# Multiparametric Ultrasound Diagnosis of Breast Diseases

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# About the Book

This monograph summarizes our extensive experience in the application of new and promising ultrasound mammography technologies that have rapidly become integrated in clinical practice. Grayscale echography, various methods of Dopplerography, color-coded techniques, ultrasound elastography, and ultrasound contrast imaging are considered to be essential components of multiparametric studies of the breast. The book provides a comprehensive overview of current ultrasound techniques, including contrast-enhanced ultrasound, and the advantages and pitfalls of several imaging modalities. The role of innovative ultrasound technologies in the differential diagnosis of inflammatory breast diseases and benign and malignant tumors is discussed. Ways of integrating the ultrasound data with the Breast Imaging Reporting and Data System (BI-RADS) are also discussed. Close attention is paid to the early diagnosis of breast cancer.

The most important benign breast diseases are described, and are illustrated with high-quality images. Several chapters cover the age-related features of these diseases, including those in children and adolescents. A separate chapter deals with the problem of breast abnormalities in men. All aspects of lymph nodes, with a special focus on the differentiation of their lesions, are reviewed in detail. Ultrasound-guided breast interventions, imaging of breast implants, and postoperative follow-up are thoroughly discussed.

The book is intended for specialists in diagnostic ultrasound, radiologists, mammologists, oncologists, gynecologists, surgeons, pediatricians, and general practitioners, and is richly illustrated with a large number of echograms, Figures, schemes, and Tables.

## Introduction

Each year dozens of new monographs, hundreds of articles, and thousands of scientific publications worldwide are devoted to the early detection and differential diagnosis of breast pathology with the use of radiological imaging. Multimillion dollar investments are being made in the search for new and effective technologies for the detection of breast cancer at earlier stages, and in monitoring the effectiveness of different types of treatment. Most of these activities are devoted to the possibilities and prospects of imaging techniques, X-ray, and ultrasound mammography in aiding the earlier detection of breast cancer.

Nevertheless, the urgency of the problem is obvious. According to the World Health Organization, in 2014, 14.1 million people worldwide were diagnosed with malignant breast tumors, and 8.2 million people died of the disease. In 2014, worldwide, 32.6 million people received regular medical check-ups in regard to breast cancer, and they had been having these check-ups for 5 years or more; 17 million of these people were citizens of developed countries and 15.6 million were citizens of developing countries. Despite the considerable progress that has been made in the significant optimization of healthcare systems, with increased diagnostic opportunities, the availability of highly effective diagnostic equipment at medical facilities, and the development of new diagnostic approaches, the proportion of patients whose disease is detected at an early stage remains low, especially in those with visually apparent tumors. Both the extent of preventive measures and practitioners' oncological alertness in the female population are still insufficient. There is a shortage of precise diagnostic equipment and highly qualified specialists, and the opinions and diagnostic strategies of various specialists often differ. The effectiveness of imaging techniques in the diagnosis of various types of breast pathology, the sequence of their use, and the complex analysis and approaches to the interpretation of the obtained results need further study, improvement, elaboration, and optimization.

Diagnostic strategies for a wide range of breast diseases are constantly being revised and improved with new developments in science and technology and the emergence of new methods and technologies in ultrasound, radiological imaging, and diagnostic equipment, as well as the expansion of their functional capabilities. In order to understand, analyze, and differentiate breast diseases, reach adequate medical conclusions, and suggest further strategies for treatment and monitoring, profound systematic knowledge of a large number of aspects of breast disease is absolutely necessary. Some of these aspects are:

- The indications and limitations of the imaging techniques employed
- Age-related breast changes
- Types of diffuse changes and focal lesions
- Peculiarities of normal breast vascularization and vascularization of neoplasms
- Topographic-anatomical relationships
- Neoplasm elasticity determined by quantitative and qualitative analysis of ultrasound elastography
- Contrast-enhanced ultrasound technologies
- Complex analysis of lymphatic drainage
- The state of other organs and systems.

Correct ultrasound evaluation of superficial organs requires profound and appropriate knowledge, the performance of complex analysis, certain experience and practical skills, the use of appropriate equipment and knowledge of its correct settings, and the effective implementation of ultrasound techniques. The availability of modern diagnostic equipment, high-level ultrasound scanners, and modern and innovative imaging

technologies operated by highly specialized diagnosticians is an important component of timely and effective diagnosis and a specific issue in providing diagnostic services.

