IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 11, June 2026
Impact Factor: 8.2

Breast Cancer-Advanced and Traditional Therapies

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Abstract: *Breast cancer is a prevalent global health issue, ranking second in cancer-related deaths among women worldwide. It originates primarily in the ductal epithelium and is influenced by various risk factors. Early detection through screening programs and awareness of symptoms like breast lumps or nipple discharge is crucial. Diagnosis involves physical examination, imaging, and biopsy, while treatment options include surgery, chemotherapy, and immunotherapy, tailored to individual tumor characteristics.*

Keywords: Breast cancer, Cooper ligaments, Lumpectomy,Tissue biopsy

I. INTRODUCTION

Breast cancer ranks second globally in terms of cancer-related deaths among women and is the most prevalent cancer diagnosed in women. The breasts are paired glands that are located superficially to the pectoralis major muscle and vary in size and density. They have lobules of milk-producing cells that are grouped together into lobes with fat scattered throughout. Acini create milk and other fluids, which are then extruded through lactiferous ducts and exit the nipple. Cooper ligaments support the breasts by anchoring them to the underlying muscular tissue.

Although it can also occur in the breast lobules (lobular carcinoma), breast cancer most frequently develops in the ductal epithelium (ductal carcinoma).Numerous breast cancer risk factors have been thoroughly documented. In Western nations, screening programs have been successful in detecting the majority of breast cancers through screening as opposed to symptoms.Nonetheless, a breast lump or unusual nipple discharge is frequently the initial sign in a large portion of the developing globe. Tissue biopsy, breast imaging, and physical examination are used to diagnose breast cancer. Surgery, chemotherapy, radiation, hormonal therapy, and, more recently, immunotherapy are among the available treatment options. Tumor markers, stage, histology, and genetic anomalies are among the variables that influence personalised Treatment choices.

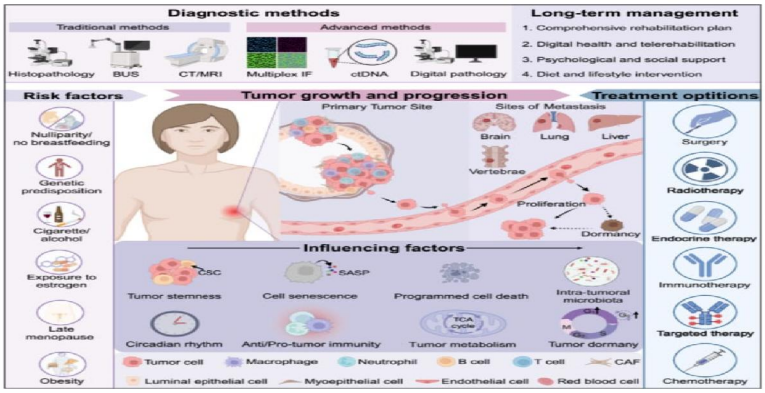

Fig: Breast cancer progression, diagnosis and treatment pathway

DOI: 10.48175/568

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II. ETIOLOGY

Breast Cancer Risk Elements Finding the variables linked to a higher risk of developing breast cancer is crucial for women's general health screening. Breast cancer risk factors include: [1] Age: As the population of females ages, the age-adjusted incidence of breast cancer keeps rising. Gender: Women are more likely to get breast cancer. Personal history: The risk of developing a second primary cancer in the contralateral breast is increased if one breast has previously experienced cancer. Histologic: One crucial class of risk factors for breast cancer is histologic abnormalities identified by breast biopsy. Lobular carcinoma in situ (LCIS) and proliferative alterations with atypia are two examples of these anomalies.

