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Breast Cancer: An Overview of Pathogenesis, Diagnosis and Advances in Therapeutic Approaches

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Abstract
A tumour (neoplasm) develops when the normal regulation of cell proliferation is disrupted, resulting in excessive or abnormal cellular growth. Neoplasms are commonly categorized as benign (non-cancerous) or malignant (cancerous). Breast cancer arises in breast tissue, particularly the ductal lining or the lobules connected to the milk ducts. The breast contains glandular components and supportive stromal tissue. Breast cancer is not a single homogeneous illness, but a group of cancers that have abnormal cells growing faster than healthy cells and that may not be recognized by the immune system or may not undergo apoptosis. According to estimates from GLOBOCAN, about 2.3 million new cases and 666,000 deaths are expected to occur globally in 2022. In 2026, these estimates were about 2.4 million cases and 694,000 deaths in 2024 all over the world. In more severe disease, cancer cells can spread to organs like the liver, lungs, brain and bones, and treatment is more complex and survival is poorer. The clinical stage is divided into stages 0 (usually non-invasive disease), stage 1, stage 2, stage 3 and stage 4 (distant metastasis); the intermediate stages are a description of the amount of tumour involvement and spread. Risk is related to age, hormonal and reproductive status, genetic predisposition, lifestyle and environment. With the advent of mammography, ultrasonography, magnetic resonance imaging (MRI), computed tomography (CT), immunohistochemistry and next-generation sequencing, diagnostic and molecular evaluation have been enhanced. Management includes surgical procedures, radiotherapy, cytotoxic chemotherapy, endocrine treatments and emerging approaches involving immune-cell modification, artificial intelligence and ultrasound-targeted microbubble destruction (UTMD).

Keywords: Neoplasm, Benign, Malignant, Non-invasive, Metastatic, Mammography, MRI, CT, Next-generation sequencing, Immunochemistry, Radiation therapy, Chemotherapy, Hormone therapy, Artificial intelligence, UTMD

1. Introduction

A tumour, also termed a neoplasm, results from disturbed control over cellular growth and an excessive or atypical increase in cell number [01]. Tumours are conventionally placed into benign (non-malignant) and malignant categories [02]. Benign lesions usually remain non-invasive [03]. They tend to grow slowly and stay restricted to the tissue where they developed, rather than infiltrating neighbouring structures or reaching distant sites. Their cells generally retain a relatively normal appearance and their boundaries are commonly distinct and smooth. Although they do not metastasize, benign lesions can still create a substantial burden on health services because they occur frequently and sometimes require operative removal. As these cells do not ordinarily spread, their clinical behaviour is generally less aggressive than that of malignant growths [04].

Unlike benign growths, malignant tumours demonstrate uncontrolled cell division, tissue infiltration and the capacity to metastasize. Carcinogenesis develops over several steps that involve alterations in DNA, epigenetic regulation and communication between tumour cells and their surrounding microenvironment. These changes can permit evasion of apoptosis, prolonged angiogenesis, invasion and distant dissemination. Changes that have been implicated in this process include activation of oncogenes such as RAS and MYC and impairment of tumor suppressors such as TP53 and BRCA1. Other features, like immune escape and metabolic reprogramming, may play a role in the development of an aggressive phenotype. Malignant cells can survive and grow without being recognized and destroyed by the T lymphocytes and natural killer (NK) cells [05]. Cancer is a diverse group of disorders where there is an abnormal regulation of the growth and division of cells that is not properly controlled. This general term covers over 100 diseases and tumors of various organs can have different clinical characteristics. The beginnings of the disease are when a cell escapes normal controls on proliferation. The term is of longstanding origin: The Greek term associated with cancer was used by Hippocrates around 2300 years ago, followed by the Latin term ‘cancer'. Further studies in the 1600s by

Hooke and in the 1800s by Virchow led to an understanding of the cell as the fundamental unit of living tissue and that new cells are formed from existing ones [06]. When malignant cells spread from the primary site to other places this is called metastasis; if they spread out without control they may kill the patient. External factors (tobacco, chemicals, irradiation and infectious organisms) and internal factors (acquired mutations and immune dysfunction, as well as inherited mutations and endocrine influences) all play a role in the development of cancer. It is multifactorial and there are incomplete explanations for its causes. Some of the factors that have been identified or suspected include diet, some infections, inactivity, obesity, and pollutants. The interplay of these factors may contribute to the malignant disease which is a leading cause of mortality to the world [07]. As a tumor grows, malignant cells can spread to normal tissue around them and cause it to become compressed. Local invasion occurs when enzymes are produced by cancer cells that break down normal tissue and allow the cancer cells to invade the surrounding tissue. A cell may then break away from the main tumor and spread in the lymph system or blood. Once they grow elsewhere within the body, it is called metastasis [08].

More than 200 forms of cancer have been described. They may be classified according to their anatomical site of origin, for example, breast, brain or lung, or according to the cell type from which the malignancy develops. This second method distinguishes, among others, tumours originating in epithelial or squamous cells. The principal categories arising from particular cell populations are summarized below [09]

S.No.	Types of Cancer	Description
01 a. b. c. d.	Carcinomas	It is most common type of cancer; these tumors form from the epithelial cells. This cancer begins in the skin or tissue that lines the internal organs. There are various forms of epithelial cells where cancer initiates, which include adenocarcinoma, basal cell carcinoma (BCC), squamous cell carcinoma, and transitional cell carcinoma (TCC).
	Adenocarcinoma	is a cancer that is formed in epithelial cells that produce fluid or mucus (breast cancer, prostate cancer, lung cancer, colon cancer).
	Basal Cell Carcinoma	basal cell cancer begins in the basal layer of the epidermis which is one individual's skin and rarely develops on mucus membranes (nodular BCC, superficial BCC, infiltrative BCC)
	Squamous Cell Carcinoma	is a cancer that forms on cutaneous squamous epithelium, which lies just beneath the outer epidermis and is also found on the lining of the throat and esophagus
	Transitional Cell Carcinoma	It is a cancer that forms in transitional epithelium also called ad urothelium, this epithelium is commonly located in the linings of the bladder, ureter and other parts of the urinary system (papillary TCC, non-papillary TCC)

02 a.	Sarcoma	sarcomas are cancers that form in connective tissue including bone, cartilage, fat, muscles, blood vessels, and fibrous tissues. They are divided into two categories-
	Soft Tissue Sarcoma	including malignant fibrous histiocytoma, liposarcoma, leiomyosarcoma, synovial sarcoma, dermatofibrosarcoma protuberans, angiosarcoma, Kaposi sarcoma, gastrointestinal stromal tumor, desmoid tumor.
b.	Primary Bone Sarcoma	include osteosarcoma, giant cell tumor, and chondrosarcoma.
03	Leukemia	is a life-threatening cancer that begins in the bloodforming tissues including bone marrow and leads to greater production of leukocytes aggressively. These cancers do not form solid tumors. There are four subtypes of leukemia based on the rapidity of proliferation (acute or chronic) and the type of cell cancer that is initiated (lymphoblastic or myeloid)
04 a.	Lymphomas	that is caused by the proliferation of B cells, T-cells, and NK cells. In lymphoma, an abnormal number of lymphocytes builds up in the lymphatic nodes and lymphatic blood vessels exceeding and invading into other organs of the body. There are two main types of lymphomas-
b.	Hodgkin Lymphoma	the occurrence of abnormal Hodgkin Reed-Sternberg cells, these originate from B cells of the host immune system
	Non-Hodgkin Lymphoma	a cancer arising from the lymph nodes
05	Multiple myeloma	cancer that begins in the plasma cells and is distinguished by an abnormal increase in the count of immunoglobulins. The abnormal plasma cells called myeloma cells are built up in the bone marrow and form tumors in the bones throughout the body, excess production of these plasma cells results in endorgan damage

