

Chapter 51

Approach to Breast Diseases



What would be the options of next step in management of the mentioned patient below?

- **A 64-year-old woman had routine screening mammogram. A cluster of micro calcifications in the left lower inner quadrant of her breast was found on mammography. Based on the spot compression magnification mammogram, calcifications were found to be suspicious and classified as BI-RADS 4.**
 - Stereotactic core needle biopsy
 - Wire localized excisional biopsy

What would be the options of next step in management of the mentioned patient below?

- **An asymmetric density in the subareolar zone of left breast was found in a 54-year-old postmenopausal woman on routine screening mammography. Sonographic imaging demonstrates 10 mm intraductal mass with ill-defined borders.**
 - Ultrasound guided core needle biopsy targeting papilloma
 - Wire localized excisional biopsy targeting papilloma
 - Seed localized excisional biopsy

What are the indications to excise a lesion diagnosed as intraductal papilloma by core needle biopsy?

- The presence of atypia associated with papilloma
- The presence of clinic-radiologic imaging discordance
- The association of atypical ductal hyperplasia with the papilloma

The original version of this chapter was revised. The correction to this chapter can be found at https://doi.org/10.1007/978-3-030-29669-8_52

Author: Güldeniz Karadeniz Çakmak

- The association of atypical lobular hyperplasia with the papilloma
- The presence of symptoms due to papilloma

What are the breast imaging-reporting and data system (BI-RADS) categories of the lesions that should be observed/follow-up?

- BI-RADS 1
- BI-RADS 2
- BI-RADS 3

What are the breast imaging-reporting and data system (BI-RADS) categories of the lesions that should be biopsied?

- BI-RADS 4
- BI-RADS 5

Which imaging modalities are used for breast imaging-reporting and data system (BI-RADS) for classification?

- Breast ultrasound
- Mammography
- Breast MRI

What does provide the sensory innervation of the breast?

- The anterior and lateral cutaneous branches of the second to sixth intercostal nerves
- The supraclavicular branches of the cervical plexus

What does provide the sensory innervation of the nipple–areola complex?

- The deep division of the lateral cutaneous branches of the fourth intercostal nerve
- The third and fourth anterior cutaneous branches of intercostal nerve

What is Berg classification of axillary lymph nodes?

- There are three groups of axillary lymph nodes according to their position relative to the pectoralis minor muscle.
- Level I lymph nodes are located laterally to the lateral margin of the pectoralis minor muscle.
- Level II lymph nodes are located behind the muscle.
- Level III lymph nodes are located medially to the medial-superior margin of the muscle.

What are the stages of breast development?

- Prenatal stage
- Infant stage
- Peripubertal stage
- Adult stage (including pregnancy and lactation)
- Postmenopausal stage

What are the characteristic features of Poland's syndrome?

- Absence of costal cartilages and a portion of the third or third and fourth rib
- Absence of the nipple or breast with accompanying hypoplasia

- Absence of subcutaneous fat
- Absence of axillary hair
- Absence of the pectoralis minor muscle
- Absence of costosternal part of the pectoralis major muscle

What are the major risk factors associated with breast cancer?

- Female gender
- Increasing age
- Past history of breast cancer
- Past history of other high-risk pathology
- Previous radiation therapy
- Genetic mutations

What are the major modifiable lifestyle risk factors for breast cancer?

- Physical inactivity
- Obesity
- Alcohol consumption
- Exogenous hormone administration (oral contraceptives, hormone replacement therapy)

What are the high-penetrance hereditary breast cancer genes?

- BRCA1 and BRCA2
- TP53
- STK11
- PTEN
- CDH1

What are the criteria for designating women at high familial risk for breast cancer according to American Cancer Society?

- Women with a known mutation in *BRCA1* or *BRCA2* or their untested first-degree relatives
- Women with Li–Fraumeni syndrome
- Women with Cowden’s syndrome
- Women with Bannayan–Riley–Ruvalcaba syndrome
- Woman with hereditary diffuse gastric cancer
- Woman with Peutz–Jeghers syndrome and their first-degree relatives
- Women having a lifetime risk equal to or greater than 20–25% according to BRCAPRO or other family history-based models

What are the criteria for breast cancer screening for high familial risk women?

