

## Breast Cancer Risk Assessment and Treatment Options with Radiation Therapy, a Review Study

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### ABSTRACT

This review aims to provide an overview of breast cancer, the most prevalent malignancy among women, with a particular focus on risk factors, diagnosis, and treatment options, emphasizing the role of radiation therapy. This study synthesizes existing literature to explore breast cancer, its risk factors (age, genetics, lifestyle, hormonal changes), diagnostic methods including biopsy, and various treatment approaches, including surgery, hormone therapy, chemotherapy, and radiation therapy. The role of multidisciplinary tumor boards in decision-making is also highlighted. Early diagnosis improves treatment outcomes, often involving surgical intervention. Treatment strategies include chemotherapy, radiation therapy, and electrocautery. Radiation therapy, which uses high-energy X-rays to kill cancer cells, is often combined with surgery and chemotherapy. Breast cancer remains a significant health challenge for women, requiring a multifaceted approach encompassing risk assessment, early detection, and tailored treatment strategies. Radiation therapy plays a crucial role in both curative and palliative settings, often in conjunction with other modalities.

**Key words:** Breast cancer, Radiotherapy, Health, Oncology, Treatments

### INTRODUCTION

Breast cancer is a malignancy creating from breast tissue, with symptoms such as lumps, nipples, and erythematous skin. Risk factors include female sex, obesity, sedentary lifestyle, alcohol consumption, hormone replacement therapy, radiation exposure, early menarche, delayed childbearing, and family history [1, 2]. Among 18 subtypes, with ductal carcinoma in situ originating from milk ducts and lobular carcinoma emerging in milk-producing sacs. Breast cancer is identified through biopsy and supplementary tests to determine metastasis. The debate about breast cancer screening is ongoing, with mammography benefits more pronounced for women aged 40-70 and biennial mammograms recommended for women aged 50-74 [3].

High-risk individuals can benefit from preventative measures like medications and mastectomy. Breast cancer treatments include surgery, chemotherapy, hormone therapy, targeted therapy, and radiation therapy. Surgical options range from mastectomy to breast-conserving surgery, with reconstruction possible. Oncoplastic surgery and sentinel lymph node biopsy are recommended [4]

Multidisciplinary tumor boards are crucial for optimal treatment decisions, especially with advanced systemic therapies like cyclin-dependent kinase 4/6 inhibitors, enhancing patient quality of life through informed, evidence-based plans. [5]

A recent study highlights cardiovascular disease as a potential consequence of breast cancer treatment. The study investigated whether female carriers of pathogenic variants of BRCA1/2 (BRCA1/2pv) were probably heading to develop CVD following breast cancer treatment compared to breast cancer patients without known BRCA1/2pv. The researchers found that BRCA1/2pv carriers did not show a statistically significant increased risk of CVD compared to other breast cancer patients after accounting for factors like smoking status, age, chemotherapy, and radiation treatment. Specifically, the study did not find evidence that breast cancer treatment was linked to an elevated risk of CVD in BRCA1/2pv carriers compared to other breast cancer patients. [6]

Breast cancer is the most prevalent malignancy among women, accounting for 25% of all cases in 2018. It is a multifaceted disease characterized by mutations in cellular pathways, like the MAPK, RB/E2F, PI3K/AKT/mTOR, and TP53 pathways [7]. Survival rates vary by cancer subtype, clinical stage, and patient age. Breast cancer is more prevalent in wealthy nations and manifests 100 times more frequently in women than in men [8].

#### *Breast cancer prevalence*

Being responsible for 26.2 million new cases in 2020 made breast cancer the most generally diagnosed cancer among women globally [9]. Breast cancer is the most prevalent malignancy and the most frequent cause of mortality among women globally, accounting for 29% of recently diagnosed cancers in the United States [10]. In 2018, around 1.2 million new patients were diagnosed, with the disease projected to expand at an annual rate of 1.3% [11].

#### *Risk factors for breast cancer*

An individual may have increased susceptibility to breast cancer due to various factors. These factors are categorized into changeable and non-modifiable types, which include: Immutable factors

**Gender:** Females are at a higher danger of breast cancer due to expanded vulnerability to hormonal stimulation, particularly estrogen and progesterone levels, despite being less common in males. [12].

