

Studying the Impact of Skin Dose on Post-Mastectomy Radiotherapy Planning for Breast Cancer

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Abstract: *Objective:* To investigate the impact of skin dose on post-mastectomy radiotherapy planning for breast cancer. *Methods:* Sixty patients undergoing radiotherapy after radical mastectomy for breast cancer were collected as research subjects and divided into a traditional group P1 and a newly designed group P2. The traditional method and a new method with the skin as an organ at risk (OAR) for dose limitation were used to set up the plans. The differences between the radiotherapy plans of the two groups were compared. All patients were followed up, focusing on the occurrence of acute skin reactions $\geq$ grade 2, to analyze whether limiting skin dose ultimately benefits patients. *Results:* According to Tables 1, 2, and 3, there was no significant increase in the target dose and the irradiated dose to organs at risk ($P > 0.05$). **Table 4** shows that the maximum skin dose decreased by 1.95%, V107% and V110% decreased by 57.32% and 73.68%, respectively, with statistically significant differences ($P < 0.05$). **Table 5** reveals that among patients without skin dose limitation, 7 developed acute skin reactions $\geq$ grade 2, whereas only 3 developed such reactions after limitation. Although the incidence of acute skin reactions $\geq$ grade 2 decreased by 13.33%, the statistical results showed no significant difference ($P > 0.05$). *Conclusion:* Limiting skin dose by considering it an organ at risk can significantly reduce the irradiated skin dose. However, reducing the skin dose in breast cancer patients does not significantly decrease the incidence of acute skin reactions $\geq$ grade 2. This suggests that reducing the skin dose in breast cancer patients does not significantly benefit them.

Keywords: Radical mastectomy; Radiotherapy; Skin reaction; Dose volume

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1. Introduction

The global number of new breast cancer cases has reached 2.26 million, surpassing lung cancer's 2.2 million cases and becoming the world's leading cancer^[1]. Combination adjuvant radiotherapy after radical mastectomy is an effective means to improve survival rates^[2,3]. However, adjuvant radiotherapy in the treatment of breast cancer may cause acute skin reactions. When the acute skin reaction is grade 2 or higher, it may lead to the interruption of radiotherapy, thereby reducing the tumor control rate. In severe cases, it can even affect the patient's quality of life^[4,5]. Some domestic scholars^[6-8] have attempted to reduce skin toxicity by creating a "skin volume" to limit skin dose. Therefore, this article explores the impact of IMRT technology on skin dose for patients after radical

mastectomy and provides suggestions for addressing skin damage.

2. Materials and methods

2.1. General information

Patients who underwent adjuvant radiotherapy after radical mastectomy for breast cancer at our hospital and Mianyang 404 Hospital from January 2022 to December 2023 were collected. Inclusion criteria: (1) Female, age ≥ 18 years old; (2) Pathologically confirmed breast cancer; (3) Patients underwent adjuvant radiotherapy after radical mastectomy. Exclusion criteria: (1) Only the chest wall area was irradiated; (2) Failed to complete the entire radiotherapy; (3) Only 90% of the target volume of the radiotherapy plan reached the prescribed dose; (4) Patients who could not be medically followed up due to geographical, social, or psychological reasons.

Patients were randomly divided into a traditional group, P_1 and a newly designed group, P_2 . The age range of the traditional group P_1 was 37–82 (median 54), while the age range of the newly designed group P_2 was 34–79 (median 53.7). There was no significant difference ($P > 0.05$), making the two groups comparable.

2.2. Methods

(1) Target Volume Delineation

All patients were positioned supine with both arms crossed in front of the forehead, immobilized using a thermoplastic head-neck-shoulder mask, and underwent contrast-enhanced spiral CT scanning with a slice thickness of 5 mm under quiet breathing. The scanned CT images were transmitted to the physician's workstation (CMS FOCAL 3.0). According to the principles outlined in ICRU Reports No. 50 and 63^[9], the gross tumor volume (GTV), including the primary tumor and positive lymph nodes^[10], was delineated by clinical physicians. The clinical target volume (CTV) was generated by expanding the GTV by 10 mm. The planning target volume (PTV) was then created by expanding the CTV by 5 mm in the anterior, posterior, left, and right directions, and by 10 mm in the superior and inferior directions, followed by retraction to 5 mm beneath the skin surface. All target volumes were delineated slice-by-slice by radiation oncologists with intermediate or higher professional titles and subsequently reviewed and confirmed by the department director with a senior professional title.

A "skin volume" was created by removing the compensator from the external contour and then retracting the resulting volume inward by 3 mm^[6,7]. This volume was used to evaluate the radiation dose delivered to the skin. For all patients, the radiotherapy plan was designed such that the prescribed dose covered 95% of the PTV volume.

