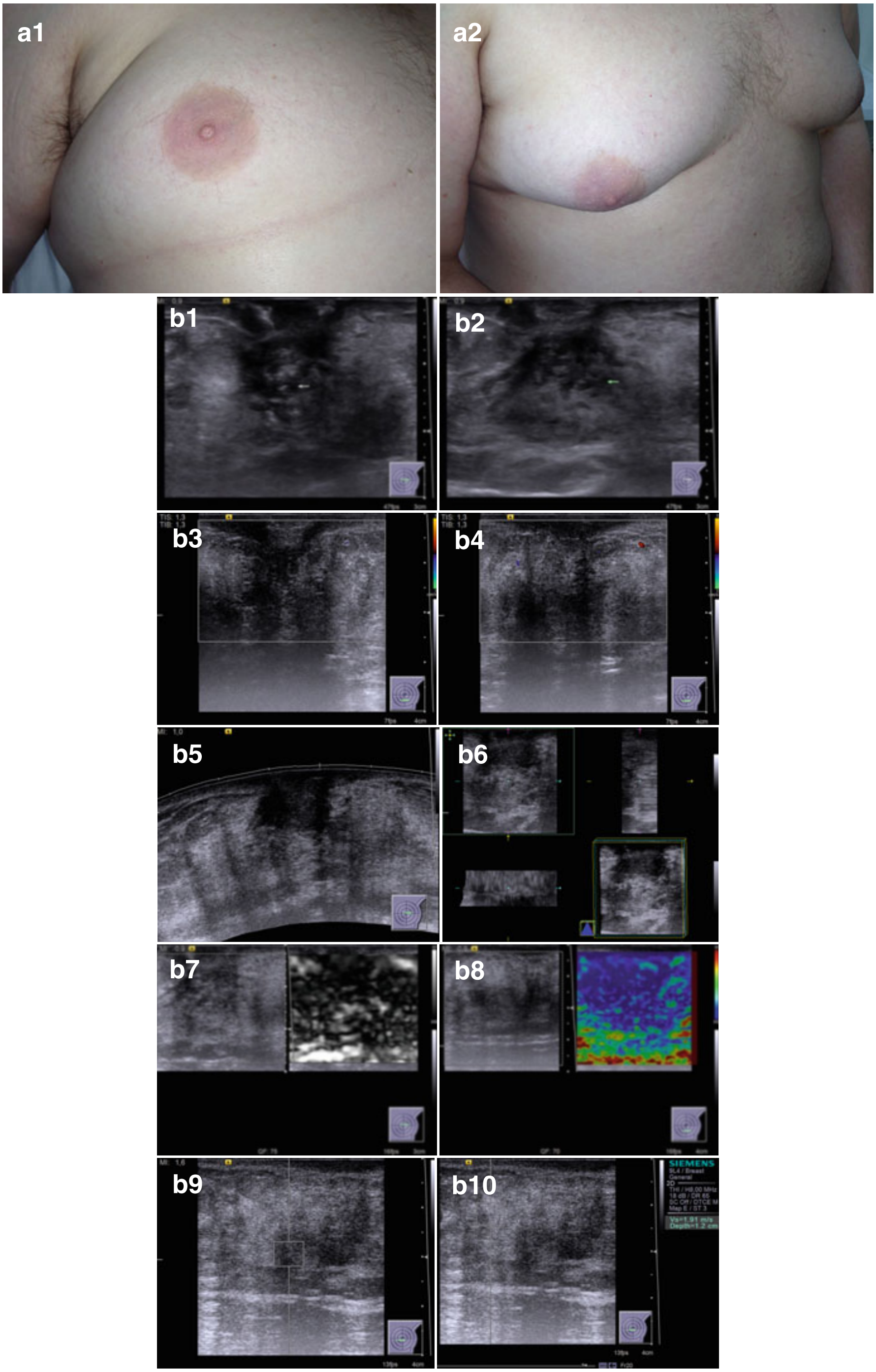

Fig. 7.3 Nodular gynecomastia. (**a**) (1, 2) Breast view. (**b**) (1–10) Grayscale US, CDI, panoramic scan, 3D, US elastography, and ARFI. (**c**) (1–4) Hematoxylin–eosin-stained smears. Original magnifications ×100 and ×400

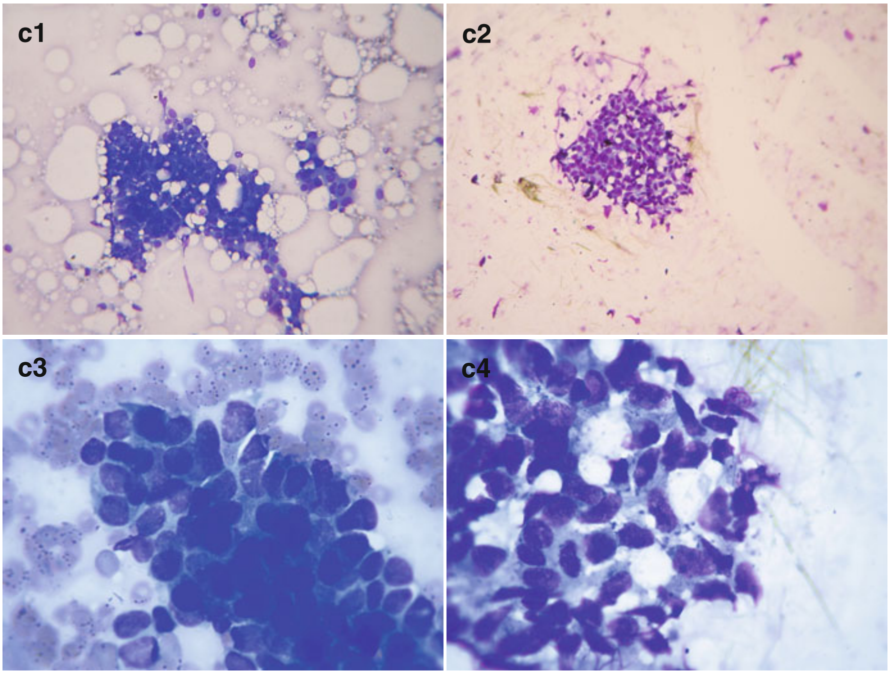

Fig. 7.3 (continued)

lateral acoustic shadows may be defined on each side of the adipose lobe. These artifacts completely disappear when the tissues are compressed with the US probe. The whole breast in false gynecomastia is composed of the adipose component, which is avascular with CDI, PDI, and 3DPD.

The development of gynecomastia passes though three clinical stages: acute, intermediate, and chronic. The acute, or active, phase of gynecomastia is a consequence of proliferation and hyperplasia of the ductal epithelium and myoepithelial tissue. US shows that healthy adipose tissue of the rudimentary gland under the nipple is substituted for by a hypoechoic field with rough indistinct contours (Fig. 7.6). The layer of fat is deformed. Such a picture can be similar to a malignant tumor. CDI is of no benefit due to its low specificity because the increased vascularity may be of inflammatory character.

As opposed to the female breast, which reacts with a change in vascularity to any pathological process, gynecomastia in men does not exhibit a local increase in vascularity. CDI reveals predominantly avascular lesions, as shown by the virtual organ computer-aided analysis (VOCAL) method of quantitative assessment of vascularity (an option incorporated in some premium-class US devices). The method is based on 3D reconstruction in an angiographic regimen with an automatic cal culation of color pixels in the volume specified by the sonographer. However, vessels may be detected in approximately 21 % of patients. They mainly exhibit a perinodular pattern in young and middle-aged men, whereas elderly patients have

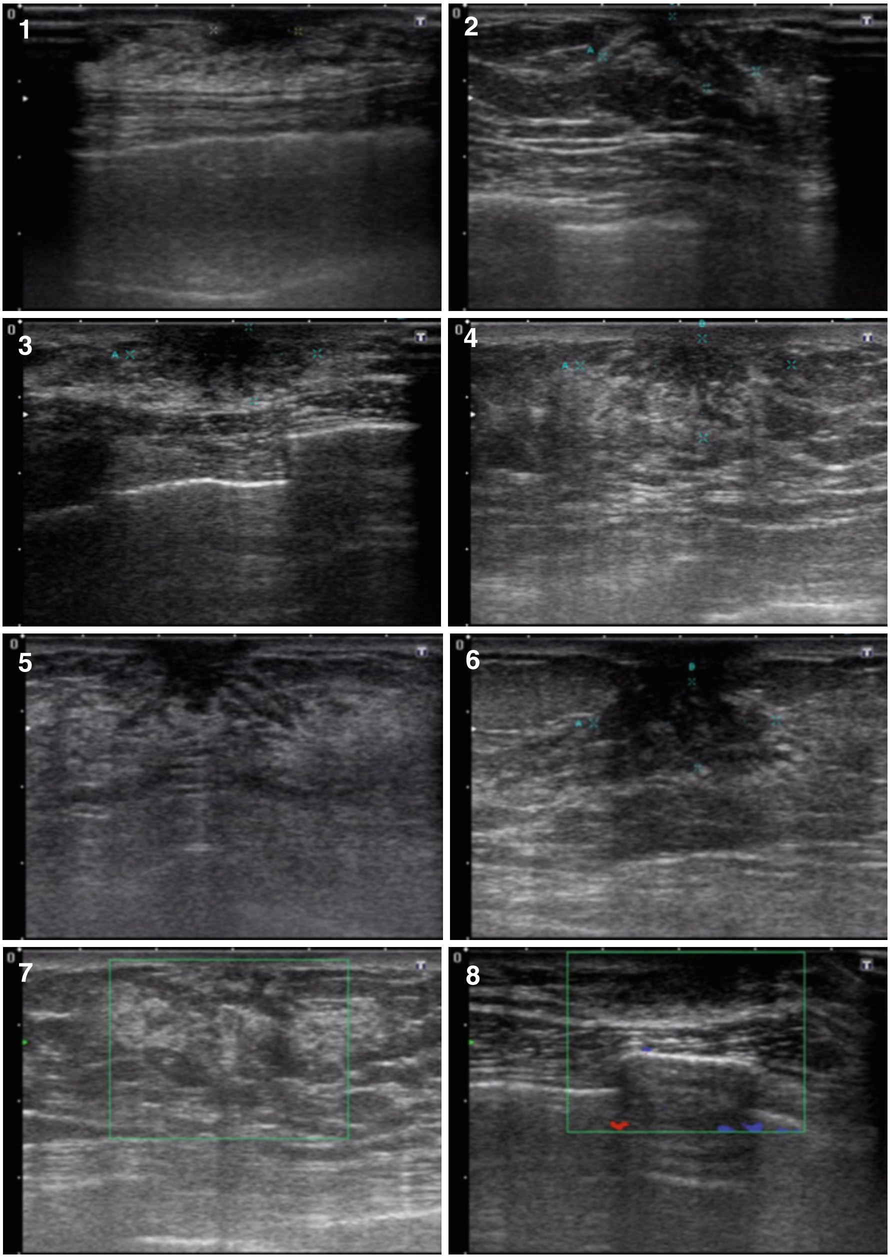

Fig. 7.4 (1–8) Treelike gynecomastia. Grayscale US, CDI, panoramic scan, 3D, and US elastography

