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A SYSTEMATIC REVIEW OF BREAST CANCER: RECENT TRENDS IN DETECTION, THERAPY, AND PREVENTION: A REVIEW

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ABSTRACT

One of the most prevalent cancers and a significant health issue affecting women worldwide is breast cancer. Recent advancements in early detection techniques and therapeutic approaches have contributed to higher survival rates and better patient care. Recent advancements in breast cancer detection, treatment, and prevention are explained in this systematic review. Mammography, ultrasound, MRI, molecular biomarkers, and artificial intelligence (AI) are examples of contemporary diagnostic techniques that assist physicians more accurately identify breast cancer at an early stage. Chemotherapy, hormonal therapy, targeted therapy, immunotherapy, and personalised medicine are examples of new therapeutic approaches that have decreased side effects and increased treatment success. The incidence and burden of breast cancer can also be decreased by preventive interventions such routine screening, genetic counselling, healthy lifestyle choices, awareness campaigns, and early diagnosis. Treatment is becoming more effective and patient-specific thanks to developments in precision medicine and molecular biology. Drug resistance, high treatment costs, and unpleasant drug reactions are still issues, nevertheless. All things considered, current developments in the management of breast cancer have enhanced patient quality of life, diagnosis, therapy, and prevention.

KEYWORDS: Breast Cancer, Tumor, Chemotherapy, Ductal Carcinoma.

1. INTRODUCTION

One of the most prevalent malignancies that affect women is breast cancer. Both internal and external factors contribute to its development. Breast cancer risk can be raised by social or psychological factors, environmental effects, and unhealthy lifestyle choices.[1,3] Genetic mutations and family history account for about 5–10% of cases of breast cancer, but factors that may be altered or controlled account for 20–30% of cases. Breast cells are where breast cancer starts. When these cells proliferate excessively, they create a malignant tumor that has the potential to spread to other areas of the body and invade neighboring tissues.[4] Changes in breast cells can occasionally result in non-cancerous diseases such cysts or atypical hyperplasia rather than cancer. Benign cancers like intraductal papillomas can also arise from these alterations.[5]

Breast cancer is among the most frequent malignancies that affect women, according to the American Cancer Society.[6] It was estimated that 230,480 women in the US will receive a breast cancer diagnosis in 2011, accounting for approximately 30% of all new cancer cases among women. The sickness was also predicted to kill about 39,520 women.[7] These figures demonstrate the severity of breast cancer and its profound impact on women's health and society. Researchers have been examining whether routine screening for breast cancer can reduce mortality rates since the 1960s.[7-9] X-ray mammography is the primary screening technique and is regarded as the gold standard for identifying breast cancer. Regular screening is crucial since early detection of breast cancer improves treatment outcomes and increases the likelihood of survival, according to studies. The appropriate age to start mammography screening, however, has been a topic of discussion.[11] Experts disagreed with the U.S. Preventive Services Task Force's recommendation to begin routine screening at age 50 rather than age 40. The majority of specialists concur that routine breast cancer screening is particularly crucial for women between the ages of 50 and 74, despite differing views regarding the advantages of mammography.[10]

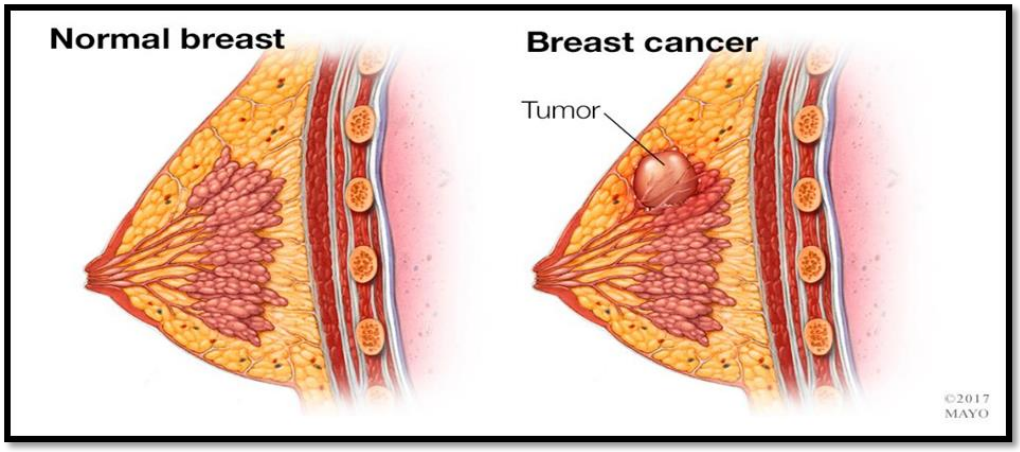


Fig. 1: Normal Breast Vs Breast Cancer.

Classification of Breast Cancer

1. Histological Classification (according to the origin of the malignancy)

A. In situ, non-invasive: These tumors do not migrate to adjacent tissues; instead, they remain where they first appear.

- **DCIS, or ductal carcinoma in situ:** Only the milk ducts contain cancer cells.
  It is the most prevalent kind of breast cancer that is not invasive.
- **LCIS, or Lobular Carcinoma in Situ:** The lobules (milk-producing glands) contain aberrant cells.

Although it raises the chance of getting breast cancer in the future, it is not regarded as a real malignancy.