(2) Treatment Plan Design

For the conventional group P_1 , an IMRT plan was designed based on the contoured target volume described above. The new design group P_2 was developed on the basis of P_1 by implementing dose constraints to the skin region, primarily restricting high doses. These constraints were progressively intensified until a target volume underdosage occurred. Radiotherapy was delivered using conventional fractionation: 50 Gy in 25 fractions over 5 weeks. It was required that at least 90% of the target volume receive the prescription dose. Dose constraints for organs at risk (OARs) were as follows: Left lung (L-lung): $V_5 < 60\%$, $V_{20} < 30\%$, $V_{30} < 20\%$, $D_{\text{mean}} < 1500$ cGy; Heart: $D_{\text{mean}} < 1000$ cGy, $V_{30} < 15\%$; Spinal cord: Cordmax < 3500 cGy; Femoral head: L-H < 5000 cGy.(3) Treatment Plan Evaluation

The dose distribution in the target area and normal organs was analyzed based on dose curves and dose-volume histograms. According to ICRU Report 83, the $D_{\max}$, $D_{2\%}$, $D_{98\%}$, and $D_{50\%}$ for the Planning Target Volume (PTV)/skin volume refer to the doses received by the maximum, 2%, 98%, and 50% volumes of the PTV/skin volume, respectively. Relevant parameters include the Homogeneity Index (HI) and the Conformity Index (CI), where $HI = (D_{2\%} - D_{98\%}) / D_{50\%}$ and $CI = (V_{T,ref} \times V_{T,ref}) / (V_T \times V_{ref})$. Here, V_T is the target volume, V_{ref} is the volume enclosed by the reference isodose line, and $V_{T,ref}$ is the target volume enclosed by the reference isodose line. An HI value closer to 0 indicates a more homogeneous dose distribution, while a CI closer to 1 indicates better conformity between the 95% prescription isodose line and the target volume. Skin volume V_{107} : the absolute volume enclosed by 107% of the prescription dose (i.e., the absolute volume enclosed by 5350 cGy). Similarly, V_{110} .

2.3. Evaluation criteria for acute skin reactions

Skin adverse reactions were evaluated according to the Acute Radiation Morbidity Scoring Criteria by the Radiation Therapy Oncology Group (RTOG) [11]:

- (1) Grade 0: No noticeable change; skin remains normal.
- (2) Grade 1: Faint erythema, dry desquamation, decreased sweating, alopecia.
- (3) Grade 2: Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema. On mucosa: marked erythema, pain, inflammatory discharge.
- (4) Grade 3: Confluent moist desquamation other than skin folds and creases; significant edema. On mucosa: ulceration, bleeding, necrosis.
- (5) Grade 4: Life-threatening or functionally severe skin or mucosal necrosis, ulceration, or fistula formation.

Evaluation was performed within 3 months after the start of radiotherapy. All patients applied a protective skin agent before radiotherapy. When acute skin reactions reached Grade 2 or higher, irradiation was immediately stopped. Wound care was provided to prevent infection, and moist burn ointment was applied if necessary. Irradiation was resumed only after the ulcerated area had healed.

2.4. Statistical analysis

Data were analyzed using SPSS 22.0 software. Except for count data, which were analyzed using Fisher's exact test, all other data were analyzed using the paired-sample t-test. All results were expressed as mean $\pm$ standard deviation (SD). A $P < 0.05$ was considered statistically significant.

3. Results

3.1. Occurrence of acute skin reactions of grade 2 or higher

In this study, a total of 77 patients undergoing radiotherapy after radical breast cancer surgery were collected. Seventeen patients were excluded (1 patient with only 90% of the target volume receiving the prescribed dose, 3 patients who did not complete radiation therapy, and 13 patients who only received radiation therapy to the chest wall area). Sixty patients were included in the study (all received radiation therapy to the chest wall and clavicle areas). Fifty-five patients (91.67%) developed acute skin reactions of grade 1, nine patients (15.00%) developed acute skin reactions of grade 2, and one patient (1.67%) developed acute skin reactions of grade 3 or higher. In the conventional plan P_1 , seven patients (23.33%) developed acute skin reactions of grade 2 or higher, while in the skin dose-limiting plan P_2 , three patients (10%) developed acute skin reactions of grade 2 or higher.

3.2. Comparison of the effects of conventional plan P1 and skin dose-limiting plan P2 on target dose

Table 1. Comparison of target doses in the chest wall region

Plan comparison	D _{max} (cGy)	CI	HI	V _{107%} (cm ³)	V _{110%} (cm ³)
P ₁	5534.20 ± 57.67	0.450 ± 0.062	0.08 ± 0.03	52.14 ± 31.68	2.29 ± 5.10
P ₂	5502.90 ± 42.73	0.451 ± 0.063	0.08 ± 0.02	40.83 ± 23.48	0.32 ± 0.60
<i>t</i> -value	2.346	0.254	1.377	3.176	2.090
<i>p</i> -value	0.066	0.601	0.179	0.04	0.046

Table 2. Comparison of target dose in the clavicle region

Plan comparison	D _{max} (cGy)	CI	HI	V _{107%} (cm ³)	V _{110%} (cm ³)
P ₁	5512.06 ± 60.34	0.599 ± 0.071	0.09 ± 0.03	13.11 ± 10.42	1.08 ± 2.38
P ₂	5489.23 ± 34.17	0.593 ± 0.073	0.09 ± 0.02	11.72 ± 8.74	0.19 ± 0.20
<i>t</i> -value	1.889	0.156	1.101	0.691	2.052
<i>p</i> -value	0.069	0.504	0.450	0.495	0.049