- Mammography begins at the age of 25–30 years or 10 years before the age at diagnosis of a first-degree relative; nevertheless, the age at onset of screening should not be younger than 25.
- Mammography and MRI are complementary examinations; both should be performed.
- Ultrasound is performed if a patient cannot undergo magnetic resonance imaging.

What are the risk reducing strategies for breast cancer?

- Surveillance
- Chemoprevention
- Risk-reducing surgery of the breasts
- Risk-reducing surgery of ovaries and fallopian tubes

What are the US National Comprehensive Cancer Network's recommendations for surveillance for BRCA1 and BRCA2 mutation carriers?

- Giving information about “breast awareness” starting at the age of 18
- Clinical breast exam every 6–12 months from the age of 25
- Annual breast screening using MRI from age 25 to 29 years
- Annual breast MRI and mammography from 30 to 75 years
- After the age of 75 years, surveillance should be considered on an individual basis

What are the options of breast reconstruction after prophylactic mastectomy?

- Implant-based reconstruction
- Autologous reconstruction

What are the possible predictors of complications after breast reconstruction?

- Smoking
- High body mass index
- Preoperative irradiation

What are the techniques of autologous breast reconstruction?

- Latissimus dorsi flap
- Transverse rectus abdominis musculo (TRAM)-cutaneous flaps
- Superficial inferior epigastric abdominal (SIEA) perforator flaps
- Transverse myocutaneous gracilis (TMG) flaps
- Deep inferior epigastric perforator flaps

What are the factors included in National Cancer Institute's breast cancer risk assessment tool (Gail model)?

- Age
- First menstrual period age
- First live birth age
- First-degree relatives with breast cancer (include only mother, sisters, and daughters)
- Previous breast biopsy
- Race

What are the available current multigene assays in breast cancer?

- Oncotype DX Breast Recurrence Score Assay
- MammaPrint
- Prosigna (PAM50)
- EndoPredict

- Breast cancer index
- Insight Dx Mammostrat

What are high-risk breast lesions?

- Flat epithelial atypia
- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Lobular carcinoma in situ
- Radial scar (RS)/complex sclerosing lesion
- Intraductal papilloma

What is the next step in management if a high-risk lesion is diagnosed on core breast biopsy specimen?

- Diagnostic surgical excision

Define ductal carcinoma in situ

- Ductal carcinoma in situ (DCIS) of the breast represents an intraductal lesion of the breast characterized by increased epithelial proliferation with cellular atypia not invading the basement membrane of the ductal lobular unit.

What is the common feature of DCIS on mammogram?

- DCIS often appears as microcalcifications or less commonly as a mass or area of architectural distortion.

What are the current treatment options routinely offered for DCIS?

- Surgery (lumpectomy/wide excision/segmental mastectomy or mastectomy)
- Radiation
- Endocrine therapy

What are the risk factors for recurrence for DCIS?

- Symptomatic presentation of DCIS
- Greater extent (size) of DCIS
- The presence of DCIS at the resection margin
- High grade
- Multifocality

What are the absolute contraindications for breast-conserving therapy to treat breast cancer?

- Radiation therapy during pregnancy
- Diffuse suspicious or malignant-appearing microcalcifications
- Widespread disease that cannot be incorporated by local excision of a single region or segment of breast tissue that achieves negative margins with a satisfactory cosmetic result
- Diffusely positive pathologic margins
- Homozygous (biallelic inactivation) for ATM mutation

What are the indications for mammography?

- Breast cancer screening
- Assessment of patients with clinical symptoms

- Image-guidance for biopsy
- Preoperative staging
- Preoperative localization
- Therapy monitoring and follow-up

What does determine the density of the breast in mammography?