Genetic mutations and family history: First-degree relatives of breast cancer patients have a two- to three-fold increased chance of developing the disease. 5% to 10% of instances of breast cancer are caused by genetic factors; however, in women under 30, this percentage may reach 25%. The most significant genes linked to an increased risk of breast cancer are BRCA1 and BRCA2. Reproductive: It is believed that breast cancer risk is increased by reproductive milestones that raise a woman's lifetime exposure to estrogen.Menarche before the age of twelve, the first live birth after the age of thirty, nulliparity, and menopause after the age of fifty-five are some of these.[2]

Exogenous hormone use: Hormone replacement treatment for postmenopausal women and contraception for premenopausal women are the most common circumstances for which therapeutic or supplementary estrogen and progesterone are administered. Other: Other variables linked to an increased risk of breast cancer include radiation, environmental exposures, obesity, and excessive alcohol intake.[3]

III. EPIDIMEOLOGY

With 11.7% of new cases in 2020, invasive breast cancer is still the most frequent cancer among women globally.[6] In the United States, 1 in 8 women and 1 in 1000 men will have breast cancer at some point in their lives.[4] 95% of new occurrences of breast cancer occur in women 40 years of age or older, and the incidence rate rises with age, from 1.5 cases per 100,000 in women aged 20 to 24 to a peak of 421.3 cases per 100,000 in women aged 75 to 79. When a woman is diagnosed with breast cancer, her median age is 61.Up until 2000, there was a sharp rise in the incidence of breast cancer; after that, it started to fall. Women under 50 years old see more notable declines. Over the past 25 years, North America and portions of Europe have seen a decline in breast cancer death rates due to early detection and substantial advancements in therapy. Between 1980 and 2020, the death rate from breast cancer in the US decreased by 43%.However, the incidence and death rates from breast cancer are still rising in several Asian and African nations (such as South Korea, India, and Uganda).[5]There are significant differences in detection and survival rates according on race and socioeconomic position even within the United States. While non-Hispanic whites have the highest prevalence, African Americans have a much higher death rate. The American Cancer Society (ACS) reports that women from different racial and ethnic groups have the following rates of breast cancer[6]

Non-Hispanic white: 128.1 in 100,000
African American: 124.3 in 100,000
Hispanic/Latina: 91.0 in 100,000 American Indian/Alaska Native: 91.9 in 100,000
Asian American/Pacific Islander: 88.3 in 100,000

IV. PATHOLOGY

Luminal breast cancers arise from the luminal epithelial cells lining the breast ducts. These cancers are characterized by hormone receptor positivity, especially estrogen receptors

1. Cell of Origin

* Originates from luminal epithelial cells of the mammary ducts
* These cells normally respond to estrogen and progesterone for growth and differentiation

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2. hormone receptor expression

*Estrogen receptors (ER-positive)

* Often progesterone receptors (PR-positive)

* Estrogen binds to ER → activates gene transcription → cell proliferation

Cancer develops when this hormone-driven growth becomes uncontrolled

3. Molecular Mechanism

* Estrogen–ER complex enters the nucleus Activates genes involved in:

* Cell cycle progression * Anti-apoptosis (cell survival)

* Mutations (e.g., *PIK3CA*) enhance survival and proliferation

* Loss of growth regulation → tumor formation

4. Subtypes of Luminal Breast Cancer

Luminal A

* ER+, PR+

* HER2 negative

* Low Ki-67 (low proliferation)

* Slow-growing, better prognosis

Luminal B

* ER+, PR low or negative

* May be HER2 positive or negative

* High Ki-67 (high proliferation)

* More aggressive than Luminal A

5. Tumor Behavior

* Growth is estrogen-dependent

* Responds well to hormonal (endocrine) therapy

* Metastasis usually occurs later compared to other subtypes

6. Clinical Correlation

* Common in adults, especially post-menopausal women

* Best prognosis among breast cancer subtypes

* Treatment targets estrogen signalling[7],[8],[9]

V. TREATMENT

Surgery

Breast-conserving surgery (BCS) followed by radiotherapy (RT) and mastectomy are well-established treatments for early breast cancer. Improvements in systemic therapy have significantly reduced locoregional recurrence (LRR). The 10-year LRR after BCS+RT is very low—2–3% in ER-positive and HER2-positive tumors and around 5% in TNBC—comparable to outcomes after mastectomy. Because BCS also offers better cosmetic and quality-of-life results, it is preferred for most eligible patients. BCS is avoided when there are diffuse micro-calcifications, multicentric lesions, inability to obtain clear margins, or contraindications to RT. Young patients, lobular carcinoma, HER2-positive disease, and TNBC are not contraindications. Neoadjuvant chemotherapy may be used to shrink large tumors and make BCS possible.[11]

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Axillary management depends on initial nodal status. Axillary lymph node dissection (ALND) is recommended for patients with clinically positive nodes, while sentinel lymph node biopsy (SLNB) is usually adequate for clinically node-negative (cN0) cases, even when 1–2 nodes are positive.