**Age:** As it has been mentioned in **Table 1**, Around 80% of breast cancer patients are over 50, with aging increasing the risk of various illnesses due to cellular alterations and exposure to carcinogens. [13]

Table 1. Relation between Genetic risk and Normal risk age in BC	
Genetic Risk	Normal Risk Age
42%	1 in 93 (1%)45
72%	1 in 33 (3%)55
80%	1 in 17 (6%)65
84%	1 in 11 (9%)75

Table1: The Relationship between genetic risk and normal risk age in BC

**Race and ethnicity:** Women of diverse racial backgrounds have differing occurrence rates of breast cancer. Non-Hispanic white women often exhibit the greatest rates of breast cancer recurrence. Conversely, breast cancer death rates are markedly elevated among black women. [14].

**Gestational age:** Studies show estrogen and progesterone exposure increases breast cancer vulnerability in women, with reproductive milestones like pregnancy, breastfeeding, menarche, and menopause influencing the breast microenvironment's carcinogenic potential. [15].

**Breast tissue density:** Breast tissue density fluctuates throughout life, with higher density in pregnant or nursing women with lower BMIs linked to enlarged breast cancer threat pre- and post-menopause [16].

**Family history of breast cancer:** A familial history of breast cancer is a substantial risk factor, explaining around 25% of all instances. Women with a parental or sibling history of breast cancer have increased vulnerability to the disease relative to those lacking such familial ties. [17].

**Having a history of radiation therapy:** Patients receiving radiation treatment have a greater danger of increasing secondary cancers, especially those before 30 years old, and a higher likelihood of developing breast cancer due to familial predisposition.

**Body Mass Index (BMI) and physical activity:** Research indicates that overweight and obesity increase the risk of breast cancer, particularly in obese postmenopausal women, with higher BMI women over 50 having a higher risk [18].

**Alcohol consumption and smoking:** Studies show alcohol consumption and smoking might increase gastrointestinal and breast cancer incidence due to elevated estrogen levels and hormonal imbalances, and correlates with elevated BMI and increased risk [19, 20].

**The consumption of processed foods:** Processed meats, classified as a Group 1 carcinogen by the WHO, significantly increase the risk of breast cancer, emphasizing the importance of maintaining a balanced diet. [21].

#### *Breast cancer classification*

Invasive breast cancer (IBC) is a diverse group of tumors with varying clinical and morphological characteristics. [22]. The most prevalent form is invasive ductal carcinoma, responsible for 40-80% of cases. About 25% of these tumors have distinct growth patterns and cytological characteristics. The onset of breast cancer is attributed to progenitor cells, which can develop various tumor forms [23]:

- luminal-like
- basal-like or triple-negative
- HER-2 enriched

In addition, depending on whether estrogen, progesterone, and epidermal growth factor receptors exist in the tumor, breast cancer is divided into four categories. which are [24]:

- HR+ / HER2–
- HR+ /HER2+
- HR– /HER2+
- triple-negative HR– /HER2–

### *Luminal breast cancer*

Luminal breast cancer, a subgroup of luminal A and B tumors, accounts for over 70% of Western cases. These low-grade, slow-growing tumors, characterized by ER transcription aspects and gene manifestation, have a favorable prognosis and are typically estrogen receptor-positive [25].

Unlike type A tumors, luminal B tumors have a higher grade and a less good prognosis. These tumors are estrogen receptor-positive (ER+) and could be progesterone receptor-negative (PR-) or human epidermal growth factor receptor 2-positive (HER2+). Genes connected to cell proliferation—including MK167 and AURKA—have higher expression in group B. nevertheless, genes linked to luminal epithelium, such PR and FOXA1, show higher expression. The ER gene's expression is nearly same in subgroups A and B, hence enabling the difference between luminal and non-luminal groups [26-38].

### *Basal-like or triple negative breast cancer*

Triple-negative breast cancer (TNBC) is a form of breast cancer, categorized by the lack of HER2, PR, and ER receptors, and is more common in women under 40, especially African-American women. It often has aggressive clinical behavior and poorer prognosis [39].