- The proportion of fibroglandular tissue and fatty tissue determines the density of the breast.

What are the categories of breast density according to the breast imaging-reporting and data system (BI-RADS®) in mammography?

- Category A: Breasts are almost entirely fatty
- Category B: There are scattered areas of fibroglandular density
- Category C: The breasts are heterogeneously dense, which may obscure small masses
- Category D: The breasts are extremely dense, which lowers the sensitivity of mammography

What are abnormal findings on mammography?

- Masses (characterized by shape, margins, and density)
- Architectural distortions
- Asymmetries
- Microcalcifications (evaluated by their morphology and distribution)
- Skin and nipple changes (thickening, retraction)
- Chest wall invasion
- Axillary lymphadenopathy

What are the frequent features of benign microcalcifications in mammography?

- A cutaneous or vascular location
- A round shape or rim appearance
- Large coarse “popcorn- like” morphology
- A large rod-like shape and a peri-, intraductal punctate pattern
- Diffusely homogeneous punctate pattern
- Amorphous dystrophic calcification after trauma
- Milk-of-calcium sediment calcifications

What are the commonest imaging findings after surgery and radiation therapy for breast cancer?

- Scarring—deformity of the breast
- Distortion of the parenchymal pattern
- Skin thickening
- Radiation fibrosis
- Postsurgical fluid collections
- Fat necrosis
- Dystrophic calcifications
- Artificial material

What are the indications of breast ultrasonography?

- Adjunct to screening mammography in dense breast
- Characterization of abnormalities found in other modalities
- Evaluation of palpable masses and other breast-related symptoms
- Evaluation and characterization of palpable masses and other breast-related signs and/or symptoms
- Evaluation of suspected or apparent abnormalities detected on mammography
- Treatment planning for radiation therapy
- Axillary staging in women with breast cancer
- Evaluation of breast implants
- Guidance of interventional procedures in the breast and axilla
- Evaluation of young, pregnant, and breastfeeding patients with clinical symptoms

What are the indications of breast magnetic resonance imaging (MRI)?

- Screening modality for women with high lifetime risk of breast cancer
- Preoperative staging
- Pretreatment evaluation of local disease extent
- Monitoring of neoadjuvant systemic treatment
- Evaluation of residual disease after neoadjuvant systemic treatment
- Unequivocal findings from other imaging modalities
- With negative mammography and ultrasound, to detect an occult primary tumor in patients with metastatic involvement of axillary lymph nodes; assessment of breast implants

What are the techniques used for preoperative marking for breast masses?

- Wire guidance
- Carbon marking
- Radioactive agent guidance marking
- Clip placement
- Skin marking
- Ultrasound guidance

What are the potential physical and psychological hazards of mammographic screening?

- Radiation exposure
- Overtreatment
- Pain
- False-positive results
- False-negative results

What are the breast cancer screening modalities that have been assessed in population-based breast screening?

- Clinical breast examination
- Breast self-examination
- Mammography

What are the clinical symptoms and signs of breast cancer?

- Breast mass
- Skin retraction
- Nipple inversion
- Changes in the size and shape of the breast
- Discoloration of the skin
- Breast pain
- Skin edema
- Axillary nodal mass

Define locally advanced breast cancer (LABC)

- Any breast cancer that is >50 mm in greatest dimension or tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules), or metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases, or metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement with no distant metastases (T3–T4, or N2–3, no metastases: M0) is defined as LABC.

What are the main features of phyllodes tumor?

- A group of rare fibroepithelial lesions.
- They have different malignant potentials.
- They represent 0.3–0.5% of all breast tumors.
- The majority of them are diagnosed in the fourth and fifth decade of life although they can appear at almost any age.
- The majority present as benign-feeling lumps often thought to be fibroadenomas clinically or on imaging but may be larger or grow more rapidly.
- In most cases, a definitive diagnosis is established after core needle biopsy and in some cases surgical excision.

What are the non-epithelial malignancies of the breast?