B. Infiltrating (Invasive): These tumors spread throughout the surrounding breast tissue from their original location.

- **IDC, or invasive ductal carcinoma:** Begins in the milk ducts and travels to adjacent tissues.

About 70–80% of cases of breast cancer are of this kind.

- **ILC, or invasive lobular carcinoma:** Spreads to the surrounding tissue after starting in the lobules.

It may spread in a widespread form and impact both breasts.

Less prevalent invasive varieties

- Carcinoma of the medulla
- Mucinous carcinoma
- Tubular carcinoma

- Inflammatory breast cancer, an uncommon yet highly aggressive form.

2. Classification by Molecular (Genetic): The genes and proteins found in cancer cells provide the basis for this classification.

Luminal A: It has the greatest prognosis and is slow growing, ER positive, PR positive, and HER2 negative.

Luminal B: ER positive and occasionally HER2 positive HER2-enriched, ER and PR negative, and more aggressive than Luminal A. rapid growth, although tailored therapy can be used to treat it.

TNBC, or triple-negative breast cancer.

HER2-enriched: HER2 negative, PR negative, and ER negative.

aggressive kind with few alternatives for focused therapy.

3. Classification Based on Receptors: When selecting the optimal course of action, this type is crucial.

- ER-positive: Estrogen receptors are present in cancer cells.
- PR-positive: Progesterone receptors are present in cancer cells.
- HER2-positive: Excess HER2 protein is produced by cancer cells.
- Triple-negative: Does not have HER2, PR, or ER receptors.

4. TNM Staging (Cancer Spread Extent): The extent of the cancer's spread is described by this system.

- T (Tumor): Tumor size
- N (Nodes): Proliferate to adjacent lymph nodes
- M (Metastasis): Dispersed throughout the body.

Phases

1) Stage 0: Non-invasive (in situ) cancer
2) Stage I–II: Breast cancer in its early stages
3) Stage III: Cancer that has spread locally
4) Stage IV: Metastatic cancer, meaning cancer that has spread to distant organs

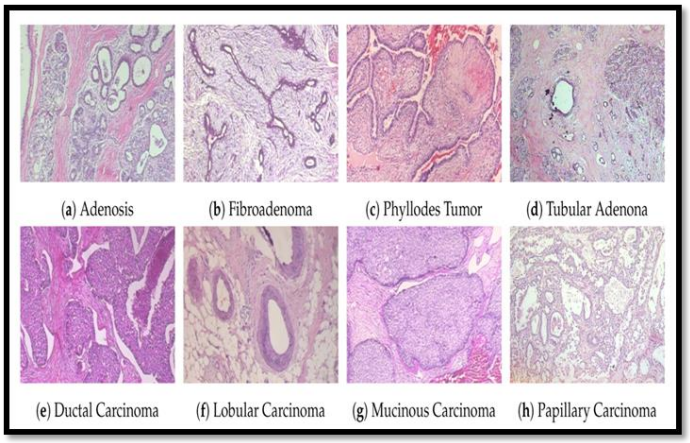


Fig. 1: Classification of Breast Cancer.

Epidemiology: Breast cancer is among the most frequent malignancies that affect women, according to the American Cancer Society. It was estimated that 230,480 women in the US will receive a breast cancer diagnosis in 2011, making up about 30% of all new cancer cases in women.[12] The sickness was also predicted to kill about 39,520 women. These figures demonstrate the severity of breast cancer and its impact on women's health and society.[13] Numerous studies have been conducted since the 1960s to determine whether routine screening for breast cancer can lower death rates.[14] X-ray mammography is the most widely used screening technique and is regarded as the gold standard for identifying breast cancer. Regular screening is highly advised because research has shown that early detection of breast cancer improves treatment success and boosts survival rates.[15] The ideal age to start mammography screening, however, has been disputed by experts. There was much debate and dispute about the U.S. Preventive Services Task Force's recommendation to begin routine screening at age 50 rather than age 40.[16] The majority of specialists concur that routine breast cancer screening is particularly crucial for women between the ages of 50 and 74, despite differing views regarding the precise advantages of mammography.[17,18]

2. Risk factors for developing breast cancer among women

2.1 Individual Breast Cancer History: Women who have previously experienced breast cancer are more likely to get it again. The cancer may spread to another breast or recur in the same breast. Although they typically do not experience recurrence, women with diseases like ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) are nonetheless at a higher risk of developing breast cancer than other women.[19]

2.2 Breast and Other Cancer Family History: A woman's chance of getting breast cancer can be raised if she has a mother, sister, or daughter who has the condition. Breast cancer is more common than anticipated in some families. Environmental influences, similar lifestyle patterns, inherited genes, or a mix of these could produce this.[20]

2.3 BRCA Gene Mutations: A genetic mutation is an alteration in a gene that can raise the risk of cancer and other disorders. Parents may pass on some of these mutations to their offspring. Inherited gene mutations are associated with 5–10% of cases of breast cancer. BRCA1 and BRCA2 are two significant genes associated with breast cancer. These genes are known as tumor suppressor genes because they often aid in regulating cell development and preventing cancer. These genes may lose their capacity to prevent the development of cancer when mutations take place in them. BRCA gene mutations are uncommon, occurring in approximately 1 in 500 individuals. These mutations can be passed down from either father to both males and women. Every child has a 50% chance of inheriting a mutant BRCA gene if one parent does.[21] According to research, women who inherit BRCA1 or BRCA2 mutations are up to 85% more likely to get breast cancer throughout their lifetime. Additionally, these women may get cancer in both breasts and are more likely to acquire breast cancer at a younger age. The chance of getting cancer in the second breast is likewise increased if one breast has cancer. Moreover, ovarian cancer risk is elevated by BRCA gene mutations.[22]

