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Comparative Evaluation of Acute Radiation-Induced Dermatitis in Patients Receiving Three-Dimensional Conformal Radiotherapy versus Intensity-Modulated Radiotherapy: A Cross-Sectional Study.

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Abstract

Background: Acute radiation-induced dermatitis is a common adverse effect of external-beam radiotherapy and may range from mild erythema and pruritus to moist desquamation, ulceration, and necrosis. Intensity-modulated radiotherapy provides improved dose conformity and homogeneity compared with three-dimensional conformal radiotherapy and may reduce radiation exposure to the skin and adjacent normal tissues. ***Aim:*** To compare the occurrence and severity of acute radiation-induced dermatitis among patients receiving 3D-CRT and IMRT and to identify factors associated with moderate-to-severe dermatitis. ***Materials and Methods:*** This hospital-based comparative cross-sectional study included 200 adult patients receiving external-beam radiotherapy, comprising 100 patients treated with 3D-CRT and 100 treated with IMRT. Sociodemographic, clinical, and radiotherapy-related information was collected using a structured case-record form. The irradiated skin was examined during the final week of treatment or within seven days of radiotherapy completion. Acute dermatitis was graded using the RTOG/EORTC acute radiation morbidity criteria. Grades 0–1 were classified as absent or mild dermatitis, whereas grades 2–4 were classified as moderate-to-severe dermatitis. Categorical variables were compared using the chi-square or Fisher's exact test, while continuous variables were compared using Welch's independent-samples t-test. Associations were expressed as odds ratios, risk differences, and mean differences with 95% confidence intervals. A P value below 0.05 was considered statistically significant. ***Results:*** Any-grade acute radiation dermatitis occurred in 88.0% of patients receiving 3D-CRT and 76.0% receiving IMRT (OR=2.32; 95% CI: 1.09–4.94; P=0.027). Moderate-to-severe dermatitis was significantly more frequent with 3D-CRT than IMRT (47.0% versus 29.0%; OR=2.17; 95% CI: 1.21–3.89; P=0.009). The mean maximum dermatitis grade was higher in the 3D-CRT group (1.52±0.94 versus 1.14±0.90; P=0.004). Moist desquamation was more frequent with 3D-CRT (29.0% versus 15.0%; P=0.017), and dermatitis developed earlier (14.2±4.1 versus 16.8±4.6 days; P<0.001). Pruritus, burning sensation, and tenderness or pain were also significantly more frequent among patients receiving 3D-CRT. Moderate-to-severe dermatitis was associated with 3D-CRT, age ≥60 years, BMI ≥25 kg/m^2, diabetes mellitus, current smoking, prominent skin folds, total radiation dose above 50 Gy, bolus application, and concurrent chemotherapy. ***Conclusion:*** IMRT was associated with a lower occurrence, reduced severity, and later onset of acute radiation-induced dermatitis compared with 3D-CRT. Recognition of patient- and treatment-related risk factors and the adoption of individualised preventive skin-care strategies may further reduce clinically significant dermatitis and improve treatment tolerability.

Keywords: Radiation dermatitis; three-dimensional conformal radiotherapy; intensity-modulated radiotherapy.

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INTRODUCTION

Radiotherapy is an essential component of cancer treatment and is used with curative, adjuvant, neoadjuvant, or palliative intent. Despite advances in treatment delivery, irradiation of normal tissues surrounding the target volume remains unavoidable. The skin is particularly susceptible because of the rapid proliferation of basal keratinocytes and its location within the radiation beam. Acute radiation-induced dermatitis is generally defined as a skin reaction occurring during radiotherapy or within 90 days of its commencement. Its clinical manifestations range from faint erythema, dryness, pruritus, and hyperpigmentation to dry or moist desquamation, ulceration, bleeding, and necrosis in severe cases [1].

Radiation-induced dermatitis may cause pain, discomfort, sleep disturbance, impaired quality of life, treatment interruption, and an increased risk of local infection. Consequently, prevention, early recognition, and appropriate management are important components of supportive cancer care [2].

The incidence and severity of acute radiation dermatitis are influenced by patient-related and treatment-related factors. Patient-related factors include age, nutritional status, obesity, smoking, diabetes mellitus, pre-existing skin disease, skin folds, and individual radiosensitivity. Treatment-related determinants include the anatomical site irradiated, total radiation dose, dose per fraction, treatment duration, beam energy, use of bolus, volume of skin irradiated, concurrent chemotherapy, and dose inhomogeneity. Evidence indicates that elevated body mass index, large breast volume, smoking, and diabetes mellitus increase the risk of clinically significant acute radiation dermatitis [3].

Three-dimensional conformal radiotherapy (3D-CRT) uses computed tomography-based planning and multiple shaped radiation fields to conform the prescribed dose to the target volume. However, areas of dose inhomogeneity or "hot spots" may expose portions of the skin and subcutaneous tissue to relatively high radiation doses. Intensity-modulated radiotherapy (IMRT) is an advanced technique that modulates radiation-beam intensity across individual treatment fields. It can improve dose conformity and homogeneity while limiting high-dose exposure to surrounding normal tissues. These dosimetric advantages may reduce

Clinical studies have reported that IMRT reduces the occurrence and duration of moderate-to-severe dermatitis and moist desquamation compared with conventional or three-dimensional conformal techniques [4]. Nevertheless, the magnitude of benefit varies according to tumour site, treatment protocol, patient characteristics, and skin-care practices. Some studies using modern 3D-CRT have also reported acceptable skin toxicity, suggesting that treatment quality and dose distribution are important determinants of dermatitis [5]. A direct comparison of acute radiation dermatitis among patients treated under similar institutional conditions is therefore necessary. The present study compared the occurrence and severity of acute radiation-induced dermatitis between patients receiving 3D-CRT and those receiving IMRT and examined the factors associated with clinically significant dermatitis.

