

Review Article

The Impact of Radiation on Breast Cancer Treatment (Case Study: Breast Cancer)

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Abstract

Radiation therapy has long been established as a cornerstone in oncological practice and remains one of the most effective modalities in the management of malignant diseases. It is a specialized field within oncology that utilizes high-energy ionizing radiation, such as X-rays or gamma rays, with the objective of eradicating cancer cells while preserving adjacent healthy tissues. This dual aim of maximizing tumor control and minimizing normal tissue toxicity underscores the critical importance of precision in treatment planning and delivery. The present study specifically examines the role of radiation therapy in the management of breast cancer, which represents one of the most prevalent malignancies among women globally. Given the availability of multiple therapeutic strategies—including surgical resection, systemic chemotherapy, hormonal interventions, immunotherapy, and targeted therapies—radiation therapy occupies a distinct position in ensuring local tumor control and reducing recurrence. This study employs a descriptive-analytical approach, drawing upon a broad review and synthesis of experimental and clinical investigations to evaluate the therapeutic efficacy and limitations of radiation therapy in breast cancer treatment. The findings consistently demonstrate that radiation therapy exerts a markedly positive effect on patient outcomes, particularly in reducing local recurrence rates, improving disease-free survival, and contributing to overall survival. However, the therapeutic impact is contingent upon several decisive factors. These include the accuracy of tumor delineation, the radiation oncologist's ability to identify and mitigate potential errors during planning and delivery, the reduction of scattered radiation beyond the treatment field, and the maintenance of a homogeneous dose distribution across the target volume. Optimization of these parameters is essential to achieving favorable clinical results while limiting acute and long-term side effects. In conclusion, radiation therapy continues to serve as an indispensable modality in the multidisciplinary management of breast cancer. Ongoing advances in imaging technologies, treatment planning algorithms, and delivery systems, such as intensity-modulated radiotherapy and image-guided radiotherapy, are expected to further enhance the precision, safety, and clinical effectiveness of this therapeutic approach. Collectively, these developments underscore the enduring and evolving role of radiation therapy in improving survival outcomes and quality of life for breast cancer patients.

Keywords

Breast Cancer, Radiation Therapy, Tumor, X-rays, Dose Distribution

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1. Introduction

Cancer is a disease characterized by the continuous and uncontrolled division of certain body cells, which invade surrounding tissues. In other words, cancer can be defined as the abnormal growth and division of cells that fail to respond to normal regulatory mechanisms [1].

Under normal circumstances, damaged or aged cells undergo programmed cell death, and new healthy cells replace them. However, in cancer, this balance is disrupted: cells that should die continue to survive, accumulate, and divide abnormally. Over time, these cells may form a mass known as a tumor. [2] The development of cancer is a complex, multi-factorial process. Although identifying a single primary cause is challenging, numerous risk factors have been established, either acting independently or in combination [3].

Well-known contributors include:

Chemical compounds and toxins: benzene, asbestos, nickel, cadmium, vinyl chloride, benzidine, tobacco smoke, and aflatoxin.

Ionizing radiation: uranium, radon, ultraviolet radiation from sunlight, alpha, beta, and gamma rays, and X-rays.

Pathogens: Human Papillomavirus (HPV), Epstein-Barr virus, hepatitis B and C viruses, Kaposi's sarcoma virus, Schistosoma species, and Helicobacter pylori.

Genetic predisposition: mutations in specific genes associated with breast, ovarian, colorectal, prostate, and skin cancers, including melanoma.

Because cancer arises from different sites and etiologies, its types are diverse and require distinct therapeutic approaches. The primary goal of treatment is either to eradicate malignant cells or to control disease progression, thereby improving patient outcomes. Depending on disease stage, tumor biology, and patient-specific factors, treatment may consist of a single modality or a combination of approaches [4].

Although treatment protocols vary by cancer type, the most commonly employed modalities include surgery, chemotherapy, immunotherapy, hormone therapy, and radiation therapy [5].

2. Radiation Therapy

Radiation therapy, also known as radiotherapy, has been used for many years in the treatment of cancer. It is a branch of medicine that focuses on delivering high-energy rays directly to the tumor or target area to treat cancer. Radiation therapy is employed in the treatment of many types of cancers, with the primary objective being the definitive treatment of the tumor while preserving adjacent healthy tissues [6].

