

Impact of Radiation Therapy on Hematological Parameters and Hormonal Profiles in Male Breast Cancer Patients

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Abstract

Introduction: Hereditary factors contribute to 5–10% of breast cancer cases, with elevated estrogen levels often implicated. Male breast cancer, although rare, presents unique challenges, particularly concerning the impact of radiotherapy on hormonal and hematological parameters. This study aimed to evaluate the effects of radiation therapy on blood components and hormone levels in male breast cancer patients. **Objectives:** The study focused on assessing changes in red blood cells (RBCs), white blood cells (WBCs), platelets, and lymphocytes, as well as estrogen, progesterone, and testosterone levels in male breast cancer patients undergoing radiotherapy. **Methods:** This prospective clinical study was conducted at the Middle Euphrates Oncology Center, involving 26 male breast cancer patients receiving radiotherapy. The average patient age was 59.88 years, with mean physical characteristics including weight (93.46 kg), height (171.15 cm), and body surface area (2.06 m²). Most patients had advanced-stage cancer and were smokers. Blood samples were collected before and after radiotherapy and analyzed using the VIDAS® 30 multiparametric immunoassay system. Radiation doses ranged from 20 Gy to 25 Gy, administered in 2 Gy fractions. **Results:** Post-radiotherapy, significant decreases were observed in RBC, WBC, platelet, and lymphocyte counts, indicating compromised bone marrow function and immune response. Hormonal analysis revealed positive estrogen receptor status in 77% of patients and progesterone receptor positivity in 81%, highlighting the potential role of hormone-targeted therapies. Testosterone levels showed a marked decline post-treatment. **Conclusion:** The findings demonstrate that radiotherapy significantly impacts hematological parameters and hormone levels in male breast cancer patients, emphasizing the need for close monitoring of these parameters during treatment. These results underscore the importance of individualized therapeutic strategies, including hormone-targeted approaches, to optimize patient outcomes. Statistical analysis confirmed the significance of these changes ($p \leq 0.05$).

Keywords: Male Breast Cancer, Blood Screen, Radiotherapy

Introduction

Male breast cancer (MBC) is rare, accounting for approximately 0.1% of all carcinomas in men. The existing body of evidence for treatment primarily stems from studies on female breast cancer (FBC) [1, 2]. The masculine endocrine environment and limited mammary tissue contribute to the rarity of breast cancer. Despite estrogen being predominantly associated with females, it is also present in males, albeit in smaller amounts. Hypoestrogenism is a significant risk factor for male breast cancer, with a majority of cases being estrogen receptor-alpha positive (ER α +) [3]. The historical context, dating back to John of Arderm in the 14th century, highlights the long recognition of this condition. Early 20th century reports, such as the 1938 case of a 50-year-old Indian male with a nonmetastatic primary breast tumor, underscored the challenges in treating male breast cancer at that time. Indeed, male breast cancer has remained rare over the past few decades, and the research focus has focused predominantly on female breast cancer. The abundance of publications on female breast cancer reflects its relatively high prevalence and extensive research [4].

The relative scarcity of information on male breast cancer underscores the need for more research to unravel the complexities of this less common disease entity and improve our understanding of its uniqueness [5]. Males share common risk factors with postmenopausal women for breast cancer, including age, family history, BRCA mutations, and exposure to therapeutic radiation. Interestingly, most male breast cancer patients present without overt risk factors. Notably, exogenous hormone therapy for prostate

cancer does not seem to increase the risk of male breast cancer. Identifying genetic and environmental risk factors continues to enhance our understanding of this rare condition. For this reason, doctors advise anyone with a family member who has had cancer to be checked out frequently [6]. Numerous variables, including the type and stage of cancer, the patient's general health, and personal preferences, play a role in determining the best course of cancer therapy [7]. Conventional cancer treatment methods include surgery, radiation therapy (which uses high-energy beams to destroy cancer cells or reduce tumor size), and internal placement of radioactive materials directly into or near the tumor. One treatment option is chemotherapy, which involves the use of medications to eradicate cancer cells or inhibit their proliferation. Immunotherapy (which involves training the immune system to identify and destroy cancer cells) is a common method for treating cancer that has metastasized or for shrinking tumors before surgery or radiation treatment. Some studies have shown encouraging results from its use in targeted therapy and hormone therapy, two approaches to cancer treatment that target hormone-sensitive malignancies such as those of the breast and prostate. Precision medicine, stem cell transplantation, and hormone-blocking all play a role in the effectiveness of this treatment [8-10].