In the past 50 years, complex ultrasound diagnosis has taken a leading position in diagnoses of the pathology of the breast and other organs. Echography has advanced very rapidly and the quality of grayscale and color-coded images has significantly improved. Three-dimensional image reconstruction and multiplanar reconstruction and panoramic scanning have been introduced. Ultrasound compression elastography and elastometry and contrast-enhanced ultrasonography have found practical applications. However, many issues and unsettled problems have arisen during this period. Accurate and timely diagnosis involves the use of a set of methods and techniques and compliance with effective and efficient examination algorithms. Data on the complex use of the most advanced and innovative ultrasound technologies in the differential diagnosis of neoplasms and tumors requires elaboration and further study. The use of contrast agents in echography for the evaluation of neoangiogenesis and the differential diagnosis of focal lesions seems quite promising.

On the basis of the literature data, our own experience in scientific research, and the results of practical activities, we have attempted to analyze and summarize controversial and unresolved issues, problems, and prospects for the early differential diagnosis of various breast diseases. Undoubtedly, we have not solved all the problems of the ultrasound diagnosis of breast diseases, but we have provided the reader with the opportunity to analyze, criticize, reflect on, and comment on various aspects of the diagnosis of breast diseases, and to carry out further scientific and practical research in this field. This publication is a small contribution to solving a big problem, and it is believed that there are still many discoveries to be made and good prospects ahead for solving this problem.

The authors hope for a favorable reception from readers; remarks, clarifications, and suggestions will be gratefully accepted, analyzed, and taken into consideration in further practical activities, as well as in professional and scientific research.

# Contents

# Abbreviations

| | |
|---|---|
| BPE | Background parenchymal enhancement |
| CDI | Color Doppler imaging |
| CEUS | Contrast-enhanced ultrasound |
| CNB | Core needle biopsy |
| CT | Computed tomography |
| 3D | Three-dimensional |
| 3DPD | Three-dimensional power Doppler imaging |
| 4D | Realtime 3D |
| EDV | End diastolic velocity |
| FA | Fibroadenoma |
| FBD | Fibrocystic breast disease |
| FGT | Fibroglandular tissue |
| FNAB | Fine needle aspiration biopsy |
| IHC | Immunohistochemistry |
| ICC | Immunocytochemistry |
| MDCT | Multidetector computed tomography |
| MIP | Maximum intensity projection |
| MIM | Minimally invasive modality |
| MRI | Magnetic resonance imaging |
| MRM | Magnetic resonance mammography |
| PCV | Peak systolic velocity |
| PDI | Power Doppler imaging |
| PET | Positron emission tomography |
| PI | Pulsatility index |
| PW | Pulsed wave Doppler |
| RI | Resistive index |
| SLNB | Sentinel lymph node biopsy |
| SWE | Shear wave elastography (elastometry) |
| TIRM | Turbo inversion recovery magnitude |
| US | Ultrasound (sonography) |

# 1 Current State of Diagnosis of Breast Diseases: Contribution of Medical Imaging Technologies

Alexander N. Sencha, Vladimir Bychenko, and Yury Patrunov

**Abstract**

Breast pathology is diagnosed in every fourth woman under the age of 30 and in 60% of older women. Accuracy of clinical examination in detecting benign and malignant tumors does not exceed 50–60%, sensitivity is 40–69%, and specificity is 88–95%. Digital mammography is the principle diagnostic method for breast pathology in women over 40 years of age. Ultrasound is now one of the most widespread and affordable imaging methods for diagnosis of breast pathology, early and differential diagnosis of breast masses, and guidance of minimally invasive modalities. US is more valuable for specification of cysts, fibroadenomas, lipomas, some malignant tumors, and duct ectasia. Both diagnostic methods would benefit from their combined use in the differential diagnosis of cysts, large benign soft tissue tumors, tumor-like masses, and malignant tumors. To assess the spread of the tumor, CT or MRI is strongly recommended. The risk of breast cancer increases with age. The basic concept of screening is the detection of the disease early enough to ensure optimistic prognosis and change of the "natural" clinical course. In female population, large-scale mammography screening can reduce mortality rate from breast cancer by 15–30%. The efficiency of mammography for screening has been tested in numerous randomized studies. In order to unify imaging findings description, a specialized BI-RADS lexicon was developed. Report categories in accordance with BI-RADS lexicon are presented. BI-RADS categories used in echography correspond to the categories used in other diagnostic procedures.