2.4 Big or Dense Breasts: Fatty tissue, milk ducts, glands, and connective tissue make up the breasts. There are less fatty tissues and more glands and connective tissue in women with thick breasts. Breast density is regarded as a hereditary trait and is typically inherited. Compared to women with less dense breasts, those with dense breast tissue are more likely to get breast cancer. A mammography is the only way to detect dense breasts. However, because fatty tissue appears dark on the scan while dense tissue and malignancies appear white, dense tissue can make mammography images more difficult to interpret. This can occasionally make it challenging to precisely identify malignancies.[23]

2.5 Menopause in Later Life: Menstruation stops when the ovaries cease making hormones like progesterone and estrogen, a condition known as menopause. The body is exposed to estrogen for a longer period of time if menopause happens later in life, particularly after the age of 55. The chance of getting breast cancer may rise as a result of this prolonged exposure.

However, because their breast tissue is exposed to these hormones for a shorter amount of time, women who go through menopause earlier are less likely to get breast cancer.[24]

2.6. Whether there are late or no pregnancies: Women who have their first pregnancy at a younger age, especially before 30, may have a lower risk of developing breast cancer. During pregnancy, exposure of breast cells to estrogen decreases, and the number of menstrual cycles in a woman's life is also reduced, which can help protect against breast cancer. Having more children may further lower the risk. On the other hand, women who never become pregnant or have pregnancies later in life may have a slightly higher risk of breast cancer.[25]

2.7. Treatment with hormone replacement: The Women's Health Initiative study found that hormone replacement treatment (HRT) elevated the risk of breast cancer much more than estrogen alone. According to the study, even short-term usage of combination HRT may increase this risk. However, a few years after discontinuing the treatment, the elevated risk seemed to decline. The study also revealed a decline in new instances of breast cancer among Canadian women aged 50-69 between 2002 and 2004. This occurred concurrently with a decline in the use of combined HRT by women. Countries including the United States, Australia, Germany, the Netherlands, Switzerland, and Norway also showed similar tendencies. Experts now think that coupled HRT may have more long-term dangers than advantages.[26]

2.8. Being overweight: After menopause, obesity can raise a woman's risk of breast cancer. Research indicates that women who have never undergone hormone replacement therapy (HRT) and have a higher body mass index (BMI) are more likely than women with a lower BMI to acquire breast cancer. The development of breast cancer is significantly influenced by estrogen. The ovaries produce the majority of estrogen before to menopause. Fat tissue starts to produce estrogen after menopause. Over time, women who have greater body fat may have higher levels of estrogen, which can raise their risk of breast cancer.[27]

2.9. Oestrogen: The risk of breast cancer is associated with both endogenous (made within the body) and exogenous (acquired from outside sources) estrogen. The ovaries are the primary source of estrogen prior to menopause, and removing them can lower the risk of breast cancer. Hormone replacement therapy (HRT) and oral contraceptives are the two main external sources of estrogen. Since the 1960s, birth control pills have been used extensively, and their formulations have been refined to minimize adverse effects. After quitting oral

contraceptives for more than ten years, the majority of women no longer have a high risk of breast cancer. Menopausal and postmenopausal women frequently use HRT to control their symptoms. Long-term HRT use, however, may raise the risk of breast cancer, according to a number of studies. Women who currently take hormone replacement therapy (HRT) have a greater risk of breast cancer than women who have never used it, according to research from the Million Women Study. According to additional research, the risk rises with extended HRT use but falls after a few years of medication cessation. HRT use may potentially increase the risk of recurrence in women with a history of breast cancer. Breast cancer cases in the US dropped by roughly 7% after the Women's Health Initiative study in 2003 made the negative effects of HRT generally recognized.[28]

2.10. Age: One of the most well-known risk factors for breast cancer is age. Although breast cancer is extremely rare in women under 30, the risk progressively rises with age. Up until the age of 80, the number of instances of breast cancer keeps increasing.Compared to younger women, women 65 years of age and beyond are far more likely to acquire breast cancer. This demonstrates that growing older is a significant factor in the development of breast cancer.[29]

2.11. Environmental and Lifestyle Factors: Similar to how smoking raises the risk of lung cancer, people are highly curious about whether lifestyle choices can influence the risk of breast cancer. Researchers are investigating the possibility of preventing cancer by altering everyday routines or abstaining from dangerous substances. But unlike lung cancer, there isn't a single lifestyle factor that significantly raises or lowers the chance of breast cancer. However, other factors might have less of an impact on the risk of breast cancer.