Objectives

This study aimed to investigate the effects of radiation on the levels of blood components, estrogen, progesterone, and testosterone, in breast and prostate cancer patients.

PATIENTS AND METHODS

Study Design and Participants

The Middle Euphrates Oncology Center conducted This Prospective Clinical Study was via a consecutive sampling technique from October 2023 to April 2024. The Middle Euphrates Oncology Center has already diagnosed 26 male patients with breast cancer. We obtained ethical written consent from each patient. The blood samples were withdrawn from 3–5 ml from each patient before radiotherapy and after 24 hours of completing the course.

The prescribed dose ranged from 20 Gy to 25 Gy, with 2 Gy per fraction. We centrifuged and analyzed the blood samples for blood screening, which included red blood cells (RBCs), white blood cells (WBCs), platelets, and lymphocytes. The blood analysis was conducted by the following laboratory at the hospital, utilizing an analyzer (Diagon D-cell5D, serial No. 171021655D, media in Hungary: 2011) to test all blood components before and after radiotherapy: After the blood samples were shaken for 15 minutes in the analyzer shaker, a metallic needle automatically descended into the tube, and

approximately 2 microliters of blood were extracted when the start button was pressed. We conducted hormonal analyses of estrogen, progesterone receptor, and testosterone levels. The hormones were analyzed via the VIDAS® 30 multiparametric immunoassay system manufactured by Biomatrix, U.S. The analyzer's screen displays all the blood results after a few seconds.

Statistical Analysis

The statistical analysis was performed using SPSS 28. The mean, standard deviation, and percentage were used to describe the data. Student-paired T-tests were conducted to compare the effects of radiation. The p-value is considered as significant if the values ≤ 0.05 .

Results

Table 1 lists the sociodemographic distribution of the cases. The age of the male patients was 59.88 ± 12.90 years. Their weight was 93.46 ± 26.28 , height was 171.15 ± 15.90 , and surface area was 2.06 ± 0.24 . Most male patients were smokers, according to the Figure 1 and Figure 2 the majority of male patients were in stage II, then stages I, III, I, and finally stage V.

Table 1: Sociodemographic Data of the Patients

Socio Demography	Mean $\pm$ SD
Age (Years)	59.88 ± 12.90 (69 – 90)
Weight (Kg)	93.46 ± 26.28 (95 – 192)
Height (Cm)	171.15 ± 15.90 (178 – 190)
Surface Area (S.A) M ²	2.06 ± 0.24 (2.1 – 2.4)
Smoking Habit	Yes 19 (73%) No 7 (27%)
Cancer Stage	I 6 (23%) II 13 (50%) III 3 (11.5%) IV 3 (11.5%) V 1 (4%)

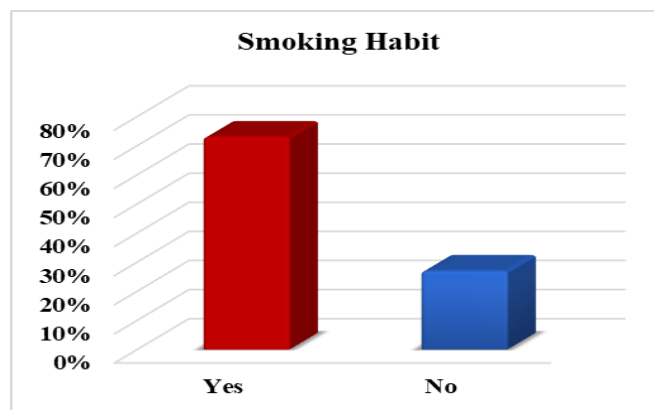


FIGURE 1: Percentage of Male Smokers.