06 a. b.	Brain and spinal cord cancers	abnormal cell growth that starts in the brain and spinal cord, as these two components together form the central nervous system. There are various forms of brain and spinal cord tumors. These tumors are named based on the type of cell in which they are formed or the origin of the tumor in the central nervous system. The most common type of brain tumor develops in the glial cells of the brain it is called glioma. Brain tumors are classified as-
	Primary tumor	which starts in the brain.
	Secondary tumor/brain metastasis tumor	they usually spread from tumors that are located outside the brain.

Breast Cancer Changes in the growth or behaviour of cells within the breast can lead to breast cancer [10]. The malignancy commonly begins in the epithelial lining of ducts or in the lobules that supply the ducts with milk. Two major tissue components make up the breast: glandular tissue, which includes the milk-producing lobules and the ducts carrying milk, and stroma, which includes fibrous connective and adipose tissue.

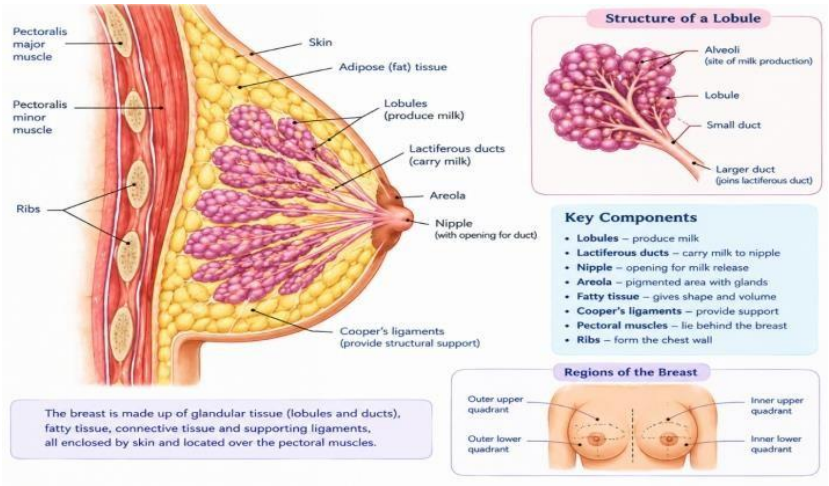

Figure 1: Structure of Breast

Lymphatic tissue in the breast is involved in immune function and also in the removal of excess cellular fluid and waste; in addition to glandular and stromal elements. Growths can be found in various parts of the breast and many of the breast changes are not cancerous. For example, fibrocystic changes may result in fluid-filled cysts, an excess of fibrous tissue, thickening, tenderness, lumpiness or pain [11]. By contrast, breast cancer is a diverse group of cancers in which cancer cells may multiply quickly and survive normal cell death and escape the immune system. These cells can get into blood or lymph vessels and spread from the original breast tumor [12]. Breast cancer is one of the most common types of cancer in women, but men also can develop the disease. It is significantly more common in women [13].

Epidemiology of Breast Cancer

2001-2010

During the period from 2001 to 2010, breast cancer emerged as a more significant public health issue for women, especially worldwide. According to estimates from around the world, in 2002 approximately 1.15 million new diagnoses and 410,000 deaths due to HIV/AIDS occurred. The respective estimates for 2008 are estimated to be around 1.38 million cases and 458,000 deaths per year. The increase was observed due to the following factors: ageing of the population, changes in reproductive behaviour, lifestyle factors and better detection and registration. Advances in the management of breast cancer during this decade included improved mammographic screening, breast-conserving surgery, radiation

therapy, and chemotherapy and endocrine therapy, such as tamoxifen. Mortality remained high, however, particularly in low-income countries, where diagnosis was often late and treatment was limited, which had a negative impact on survival [14].

2011-2020

Breast cancer continued to grow in significance globally from 2011-2020. There were an estimated 1.67 million incident cases and 522,000 deaths in 2012, and 2.1 million cases and 627,000 deaths in 2018 [14]. Breast cancer was the most diagnosed cancer in the world in 2020, overtaking lung cancer. IARC estimates indicated nearly 2.3 million new cases and 685,000 deaths in that year. Approximately 11.7% of all new cancers were breast cancers, making the condition a leading cause of cancer mortality among women. Despite continuing progress in screening, molecular characterization, targeted drugs and other treatments, large inequalities in mortality persisted between high-income and lower-income settings [15].

2021-2026

Between 2021 and 2026, advances in detection and treatment did not eliminate the considerable worldwide burden of breast cancer. GLOBOCAN 2022 reported approximately 2.3 million newly diagnosed cases and 666,000 deaths. Estimates published in 2026 relating to 2024 suggested around 2.4 million new cases and 694,000 deaths. Figures from different years are not necessarily directly comparable because cancer registration, estimation methods and available data can change. Breast cancer continues to rank among the most frequently diagnosed cancers in women and remains an important cause of cancer-associated mortality. The World Health Organization introduced the Global Breast Cancer Initiative in 2021, with the objectives of reducing annual mortality by 2.5% and preventing 2.5 million deaths by 2040. Its priorities include earlier diagnosis, access to prompt care, molecularly guided therapy and equitable cancer services. Many high-income countries have achieved substantial reductions in mortality, whereas diagnosis delays and obstacles to comprehensive treatment continue to affect several resource-limited populations. As complete global mortality figures for 2026 are not yet available, this overview uses the published estimates for 2024 as its most recent global figures [16].

History of Breast Cancer

Earliest Historical Record of Breast Cancer

Historical accounts of breast disease extend to approximately 1600 BC. The Edwin Smith Papyrus contains descriptions of 48 surgical cases, eight involving the breast, including a lesion thought to have been a tumour. Its original source material may date to around 3000 BC. The account mentions cauterization as an intervention but records that no effective cure for breast cancer was available at the time.

Early Surgical Treatment

During the first century AD, Leonides of Alexandria described operative treatment of breast cancer. His approach included excision of the lesion together with nearby tissue and skin. Cautery was applied for haemostasis while the procedure continued until removal of the tumour and breast was completed.

Development of Radical Mastectomy

In 1894, William Halsted and Willy Meyer independently reported about the operative approaches to breast cancer. Halsted's radical mastectomy included the removal of the axillary (underarm) nodes, pectoral muscles, and the affected breast. It was a breakthrough in the surgical management and control of the disease in the local area.

Following Wilhelm Conrad Röntgen's discovery of X-rays in 1895, radiation began to be applied in breast cancer care to limit recurrence following surgery and alleviate pain in advanced disease. Later improvements in imaging supported detection of lesions that could not be palpated and helped make breast-sparing procedures feasible, including lumpectomy, quadrantectomy and segmentectomy.