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## 1.1 Imaging Techniques in the Diagnosis of Breast Diseases

Diagnosis of breast diseases is one important problem of women's health globally. Breast pathology is diagnosed in every fourth woman under the age of 30 and in 60% of older women; 50–95% of women suffer from diffuse fibrocystic breast disease (Rozhkova 1993; Radzinsky et al. 2016).



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The issues of early detection of breast tumors remain relevant due to the high morbidity and mortality of the female population. Breast cancer takes one dominating malignancy in women around the world. According to the WHO, each year more than 1,300,000 new cases are detected globally. The incidence of cancer has also increased in the majority of countries in Europe and in the world over the past decades. In 2012, 1.67 million patients with breast cancer were registered worldwide. More than half of the breast cancer cases are registered in economically developed countries, where breast cancer occurs in 6% of the female population throughout life. Morbidity in the Russian Federation for the last 10 years is shown in Fig. 1.1 (Kaprin et al. 2017).

Over the past 10 years, the number of patients with malignant breast tumors (malignant tumors) in the Russian Federation has increased by 30%; the most dramatic growth (34%) was observed in women aged 19–39 years: 68,205 cases in 2016 (439 cases per 100,000 of population). In 2016, 642,720 women with breast cancer were registered in Russian oncologic dispensaries.

Despite the increasing incidence of the disease, there has been a significant increase in the 5-year survival rate in Russia for the last decade, which was 61.9% in 2016 (Fig. 1.2) (Kaprin et al. 2017).

Breast cancer amounts to 25.2% of all malignant tumors in the structure of oncological morbidity. It is the leading cause of cancer mortality among women. This is the result of late detection and, consequently, advanced stage at the time of diagnosis (Kaprin et al. 2017).

One important prognostic criterion for cancer is the extent of the tumor spread at the time of detection. An objective assessment of the changes in primary tumor size and regional lymph nodes in the process of preoperative systemic therapy is an essential part of the treatment (Semiglazov 2001). Decisions on the duration of preoperative treatment, the type of surgery, and the need for additional treatment methods depend on it.

High rates of morbidity and mortality from breast cancer force the development of new approaches to diagnosis. Early differential diagnosis of benign and malignant processes and evaluation of the severity and extent of malignancy are among the most burning problems. Despite the apparent availability and simplicity of breast examination, the incidence of detection of advanced disease was about 40%. In 2016, 24.7% of breast cancer were diagnosed in the first stage, 45% in the second stage, 21.5% in the third stage, and 8.2% in the fourth stage of the disease (Kaprin et al. 2017). 29.6% of cases of breast cancer were detected in late stages (III–IV); this is the evidence of low attention to obvious disease.

Nine hundred cases of breast carcinoma in situ were detected in Russia in 2016, which corresponds to 1.3 (2015—2.6) of cases per 100 of all newly diagnosed cases of cancer according to

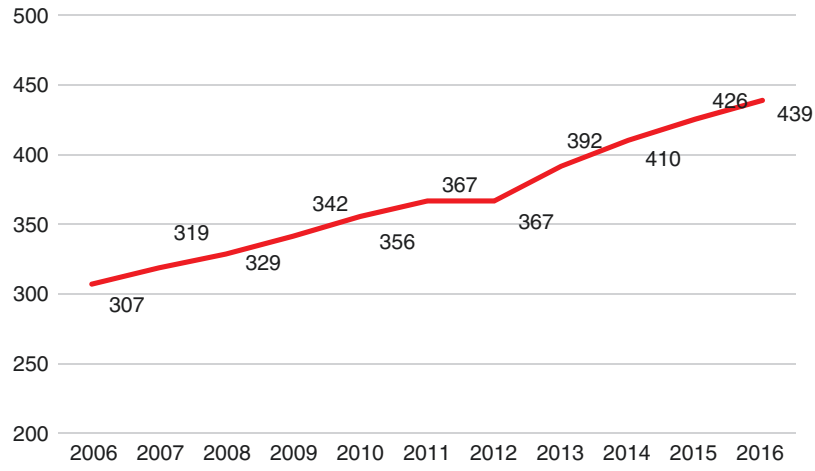


**Fig. 1.1** The incidence of malignant breast tumors in Russia in 2006–2016. The number of patients is indicated per 100,000 of population

