JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Breast cancer - A comprehensive review

By Dr. Rinkal Nakawala (MD), associate professor in Roganidana deparment, Shree O.H.Nazar Ayurved college, Surat (Gujarat), India.

Abstract

Breast cancer is the most frequently diagnosed malignancy among women worldwide and remains one of the leading cause of cancer related mortality despite remarkable advances in screening, diagnosis, and treatment. According to recent global estimates, more than 2.3 million new cases are diagnosed annually, accounting for approximately one quarter of all female cancers. In India, breast cancer has surpassed cervical cancer as the most common cancer among women, with increasing incidence in both urban and rural populations. Breast cancer is a biologically heterogeneous disease characterized by diverse histopathological features, molecular alterations, and clinical behaviour. The identification of molecular sub-types, including Luminal A, Luminal B, HER2-enriched, and Triple-Negative Breast Cancer (TNBC), has transformed therapeutic strategies and improved patient outcomes through personalized medicine. Risk factors include increasing age, female sex, prolonged estrogen exposure, reproductive factors, obesity, alcohol consumption, ionizing radiation, and hereditary mutations in susceptibility genes such as BRCA1, BRCA2, TP53, PALB2, CHEK2, and ATM. Recent advances in molecular biology have elucidated key signaling pathways involved in carcinogenesis, including the PI3K/AKT/mTOR, HER2, MAPK, and DNA damage repair pathways. Diagnosis relies on the principle of triple assessment, consisting of clinical examination, imaging, and pathological confirmation. Mammography remains the cornerstone of breast cancer screening, supplemented by ultrasonography and magnetic resonance imaging is selected populations. Histopathological examination combined with immunochemistry for estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67 provides essential prognostic and predictive information.
Management requires a multidisciplinary approach incorporating surgery, radiotherapy, chemotherapy, endocrine therapy, and novel targeted agents. Breast-conserving surgery with sentinel lymphnode biopsy has become standard treatment for early-stage disease, whereas systemic therapy is individualized according to molecular sub type and stage. Recent developments such as antibody-drug conjugates, immune check point inhibitors, PARP inhibitors, liquid biopsy, genomic profiling, artificial intelligence- assisted imaging and precision oncology are redefining the management landscape. This article provides an evidence-based overview of breast cancer, including epidemiology, molecular pathogenesis, pathology, diagnosis, staging, and future therapeutic directions.

Keywords

Breast cancer, breast neoplasms, carcinoma breast, Triple assessment, Mammography, Molecular classification, BRCA1, BRCA2, HER2, Estrogen receptor, Progesterone receptor, Triple-negative Breast cancer, AJCC TNM Staging, Precision Oncology, Immunotherapy, Targeted therapy

1. Introduction

Breast cancer is a malignant neoplasm arising from the epithelial lining of the terminal duct lobular unit (TDLU), which is the functional and anatomical unit of the breast. It represents a heterogeneous group of diseases with varying genetic, molecular, histological, and clinical characteristics. This heterogeneity accounts for differences in prognosis, response to treatment, and survival.

Breast cancer has emerged as a major global public health challenge. Improvements in screening programs and public awareness have facilitated earlier diagnosis in developed nations; however, late-stage presentations remains common in low and middle-income countries, including India. Consequently, breast cancer continues to impose substantial social, psychological, and economic burdens on patients, families, and healthcare systems.

The pathogenesis of breast cancer involves the accumulation of genetic and epigenetic alterations leading to uncontrolled cellular proliferation, resistance to apoptosis, angiogenesis, immune evasion, and metastatic spread. Both environmental and hereditary factors contribute to disease development. Approximately 5-10 % of breast cancers are hereditary, with germline mutations in BRCA1 and BRCA2 accounting for the majority of inherited cases.

The introduction of molecular classification based on gene-expression profiling has revolutionized breast cancer management. Molecular subtypes - including Luminal A, Luminal B, HER2-enriched, and Triple-Negative Breast Cancer (TNBC)- provide valuable prognostic information and guide therapeutic decisions. Patients with hormone receptor positive tumors benefit from endocrine therapy, whereas HER2-positive tumors respond to HER2- targated agents such as transtuzumab. Triple-negative breast cancers, lacking expression of ER, PR, and HER2, are generally associated with aggressive clinical behavior but may respond to chemotherapy and selected immunotherapeutic approaches.

The management of breast cancer has evolved from radical surgical procedure to personalized multi modal treatment integrating surgery, radiotherapy, and immunotherapy. Advances in molecular diagnostics, genomic profiling, and precision medicine continue to improve survival and quality of life while minimizing treatment-related morbidity.

2. Epidemiology

Breast cancer is the most frequently diagnosed cancer in women worldwide and remains one of the leading causes of cancer related mortality. Approximately 2.3 million new cases are diagnosed annually and responsible for approximately 685,000 deaths per year

worldwide. One in eight women is estimated to develop breast cancer during her lifetime. Incidence is highest in North America, Western Europe, Australia, and New Zealand, whereas mortality rates remain disproportionately higher in low- and middle-income countries due to delayed diagnosis and limited access to treatment. Breast cancer has become the commonest cancer among Indian women, surpassing cervical cancer in many regions. Increasing incidence in both urban and rural population.

3. Burden of Disease

Breast cancer imposes significant medical, psychological, social, and economic burdens. It may cause Long term morbidity following surgery, chemotherapy, radiotherapy, and endocrine therapy.