Development of Hormonal Therapy and Chemotherapy

George Thomas Beatson observed regression of breast tumours after bilateral oophorectomy in two patients in 1896. This finding helped establish the foundation of hormonal treatment. Subsequent identification of hormone receptors in malignant breast cells clarified the relationship between endocrine signals and tumour growth. Recognition that malignant cells could disseminate through the circulation also supported the development of systemic chemotherapy for metastatic disease [17].

Stages of Breast Cancer

Stage 0

In stage 0, the abnormal cells are limited to where they began in the breast and there is no spread of the cancer into the surrounding tissue. Ductal carcinoma in situ (DCIS) is an example of this non-invasive stage.

Stage I

Stage I is early invasive breast carcinoma and is subclassified into stage IA and stage IB. Stage IA is for a tumor that is 2 cm or less and hasn't spread to the lymph nodes. In Stage IB, tiny clusters of cancer cells (cancer deposits) are found in a lymph node that is more than 0.2 mm in size.

Stage II

Stage II is divided into IIA and IIB. In stage IIA the size of the tumours and the presence or absence of lymph glands in the areas around the tumour vary, and the original report included an option of spread into the lymphatic system but not into the chest cavity. In stage IIB, the lesion is > 5cm in size and without axillary nodal involvement. The difference between the two is thus related to tumor size and the extent of regional involvement and therefore has a prognostic significance.

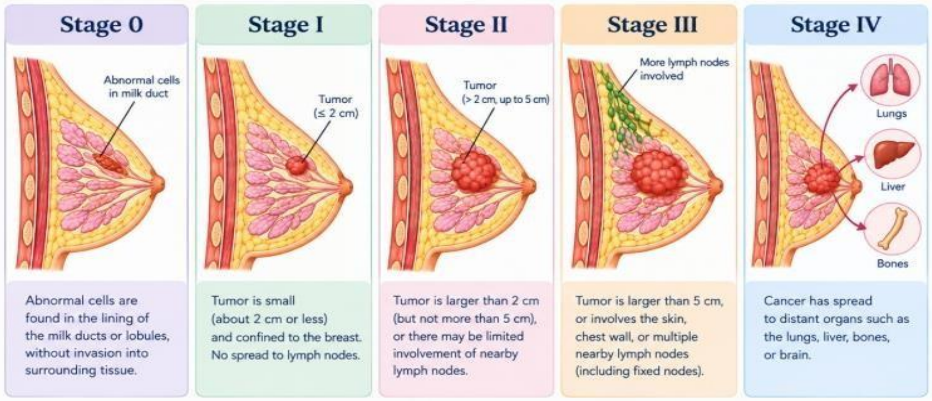

Figure 2: Stages of Breast Cancer Stage III

Stage III represents more widespread regional disease and is subdivided into stages IIIA, IIIB and IIIC. Some cases have been described in the original classification as having between 4 and 9 affected axillary or sentinel nodes, but without a palpable breast mass. A tumour of any size may be present in Stage IIIB along with swelling, ulceration of the breast skin and possible involvement of the regional nodes. Inflammatory breast cancer may present with redness, warmth and swelling. There are also some cases that have mention of the presence of ten or more axillary nodes (above and below the collar bone) as a more advanced regional spread characteristic. The presence of regional nodes therefore remains an important part of the description of the disease as do skin changes.

Stage IV

In the event malignant cells have spread to other organs such as bones, lungs, liver or brain, the situation is known as stage IV (metastatic breast cancer) [18].

Etiology of Breast Cancer

Age- Age is a risk factor for breast cancer, and the age of diagnosis is most often after 50. According to Surveillance, Epidemiology, and End Results (SEER) data, the risks of breast cancer are 2.4% for women aged 50-59, 3.5% for those aged 60-69 and 7.0% for women older than 70. This age-related pattern is similar to that found in numerous other cancers and could be a sign of a progressive accumulation of cellular changes and a progressive progression of cancer-causing processes. Prognosis is also dependent of age at diagnosis. Patients with a diagnosis at 50 to 70 years of age are more likely to survive than patients with a diagnosis prior to the age of 50. One possible explanation is the relatively greater frequency of aggressive triple-negative disease in patients aged 40 or younger [19].

In the United States, 280,000 women are diagnosed with breast cancer each year and 3,000 men. The likelihood of breast malignancy is consequently around 100 times greater among women. This difference is often associated with differences in exposure to estrogen and progestin. In postmenopausal women, increased levels of circulating estrogens and androgens have been linked to an increased risk of breast cancer. In men, a higher E:A ratio (more estrogen, or lower levels of androgen) also has been linked to risk. Sex-hormone levels also fluctuate more during the reproductive and post reproductive years in women, which can lead to their increased susceptibility [19].

There has been some link between obesity (excess weight) and breast cancer, but this association is not the same for pre- and post- menopausal women. This relationship of BMI to malignancy, particularly estrogen receptor positive cancer, seems particularly relevant following menopause. There have been reports of a BMI of 30 kg/m^2 or more being associated with increased postmenopausal risk. The source mentioned a relative risk of 1.1 per 5 BMI units (reported 95% confidence interval, 1.1–1.2). One explanation is that the greater production of estrogen in fat tissue. This study, which documents an association between higher body fat percentage and breast cancer even in women who have a normal BMI, further supports the link between body fat and breast cancer. However, among premenopausal women, some studies have found a relationship

between a lower BMI and an increased risk of breast cancer [19].

Family history – If family members have had breast cancer, this is an important risk factor. Around 13 - 19% of people who have been diagnosed with the disease report that a relative in their first degree of relationship (parent, child, sibling, or spouse) was affected. There is increased risk if multiple first-degree relatives have been diagnosed, especially if diagnosed early (before age 50). There are reports of an increase in incidence in all age groups when there is a family history. This may be due to inherited traits, epigenetic changes, and common environmental factors. Families with a history of ovarian cancer also may be at higher risk for breast cancer, particularly those with BRCA1 or BRCA2 variants [20].

Alcohol and Smoking Intake- Evidence is a study that correlates alcohol use with gastrointestinal cancer and breast cancer. The amount of alcohol consumed, not the type of alcohol drink, seems to be most important. Alcohol can increase estrogen levels and disrupt the regulation of the hormones, which can play a role in carcinogenesis. Increased body weight associated with drinking, the effects of alcohol metabolites and changes in nutrient intake have also been proposed as mechanisms. There has been some research suggesting a stronger link to the ER-positive breast cancers. Eating before first pregnancy has been associated with changes in breast tissue that could make them more susceptible to later developing cancer. The tobacco smoke contains carcinogens that can enter the breast tissue and lead to alterations in the oncogenes and tumor suppressors such as p53. Both direct and second-hand smoke exposure have been discussed as contributors. Prolonged smoking histories and smoking before a first full-term pregnancy may add risk, particularly among women with affected relatives [20].