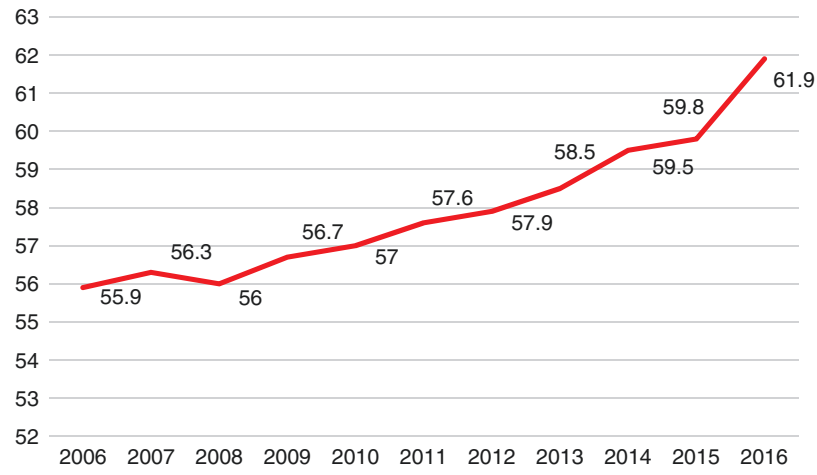


**Fig. 1.2** Percentage of patients with breast cancer followed-up for ≥5 years in Russian oncologic facilities

Kaprin et al. (2017). Early detection of breast malignancies is a priority. In this regard, the issues of effective detection of breast cancer, especially in the preclinical stage, are urgent. Secondary cancer prevention, especially screening, involves tests aimed at earlier detection of the disease, i.e., before the onset of signs and symptoms, which makes patients apply for medical assistance. The value of early diagnosis is that early cancer stage is curable.

Over the last decade, the number of patients with breast cancer has increased by 76.7% in Russia (from 21.9 to 38.7%), primarily due to preventive mammography (Kaprin et al. 2017). Technical equipment of medical facilities provides opportunities for solving the problems of the so-called secondary prevention of breast cancer (screening) by means of preventive examination of asymptomatic women.

High efficacy of diagnosis of early breast cancer makes it possible to use a highly effective complex of treatment and perform breast-conserving operations in combination with optimized programs of radiation and chemical therapy.

**Methods of Breast Cancer Diagnosis**

1. Preoperative:

   *Main:*

   (a) Noninvasive:
   - Clinical examination (medical history, examination, palpation)
   - X-ray mammography
   - Ultrasound mammography

   (b) Invasive:
   - Stereotactic core needle biopsy with histological investigation of biopsy samples
   - US-guided FNA with cytological examination
   - Vacuum aspiration biopsy under ultrasound or X-ray control
   - Cytological evaluation of nipple discharge
   - Preoperative labeling of impalpable tumors by marking needles

   *Supplementary* (upon indication):
   - Ductography
   - MRI
   - CT
   - Scintigraphy
   - Others (electrical impedance tomography, radiothermometry, etc.)

2. Intraoperative:
   - Urgent histological investigation
   - X-ray study of removed breast sector

3. Postoperative:
   - Histological examination of a specimen

Asymmetry of breasts, areolas, and nipples and deformity and dimpling of the skin and nipple when the arm is raised are *clinical manifestations* of breast tumors. Palpation usually reveals dense immobile tumor with rough surface.

Ulceration may be observed in advanced stages. The skin and areola above the tumor are thickened (Krause symptom). Skin shrinkage and dimpling over the tumor or a symptom of "peau d'orange" are possible. Many breast diseases and tumors (benign and malignant) in the initial stages are asymptomatic.