### *HER2-Enriched Breast Carcinoma*

Approximately 15 to 20 percent of breast cancer cases belong to the HER2-Enriched subgroup. This subgroup shows increased HER2 gene indication and the absence of estrogen receptor (ER) and progesterone receptor (PR) expression. Tumors in this category predominantly express genes and proteins associated with cellular proliferation, such as HER2, ERBB2, and GRB7, rather than luminal, basal, or cluster genes. HER2-Enriched breast cancers typically have a more rapid growth rate than luminal subtypes. About 30 percent of HER2-Enriched tumors are clinically designated as HER2-positive by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH) techniques. [40-45]. The second hypothesis suggests breast cancer carcinogenesis begins from random mutations in various cell types, with pathological morphology and immunohistochemistry markers crucial for determining effective treatment protocols [46].

### *Breast cancer-associated suppressor genes*

Numerous studies have identified multiple genes linked to breast cancer, indicating that alterations in oncogenes and tumor suppressor genes (TSGs) are critical factors in the initiation and progression of carcinogenesis. Oncogenes, frequently identified as tumorigenic genes, are typically the first genes to undergo mutation in the carcinogenesis process. These genes frequently encode compounds critical for cellular proliferation and cell cycle regulation [47]. Consequently, modifications in these oncogenes can disrupt normal cellular proliferation, thereby promoting cancer advancement. In contrast to oncogenes that support cell development and proliferation, tumor suppressor genes (TSGs) hinder these processes. TSGs are crucial in regulating cell division, particularly in instances of DNA damage during replication. The next section examines many notable TSGs [48].

### *RB*

The retinoblastoma gene is involved in 80% of human malignancies. In breast cancer, RB activity is impaired through chromosomal deletions, overexpression, intragenic mutations, and transcriptional repression. Mutations in other genes, like TP53, are similarly critical for tumor initiation and progression.

### *TP53*

The TP53 gene, placed on chromosome 17p13, is a 53 kDa phosphoprotein involved in various physiological activities, including cell cycle arrest, apoptotic induction, DNA repair, cell differentiation, and angiogenesis prevention. [49, 50] TP53, the "Guardian of the Genome," is crucial for DNA integrity, but mutations can

promote carcinogenesis, with mismatch mutations in 50% of cancer cases [51].

#### *PTEN*

PTEN gene, in cell cycle arrest, apoptosis induction, and adhesion regulation, contributes to 80% of breast cancer cases, with deficiency causing aggressive variations and poor prognosis. [52]

#### *BRCA1 and BRCA2*

The BRCA1 and BRCA2 genes are crucial for maintaining genomic integrity and are found in 80% of familial breast cancer cases [53, 54]. Mutations in these genes account for 5% to 10% of total breast cancer occurrences, with high-penetrance variants in certain ethnic groups. Mutations in these genes increase cancer risk as individuals age and have earlier onset of the disease. The BRCA1 gene, located at 17q21, encodes a nuclear phosphoprotein and is essential for DNA reparation processes and tumor suppressor genes. The BRCA2 gene, on 13q12, is crucial for DNA repair and interacts with other proteins [55, 56].

#### *The most important biomarkers to be investigated in breast cancer*

##### *Estrogen Receptor*

Estrogen receptor (ER) status is an influential factor in breast cancer, with overexpression observed in 70%-75% of invasive cases. Estrogen has a crucial function in breast development and carcinogenesis, but its involvement in breast cancer initiation remains a topic of debate [57]. ER $\alpha$  isoforms are key mitogenic factors in breast tissue, overexpressing in the early stages of cancer. Over 50% of estrogen receptor-positive breast cancer patients show PR gene enlarged expression. [58]. HER2 expression, present in 15-20% of breast cancer patients, indicates breast cancer development, with elevated levels increasing metastatic detection rates and recurring tumors [59].