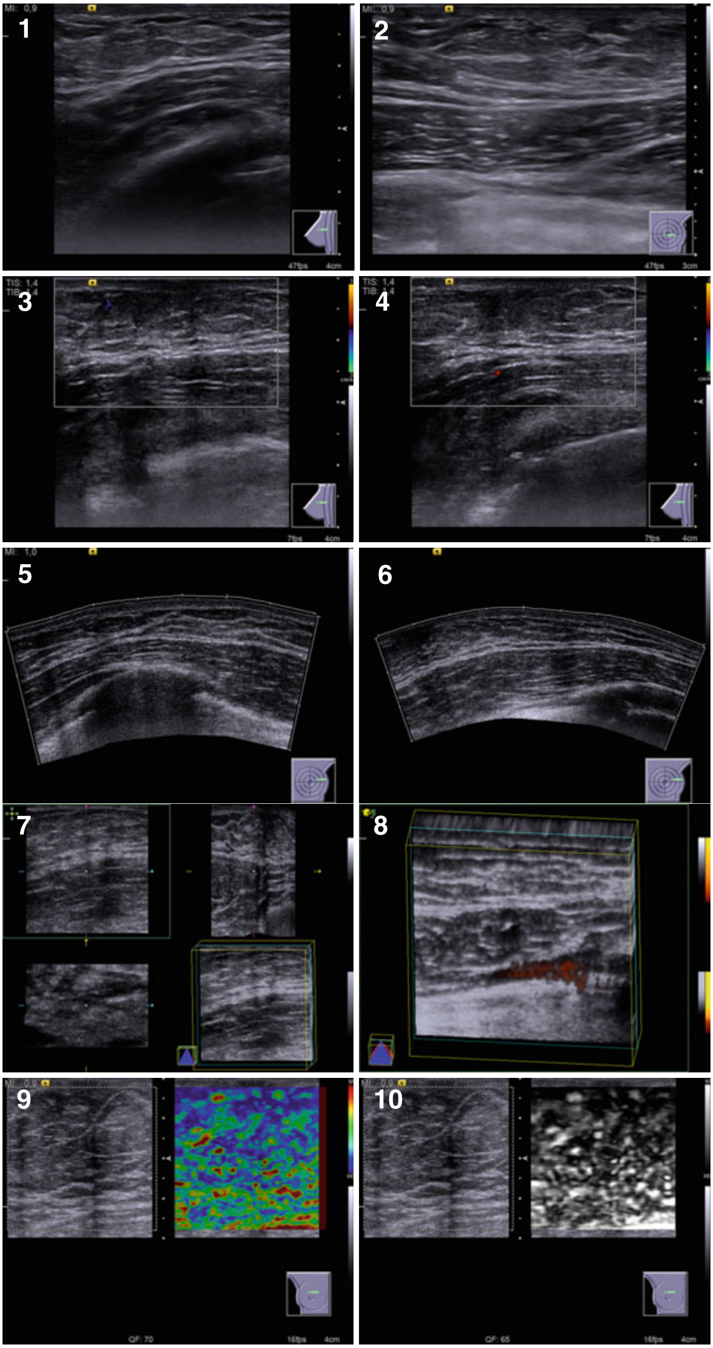

Fig. 7.5 (1–10) Diffuse glandular gynecomastia. Grayscale US, CDI, panoramic scan, 3D, and US elastography

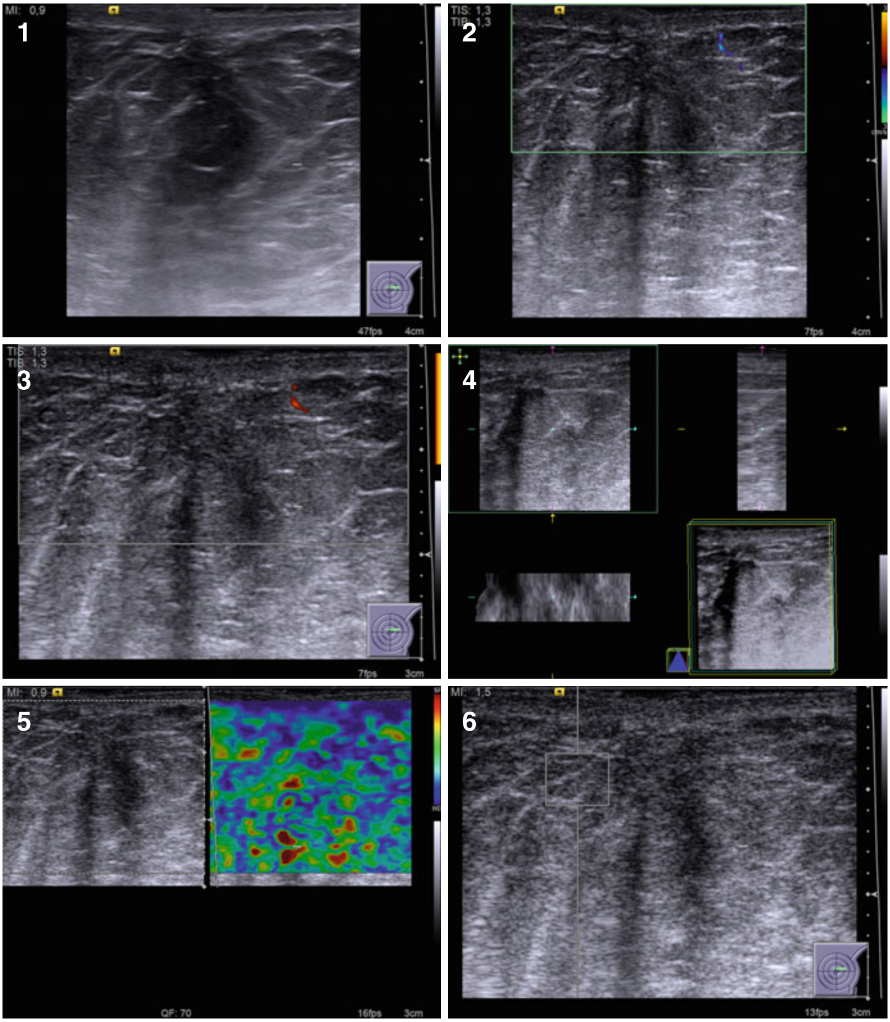

Fig. 7.6 (1–6) Diffuse glandular gynecomastia. Acute phase. Grayscale US, CDI, PDI, 3D, US elastography, and ARFI

an intranodular type of vascularity more often (Ivanov et al. 2013). The vascularization is usually poor. One or two tortuous vessels of small caliber may be identified. More than 75 % of reported vessels exhibit venous blood flow with spectral Doppler characterized by monotonous spectrum and velocity of less than 10 cm/s. Arterial blood flow is more often reported in young men; the number of detected arteries decreases with age. True gynecomastia is most often characterized with high resistance (resistive index (RI) > 0.6) and slow (peak systolic blood flow velocity (PSV) <10 cm/s) blood flow (Ivanov et al. 2013). There is no dependence between the increase in vascularity or collections of intranodular and perinodular vessels and

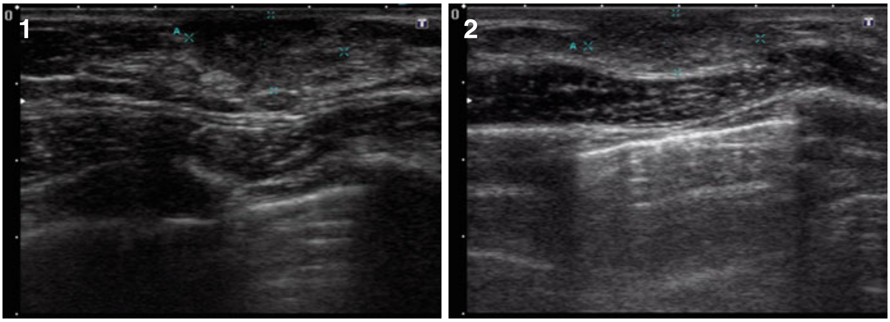

Fig. 7.7 (1, 2) Diffuse glandular gynecomastia. Intermediate phase. Grayscale US

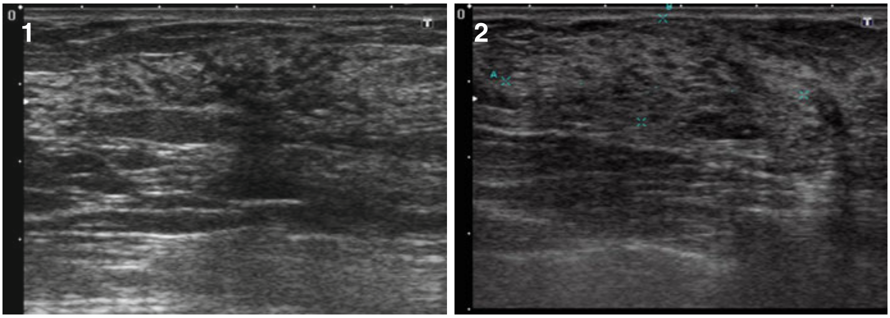

Fig. 7.8 (1, 2) Diffuse glandular gynecomastia. Chronic phase. Grayscale US

the severity of process or proliferative activity of a lesion. Differential diagnoses of breast lesions should not be based solely on quantitative Doppler data.

The intermediate (mixed, transitional) phase is histologically characterized with a proliferation of the ductal epithelium in combination with moderate fibrosis around the ducts. US reveals a significantly hypoechoic area under the nipple and an echogenic field of glandular tissue, which is identical to the US image of a healthy female breast (Fig. 7.7). It is possible to specify subareolar ducts and their branches. Such tissue can be accompanied with posterior shadowing of a random character depending on the position of the US probe and scan angle, which distinguishes this kind of shadowing from the shadow behind a malignant tumor.

In the chronic phase, dense fibrous tissue deposits appear around the ducts. US images are similar to those of healthy female breasts (Fig. 7.8). Glandular tissue, subareolar ducts, and their branches are well defined.

Fibrosis, which is defined clinically and sonographically, is the principal cause of poor prognosis of the involution of gynecomastia if its volume exceeds 70 cm^3 and the disease lasts longer than 1.5 years. Retrospective assessment of the results of histological examinations showed that full involution is possible with a smaller volume of gynecomastia, absence of fibrosis, and small duration of the disease;

partial involution is possible at the expense of the reduction of intramammary fat in diffuse and mixed types. Involution of focal gynecomastia is improbable (Brovin 2006).