2.12. Drinking Alcohol: Breast cancer risk may be somewhat elevated by alcohol use. Because alcohol can have a variety of effects on the body, including harming DNA, impairing the body's capacity to repair cells, or altering nutrients that aid in cancer prevention, researchers think this might occur.[30] Nonetheless, alcohol's overall impact on the risk of breast cancer is thought to be minimal. According to studies, consuming one alcoholic beverage or less each day does not significantly raise the risk. Higher alcohol consumption somewhat increases the risk.[31-34] Women who drink two or three drinks a day may be somewhat more likely to develop breast cancer than non-drinkers.[35] Additionally, research indicates that women with a higher body mass index (BMI) or a family history of breast

cancer may be at higher risk.[36] There was no discernible difference between wine, beer, or spirits.[37]

2.13. Index of Body Mass: Particularly in older women, the Body Mass Index (BMI), which is determined by height and weight, may have an impact on the risk of breast cancer.[38] According to a big research of Norwegian women, BMI has little to no impact on premenopausal women's risk of breast cancer and may even offer some protection.[39] However, a greater BMI was associated with an increased risk of breast cancer in postmenopausal women.[40] This is due to the fact that adipose tissue becomes a significant source of estrogen following menopause. Elevated body fat can raise estrogen levels, which over time may encourage the growth of breast cancer.[41,42] Additionally, research indicates that women with higher BMIs may have greater levels of insulin and insulin-like growth factor, which are also associated with an increased risk of breast cancer.[43] These hormonal changes are particularly linked to abdominal obesity, which is prevalent after menopause and may raise the risk even more.[44]

2.14. Treatment with Hormone Replacement: Postmenopausal women frequently take hormone replacement therapy (HRT) to lessen menopausal symptoms and help prevent osteoporosis.[45] HRT was being used by a large number of American women by 1995. Researchers later discovered that long-term HRT use may raise the risk of breast cancer.[46] The Women's Health Initiative conducted a sizable research to look at how HRT affected postmenopausal women.[47] According to the study, women who had combination estrogen and progesterone therapy were more likely to develop breast cancer, particularly after a number of years of use. Because the hazards, which included heart disease, stroke, and breast cancer, outweighed the benefits, a portion of the trial was discontinued in 2002.[48] The study discovered that five years of concurrent HRT treatment increased the risk of breast cancer by almost 26%. However, present or recent users were the ones who were most at risk.[49] The risk was comparable to that of women who never used HRT if they stopped using it for more than five years. The studies primarily associated combined estrogen-plus-progesterone therapy with an increased risk of breast cancer. In certain investigations, estrogen-only therapy did not demonstrate the same significant increase in risk.[50]

2.15. Radiation Exposure: High radiation exposure can raise the risk of breast cancer. Studies of atomic bomb survivors provided earlier information regarding radiation-related

cancer, but medical radiation exposure is now thought to be a more significant cause.[51] Research revealed that women who received fluoroscopy treatments or frequent chest X-rays for conditions like tuberculosis were more likely to acquire breast cancer in the future. Younger women were more at risk, which often manifested 10–15 years after radiation exposure and persisted throughout life.[52] Women who underwent chest radiation therapy for Hodgkin's lymphoma are also more likely to develop breast cancer, particularly if the treatment was administered between puberty and the age of thirty. These tumors frequently appear years after treatment, sometimes even before women start routine screening for breast cancer.[53]

2.16. Reproductive Elements: Reproductive factors can influence the risk of breast cancer. According to studies, women who enter menopause later in life (after 55 years) or begin menstruation earlier (before 12 years) may be somewhat more likely to get breast cancer.[54] This is because their bodies are exposed to estrogen for a longer period of time. Researchers believe that the more ovulatory menstrual cycles a woman has during her lifetime, the greater the exposure of breast tissue to hormones, which may increase breast cancer risk. Breast cancer risk was found to be decreased in women who had both ovaries removed before the age of 40.[55-57] Pregnancy also affects breast cancer risk. Compared to women who give birth earlier in life, women who never have children or who deliver their first kid after the age of thirty may be at greater risk.[58] There seems to be some protection against breast cancer from an early full-term pregnancy. This protective effect may occur because breast cells become more mature and less likely to develop cancer after full-term pregnancy and breastfeeding.[59]

Detection Of Breast Cancer: In its early stages, breast cancer typically does not cause pain. A breast lump that is painless is frequently regarded as more suspicious than one that is painful. Women without major risk factors are generally advised to have a mammogram every year starting at the age of 40.[60] Even if the tumor is huge, some breast cancers may not show up on a mammogram. However, mammography can assist detect extremely tiny cancers. Therefore, a normal mammogram does not always mean that cancer is absent.[61] When a woman has a solid or worrisome breast lump, the mammography is primarily used to look for hidden tumors in the surrounding breast tissue and the other breast. If the lump is suspicious or does not go away after fluid evacuation, a biopsy is typically required to determine whether it is malignant. A biopsy is typically required to determine whether the lump is malignant if it does not go away after fluid evacuation or if it is still suspicious.[62]

Detection And Diagnosis Of Breast Cancer Using Mammography: The breast is examined using a variety of imaging techniques, including X-ray, magnetic resonance imaging (MRI), and ultrasound. The most popular and successful technique for identifying breast cancer before a lump is felt is mammography.[63] A low-dose X-ray is used in mammography to produce images of the breast. It is widely recommended for routine breast cancer screening. The American Cancer Society states that beginning at age 40, women between the ages of 40 and 49 should have a mammogram every one to two years.[64]

There are two main types of mammography

1. **Film Mammography:** Images are directly printed on film.
2. **Digital Mammography:** A computer stores the images electronically.