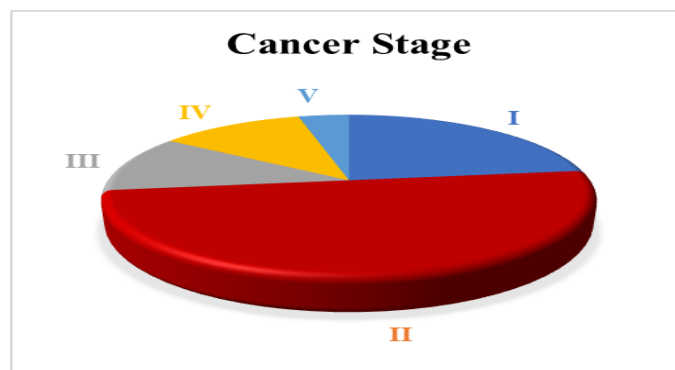


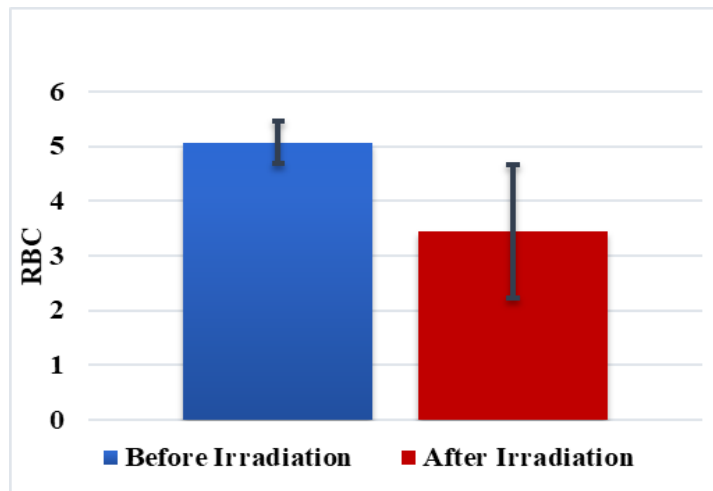
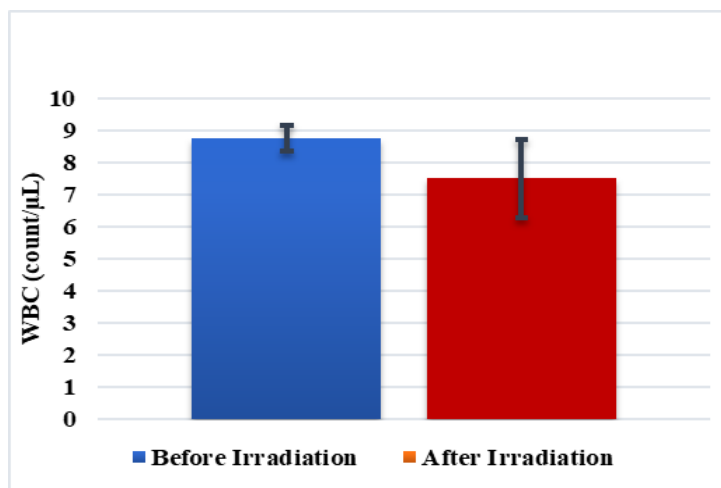
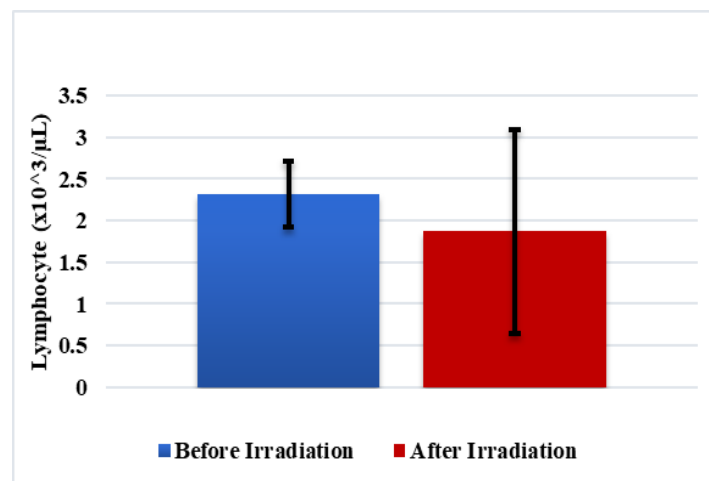
FIGURE 2: Percentage of Cancer-Stage Patients with Breast Cancer.

Table 2: Blood Test Results Before and After a Course of Radiotherapy with a Dose of 20 Gy to 25 Gy at a Rate of 2 Gy per Treatment Session.