- Angiosarcoma
- Osteogenic sarcoma
- Embryonal rhabdomyosarcoma
- Lymphoedema-associated lymphangiosarcoma
- Lymphoma
- Metastatic tumors

What are the most common organs that breast cancer metastasizes?

- Bone
- Lung
- Liver
- Brain

What are the methods of breast biopsy in use to diagnose breast cancer?

- Fine needle aspiration (FNA) biopsy
- Core biopsy (CB)
- Vacuum-assisted biopsy
- Punch biopsy
- Incisional biopsy
- Excisional biopsy

What are the elements of 8th ed. AJCC UICC-TNM clinical prognostic staging classification for breast cancer?

- Tumor size
- Lymph node status
- Distant metastasis
- Grade
- Human epidermal growth factor receptor 2 (HER2) status
- Estrogen receptor (ER) status
- Progesterone receptor (PR) status

What are molecular or intrinsic subtypes of breast cancer?

- Luminal A: ER+ and PR+, low grade, HER2–, non-proliferative 5
- Luminal B: ER+ and PR–, or PR low/high grade/proliferative, or HER2+
- HER2 + : HER2+, ER–
- Basal like–Triple negative: ER–, PR–, HER2–

Define sentinel lymph node for breast tumor

- A sentinel node is defined as the first lymph node that drains a breast tumor along a direct lymphatic pathway from the primary tumor.

What is oncoplastic breast surgery?

- Breast surgery to treat breast cancer focusing on optimizing both oncologic and esthetic outcomes, irrespective of the type(s) of surgery performed.

What is radical mastectomy (Halsted)?

- Removal of the totality of the glandular breast tissue, overlying skin, nipple-areola complex, pectoralis major and minor muscles and ipsilateral axillary lymph nodes

What is modified radical mastectomy?

- Removal of the totality of the glandular breast tissue, overlying skin, nipple-areola complex, and concurrent level I–II axillary lymph node dissection

What is skin-sparing mastectomy?

- Removal of the totality of the glandular breast tissue, removal of the nipple-areola complex, preservation of the skin envelope overlying the breast (followed by immediate reconstruction)

What is nipple-sparing mastectomy?

- Removal of the totality of the glandular breast tissue, preservation of nipple-areola complex and skin envelope (followed by immediate reconstruction)

What are indications for mastectomy in breast cancer management?

- Extensive, multicentric, invasive, or in situ disease not amenable to breast-conserving surgery
- Second ipsilateral in-breast event (recurrence or second primary cancer) following previous breast-conserving surgery and radiotherapy
- Patient choice (instead of breast-conserving surgery)
- Prophylactic (risk-reduction) surgery in patients with high family risk of breast cancer (i.e., BRCA or p53 mutation carriers, or non-carriers with >30% overall lifetime risk of breast cancer)
- Inflammatory breast cancer
- Previous mantle radiotherapy for Hodgkin's disease

What are the dissection borders when performing modified radical mastectomy?

- Dissection is carried out up to the level of the clavicle *superiorly*, down to the inframammary fold and rectus sheath *inferiorly*, lateral to the sternum *medially* and up to the anterior border of the latissimus dorsi *laterally*.

What are the methods for impalpable tumor localization?

- Guidewire localization
- Radioguided occult lesion localization (Roll)
- Radioactive seed localization
- Intraoperative ultrasound localization
- Carbon dye injection localization
- Superparamagnetic iron oxide localization

What are the indications of oncoplastic surgery?

- Adverse tumor volume to breast volume ratio
- Adverse tumor location (supero-medial, central/sub-areolar, inferior)
- Multifocal and multicentric disease
- Macromastia
- Redo conservation surgery

What are the methods used for sentinel lymph node detection?

- A radioactive tracer
- A vital blue dye
- The combination of a radioactive tracer and a vital blue dye
- Super paramagnetic iron oxide

What are the indications for sentinel lymph node biopsy for axillary staging?