US technologies are highly efficient in the differentiation of the density of breast parenchyma and specification of breast lesions in men with gynecomastia. The sensitivity of US in gynecomastia is 86 %, with a specificity of 82 % (Ivanov et al. 2013; Sencha et al. 2013a, b).

Dynamic follow-up with examinations every half a year is indicated in cases of pubertal gynecomastia accompanied with the absence of clinical symptoms of endocrine or somatic pathology and the lesion not exceeding the diameter of the areola. In cases when gynecomastia is larger than the areola or/and gynecomastia arises prior to puberty without any symptoms of endocrine or other pathology, the patient should undergo basic examination with routine blood and urine tests, biochemical and hormone blood tests (LH, FSH, testosterone, estradiol, prolactin, TSH, T4, anti-TPO antibodies). If clinical or laboratory signs of endocrine or/and other pathology arise, further radiological examination is necessary (Ivanov et al. 2013).

An *example US report* of a patient with gynecomastia is:

First name, middle initial, last name:
Age:
Date:
The breasts are of masculine type, mainly composed of adipose tissue. Fibrous tissue is moderately expressed in all regions.
A heterogeneous hypoechoic area, 7 × 20 mm in size, with irregular indistinct margins, avascular with CDI and PDI, irregular with US elastography, and moderately painful with compression is detected in the retroareolar area of the left breast. The average shear-wave velocity with ARFI within the described area is 2.8 m/s.
Lactiferous ducts are not observed. Axillary, supraclavicular, and subclavian lymph nodes are not enlarged.
CONCLUSION: US imaging results suggest an acute phase of nodular gynecomastia in the left breast.

7.2 Benign Breast Pathology in Men

Other possible causes of palpable breast masses in men can be benign lesions: lipoma, fibroadenoma, atheroma, schwannoma, angiolipoma, intraductal papilloma, cyst, and inflammatory changes, such as mastitis, subareolar sepsis, abscess, posttraumatic hematoma, adipose necrosis, tuberculosis, syphilis, etc. Newborn boys may develop galactocele. Benign breast tumors in men are rare. They comprise approximately 4.6 % of all male breast diseases (Ostrovskaya et al. 1988). The principal diagnostic feature is the detection of a mass within the breast (Fig. 7.9).

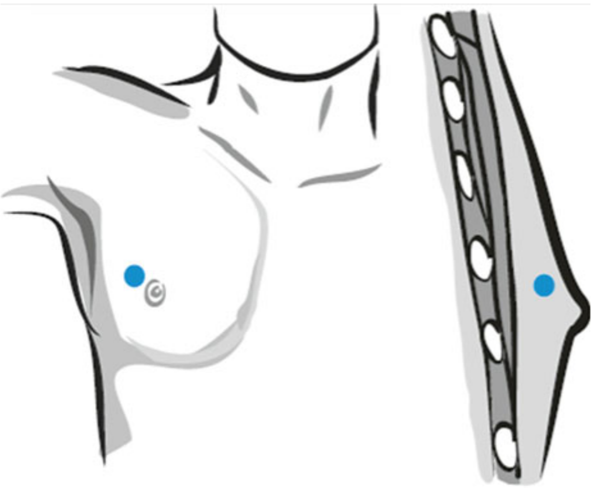

Fig. 7.9 Benign breast lesion. Scheme

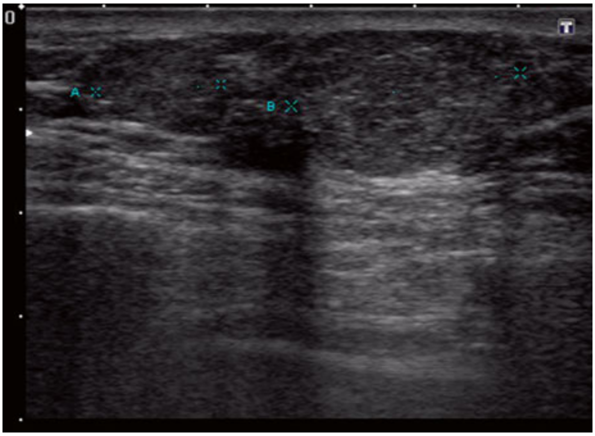

Fig. 7.10 Male breast lipoma. Grayscale US

Lipoma is a benign tumor originating from adipose tissue. It accounts for 9 % of all breast lesions (Rozhkova 1993). Lipomas that develop in the rudimentary breast of a man can be solitary or multiple. True lipoma consists of mature adipose tissue surrounded by a capsule. It presents as a mobile soft lesion of roundish or oval shape with palpation, which is often (not always) accurately delimited from the surrounding tissues. US diagnosis of breast lipoma is generally not difficult. US features of lipomas in men are the same as in women. They are almost always represented by a superficially located lesion of roundish or ovoid shape and exhibit some more typical features, such as (Fig. 7.10):

- Decreased or normal echodensity, comparable to healthy adipose tissue
- Sometimes irregular structure at the expense of fibrous incorporations

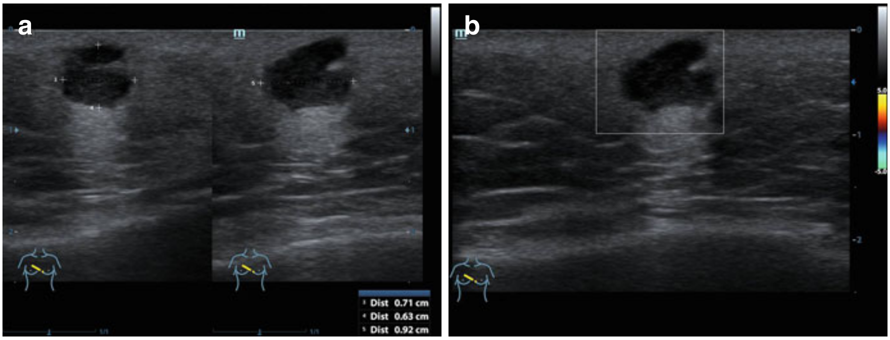

Fig. 7.11 Epidermal breast cyst. (**a**) Grayscale US. (**b**) CDI

- Easily deformed with compression
- Without posterior enhancement or shadow
- Always avascular with CDI, PDI, and 3DPD
- Regular mosaic staining with US elastography
- Average shear-wave velocity with ARFI is 1.9 m/s, strain ratio 1.1–1.2 as compared with healthy surrounding tissues

Differential diagnosis with liposarcoma is always necessary. The latter exhibits fast growth, relatively decreased echodensity, tuberous margins, increased density with elastography and palpation, and pathological vascularization. Tumor biopsy verifies the diagnosis.

Epidermal cyst is the third in the list of the most widespread benign lesions in a male breast. These cysts arise as a result of occlusion of hair follicles, in places of skin damage after trauma, surgeries, or bites of insects. US imaging may reveal a hypoechoic lesion of roundish or irregular shape adjacent to the skin (Chen et al. 2006) (Fig. 7.11).

Atheroma is a retention cyst of the sebaceous gland located in the skin and subdermal tissues. However, in some cases, it may exhibit both clinical and US features of a benign breast tumor. The correct diagnosis is based on the mammographic data, obtained in the projections with the atheroma positioned on the breast margin. This reveals a roundish homogeneous lesion with distinct, even contours. The image is similar to fibroadenoma. Its connection to the breast skin is clearly identified. One characteristic feature is skin prominence in the location of the atheroma. Acute angles between the skin line and the lesion are typical for atheroma. Long-existing atheromas with slow increases in size compress the surrounding tissues, resulting in the characteristic "rim of safety."

Atheroma exhibits the following US features (Fig. 7.12):

- A lesion comparable in echodensity to adipose tissue, most often isoechoic
- Distinct contours
- Homogeneous or heterogeneous structure (because of fibrous incorporations)
- Always avascular with CDI, PDI, and 3DPD
- Without or having poor homogeneous color pattern with US elastography

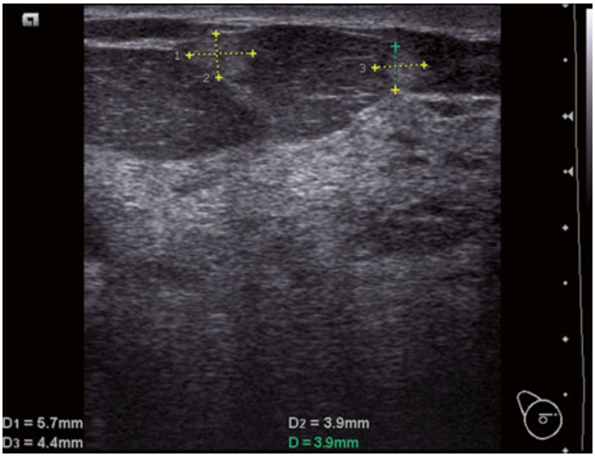

Fig. 7.12 Breast atheroma in a man. Grayscale US

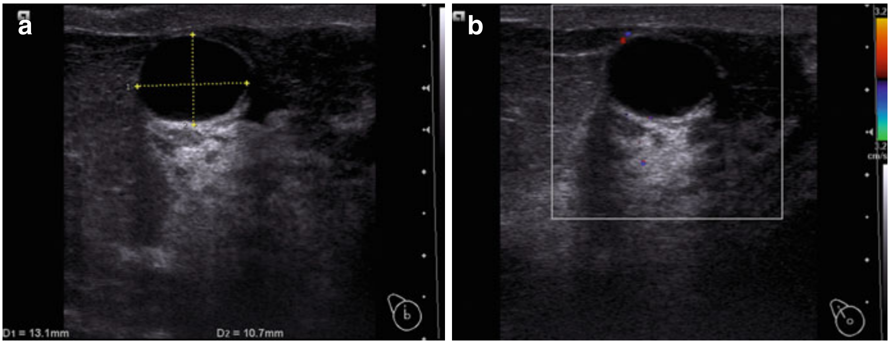

Fig. 7.13 Simple breast cyst. (**a**) Grayscale US. (**b**) CDI

- Average shear-wave velocity within the lesion of 1.6 m/s with ARFI, average strain ratio of 1.1–1.2 in relation to healthy tissue

True breast cysts in men are rare. Cysts in men have the same origin and exhibit the same US features as in women. The adipose background of the male breast permits accurate differentiation of the cystic wall. In cases of inflammation within the cyst or gynecomastia, cystic margins are difficult to specify. Hence, one may experience some difficulties in the differentiation of the cyst from breast malignancies. Complete information regarding the inner and outer contours of a cyst, as well as the wall thickness and presence of luminal masses, may be obtained with pneumocystography.

Cysts can have clinical symptoms. They may be palpable as individual or multiple elastic lesions, which are easily movable and often painful. They can be individual, multiple (more often), unilateral, bilateral, simple, or complex. US imaging permits a precise differentiation of cysts in 100 % of cases.