Genetic Mutations- inherited genetic changes (genetic mutations) play an important part in susceptibility for breast cancer. Two high-penetrance genes, BRCA1 on chromosome 17 and BRCA2 on chromosome 13, have been identified. There are pathogenic changes known to occur in these genes that are strongly linked to breast cancer and are typically inherited in an autosomal dominant fashion but can also be non-inheritable. TP53, CDH1, PTEN and STK11 are other genes with high penetrance. Women with some harmful changes in their DNA may also have a higher risk for ovarian cancer. Genes participating in DNA repair, such as ATM, PALB2, BRIP1 and CHEK2, can interact with BRCA-related pathways and may contribute to breast carcinogenesis, although their penetrance is generally more moderate. A Polish investigation also suggested a possible association between XRCC2 alterations and breast cancer susceptibility [20].

Hormonal Factors- Prolonged exposure to estrogen is linked to a higher probability of developing breast cancer, while reduced lifetime exposure may be protective.

Risk factors have been identified including conditions that place women on more cycles such as early menarche, and not having had any children, and being an older age at menopause. However, moderate physical activity and longer breastfeeding can help to reduce lifetime cycles. However, long-term HRT has been associated with higher risk than shorter HRT use in post-menopausal women. Another factor that is relevant after menopause, which is related to obesity, is the conversion of androstenedione to estrone in adipose tissue; this may result in chronic exposure to estrogen. In addition to the use of oral contraceptives, other factors associated with changes in body weight or hormonal exposure, such as age at menopause and duration of menopause, have been associated with breast cancer risk and should be considered [21].

A dietary pattern with vegetables, fruit, fiber, and complex carbohydrates and relatively little fat has been suggested as protective against breast malignancy. The association between dietary fat and breast cancer is inconsistent; however, fat density of the diet may be related to overweight or obesity, which may influence risk. The source also notes the importance of maintaining a healthy body mass index (BMI) and engaging in regular activity, such as walking, exercising, or taking yoga classes, at least three times a week [22].

The chances of developing breast malignancy may be affected by lifestyle factors, which include individual behaviours and daily habits. There have been mentions of dietary patterns high in processed or sugary foods, consumption of alcohol, and physical inactivity, which are more likely to occur in higher income countries. More detailed explanations of these associations are provided through previous studies that explain the biological pathways. Better identification of modifiable lifestyle factors may support individual risk assessment and the design of preventive public-health interventions [23] (Etiology of BC 4).

Reproductive Factors- Timing of reproductive events is associated with breast cancer susceptibility. An early onset of menstruation, late menopause, first childbirth at an older age and having fewer children have all been linked to greater risk. The source reports a 3% increase in risk for each additional year before menopause and a 5–10% reduction for each later year of menarche or additional birth. A Norwegian cohort study reported a hazard ratio of 1.54 when comparing first childbirth at 35 years with

childbirth at 20 years. The associations may differ by estrogen receptor (ER) status: the cited odds ratios for parity were 0.7 versus 0.9 for three births compared with no births, while the values for first childbirth at age 30 versus 25 were 1.6 and 1.2 for ER-positive and ER-negative breast cancer, respectively [24] (Etiology of BC 6).

Pathophysiology of Breast Cancer

Breast malignancy usually emerges through successive genetic and molecular changes in epithelial cells of the breast. At the outset, inherited alterations affecting BRCA1, BRCA2 or TP53, exposure to estrogens or environmental carcinogens, and reduced immune surveillance may facilitate DNA injury. Disturbances in pathways such as PI3K/AKT and RAS/MEK/ERK then support persistent proliferation and diminish apoptosis. Progressing tumours interact with stromal fibroblasts, immune cells and the vasculature, producing a heterogeneous tumour microenvironment.

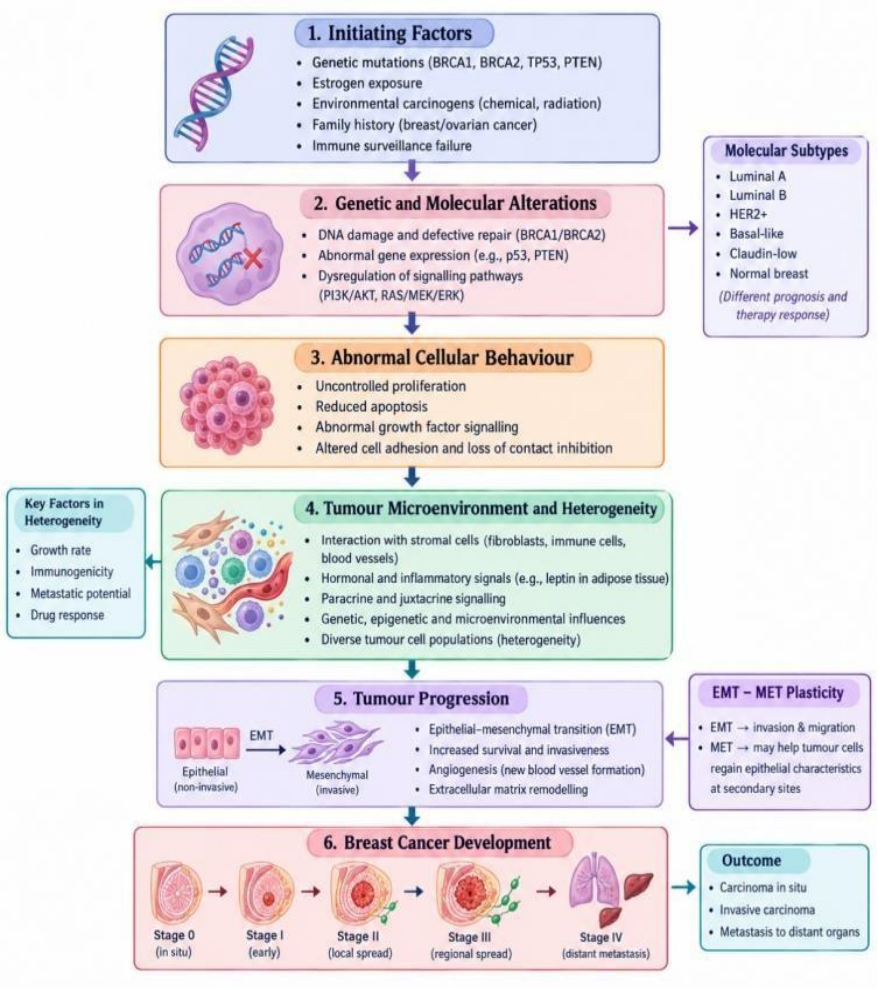

Figure 3: Pathophysiology of Breast Cancer

Further tumour development involves new blood-vessel formation, changes to the extracellular matrix and epithelial–mesenchymal transition (EMT), processes associated with invasion and cellular movement. Conversely, mesenchymal–epithelial transition (MET) may assist the growth of disseminated cells at secondary locations. Disease progression can extend from carcinoma in situ to invasive cancer and eventually, in some patients, to distant metastasis. Molecular categories such as luminal A, luminal B, HER2-positive and basal-like disease have different clinical outcomes and responses to treatment [25].