4. Risk factors

Breast cancer is multifactorial.
A. Non-modifiable Risk factors

Female gender - More than 90 % of cases occur in women
Increasing age - Risk increases progressively after 40 years and peaks after menopause
Family history - Risk doubles when a first-degree relative is affected
Genetic mutations - Important hereditary mutations include:
BRCA1, BRCA2, TP53, PALB2, CHEK2, ATM, PTEN, CDH1, STK11
Previous breast cancer - Women previously treated for breast cancer have increased risk of developimg a second primary tumour
Dense Breast Tissue - High mammographic density independently increases breast cancer risk.

B. Hormonal and Reproductive Factors

Prolonged estrogen exposure increases risk. Examples include :
Early menarche (<12 years)
Late menopause (> 55 years)
Nulliparity
First child birth after age 30
No breastfeeding
Hormonal replacement therapy
Long duration combined estrogen-progestin therapy

C. Lifestyle factors

Obesity
Especially postmenopausal obesity due to increased peripheral estrogen production.
Physical inactivity - Associated with increased risk
Alcohol consumption - Risk increases in a dose-dependent manner

Smoking - Particularly associated with early initiation and prolonged duration
Diet - High fat diets and processed foods may contribute, whereas diets rich in fruits, vegetables, and fiber appear protective.

D. Environmental factors
It includes - Ionizing radiation, occupational exposure, environmental pollutants, Night-shift work (possible association through circadian rhythm disruption)

5. Protective Factors

. Early first pregnancy
. Multiparity
. Breastfeeding
. Regular physical inactivity
. Healthy body weight
. Limited alcohol intake

6. Breast Anatomy

The adult female breast is a modified sweat gland situated in the superficial fascia of the anterior chest wall. Each breast contains: 15-20 lobes, lobules, Terminal duct-lobular units (TDLUs), lactiferous ducts and sinuses, fibrofatty connective tissue.
The terminal duct lobular unit (TDLU) is the site of origin for most breast cancer.

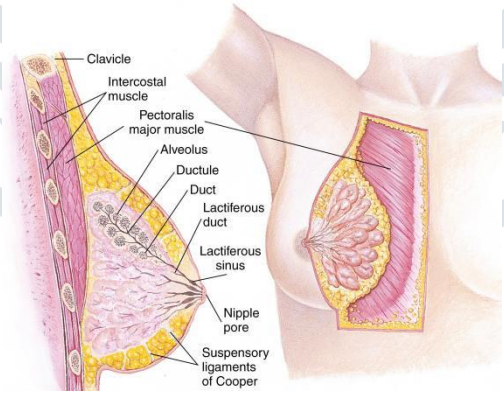


Fig.1 Normal female breast anatomy

7. Molecular Biology of Breast Cancer
Breast cancer is a generically and biologically heterogeneous disease that develops through the accumulation of genetic mutations, epigenetic alterations, and dysregulation of signaling pathways controlling cell proliferation, apoptosis, DNA repair, angiogenesis, and metastasis.
The transformation f normal breast epithelial cells into malignant cells is a multi-step process involving :
. Activation of oncogenes
. Inactivation of tumour suppressor genes
. Defective DNA repair mechanisma
. Epigenetic modifications

. Interaction with the tumour microenvironment

These molecular alterations influence tumour behavior, prognosis, and response to treatment.

8. Genetic Basis of Breast Cancer

Hereditary breast cancers are usually associated with germ line mutations in high penetrance genes.

Major Susceptibility Genes

Gene	Chromosome	Function	Clinical Significance
BRCA1	17q21	DNA repair	High risk of breast and ovarian cancer; often triple-negative phenotype
BRCA2	13q12	DNA repair	Increased risk of breast, ovarian, pancreatic, and prostate cancers
TP53	17q13	Tumour suppressor	Association of Li Fraumeni syndrome
PALB2	16p12	BRCA2 partner in DNA repair	High lifetime breast cancer risk
CHEK2	22q12	Cell-cycle checkpoint kinase	Moderate-risk susceptibility gene
ATM	11q22	DNA damage response	Moderate increase in bresat cancer risk
PTEN	10q23	PI3K pathway regulation	Cowden syndrome
CDH1	16q22	Cell adhesion	Lobular breast carcinoma; hereditary difffiuce gastric ulcer
STK11	19p13	Cell growth regulation	Peutz-Jeghers syndrome

9. BRCA1 and BRCA2

BRCA1

. Encodes a tumour suppressor protein involved in DNA double-strand break repair via homologous recombination.
. Germline mutations increases the lifetime risk of breast cancer to approximately 55-72%

. Frequency associated with :
. Triple-negative breasr cancer
. High-grade tumours
. Basal-like molecular subtype

BRCA2
. Also participate in homologous recombination repair.
. Lifetime breast cancer risk is approximately 45-69 %.
. More commonly associated with hormone receptor-positive tumors than BRCA1

Clinical Importance
. Genetic counselling and testing in selected patients
. Risk-reducing bilateral mastectomy and salpingo-oophorectomy in high-risk individuals

10. Carcinogenesis

Breast carcinogenesis involves progressive transformation through:
1. Normal epithelium
2. Usual ductal hyperplasia
3. Atypical ductal hyperplasia
4. Ductal carcinoma in situ (DCIS)
5. Invasive carcinoma
6. Metastatic disease

Key hallmarks include:
. Sustained proliferative signaling
. Evasion of apoptosis
. Replicative immortality
. Angiogenesis
. Invasion and metastasis
. Immune evasion
. Metabolic reprogramming

11. Major Molecular Pathways

A. HER2 Signaling Pathway

HER2 is a receptor tyrosine kinase belonging to the epidermal growth factor receptor family. Activation leads to cell proliferation, survival, migration and angiogenesis. HER2 amplification occurs in approximately 15-20 % of breast cancers.

