

## Skin Reaction in Radiation Therapy for Breast Cancer

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### Abstract

#### Introduction

The first medical intervention for many breast cancer patients is breast conserving surgery (BCS) and/or modified radical mastectomy (MRM). Most of these patients undergo radiation therapy, following surgery. The most common side-effect of breast radiotherapy is skin damage. In the present study, the severity of acute skin changes and the underlying causes were investigated in patients undergoing BCS and radiotherapy.

#### Materials and Methods

This prospective, cohort study was performed on 31 female patients, undergoing breast surgery therapy at Shahid Rajaie Babolsar Radiotherapy Center from September 2011 to July 2012. A questionnaire was designed, including the patient's characteristics, details of radiotherapy technique, and skin damage; the questionnaire was completed for each patient. The obtained results were analysed by performing ANOVA and Fisher's exact tests. Complications were graded using the radiation therapy oncology group (RTOG) scale.

#### Results

Grade 0 or 4 of skin damage was observed in none of the patients. Among the evaluated patients, 58%, 35.5%, and 6.5% of the patients had grade 1, grade 2, and grade 3 of skin damage, respectively. There was no statistically significant relationship between regional skin burns and factors such as average tangential field size, internal mammary field, chemotherapy, prior history of diseases, tamoxifen use, previous radiotherapy in breast area, or skin type ( $p>0.05$ ). However, there was a significant relationship between skin burns and presence of supraclavicular field ( $p=0.05$ ).

#### Conclusion

Considering the significant relationship between skin burn and supraclavicular field, special attention needs to be paid to factors affecting the treatment planning of supraclavicular field such as field size and photon energy.

**Keywords:** Breast Cancer; Radiotherapy; Skin Burns; Breast Conserving Surgery; Surgery

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## 1. Introduction

Breast cancer is the most common malignancy and the second leading cause of cancer death (after lung cancer) among women in the United States [1, 2]. Additionally, breast cancer is the most prevalent malignancy (other than skin cancer) and the fifth most lethal cancer among women in Iran [3, 4]. As a previous study indicated, on average, one in eight women will develop breast cancer during their lifetime [5].

Risk factors associated with breast cancer include age, personal or family history of breast cancer, delayed first parturition, early menstruation and late menopause, obesity (high body mass index), patient's previous biopsy with atypical hyperplasia or hyperplasia, high-density breast tissue, radiation exposure at a young age, alcohol use, and postmenopausal hormone therapy [2].

Special attention should be paid to the choice of treatment modality and its therapeutic effects, given the high incidence rate of breast cancer [6, 7]. Treatment of breast cancer includes surgery, radiotherapy, chemotherapy, and hormone therapy. The sequence of these modalities has a significant impact on the outcomes of patient treatment [8-10].

Effective factors in the selection of treatment modalities include patient's age, tumour size, menopausal status, tumour marker, lymph node status, estrogen or progesterone receptors [11], and side-effects of selected modalities [5]. The first treatment choice for patients is surgery (except in advanced diseases) [12]. Surgery can be carried out as breast conserving surgery (BCS) or modified radical mastectomy (MRM) [13].

After BCS, most patients undergo radiation therapy. BCS, followed by radiotherapy, known as breast surgery therapy (BST), has been confirmed as a standard treatment for most women with early stage of breast cancer. BST is a suitable method for primary therapy for most women, diagnosed with stage I or II of breast cancer. This method is considered desirable since the associated survival rate is similar to that of total mastectomy and axillary dissection, while preserving the breast [2].

Radiotherapy, as a treatment for breast cancer, normally leads to acute or chronic side-effects. The acute side-effects occur a few days to a few weeks after radiation therapy [2, 14, 15]. The most common acute side-effect is skin change [16], which appears as erythema, hypersensitivity, edema, alopecia, hyperpigmentation, and/or desquamation at higher radiation doses.

The first skin change is erythema and its severity varies with dose. Erythema usually occurs in the second or third week of a standard fractionated radiotherapy course with irradiation of 20-40 Gy by a megavoltage beam. In higher doses, hyperpigmentation, epilation, or desquamation may occur. Epilation appears approximately 3 weeks after irradiation with a dose of 20 Gy. Hyperpigmentation and dry desquamation appear by irradiation of 45 Gy, but moist desquamation may occur when the dose is >45 Gy [2].

Skin complications are affected by factors including irradiated volume, total dose, history of previous exposure of the treated site, clinical conditions such as diabetes, immune status, smoking, steroid therapy, weak diet conditions [14], chemical compounds, obesity, characteristics of the radiation field, and use of bolus [17].

Considering the importance of these issues, the extent of skin damage and the effective factors were investigated in the present study.