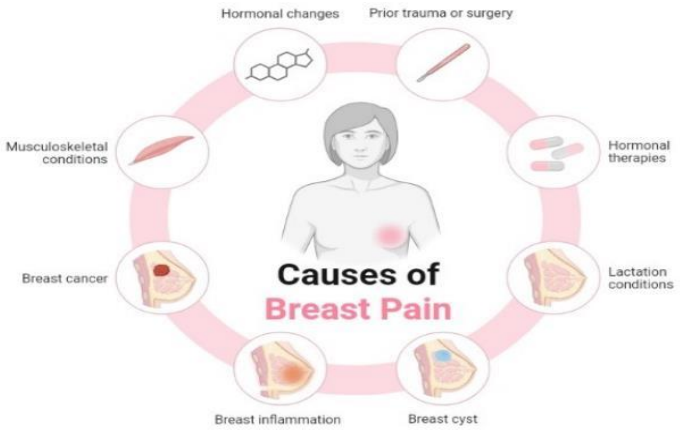

Figure 4: Causes of Breast Cancer

Breast Cancer Treat with Medicinal Plants

S. No.	Plant Name	Phytochemical Constituent	Uses	Ref.
01.	Aristolochia indica	Aristolochic-acids, aristoloactams, phenanthrene derivatives, sesquiterpenes, and steroids, ishwarone, ishwarol, aristolochene, aristolactam glycosides, β-sitosterol glucoside, and methyl aristolate, alkaloids, flavonoids, tannins, saponins, steroids, cardiac glycosides, lignans, clerodane diterpenes, and naphthoquinones, volatile oil, trans-pinocarveol, α-pinene, and pinocarvone	Antimicrobial, antioxidant, antivenom, immunomodulatory, anti-diabetic, anticancer,and antiinflammatory, breast cancer	26, 27 & 28
02.	Peganum harmala	alkaloids, flavonoids, triterpenoids, phenolic acids, anthraquinones, and fatty acids, harmaline, harmine, and vasicine, amino acid proline and lysine	Breast cancer, abortificant,aphrodisiac, sedative, vermifuge and soporific, prolapse of the womb, analgesic, antibacterial, antidiabetic,uterine contraction, anticancer, antioxidant antiviral, CNS depressant, antineoseptic, antiinflammatory, genoprotective, muscle stimulant,Antileishmanial, Anti helminthic	29, 30 & 31
03.	Artemisia annua	Sesquiterpenoids / Terpenoids, Flavonoids, Phenolic Acids, Coumarins, Glycosides, Fatty Acids	Anti-cancer activity like pro-apoptotic, anti-proliferative, anti-angiogenesis and anti-metastatic, breast-cancer, antimicrobial, antifungal, antiviral, anti-inflammatory, immunomodulatory, anti-oxidant, antibacterial, anti-fungal, antiparasitic, anti-helminthic	32, 33, 34 & 35

04.	Evodia	Alkaloids,terpenoids, steroids, limonoids, phenylpropanoids, flavonoids, phenolic acids, anthraquinones,and essential oils, rutecarpine c	Anti-tumor activity like breast cancer, liver cancer, lung cancer, colon cancer, human melanin, cervical cancer, thyroid cancer, pancreatic cancer, bladder, prostate cancer, leukemia, gastric cancer, glioblastoma, urothelial cell carcinoma, ovarian epithelial carcinoma, cholangiocarcinoma, osteo sarcoidoma, and oral cancer, Anti-hypertensive, Anti-Alzheimer's, Antidepressant, Anti-lipogenic, Antigluconeogenic, Antimicrobial,	36 & 37
05.	Inula helenium	phenolic acids (specifically chlorogenic, dicaffeoylquinic, and hydroxybenzoic acids), flavonoids such as epicatechin, catechin gallate, and quercetin3-O-β-glucopyranoside,alanlactone, isoalanlactone, rutin, kaempferol, luteolin, metabolites, including sesquiterpene lactones, essential oils, phenolic acids, polysaccharides	Anticancer like breast cancer, colorectal cancer, liver cancer, lung cancer, pancreatic cancer, gastric cancer, cervical cancer, osteosarcoma, antiinflammatory, antiseptic,anthelmintic, antimicrobial,antioxidant, antiaggregatory, anticoagulant	38, 39, 40 & 41
06.	Tripterygium wilfordii	sesquiterpenes, diterpenes, triterpenes, alkaloids,flavonoids,lignans, glycosides, triptolide, celastrol, and wilforlide	Breastcancer,Antiinflammatory, immunosuppressive, antioxidant, antiobesity,neuroprotective, anti-bacterial,antiparasitic,insecticidal, antiviral,antidepressant, anti-fibrotic	42 & 43
07.	Annona squamosa	Coumarins, tannins, cardiac glycosides,flavonoids,polysaccharides, saponins, annonaceous acetogenins, diterpenes, alkaloids, and cyclopeptides, anonaine, asimilobine, nur nuciferine, liriodenine, corypalmine, and reticuline, (E)-caryophyllene,bicyclogermacrene, caryophyllene oxide, germacreneD, spathulenol, pinene, limonene, -elemene, roemerolidine, nitroso xylophone, and duguevalline alkaloid, phenolics, terpenoids, essential oils are composed of mono- and sesquiterpenes, such as α-pinene, β-caryophyllene, and germacrene-D, germacrene D, spathulenol, pinene, limonene, -elemene, roemerolidine, nitroso xylophone, and duguevalline alkaloid, phenolics, terpenoids, essential oils are composed of mono- and sesquiterpenes, such as α-pinene, β-caryophyllene, and germacrene-D	Anticancer like breast, colon, liver and lung,Antimicrobial like Gram-positiveandGram-negative bacteria, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans, Antidiabetic,Antioxidant, Antiinflammatory,Neuroprotective, Hepatoprotective, Cardioprotective, Analgesic	44, 45 & 46

08.	Paeonia suffruticosa	Flavonoids, tannins, amino acids, polysaccharides, volatile oils, sterols, MonoterpeneGlycosides, Phenols,triterpenoids, Anthocyanins, saponins	Breast cancer, macula, epilepsy, menstrualdisorders, atherosclerosis,infection, inflammation,antioxidant, antimutagenic,antiproliferative, antiinvasive,antiinfective, antihypertensive, antiarrhythmic, anti-diabetic, anti-obesity and neuroprotective	47 & 48
09.	Plumbago zeylanica	Triterpenoids, flavonoids, gums, mucilage, protein, fatty acids saponins, naphthoquinones, alkaloids, glycosides, steroids, tannins, phenolic compounds, fixed oils, plumbagin, chitranone, 3-biplumbagin, chloroplumbagin, elliptone, coumarins includes seselin, 5methoxy seselin, xanthyletin, suberosin, plumbagic acid, β sitosterol, 2-dimethyl-5 hydroxy-6-acetylchromene, saponaretin, and isoaffinetin, naphthoquinones, difuranonaphthoquinones binaphthoquinones, di-phenyl sulfone, carboxylic acids and esters, monoterpenes, anthraquinones	Anticancer like breast cancer, hepatoprotective,antiinflammatory, anti-diabetic, hyperlipidemic, Antiulcer, Wound Healing, Antimicrobial, Antiinflammatory, Antiobesity, Nephroprotective, Antifertility	49 & 50
10.	Thymus vulgaris	Saponins, tannins, flavonoids, alkaloid, terpenoids, essential oil (thymol, carvacrol), phenolic acids, trans ocimene, γ-terpinene, limonene, α-pinene, α-thujene, α-cymene, βmyrcene, sesquiterpene, pcoumaric, Rosmarinic acid, Ferulic acid, Creosol 2methoxy-4-methyphenol	Breast cancer, Antioxidant, Antibacterial, Antifungal, Antispasmodic, Cytotoxicity, Cardiovascular, Antimicrobial, Antidermatophytic, Anti-inflammatory, Anti-viral,	51 & 52

Diagnosis:

Traditional diagnostic methods-

Mammography: Mammographic imaging is regularly used to screen for breast cancer because it is relatively inexpensive, accessible, and has a standard imaging protocol. However, there are limitations to screening, especially when screening on dense tissue. Acknowledging these limitations, the United States' breast density requirements may encourage further imaging. The estimated overdiagnosis rates vary widely across studies, screening strategies and analytic approaches, and published rates have ranged from about 1% to 50% [53].