In locoregional recurrence, surgery remains essential. After initial BCS, total mastectomy provides good control (85–95%). After prior mastectomy, wide local excision of recurrent chest-wall disease is preferred, as limited resection is associated with a high risk of further recurrence.[12]

Technique or Treatment

1. Lumpectomy

Breast-conserving surgery includes procedures like lumpectomy, partial mastectomy, and quadrantectomy, all designed to remove the tumor while keeping most of the breast intact. Quadrantectomy removes a larger portion of tissue (2–3 cm margin with fascia and skin), whereas lumpectomy removes the tumor with a smaller 1 cm margin, which is suitable for most early-stage cancers. Non-palpable tumors require image-guided localization.

During a lumpectomy, the incision is planned based on tumor position and cosmetic factors. After creating subcutaneous flaps, the tumor is removed and properly oriented for pathology. Intraoperative imaging ensures the biopsy clip and markers are included. If margins are close, extra tissue (0.5–1 cm) or thin "shave margins" may be excised to reduce the likelihood of re-excision. Radiopaque clips are placed in the cavity to assist with radiation planning. The incision is then closed in layers, usually with absorbable sutures. [13]

2. Mastectomy

Mastectomy techniques have advanced greatly from the original radical mastectomy described by Halsted in the 1890s, which removed theentire breast, pectoralis major muscle, and axillary lymph nodes, often resulting in high morbidity and poor cosmetic outcomes. Madden introduced the modified radical mastectomy (MRM) in 1972, a procedure that remains widely practiced today. This procedure uses an elliptical incision, includes removal of all breast tissue and the pectoralis major fascia, and involves dissection of level I–III axillary lymph nodes, while preserving the pectoralis major muscle. In contrast, a simple mastectomy removes only the breast tissue and nipple–areolar complex and does not require full axillary node dissection.

A typical mastectomy involves creating an elliptical incision and elevating uniform skin flaps (5 mm–1 cm thick) to ensure complete removal of breast tissue while maintaining adequate skin perfusion. These flaps extend to the clavicle superiorly, the sternum medially, the inframammary fold inferiorly, and the anterior border of the latissimus dorsi laterally.Modern variations include skin-sparing and nipple-sparing mastectomies, both commonly paired with immediate reconstruction. In nipple-sparing procedures, a frozen section of the nipple–areolar complex on the tumor side is examined to confirm the absence of disease before preservation.. [14]

3. Sentinel Node Biopsy

Sentinel lymph node biopsy (SLNB) is a key staging procedure for early breast cancer patients who have no clinical lymph node involvement. Short-acting neuromuscular blockers are preferred during anesthesia to allow clear identification of major nerves and prevent accidental injury.

For optimal detection, surgeons usually use a dual-tracer approach. Technetium-99m sulfur colloid is injected intradermally, and a blue dye (busulfan blue or diluted methylene blue) is injected into the areolar Possible spelling mistake found. plexus. A gamma probe then identifies the radioactive sentinel node.

After a small incision and dissection to the Possible spelling mistake found. fascia, the "hottest" node is removed. Additional nodes are excised if they show >10% of the sentinel node's radioactive count, are stained blue, or appear unusual. All retrieved nodes are sent for frozen or permanent histopathologic evaluation.Axillary Node Dissection[15]

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4. Axillary Node Dissection

ALND is performed for selected patients. The procedure involves:

Incision & Flap Creation: A "inactive S" incision is made over the maxilla. Electrocautery is used to dissect subcutaneous tissue and raise skin flaps, with the inferior flap extended to the 5th rib.Exposure of Maxilla: Axillary borders include the axillary vein, pectoralis major and minor, and latissimus dorsi. The lateral border of pectoralis major is elevated to expose and dissect intersectoral (Rotter's) nodes.

Node Dissection: Axillary fascia is divided to free the lateral edge of pectoralis minor, allowing excision of axillary lymph nodes. In bulky disease, the pectoralis minor may be divided for better access.