Blood Test (mL)	Before Irradiation	After Irradiation (Gy)	P-Value
RBC	5.07 ± 0.39	3.45 ± 1.22	<0.0001*
WBC	8.76 ± 2.07	7.51 ± 1.99	0.04051*
PLT	266.11 ± 79.646	205.73 ± 76.33	0.10736
Lymph	2.32 ± 0.71	1.87 ± 0.95	0.02831*

* Significant difference at p – p value ≤ 0.05

gray (Gy) is the international system of units (SI) equivalent of 100 rads

**FIGURE 3:** RBC Analysis Before and After the Radiotherapy Course.**FIGURE 4:** WBC Analysis Before and After Radiotherapy.**FIGURE 5:** Lymphocyte Analysis Before and After Radiotherapy

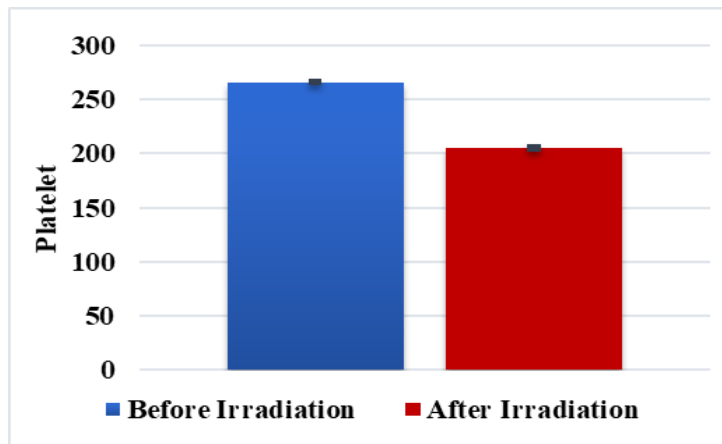


FIGURE 6: Platelet (PLT) Analysis before and after the Radiotherapy Course

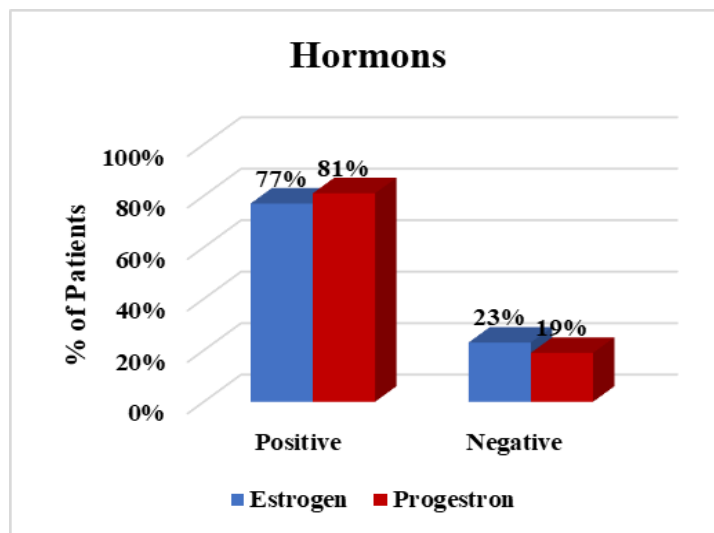


FIGURE 7: Hormone Receptor Levels of Estrogen and Progesterone and After Radiotherapy Before and After Radiotherapy.