In radiation therapy, X-rays are frequently used, although other forms of energy, such as protons or other particles, can also be utilized. One crucial feature of proton therapy is how the absorbed dose of these particles is delivered to the tissue. The absorbed dose percentage curve in the tissue, depending on the energy used, exhibits a maximum peak at a specific

depth known as the "Peak Bragg," which can deliver the highest radiation dose precisely at the tumor location [7].

In radiation therapy, efforts are generally made to minimize the radiation dose to surrounding healthy or vital tissues. The dose reaching the surrounding area (secondary or scattered dose) depends on factors such as the distance from the radiation field edge, radiation energy, field size, and the presence of accessory devices attached to the machine (such as trays, wedges, blocks, etc.) [8].

Radiotherapy can be administered through external or internal sources. When the source of radiation is internal, it is called brachytherapy, whereas external radiation therapy is referred to as external beam radiotherapy. In the past, external beam radiotherapy was primarily performed in two dimensions using rectangular fields and conventional imaging. However, it has now been replaced by "Image-Guided 3D Conformal Radiotherapy." This advanced approach utilizes techniques such as CT scans and other imaging modalities to precisely delineate treatment volumes, including the Gross Tumor Volume (GTV), Clinical Target Volume (CTV) considering microscopic tumor extension and clinical conditions, Internal Target Volume (ITV) accounting for internal body motions, and Planning Target Volume (PTV) as well as relevant sensitive organs with high accuracy for treatment planning [9].

The use of radiotherapy in cancer treatment offers several benefits, including:

1. Pain reduction
2. Improved quality of life in cases where a cure is not possible
3. Reduction of disease symptoms by shrinking the tumor size
4. Preoperative radiotherapy can reduce the size of certain tumors, making them easier to remove surgically
5. Postoperative radiotherapy can target small residual cancer cells that may not be visible to the surgeon
6. Radiotherapy can be employed to alleviate cancer-related pain.

In some cases, radiotherapy is combined with chemotherapy, and it can be used to sensitize cancer cells to radiation, making them more susceptible to destruction [10].

Although radiation therapy has many advantages in cancer treatment, it can potentially cause side effects in some patients. Radiation therapy-related side effects vary among individuals due to factors such as the patient's body condition, the type and extent of the disease, the radiation type, the duration and intensity of radiation, and the location of radiation exposure. Some side effects may occur during or immediately after the completion of radiotherapy sessions, while others may develop months or even years later. These side effects usually resolve several weeks to months after treatment completion but can sometimes have a long-lasting impact on the patient's life [7].

3. Radiation Therapy and Breast Cancer

Breast cancer is one of the most common malignant tumors in women, often detected through X-rays or by palpation. It is important to note that not all breast masses are necessarily cancerous. Sometimes, these masses are small fluid-filled cysts or are related to conditions other than cancer, such as fibrocystic breast disease [11].

Breast cancer typically does not present specific symptoms in its early stages, but individuals may notice the presence of a breast lump upon self-examination. Factors contributing to the development of breast cancer include a family history of the disease, advanced age (over 53 years old), early onset of menstruation before the age of 12, late onset of menopause, obesity, nulliparity, and more [12].

Extensive research has been conducted on breast cancer and its treatment strategies, focusing on finding new therapeutic approaches and improving the quality of established treatment methods. One of the most critical treatments for targeting cancer cells in the affected area is radiation therapy. Radiation therapy plays a vital role in breast cancer treatment and has been reported in several studies to improve survival rates and reduce local recurrence [13].

Given the widespread prevalence of breast cancer and the importance of dealing with it, as well as the significance of radiation therapy in its treatment, the necessity of further studies in this field to enhance the effectiveness of this treatment method and minimize its side effects becomes evident. Currently, for breast irradiation, both an internal medial tangential field, which passes approximately through the midline of the chest, and an external lateral tangential field are used as long as the breast tissue is palpable [14].