##### *Ki-67 antigen*

*The Ki67 protein, a non-histone nuclear protein, is a crucial diagnostic biomarker in breast cancer, indicating cancer cell proliferation. Initially identified in 1983, it is involved in cell division and ribosomal RNA synthesis. Ki67 expression is commonly assessed by immunohistochemistry and may distinguish between luminal A and luminal B subtypes [60].*

#### *Methods for Diagnosing Breast Cancer*

*A variety of diagnostic tests for breast cancer now available, which will be detailed below.*

##### *Mammography and Breast Ultrasound*

Mammography uses X-rays to detect breast cancer in asymptomatic women, while breast ultrasonography uses ultrasonic waves to detect worrisome breast tissue. [61].

##### *Magnetic Resonance Imaging*

MRI is a valuable tool for assessing breast cancer size, location, and detecting additional abnormal tissues, particularly beneficial for women with genetic predisposition or elevated breast density. [62].

##### *Biopsy*

A biopsy entails the removal of tissue or, in some cases, fluid from the affected area utilizing specialized needles. The sample is next tested in a laboratory for a thorough pathological assessment [63].

##### *Molecular Diagnostic Laboratory Assessments*

The Oncotype DX test, a multigene evaluation method, uses reverse transcriptase PCR to analyze 21 genes in early-stage breast cancer patients, identifying ineffective chemotherapy and assessing recurrence risk.[64, 65]:

*Proliferation genes*

- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2
- Invasion
- Stromelysin 3
- Cathepsin L2
- HER2
- GRB7
- HER2
- Estrogen
- ER
- PR
- Bcl2
- SCUBE2
- Others
- GSTM1
- BAG1
- CD68
- Reference
- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC
- The Oncotype DX test evaluates ER-regulated genes and ER mRNA expression, providing insights into ER function and predicting recurrence score (RS) for chemotherapy and endocrine therapy.[66, 67]. Prosigna (PAM50) assay  
The Prosigna test predicts secondary breast cancer metastasis in postmenopausal women with hormone

receptor-positive inflammatory breast cancer within ten years of diagnosis using RNA from FFPE breast tumor tissue, potentially useful for advanced lymph nodes. [68, 69].

#### *Low risk*

Genetic assays improve risk assessment and tailor breast cancer treatment options by analyzing tumor tissue gene expression profiles, predicting recurrence likelihood, and guiding adjuvant therapy use.

#### *Analysis of the Oncotype DX Recurrence Score (RS)*

The probability of distant reappearance is associated with the Recurrence Score (RS), created by the Oncotype DX assay, which ranges from 0 to 100. The following RS categories are commonly utilized for interpretation:

**Low Risk:** A distant metastasis is deemed improbable after ten years if the RS ranges from 0 to 40 [70].

**Intermediate Risk:** Intermediate risk patients have a Risk Score (RS) ranging 41-60, requiring personalized chemotherapy decisions based on clinical condition evaluation. High risk patients have a RS between 61-100, requiring adjuvant chemotherapy [71, 72]

#### *Assays for MammaPrint and Blueprint*

The MammaPrint assay is a microarray-based test that calculates the expression of 70 genes linked to breast cancer spread, categorizing patients into low or high-risk groups. It is commonly used in patients with estrogen receptor-positive or ER-breast cancer, particularly those with stage I or II tumors less than 5 cm. The Blueprint assay, which measures 80 genes, classifies tumors into three molecular subtypes [73, 74].

#### *Biotheranostics BCI*

The Breast Cancer Index (BCI) measures the expression of HOXB13 and IL17BR genes, predicting the effectiveness of extended endocrine therapy and the risk of late recurrence, a risk that occurs 5-10 years after diagnosis.

#### *Breast cancer treatment methods*

After definitively diagnosing breast cancer in a patient and determining the extent of the disease's progression, various treatment is available [75]. although these technics only should be used on non-pregnant people. During pregnancy Management includes prompt biopsy of suspicious breast masses while avoiding mammography and CT scans, and utilizing MRI for staging, with surgery and chemotherapy generally safe during specific trimesters should consider [76].

#### *Surgery*

Surgical intervention, including mastectomy and breast-conserving surgery (BCS), is a common cure for breast cancer. BCS involves partial mastectomy, while mastectomy removes the entire breast. Treatment selection depends on factors like tumor size, patient symptomatology, surgical feasibility, and patient preference. [77].