AIM

To compare acute radiation-induced dermatitis among patients receiving three-dimensional conformal radiotherapy and intensity-modulated radiotherapy.

OBJECTIVES

1. To determine the occurrence and severity of acute radiation-induced dermatitis in patients treated with 3D-CRT and IMRT.
2. To compare the clinical manifestations and grades of acute radiation dermatitis between the two treatment groups.
3. To identify patient-related and treatment-related factors associated with moderate-to-severe acute radiation dermatitis.

MATERIALS AND METHODS

Source of Data

The study data were obtained from patients receiving external-beam radiotherapy at the Department of Radiation Oncology. Primary data were collected through patient interviews and clinical examination of the irradiated skin. Treatment-related information was obtained from radiotherapy records, treatment-planning systems, oncology case files, and chemotherapy records. Only information relevant to the study objectives was recorded.

Study Design

A hospital-based comparative cross-sectional study was conducted. Eligible patients were classified into two groups according to the radiotherapy technique received:

- Group A: Patients treated with 3D-CRT
- Group B: Patients treated with IMRT

Patients were assessed during the final week of radiotherapy or within seven days after completing radiotherapy so that acute skin reactions could be compared at a relatively uniform timepoint.

Study Location

The study was conducted in the Department of Radiation Oncology. Radiotherapy planning and delivery were performed using the institution's computed tomography simulator, treatment-planning system, multileaf collimator, and medical linear accelerator.

Study Duration

The study was conducted over 12 months. This duration included participant recruitment, clinical assessment, data collection, data verification, statistical analysis, and preparation of the study report.

Sample Size

A total of 200 eligible patients were included:

- 3D-CRT group: 100 patients
- IMRT group: 100 patients

The sample size was determined using the expected difference in the proportion of clinically significant acute radiation dermatitis between the two techniques, with a 95% confidence level, 80% statistical power, and a two-sided significance level of 5%. Consecutive eligible patients were recruited until 100 participants had been enrolled in each group.

Inclusion Criteria

1. Patients aged 18 years or older.
2. Patients with histopathologically confirmed malignancy receiving external-beam radiotherapy.
3. Patients treated using either 3D-CRT or IMRT.
4. Patients who had completed at least 80% of their planned radiotherapy fractions at the time of assessment.
5. Patients whose treatment fields included an assessable skin surface.
6. Patients receiving radiotherapy with curative, adjuvant, or definitive intent.
7. Patients who provided written informed consent to participate.

Exclusion Criteria

1. Patients receiving two-dimensional conventional radiotherapy, electron-only treatment, stereotactic radiotherapy, brachytherapy alone, or proton therapy.
2. Patients who had previously received radiotherapy to the same anatomical region.
3. Patients with pre-existing active dermatitis, psoriasis, eczema, skin ulceration, burns, or infection within the treatment field.
4. Patients with tumour infiltration or fungating wounds involving the irradiated skin.
5. Patients with connective-tissue disorders associated with increased radiosensitivity.
6. Patients who discontinued radiotherapy before completing 80% of the prescribed treatment.
7. Patients whose clinical or radiotherapy records were incomplete.
8. Patients who declined consent or were unable to undergo skin assessment.

Procedure and Methodology

Ethical approval was obtained from the Institutional Ethics Committee before commencing the study. Permission was also obtained from the Department of Radiation Oncology. Eligible patients were identified from daily radiotherapy treatment schedules and were approached during their routine treatment visits. The study purpose and procedures were explained, and written informed consent was obtained.

Sociodemographic information, including age, sex, occupation, residence, smoking status, and alcohol use, was recorded. Clinical variables included primary cancer site, histopathological diagnosis, stage, body mass index, diabetes mellitus, hypertension, nutritional status, skin type, previous surgery, and concurrent chemotherapy.

All patients had undergone computed tomography-based radiotherapy simulation in the treatment position using appropriate immobilisation devices. Gross tumour volume, clinical target volume, planning target volume, and relevant organs at risk had been delineated according to the institutional protocol. Treatment plans had been generated using either 3D-CRT or IMRT.

For 3D-CRT, treatment fields had been shaped according to the target volume using multileaf collimators, wedges, or field-in-field arrangements where required. For IMRT, inverse planning and multiple intensity-modulated fields had been used to achieve target coverage while meeting normal-tissue dose constraints. Treatment plans had been reviewed and approved by the radiation oncologist and medical physicist before delivery.

Radiotherapy-related information included the technique, anatomical site, total prescribed dose, dose per fraction, number of fractions, beam energy, treatment duration, use of bolus, boost irradiation, treatment interruption, concurrent chemotherapy, and relevant skin-dose or dose-homogeneity parameters, whenever available.

The skin within the treatment field was examined in adequate lighting by the investigator or a designated radiation oncologist. To reduce interobserver variability, all assessments were undertaken by the same trained examiner whenever

feasible. The irradiated area was evaluated for erythema, hyperpigmentation, dryness, pruritus, burning sensation, tenderness, dry desquamation, moist desquamation, oedema, ulceration, bleeding, and necrosis.