## 2. Materials and Methods

### 2.1. Patients

This prospective, cohort study was performed on 31 female patients with BST at Shahid Rajaie Babolsar Radiotherapy Center from September 2011 to July 2012. The patients were treated by radiotherapy and the irradiated breasts were examined at Shahid Rajaie Babolsar Radiotherapy Center, Babolsar, Iran.

### 2.2. Characteristics of patients' radiotherapy

In this research, the patients were treated by 6 MV photon beams, delivered from Siemens linear accelerator. Whole breast irradiation of 5000 cGy was performed, followed by a 1000

cGy boost (with photon). All patients were treated with standard fractionation (200 cGy per fraction) and treatments were performed 5 days a week. For patients' treatment, various radiation fields were used including tangential, supraclavicular, and internal mammary fields. Depending on lymph node involvement and other parameters, two (tangential field for 22.5% of patients), three (tangential and supraclavicular fields for 61.5% of patients), or four fields (tangents, supraclavicular, and internal mammary fields for 16% of patients) were used.

### 2.3. Evaluation of skin damages

Since there was a possibility that each patient would have conditions such as skin sensitivity, previous skin changes, and previous radiotherapy on their irradiated breast skin, breast skin of these patients was examined by a radiation oncologist before radiotherapy.

A questionnaire was completed for each patient by the radiation oncologist, which included the patient's name, file number, sex, age, total dose, radiation field setup, irradiation field size, depth of tumour, and other factors such as chemotherapy, pathologic findings, history of previous illnesses, date of diagnosis, use of tamoxifen, and skin type. The most important part of the questionnaire, which included skin changes, was completed every week. Table 1 lists the classification system of skin types [18].

Table 1. Fitzpatrick skin type classification system

Skin types	Skin reaction and solar radiation
1	Always burns, never tans
2	Usually burns, tans less than average (with difficulty)
3	Sometimes mild burn, tans about average
4	Rarely burns, tans more than average (with ease)
5	Rarely burns and tans easily (brown-skinned people)
6	Almost never burns and tans easily (black-skinned people)

The radiation therapy oncology group (RTOG) protocol on skin changes includes 5 grades, which are as follows: Grade 0: no change; Grade 1: mild erythema; Grade 2: clear redness, pruritus and dry desquamation; Grade 3: moist desquamation, creation of voids, and edema; and Grade 4: necrosis and bleeding [13].

Finally, the results were analysed by ANOVA and Fisher's exact tests, using SPSS version 11.5. RTOG was used as the scoring system, and P-value  $\leq 0.05$  was considered statistically significant.

### 3. Results

The average age of patients was  $49 \pm 13$  years and the minimum and maximum of age were 18 and 80 years, respectively. The average tangential field size was  $198 \pm 79$  cm<sup>2</sup>. In total, 39% of the patients had undergone chemotherapy. The analysis of histopathological samples of patients showed that 97% of patients had carcinoma and 3% had sarcoma.

Also, 6.5% of the patients had a previous history of conditions such as high blood pressure. Furthermore, 23% of the patients had received tamoxifen, and 93.5% of the subjects had undergone radiation therapy for the first time. As the results indicated, 3%, 74%, and 23% of the patients had skin type II, type III, and type IV, respectively.

None of the patients showed grade 0 or 4 of skin damage. However, 58%, 35.5%, and 6.5% of the patients had grade 1, grade 2, and grade 3 burns, respectively (Fig. 1). Sections (a), (b), and (c) in Fig. 2 illustrate grades 1, 2, and 3, respectively.

Kolmogorov-Smirnov test confirmed the normality of patients' age and field size ( $p=0.30$  and  $p=0.52$ , respectively). Afterwards, ANOVA test was used for comparing the averages to assess the statistical relationship between different groups of cutaneous complications, average age, and average field size. The average age of patients was similar in different groups of cutaneous complications and there was no significant difference ( $p=0.93$ ).