#### *Chemotherapy*

Adjuvant chemotherapy is frequently administered following surgical resection of breast cancer, which may include either breast-conserving surgery or mastectomy. This treatment modality employs a combination of cytotoxic agents to eradicate residual cancer cells that may be present but clinically undetectable, thereby mitigating the risk of disease recurrence. Commonly utilized chemotherapeutic agents include cyclophosphamide, taxanes (e.g., paclitaxel and docetaxel), 5-fluorouracil/capecitabine, and anthracyclines (e.g., doxorubicin and epirubicin) [78].

#### *Radiation therapy*



Radiation therapy is a local treatment that is often used after surgery and chemotherapy. The reason for this is to ensure that all cancer cells are destroyed and to minimize the chance of breast cancer coming back. In addition, radiation therapy is desirable in cases of metastatic or unresectable breast cancer [79].

#### *Hormone therapy*

Hormonal therapy, including Tamoxifen, Toremifene, and Fulvestrant, is used as an adjuvant treatment for Luminal BC breast cancer, aiming to reduce estrogen levels or inhibit estrogen stimulation. [80].

#### *Immunotherapy*

While melanoma and lung cancer are thought to be more immunogenic than BC, immunotherapy is a relatively new type of BC therapy. [81]. While not a novel therapeutic strategy in breast cancer (BC), immunotherapy has demonstrated evolving applications. Monoclonal antibodies (mAbs), such as Trastuzumab, have a well-established role in passive immunotherapy for BC. More recently, modalities like antibody-drug conjugates (ADCs) and immune checkpoint inhibitors (ICIs) have garnered increasing attention as both preventative measures and therapeutic interventions for BC.[82]

#### *Unavoidable factors*

- Age
- Sex
- Blood androgen levels
- Blood estrogen levels: High levels of estrogen in the blood of premenopausal women [21]
- Family history: Breast cancer in the family, inherited mutations in the BRCA1 and BRCA2 genes, (short for breast cancer type1 and breast cancer type2) have been found in many people with breast and ovarian cancer) [83]
- Bone density

#### *Breast tissue density*

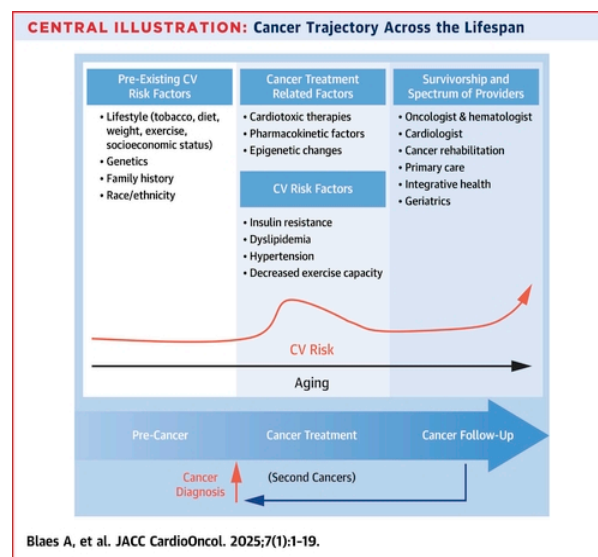
- Increased exposure to the hormone estrogen in women, which occurs in the following situations:
- First menstrual period (menarche) before age 13
- Menopause after age 51
- Applying estrogen in hormone replacement therapy
- People who have never been pregnant or whose first pregnancy was after age 30
- High levels of insulin-like growth factor in the blood of premenopausal women
- A previous history of breast cancer or some other abnormality in breast tissue
- Genetics

#### *Preventable factors*

- Obesity.
- Age of first pregnancy and number of pregnancies
- Start of period
- Alcohol consumption



- Birth control pills
- Menopausal hormone therapy
- Type of nutrition: Sweets consumption raises the danger of heart disease, metabolic disorders, obesity, diabetes, and breast cancer along with these conditions' risks of metastasis. [84]
- Life style [85] (**Figure 1**).