Compared to film mammography, digital mammography offers the following benefits

- Improved contrast and image quality
- Reduced radiation exposure
- Quicker processing of images
- The capacity to modify and improve photos

According to studies, both methods are generally equally effective; however, premenopausal women, women under 50, and women with thick breasts may benefit more from digital mammography.[65]

Additionally, there are two kinds of mammograms

1. **Screening Mammography:** Used to find cancer early in women who do not exhibit symptoms.
2. **Diagnostic Mammography:** Used in cases with symptoms such an abnormal screening result or a breast lump. It offers a more thorough assessment and could assist in determining whether a biopsy is required.[66]

Breast cancer fatalities have decreased and early detection of the illness has increased because to mammography. However, because the pictures may have low contrast, mammograms can occasionally be challenging to interpret. This may result in false-negative (missing cancer) or false-positive (showing cancer when there is none) results.[67]

Some hospitals employ the following to increase accuracy

1. **Computer-Aided Detection (CAD):** A computer system assists radiologists in identifying worrisome areas. CAD functions as a "second pair of eyes" and can enhance early cancer detection while lessening the strain for physicians.

2. **Double Reading:** Two radiologists review the same mammography.

3. **Computer-Aided Detection (CAD):** Radiologists can find suspicious spots with the aid of a computer system. By acting as a "second pair of eyes," CAD can lessen the strain for physicians while enhancing early cancer diagnosis.[68-71]

Computer, Based Breast Cancer Detection & Diagnosis: Radiologists can more precisely identify and diagnose breast cancer with the use of computer-aided detection (CAD). It integrates computer science, image processing, pattern recognition, and artificial intelligence (AI) with medical imaging. By assisting physicians in identifying questionable regions in mammograms, CAD functions similarly to a "second opinion."[72]

CAD systems come in two primary varieties

1. **Film-based CAD systems:** For computer analysis, traditional mammography films are scanned and transformed into digital images.
2. **Digital CAD systems:** These employ full-field digital mammography (FFDM), which improves image quality, contrast, and clarity.

A number of commercial CAD systems are available in the United States, including:

- R2 Technology
- iCAD
- Kodak systems

Research has shown that CAD can improve early breast cancer detection and reduce the workload of radiologists; however, some studies suggest that current CAD systems still need improvement because they may occasionally reduce accuracy or produce incorrect results. Overall, CAD is considered a promising tool for breast cancer screening and diagnosis, but further research and development are needed before it can be fully reliable and widely used in hospitals and screening centers.[73]

Ultrasound of the breast: A helpful imaging technique for looking at possible breast issues or tumors is breast ultrasonography. It can examine the lymph nodes under the armpit as well as the breast tissue. The patient often lies on her back during the examination while the physician uses an ultrasound machine to scan the breast and armpit regions.

Breast Ultrasound Indications

1. For young women, pregnant women, and nursing mothers with breast issues, breast ultrasonography is frequently recommended.
2. It aids in verifying whether a breast lump or other questionable alterations are present.
3. After breast implant surgery, it can be used to check the breasts.
4. It also aids in directing operations like fluid extraction from breast lesions or needle biopsies.

MRI, or magnetic resonance imaging: Typically, magnetic resonance imaging (MRI) is not utilized as a screening test for breast cancer. But in some circumstances, it is quite helpful.[74]

Doctors can benefit from MRI

- Ascertain the amount and stage of breast cancer
- Determine the extent of the tumor's spread inside the same breast.
- Find many tumors in one or both breasts.
- During the initial diagnosis, look for hidden cancer in the opposite breast.
- Examine the tumor both prior to and following chemotherapy.
- Track the effectiveness of the treatment.
- Determine whether breast-conserving surgery is feasible.

When more information is required than what mammography or ultrasound can offer, magnetic resonance imaging (MRI) is particularly useful.

Histopathological Examination: The most crucial technique for verifying the diagnosis of breast cancer is histopathological examination, which involves examining a small sample of breast tissue under a microscope to detect cancer cells. This test aids in the final and accurate diagnosis and directs the course of treatment. To make an accurate diagnosis, physicians require comprehensive clinical data and a high-quality tissue sample that is obtained at the appropriate time.

The most crucial technique for verifying the diagnosis of breast cancer is histopathological investigation. This test looks for cancer cells by using a microscope to analyze a small sample of breast tissue. This test directs the course of treatment and aids physicians in making a definitive and precise diagnosis. Doctors require comprehensive clinical data and a high-quality tissue sample taken at the appropriate time in order to make an accurate diagnosis.[75]

Tissue Fixation Standard

- **Fixative:** For tissue fixation, 10% neutral formalin is frequently utilized.
- **Fixative volume:** The volume of the tissue sample should be at least twice that of the fixative. The fixative may need to be replaced once during the procedure if the tissue is thick or big.
- **Temperature:** Fixation is typically carried out at room temperature.
- **Fixation time:** The size and kind of the tissue specimen determine how long it takes.

Sampling and Processing of Tissue Specimens: Sampling and Processing of Tissue Specimens In order to properly examine tissue samples during surgery, the following steps must be taken: 1. The tissue sample and patient details are checked and verified; 2. The specimen is carefully observed, measured in length, width, and height, and its appearance is recorded; occasionally photos or diagrams are also taken; 3. A small sample is taken from the suspicious area, quickly frozen, and sliced for examination; if cancer is found, additional tissue samples may be fixed for 12 to 24 hours after the completion of the examination report.