B. PI3K/AKT/mTOR Pathway

This pathway regulates cell growth, protein synthesis, survival and metabolism. PI3KCA mutation are common in hormone receptor-positive breast cancers.

C. MAPK Pathway
It mediates cell proliferation and differentiation.

Dysregulation contributes to tumour progression and resistance to therapy

D. Estrogen Receptor Pathway

Estrogen binds to estrogen receptors (ERα and ERβ), promoting transcription of genes involved in cell proliferation

E. DNA Damage Repair Pathway

Homologous recombination repairs double-strand DNA breaks.
Defects in BRCA1/2 increase genomic instability and sensitivity to PARP inhibition.

12. Tumor Microenvironment

The breast tumour microenvironment includes:
. Cancer-associated fibroblasts
. Immune cells
. Macrophages
. Lymphocytes
. Endothelial cells
. Extracellular matrix

Interaction between tumor cells and the microenvironment influence:
. Angiogenesis
. Metastasis
. Immune escape
. Therapeutic response

13. Molecular Classification (Intrinsic Subtypes)

Gene- expression profiling has identified four major sub types:

Subtype	ER	PR	HER2	Ki-67	Prognosis	Treatment
Luminal A	Positive	Positive	Negative	Low	Excellent	Endocrine therapy

Luminal B	Positive	Variable	Positive or Negative	High	Inermediate	Endocrine therapy and/or chemotherapy
HER2-enriched	Negative	Negative	Positive	High	Aggressive but responsive to HER2-targeted therapy	Anti-HER2 therapy + Chemotherapy
Triple-negative (Basal-like)	Negative	Negative	Negative	High	Aggressive	Chemotherapy and/or immunotherapy

Clinical Significance of Molecular Classification

Molecular classification is essential because it :
. Predict prognosis
. Guides systemic therapy
. Identifies patients for targeted treatments
. Helps estimate recurrence risk
. Supports precision medicine approaches

14. Histopathology of Breast Cancer

Histopathological examination is the gold standard for the diagnosis of breast cancer. It confirms malignancy, determines the histological subtypes and grade, evaluates surgical margins, assesses lymphovascular invasion, and provides tissue for immunohistochemical and molecular studies.
Most breast carcinomas arises for the terminal duct-lobular unit (TDLU). The disease progresses through a spectrum ranging from epithelial hyperplasia to atypical hyperplasia , carcinoma in situ, invasive carcinoma, and eventually metastatic disease.

15. WHO Classification of Breast Tumours

The World Health Organization (WHO) classifies breast tumors into benign, in situ, invasive epithelial, mesenchymal, fibroepithelial, and other rare neoplasms.

A. Benign Epithelial Lesions
. Fibrocystic changes
. Fibroadenoma
. Intraductal papilloma
. Adenosis
. Sclerosing adenosis
. Radical scar/complex sclerosing lesion

These lesions are generally non-invasive but some proliferative lesions with atypia are associated with an increased future risk of breast cancer.

B. Pre-invasive (In Situ) Carcinomas

1. Ductal Carcinoma in Situ (DCIS)

DCIS is characterized by malignant epithelial cells confined within the ductal system without invasion through the basement membrane.

Clinical features

. Often asymptomatic
. Commonly detected by screening mammography as microcalcifications
. Occasionally presents with nipple discharge or palpable lesion

Histologic pattern

. Comedo
. Cribriform
. Soild
. Papillary
. Micropapillary

Features

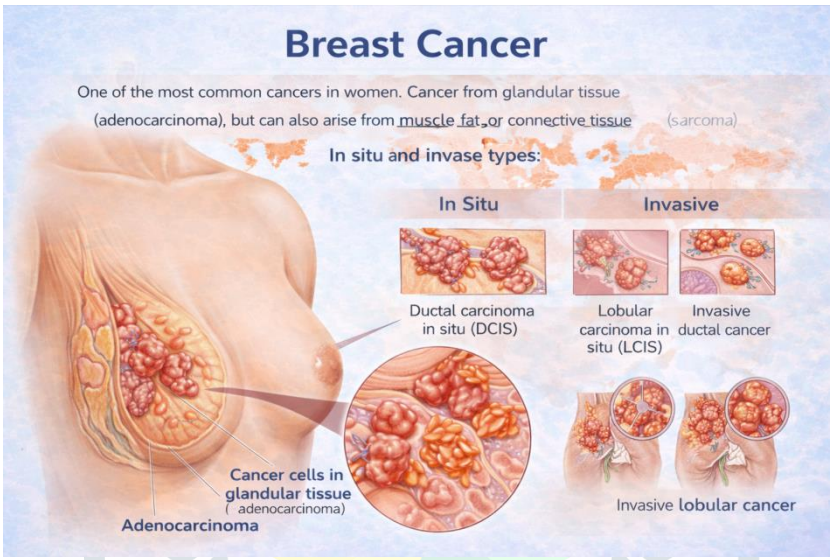
. Basement membrane remains intact
. No stromal invasion
. Excellent prognosis after appropriate treatment

2. Lobular Carcinoma in Situ (LCIS)

LCIS is a proliferation of dyscohesive neoplastic cells within lobules due to loss of E-cadherin (CDH1) expression

Characteristics

. Usually an incidental microscopic findings
. Frequently multifocal and bilateral
. Marker of increased future breast cancer risk rahther than an obligate precursor
. More commonly associated with invasive lobular carcinoma



16. Invasive Breast Carcinoma

Invasive carcinoma is defined by tumour cells penetrating the basement membrane and infiltrating the surrounding stroma.