**Figure 1.** Central illustration, Blaes et al. In 2025.

### *Sedentary lifestyle and low physical activity*

According to experts, abstaining from fertility and limiting childbearing, along with nutrition, increases the risk of breast cancer [86]

### *Grading*

Histopathological grading is a method used by pathologists to assess tumor cells under a microscope, focusing on their proliferation and differentiation rates. Grade 1 (Well Differentiated) cells grow slowly, Grade 2 (Intermediate/Moderate grade) cells grow slightly faster, and Grade 3 (Poorly Differentiated) cells multiply rapidly.[87]


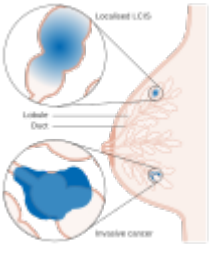



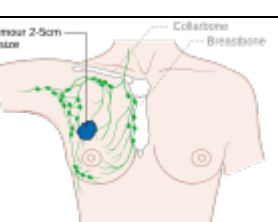
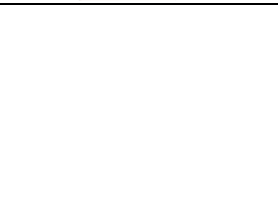
### *TNM staging*

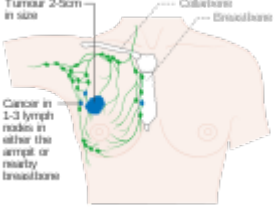



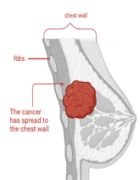
The Tumor-Node Model (TNM) is a medical tool used to determine cancer stages. It uses three factors: the tumor's size, the lymph nodes surrounding it, and the tumor's ability to spread to other organs. The system consists of five phases: non-invasive ductal carcinoma in situ (DCIS) and invasive breast cancer. Staging helps doctors collaborate to select the most effective treatment method. TNM stands for tumor (T), nodes (N), and metastases (M).[87]


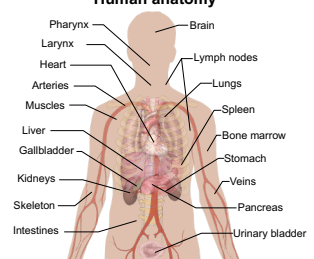
### *Staging*

Stage is a cancer classification method used by doctors to determine the most effective treatment and predict the patient's prognosis, with different stages for different types of cancer. (**Figure2**)[87].

### **Stages of breast cancer** <sup>[12]</sup>

Steps	Image	Evaluation TNM	Description
		Tis, N0, M0 (Ductal carcinoma in situ)	The disease has not yet spread to the surrounding tissue; it is restricted to the breast tissue's ducts and lobules. Another term for it is non-invasive cancer.
		Tis, N0, M0 (Lobular carcinoma in situ)	
1A		T1, N0, M0	The tumor cells has not yet spread out of the breast and is no more than 2 centimeters.
1B		T0 ou T1, N1mic, M0	A limited potation of breast cancer cells is seen in lymph nodes close the breast, or no lump is seen in the breast, or the lump is smaller than 2 centimeters.
2A		T0, N1, M0	There is no obvious evidence of a tumor in the breast, although the cancer has spread to the lymph nodes in the armpit.
		T1, N1, M0	One to three lymph nodes next to the breast have cancer cells, and the tumor is less than two cm in size..
		T2, N0, M0	Tumor larger than 2 cm and smaller than 5 cm without any evidence of lymph node spread.

<b>2B</b>		T2, N1, M0	The tumor is bigger than 20 mm, smaller than 50 mm, it has reached one to three lymph nodes in the axilla.
		T3, N0, M0	The tumor is larger than 50 mm however has not yet spread to the lymph nodes in the armpit.
<b>3A</b>		T0, T1, T2 ou T3, N2, M0	Any tumor has been seen in the breast, but any size may be found in 4 to 9 lymph nodes under the arm or next to the breast.
		T3, N1, M0	A tumor greater than five centimeters that is spreading to more than three lymph nodes in the armpit or close to the chest, or a tumor larger than five centimeters with a cluster of cancer cells in the lymph nodes.
<b>3B</b>		T4; N0, N1 ou N2; M0	Cancer spreads to chest, skin, or armpit, leading to sores or swelling, and may affect over nine lymph nodes. Inflammatory breast cancer may develop.