One of the initial considerations in radiation therapy is accurate and precise treatment planning. Proper treatment planning ensures that the tumor receives the maximum dose while minimizing the radiation exposure to normal tissues in the path of the radiation beams. As a result, one of the first steps in breast cancer treatment through radiation therapy is diagnosing and quantifying the errors that occur during treatment. This can significantly enhance the efficacy of this treatment method. Mahmoud Alaahverdi and his colleagues [15] conducted a study titled "Investigating the Accuracy of the Delivered Dose in Breast Cancer Radiotherapy Using Thermoluminescence Dosimetry." In this study, they measured the dose at entry and exit points of the patients' bodies using TLD chips and compared it with the calculated dose in the patient's treatment plan. The measured doses at the entry and exit points were then compared with the calculated doses in the patient's treatment plan. The dose discrepancies were calculated, and the results were plotted as histograms. The sources of error in this study, as determined by in-vivo dosimetry, included errors in computational algorithms, especially those related to heterogeneous calculations and patient contours, errors in patient setup, patient motion, output factor errors of the machine, and errors due to data transfer. The

results of Alaahverdi and his colleagues' research showed that in-vivo dosimetry could play a crucial role in the quality control of the radiotherapy department for the enhancement of breast cancer patient treatment quality [15].

Another important consideration in breast cancer treatment through radiation therapy is the potential scattering of radiation beams from the treatment accelerator, scattered radiation from within the patient's body, and unwanted neutrons reaching areas outside the treatment field. Therefore, measuring the dose received by the contralateral breast surface is crucial. Although the dose levels outside the treatment field are lower than inside the treatment field, these dose levels can lead to long-term hidden secondary cancers [16].

Babak Shekarchi and his colleagues [17] conducted a study to measure the doses of thermal neutron and photon radiation reaching the contralateral breast surface during breast cancer radiation therapy for different treatment fields in the presence of physical and dynamic wedges. Shekarchi and his team measured dose values for 11×13 , 11×17 , and 11×21 square centimeter treatment fields with both physical and dynamic wedges. The results of their investigation showed that the dose values received (resulting from both photon and thermal neutron radiation) at the contralateral breast surface in the presence of a physical wedge for 11×13 , 11×17 , and 11×21 square centimeter fields were 12.06%, 15.75%, and 33.40% of the prescribed dose, respectively. In the presence of a dynamic wedge, the corresponding values were 9.18%, 29.26%, and 12.92% of the prescribed dose. These values indicated that with an increase in the field size, the dose values of both photon and thermal neutron radiation reaching the contralateral breast surface increased. Furthermore, the dose values of photon and thermal neutron radiation reaching the contralateral breast surface were lower in the presence of a dynamic wedge compared to a physical wedge. Based on their findings, Babak Shekarchi and his colleagues concluded that during breast cancer radiation therapy with the wedge technique, especially for internal medial tangential fields, the use of a dynamic wedge is preferable. They also recommended avoiding the use of an 18 MeV energy level to minimize neutron dose and using lower energies such as 10 MeV or 8 MeV instead [17].

Another important consideration in breast cancer radiation therapy techniques is the uniformity of dose distribution within the target volume. This factor is crucial in the effectiveness of this therapeutic technique. The level of dose uniformity within the target tissue varies depending on the specific conditions of each treatment protocol. In radiotherapy, points that receive less than half of the prescribed dose are called cold spots, while points that receive approximately twice or more than the prescribed dose are called hot spots. Non-uniformity in dose distribution within the target tissue results in the formation of cold and hot spots within the volume of interest. Hot spots are formed at points where treatment fields overlap, while cold spots are predominantly created in the empty space between two treatment fields,

depending on the conditions specific to each radiotherapy technique [18].

Abbas Haghparsat and his colleagues [19] conducted research to investigate this issue. They utilized three techniques: photon tangential technique, electron technique with two perpendicular beams at 90 degrees to each other, and electron technique with two beams at 45 degrees to each other to achieve their research goals. In the photon tangential technique, they used two MV6 energy photon fields with an angle of 180 degrees relative to each other. To create dose uniformity within the target volume against each field, they also used a 15-degree wedge with the thick part facing towards the chest wall to compensate for the non-uniformity present in the chest wall. This ensured that the radiation dose to each part of the chest wall was proportional to the volume of the area of interest.