Tissue samples must be handled swiftly and carefully during surgery in order to be properly examined.

1. The tissue sample and patient information are first examined and confirmed.
2. The item is closely examined, its length, width, and height are measured, and its appearance is noted. Diagrams or pictures are occasionally also taken.
3. A tiny sample is extracted from the questionable area, promptly frozen, and cut for analysis. Additional tissue samples may be preserved for specialized examinations like immunohistochemistry if malignancy is found.
4. The leftover tissue samples are preserved for 12 to 24 hours for additional in-depth analysis after the examination report is finished.[76]

Breast Cancer Pathological Categorization and pTNM Staging: Based on how cancer cells appear under a microscope, pathological categorization is used to determine the kind of breast cancer.

The TNM staging system describes the extent to which the cancer has spread

- T (Tumor): The primary tumor's size and extent
- N (Nodes): If adjacent lymph nodes are impacted
- M (Metastasis): The pathological staging carried out following surgery and microscopic analysis of tissue samples determines whether the malignancy has migrated to other bodily parts. It aids medical professionals in identifying the precise stage of breast cancer and developing the best course of action.

Role of the Prolactin Receptor in Breast Cancer: Function of the Prolactin Receptor in Breast Cancer: Prolactin is a hormone that acts through the prolactin receptor (PRLr), which is present in extremely high concentrations in over 95% of cases of breast cancer, including both hormone-positive and hormone-negative cancers. The PRLr influences key hormones like progesterone and estrogen, which causes the levels of these receptors to drop when the prolactin receptor is lost or reduced.[77] The prolactin receptor (PRLr) is how the hormone prolactin functions. Over 95% of cases of breast cancer, both hormone-positive and hormone-negative, have extremely high levels of this receptor.[78] By regulating vital hormones including progesterone and estrogen, the PRLr promotes the growth of breast cancer cells. Estrogen and progesterone receptor levels similarly drop when the prolactin receptor is deleted or diminished, indicating that PRLr is crucial for the development of cancer. Numerous cellular pathways connected to tumor development and fast cell proliferation are triggered by the prolactin receptor.[79] These pathways aid in the survival, proliferation, and dissemination of cancer cells. Additionally, PRLr interacts with other receptors that are important in the development of breast cancer, including integrin receptors, estrogen receptors, and epidermal growth factor receptors (EGFR). According to recent studies, the prolactin receptor may also directly influence gene activity within the cell nucleus, accelerating the development of breast cancer.[80]

MANAGEMENT

Surgery: Surgery for breast cancer has evolved significantly over time. William Halsted, a surgeon, invented the radical mastectomy at Johns Hopkins Hospital in 1882.[81] The entire

breast, surrounding skin, chest muscles, and lymph nodes behind the arm were removed during this procedure. This procedure significantly reduced the risk of cancer returning, but it resulted in severe body deformities, lymphedema (arm swelling), and loss of sensation in the arm and chest.[82] Later, medical professionals discovered that it was frequently not required to remove the chest muscles. Because cancer rarely spread to these muscles, doctors like J. B. Murphy ceased removing them by 1912. David Patey advocated for the less invasive and less complicated modified radical mastectomy in 1948.[83] Surgery got less aggressive with time. Bernard Fisher's research revealed that for many patients, removing just the breast's malignant portion and a few lymph nodes could be equally beneficial. This aided medical professionals in transitioning to lumpectomy, a procedure that preserves the majority of the breast.[84]

Currently, the following are typical treatments for operable breast cancer:

- Mastectomy (removal of the breast) or lumpectomy (removal of the tumor alone).
- Sentinel lymph node biopsy or lymph node dissection to monitor the spread of malignancy. Neoadjuvant chemotherapy, which shrinks the tumor before surgery, is frequently administered to patients with locally advanced breast cancer.[86] Depending on the patient's health, surgeons may then perform a modified radical mastectomy or breast-conserving surgery.[85]

Radiation treatment: Since the early 1900s, radiation therapy has been utilized to treat breast cancer. Physicians found that radiation could help slow the spread of cancer, particularly in patients who were too frail or unwilling to undergo surgery.[86] George Pfahler, a physician, reported positive outcomes from radiation therapy for patients with breast cancer in 1932. Following treatment, many women with early-stage cancer lived for several years. Later, in 1937, Geoffrey Keynes treated breast cancer with radium needles while keeping the breast intact. The outcomes for survival were comparable to those of radical mastectomy. However, because radium was challenging to handle and occasionally caused tissue damage, this approach was not extensively used.[87] Robert McWhirter demonstrated in the middle of the 20th century that radiation therapy combined with straightforward breast surgery might be just as successful as radical mastectomy. This demonstrated that cancer cells in adjacent lymph nodes might be effectively treated with radiation.[88]

Antoine Lacassagne Baclesse discovered in the 1940s that many breast tumors react favorably to radiation therapy, particularly when the tumor is tiny. Subsequent research verified that for many individuals, radiation therapy after breast-conserving surgery is just as successful as total breast removal.[89] Additionally, studies have demonstrated that managing cancer in the breast and surrounding lymph nodes increases survival and slows the disease's spread to other body areas.