Closure: Wound is irrigated, hemostasis ensured, and a single drain placed below the axillary vein. Closure is done with deep dermal absorbable sutures and skin adhesive or absorbable sutures.[16]

VI. CHEMOTHERAPY

Chemotherapy is the use of cytotoxic drugs to destroy cancer cells, reduce recurrence, and improve survival in breast cancer patients.[17,18,19,20]

Types/Modalities:

1. **Neoadjuvant Chemotherapy (NAC):** Administered before surgery to shrink tumors, downstage the axilla, enable breast conservation, convert inoperable tumors to operable, and eliminate micrometastases. Recommended for large tumors, multiple node involvement, and aggressive subtypes (TNBC, HER2-positive). NAC also helps assess treatment response, guide prognosis, and inform further therapy. It reduces mastectomy rates by ~17%.

2. **Adjuvant Chemotherapy (AC):** Given after surgery to eradicate residual disease. Indicated for high-risk patients, such as those with large tumors, nodal involvement, low hormone receptor expression, younger age, or lymphovascular invasion. AC should ideally start within 3 months post-surgery; dose-dense schedules (every 14 days) improve disease-free and overall survival compared to conventional 21-day intervals.

3. **Salvage Chemotherapy:** Used for recurrent or metastatic breast cancer.

4. Regimens:

• Standard: Taxane with or without anthracycline (sequential or combination). Anthracyclines remain important for high-risk TNBC and HER2-positive patients.

TNBC-specific options:

Adding platinum increases pathological complete response (pCR).

• Docetaxel + carboplatin improves disease-free and relapse-free survival, with similar overall survival to standard regimens.

• Low-dose, high-frequency capecitabine maintenance enhances 5-year distant disease-free survival as consolidation therapy.

Additional Points

• Sandwich chemotherapy is discouraged outside clinical trials.

• Multigene assays and molecular subtypes help identify patients who will benefit most.

• Timely initiation of AC is critical; delays beyond 91 days are associated with worse outcomes, especially in TNBC.

Summary: Chemotherapy, through NAC or AC, significantly reduces recurrence (~30%) in early breast cancer. Optimal regimen selection, scheduling, and patient stratification are key for maximizing benefits.[17],[18],[19],[20].

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VII. RADIOTHERAPY

1. After Breast-Conserving Surgery (BCS)

Two major randomized trials have shown that for low-risk patients, skipping radiotherapy (RT) is unsafe. Therefore, adjuvant RT is essential after BC Whole breast irradiation (WBI) is still the standard treatment after BCS.

Hypofractionated whole breast irradiation (WBI) offers similar local control, survival rates, and side effects as traditional schedules. It is recommended for early-stage breast cancer without lymph node involvement.

Partial breast irradiation (PBI) has comparable local recurrence rates. It also improves cosmetic outcomes and reduces side effects, making it a suitable choice for some low-risk patients.

Accelerated PBI (APBI) is another valid option for certain early-stage cases. It shows lower recurrence rates in specific patient groups compared to WBI.

Brachytherapy has similar recurrence outcomes to external beam RT. However, it should be used selectively because of limited strong evidence.

2. After Mastectomy

Postmastectomy radiation therapy (PMRT) is highly recommended for patients with four or more positive axillary lymph nodes (ALNs).For patients with 1 to 3 positive ALNs, the benefits of PMRT are less clear. Earlier studies showed significant reductions in recurrence and breast cancer mortality.More recent studies, which reflect improvements in systemic therapy, do not consistently show survival benefits.

As a result, PMRT should be adjusted for each patient, especially those at higher risk. This includes younger patients, those with a greater tumor burden, or individuals with aggressive tumor biology.

The 8th AJCC pathological prognostic staging, which includes molecular subtype, may offer more guidance for PMRT decisions in N1 disease.

3. Regional Nodal Irradiation (RNI)

For patients with positive nodes, irradiating the chest wall and infra-/supraclavicular nodal regions provides clear benefits. The MA.20 trial showed that adding comprehensive RNI improved disease-free survival by 24%. The role of internal mammary node (IMN) irradiation is still uncertain. Some studies report improved overall survival but also point out increased risks of heart and lung issues, lymphedema, and non-breast cancer mortality.Other trials find no significant survival benefit from IMN irradiation.Further research is needed to clarify the exact value of IMN irradiation in modern breast cancer treatment.