The majority of breast cysts exhibit these typical US features (Fig. 7.13):

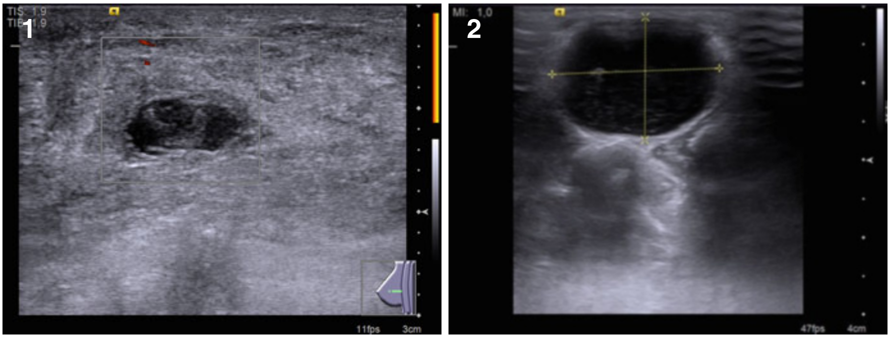

Fig. 7.14 (1, 2) Complex breast cyst. Grayscale US

- Anechoic structure
- Homogeneous structure
- Roundish or oval shape
- Distinct margins
- Posterior echo enhancement
- Easy deformation and painless with compression
- Avascularity with CDI and PDI
- Absence of color pattern within the lesion with US elastography

Up to 95 % of breast cysts have no solid component on the capsule (Korzhenkova 2004). Such cysts are characterized as simple (typical) and uncomplicated. There are also breast microcysts (with sizes of 1–2 mm) and macrocysts (simple and multilocular), individual and multiple. Breast cysts in some cases may not exhibit such a characteristic symptom as posterior echo enhancement. This happens more often in small cysts, cysts surrounded by dense structures, near to the thorax, or in cysts with an expressed fibrous capsule. Atypical cysts may be sometimes observed among fluid breast lesions (Sergeeva and Sotskova 2009). There are long-existing, recurrent cysts and cysts with inflammation.

US features of atypical cysts are (Fig. 7.14):

- Thick cystic walls
- Contents with inclusions
- Solid component with different types of vascularization
- Staining of the walls (especially, posterior) and solid component with US elastography

Malignant lesions more often cause complex cysts in men than in women. Atypical US images of cysts in up to 2 % of cases can be the result of intracavitary growth originating from the cystic wall (Korzhenkova 2004). Seventy-five percent of them are papillomas of benign nature. Twenty percent of intracystic breast lesions are associated with papillary cancer. All kinds of growth connected with the cystic wall, especially if vascularized, require US-guided biopsy with cytology and are indicated for sector resection with urgent histology (Fig. 7.14).

Fig. 7.15 Intraductal papilloma in a man. Grayscale US

Intraductal papilloma presents with a lesion that grows within the lumen of lactiferous ducts of the breast. Solitary or multiple lesions may arise. Intraductal papilloma is associated with abnormal discharge from the nipples. Similar discharge less often occurs in duct ectasia or mastitis. However, 13 % of cases of bloody nipple discharge and 7 % of cases of serous discharge are consequences of ductal breast carcinoma. The only method of revealing intraductal masses is ductography – the method of artificial contrasting of lactiferous ducts with iodine-containing water-soluble agents while performing X-ray mammography. Intraductal lesions are an absolute indication for breast surgery. Ductography usually follows routine mammography and cytology of nipple discharge smears. A triad of cytologic features including macrophages, erythrocytes, and papillary structures or separate glandular epithelial cells is typical for intraductal papilloma. Nevertheless, ductography is contraindicated in patients with inflammatory process in breast ducts or breast carcinoma. This aims to avoid spreading the infection in the first case and cancer cells in the second. The value of US in the diagnosis of intraductal pathology is limited by such factors as the resolution of the equipment (a conventional scanner detects lesions greater than 2–3 mm) and the size of the intraductal lesion (tumors are often smaller than 2 mm).

Intraductal papilloma can cause isolated dilation of a duct (ducts) in the retroareolar area or breast periphery. The tumor itself looks like a solid papillary lesion of ordinary or increased echodensity with a lobulated border located within a cystic cavity.

Papillomas are often characterized by the following US features (Fig. 7.15):

- Solid papillary structures in the lumen adjacent to the walls.
- Isoechoic or hyperechoic, lobulated structures with rough borders against the surrounding fluid component. Ductal papillomas diagnosed at the level of peripheral ducts (>3 cm from the nipple) and accompanied with atypical epithelial hyperplasia on the data of FNAB with cytology are always suspicious for ductal cancer.

- Hypovascularization or hypervascularization of solid component.
- Staining of the walls (especially, posterior) and solid component with US elastography.

Fibroadenoma in a man is an extremely rare finding (Ostrovskaya et al. 1988). Unlike fibroadenomas in women, fibroadenomas in men seldom grow larger than 2 cm.

Fibroadenoma usually has the following US features:

- Solid breast lesion of decreased echodensity
- Homogeneous structure
- Spherical or oval shape
- Accurate smooth borders
- Avascular or hypovascular in CDI and PDI
- Irregular mosaic staining with US elastography different from the surrounding structures

The tumor grows slowly throughout several years and compresses the surrounding tissue. Hence, it is often possible to define the capsule of the lesion. It should be differentiated from breast carcinoma and sarcoma.

Breast sarcoma is also a rare disease. It accounts for 2–5 % of all malignant breast lesions in men and 0.6–1 % in women (Warshavsky et al. 1980; Ostrovskaya et al. 1988; Treyvand and Nessler 1982). Men with breast sarcoma are 10–20 years younger than men with breast carcinoma. Sarcoma exhibits fast enlargement of a solitary or multiple nodules of the tumor. The skin over the tumor becomes stretched, thin, glittering with reddish and bluish tint and prominent vascular rete. Fibrosarcoma in men, as well as in women, is the most frequent histological type (Ostrovskaya et al. 1988).

7.3 Inflammatory Processes

Nonspecific inflammatory process (mastitis) in male breast is reported significantly less often than in women. It is the rarest condition (2.6 %) among all benign abnormalities in men (Ostrovskaya et al. 1988). Nevertheless, its diagnosis is extremely difficult. The inflammation is so indistinctly expressed that neither the results of the physical examination nor local symptoms with careful correlation to mammography ensure the correct diagnosis. The history of the disease and follow-up are extremely important in such cases. Generally, the inflammation appears in young and active men who note the trauma of the breast or anterior aspects of the thorax soon before the disease.

Almost all cases of inflammation are associated with retraction of the nipple, local skin edema (with hyperemia in some cases), and enlargement of regional lymph nodes. It is accompanied with a change in the general somatic status of a man and abnormal laboratory test results.

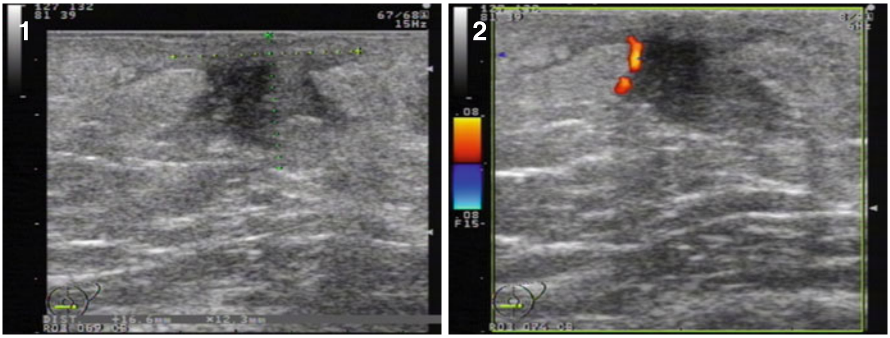

Fig. 7.16 (1, 2) Mastitis. Grayscale US and CDI

The inflammatory process can be acute or chronic and local or diffuse. Acute mastitis exhibits the following phases of development: serous inflammation, infiltration, and abscess.

Mastitis has the following US features (Fig. 7.16):

- Thickening of the skin over the area of inflammation (as compared to the skin in healthy areas and the other breast)
- Increase in echodensity of subcutaneous fat
- Indistinct margin between the deep layer of derma and adjacent structures
- Poor differentiation of breast structures
- One or several hypoechoic areas with distinct or vague margins within the breast
- Underlined connective tissue component
- Enlargement of axillary lymph nodes

The expression of US features directly depends on clinical symptoms. In some cases, such as late or inadequate treatment, the inflammation develops from serous infiltration to diffuse purulent stage with fine foci of purulent fusion of the parenchyma, which aggregate and form abscesses. Breast abscesses can be classified in accordance with their location into subcutaneous, subareolar, intramammary, and retromammary. In the majority of cases, the infection enters the breast tissue through the damaged skin of the nipple, areola, or epithelium of lactiferous ducts. However, the infection may develop because of a weak immune response with hematogenous or lymphogenous contamination. The knowledge of clinical signs of acute mastitis is important for differential diagnosis with the infiltrative type of breast carcinoma. Acute mastitis begins acutely, with severe pain, local edema and hyperemia, dense infiltration, local hyperthermia, and fever. The formation of an abscess is usually characterized with a decrease in pain and the development of fluctuation in the area of inflammation.

Breast abscess in men, subareolar abscess in particular, is sonographically characterized with a mass of heterogeneous structure caused by anechoic necrotic foci and echogenic detritus, which is accurately bordered by an echogenic

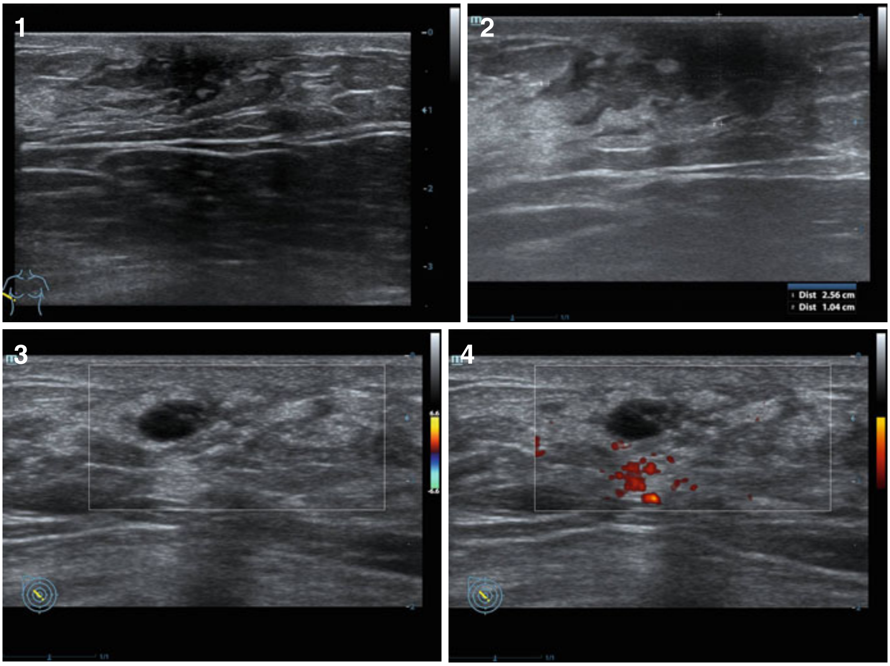

Fig. 7.17 (1–4) Subareolar infiltrate developing breast abscess. Grayscale US and PDI

pseudocapsule (Fig. 7.17). An abscess can have a mainly hypoechoic or anechoic structure. It is avascular with CDI and PDI and often surrounded with the zone of increased vascularity. Vessels in acute mastitis are generally regular with uniform caliber without dilations and diverticula. Follow-up of patients with acute mastitis with appropriate conservative treatment generally reveals the normalization of skin thickness and breast tissue structure (decrease in the number and size of hypoechoic and anechoic areas and disappearance of reactive lymph nodes).