A compression plate, which is used to flatten the breast, is used during the exam to get a picture of it. Low-energy X-rays, typically around 20–30 kVp, are fired through the breast and create a two-dimensional mammogram [54].

During biopsy, mammographic guidance could also be used to accurately identify a suspicious region [55].

Screening mammography is intended to detect malignancy before it is clinically detectable, so that it can be addressed at a point when there is a greater chance of cure [56].

Ultrasound: Ultrasound imaging is not associated with the use of radiation and is especially helpful for women who have dense breast tissue as an additional tool for evaluation. It can be able to show tiny invasive lesions that cannot be seen on mammography. A major drawback is operator dependency and therefore difficulties in repeatability. This is partially addressed by automated breast ultrasonography, which has more significant cost, but may be more effective in its implementation [53].

In a clinical setting, breast ultrasonography is typically performed in conjunction with mammography and physical examination, even in people that may be at higher risk [54].

Magnetic resonance imaging (MRI): Breast MRI is a highly sensitive supplementary imaging technique, especially for patients with elevated risk, including carriers of BRCA mutations. It can reveal tumours not seen with mammography. Its application to routine population screening is restricted by expense, prolonged examination times and a comparatively high rate of false-positive findings. Consequently, it is most often recommended in combination with mammography or ultrasound for high-risk patients [54,53].

Computed Tomography (CT): CT employs X-ray measurements acquired from several angles to obtain cross-sectional information about internal structures. Computer-assisted reconstruction combines these observations into detailed two- and three-dimensional anatomical images [56].

Biopsy and histopathology: The diagnosis of breast cancer is made definitively by taking tissue. During a biopsy, cells or tissue are removed to be studied using a microscope and other tests. This depends in part on the palpable or not of the suspected lesion. Most biopsies are done on an outpatient basis, and these procedures can be completed in a few hours and patients can go home on the same day. Fine-needle aspiration (FNA), excisional sampling and core-needle biopsy. Core-needle sampling may be preferred, as it preserves tissue architecture and allows testing of tissue-receptive receptors [57,55].

Thermal imaging (thermography) uses infrared cameras to measure temperature differences and does not use ionizing radiation. The technique can be classified as static infrared thermography (SIT) or dynamic infrared thermography (DIT). While relatively stable surface temperature patterns are captured by SIT, changing thermal responses are captured by DIT, and have been more robust and faster [56].

Digital breast tomosynthesis (DBT): DBT is like conventional 2-D mammography but uses multiple images to create a 3-D image to minimize the issue of overlapping tissue. Cancer detection and recall benefits have been reported, which could indicate higher sensitivity with fewer false positive assessments [53].

Molecular and genomic diagnostics-

Immunohistochemistry: Immunohistochemistry represents an advanced, more complex tool in the diagnosis of breast cancer. It also allows the detection of protein biomarkers within the tumor tissues. The technique is usually standardized globally; although some variation can occur within individual laboratories, reflecting the importance of quality control and expert interpretation [57].

Liquid biopsy: role of circulating tumor DNA and exosomal miRNAs: Liquid Biopsy is an advanced and emerging form of non-invasive and dynamic technique that detects and analyzes the biomarkers present in the bloodstream for the genotyping of an existing tumor. Liquid biopsies also enable the early detection of the recurrence of tumors, the assessment of minimum residual disease, and the evaluation of treatment responses without the need for repeated biopsies [57].

Next-generation sequencing: Recent advances in the field of next-generation sequencing (NGS) have completely revolutionized the field of cancer genomics. It has allowed researchers and clinicians to perform comprehensive profiling of tumor DNA to identify somatic mutations, copy number variations, cis and trans gene fusions, splicing events, and more [57].

Artificial intelligence and machine learning in diagnostic approaches- The role of AI technology and ML techniques is becoming integral in the field of breast cancer diagnosis [57]. For AI algorithms, high-quality training images are required. Qualitative evaluation of AI can quickly and accurately identify cell types and provide corresponding tissue morphology and biological patterns. Integrating AI into screening and diagnostic methods, such as biopsy, can significantly improve the success rate of breast cancer screening and/or treatment. Machine learning and deep learning are the key aspects of AI in breast cancer imaging. Machine learning is used to store a large dataset, which is then used to train prediction models and interpret generalization. AI-driven techniques are effective not only for image analysis but also for risk assessment, tumor characterization, and treatment monitoring. For example, AI-based mammography has demonstrated superior diagnostic accuracy in dense breast tissue compared with traditional radiological assessments. AI models trained on extensive datasets also exhibit reduced false-positive and false-negative rates, thereby minimizing diagnostic inconsistencies and missed diagnoses. AI in breast pathology has been applied in various tasks to diagnose and classify breast lesions, histopathological grade, BC, and metastatic deposits [58-60].

Advance Treatments of Breast Cancer

Surgery: To prevent or reduce the disease's spread and remove cancer from the body, surgeons may remove lymph nodes. Surgeries are used for the solid tumor, which is the local treatment because it contained in one area. Surgery is not used for metastatic cancer or leukemia i.e., blood cancer. Surgeries are used for the solid tumor, which is the local treatment because it contained in one area. Surgery is not used for metastatic cancer or leukemia i.e., blood cancer. surgery of the intestine, mouth, throat or stomach. The food is given in an IV or

feeding tube.

It is most effective for solid tumors that have not spread to other parts of the body [62,61]. Other surgeries also present for treatment of cancer which does not involve any cuts are:

Cryosurgery / Cryotherapy: This therapy is used to treat precancerous growth on the cervix and skin by argon gas and nitrogen gas to destroy abnormal cells from extreme cold.

Lasers: This treatment is used for more precise surgeries because it has an accurate focus on small areas and it is also used to shrink or destroy a tumor.

Hyperthermia: In this therapy, the small body part is exposed to a high temperature so this heat kills cancer cells and makes sense to radiation or chemotherapy drugs. Photodynamic Therapy: In this therapy, photodynamic drugs are used to treat cancer cells.

Radiation therapy: In this therapy high doses of radiation are used to treat cancer by shrinking tumors, killing cancer cells, and slow the growth of cancer cells by damaging their DNA because the damaged DNA does not repair and the cell die which is removed by the body. It can be used as the main treatment or in combination with surgery or chemotherapy [01]. Although the patient experiences a couple of side effects after the treatment, the radiotherapy has a significant impact on the life expectancy of the patient with the disease.