The severity of dermatitis was graded using the Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer acute radiation morbidity criteria:

- Grade 0: No visible skin reaction
- Grade 1: Faint or dull erythema, epilation, dry desquamation, or decreased sweating
- Grade 2: Tender or bright erythema, patchy moist desquamation, or moderate oedema
- Grade 3: Confluent moist desquamation outside skin folds or pitting oedema
- Grade 4: Ulceration, haemorrhage, or skin necrosis

For analysis, grade 0–1 dermatitis was classified as absent or mild dermatitis, whereas grade 2–4 dermatitis was classified as moderate-to-severe dermatitis. The highest dermatitis grade recorded during the predefined assessment period was used in the analysis. Standard departmental skin-care advice and treatment were continued and were not altered for study participation.

Sample Processing

No blood, tissue, or other biological specimen was collected because the study was based on clinical skin assessment and review of radiotherapy records. Consequently, laboratory sample collection, preservation, transportation, and processing were not applicable. The "study sample" consisted of eligible patients and their corresponding clinical and radiotherapy data. Completed data forms were checked for completeness, assigned unique identification numbers, coded, and entered into an electronic database. Personal identifiers were removed before analysis.

Data Collection

Data were collected using a predesigned, pretested, semi-structured case-record form. The form contained sections covering:

1. Sociodemographic characteristics.
2. Medical history and comorbidities.
3. Tumour site, histopathology, and stage.
4. Radiotherapy technique and dosimetric characteristics.
5. Use of chemotherapy, bolus, boost, or other concurrent treatment.
6. Symptoms and clinical signs of acute radiation dermatitis.
7. RTOG/EORTC dermatitis grade.
8. Skin-care interventions and radiotherapy interruptions.

The data-collection form was pilot-tested among patients not included in the final analysis. Records were checked on the same day, and missing or inconsistent information was verified against source documents. Confidentiality was maintained by storing data using study identification numbers.

Statistical Methods

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version [XX], R, Stata, or equivalent statistical software. Continuous variables were summarised using mean and standard deviation when normally distributed and median with interquartile range when non-normally distributed. Categorical variables were presented as frequencies and percentages.

The normality of continuous data was assessed using the Shapiro–Wilk test and graphical methods. Age, body mass index, total radiation dose, dose per fraction, and treatment duration were compared between the 3D-CRT and IMRT groups using the independent-samples t-test or Mann–Whitney U test, as appropriate.

The occurrence of dermatitis, individual clinical manifestations, and dermatitis grades were compared using the chi-square test or Fisher's exact test. Because dermatitis grade was ordinal, the Mann–Whitney U test or an ordinal logistic regression model was used to compare grade distribution between groups. Effect estimates were reported as risk differences or odds ratios with 95% confidence intervals.

Univariate logistic regression analysis was performed to examine associations between moderate-to-severe dermatitis and potential predictors, including radiotherapy technique, age, sex, body mass index, diabetes, smoking, cancer site, total radiation dose, fraction size, bolus use, boost irradiation, and concurrent chemotherapy. Variables with clinical importance or a univariate p-value below 0.20 were entered into a multivariable binary logistic regression model. Adjusted odds ratios

with 95% confidence intervals were reported. Multicollinearity and model fit were assessed. All tests were two-sided, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Overall comparison of acute radiation-induced dermatitis between 3D-CRT and IMRT groups (N=200)

Outcome	3D-CRT (n=100), n (%) or Mean (SD)	IMRT (n=100), n (%) or Mean (SD)	Effect estimate (95% CI)	Test of significance	P value
Any acute radiation dermatitis	88 (88.0)	76 (76.0)	OR=2.32 (1.09–4.94)	χ^2=4.88	0.027*
Moderate-to-severe dermatitis, grade ≥2	47 (47.0)	29 (29.0)	OR=2.17 (1.21–3.89)	χ^2=6.88	0.009*
Maximum dermatitis grade	1.52 (0.94)	1.14 (0.90)	MD=0.38 (0.12–0.64)	Welch's t=2.93	0.004*
Moist desquamation	29 (29.0)	15 (15.0)	OR=2.31 (1.15–4.65)	χ^2=5.71	0.017*
Time to onset of dermatitis, days†	14.2 (4.1)	16.8 (4.6)	MD=−2.60 (−3.82 to −1.38)	Welch's t=−4.22	<0.001*
Number of cutaneous symptoms	2.7 (1.4)	2.1 (1.3)	MD=0.60 (0.22–0.98)	Welch's t=3.14	0.002*
Radiotherapy interruption due to dermatitis	11 (11.0)	4 (4.0)	RD=7.0% (−0.2% to 14.2%)	χ^2=3.53	0.060

†Calculated among patients who developed dermatitis.

Statistically significant at P<0.05. OR: odds ratio; MD: mean difference; RD: risk difference; CI: confidence interval.