- All patients with invasive breast cancer with a clinically negative axilla at primary surgery
- For patients with DCIS and going to undergo mastectomy

What are the factors associated with an increased risk of postoperative complications after breast surgery?

- Age
- Obesity

- Smoking
- Excessive use of alcohol or recreational drugs
- Diabetes mellitus
- Chronic renal failure or chronic obstructive pulmonary disease
- Atherosclerosis and cardiovascular disease
- Autoimmune and connective tissue disorders
- Preoperative chemotherapy
- History of irradiation to the chest wall
- Previous surgical procedures on the breast

What are the indications for neoadjuvant chemotherapy for breast cancer?

- Inflammatory breast cancer
- Inoperable breast cancer
- To facilitate breast conservation surgery
- If the same systemic therapy would also be indicated in the adjuvant setting
- If adjuvant chemotherapy is likely to be advised and complex surgery is planned which may otherwise delay systemic therapy
- If adjuvant chemotherapy is likely to be advised and the results of gene testing are awaited which may affect subsequent treatment decisions

What are the indications for adjuvant radiation therapy after mastectomy for breast cancer?

- Tumor >5 cm
- Four or more positive axillary lymph nodes (post-mastectomy radiotherapy mandatory)
- One to three axillary lymph nodes (post-mastectomy radiotherapy is recommended)
- Positive surgical margins when further surgery is not possible
- Chest wall/skin infiltration (T4a, T4b, T4c)
- Inflammatory cancer (T4d)
- Pectoral muscle invasion

Suggested Reading

1. Wyld L, Markopoulos C, Leidenius M, Senkus-Konefka E, editors. Breast cancer management for surgeons: a European multidisciplinary textbook. New York: Springer; 2018.
2. Burstein HJ. Tumor, node, metastasis (TNM) staging classification for breast cancer. UpToDate (Accessed June 2019).
3. Taghian A, El-Ghamry MN, Merajver SD. Overview of the treatment of newly diagnosed, non-metastatic breast cancer. UpToDate (Accessed June 2019).
4. Joe BN. Clinical features, diagnosis, and staging of newly diagnosed breast cancer. (Accessed June 2019).
5. Khan S, Diaz A, Archer KJ, et al. Papillary lesions of the breast: to excise or observe. *Breast J.* 2018;24:350–5.
6. Cooper AP. On the anatomy of the breast. London: Longman, Orme, Green, Brown and Longmans; 1840.