There are 2 kinds of treatments used in the radiotherapy of a patient with the disease; specifically, they are as follows: (a) EBRT and (b) Brachytherapy [57].

Chemotherapy: In this therapy, chemicals are used to treat cancer by stopping or slowing the growth of cancer cells or by killing cancer cells or also by shrink tumors that causing pain and other problems but have severe side effects. It may be used before or after surgery, or as the main treatment for cancers that have spread to other parts of the body [62,13].

Immunotherapy: Immunotherapy works by boosting the body's immune system to recognize and attack cancer cells. It is often used to treat cancers that have spread to other parts of the body, and is sometimes combined with other treatments [62]. Immunotherapy can help the immune system recognize and attack cancer cells more effectively. One type of immunotherapy is checkpoint inhibitors, which work by blocking proteins on cancer cells or immune cells that prevent the immune system from attacking cancer cells. These proteins are known as checkpoints, and they are designed to prevent the immune system from attacking healthy cells in the body. By blocking these checkpoints, checkpoint inhibitors can help the immune system recognize and attack cancer cells [61].

HER2 Block: Targeting Oncogenic Signaling Pathways in Cancer Therapy-

HER2(human epidermal growth factor receptor 2), also known as ERBB2, is a trans membrane glycoprotein and tyrosine kinase receptor that belongs to the ERBB family of epidermal growth factor receptors (EGFRs). It is a key regulator of intracellular signaling pathways that govern essential cellular processes, including cell growth, proliferation, survival, differentiation, and migration. HER2's ability to enhance signaling efficiency makes it essential in normal cellular function and development. The mechanism of action for HER2 blockade focuses on interrupting the signaling pathways mediated by HER2 that are frequently overexpressed or amplified in aggressive cancers, such as breast and gastric cancers. By blocking HER2mediated signaling, therapies aim to restore control over these pathways, suppressing tumor progression and enhancing the susceptibility of cancer cells to other treatments, ultimately improving patient outcomes [63].

Immune Checkpoint Inhibition: Revolutionizing Cancer Immunotherapy-

The advent of ICIs has revolutionized the field of oncology, introducing a groundbreaking approach that leverages the body's immune system to combat cancer. These therapies specifically target key regulatory pathways in T-cells that are often hijacked by tumors to evade immune detection and destruction. By blocking these inhibitory signals, ICIs restore and enhance immune system activity, enabling a more effective antitumor response [62,63].

Chimeric Antigen Receptor Macrophages (CAR-M) as a Novel Immunotherapeutic Approach in Breast Cancer-

Breast cancer remains a leading cause of cancer-related mortality worldwide, necessitating the development of innovative therapeutic strategies to improve patient outcomes. Chimeric antigen receptor macrophages (CAR-M) have emerged as a novel immunotherapeutic approach, leveraging the innate phagocytic and antigen-presenting capabilities of macrophages to target and eliminate tumor cells [63].

Targeted therapy: Targeted therapy uses drugs or other substances to identify and attack specific cancer cells without harming normal cells. It is often used for cancers that have specific genetic mutations. This therapy can treat cancer in different ways, include- It helps the immune system to destroy cancer cells by marking the cells by which the immune system can easily identify and destroy the cancer cells. It can cause the death of cancer cells by the natural process of cell death.

Types of Target Therapy:

Monoclonal Antibody: These antibodies are get attached to specific targets found on cancer cells and mark cancer cells and help the immune system to find and destroy it. Some antibodies also stop the growth of cancer cells and made self-destructed. These antibodies are proteins that are made in a laboratory [62].

Trastuzumab and pertuzumab are two monoclonal antibodies approved by the U.S. Food and Drug Administration (FDA) that target the extracellular domain of HER2. Trastuzumab (Herceptin) binds to subdomain IV of the extracellular domain of the HER2 receptor. By blocking this region, trastuzumab inhibits HER2 from forming het erodimers with other members of the ERBB receptor family, thereby disrupting downstream signaling pathways that drive cell proliferation and survival.

Pertuzumab (Perjeta) binds specifically to subdomain II of the HER2 extracellular domain, effectively blocking the formation of HER2/HER3 heterodimers, which are critical drivers of HER2-mediated signaling and tumorigenesis. By targeting this unique mechanism, pertuzumab complements the action of trastuzumab, which binds to a different region of HER2 (subdomain IV) [63].

Small Molecule Drugs: By their small size these drugs can easily enter inside the cell and used for targets.

Hormone therapy: Hormone therapy is used to treat cancers that are hormone-sensitive, such as breast and prostate cancer. It works by blocking the hormones that fuel the growth of cancer cells [13,61].

Hormonal therapies are crucial in treating HR+ breast cancer, particularly ER+ tumors. These therapies aim to interfere with hormonal signaling pathways and block the effects of estrogen or progesterone on tumor growth and progression. AIs, including anastrozole, letrozole, and exemestane, are another class of hormonal therapies. AIs block the enzyme aromatase, which converts androgens into estrogens. By reducing estrogen production, AIs effectively inhibit estrogen-mediated cell growth. AIs are primarily used in postmenopausal women with HR+ breast cancer. Other hormonal therapies include selective ER down regulators (SERDs) like fulvestrant, which binds to the ER and promotes its degradation, and luteinizing hormonereleasing hormone (LHRH) agonists, such as goserelin, which suppress ovarian function and reduce estrogen production [64].

Stem cell transplant: Stem cell transplant, also known as bone marrow transplant, may be used to treat certain types of cancer, such as leukemia, lymphoma, and multiple myeloma. It involves replacing diseased or damaged bone marrow with healthy stem cells to promote the growth of new, healthy blood cells. It is important to note that the best treatment approach for cancer depends on many factors, including the type and stage of cancer, the patient's overall health, and their individual preferences [62,61].

Gene Therapy: Gene therapy is a type of cancer treatment that involves altering the genetic material of cancer cells to either correct or eliminate a specific genetic mutation that is driving their growth and survival. Gene therapy can also be used to enhance the immune system's ability to recognize and attack cancer cells. There are several types of gene therapy, including:

Insertion of normal genes: This approach involves inserting a normal copy of a gene into the cancer cells that have a mutated or missing version of that gene. This approach can help to restore the normal function of the gene, which can help to slow or stop the growth of cancer cells.

Inactivation of oncogenes: Oncogenes are genes that can cause cancer when they become overactive or mutated. Gene therapy can be used to inactivate these genes, which can help to stop the growth of cancer cells.

Introduction of suicide genes: Suicide genes are genes that can be activated in cancer cells to induce cell death. Gene therapy can be used to introduce these genes into cancer cells, which can help to eliminate them.

Modification of immune cells: Gene therapy can be used to modify immune cells, such as T cells, to recognize and attack cancer cells. This approach can be done using chimeric antigen receptor (CAR) T-cell therapy, which involves collecting and genetically modifying a patient's T cells to specifically target cancer cells [61].