Radiation therapy is now far safer and more sophisticated. Modern techniques include

1. 3D Conformal Radiotherapy (3DCRT) more precisely targets the tumor.
2. Normal tissue damage is lessened with Intensity Modulated Radiation Therapy (IMRT).
3. By merely treating a portion of the breast, Accelerated Partial Breast Irradiation (APBI) reduces the duration of treatment.
4. Radiation is administered during surgery using intraoperative radiation therapy (IORT).

Nowadays, radiation is frequently administered

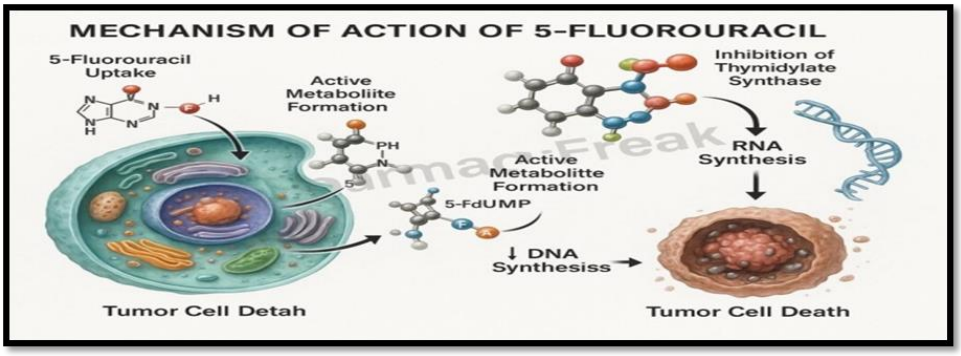
- Following a modified radical mastectomy (MRM) of the chest wall.
- Following breast-conserving surgery, the residual breast tissue.

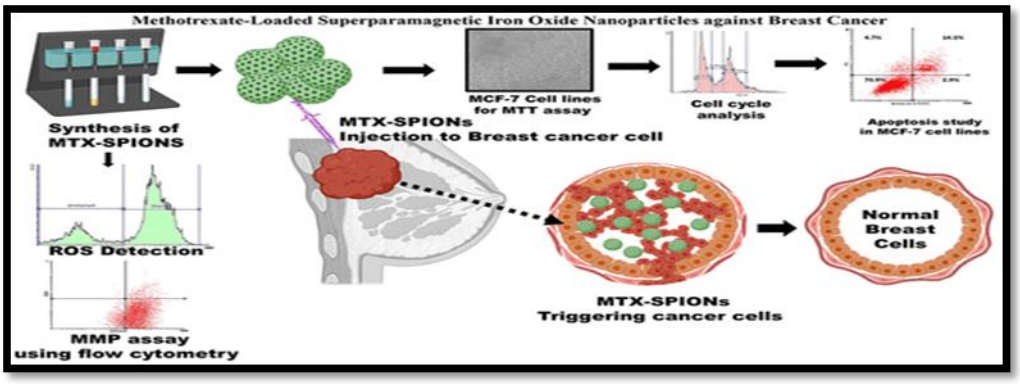
Radiation therapy is also used to improve the quality of life for patients with advanced breast cancer by reducing pain and other symptoms.[90]

Chemotherapy: In the middle of the 20th century, chemotherapy emerged as a significant cancer treatment. It enabled medical professionals to effectively treat a variety of advanced malignancies, including breast cancer.[91] When breast cancer had spread and was no longer responding to hormone therapy, doctors initially treated it with single chemotherapy medicines. Among the first medications were

1. Cyclophosphamide
2. Methotrexate
3. 5-Fluorouracil
4. Vincristine And Vinblastine.

Mechanism of Action Anticancer drug in Breast Cancer





However, there was little effectiveness with a single medication. Later, medical professionals found that combining multiple medications produced superior results.[92] Gianni Bonadonna created the well-known CMF regimen at the Milan Cancer Institute, which included:

1. Cyclophosphamide
2. Methotrexate
3. 5- Fluorouracil

Research conducted in 1976 revealed that CMF increased the survival rate of individuals whose breast cancer had progressed to lymph nodes following surgery. In the 1970s, CMF was one of the most widely used chemotherapy therapies due to its effectiveness and lower incidence of serious adverse effects.[93] Newer medications known as anthracyclines, such doxorubicin, became the norm for treating early-stage breast cancer in the 1990s. These medications dramatically decreased the number of deaths from breast cancer, according to research.[94] Later, treatment outcomes were further enhanced by a different class of medications known as taxanes.

Key taxane medications consist of

1. Paclitaxel

2. Docetaxel

Addition of taxanes to chemotherapy combinations improved survival and decreased cancer recurrence in individuals with early-stage breast cancer, according to extensive clinical research.[95]

Chemotherapy is now utilized in many phases of the treatment of breast cancer

- Neoadjuvant chemotherapy: used prior to surgery in order to reduce tumor size
- Adjuvant chemotherapy is administered to eradicate any cancer cells that remain after surgery.
- When cancer has spread to other areas of the body, metastatic chemotherapy is utilized. Over time, patient survival and breast cancer treatment have significantly improved thanks to modern chemotherapy.[96]

NANOTECHNOLOGY: The use of nanotechnology in the treatment of breast cancer is growing. Researchers are creating nanoparticles, which are minuscule drug delivery systems that can transport cancer medications straight to tumor cells. Currently, over 150 clinical trials are evaluating cancer treatments based on nanotechnology. Making chemotherapy safer and more efficient is one of nanotechnology's main objectives. Conventional chemotherapy medications, such as doxorubicin, are effective against cancer but can harm healthy organs, particularly the heart. Researchers created liposomal doxorubicin formulations to lessen these adverse effects. These medications help deliver the medication to cancer cells more safely by encasing it in liposomes, which are tiny fat-like particles.