In cases of difficulty in the differentiation of acute mastitis and diffuse breast carcinoma, special care should be paid to case history, clinical data, mammographic features, and US features. Biopsy of the breast and abnormal lymph nodes with cytology or histology is of great benefit. Core biopsy in cases of expressed inflammatory process is often impossible and, in the diffuse type of breast carcinoma, appears not to be informative.

Breast tuberculosis is seldom reported and mainly affects women. Men comprise approximately 4 % of all patients with breast tuberculosis. Nodular, fistulous, ulcerative, and sclerosing types of breast tuberculosis are specified. The nodular type is characterized by dense painful nodules, which merge and form an infiltration with the nipple retracted. Axial lymph nodes are enlarged and dense. This stage of tuberculosis can be mistaken for breast cancer. Further development of tuberculous granulomas results in their destruction with chronic fistulas and purulent discharge. Ulceration of the skin over the infiltrations shows rough thick edges and poor granulations at the bottom.

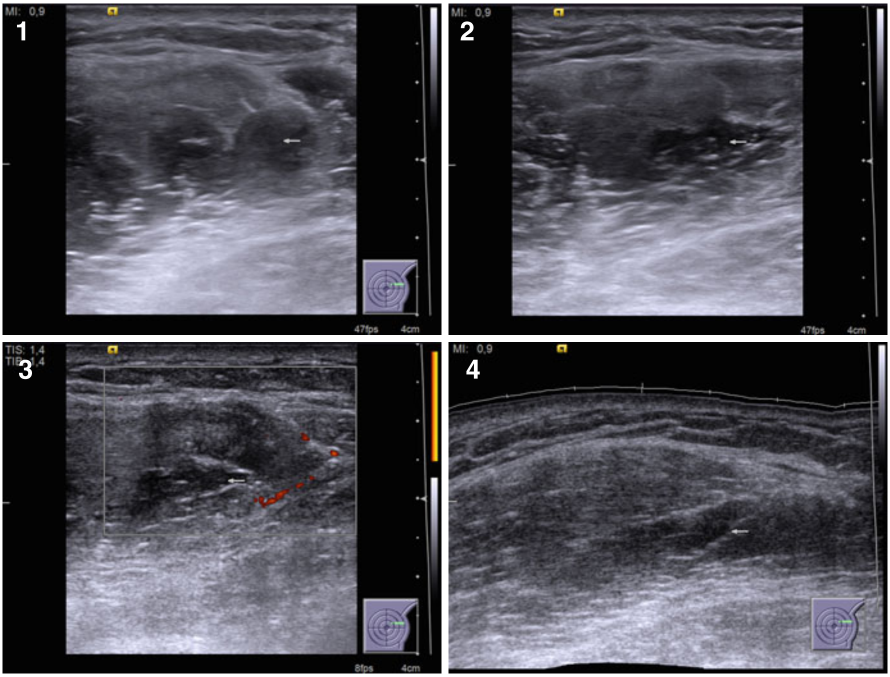

Fig. 7.18 (1–4) Breast bruise and edema of soft tissues. Grayscale US, PDI, and panoramic scan

Ulcers in the nipple and areolar area are similar to those seen in Paget disease. The combination of tuberculosis and cancer of the breast in a man with involvement of axillary lymph nodes was described by L. Zappala (1959). Differential diagnosis of these diseases is difficult, because breast tuberculosis in modern conditions often has a solitary character. It complicates differentiation from cancer and suggests hematogenous contamination from old foci of tuberculosis (Ostrovskaya et al. 1988).

7.4 Breast Trauma

Breast trauma in men is reported much more often than in women and comprise 1–2 % of all breast pathologies. The trauma may be closed or open, isolated or combined. Bruises and hematomas form the closed type of breast trauma. Open damages include cut, gunshot, bitten, and other wounds. Breast traumas can be combined with damage of the thorax (such as fractures of the ribs or breastbone, pneumothorax, hemothorax) and the organs of the thoracic cavity. Any breast trauma can be complicated by bleeding or infection. Injury leads to the rupture of vascular walls and hemorrhage. Small hemorrhages usually stop spontaneously (Fig. 7.18). Breast tissues withstand direct trauma well. However, good innervations may result in traumatic shock, especially if paraareolar or papillary areas are damaged.

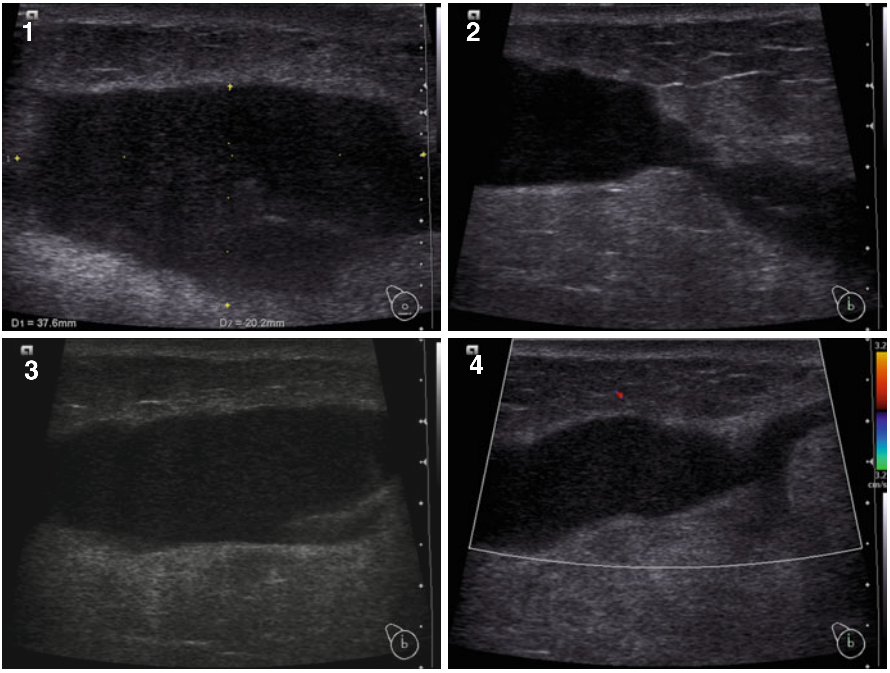

Fig. 7.19 (1–4) Posttraumatic breast hematoma. Grayscale and CDI

US is best used for the specification of hemorrhage and breast hematoma. Posttraumatic changes include the following periods: acute, the first 4–7 days; intermediate, up to 2 weeks; and late, a year and longer after the trauma. Division into the periods is necessary for the correct interpretation of sonographic and clinical signs. Breast hematoma requires special attention because it can be the first sign of a malignant tumor, considering neoangiogenesis (because vessels within a malignant neoplasm have no muscular layer, are fragile, and are easily damaged).

During the first few days and weeks, hematoma is detected with US as a lesion with the following features (Fig. 7.19):

- Anechoic
- Roundish or irregular shape
- Of various sizes
- Avascular with CDI and PDI
- Poorly colored with elastography
- Generally located superficially

Hematomas undergo slow resorption and/or organization. Breast trauma can also induce breast fat necrosis, which is rare in men as compared with women. It is defined as hypoechoic or echogenic breast fields of irregular shape with indistinct or distinct margins, often with posterior acoustic shadow (Fig. 7.20).

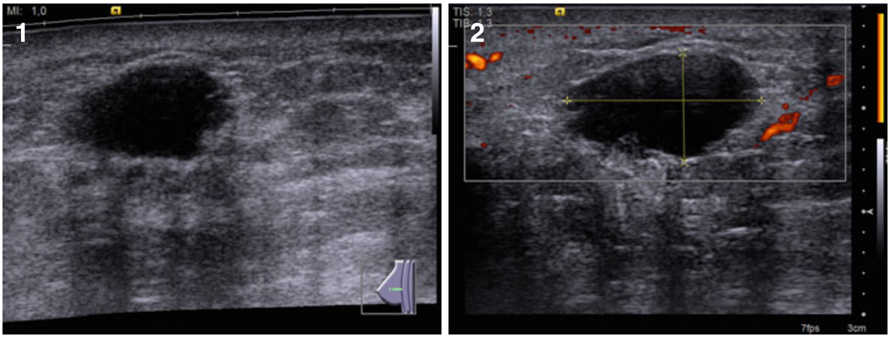

Fig. 7.20 (1, 2) Posttraumatic breast in a man. Panoramic scan and PDI

The architectonics of the surrounding tissues is quite often affected. Coarse calcifications also appear, which have irregular shapes or correspond to the roundish margins of the lesion. The location of such masses corresponds to the place of the former trauma or hematoma. Surgical interventions, inflammatory processes, local ischemia, and other conditions also can lead to such lesions. They need to be differentiated with breast malignancies. Breast trauma or surgery in a patient's history and absence of malignant signs with US and mammography suggest lipogranuloma. It is necessary to remember that there is a possibility of recurrent breast carcinoma in the scar. FNAB and cytology assist in the correct diagnosis. Breast MRI and excision biopsy may be indicated in most ambiguous cases.

Treatment Strategies for Breast Diseases, Types of Breast Surgery, the Postoperative Breast, and Follow-Up Principles

8

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Different breast diseases in men implicate different diagnostic and treatment strategies. Breast pathology is treated several ways. Unfortunately, today, there is no common view regarding the therapy of gynecomastia, inflammatory and traumatic breast diseases, benign lesions, and cancer in men. The principles of treatment of many of them are based on knowledge obtained during the treatment of women with similar pathology. Breast diseases in men are rare, and it takes a long time to collect enough data for analysis. Meanwhile, the diagnostic and treatment methods of breast diseases can change. This fact complicates the study of the treatment of male breast diseases.