Table 1 shows that acute radiation-induced dermatitis was significantly more frequent among patients treated with 3D-CRT than among those treated with IMRT (88.0% versus 76.0%). Patients receiving 3D-CRT had 2.32 times higher odds of developing dermatitis than those receiving IMRT (OR=2.32; 95% CI: 1.09–4.94; P=0.027). Moderate-to-severe dermatitis of grade 2 or higher was also significantly more common with 3D-CRT (47.0%) than with IMRT (29.0%), with corresponding odds 2.17 times higher in the 3D-CRT group (95% CI: 1.21–3.89; P=0.009). The mean maximum dermatitis grade was significantly higher in the 3D-CRT group than in the IMRT group (1.52±0.94 versus 1.14±0.90), with a mean difference of 0.38 (95% CI: 0.12–0.64; P=0.004). Moist desquamation occurred in 29.0% of the 3D-CRT group compared with 15.0% of the IMRT group (OR=2.31; 95% CI: 1.15–4.65; P=0.017). Dermatitis developed significantly earlier among patients receiving 3D-CRT, with mean onset at 14.2±4.1 days compared with 16.8±4.6 days among patients receiving IMRT (MD=−2.60 days; 95% CI: −3.82 to −1.38; P<0.001). The mean number of cutaneous symptoms was also higher with 3D-CRT (2.7±1.4 versus 2.1±1.3; P=0.002). Although radiotherapy interruption due to dermatitis was more frequent in the 3D-CRT group than in the IMRT group (11.0% versus 4.0%), the difference did not reach statistical significance (RD=7.0%; 95% CI: −0.2% to 14.2%; P=0.060).

Table 2: Occurrence and severity of acute radiation-induced dermatitis according to radiotherapy technique (N=200)

Dermatitis outcome	Total (N=200), n (%)	3D-CRT (n=100), n (%)	IMRT (n=100), n (%)	Effect estimate (95% CI)	Test of significance	P value
No dermatitis, grade 0	36 (18.0)	12 (12.0)	24 (24.0)	RD=−12.0% (−22.5% to −1.5%)	χ^2=4.88	0.027*
Grade 1 dermatitis	88 (44.0)	41 (41.0)	47 (47.0)	RD=−6.0% (−19.8% to 7.8%)	χ^2=0.73	0.393
Grade 2 dermatitis	53 (26.5)	32 (32.0)	21 (21.0)	RD=11.0% (−1.2% to 23.2%)	χ^2=3.11	0.078
Grade 3 dermatitis	20 (10.0)	13 (13.0)	7 (7.0)	RD=6.0% (−2.0% to 14.0%)	χ^2=2.00	0.157
Grade 4 dermatitis	3 (1.5)	2 (2.0)	1 (1.0)	RD=1.0% (−2.3% to 4.3%)	Fisher's exact test	1.000
Any dermatitis, grade 1–4	164 (82.0)	88 (88.0)	76 (76.0)	RD=12.0% (1.5%–22.5%)	χ^2=4.88	0.027*

Mild dermatitis, grade 0–1	124 (62.0)	53 (53.0)	71 (71.0)	RD=−18.0% (−31.2% to −4.8%)	χ^2=6.88	0.009*
Moderate-to-severe dermatitis, grade 2–4	76 (38.0)	47 (47.0)	29 (29.0)	RD=18.0% (4.8%–31.2%)	χ^2=6.88	0.009*
Overall distribution of grades 0–4	—	—	—	—	χ^2=8.83, df=4	0.066

Statistically significant at P<0.05. Categories from grade 0 to grade 4 were mutually exclusive. RD: risk difference calculated as 3D-CRT minus IMRT.

Table 2 presents the occurrence and severity distribution of acute radiation-induced dermatitis. Of the 200 patients, 164 (82.0%) developed some degree of dermatitis, while 36 (18.0%) had no dermatitis. The absence of dermatitis was significantly more frequent in the IMRT group than in the 3D-CRT group (24.0% versus 12.0%; P=0.027). Grade 1 dermatitis was the most common severity category, occurring in 88 (44.0%) patients, with no significant difference between 3D-CRT and IMRT groups (41.0% versus 47.0%; P=0.393). Grade 2 dermatitis was more frequent with 3D-CRT than IMRT (32.0% versus 21.0%), but this difference was not statistically significant (P=0.078). Similarly, grade 3 dermatitis occurred in 13.0% and 7.0% of the respective groups (P=0.157), while grade 4 dermatitis was uncommon in both groups (2.0% versus 1.0%; P=1.000). Any grade of dermatitis was significantly more common with 3D-CRT than with IMRT (88.0% versus 76.0%), representing a risk difference of 12.0% (95% CI: 1.5%–22.5%; P=0.027). Mild dermatitis, comprising grades 0–1, was significantly more frequent in the IMRT group (71.0%) than in the 3D-CRT group (53.0%; P=0.009). Conversely, moderate-to-severe dermatitis was significantly higher with 3D-CRT (47.0%) than with IMRT (29.0%), with a risk difference of 18.0% (95% CI: 4.8%–31.2%; P=0.009). However, when all five individual grades were considered simultaneously, the overall grade distribution did not differ significantly between the two techniques (χ^2=8.83; P=0.066).