4. Endocrine therapy

Endocrine therapy is the standard adjuvant treatment for HR-positive breast cancer for 5–10 years, with its effectiveness depending on the level of hormone receptor expression.

A, Premenopausal Patients

- Tamoxifen 20 mg/day for 5 years lowers recurrence by about 50% in the first 4 years and by over 30% during years 5–9.
- The ATLAS trial showed that extending tamoxifen to 10 years provides an additional 2% reduction in breast cancer mortality, supporting extended therapy.

B, High-Risk Premenopausal Patients

- Patients 35 years or younger or those who have undergone chemotherapy may achieve better outcomes with ovarian suppression combined with tamoxifen.
- This intensified treatment approach, however, is associated with higher toxicity compared with tamoxifen alone.

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C, Postmenopausal Patients

- Options include tamoxifen, five years of endocrine therapy, or sequential therapy.
- Endocrine agents used in this group offer a significant reduction in breast cancer mortality and are preferred in high- risk patients and those with lobular carcinoma.
- If patients develop bone-adverse effects, alternative endocrine agents such as tamoxifen can be considered.
- Treatment duration should be individualized, and tools like multigene assays may assist in determining the most suitable length of therapy related adverse effects, alternative endocrine agents such as tamoxifen can be considered.

5. Targeted Therapy

HER2-positive breast cancer is now much more effectively managed and treated with anti-HER2 targeted therapy, and trastuzumab has shown notable survival benefits when combined with anthracycline and taxane-based chemotherapy, both in the adjuvant and neoadjuvant settings. Although other chemotherapy regimens also enhance overall survival, several studies have demonstrated that trastuzumab plus paclitaxel reduces toxicity and decreases recurrence rates in patients with small, node-negative tumors, so the standard treatment for HER2-positive breast cancer is now one year of trastuzumab plus chemotherapy. Additional anti-HER2 medications have further enhanced treatment efficacy; for example, pertuzumab is recommended for stage II–III disease And significantly increases pathological complete response rates when used in combination with trastuzumab and docetaxel in the neoadjuvant setting. Other examples include dual HER2 blockade using lapatinib and trastuzumab. [21],[22],[23],[24],[25],[26],[27],[28]

VIII. DIAGNOSIS

Techniques for Diagnosis or Detection of Breast Cancer

A successful course of treatment for breast cancer depends on early diagnosis. T3 tumors, which are largely the consequence of delayed diagnosis, have a 10-year survival of less than 60%, whereas T1 tumors with a diameter of less than 2 cm have a 10-year survival of over 85%.

Imaging techniques commonly used for detection of breast cancer are summarized in Table 1.

Table -1

Summary of various imaging modalities for screening of breast cancer.

Imaging Modality	Principle	Diagnostic Accuracy	Advantages	Limitations
Mammography (First-line tool for breast screening)	Low-dose ionizing x-ray creates detailed images of the breast.	Sensitivity: 75–90% Specificity: 90–95% Spatial Resolution: 50 µm	Most cost-effective. Good response with high specificity and sensitivity. Portable device.	Uses ionizing radiation. Sensitivity decreases with increasing breast density. Accuracy is low in young women. High false-positive results in young women due to dense breasts. Poor contrast compared to MRI.
Magnetic Resonance Imaging	Uses low-energy radio waves and strong magnets to obtain detailed images of structures within	Sensitivity: 75–100% Specificity: 83–98.4% Spatial Resolution:	Ability to detect breast malignancies that often escape from clinical, mammograms, and ultrasound detection.	Expensive, inability to standardize the test. Unnecessary breast biopsies due to inability to distinguish between malignant and benign lesions.