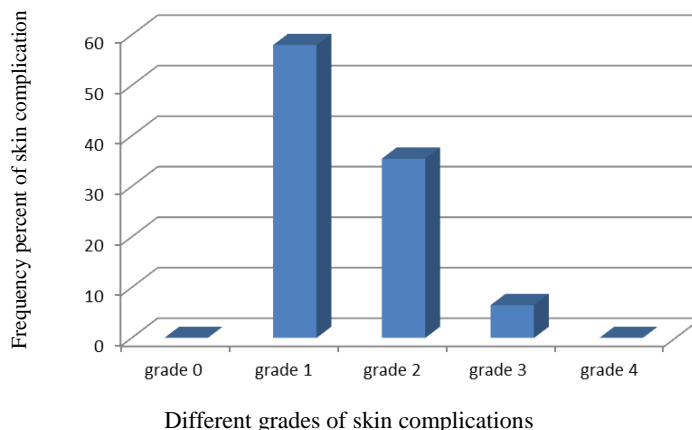


Fig. 1. Frequency percentage of different grades of skin complications

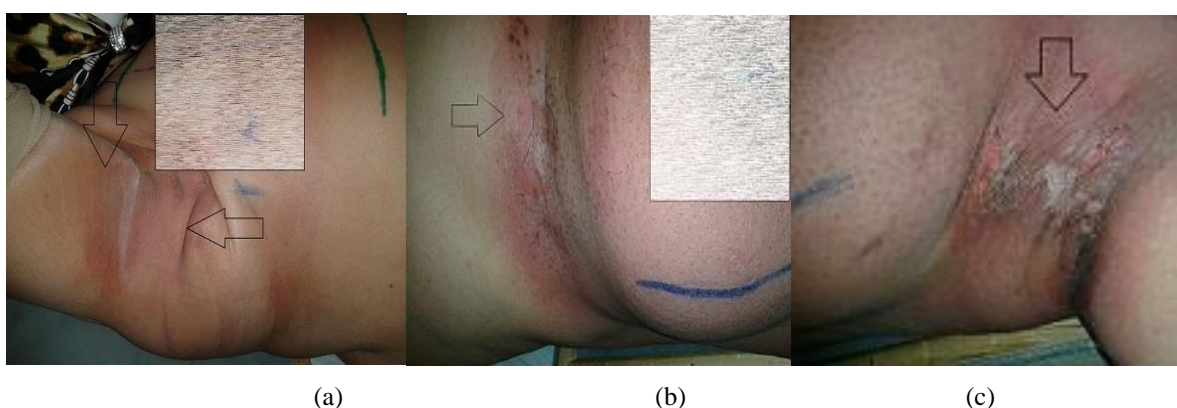


Figure 2. (a). Burn of grade 1 (erythema); (b). Burn of grade 2 (dry desquamation); (c). Burn of grade 3 (moist desquamation)

Besides, the average tangential field size was equal in different groups of cutaneous complications and there was no significant difference ( $p=0.192$ ).

Cross tabulation and Fisher's exact test showed no significant relationship between different groups of cutaneous side-effects and chemotherapy ( $p=0.62$ ). Also, there was no significant relationship between different groups of cutaneous side-effects and tamoxifen use ( $p=0.63$ ). There was also no significant relationship between different groups of cutaneous side-effects and skin type ( $p=0.15$ ).

No significant correlation was found between different groups of cutaneous side-effects and pervious radiotherapy ( $p=0.57$ ). In addition, there was no significant correlation between different groups of cutaneous side-effects and internal mammary field ( $p=0.54$ ). However, there was a statistically significant relationship

between different groups of cutaneous complications and presence of supraclavicular field ( $p=0.050$ ).

#### 4. Discussion

Since BCS, followed by radiotherapy, is a standard procedure for the treatment of stage I and II breast cancer, attention needs to be paid to the side-effects of radiation. Therefore, factors influencing radiation-induced complications such as field type (especially axillary), irradiated volume, total dose, patients' clinical status, and chemicals should be considered.

According to the report by National Health Service Quality Improvement Scotland (NHS QIS) in 2004, any type of skin damage is anticipated about 10 to 14 days after the first fraction of radiotherapy [15]. In a report presented by NHS, acute reactions after

radiotherapy occur 10 to 14 days after the onset of treatment and continue until the end of treatment [14].

In a study carried out by Jalilian and Arbabi [13] on 200 patients with breast cancer, who had undergone mastectomy and radiotherapy using electron beams, the results showed that 31.5%, 64.5%, and 4% of burns were grade 1, grade 2, and grade 3, respectively; also, grade 0 or 4 was observed in none of the cases. In the mentioned report, there was a statistically significant relationship between different groups of cutaneous complications and posterior axillary field.

The current study was performed on patients, who had undergone BCS followed by radiation therapy with photon beams, while the study by Jalilian and Arbabi evaluated patients who had undergone mastectomy followed by radiation therapy with electron. In both studies, grades 0, 3, and 4 were observed with relatively the same prevalence. However, the incidence of grades 1 and 2 differed between the studies. This is because the skin is part of the target volume in mastectomy and should receive sufficient radiation dose.

On the other hand, since the range of electrons is smaller than that of photons, the severity of burns in radiotherapy with electron beams is expected to be greater than that in radiotherapy with photon electron beams. Furthermore, in electron beam radiotherapy, higher energy is deposited on the surface. This effect could be the reason for the higher percentage of grade 2 burns in the current study (compared to grade

1), compared to that observed in the study by Jalilian and Arbabi.