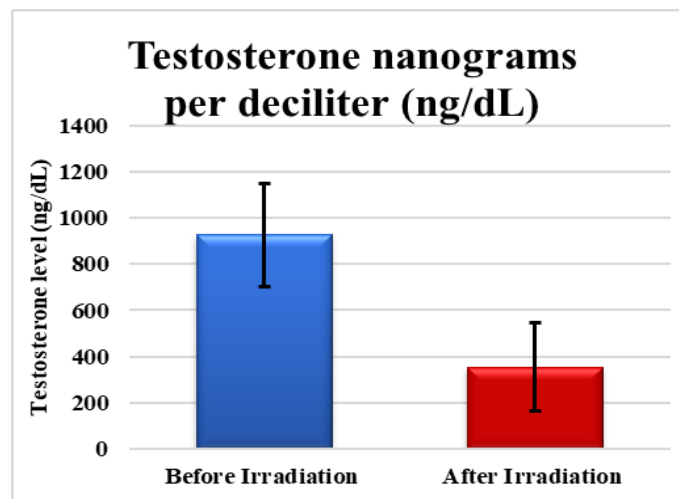


FIGURE 8: Testosterone Hormone Levels Before and After Radiotherapy

Figure 7 illustrates the classification of estrogen and progesterone receptors into negative and positive categories. The analysis revealed that 77% of male cancer patients were positive for estrogen and that 81% were positive for progesterone. We analyzed testosterone levels before and after radiotherapy. The results revealed a significant decrease in testosterone levels after irradiation ($p\text{-value} = 0.0352$), as shown in Figure 7.

Discussion

Guidelines for women with breast cancer should be followed while providing radiation treatment after surgery [11]. More than one study of men with breast cancer reported that R.T. after surgery improved L.C. and overall survival [12, 13]. Much less radiation exposure to healthy tissues is now possible because of developments in

contemporary radiation therapy (RT) and treatment methods [14]. The majority of male patients were classified as having stage II cancer, with stages I, III, IV, and V followed closely behind. The distribution provides insight into the severity and progression of the disease among the study participants. Realistically, male breast cancer patients seldom receive radiation therapy after surgery [15, 16]. Fewer than half of the males diagnosed with stage I breast cancer who underwent breast-conserving surgery underwent radiation treatment, according to data from the SEER database [17]. Multiple observational studies have shown that radiation therapy (RT) is beneficial for men with early-stage or locally advanced breast cancer, including node-positive or stage III illness, even though only 50% of men in the worldwide Male Breast Cancer Program have adjuvant RT [18-20]. This research assessed several blood parameters, including RBCs, WBCs, PLTs, and lymphocytes, to determine the effects of radiation treatment. The findings revealed that red blood cells, white blood cells, and lymphocytes were significantly lower following radiation therapy than before radiation therapy. These findings suggest that radiation treatment may reduce bone marrow activity and thus blood cell generation. To manage any side effects and guarantee patient safety, monitoring blood parameters before, during, and after radiation treatment is crucial. The statistical analysis in this study revealed that the RBC, WBC, and lymphocyte counts decreased significantly below normal levels after irradiation. These findings suggest that radiation therapy may have a suppressive effect on blood cell production and immune function. The bone marrow is responsible for the production of blood cells, which mature at a rapid rate, making them very vulnerable to the effects of chemotherapy. Chemotherapy eliminates a significant number of bone marrow cells, resulting in a decrease in white blood cells and red blood cells. Compared with the irradiation zone, the impact zone is restricted to the region immediately around the bone marrow. If radiation is administered to significant sections of the body, especially the major bones that contain the most bone marrow, such as the pelvis, legs, and torso, it can damage the blood vessels near the irradiated tumor location, as well as white and red blood cells. It has the potential to produce low levels of red and white blood cells. Radiation directly affects lymphocytes located close to the tumor [21]. This study's findings corroborated those of a 2018 investigation by Baydaa T. Sih [22] on the effects of radiation and chemotherapy on blood cell components in breast cancer survivors. The study involved 32 female participants, of whom 18 received chemotherapy and the remaining 12 received radiation. Researchers have investigated several blood cell properties, including white blood cell (WBC), red blood cell (RBC), lymphocyte (lymphocyte), and hemoglobin (HGB) contents. Compared with radiation patients, chemotherapy patients experienced faster decreases in white blood cell (WBC), red blood cell (RBC), and lymphocyte counts. However, after four cycles, no treatment strategy significantly affected the HGB concentration. These results suggest that radiation therapy may be safer than chemotherapy for breast cancer patients. This highlights the need to consider the potential effects of various therapies on different components of blood cells when strategies for the management of breast cancer patients are formulated. A study by İnanç and colleagues [23]. This study examined the impact of radiation treatment on human red blood cells (RBCs) in vitro. The cells were exposed to different radiation doses (2 Gy, 12 Gy, and 25 Gy) and compared to those in the control group. We evaluated the differences between the groups via the deformability index (DI). Compared with the groups receiving the highest dose of 25 Gy, the control group presented significantly different deformability. This study suggested that radiation treatment can alter the deformability of