A. Invasive Carcinoma of No Special Type (NST)

Previously known as Invasive Ductal Cacinoma (IDC)

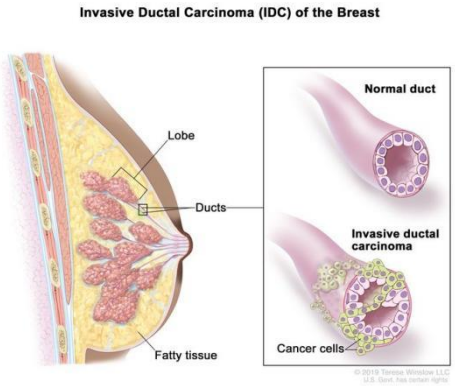
Accounts for approximately 70 - 80 % of invasive breast cancers

Microscopic features

. Malignant glands, nests, cords, and sheets infiltrating fibrous stroma
. Variable tubule formation
. Nuclear pleomorphism
. Mitotic activity

Clinical significance

Most common subtype and variable prognosis depending on stage, grade, and molecular sub type



B. Invasive Lobular Carcinoma (ILC)

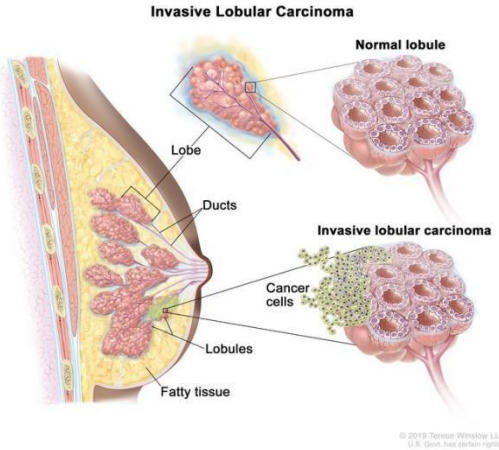
Approximately 10 -15 % of invasive breast cancers

Microscopic features

. Small, uniform, discohesive tumour cells
. Classic single-file (Indian file) infiltration
. Loss of E-cadherin expression

Clinical significance

. Frequnetly bilateral or muti-focal
. Difficult to detect on mammography
. Tendency for unusual metastatic sites (peritoneum, gastrointestinal tract, ovaries, meninges)



C. Special Histological Types

Histological type	Key features	Prognosis
Tubular carcinoma	Well-formed tubules, low grade	Excellent
Mucinous (colloid) carcinoma	Extracellular mucin pools	Favorable
Medullary carcinoma	Syncytial growth, lymphoplasmacytic infiltrate	Intermediate to favorable
Papillary carcinoma	Papillary architecture	Generally favorable
Cribriform carcinoma	Cribriform glands	Favorable
Metaplastic carcinoma	Squamous or mesenchymal differentiation	Poor
Micropapillary carcinoma	Lymphovascular invasion common	Aggressive

17. Histological Grading (Nottingham/Elston-Eills Modification of the Scarff- Bloom-Richardson System)

The Nottingham grading system evaluates three morphological parameters:
1. Tubule formation
2. Nuclear pleomorphism
3. Mitotic count

Each parameter is scored from 1 to 3.

Total score	Grade	Description
3-5	Grade I	Well differentiated
6-7	Grade II	Moderately differentiated
8-9	Grade III	Poorly differentiated

Clinical significance
. Higher grades are associated with increased recurrence risk and poorer survival.
. Histological grade is incorporated into prognostic models and treatment decisions.

18. Immunohistochemistry (IHC)

IHC is routinely performed on invasive breast cancers to determine predictive and prognostic biomarkers.

A. Estrogen Receptor (ER)
ER-positive tumors respond to endocrine therapy and it indicates favourable prognosis

B. Progesterone Receptor (PR)
Reflects functional estrogen receptor signaling and PR positivity supports endocrine responsiveness.

C. HER2 (Human Epidermal Growth Factor Receptor 2)
Membrane receptor tyrosine kinase. Over-expressed in approximately 15-20 % of breast cancers.

D. Ki-67 Proliferation Index
Ki-67 is a nuclear marker of cell proliferation.
Low Ki-67 suggest indolent disease and High Ki-67 indicates aggressive tumour biology and may support the use of chemotherapy

19. Other Biomarkers
Additional markers may be used in selected settings:
. Angrogen receptor (AR)
. PD-L1 (for immunotherapy eligibility)
. BRCA1/BECA2 mutation analysis

20. Differential diagnosis

Important conditions that may mimic breast carcinoma include:
. Fat necrosis
. Sclerosing adenosis
. Radial scar
. Granulomatous mastitis
. Fibroadenoma
. Primary breast lymphoma
. Phyllodes tumour

Correlation of clinical findings, imaging, histopathology, and immunohistochemistry is essential for accurate diagnosis.

21. Clinical Importance of Histopathology

Histopathological examination provides information on :
. Histological subtype
. Tumour grade
. Tumour size
. Margin status
. Lymphovascular invasion
. Nodal metastasis

. Biomarker status (ER, PR, HER2, Ki-67)

These findings form the basis for staging, prognosis, and individual treatment planning.

22. Clinical Presentation

The clinical presentation of breast cancer varies according to tumour size, location, biological sub type, stage at diagnosis. Early stage disease may be asymptomatic and detected through screening, whereas advanced disease often presents with obvious local or systemic manifestations.