Treatment of different types of gynecomastia can differ. Indications for surgery in boys with gynecomastia are relative. They are based on psychological and social aspects resulting from cosmetic defect. Surgical treatment of gynecomastia permits optimal cosmetic results. It consists of surgical repair of the subcutaneous adipose layer of the anterior thoracic wall, reduction of the areola in cases of significant estrogenization (diameter >5 cm), reduction of the peripapillary area in breast ptosis (if the inferior pole and areola are located under the inframammary fold), and nipple

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_8

eventration for nipple–areolar complex dystrophy (thinning of the areola, depression of papillary reflex) (Brovin 2006). Surgery for gynecomastia is indicated when the cosmetic defect invokes psychosocial problems, and prognosis of spontaneous breast involution is poor. In all cases, regardless the breast volume, subareolar surgical access is used. After excision of the gynecomastia, the defect with the fat from the surrounding area is repaired.

Breast carcinoma of locally extended and generalized types is subject to a complex approach that includes both local methods for treatment of the primary tumor (operation and/or radiation therapy) and systemic influence (chemotherapy, hormone therapy, etc.). The principal treatment of breast carcinoma in men is surgical and usually consists of radical mastectomy with conservation of pectoral muscles. Depending on the local status of the tumor, it is performed during the first stage of treatment. Preoperative treatment allows the reduction of the mass of the primary tumor influencing the micrometastases, which are often detected in men at the time of the initial diagnosis. Despite the significant number of clinical trials on the efficacy of various schemes of treatment, there is no accurate data regarding the combinations of medical influences on tumoral process that yield the best results.

The type of surgery is defined by the character of the breast pathology, the affected breast volume, and the degree of invasion into surrounding tissues. The following types of operations may apply in different situations:

1. Operations for inflammatory processes (acute or chronic mastitis) – dissection and abscess drainage
2. Operations for benign and malignant neoplasms (e.g., nodular gynecomastia, breast carcinoma)
   - Lumpectomy or excisional biopsy
   - Segmental mastectomy
   - Partial mastectomy; less than total mastectomy
   - Total mastectomy
   - Axillary dissection
3. Plastic surgery

Radical breast resection removes gland sectors with the tumor (one third or one half of the breast volume), the adjacent fascia of the pectoralis major and the pectoralis minor, and adipose tissues of the subclavian, axillary, and subscapular areas at early stages of cancer. Excision of a benign tumor or breast tissue suspicious for carcinoma can be performed with sector resection or lumpectomy. This is a method of choice in masses suspicious for breast carcinoma to verify the diagnosis and in benign lesions (lipoma, granuloma, chronic mastitis, etc.). Total biopsy of the tumor is an excision of only the breast lesion without surrounding tissues. It is used for benign lesions with a capsule or pseudocapsule, such as lipoma, cyst, or fibroadenoma.

Radical mastectomy involves the removal of the breast tissue, nipple, and areolar complex and a variable amount of the skin, pectoralis minor, and/or pectoralis major, as well as en bloc axillary dissection. A total (simple) mastectomy removes all breast tissue, the fascia of pectoralis major, the nipple, and the areolar complex.

An axillary dissection and a dissection of pectoral muscles are not performed, but sentinel lymph nodes may be removed. Hemimastectomy with lymph node dissection aims to remove one half of the breast with the adipose tissue of the axillary, subscapular, and subclavian regions. The pectoralis major and minor muscles are not removed. Simple mastectomy, mastectomy with lymph node dissection, and hemimastectomy with lymph node dissection are not widely used because of difficulties in the complete removal of adipose tissue with lymph nodes.

Different types of mastectomies can be accompanied by several complications. The most frequent are:

- Bleeding in the early postoperative period.
- Abundant lymphorrhea with collection of a significant amount of lymphatic fluid under the skin. Moderate lymphorrhea is a natural consequence of mastectomy because the excision of lymph nodes and vessels inevitably leads to abnormal lymph drainage.
- Infectious complications in the postoperative wound.

Breast reconstruction surgery aims to recover the shape and volume of the breast after mastectomy, trauma, or other injuries and is rarely performed in men.

There is no consent regarding the value of radiation therapy in the postoperative period in patients with breast carcinoma. Some authors report that radiation therapy in men who have undergone surgery for breast carcinoma does not increase the survival rate or influence local recurrence. Other data suggest the opposite. The only area of agreement is that a single radiation therapy in the postoperative period is not efficacious. Therefore, the general treatment of breast carcinoma includes radical mastectomy and radiation therapy for patients of high risk or with lymph node metastases (Letyagin 2006; Giordano 2005; Contractor et al. 2008). The greatest value of radiation therapy is expected in patients with a high risk of local recurrence of breast cancer. Hence, the principal aim of radiation therapy of breast cancer in men is a decrease in the number of recurrent tumors and metastases in regional lymph nodes. It is indicated in large primary tumors, tumors with a medial or central location, multicentric growth, a large number of surgically removed metastatic lymph nodes, and when radical operation is not possible (Fig. 8.1).

Chemotherapy and hormone therapy of breast carcinoma in men are based entirely on the principles that have proven efficacy in the treatment of the same pathology in women; no definitive data regarding the efficacy of adjuvant chemotherapy in male breast carcinoma exist.

Before the 1970s, orchiectomy was used in many men along with surgery and radiation therapy for breast cancer. Early works devoted to the efficacy of this kind of treatment reported the increase in lifetime in patients with stage IV cancer from 38 to 56 months (Letyagin 2006). Meanwhile, despite the efficacy of hormone therapy, it is not the principal method for palliative therapy. Many men reject this treatment. Additionally, adrenalectomy or hypophysectomy are associated with high risks of complications. Further studies revealed that they do not increase the survival rate. Hence, alternative chemotherapy and hormone therapies that allow avoidance of surgical interventions appear beneficial in such cases.

Fig. 8.1 Condition after radiation therapy of breast cancer in a man. Photograph

Antiestrogens were tested in male breast cancer. Tamoxifen is quite effective, although it induces more side effects in men than in women (Letyagin 2006). Many authors consider tamoxifen as a gold standard in the treatment of breast cancer in men (Giordano 2005).

Despite the complications that can accompany antiestrogen treatment of breast carcinoma in men, the idea of their use has not been rejected. The benefits of this treatment are significantly greater than the potential side effects. Therefore, antiestrogens should be included in all schemes of adjuvant treatment of hormone receptor-positive male breast cancers (Letyagin 2006; Korde et al. 2010). Clinical experience of endocrine therapy shows that a remission of an average duration of 17 months can be achieved in 69 % of patients (even with metastases in bones in some cases). Remission in men is often reached faster than in women (Makarenko 1998).

Chemotherapy for male breast cancer is not widely discussed. Polychemotherapy with cyclophosphamide, methotrexate, and fluorouracil (5-FU) is used in early stages as adjuvant treatment. The 5-year survival rate in the group with chemotherapy was 80 %. That was significantly higher than in other groups. In other reports, adjuvant chemotherapy in men with breast carcinoma of stage II or operable stage III provided a 5-year survival rate of 85 % (Letyagin 2006; Korde et al. 2010). Hence, initial stages of male breast cancer require adjuvant chemotherapy and hormone therapy. In these cases, the status of axillary lymph nodes, risk of local recurrence, and the hormone receptor status of a tumor should be considered. Adjuvant chemotherapy plus tamoxifen in estrogen receptor-positive cancers and only chemotherapy in estrogen receptor-negative tumors are recommended.

The majority of authors use tamoxifen for hormone therapy in the palliative treatment of breast carcinoma in men. This antiestrogen medicine is tolerated satisfactory. Its efficacy ranges from 25 to 58 % with an average duration of treatment of 7–21 months. It directly depends on the status of hormone receptors. In cases of hormone-negative tumors, the result of hormone therapy is generally significantly

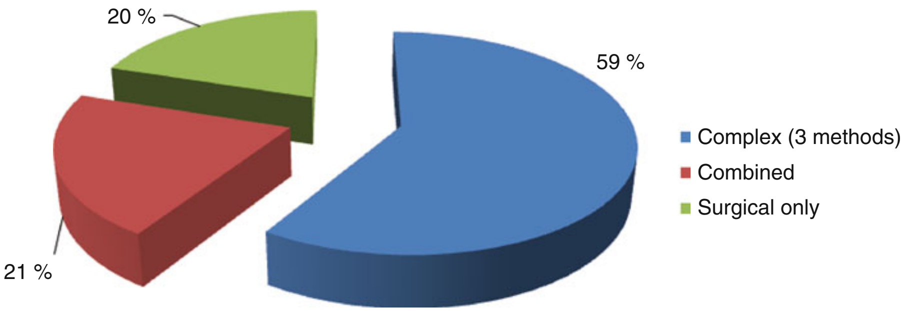

Fig. 8.2 Types of treatment of men with breast carcinoma

worse. Gonadotropin-releasing hormones and their analogs and antiandrogens may exhibit various side effects, such as hot flashes, loss of libido, erectile dysfunction, and gynecomastia. However, these side effects are rare. Other hormonal agents that cause temporary regression of remote metastases include estrogens, progestins, androgens, corticosteroids, and aromatase inhibitors. Optimum regimens of polychemotherapy for the treatment of metastatic breast cancer in men are not defined yet because of the absence of sufficient data for analysis (Giordano 2005; Letyagin 2006).

The medical approaches used for the treatment of men with breast cancer in our clinics depended on the local features and the character of the development of breast carcinoma. All 122 patients had surgical treatment (Fig. 8.2). A complex treatment that included a combination of more than three methods (chemotherapy, radiation therapy, hormone therapy) was applied in 59 % of cases. Combined treatment was used in 21 % of patients. Surgery only was performed in 20 % of patients. A radical mastectomy with conservation of pectoral muscles was performed in 118 patients (96.7 %) and a modified radical mastectomy (Patey) in 4 patients (3.3 %). The follow-up of men (as well as of women) with breast carcinoma is primarily based on imaging modalities, such as ultrasound (US), mammography, magnetic resonance imaging (MRI), computed tomography (CT), and scintigraphy.

The tissues of the postoperative scar (connective tissue with collagen fibers and fibrosis), local edema, and aseptic inflammation lead to a diversity of variants of US images of the postoperative breast (Fig. 8.3). US shows scars as areas of decreased or increased echodensity, heterogeneous echostructure, of linear (sometimes irregular) shape, rarely with posterior shadowing, avascular with color Doppler imaging (CDI) and power Doppler imaging (PDI), and moderately irregularly colored with US elastography. Alternatively, US sometimes reveals a total absence of any features of a scar. Fat in the area of surgery often exhibits a diffusely dense irregular structure, sometimes with echogenic incorporations of various dimensions and shapes (Fig. 8.4).