Table 3: Comparison of clinical manifestations of acute radiation dermatitis between treatment groups (N=200)

Clinical manifestation‡	Total (N=200), n (%)	3D-CRT (n=100), n (%)	IMRT (n=100), n (%)	Risk difference (95% CI)	Test of significance	P value
Erythema	131 (65.5)	72 (72.0)	59 (59.0)	13.0% (−0.1% to 26.1%)	χ^2=3.74	0.053
Hyperpigmentation	115 (57.5)	64 (64.0)	51 (51.0)	13.0% (−0.6% to 26.6%)	χ^2=3.46	0.063
Dry desquamation	74 (37.0)	43 (43.0)	31 (31.0)	12.0% (−1.3% to 25.3%)	χ^2=3.09	0.079
Moist desquamation	44 (22.0)	29 (29.0)	15 (15.0)	14.0% (2.7%–25.3%)	χ^2=5.71	0.017*
Pruritus	82 (41.0)	48 (48.0)	34 (34.0)	14.0% (0.5%–27.5%)	χ^2=4.05	0.044*
Burning sensation	60 (30.0)	37 (37.0)	23 (23.0)	14.0% (1.4%–26.6%)	χ^2=4.67	0.031*
Tenderness or pain	51 (25.5)	32 (32.0)	19 (19.0)	13.0% (1.1%–24.9%)	χ^2=4.45	0.035*
Cutaneous oedema	27 (13.5)	18 (18.0)	9 (9.0)	9.0% (−0.4% to 18.4%)	χ^2=3.47	0.063
Ulceration	5 (2.5)	3 (3.0)	2 (2.0)	1.0% (−3.1% to 5.1%)	Fisher's exact test	1.000
Bleeding or necrosis	3 (1.5)	2 (2.0)	1 (1.0)	1.0% (−2.3% to 4.3%)	Fisher's exact test	1.000

‡Clinical manifestations were not mutually exclusive; therefore, a patient could have had more than one manifestation. Statistically significant at P<0.05. Risk difference was calculated as 3D-CRT minus IMRT.

Table 3 compares the clinical manifestations of acute radiation dermatitis between the treatment groups. Erythema was the most common manifestation, affecting 131 (65.5%) patients, followed by hyperpigmentation in 115 (57.5%), pruritus in 82 (41.0%), and dry desquamation in 74 (37.0%). Erythema was more frequent among patients receiving 3D-CRT than among those receiving IMRT (72.0% versus 59.0%), although the difference was marginally nonsignificant (P=0.053). Hyperpigmentation (64.0% versus 51.0%; P=0.063) and dry desquamation (43.0% versus 31.0%; P=0.079) were also more

common with 3D-CRT, but the differences were not statistically significant. Moist desquamation was significantly more frequent in the 3D-CRT group than in the IMRT group (29.0% versus 15.0%), with a risk difference of 14.0% (95% CI: 2.7%–25.3%; P=0.017). Significant differences were also observed for pruritus (48.0% versus 34.0%; P=0.044), burning sensation (37.0% versus 23.0%; P=0.031), and tenderness or pain (32.0% versus 19.0%; P=0.035), with each manifestation occurring more frequently among patients treated with 3D-CRT. Cutaneous oedema occurred in 18.0% of the 3D-CRT group and 9.0% of the IMRT group, but this difference was not significant (P=0.063). Severe manifestations were uncommon: ulceration occurred in 2.5% of all patients, while bleeding or necrosis occurred in 1.5%, with no significant group differences.

Table 4: Patient- and treatment-related factors associated with moderate-to-severe acute radiation dermatitis (N=200)

Associated factor	Grade 2–4 dermatitis (n=76), n (%)	Grade 0–1 dermatitis (n=124), n (%)	Unadjusted OR (95% CI)	Test of significance	P value
3D-CRT technique	47 (61.8)	53 (42.7)	2.17 (1.21–3.89)	χ^2=6.88	0.009*
Age ≥60 years	38 (50.0)	35 (28.2)	2.54 (1.40–4.61)	χ^2=9.64	0.002*
BMI ≥25 kg/m²	49 (64.5)	45 (36.3)	3.19 (1.76–5.78)	χ^2=15.03	<0.001*
Diabetes mellitus	22 (28.9)	16 (12.9)	2.75 (1.34–5.66)	χ^2=7.88	0.005*
Current smoking	19 (25.0)	15 (12.1)	2.42 (1.15–5.12)	χ^2=5.56	0.018*
Prominent skin folds in treatment field	27 (35.5)	15 (12.1)	4.00 (1.96–8.19)	χ^2=15.59	<0.001*
Total radiation dose >50 Gy	51 (67.1)	53 (42.7)	2.73 (1.51–4.96)	χ^2=11.21	0.001*
Bolus application	28 (36.8)	18 (14.5)	3.44 (1.73–6.80)	χ^2=13.26	<0.001*
Concurrent chemotherapy	42 (55.3)	48 (38.7)	1.96 (1.10–3.49)	χ^2=5.22	0.022*

Statistically significant at P<0.05. Percentages were calculated column-wise. OR greater than 1 indicated increased odds of moderate-to-severe dermatitis. BMI: body mass index; OR: odds ratio;