A. Common Symptoms

. Painless breast lump (most common presenting complaint)
. Breast asymmetry
. Localized breast pain (less common)
. Nipple discharge (especially bloody or serasanguinous)
. Nipple retraction or inversion
. Skin dimpling or tethering
. Breast swelling
. Axillary swelling due to lymphnode enlargement

B. Signs on Physical Examination

Breast Examniation

The clinician should assess:

. Breast size and symmetry
. Skin changes
. Visible masses
. Nipple abnormalities
. Palpable breast lump
. Mobility of the lesion
. Fixity to skin or chest wall

Skin changes

Characteristic skin manifestations include:

. Peau d’orange (orange-peel appearance due to dermal lymphatic obstruction)
. Skin ulceration
. Skin nodules
. Satellite lesions

Nipple changes

. Retraction
. Ulceration

. Bloody discharge
. Eczema-like changes (suggestive of Paget disease of the breast)



A 55-year-old female having ca. Breast

23. Triple Assessment

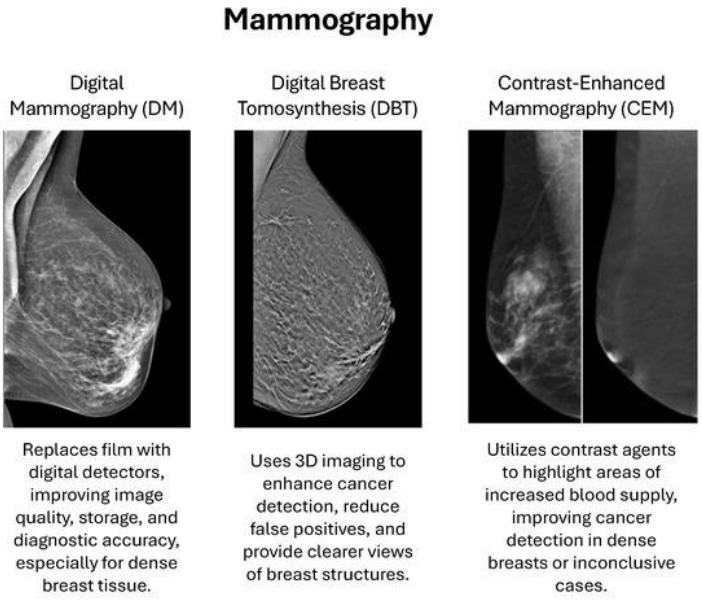
Triple assessment is the gold standard for evaluation a suspected breast lesion. When all three components are concordant, diagnostic accuracy exceeds 99 %.
The three components are :
1. Clinical examination
2. Imaging
3. Pathological Assessment

A. Clinical Examination

A systemic examination should include:
. Inspection (arms at sides, raised, and on hips)
. Palpation of both breasts
. Examination of axillary, supraclavicular, and infraclavicular lymph nodes
. Assessment of tumour size, mobility, consistency, and skin/chest involvement

B. Imaging
1. Mammography
Mammography is a primary modality for breast cancer screening and detects microcalcifications and early non-palpable lesions.

Advantages
. High sensitivity in fatty breasts
. Useful for screening asymptomatic women
. Detects ductal carcinoma in situ (DCIS)



2. Ultrasonography (USG)

Indications

. Evaluation of palpable masses
. Dense breast tissue
. Distinguishing cystic from solid lesions
. Image guided biopsy

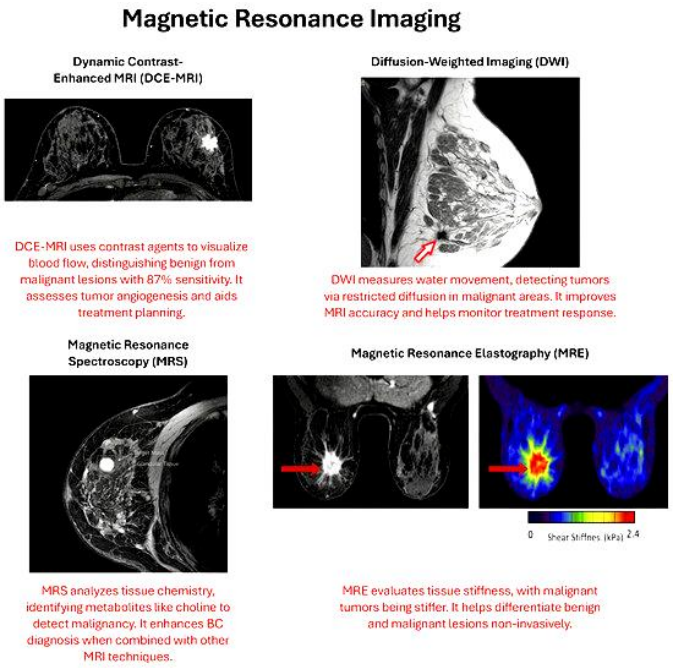
Typical malignant features

. Irregular shape
. Spiculated margins
. Hypoechoic appearance
. Posterior acoustic shadowing
. Taller-than-wide orientation

3. Magnetic Resonance Imaging (MRI)

MRI is not routinely used for screening average-risk women but is valuable in selected situations.