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	the breast	25–100 µm		
Magnetic Resonance Spectroscopy	Employs magnetic field on body fluids and tissue samples to obtain chemical information of that region	Sensitivity: 93% Specificity: 70% Spatial Resolution: up to 0.25 cm^3	Overcomes limitations of mammography. Radiation-free imaging technology. Excellent Sensitivity. Excellent spatial resolution. All imaging planes possible.	Expensive and time-consuming. Low specificity. Not portable. False-positive results in some benign tumors.
Dynamic Contrast Enhanced MRI (DCE-MRI)	Multiple MRI scans taken post i.v. injection of contrast agent	Sensitivity: 89–99% Specificity: 37–86% Spatial Resolution: 25–100 µm	Exhibits good performance in monitoring response post therapy.	False-negative results observed due to artifacts based on bleeding and tumor structure.
Diffusion-Weighted Imaging	Employs diffusion of water molecules to generate contrast.	Sensitivity: 83% Specificity: 84% Spatial Resolution: 25–100 µm	Non-radioactive imaging technique	Failure to detect high water content malignant lesions due to high apparent diffusion coefficients.
MR Elastography (MRE)	Dynamic elasticity imaging technique that combines MRI imaging with low frequency. Employs mechanical waves to create an elastogram to assess tissue stiffness.	Sensitivity: 90–100% Specificity: 37–80% Spatial Resolution: 25–100 µm	Non-invasive, non-ionizing and cross-sectional imaging modality	Lacking in spatial resolution and detection of small focal lesions.
Positron Emission Tomography conjugated with computed Tomography (PET-CT)	Combines nuclear medicine technique and computed tomography resulting in high detailed images.	Sensitivity: 90–100% Specificity: 75–90% Spatial Resolution: 2–10 mm	Non-invasive. Provides twice the diagnostic benefits (Elevated activity within the body detected by PET scan and intricate images of tissues and	High-cost. Unable to detect tumors less than 8 mm.

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organs by CT scan).

Sentinel lymph node biopsy (SLNB)	Surgical procedure to detect spreading of cancer in lymphatic system.	Sensitivity: 90.5% Specificity: 85.7% Spatial Resolution: Not Applicable	Significantly reduces post-operative complications	Not useful for patients with locally advanced cancers and inflammatory breast cancer.
Breast Specific Gamma Imaging	Employs use of a radiotracer. Image captured using a special camera.	Sensitivity: 90–96% Specificity: 71–80% Spatial Resolution: ≥7 mm	Able to identify smaller lesions (<1 cm)	High radiation dose. Not suited for routine tumor screening.
Ultrasound	Employs sound waves to image breast tissues	Sensitivity: 80–89% Specificity: 34–88% Spatial Resolution: 50–500 µm	Accessible, real-time lesion visualization, cost-effective, patient compliant.	Failure to detect microcalcifications, possibility of false-positives.

1. Mammography

An x-ray of the breast called a mammography can show abnormalities that are either benign or cancerous. An x-ray image is created by passing a tiny amount of radiation through the breast after it has been compressed between two plates. Mammograms can be used for diagnosis as well as screening. In order to reduce mortality through early diagnosis, mammography screening is done in an effort to find any early indications of breast cancer, even before symptoms appear. If a woman has symptoms, such as a palpable lump in her breast, a diagnostic mammography can help identify breast cancer. The U.S. Preventive Services Task Force (USPSTF) released new mammography screening guidelines in 2009, recommending that routine screening mammography is not necessary for women under 50. Prior to this, the USPSTF's position was in line with American Cancer Society guidelines, which recommended mammography every one to two years for all women 40 and older. Furthermore, breast density cannot be used to deduce the information embedded in a mammogram since radiologists evaluate data subjectively [35]. For example, patients may have the same breast density assessment value but noticeably different mammograms, each with very different results. In earlier research, statistics pertaining to glandular tissue volume were developed using mammography results. Nevertheless, these automated techniques for assessing breast density are insufficient to forecast the incidence of breast cancer. Gold-based nanoformulations have recently demonstrated promise in greatly improving mammography picture contrast. The precision of breast cancer risk models can be enhanced by mammographic density. A deep learning (DL) model based on mammography can also provide more precise risk prediction

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2. Magnetic Resonance Imaging