Typical instances consist of:

- DaunoXome
- Myocet
- Caelyx and Doxil

These medications have anti-cancer properties comparable to those of standard doxorubicin, but they also have fewer adverse effects and a decreased risk of heart damage. Abraxane is another significant nanotechnology-based medication that contains albumin protein particles bound to the chemotherapeutic chemical paclitaxel. Because regular paclitaxel does not dissolve readily in water, dangerous chemicals were formerly required to do so, which resulted in allergic responses and nerve damage.

To increase the drug's solubility and lessen these harmful effects, albumin-bound paclitaxel was created. Patients can now receive therapy in a more comfortable and safe manner.

In general, breast cancer treatment is becoming more focused, efficient, and less damaging to healthy tissues thanks to nanotechnology.

Future directions: Enhancing early detection, individualized therapy, and patient survival are the primary goals of future approaches in breast cancer research and treatment. Among the crucial future paths are:

- **Customized Healthcare:** For greater efficacy and fewer adverse effects, treatments will be tailored to a patient's genetic composition and tumor features.
- **Targeted Treatment:** creation of medications that target cancer cells specifically, such as hormone treatments and HER2-targeted medicines.
- **Immunotherapy:** Research on the body's immune system's ability to identify and eliminate cancer cells is growing in importance.
- Artificial Intelligence (AI) in Diagnosis Early diagnosis, treatment outcome prediction, and mammography interpretation could all be enhanced by AI and machine learning.
- **A liquid biopsy:** Without invasive procedures, blood-based testing can track recurrence, assess treatment response, and potentially diagnose cancer early.
- In order to better understand hereditary breast cancer and develop new treatments, researchers are studying genes such as BRCA1 and BRCA2.
- **Nanotechnology-Based Drug Delivery:** Nanoparticles may deliver anticancer drugs directly to tumor cells, reducing damage to healthy tissues.
- **Prevention and Lifestyle Research**: More emphasis is being placed on diet, exercise, environmental factors, and awareness programs to reduce breast cancer risk.
- **Combination Therapies**: Chemotherapy, immunotherapy, and long-term survivorship care.
- To better understand hereditary breast cancer and create novel treatments, researchers are examining genes like BRCA1 and BRCA2.
- **Drug Delivery Using Nanotechnology:** By delivering anticancer medications straight to tumor cells, nanoparticles may lessen harm to healthy tissues.
- **Research on Lifestyle and Prevention:** To lower the risk of breast cancer, more attention is being paid to food, exercise, environmental factors, and awareness campaigns.

- **Combination Treatments:** Treatment outcomes may be enhanced by combining chemotherapy, immunotherapy, radiation, and targeted therapy.
- **Enhanced Survivors' Quality of Life:** Future care will also concentrate on long-term survivorship care, mental health, rehabilitation, and fertility preservation.
- Future treatments for breast cancer should be more precise, less harmful, and more effective thanks to these developments.

CONCLUSION

One of the most prevalent and dangerous tumors that impact women globally is breast cancer. Numerous genetic, hormonal, environmental, and lifestyle factors affect its development. Breast cancer is classified into many categories according to histological and molecular features, which aids in choosing the best course of treatment and enhancing patient outcomes. According to epidemiological research, breast cancer is becoming more commonplace worldwide, which is a serious public health issue. Women are more likely to develop breast cancer due to a number of risk factors, including age, family history, hormonal imbalance, obesity, late menopause, alcohol usage, and genetic abnormalities like BRCA1 and BRCA2. In order to lower mortality and increase survival rates, early detection is essential. The prolactin receptor (PRLR) also plays a significant role in the progression and development of breast cancer; overexpression of PRLR in breast cancer cells contributes to tumor growth, cell proliferation, and survival. Screening methods, such as self-breast examination, clinical breast examination, and advanced imaging techniques, are important for identifying cancer at an early stage. Mammography continues to be one of the most effective and widely used tools for the early diagnosis of breast cancer.

Mammography is still one of the most popular and successful diagnostic techniques for the early detection of breast cancer. It increases the likelihood of a successful course of treatment by assisting in the detection of aberrant alterations in breast tissue before clinical symptoms manifest. Furthermore, new developments in molecular diagnostics and imaging have increased the accuracy of diagnoses.

The development and progression of breast cancer are also significantly influenced by the prolactin receptor (PRLR). In breast cancer cells, overexpression of PRLR promotes tumor development, cell division, and survival. Gaining insight into the molecular mechanisms

behind prolactin receptor signaling may open up new possibilities for customized treatment plans and targeted medicines.

To improve breast cancer prevention, diagnosis, and treatment, ongoing research in early detection, molecular biology, targeted therapy, and patient awareness is crucial. Future developments in customized medicine and cutting-edge treatment approaches could greatly lessen the impact of breast cancer and enhance the lives of those who are impacted.

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