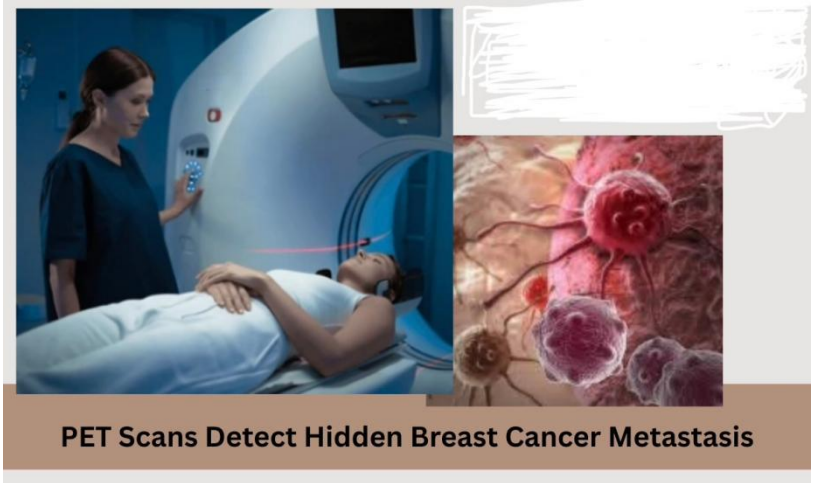
It is indicated in high risk-patients (e.g. BRCA mutation carriers), evaluation of multifocal or multicentric disease, assessment of implant integrity, monitoring response to neoadjuvant chemotherapy, problem solving when mammography and ultrasound are inconclusive.



4. PET-CT

It is indicated in suspected metastatic disease, assessment of recurrence and evaluation of treatment response in selected patients.

PET-CT is not routinely recommended for staging early breast cancer.



24. BI-RADS Classification

The breast imaging reporting and data system (BI-RADS) standardizes breast imaging interpretations and management.

BI-RADS Category	Interpretation	Recommended Management
0	Incomplete	Additional imaging required
1	Negative	Routine screening
2	Benign finding	Routine screening
3	Probably benign (2% risk)	Short-interval follow up
4	Suspicious abnormality	Tissue diagnosis (biopsy)

5	Highly suggestive of malignancy (>95 % risk)	Appropriate treatment after biopsy confirmation
6	Known biopsy proven malignancy	Definitive treatment planning

25. Tissue Diagnosis

Fine-Needle Aspiration Cytology (FNAC)

It is simple, rapid and minimally invasive but have some limitations such as it cannot reliably distinguish in situ from invasive carcinoma and has limited assessment of tumour architecture

Core Needle Biopsy (CNB)

Core needle biopsy is the preferred diagnostic technique. It provides tissue architecture, enables histological grading, allows immunochemistry and more accurate than FNAC

Vaccum-Assisted Biopsy

It is useful for small lesions, microcalcifications and selected benign lesions requiring excision

26. Metastatic Work-up

Additional investigations are performed according to clinical stage and symptoms.

Laboratory Tests

. Complete blood count
. Liver function tests
. Renal function tests
. Serum alkaline phosphatase
. Calcium levels

Imaging

. Chest CT
. Abdominal CT or ultrasound
. Bone scan
. PET-CT (selected cases)
. Brain MRI (if neurological symptoms are present)

27. Anatomical Stage Grouping (Simplified)

Stage	TNM (Typical Pattern)
Stage 0	Tis N0 M0
Stage I	Small tumour (T1), N0, M0
Stage II	Large tumour and/or limited nodal involvement
Stage III	Locally advanced disease with extensive nodal involvement or chest wall/skin invasion
Stage IV	Any T, any N, M1

28. AJCC 8th Edition TNM Staging

The TNM system classifies breast cancer based on:
. T = Primary tumour
. N = Regional lymph nodes
. M = Distant metastasis
It also incorporates tumour grade and biomarker status into prognostic staging.

T - Primary Tumour

Category	Definition
Tis	Carcinoma in situ (DCIS, LCIS, Paget disease without invasive carcinoma)
T1	Tumour < 20 mm
T1mi	< 1 mm microinvasion
T1a	> 1-5 mm
T1b	> 5-10 mm
T1c	> 10-20 mm
T2	> 20-50 mm
T3	> 50 mm
T4	Tumour of any size with direct extension to chest wall and/or skin
T4a	Chest wall involvement
T4b	Skin ulceration, satellite nodules or oedema (including peau d'orange)
T4c	Both T4a and T4b
T4d	Inflammatory breast cancer

N-Regional Lymph Nodes

Category	Definition
N0	No regional lymph node metastasis
N1	Metastasis to movable ipsilateral level I or II axillary lymph node
N2	Fixed/matted axillary nodes or clinically detected internal mammary nodes without axillary involvement
N3	Infraclavicular, supraclavicular, or combined axillary/internal mammary node involvement

M- Distant Metastasis

Category	Definition
M0	No distant metastasis
M1	Distant metastasis present

Common metastatic sites include:
. Bone (most common)
. Lung
. Liver
. Brain

29. Anatomical Stage Grouping (Simplified)

Stage	TMN (Typical Pattern)
Stage 0	Tis N0 M0
Stage I	Small tumour (T1), N0, M0
Stage II	Larger tumour and/or limited nodal involvement
Stage III	Locally advanced disease with extensive nodal involvement or chest wall/skin invasion
Stage IV	Any T, any N, M1

The AJCC 8th edition also uses prognostic stage groups that incorporate ER, PR, HER2 status, and histological grade, which can alter assignment compared with anatomical staging.

30. Management of Breast Cancer

Breast cancer treatment is individualized based on:
. AJCC stage
. Tumour size
. Histological grade
. ER. PR, and HER2 status
. Molecular subtype

. Patient age and menopause status
. Performance status
. Genetic mutation (e.g. BRCA 1/2)
. Patient preference

1. Surgical Management

Surgery remains the primary treatment for most patients with early-stage breast cancer.