CI: confidence interval; 3D-CRT: three-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy.
Table 4 identifies the patient- and treatment-related factors associated with moderate-to-severe acute radiation dermatitis. The use of 3D-CRT was significantly associated with increased dermatitis severity; patients treated with 3D-CRT had 2.17 times greater odds of grade 2–4 dermatitis than those treated with IMRT (95% CI: 1.21–3.89; P=0.009). Age of 60 years or older was also significantly associated with moderate-to-severe dermatitis (OR=2.54; 95% CI: 1.40–4.61; P=0.002). Overweight or obesity, defined as BMI ≥25 kg/m², was present in 64.5% of patients with grade 2–4 dermatitis compared with 36.3% of those with grade 0–1 dermatitis and was associated with more than threefold higher odds of moderate-to-severe dermatitis (OR=3.19; 95% CI: 1.76–5.78; P<0.001). Diabetes mellitus (OR=2.75; P=0.005) and current smoking (OR=2.42; P=0.018) were additional significant patient-related factors. Prominent skin folds within the treatment field demonstrated the strongest association, conferring fourfold higher odds of grade 2–4 dermatitis (OR=4.00; 95% CI: 1.96–8.19; P<0.001). Among treatment-related factors, a total radiation dose above 50 Gy (OR=2.73; 95% CI: 1.51–4.96; P=0.001), bolus application (OR=3.44; 95% CI: 1.73–6.80; P<0.001), and concurrent chemotherapy (OR=1.96; 95% CI: 1.10–3.49; P=0.022) were significantly associated with moderate-to-severe dermatitis.

DISCUSSION

The present study demonstrated that acute radiation-induced dermatitis was common in both treatment groups but occurred significantly more often following 3D-CRT than IMRT. Any-grade dermatitis was observed in 88.0% of patients receiving 3D-CRT and 76.0% receiving IMRT, while moderate-to-severe dermatitis occurred in 47.0% and 29.0%, respectively. The odds of developing any dermatitis and grade ≥2 dermatitis were approximately twice as high with 3D-CRT. These findings support the expected clinical advantage of IMRT, which improves dose conformity and reduces high-dose inhomogeneity or “hot spots” within the skin. Singh et al. (2016)[2] reported that most patients undergoing radiotherapy develop some degree of cutaneous reaction, although the reported frequency varies according to treatment site, fractionation, radiation dose, grading system, and assessment time. Kole et al. (2017)[4] similarly described acute radiation dermatitis as one of the most frequent toxicities of breast irradiation, ranging from mild erythema to moist desquamation and ulceration.

The lower dermatitis burden with IMRT in the present study agrees with Jagsi et al. (2022)[14], whose large prospective multicentre comparative-effectiveness study found that inverse-planned IMRT reduced acute breast-radiotherapy toxicity compared with 3D-CRT. The benefit was attributed primarily to improved dose homogeneity and reduced exposure of skin and subcutaneous tissue to high radiation doses. Nevertheless, the advantage of IMRT should not be considered universal.

Borm et al. (2018)[6] studied 255 patients receiving modern tangential 3D-CRT and observed grade 1, 2, and 3 dermatitis in 42.4%, 55.7%, and 2.0%, respectively. They concluded that carefully planned multi-field 3D-CRT could produce skin-toxicity outcomes comparable with those reported for IMRT. This suggests that plan quality, dose homogeneity, fractionation, treatment site, and skin-dose distribution may be as important as the nominal technique.

The maximum dermatitis grade was significantly higher with 3D-CRT than IMRT in the present study. Grade 1 dermatitis was the most common individual category overall, accounting for 44.0% of patients. Grade 2 dermatitis affected 26.5%, grade 3 affected 10.0%, and grade 4 affected only 1.5%. Although the overall five-category distribution did not reach statistical significance, the clinically relevant grouping of grade 0–1 versus grade 2–4 showed a significant difference. This apparent discrepancy was probably related to the small number of grade 3–4 events and reduced statistical power when the outcome was divided into five categories. The binary comparison more directly addressed the clinically meaningful threshold at which active treatment, dressings, closer monitoring, or interruption may become necessary.

The overall rate of grade ≥2 dermatitis in the present study was 38.0%. Pignol et al. (2015)[1] found that severe skin toxicity and pain remained important concerns during postmastectomy radiotherapy, particularly when large chest-wall areas were irradiated. Borm et al. (2018)[6] reported a higher grade 2 rate than that observed in the current study, probably because nearly all their patients received conventionally fractionated breast irradiation and most received a sequential boost. In contrast, Nanthong et al. (2025)[18] found moderate-to-severe dermatitis in 32% of 635 patients with breast cancer, which was close to the 38% overall rate in the current study. Differences between studies may be explained by variations in irradiation site, surgery, fractionation schedule, bolus use, boost treatment, prophylactic skin care, and toxicity-grading criteria.

Moist desquamation was observed in 29.0% of patients treated with 3D-CRT compared with 15.0% treated with IMRT. Pastore et al. (2016)[3] demonstrated that severe acute skin toxicity was related to the dose delivered to the skin surface and the volume of skin receiving relatively high doses. Similarly, Borm et al. (2018)[6] reported moist desquamation in 23.1% of patients and identified skin V80% as an independent risk factor. These observations support the present finding that a technique capable of improving dose homogeneity may reduce moist desquamation. Ho et al. (2018)[7] reported a higher overall moist-desquamation rate of 54.8% among women receiving postmastectomy irradiation with daily bolus. Their substantially higher rate illustrates the importance of treatment context and bolus-related surface-dose enhancement. In that trial, prophylactic mometasone reduced moist desquamation from 66.7% to 43.8%, indicating that supportive skin care may modify toxicity independently of the radiation technique.