3C		qualquer T, N3, M0	A tumor, varying in size, has spread to the skin, causing swelling and inflammation. It may also spread to over 10 lymph nodes, the collarbone, or lymph nodes behind the arm or chest.
* (Metastatic)		qualquer T, qualquer N, M1	Any size tumor is possible. There may be cancer cells in the lymph nodes. The cancer develops metastases to different organs in the body, like the lungs, bones, liver, or brain.

**Figure2. The stage of breast cancer is determined by combining the N, T, and M parameters [87].**

### *Treatment*

Early breast cancer diagnosis improves treatment outcomes, often involving surgical intervention. [88]. Treatment strategies include chemotherapy, radiation therapy, and electrocautery. Radiation therapy uses penetrating radiation to eradicate or inhibit malignant tissue growth, causing DNA damage within targeted cells [89, 90]. It has primary clinical applications for curative treatment and symptom palliation. Adjuvant radiation therapy, administered postoperatively, eradicates residual microscopic disease and influences the tumor microenvironment. Postoperative radiotherapy is a standard component of breast cancer treatment, reducing recurrence risk by 50-66%. [91].

### *Radiotherapy*

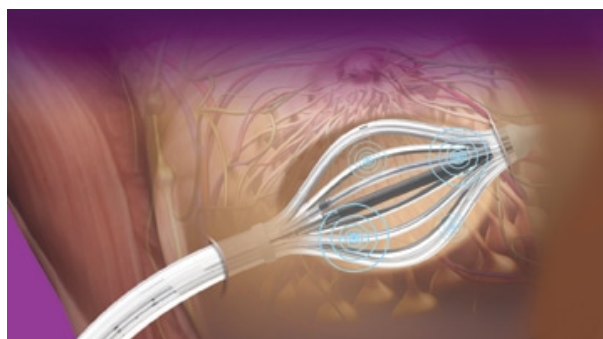
Radiotherapy is a cancer treatment using high-energy X-rays to kill cancer cells, often combined with surgery and chemotherapy. It's painless, effective, and can be given at different stages of breast cancer. [92].

### *Types of radiotherapy for breast cancer*

**Internal radiation therapy:** In this method, a radiation source is placed in a protective sheath near the tumor site. The better the tumor area in the breast is defined, the more accurate the radiotherapy results will be. In an experiment A total of 4541 patients were registered between January 2007 and May 2014. The characteristics of the patients have been distributed equally. between right- and left-handed patients. Median follow-up for OS was 13.7 years. Patients with IMNI had a 15-year survival rate of 65.0%, whereas those without had a rate of 60.8%. As a result, the adjusted HR for OS was 0.85 (95% CI, 0.76–0.94;  $p = 0.0016$ ). The equivalent HR for distant metastases was 0.87 (95% CI, 0.78-0.98;  $p = 0.026$ ) and for breast cancer mortality it was 0.84 (95% CI, 0.74-0.95;  $p = 0.0077$ ). There were no subgroups found to be excluded by IMNI. For patients with ischemic or valvular heart disease, the 15-year cumulative incidence of death was 0.2% (95% CI, 0.0-0.5) for those on the right side and 0.7% (95% CI, 0.4-1.2) for those on the left. Also, it can be noticed that while internal mammary node irradiation typically improves overall survival in node-positive breast cancer patients, this benefit hasn't been seen with newer systemic therapies and 3D-based radiotherapy [93].

**Intraoperative radiation therapy:** External radiation therapy is a common method for treating localized tumors that cannot be completely removed and are likely to recur, particularly in breast cancer.

**External radiation therapy:** It is usually performed by devices that send radiation from outside the body, such as devices similar to CT scans used in imaging. In this way, the patient visits the treatment site and lies on a bed, and the radiation device is irradiated to the desired area. X-rays, gamma rays, electrons, protons and other rays are used for treatment (**Figure 3**) [94].



**Figure 3.** Types of radiotherapy in the treatment of breast cancer

#### *Radiotherapy after lumpectomy*

Radiotherapy is typically used after a lumpectomy to diminish the danger of cancer relapse. It eliminates detectable cancer cells, preventing the disease from returning. This conservative treatment, often referred to as lumpectomy with radiotherapy, has been revealed to significantly decrease breast cancer recurrence, suggesting doctors may recommend multiple stages of radiotherapy in high-risk cases. [95].