US is a highly effective method of diagnosis of early postoperative complications, such as local infection, hemorrhage, and others. After surgery, US is used to detect complications caused by clumps of blood or lymphatic fluid caused by insufficient drainage in the early postoperative period. Abundant lymphorrhea results in fluid

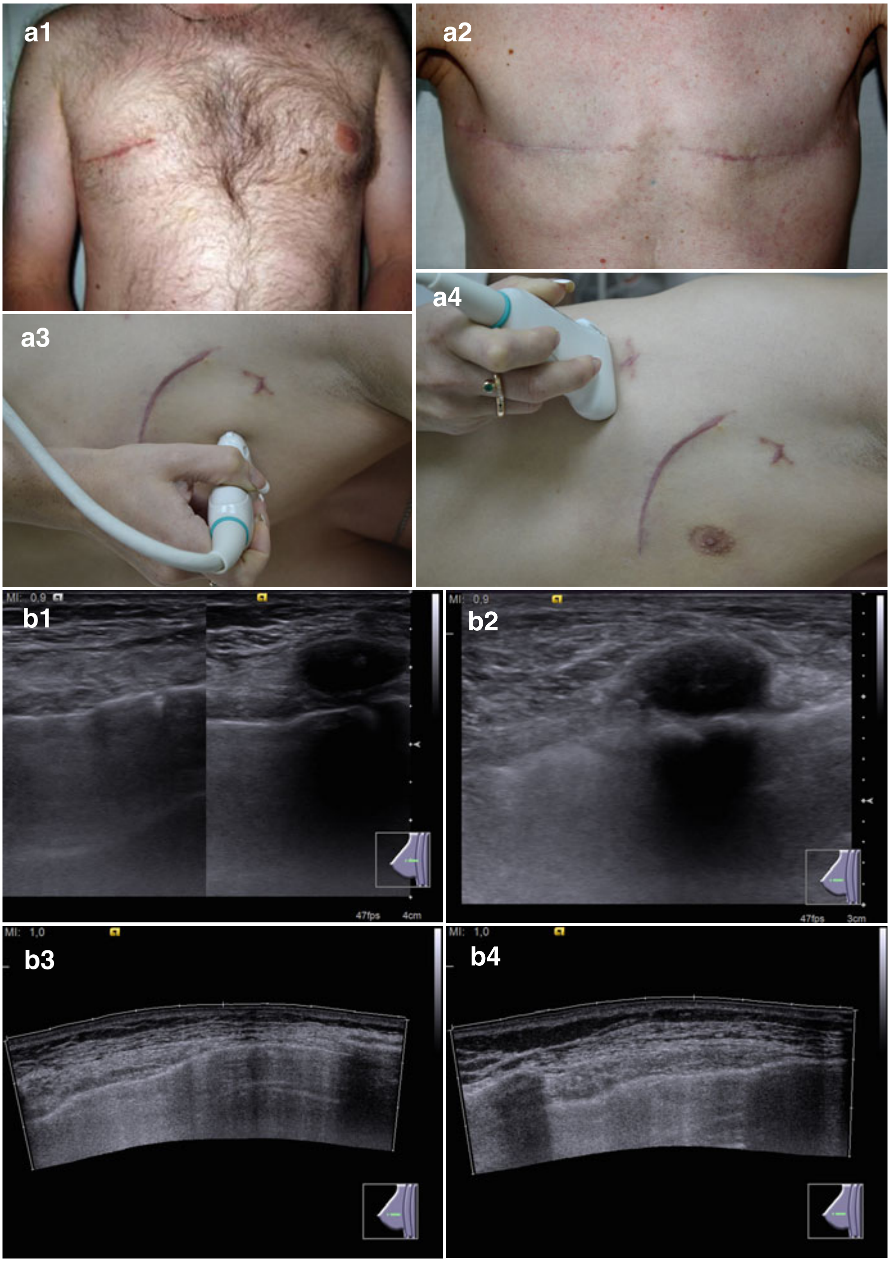

Fig. 8.3 Status after mastectomy. Anterior thoracic wall scar. (**a**) (1–4) Photograph. (**b**) (1–4) Grayscale US and panoramic scan

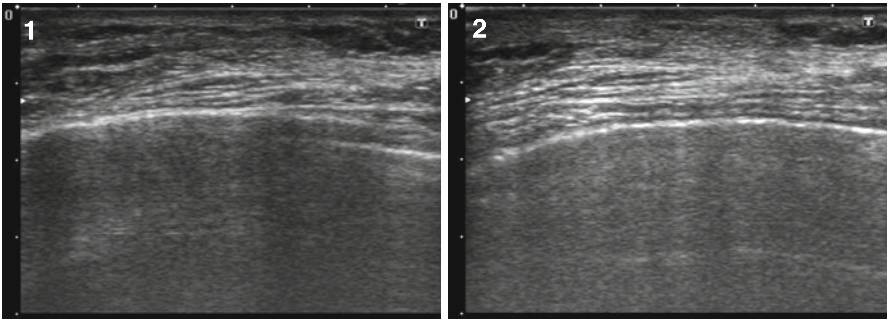

Fig. 8.4 (1, 2) Status after mastectomy. Local fibrosis. Grayscale US

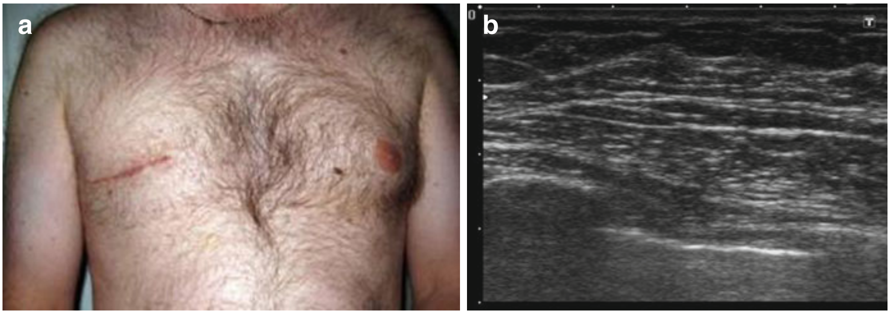

Fig. 8.5 Status after radical breast resection. (**a**) Photograph. (**b**) Grayscale US

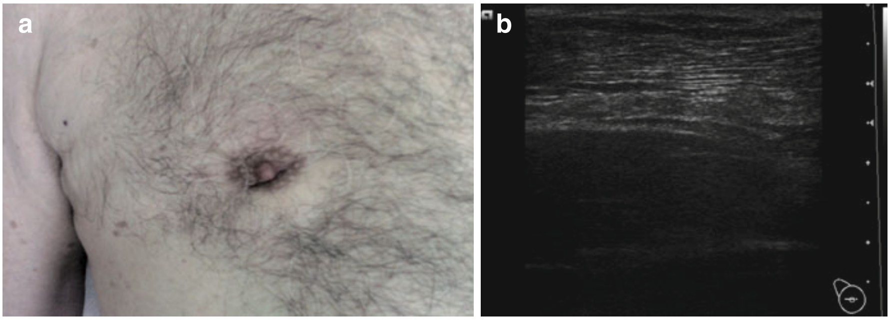

Fig. 8.6 Status after segmental breast resection. (**a**) Photograph. (**b**) Grayscale US

collection within operated tissues. It is sonographically registered as anechoic areas of various sizes with indistinct rough borders, located subcutaneously and/or in interfascial spaces, and leads to seroma. The increase in echodensity of the skin and subcutaneous tissues is a consequence of lymphedema (local lymphostasis in the postoperative region) (Figs. 8.5, 8.6, and 8.7). Hematoma is observed as an anechoic

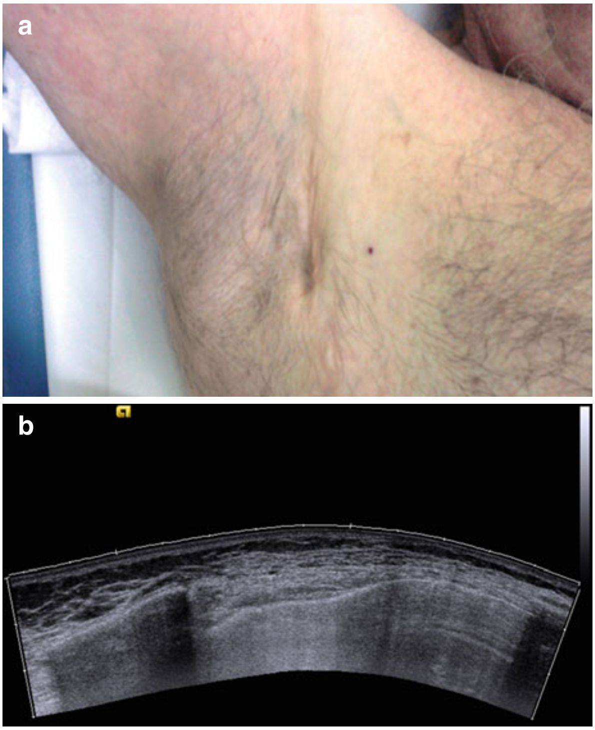

Fig. 8.7 Status after lymph node dissection. (**a**) Photograph. (**b**) Grayscale panoramic US

or hypoechoic lesion of regular (rarely, irregular) shape with accurate distinct margins and heterogeneous structure. It often contains linear echogenic incorporations and septations. CDI, PDI, and three-dimensional power Doppler vascular image reconstruction (3DPD) detect no blood vessels. If the volume of fluid collections is large and accompanied by fever or general inconvenience, US-guided puncture may be performed to aspirate the contents.

Recurrent Breast Cancer

9

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Studies devoted to survival analysis in men with breast carcinoma are significantly smaller than similar studies in women. In most cases, only the general survival rate is evaluated. The majority of authors agree that the prognosis in men with breast cancer is significantly worse than in women with similar disease (Dymarsky 1980; Guinee et al. 1993). The lower general survival rate in men results from an older age and later stages of the disease at the time of the diagnosis. According to the literature, the 5-year survival rate in men with breast carcinoma ranges from 36 to 66 % (Korde et al. 2010). The 10-year survival rates in patients with stage I–Ia is 91.5 %, IIb is 72.5 %, III is 44.2 %, and IV does not exceed 3.2 % (Guinee et al. 1993; Letyagin 2006).

The search for factors that permit accurate prognosis of breast carcinoma in men is still in progress. The most significant features are:

- Size of the primary tumor
- Histological type and degree of malignancy
- Presence of pseudocapsule and lymphatic and plasmacytic infiltration merging into surrounding tissues
- Status of regional and distant lymph nodes

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A.N. Sencha (ed.), *Imaging of Male Breast Cancer*,
DOI 10.1007/978-3-319-06050-7_9

According to many authors, breast cancer in men develops more slowly than in women; therefore, they seek medical attention later than women. At the same time, considering the small size of the male breast, it is reasonable to expect a shorter anamnesis in men than in women. However, clinical data show a longer history in men. According to Crichlow (1972), the average duration of the case history in men is 10–18 months. Later publications also demonstrate its long average duration, from 11 to 32 months (Todua 1980). Men with tumor sizes of 2–5 cm have a 40 % higher risk of death than men with tumors smaller than 2 cm (Letyagin 2006).