Accuracy of the clinical examination in detecting benign and malignant tumors does not exceed 50–60%, sensitivity is 40–69%, and specificity is 88–95% (Shevchenko 1997; Korzhenkova 2004) (Fig. 1.3). Palpation also often fails to detect regional lymph nodes affection. The rate of errors in detection of metastatic lymph nodes reaches 32–45.8%.

Imaging techniques, particularly X-ray and ultrasound mammography, are essential in the diagnosis of breast pathology.

*Mammography* is a technology of obtaining a negative photographic image of the breast that reflects the projected attenuation of the X-ray radiation from mammography device passing through various tissues. First X-ray images of the breast were produced on amputated breasts by A. Salomon in 1913. Primary tumor with spread to the axillary lymph nodes was visualized. To now, the mammography is recognized worldwide as one of the most valuable diagnostic methods for a wide range of diseases, including breast tumors. Digital mammography is the principle diagnostic method for breast pathology in women over 40 years of age.

Mammography represents a two-dimensional image of the breast, which permits assessment of the thickness, glandular tissue density, and specification of the location, shape, borders, and size of focal lesions (Fig. 1.4). As a rule, mammography is performed in frontal (craniocaudal) and oblique (mediolateral) projections. Two projections provide imaging of the whole breast,

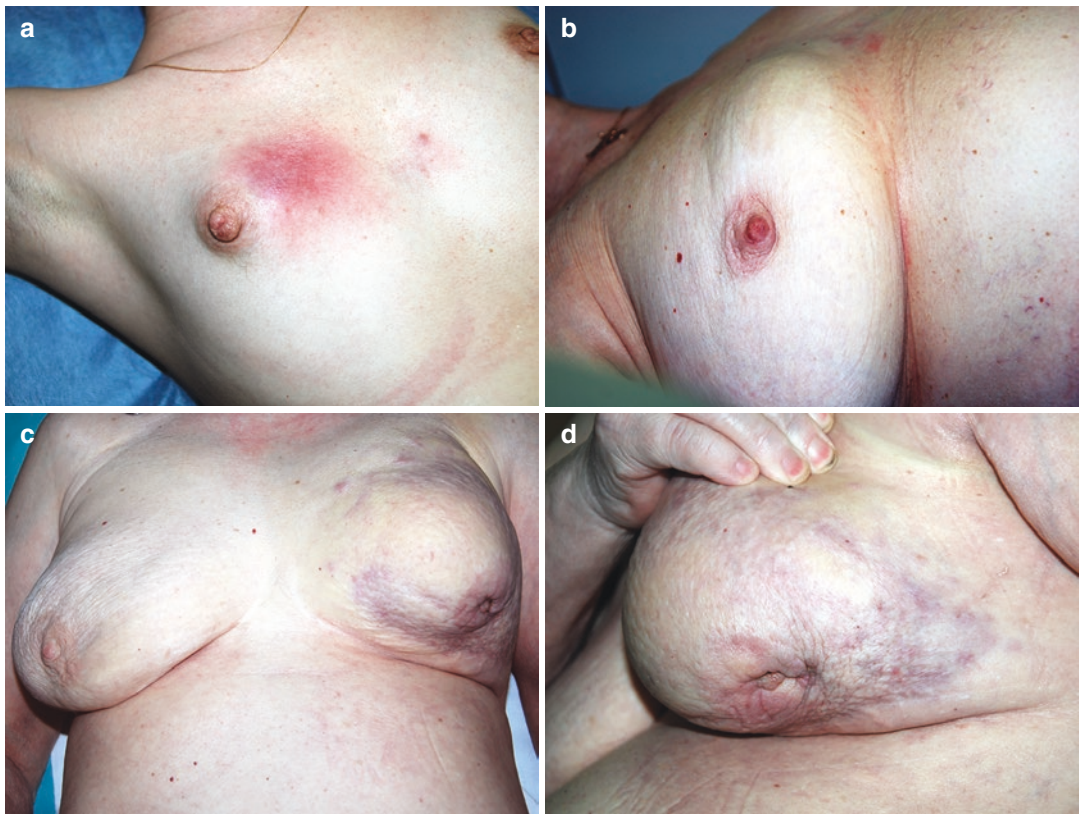


**Fig. 1.3** (**a**–**d**) Visual inspection in patients with breast cancer

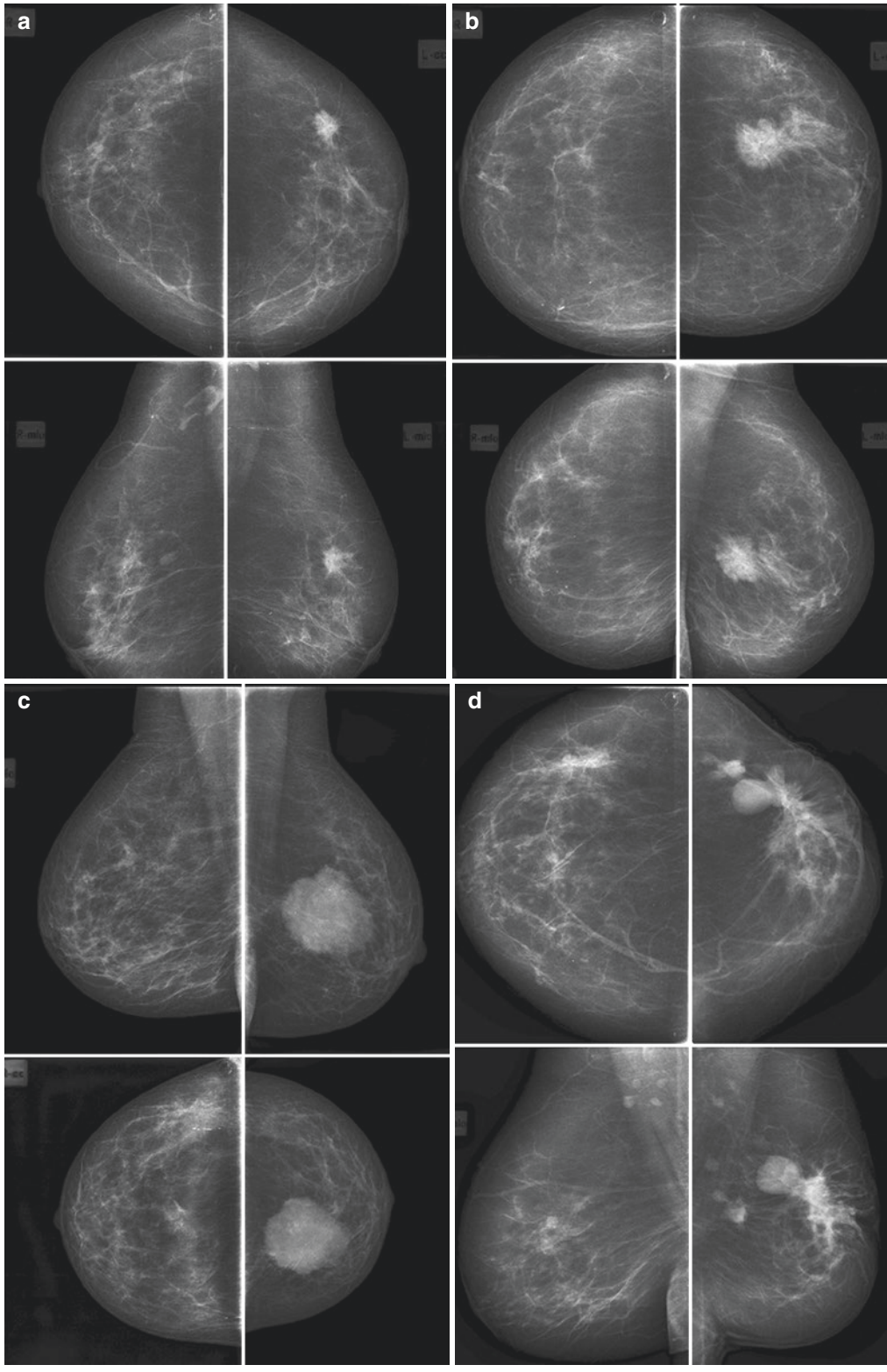


**Fig. 1.4** (**a**–**h**) X-ray mammography. Breast cancer