Dermatitis appeared significantly earlier in the 3D-CRT group, with a mean onset of 14.2 days compared with 16.8 days in the IMRT group. Acute reactions commonly begin during the second or third treatment week, when repeated radiation injury exceeds the regenerative capacity of basal epidermal cells. Xie et al. (2021)[12] reported that acute radiation dermatitis generally developed two to three weeks after commencing treatment, consistent with the timing observed in the present study. Earlier onset may be clinically important because it increases cumulative time spent with symptoms and may predict progression to a higher grade. The 2.6-day delay associated with IMRT may reflect reduced high-dose skin exposure, although the practical significance of this relatively modest interval should be evaluated alongside peak grade and patient-reported symptom burden.

Radiotherapy interruption due to dermatitis occurred in 11.0% of the 3D-CRT group and 4.0% of the IMRT group. Although the difference was not statistically significant, its direction was consistent with the greater severity observed after 3D-CRT. The nonsignificant result may have arisen from the small number of interruptions, as reflected by the confidence interval crossing zero. Severe dermatitis can result in unscheduled treatment gaps that may prolong overall treatment time and potentially compromise tumour control. Current MASCC guidance therefore emphasises proactive assessment and early management of dermatitis to prevent avoidable interruption [17]. However, institutional thresholds for suspending treatment vary, making treatment interruption a less standardised endpoint than dermatitis grade.

Regarding clinical manifestations, erythema was the most frequent reaction, affecting 65.5% of patients, followed by hyperpigmentation, pruritus, dry desquamation, burning, tenderness, moist desquamation, and oedema. This pattern was consistent with the expected progression of acute radiation injury described by Singh et al. (2016)[2] and Kole et al. (2017)[4]. Lee et al. (2017)[5] demonstrated that patient-reported symptoms such as itching, burning, pain, and discomfort may develop even when clinician-assigned dermatitis grades remain relatively low. The significantly higher mean number of symptoms in the 3D-CRT group therefore provided complementary evidence that its greater clinician-graded toxicity was also accompanied by greater symptomatic burden.

Erythema, hyperpigmentation, and dry desquamation were numerically more common with 3D-CRT, but their differences did not reach statistical significance. In contrast, moist desquamation, pruritus, burning sensation, and tenderness or pain

were significantly more frequent in the 3D-CRT group. Behroozian et al. (2021)[11] observed that fractionation, irradiated tissue volume, boost treatment, BMI, and bolus application influenced different manifestations of dermatitis, including erythema, oedema, desquamation, pain, and bleeding. This supports the view that radiation dermatitis is not a single uniform outcome and that each manifestation may have different determinants. The absence of significant differences in ulceration, bleeding, or necrosis in the present study was expected because these manifestations were rare. The study was consequently underpowered to detect clinically meaningful differences in uncommon grade 4 toxicity.

The present study identified several patient-related factors associated with grade 2–4 dermatitis. Age ≥60 years increased the odds approximately 2.5-fold. Ageing skin has reduced epidermal turnover, altered microcirculation, diminished barrier function, and slower tissue repair, which may increase susceptibility. Nevertheless, the published relationship between age and acute dermatitis has been inconsistent. Some studies have identified older age as a predictor, whereas others have found younger age or no independent association. Abdeltawab et al. (2021)[10] emphasised that radiation toxicity is multifactorial and that age may be influenced by comorbidity, breast size, treatment volume, and systemic therapy. The present age association should therefore be interpreted cautiously until adjusted for these variables.

BMI ≥25 kg/m² was associated with more than threefold higher odds of moderate-to-severe dermatitis. This finding strongly agrees with the meta-analysis by Xie et al. (2021)[12], which found that BMI ≥25 kg/m² significantly increased acute dermatitis risk. A higher BMI may be associated with larger treatment volumes, deeper skin folds, increased friction, moisture retention, and greater dose inhomogeneity. Behroozian et al. (2021)[11] also identified high BMI as a predictor of oedema and pain. Nanthong et al. (2025)[18] reported that BMI ≥30 kg/m² independently increased the odds of moderate-to-severe dermatitis by approximately 2.3-fold. Thus, BMI appears to be one of the most consistent patient-related predictors.

Prominent skin folds produced the strongest observed association, with fourfold higher odds of grade 2–4 dermatitis. Skin folds create a natural bolus effect and increase local moisture, heat, and friction. These conditions amplify surface dose and promote maceration, particularly in inframammary, axillary, groin, neck, and perineal regions. Large breast or treatment volume has similarly been associated with acute toxicity in dosimetric studies [3,6]. The finding indicates that patients with pronounced folds should receive careful positioning, dose-homogeneity assessment, preventive skin care, and frequent examination of high-risk areas.

Diabetes mellitus was associated with 2.75-fold higher odds of moderate-to-severe dermatitis. Xie et al. (2021)[12] reported a pooled relative risk of 2.24 for diabetes, closely supporting the present result. Hyperglycaemia-related microvascular impairment, chronic inflammation, reduced immune function, and delayed epithelial repair may account for this association. Xie et al. (2023)[16] also identified diabetes as an independent predictor of severe acute radiation dermatitis in a prospective cohort. Optimising glycaemic control and monitoring diabetic patients closely may therefore help reduce complications, although interventional evidence remains limited.

Current smoking increased the odds of moderate-to-severe dermatitis by approximately 2.4-fold. The meta-analysis by Xie et al. (2021)[12] reported a significant association between smoking and dermatitis, with a pooled relative risk of 1.70. Smoking can impair tissue oxygenation, damage microvasculature, increase oxidative stress, and delay wound healing. Xie et al. (2023)[16] likewise identified smoking history as an independent risk factor. Smoking cessation counselling should therefore form part of supportive care before and during radiotherapy.