The histological type of breast carcinoma influences the prognosis (Paltsev and Anichkov 2005). Some histological types of invasive carcinoma are associated with rather good prognoses. They are so-called special histological variants – medullary, papillary, and mucous carcinomas. The morphology of male breast cancer is studied insufficiently because of a small number of observations available for individual researchers. In particular, there are discordant data regarding the existence of lobular and noninvasive types of ductal carcinoma in men (Ostrovskaya et al. 1988). One valuable morphological criterion for the prognosis of breast cancer in women is the indicator of proliferative activity of tumor cells. However, this is not mentioned in the literature with reference to male breast carcinoma.

The degree of malignancy of breast tumors influences the disease prognosis. The higher the degree of malignancy, the shorter the patient's life expectancy is. Patients with tumors of the first degree of malignancy live 5 years and longer after operation in 75 % of cases and longer than 10 years in 45 % of cases and with tumors of second and third degrees for longer than 5 years in 53 and 31 % and for longer than 10 years in 27 and 18 % of cases, respectively.

For breast carcinoma, the presence of a pseudocapsule; lymphatic and plasmacytic infiltration; invasion of extramammary tissues, lymphatics, and veins; and the presence of metastases are of important prognostic value (Letyagin 2006). These features should be mentioned in the diagnosis. The number of affected lymph nodes with metastases also influences the prognosis. Letyagin (2006) divided patients into three groups: without metastases in the axillary lymph nodes, with one to three metastatic lymph nodes, and with four or more metastatic nodes. The 5-year survival rates were 90, 73, and 55 %, respectively.

Early detection of recurrence of malignant tumors is a principal problem of modern oncology. According to the literature, the incidence of recurrence of breast carcinoma after radical resection or radical mastectomy ranges from 2.8 to 71 %. Even in patients without metastases in regional lymph nodes, the recurrence of cancer is reported as 25–30 % (Ciatto et al. 1994).

Despite complex and combined approaches to the treatment of patients with breast cancer, 40–50 % of men, as well as women, develop tumoral dissemination within 5 years after radical treatment. Factors other than the degree of local spreading define disease development. Different preoperative therapies influence not only the duration of the period without recurrence but also the localization of metastases (Goldhirsch et al. 2001). The efficiency of treatment of cancer recurrence and its metastases depends on the localization and the stage of cancer and the character of treatment of the primary tumor.

The basic prognostic criteria that characterize the biological properties of a tumor are the type, histological structure, and clinical stage of the malignant process. The diffuse type of carcinoma has a 10–16 times worse prognosis than the nodular type; and scirrhous structure exhibits two to three times worse prognosis than glandular. When the process is generalized, these prognostic features appear insignificant. Localization, the duration of disease, and the rate of tumor growth are relative prognostic tests in breast carcinoma. Results of numerous studies underline the high risk of recurrence of breast carcinoma in men and young women, especially with breast-conserving surgeries. According to Fowble (1997), local recurrence appeared in 40 % of patients younger than 35 years and only in 13 % of patients older than 50 years during 4.5 years of follow-up. Local recurrence results in the dissemination of tumoral process in 20–40 % of cases. The risk of cancer recurrence is higher in the first 5 years, and it still exists within 15–20 years after surgery.

Some clinical features influence the rate of recurrence of breast carcinoma. The incidence of local recurrences corresponds with the size of the primary tumor and its local extension. Lobular breast carcinoma is quite often associated with local recurrence. It may be the consequence of the high incidence of multicentric growth, frequent bilateral location, clinically latent involvement of lymph nodes, and positive edge of resection in a greater number of cases. Meanwhile, some retrospective studies did not reveal any significant difference in long-term results after different types of surgeries in patients with invasive lobular carcinoma. Multicentric growth of breast tumors is associated with an increased incidence of recurrence. Many studies demonstrated that the rate of local recurrence increases in patients with metastases in lymph nodes correlates with their number.

Routine ultrasound (US) is an affordable method of early detection of the recurrence of breast carcinoma and its regional and remote metastases (Solbiati and Rissato 1995; Zabolotskaya and Zabolotsky 1997; Sinyukova and Sholokhov 2010; Sencha et al. 2011a, b). The complex use of standard and new US technologies permits the supervision of the efficacy of treatment (Sinyukova and Sholokhov 2010; Evseeva et al. 2011). However, the interpretation of US images is difficult. This is especially true for US examination of patients who have had surgery for breast cancer or after radiation therapy. The difficulties arise because of frequent fibrosis within the breast and anterior thoracic wall. It significantly complicates early detection and differential diagnosis of carcinoma recurrence in the region of primary surgery.

Local recurrence of breast carcinoma in the region of radical resection or mastectomy usually exhibits the following US features (Sencha et al. 2011a, b) (Fig. 9.1):

- Solid lesion
- Size of 1–2 cm
- Decreased echodensity
- Homogeneous structure
- Irregular or roundish shape
- Rough borders
- Indistinct contours

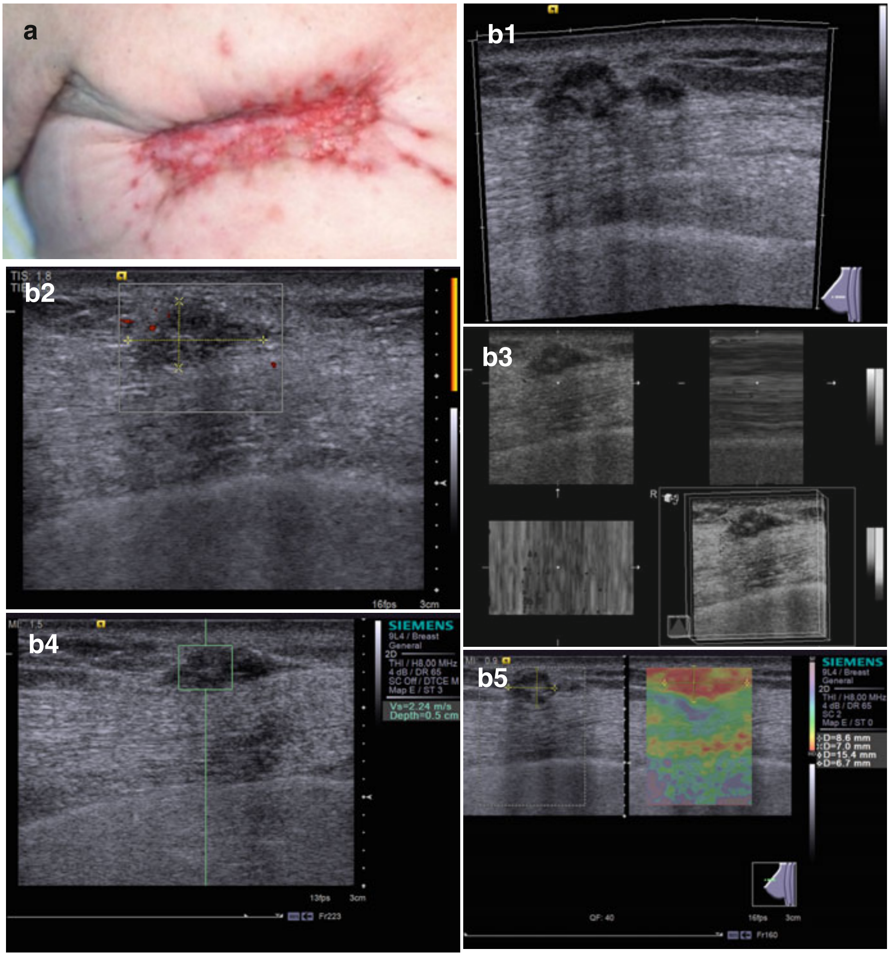

Fig. 9.1 The status after radical resection of the breast in a man. Local recurrence of breast carcinoma. (**a**) Photo. (**b**) (1–5) Grayscale US, panoramic scan, PDI, 3D, ARFI, and US elastography

- Intranodular blood flow pattern in color Doppler imaging (CDI), power Doppler imaging (PDI), and three-dimensional power Doppler vascular image reconstruction (3DPD)
- Intensive hard (blue) staining with US elastography
- Average shear-wave velocity with acoustic radiation force impulse (ARFI) of 2.9 m/s
- Strain ratio of 2.6

Any surgical intervention may be accompanied by oleogranuloma or adipose necrosis in the late postoperative period (3–6 months and later after surgery). Lipogranuloma can be detected along the postoperative scars as a lesion of various echodensity (anechoic, hypoechoic, or hyperechoic) and size (more often <10 mm) of roundish shape with clear margins, homogeneous (or impure) echostructure, and avascular with CDI, PDI, and 3DPD. It is often accompanied with acoustic shadow, especially in cases of calcifications, which are characteristic for lipogranuloma. Surrounding tissues are usually intact or exhibit the signs of lymphostasis. Adipose necrosis and lipogranuloma are difficult to differentiate from recurrent breast carcinoma. Recurrent tumors of small sizes can have the same echodensity, echostructure, shape, contours, and vascularity.

Local fibrosis (Fig. 8.3) is characterized by decreased echodensity (100 %) and layered structure (93 %) and lipogranuloma with average or mixed echodensity (29 and 45 %, respectively), heterogeneous structure (97 %), small calcified incorporations (68 %), "eggshell" calcification (32 %), and fluid component (29 %). Acoustic shadows can be observed significantly more often in patients with lipogranulomas (87 %) than in recurrent tumors (2 %). Posterior enhancement of US does not depend on the type of the mentioned lesions. Lipogranulomas, local fibrosis, and cystic lesions are usually avascular, whereas recurrent breast carcinoma is vascularized in CDI, PDI, and 3DPD in 83 % of cases.

US and X-ray mammography are always used together to diagnose local recurrence of breast carcinoma. However, US is unique, widely accessible, and cost-effective as an imaging technique for recurrences in the region of a radical mastectomy (Sencha et al. 2011a, b). The sensitivity of US in the diagnosis of recurrent breast carcinoma in the region of radical resection is 91–93 %; the specificity, 96 %; and the diagnostic accuracy, 93–94 %. The corresponding figures for X-ray mammography are 87, 84, and 86 % (Sinyukova and Sholokhov 2010). Puncture biopsy of solid masses in the postoperative scar and the bed of the operated breast is obligatory to verify the lesion's nature. Oncologic awareness of female population and general practitioners associated with mammographic and US screening can lead to the early diagnosis of breast tumors, increase the life expectancy of patients, and improve life quality.

Conclusion

Difficulties in the diagnoses of breast diseases in men result from late referral to the doctor, diversity of abnormalities, special clinical features, frequently aggressive development of breast carcinoma, and not always high efficacy of modern diagnostic methods. The analysis of different diagnostic methods shows that the use of modern modalities and their combinations does not always allow solutions for the problems of early and differential diagnosis of breast carcinoma. Early and effective diagnosis of regional and remote metastases remains a problem. The inadequate efficacy of existing diagnostic methods often provokes increased surgical activity.

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