In the electron technique with two perpendicular beams at 90 degrees to each other, they used two electron beams with MeV12 energy. In this method, the first field was directed vertically, and the second field was directed horizontally on the phantom surface. In the electron technique with two beams at 45 degrees to each other, they also used two electron beams with MeV12 energy. In this approach, the first field was directed vertically, and the second field was directed at a 45-degree angle relative to the first field and inclined towards the phantom surface.

Considering the obtained curves and practical dose results within the target volume for different techniques, it was concluded that the average received dose within the target volume is significantly higher in electron techniques compared to photon techniques. Additionally, due to the use of adjacent fields in electron techniques, some parts of the target volume received doses two times or more than the prescribed dose, indicating that dose distribution in the photon tangent technique is more uniform. Ultimately, with fewer field overlaps and the average received dose in the tangential photon technique, Haghparsat and his colleagues concluded that the tangential photon technique has a superior advantage over other radiation therapy methods in breast cancer treatment [19].

Another point to consider is the potential complications of radiation therapy in the treatment of left breast cancer, with the most important being heart-related issues. It seems that in patients with left breast cancer, the risk of radiation-related complications due to radiation exposure to the heart is higher compared to patients with right breast cancer. This can affect all three components of the heart, including the pericardium, myocardium, and coronary arteries [20].

In a study conducted by Salarie and his colleagues [21], they investigated the frequency of acute and subacute cardiac complications in patients who underwent radiation therapy following left breast cancer, particularly after mastectomy or lumpectomy. Their study involved 53 patients. The evaluation method involved electrocardiography, echocardiography, and electrocardiography performed before the initiation of radiotherapy and then again three and six months after radiotherapy.

The patients received radiotherapy to the chest wall region with a dose of F/25 Gray 50. The findings of Salarie and his colleagues showed that complications following radiotherapy were observed in 10 patients, with the most common being mild pericardial effusion in 7 cases, mild mitral valve regurgitation in 3 cases, and right bundle branch block in 2 cases. Based on this, it can be concluded that acute and subacute cardiac complications in breast cancer patients undergoing radiotherapy are not severe and do not hold significant clinical importance. However, Salarie and his colleagues acknowledged that some previous studies [22] have confirmed a relationship between left breast radiotherapy and cardiac complications. They suggested that one of the reasons for the lack of severe cardiac complications in their study may be the small sample size or the relatively short follow-up duration. Therefore, they recommended extending the follow-up period in future studies, considering that chronic pericardial diseases are observed within six months to one year after radiotherapy [21].

Please note that the years provided in Persian articles are based on the Iranian calendar, which is about 621 years ahead of the Gregorian calendar. Therefore, the mentioned years should be adjusted accordingly for the Gregorian calendar.

4. Conclusion

Radiation therapy is a form of treatment that utilizes high-energy waves such as X-rays for cancer treatment. In this method, in addition to targeting cancer cells, healthy cells are also exposed to radiation, which can result in side effects. However, according to researchers, these side effects are generally not severe, as healthy cells can often repair themselves. When healthy cells regenerate, the side effects of radiation therapy also improve.

The results of the investigation into the impact of radiation therapy on breast cancer, as discussed, indicate that the effects of radiation on breast cancer treatment are generally positive and acceptable. To enhance the applicability of this therapeutic approach, the therapist's ability to diagnose and determine errors that occur during radiation therapy, control scattered radiation to areas outside the treatment field, and ensure uniform dose distribution within the target volume should be considered.

Abbreviations

CTV	Clinical Target Volume
GTV	Gross Tumor Volume
HPV	Human Papillomavirus
IMRT	Intensity-Modulated Radiation Therapy
ITV	Internal Target Volume
MeV	Mega Electron Volt
MV	Mega Volt
PTV	Planning Target Volume

TLD	Thermoluminescence Dosimetry
VMAT	Volumetric Modulated Arc Therapy
WHO	World Health Organization
X-ray / X-rays	X-radiation

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Author Contributions

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Conflicts of Interest

The authors declare no conflicts of interest.

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