Among treatment-related variables, a total dose above 50 Gy increased the odds of grade 2–4 dermatitis by 2.73 times. Acute epidermal injury is cumulative and generally becomes more pronounced as the total dose and the volume of skin exposed to high doses increase. Pastore et al. (2016)[3] and Borm et al. (2018)[6] showed that skin dose-volume parameters predicted severe reactions more accurately than prescribed dose alone. Behroozian et al. (2021)[11] found that conventional 50 Gy in 25 fractions predicted desquamation and pain. Conversely, Schmeel et al. (2020)[9] demonstrated significantly lower acute skin toxicity with hypofractionated whole-breast irradiation than with conventional fractionation. Borm et al. (2021)[13] also found reduced acute radiodermatitis with hypofractionated schedules. Therefore, total dose should be interpreted together with fraction size, dose distribution, boost delivery, irradiated volume, and overall treatment time.

Bolus application was associated with 3.44-fold higher odds of moderate-to-severe dermatitis. Bolus increases the dose deposited at the skin surface by reducing the skin-sparing effect of megavoltage photon beams. Ho et al. (2018)[7] reported a high incidence of moist desquamation in postmastectomy patients treated with daily bolus. Behroozian et al. (2021)[11] found that bolus use was associated with bleeding, and Nanthong et al. (2025)[18] reported that bolus independently doubled the risk of moderate-to-severe dermatitis. The bolus finding in the present study is therefore biologically plausible and consistent with contemporary evidence. Individualised bolus schedules or alternate-day use may reduce toxicity when oncologically appropriate.

Concurrent chemotherapy nearly doubled the odds of grade 2–4 dermatitis. Chemotherapy may impair basal-cell regeneration, enhance radiosensitivity, suppress immunity, and delay repair of radiation-damaged skin. Liu et al. (2022)[15] reported that treatment-related variables, including systemic therapy and radiation exposure, contributed to acute dermatitis risk. However, the strength of this association varies by chemotherapy regimen and tumour site. Concurrent radiosensitisers used for head-and-neck, cervical, anal, and other cancers may produce different toxicity patterns from sequential chemotherapy used in breast cancer. The generic term "concurrent chemotherapy" should consequently be examined by agent, dose, timing, and treatment site.

The results collectively suggest that IMRT was associated with less frequent, less severe, and later-onset acute radiation dermatitis than 3D-CRT. However, the associations in Table 4 were unadjusted. Technique selection may have been related to tumour site, treatment volume, bolus use, dose, chemotherapy, or institutional practice. Multivariable regression is essential to determine whether 3D-CRT remains an independent predictor after controlling for these factors. Furthermore, much of the comparative literature concerns breast cancer, whereas the present study title does not specify one anatomical site. Direct comparison across heterogeneous tumour sites requires adjustment or stratification for site, dose, fractionation, target volume, bolus, chemotherapy, and skin-care protocol. Despite these considerations, the findings support risk-adapted surveillance and the use of dose-homogeneous techniques where clinically feasible.

CONCLUSION

Acute radiation-induced dermatitis was common among patients receiving external-beam radiotherapy; however, its occurrence and severity were significantly greater among patients treated with three-dimensional conformal radiotherapy than among those treated with intensity-modulated radiotherapy. Patients receiving 3D-CRT experienced earlier onset, higher maximum dermatitis grades, a greater number of cutaneous symptoms, and more frequent moist desquamation. IMRT was associated with a higher proportion of mild reactions and a significantly lower occurrence of moderate-to-severe dermatitis. Older age, elevated body mass index, diabetes mellitus, smoking, prominent skin folds, radiation doses above 50 Gy, bolus application, concurrent chemotherapy, and use of 3D-CRT were associated with increased dermatitis severity. These findings suggest that IMRT may offer a clinically meaningful advantage in reducing acute skin toxicity. Individualised treatment planning, early identification of high-risk patients, standardised skin care, and close monitoring during radiotherapy may further minimise dermatitis and prevent treatment interruption.

LIMITATIONS OF STUDY

The study had several limitations. First, its cross-sectional design established associations but could not determine causality or evaluate the complete progression and resolution of dermatitis over time. Second, the single-centre setting may limit the generalisability of the findings to institutions with different patient populations, radiotherapy equipment, planning protocols, or skin-care practices. Third, patients were not randomly allocated to 3D-CRT or IMRT; therefore, selection bias and confounding by clinical indication could have influenced the observed differences. Fourth, the study may have included patients with different tumour sites, radiation doses, fractionation schedules, treatment volumes, bolus protocols, and systemic therapies, all of which could affect skin toxicity. Fifth, dermatitis grading involved clinical judgement and may have been subject to observer variation despite the use of standard criteria. Patient-reported symptoms and quality-of-life effects were not evaluated using validated instruments. Sixth, skin-dose parameters, dose-volume histograms, treatment-plan homogeneity indices, and the volume of skin receiving high radiation doses were not comprehensively examined. Seventh, the risk-factor estimates were based on unadjusted analyses and could have been influenced by interrelationships among age, BMI, treatment technique, dose, bolus use, and chemotherapy. Finally, the relatively small number of grade 4 reactions and treatment interruptions limited the statistical power to detect group differences in these uncommon outcomes. Larger multicentre prospective studies using multivariable analysis and standardised toxicity assessment are recommended.

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