Objectives

. Complete tumour excision with negative margins
. Accurate staging of regional lymph nodes
. Preservation of cosmetic appearance where appropriate

A. Breast-Conserving Surgery (BCS)

It is also known as lumpectomy, wide local excision or partial mastectomy. It is indicated in solitary tumour, Tumor-to-breast size ratio suitable for good cosmetic outcome or patient willing to receive postoperative radiotherapy.

B. Mastectomy

Types
1. Simple (total) mastectomy
2. Skin-sparing mastectomy
3. Nipple-sparing mastectomy
4. Modified radical mastectomy (MRM)
5. Radical mastectomy (rarely performed today)

Indications
Main indications for mastectomy are large tumor relative to breast size, multicentric disease, patient preference, contradiction to radiotherapy and inflammatory breast disease cancer (after neoadjuvant therapy)

C. Oncoplastic Breast Surgery
Combines oncologic resection with plastic surgical techniques to improve cosmetic outcomes while maintaining oncologic safety.

31. Axillary Management

Sentinental Lymph Node Biopsy (SLNB)

SLNB is the standard procedure for clinically node-negative patients. It lowers the rates of lymphedema, pain and shoulder dysfunction compared with axillary lymph node dissection (ALND)

Axillary Lymph Node Dissection (ALND)

Typically it involves removal of level I and II axillary nodes.
It is indicated in clinically node-positive disease, persistent nodal disease after neoadjuvant therapy in selected patients and selected patients with multiple positive sentinel nodes.

32. Radiotherapy

Radiotherapy reduces local recurrence and improves survival in selected patients.
It is indicated after breast-conserving surgery, selected patients after mastectomy (e.g.large tumors, positive nodes, close/positive margins).

33. Systemic therapy

A. Chemotherapy

Common indications
. Triple-negative breast cancer (TNBC)
. HER2-positive disease
. High-risk hormone receptor-positive tumors
. Node-positive disease
. High-grade tumors

Common Adverse effects
. Myelosuppression
. Alopecia
. Nausea and vomiting
. Peripheral neuropathy
. Cardiotoxicity
. Infertility

. Febrile neutropenia

B. Endocrine therapy
Used in ER-positive and/or PR positive breast cancers.

C. HER2-Targated Therapy
For HER2-positive breast cancer

D. CDK4/6 inhibitors
For hormone receptor-positive, HER2-negative advanced breast cancer.

E. PI3K and mTOR Inhibitors
Alpelisib indicated for PIK3CA-mutated, hormone receptor-positive, HER2-negative advanced disease and Everolimus for mTOR inhibitor used with endocrine therapy in selected patients.

F. PARP Inhibitors
For patients with gremline BRCA1/2 mutations.

G. Immunotherapy
Immune checkpoint inhibitors are used in selected cases of triple-negative breast cancer.

34. Neoadjuvant Therapy
Administered before surgery to downstage tumors, increase eligibility for breast-conserving surgery, assess treatment response and treat micro metastatic disease early and preferred for HER2-positive disease, Triple-negative breast cancer, locally advanced breast cancer.

35. Adjuvant Therapy
Administered after surgery to reduce recurrence risk. It may include chemotherapy, radiotherapy, endocrine therapy, HER2-targeted therapy, bone-modifying agents in selected patients.

36. Management of Metastatic Breast Cancer
Goals are prolonged survival, control symptoms and preserve quality of life. Treatment depends on hormone receptor status, HER2 status, disease burden, prior therapies and patient preference.

37. Follow-up and Survivor ship

Recommended follow-up includes:
. Regular history and physical examination
. Annual mammography of the preserved or contra lateral breast
. Monitoring for treatment-related adverse effects
. Assessment of bone health in patients receiving aromatase inhibitors
. Psychological support
. Lifestyle counseling (exercise, weight management, smoking cessation, limiting alcohol)

Routine imaging or tumour marker testing in asymptomatic patients is not recommended unless clinically indicated.

38. Preventive aspect of breast cancer

The preventive aspect of breast cancer focus on reducing risk, detecting caner early, and improving outcomes. While not all cases can be prevented, several measures are associated with a lower risk or earlier diagnosis.

1. Maintain a Healthy Lifestyle
. Exercise regularly
. Maintain a healthy body weight, especially after menopause.
. Eat a balanced diet rich in fruits, vegetables, whole grains and lean protein.
. Limit consumption of processed food and saturated fats.

2. Limit Alcohol and Avoid Smoking
. Alcohol increases the risk of breast cancer, and risk rises with greater consumption.
. Avoid smoking as it is linked to several cancers, including breast cancer

3. Breastfeeding
. Breastfeeding particularly for several months or longer, is associated with a reduced risk of breast cancer.

4. Hormone Therapy
. Long term combined hormone replacement therapy (HRT) after menopause may increase breast cancer risk.

5. Regular Screening

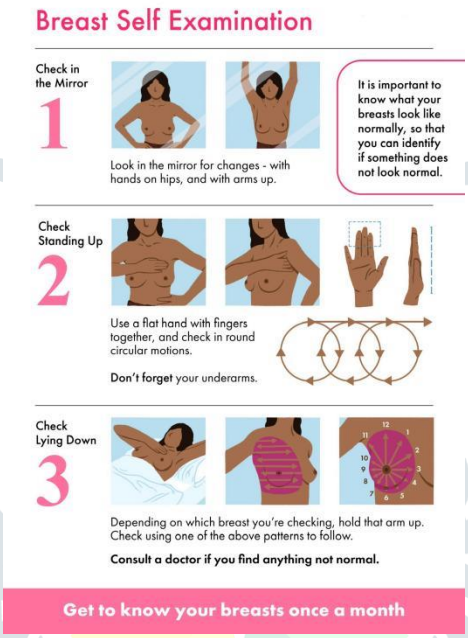
Early detection improves the chance of successful treatment.