#### *Radiotherapy after mastectomy*

Breast cancer recurrence is often high after mastectomy, leading to the recommendation of post-mastectomy radiotherapy. This therapy is typically taken 5 days a week for 5 to 6 weeks. Factors boosting the likelihood of breast cancer returning include lymph node symptoms, tumor size, and cancerous tissue margins. These factors can increase the risk of cancer recurrence in the lymph nodes or chest wall. [96].

When considering radiation therapy after mastectomy with reconstruction, it's important to evaluate the potential for implant-related complications, by investigating the impact of hypo fractionated PMRT on this complication it has been noted that hypo fractionated PMRT does not significantly increase the risk of major implant-related problems compared to conventional fractionation PMRT [97].

#### *What are the possible complications of radiotherapy for breast cancer?*

##### *Swelling of breast tissue*

Skin alterations that resemble a little sunburn in the treated area. Therefore, it is recommended that the patient not be exposed to direct sunlight during radiotherapy. Skin complications usually improve within a few months, which may vary between 6 and 12 months [98].

##### *Fatigue, which is usually not very severe.*

External radiotherapy can cause complications like lymphedema and cardiac and pulmonary issues, but with advanced devices and proper treatment by a radiotherapy and oncology specialist. [99].

*What are the complications of radiotherapy in breast cancer?*

While radiotherapy can cause complications, it remains a highly successful therapy for breast cancer, and further advancements are expected to improve its effectiveness [100]. Radiotherapy can have two types of complications, which are:

*Acute complications of radiotherapy*

Following radiation therapy, acute problems may occur, including stiffness, fatigue, nausea, coughing, shortness of breath, rib pain, and skin issues like redness, dryness, and sensitivity.

*Late complications of radiotherapy*

Late complications of radiotherapy, typically manifesting several months to years' post-treatment, may include dermatological effects, cardiac dysfunction, lymphedema, and cardiopulmonary sequelae. Based on experiment that had done with 829 survivors monitored via echocardiograms, revealed a cumulative incidence of cardiac dysfunction increasing from 1.8% at 2 years to 15.3% at 15 years post-cardiotoxic therapy.[101]

Cardiopulmonary complications are infrequent and generally asymptomatic. Lymphedema, characterized by the accumulation of interstitial fluid in any anatomical location, can arise from any disruption to the lymphatic system's structural or functional integrity, resulting in localized swelling [102]. despite this some rare life treating condition, can occur in women with a history of thoracic radiation therapy and congenital coronary anomalies. in an experiment of 22 patients found that LAD dissection in this group is linked to both radiation-induced vascular injury and congenital coronary anomalies .it might note that the importance of advanced imaging for diagnosis and individualized management based on patient stability and disease severity . The mean interval between thoracic radiation therapy and the LAD dissection was  $15.2 \pm 6.7$  years.[103]

*Complications of radiotherapy for breast cancer that last for a long time include [104]*

- Lymphedema, a condition resulting from lymph node removal during surgery, is common. Skin discoloration due to rapid tissue turnover can cause side effects. Breast shape and size change, and respiratory problems like cough and shortness of breath may occur after treatment.[105]
- Radiation therapy, despite being crucial for lymphoma treatment, can cause late toxicities in survivors, increasing cardiovascular risks and secondary cancers. [94,106]. Accurate toxicity predictions are essential for early management, technology evolution, and patient monitoring. [107]
- 
- Bone problems; Which occur as a result of weakening of the bone tissue.
- Nerve damage in the arm area; Which causes symptoms such as tingling, numbness, pain and weakness and makes it difficult to move the arm and shoulder.[108]

**Conclusion**

The article highlights the importance of radiotherapy in breast cancer treatment, with a significant percentage of cases responding positively. Advancements in targeted therapy, hormone therapy, and chemotherapy have improved patient outcomes. The article emphasizes the need for ongoing research and development of precise radiation technologies to improve treatment planning and administration, potentially leading to total eradication.

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