There was a statistically significant relationship between skin burns and presence of supraclavicular field. This may be due to the presence of adjacent (tangential and supraclavicular) or overlapping fields. Thus, the supraclavicular field can affect the severity of burns in breast cancer patients with involved supraclavicular lymph nodes.

## 5. Conclusion

In the present study, no statistically significant relationship was observed between regional skin burns and average tangential field size, internal mammary field, chemotherapy, history of previous diseases, tamoxifen use, previous radiotherapy in breast area, or skin type in patients with breast cancer, who had undergone BST. However, a statistically significant relationship was found between skin burns and presence of supraclavicular field. Therefore, it is suggested that in treatment planning of supraclavicular field, the field size, beam energy, total dose, and depth of the tumour be taken into account.

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## References

1. American Cancer Society. Cancer Facts & Figures 2013. Atlanta: American Cancer Society; 2013. Available at: <http://www.cancer.org/research/cancerfactsfigures/cancerfactsfigures/cancer-facts-figures-2013>. Accessed Aug 4, 2014.
2. Halperin EC, Perez CA, Brady LW. Perez and Brady's principles and practice of radiation oncology. 5th Ed. USA: Wolters Kluwer Health; 2008: 330-1207.
3. Akbari ME. Iran cancer report. Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Qom: Darolfekr; 2007.
4. Akbari ME, Khayamzadeh M, Khoshnevis SJ, Nafisi N, Akbari A. Five & ten years survival in breast cancer patients mastectomies vs. breast conserving surgeries, personal experience. Iranian J cancer prevention 2008; 1(2): 53-7.
5. Levitt SH, Purdy JA, Perez CA, Vijayakumar S. Technical basis of radiation therapy practical clinical applications. 4th Ed. Germany: Springer-Verlag Berlin Heidelberg; 2006: 486-492.

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6. Krauss DJ, Kestin LL, Raff G, Yan D, Wong J, Gentry R, et al. MRI-based volumetric assessment of cardiac anatomy and dose reduction via active breathing control during irradiation for left-sided breast cancer. *Int J Radiat Oncol Biol Phys.* 2005;61(4):1243-50.
7. Laliberte L, Fennell ML, Papandonatos G. The relationship of membership in research networks to compliance with treatment guidelines for early-stage breast cancer. *Med Care.* 2005;43(5):471-9.
8. Bellon JR, Come SE, Gelman RS, Henderson IC, Shulman LN, Silver BJ, et al. Sequencing of chemotherapy and radiation therapy in early-stage breast cancer: updated results of a prospective randomized trial. *J Clin Oncol.* 2005;23(9):1934-40.
9. J. Liu M, Hawk H, Gershman ST, Smith SM, Karacek R, Woodford ML, et al. The effects of a National Breast and Cervical Cancer Early Detection Program on social disparities in breast cancer diagnosis and treatment in Massachusetts. *Cancer Causes Control.* 2005;16(1):27-33.
10. Katz SJ, Lantz PM, Janz NK, Fagerlin A, Schwartz K, Liu L, et al. Patterns and correlates of local therapy for women with ductal carcinoma-in-situ. *J Clin Oncol.* 2005;23(13):3001-7.
11. Tobler M, Leavitt DD. Design and production of wax compensators for electron treatments of the chest wall. *Med Dosim.* 1997;21(4):199-206.
12. Kao J, Conzen SD, Jaskowiak NT, Song DH, Recant W, Singh R, et al. Concomitant radiation therapy and paclitaxel for unresectable locally advanced breast cancer: results from two consecutive phase I/II trials. *Int J Radiat Oncol Biol Phys.* 2005;61(4):1045-53.
13. Jalilian M, Arbabi F. Cutaneous complication after electron beam therapy in breast cancer. *J Res Med Sci.* 2005;10(6):368-70.
14. Scotland NQI. The new castle upon tyne hospitals NHS foundation trust skin care guidelines for radiotherapy patients. Scotland: NHS Quality Improvement Scotland; 2011.
15. Scotland NQI. Skincare of patients receiving radiotherapy. Scotland: NHS Quality Improvement Scotland; 2004.
16. National Cancer Institute. Radiation therapy and you: Support for People with Cancer. USA: National Institutes of Health; 2012: 21
17. Scotland NQI. Skincare of patients receiving radiotherapy. Scotland: NHS Quality Improvement Scotland; 2010.
18. Ravnbak MH. Objective determination of Fitzpatrick skin type [Thesis]. Dan Med Bull: University of Copenhagen; 2010.