. Perform self breast examination (SBE) and become familiar with the normal appearance and feel of your

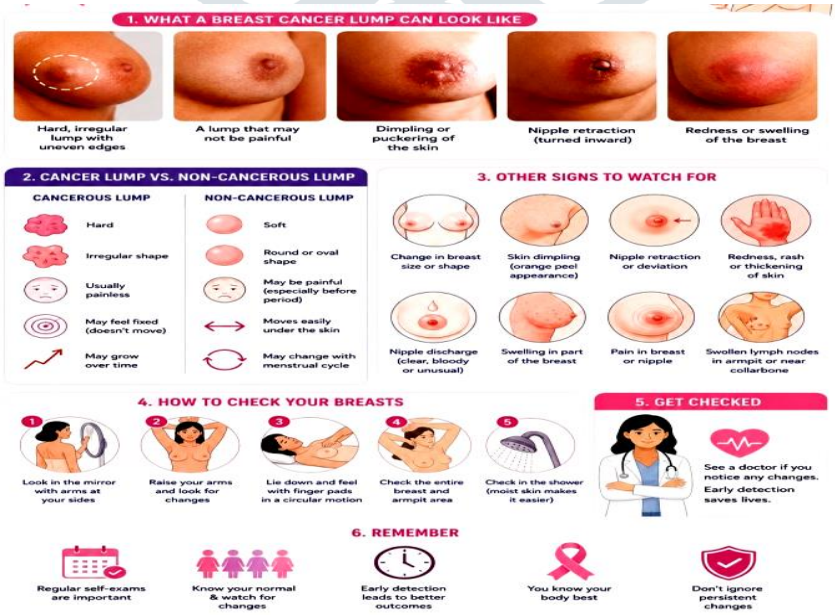
Breast and reporting any changes promptly.

. Have clinical breast examination if recommended by healthcare provider

. Undergo mammography according to age, risk level, and local screening guidelines.



Breast cancer lumps (Visual guide for patients)



6. Family history

People with a strong family history may benefit from genetic counseling and testing for inherited mutations such as BRCA1 or BECA2 .

39. Rare condition

Male breast cancer is classified under **ICD-10-CM category C50**, which covers malignant neoplasms of the breast. Although breast cancer is far more common in women, men can also develop it, typically between ages 60 and 70, and it accounts for about 1% of all breast cancer cases.



A 62-year-old male patient with carcinoma of breast

40. Conclusion

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and is a major cause of cancer-related mortality. Despite its increasing incidence, significant advances in screening, molecular diagnostics, imaging, surgery, radiotherapy, systemic therapy, and precision medicine have substantially improved survival and quality of life.

Breast cancer is a heterogeneous disease with diverse histopathological and molecular characteristics. The identification of intrinsic molecular sub types - Luminal A, Luminal B, HER2-enriched, and Triple-Negative Breast Cancer-has transformed management by enabling personalized treatment based on tumor biology. Immunochemical assessment of estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67 is essential for prognostication and therapeutic decision making.

The principle of tripe assessment (clinical examination, imaging, and tissue diagnosis) remain the cornerstone of diagnosis. Accurate staging using the AJCC TNM classification, coupled with biomarker evaluation, guides the selection of surgery, radiotherapy, chemotherapy, endocrine therapy, targeted therapy, and immunotherapy. A multidisciplinary team approach ensures optimal patient care throughout diagnosis, treatment, rehabilitation, and survivorship.

Emerging technologies, including artificial intelligence-assisted imaging, genomic profiling, liquid biopsy, antibody-drug conjugates, PARP inhibitors, CDK4/6 inhibitors, and precision oncology, are reshaping breast cancer management and are expected to further improve outcomes. Continued research, equitable access to modern therapies, organized screening programs, and public awareness are essential to reduce burden of breast cancer, particularly in low- and middle-income countries.

Further strategies should emphasize early detection, individualized treatment, survivorship care, and integration of molecular medicine into routine clinical practice. With ongoing advances in transitional research and targeted therapeutics, the outlook for patients with breast cancer continues to improve, making personalized, evidence-based care the cornerstone of modern breast oncology.

References

1. Sung H, Ferlay J, Siegel RL. et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and martality worldwide for 36 cancers in 185 countries. CA cancer J Clin. 20121;71(3):209-249
2. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2024. CA cancer J Clin.2024
3. World Health Organization. WHO Classification of Tumors: Breast Tumours. 5th edition Lyon 2019
4. Amin MB, Edge SB, Greene FL, et al., editors. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017
5. National comprehensive cancer network. NCCN Clinical practice guidelines in oncology: Breast cancer. 2020
6. Cortes J, Cescon DW, Rugo HS, et al. Transtuzumab deruxtecan in HER2-low advanced breast cnacer. N Engl J Med 2022; 387:9-20
7. Robson M. Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in BRCA mutation carriers, N Engl J Med. 2017;377; 523-533
8. Slamon DJ,Clark GM, wing SG, et al. Human breast cancer : correlation of relapse and survival with amplification of the HER2/ neu oncogene. Science. 1987; 235 : 177-182
9. Polyak K. Heterogeneity in breast cancer. J Clin Invest 2011;121: 3786-3788
10. Early breast caner trialists' Collaborative group (EBCTCG). long term outcomes after breast cancer therapy, lancet. 2022