7. Schlenz I, Kuzbari R, Gruber H, Holle J. The sensitivity of the nipple-areola complex: an anatomic study. *Plast Reconstr Surg.* 2000;105(3):905–9.
8. Sohn V, Keylock J, Arthurs Z, et al. Breast papillomas in the era of percutaneous needle biopsy. *Ann Surg Oncol.* 2007;14:2979–84.
9. Sydnor MK, Wilson JD, Hijaz TA, Massey HD, Shaw de Peredes ES. Underestimation of the presence of breast carcinoma in papillary lesions initially diagnosed at core-needle biopsy. *Radiology.* 2007;242:58–62.
10. D’Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. *ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System.* Reston: American College of Radiology; 2013.
11. Berg JW. The significance of axillary node levels in the study of breast carcinoma. *Cancer.* 1955;8(4):776–8.
12. Skandalakis J. Embryology and anatomy of the breast. In: *Breast augmentation.* Berlin: Springer; 2009. p. 3–24.
13. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT, et al. Effect of physical inactivity on major non-communicable diseases 94. Worldwide: an analysis of disease and life expectancy. *Lancet.* 2012;380(9838):219–29.
14. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer.* 2015;112(3):580–93.
15. Munsell MF, Sprague BL, Berry DA, Chisholm G, Trentham-Dietz A. Body mass index and breast cancer risk according to post-menopausal estrogen progestin use and hormone receptor status. *Epidemiol Rev.* 2014;36(1):114–36.
16. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin.* 2007;57(2):75–89.
17. Mainiero MB, Lourenco A, Mahoney MC, Newell MS, Bailey L, Barke LD, et al. ACR appropriateness criteria breast cancer screening. *J Am Coll Radiol.* 2013;10(1):11–4.
18. Rajan S, Sharma N, Dall BJ, Shaaban AM. What is the significance of flat epithelial atypia and what are the management implications? *J Clin Pathol.* 2011;64(11):1001–4.
19. Sickles EA, D’Orsi CJ, Bassett LW, et al. *ACR BI-RADS® mammography. ACR BI-RADS® atlas, breast imaging reporting and data system.* Reston: American College of Radiology; 2013.
20. Berg WA, Blume JD, Cormack JB, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA.* 2008;299(18):2151–63.
21. Tagliafico AS, Calabrese M, Mariscotti G, Houssami N, et al. Adjunct screening with tomosynthesis or ultrasound in women with mammography negative dense breasts: interim report of a prospective comparative trial. *Clin Oncol.* 2016;34(6):1882–8.
22. Houssami N, Irwig L, Simpson JM, McKessar M, Blome S, Noakes J. Sydney breast imaging accuracy study: comparative sensitivity and specificity of mammography and sonography in young women with symptoms. *AJR Am J Roentgenol.* 2003;180:935–40.
23. Corsi F, Sorrentino L, Bossi D, Sartain A, Foschi D. Preoperative localization and surgical margins in conservative breast surgery. *Int J Surg Oncol.* 2013;2013:793–819.
24. *Breast Screening Programme, England: 2014–15.* Health and Social Care Information Centre; 2016.
25. Berrington de González A. Estimates of the potential risk of radiation-related cancer from screening in the UK. *J Med Screen.* 2011;18(4):163–4.
26. Whelan P, Evans A, Wells M, et al. The effect of mammography pain on repeat participation in breast cancer screening: a systematic review. *Breast.* 2013;22(4):389–94.
27. Alexander FE, Anderson TJ, Brown HK, Forrest AP, Hepburn W, Kirkpatrick AE, McDonald C, Muir BB, Prescott RJ, Shepherd SM. The Edinburgh randomized trial of breast cancer screening: results after 10 years of follow-up. *Br J Cancer.* 1994;70(3):542–8.

28. Anthony M, To T, Baines CJ, Wall C. Canadian National Breast Screening Study-2: 13-year results of a randomized trial in women aged 50–59 years. *J Natl Cancer Inst.* 2000;92(18):1490–9.
29. Amin MB, Edge SB, Greene FL, et al., editors. *AJCC (American Joint Committee on Cancer) cancer staging manual*; 8th edition, 3rd printing. Chicago: Springer; 2018.
30. Sabel MS. Overview of benign breast disease. (Accessed June 2019).
31. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: an analysis of 170 cases. *Cancer.* 1996;77(5):910–6.
32. Tan BY, Acs G, Apple SK, Badve S, Bleiweiss IJ, Brogi E, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology.* 2016;68(1):5–21.
33. Young JL Jr, Ward KC, Wingo PA, Howe HL. The incidence of malignant non-carcinomas of the female breast. *Cancer Causes Control CCC.* 2004;15(3):313–9.
34. Nicholson BT, Bhatti RM, Glassman L. Extranodal lymphoma of the breast. *Radiol Clin North Am.* 2016;54(4):711–26.
35. Williams SA, Ehlers RA 2nd, Hunt KK, Yi M, Kuerer HM, Singletary SE, et al. Metastases to the breast from nonbreast solid neoplasms: presentation and determinants of survival. *Cancer.* 2007;110(4):731–7.
36. Alva S, Shetty-Alva N. An update of tumor metastasis to the breast data. *Arch Surg (Chicago, Ill 1960).* 1999;134(4):450.
37. Coates AS, Winer EP, Goldhirsch A, Gelber RD, Gnant M, Piccart-Gebhart M, et al. Tailoring therapies-improving the management of early breast cancer: St Gallen International Expert Consensus on the primary therapy of early breast cancer 2015. *Ann Oncol.* 2015;26(8):1533–46.