red blood cells, with the degree of change determined by the dose. Dual-beam optical tweezers, which are sensitive biomarkers for investigating biological responses to radiation, can measure the deformability index. Researchers are investigating estrogen and progesterone receptor levels in cancerous tissue. Laboratory testing of specific tumor samples is necessary to establish whether estrogen and progesterone are thought to influence the progression of breast cancer [24, 25]. The data show that hormone treatment might halt the progression of cancer [26]. Understanding the receptor status is vital for selecting the appropriate treatment method. Given the potential effectiveness of hormone therapy for hormone receptor tumors, this study revealed that the majority of male breast cancer patients experienced positive outcomes. Radiation caused a dramatic decrease in testosterone levels, according to these findings. These results suggest that radiation therapy for breast cancer in males could reduce testosterone levels. Changes in testosterone levels may have different effects on men's libido, mood, and energy levels. Testosterone deficiency has been linked to many negative health outcomes, including but not limited to decreased lean body mass and muscle mass, elevated fat content, impaired sexual performance, altered bone mineral density and osteoporosis risk, increased weariness, melancholy, and decreased intellectual activity [27]. It is reported that bone mineral density and lean body mass improved in men whose hypogonadal symptoms were caused by organic diseases [28]. after testosterone replacement treatment. Subjects whose baseline testosterone levels were less than normal (less than 8 nmol/l) reported a 20–40% improvement in their physical performance after replacement medication, according to the placebo-controlled study. These findings suggest that low testosterone levels can have serious consequences. The degree to which rectal cancer patients who undergo radiation treatment experience a long-term decrease in testosterone levels, and therefore, any symptoms associated with low testosterone levels, is an open question. Additionally, whether testosterone replacement treatment could help these people is still unknown. However, since radiation treatment and surgery damage nerves and arteries, the severely diminished sexual function observed in these individuals is unlikely to recover.

Conclusion

This study revealed that stage II cancer was the most common diagnosis for male breast cancer patients, underscoring the importance of early detection and treatment. Blood screening analysis revealed significant decreases in red blood cell, white blood cell, and lymphocyte counts after irradiation, highlighting the impact of radiotherapy on bone marrow function and the immune response. Hormone receptor status assessment revealed that a significant proportion of male cancer patients were positive for estrogen and progesterone receptor status, suggesting the potential efficacy of hormone-targeted therapies. However, a significant decrease in testosterone levels after irradiation suggested a possible adverse effect of radiotherapy on testosterone production in male patients with breast cancer.

Limitations of the study

Sample size and selection bias: This study involved only 26 male breast cancer patients from a single oncology center, potentially limiting its generalizability to the broader male breast cancer population. Predominantly older age and advanced cancer stages in the sample may introduce selection bias.

Short Follow-Up Period: The lack of a specified follow-up postradiotherapy duration hinders the understanding of the long-term effects on hematological parameters and hormone receptor status.

Smoking and other comorbidities: A high prevalence of smoking and other comorbidities among participants could complicate the interpretation of outcomes related to hematological changes and hormone receptor status.

Generalizability: Caution is needed when findings are applied to younger patients or those with earlier-stage cancers because of the specific demographic and clinical characteristics of the study sample.

Key Point

This research was conducted at the Middle Euphrates Oncology Center on 26 male patients diagnosed with breast cancer who were receiving radiation treatment. The study included primarily middle-aged and elderly individuals who were in the late stages of cancer, with the majority of them being smokers. Following radiation exposure, there were notable reductions in red blood cells, white blood cells, platelets, and lymphocytes. Among the patients, 77% tested positive for estrogen receptors, and 81% tested positive for progesterone receptors.

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Therapy led to a considerable decrease in testosterone levels. These findings highlight the influence of radiation on bone marrow and immunological function, emphasizing possible consequences for patient care and management techniques, particularly hormone-targeted medicines.

Acknowledgments

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Ethical Issues

The Ethics Committee of Baghdad University of Medicine approved the research in this study, adhering to the principles outlined in the Declaration of Helsinki (Ethical Code No. 153 IN 1/7/2024). Before any intervention, all participants provided written informed consent. The Department of Physiology at this university extracted the study from their thesis, "The Effects of Radiation on Blood Components and Hormones in Patients with Breast and Prostate Cancer." The authors fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

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