Breast MRI is a non-invasive, non-ionizing diagnostic imaging technique that uses a magnetic field and low-energy radio frequency radiation to produce finely detailed images of the breast's internal structures. In women who have previously been diagnosed with breast cancer, MRI can be used to evaluate the cancer's size and search for metastasized tumors. MRI has been used to precisely identify and measure tumors that are smaller than or equal to 2 cm. However, because of the aberrant breast tissue surrounding the lesion, larger breast tumors are frequently exaggerated, which can result in higher mastectomy rates. Forty years ago, Goldsmith et al. initially reported using nuclear magnetic resonance position was in line with American Cancer Society guidelines, which recommended mammography every one to two years for all women 40 and older. Furthermore, breast density cannot be used to deduce the information embedded in a mammogram since radiologists evaluate data subjectively [35]. For example, patients may have the same breast density assessment value but noticeably different mammograms, each with very different results. In earlier research, statistics pertaining to glandular tissue volume were developed using mammography results. Nevertheless, these automated techniques for assessing breast density are insufficient to forecast the incidence of breast cancer. Gold-based nanoformulations have recently demonstrated promise in greatly improving mammography picture contrast. The precision of breast cancer risk models can be enhanced by mammographic density. A deep learning (DL) model based on mammography can also provide more precise risk prediction

.3. Dynamic Contrast Enhanced (DCE-MRI)

Analyzing the temporal enhancement pattern of a tissue after an intravenous infusion of a paramagnetic contrast agent is how dynamic contrast-agent-enhanced breast MRI operates. The degree of tissue vascularization, the makeup of the interstitial space, and the differentiation of lesions are all quantitatively determined by this non-invasive imaging method [48]. Tumor angiogenesis, overall recurrence, and overall breast cancer patient survival can all be shown using this imaging method. Therefore, this imaging modality can also be used to predict lymph node metastases caused by increased angiogenesis in breast cancer. Estrogen receptor positive (ER+) breast cancer subtypes can also be identified using DCE-MRI in conjunction with a computer-aided diagnosis tool like texture analysis. The non-invasive, three-dimensional DCE-MRI method enables the viewing of the disease's extent prior to morphological changes and aids in the prediction of the overall response either prior to the initiation of therapy or early during treatment. DCE-MRI is not constrained by breast tissue density, in contrast to mammography. However, DCE-MRI's non-specificity is a major drawback

.4.. Magnetic Resonance Elastography

Details about the mechanical characteristics of tissues in vivo can be obtained using magnetic resonance elastography (MRE) [56]. Breast MRE, a non-invasive, non-ionizing, cross-sectional imaging technique, may measure the viscoelastic characteristics of breast tissues once an external stress is applied. Compared to normal surrounding tissues and benign lesions, breast tumors frequently exhibit greater stiffness due to an increase in cells, collagen, and proteoglycans. Despite being widely used for routine breast screening, manual palpation is not sensitive or specific. Here, MRE scanning of the breast can help overcome the limitations of manual palpation. The most important constraint for MRE in breast cancer is spatial resolution and detection of small localized lesions because the elasticity ranges of stiff benign lesions and soft malignant tumors overlap, despite the optimistic initial results.

5. Diffusion-Weighted Imaging

Using high magnetic field strengths (usually 11–14 T) on bodily fluids, cell extracts, and tissue samples, magnetic resonance spectroscopy (MRS) can quantify a chemical "spectrum" in the area, providing more details on the chemical content in the area. The addition of an MRI technique to the in vivo 1H MRS protocol extends the total collection time by about 10 minutes and has the benefit of increasing the diagnostic accuracy of clinical breast MR. One of the limitations of this imaging modality is the need for slightly larger lesions and low sensitivity to detect total choline

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(tCho), a phosphocholine metabolite elevated in breast malignancies and used as a diagnostic biomarker signal. The MRS specificity has been reported to be about 88%.Breast MRS has advanced significantly over the past 10 years, but before using this imaging modality in a clinical context, a number of issues that could limit MRS, such as the complexity of acquisition processes and the optimization of analytic techniques, must be resolve.