Emerging Technologies: Emerging technologies in cancer treatment refer to a variety of novel approaches that are being developed to improve cancer therapy. Here are some examples of emerging technologies in cancer treatment:

Nanotechnology: Nanoparticles can be designed to deliver drugs to specific cells or tissues, including cancer cells. These nanoparticles can be engineered to be highly selective in targeting cancer cells while leaving healthy cells unaffected. By encapsulating cancer drugs in nanoparticles, it may be possible to reduce the toxicity and side effects associated with chemotherapy. Nanocarriers improve the pharmacokinetics (PK) of medications, enhancing tissue penetration and retention at the tumor site, which is critical for successful therapy. AI has furthered the use of nanoparticles in imaging and therapeutic interventions. Technologies such as

quantum dots and gold nanoparticles, refined using AI, improve image resolution, facilitating earlier and more precise tumor identification. These discoveries underscore the dual capabilities of AI-driven nanoparticles in cancer diagnosis and treatment [61,65].

Liquid biopsies: Liquid biopsies involve analyzing a patient's blood or other bodily fluids for the presence of circulating tumor cells, cell-free DNA, or other cancer biomarkers. This approach can provide a non-invasive way to monitor a patient's response to treatment and detect cancer recurrence earlier than conventional imaging techniques.

Artificial intelligence: In the near future, AI algorithms may play a part in enhancing this procedure since they can analyze enormous volumes of multimodal data to find signals that would otherwise be hard to spot. AI algorithms can be trained to analyze large amounts of data, including genomic data, radiological images, and electronic medical records. This approach can help to identify patterns and biomarkers that are associated with specific types of cancer, which can improve the accuracy of cancer diagnosis and treatment. AI algorithms can precisely analyze mammograms, ultra sounds, and MRI data. These algorithms detect nuanced pat terns and abnormalities that may be missed by human observation, resulting in earlier and more accurate diagnoses. AI is incorporated with traditional imaging modalities such as mammography, ultrasound, and MRI to enhance diagnostic efficacy [61, 65, 66].

Oncolytic viruses: Oncolytic viruses are viruses that can selectively infect and kill cancer cells while sparing normal cells. These viruses can be engineered to replicate specifically in cancer cells, leading to their destruction. In addition, some oncolytic viruses can stimulate the immune system to attack cancer cells. dsDNA viruses such as Adenovirus have distinct replication processes. Oncolytic adenoviruses target cancer using two main strategies: transductional targeting, which enables specific infection of cancer cells, and transcriptional targeting, allowing viral replication specifically within cancer cells [61,67].

CAR-T cell therapy: CAR-T cell therapy involves collecting a patient's own immune cells, engineering them to recognize and attack cancer cells, and then infusing them back into the patient's body. This approach has shown promising results in treating certain types of blood cancers, such as leukemia and lymphoma [61].

CRISPR/Cas9: CRISPR/Cas9 is a gene-editing technology that can be used to modify the DNA of cancer cells. By selectively targeting cancer genes or pathways, CRISPR/Cas9 may be able to turn off genes that promote cancer growth or turn on genes that suppress tumor growth. In BC, oncogenes such as HER2, MYC, CXCR4, ACKR3, MAP3K11, and OPN are commonly deregulated. CRISPR/Cas9 can target these oncogenes to inhibit cell proliferation and tumorigenicity [61,67].

Machine learning-guided therapeutic decision-making: DL and ML have significantly improved breast cancer imaging techniques via AI. The analysis of intricate patterns and generalizations in data is enhanced by using extensive datasets to develop predictive models via ML. ML is employed to store extensive datasets, which are subsequently employed to train predictive models and develop generalizations. The most recent branch of ML is DL, which establishes a framework of ANNs capable of identifying and categorizing images effectively [65].

Ultrasound-Targeted Microbubble Destruction Technology in Adjuvant Breast Cancer Therapy:

UTMD in the Chemotherapy of Breast Cancer: Notably, conventional chemotherapy methods often face issues with non-specificity and high toxicity.75 To address these challenges, the integration of nanocarriers or other drug delivery systems can enhance drug specificity and mitigate toxic side effects.76,77 In a recent study, researchers developed lipid microbubbles loaded with paclitaxel (PTX) and LyP- 1 peptides to validate their in vitro tumor targeting efficiency and chemotherapeutic efficacy. The results demonstrated that the targeted drug-loaded microbubbles exhibited efficient and stable attachment to breast cancer cells under both static and dynamic conditions [68].

UMTD in the Radiotherapy of Breast Cancer: Ultrasound molecular tomography (UTMD) offers a potential role in enhancing treatment efficacy by targeting tumor microvasculature and blood flow dynamics.105,106 Several studies have investigated the synergistic effects of radiation therapy and ultrasound-guided focused ultrasound (FUS) in preclinical breast cancer models. These studies employed ultrasound stimulation of microbubbles to induce vascular damage, thereby enhancing tumor radiosensitivity. This approach has demonstrated compromised tumor vasculature and improved response to radiation therapy [68].

UTMD in Targeted Immunotherapy for Breast Cancer: Immune checkpoint inhibitors (ICIs) represent the foremost class of therapeutics currently employed in breast cancer immunotherapy. This strategy offers a novel approach to targeted therapy, even in cases where the tumor cells lack conventional therapeutic targets. However, thanks to immune checkpoint blockade (ICB), explicitly targeting the tumor microenvironment (TME) rather than the tumor cells themselves provides a new

approach to targeted therapy, even if the tumor cells lack actionable targets [68].

UTMD in Hormonal Therapy of Breast Cancer: HER2+ breast cancer is a highly aggressive subtype, and precise assessment of HER2 expression status is crucial for determining patient eligibility for targeted anti-HER2 therapy. Hormone therapy for breast cancer targets hormone receptor- positive (ER+/PR+) subtypes.134 Moreover, microbubble-enhanced and ultrasound-guided (MB+US) drug delivery has demonstrated promise across various therapies, including HER2+ breast cancer, due to its tunable, noninvasive, and spatially targeted nature. Researchers have developed ultrasound imaging combined with poly (lactic acid- hydroxy acetic acid) nanocarriers to dynamically monitor tamoxifen resistance. This technology, which integrates hormone therapy with ultrasound to create targeted nanobubbles for ultrasound molecular imaging, offers a promising tool for real-time monitoring of drug resistance in the clinic. While these therapies have proven effective in clinical settings, challenges such as drug resistance and side effects persist. UTMD has shown potential in managing side effects and providing new insights into drug resistance. Consequently, there is a need to continually explore and develop more effective treatment options for breast cancer, particularly in the application of ultrasound nanobubbles [68].

UTMD in Radiofrequency Ablative Therapy for Breast Cancer: Imaging-guided Radiofrequency ablation (RFA) of breast cancer has become an important tool in modern breast therapy. Among these techniques, ultrasound-guided RFA is a new minimally invasive breast surgical modality widely used in clinical practice. RFA generates heat locally by causing ionic oscillations through the high-frequency alternating current flowing around the electrodes, leading to protein denaturation and coagulative necrosis of tissues, as well as apoptosis and inactivation of tumor cells. Currently, RFA has shown good results in the treatment of breast cancer. Early studies have confirmed that radiofrequency ablation can cause complete necrosis of ablated tumor cells in various types of breast diseases. The rate of complete tumor necrosis after ablation, as observed through pathological examination, ranges from 76% to 100% [68].

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