6. Positron Emission Tomography (PET)

Scanning and PET In Conjunction with Computer-aided Tomography (CT) Scanning (PET-CT)In cancer, positron emission tomography (PET) imaging has gained widespread acceptance as a crucial clinical tool. The most popular US FDA-approved PET radiotracer that capitalizes on the increased glucose metabolism of cancer cells is 2-deoxy-2-(18F)fluoro-D-glucose (FDG), despite the fact that numerous PET radiotracers have been created to non-invasively examine in vivo tumor metabolism. Compared to normal cells, cancerous cells have a faster rate of glucose metabolism and are extremely proliferative. Tumor cells absorb more FDG PET radiotracers than healthy cells do because they enter cells through the glucose transporter. Prognosis and FDG uptake have an inverse relationship.

PET-CT is a nuclear medicine method that combines CT with PET to get extremely detailed images of the body. Positron emission mammography (PET) has found practical use in the investigation of primary tumors because to the enhanced spatial resolution and sensitivity of breast-specific PET scanners. Several studies have demonstrated that cellular glucose absorption, which is increased in malignant lesions, can be determined using hybrid imaging with 18F-FDG PET/CT. Following nanoparticle-assisted photothermal therapy, Jørgensen et al. found that tumor cells greatly reduced their uptake of 18F-FDG, suggesting that it can be used as a marker to evaluate treatment responses. PET-CT studies are used by doctors to diagnose and stage cancer, plan treatment, assess treatment efficacy, and oversee continuing care.

7. Molecular Image-Guided Sentinel Node Biopsy

A cutting-edge, minimally invasive technique for determining whether metastases has occurred in individuals with early-stage breast cancer is sentinel lymph node biopsy (SLNB). SLNB is typically performed to determine the best course of treatment based on the nodal metastatic status. Compared to traditional axillary lymph node dissection, the SLNB approach is widely known for having substantially less post-operative problems [87,88]. Effective SLNB care is therefore essential to a successful diagnosis and course of treatment for breast cancer. In order to improve the staging accuracy in women with invasive breast cancer, accurate SLNB guidance should reduce the number of invasive procedures required and identify whether multiple-basin drainage is taking place by localizing sentinel lymph nodes.

8. Breast Specific Gamma Imaging

With a sensitivity and specificity comparable to magnetic resonance imaging (MRI), breast specific gamma imaging (BSGI), a molecular breast imaging technique, is a specialist nuclear medicine imaging test that can identify sub-centimeter and mammographically occult breast cancer. A radiotracer, such as Technetium Tc99m Sestamibi, is injected into the patient's circulation during BSGI, and a specialized camera is used to seethe breast. Breast density has no effect on BSGI, in contrast to mammography. Compared to scintimammography, the sensitivity of the current BSGI is higher for the identification of sub-centimeter lesions [95]. The main disadvantage of this method is that it cannot be used for routine breast cancer screening because the entire body is exposed to radiation.

9. Ultrasound

Despite being the gold standard for imaging breast cancer, mammography has limits when it comes to dense breasts, hence an additional screening method is needed. For women with dense breast tissues, ultrasound is an additional tool that can be used to examine worrisome areas not visible on a mammogram as well as certain breast alterations. Widespread accessibility and the lack of radiation exposure for patients are two benefits of this method. However, it is constrained by several things at the same time. Most importantly, it might miss some early indicators of cancer and fail

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 11, June 2026
Impact Factor: 8.2

to identify microcalcifications. Due to this restriction, this method is only utilized in certain circumstances and is not used to test for breast cancer. Combining ultrasonography with additional modalities . Important tools for the treatment of breast cancer patients include ultrasound imaging methods and ultrasound-guided biopsies. Nowadays, ultrasound elastography is a common noninvasive method for determining the hardness or consistency of tissues in order to distinguish between benign and malignant breast tumors. Other methods that could be helpful in the noninvasive prediction of breast cancer prognostic variables include contrast-enhanced ultrasonography and other modalities combined with ultrasound. When used by professionals, complementary high resolution ultrasonography is a great way to find breast lesions [103]. According to the literature currently in publication, combining ultrasound with other modalities may be a useful primary detection method for breast lesions, especially in low- and middle-income nations with limited resources where mammography and other costly methods are unavailable.[29,30,31,32,33].

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IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
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ISSN: 2581-9429
Volume 6, Issue 11, June 2026
Impact Factor: 8.2

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