3.3. Comparison of the impact of conventional plan P1 and skin dose-limiting plan P2 on organ-at-risk doses

Table 3. Comparison of organ-at-risk doses

Plan comparison	Affected Lung				Heart		Spinal Cord	Esophagus D _{max}
	V ₅	V ₂₀	V ₃₀	D _{mean}	V ₃₀	D _{mean}	D _{max}	
P ₁	57.36 ± 5.11	24.61 ± 2.01	17.20 ± 1.36	1389.90 ± 52.29	6.76 ± 2.23	735.40 ± 138.25	1720.94 ± 975.82	5115.00 ± 308.44
P ₂	56.18 ± 4.56	24.91 ± 2.06	17.69 ± 1.74	1380.13 ± 50.99	6.62 ± 1.72	685.00 ± 161.07	1767.05 ± 948.31	4931.70 ± 542.96
<i>t</i> -value	0.930	-0.518	-1.164	1.322	0.256	1.238	0.296	1.536
<i>p</i> -value	0.360	0.609	0.254	0.193				

3.4. Impact of limiting skin dose on acute skin reactions

Table 4. Comparison of skin region doses

Plan comparison	D _{max}	V _{107%} (cm ³)	V _{110%} (cm ³)
P ₁	5530.47 ± 80.64	8.95 ± 5.89	0.38 ± 0.64
P ₂	5424.67 ± 63.36	3.82 ± 5.07	0.10 ± 0.23
<i>t</i> -value	6.810	3.777	2.285
<i>p</i> -value	0.00	0.01	0.03

Table 5. Impact of limiting skin dose on acute skin reactions

Group	No $\geq$ Grade 2 acute skin toxicity (n)	$\geq$ Grade 2 acute skin toxicity (n)	t-value	p-value
P ₁	23	7	1.920	0.299
P ₂	27	3		

4. Discussion

Currently, adjuvant radiotherapy after radical mastectomy remains the primary treatment for advanced breast cancer^[12–14]. However, adjuvant radiotherapy in the treatment of breast cancer may cause acute skin adverse events. Grade 2 or higher acute skin toxicity can affect patients' quality of life, and severe cases may even lead to treatment interruption, thereby reducing tumor control rates^[15–17]. Therefore, reducing skin dose and determining whether patients can truly benefit from it has always been an issue that medical workers need to pay attention to.

Zhang et al.^[8] generated skin by reducing the outer contour of the neck by 3mm, and set a plan to limit the skin as an organ at risk (OAR). Studies have shown that compared with the control group, the dIMRT technology research group reduced skin D_{mean} , V_{10} - V_{60} by 7%, 8%, 22%, 25%, 38%, 59%, and 85% respectively ($P = 0.00$, 0.00, 0.00, 0.00, 0.00, 0.00, 0.00). The results showed that limiting the dose of neck skin as an OAR could significantly reduce the exposure of neck skin. Wu's^[18] research results showed that the dIMRT technology made the newly designed group lower than the traditional group in terms of neck skin V_{10} - V_{60} and D_{mean} . The conclusion was that limiting the dose by treating the neck skin as an organ at risk could significantly reduce neck skin exposure. According to Tables 1, 2, 3, and 4, the maximum dose in the skin area decreased by 1.95%, $V_{10\%}$ and $V_{110\%}$ decreased by 57.32% and 73.68% respectively, and the differences were statistically significant ($P < 0.05$), while the target dose and the exposed dose of organs at risk did not increase significantly ($P > 0.05$). This indicates that generating skin by reducing the outer contour of breast cancer by 3 mm and limiting the dose of skin as an OAR can also significantly reduce the skin exposure of breast cancer.

Pasquier et al.^[19] designed a two-center prospective clinical study where 36.8% of patients experienced acute skin adverse reactions of grade 2 or higher, and 4 patients developed acute radiation dermatitis of grade 3, with an incidence rate of 1.38%. These findings are generally consistent with the results of this study, where among the 60 enrolled cases, 9 patients developed acute skin adverse reactions of grade 2, and 1 patient developed an acute skin adverse reaction of grade 3.

According to **Table 4**, limiting the dose to the skin as an organ at risk (OAR) can significantly reduce the skin exposure in breast cancer patients. However, as shown in **Table 5**, among patients without skin dose limitations, 7 developed acute skin reactions of grade 2 or higher. After applying the limitations, the number of patients with acute skin reactions of grade 2 or higher decreased to 3. Although the incidence of acute skin reactions of grade 2 or higher decreased by 13.33% ($P > 0.05$), this suggests that while limiting the skin dose as an OAR can significantly reduce skin exposure in breast cancer patients, reducing the skin dose in breast cancer patients does not significantly benefit the patients.

5. Conclusion

In summary, adopting dose limitations to the skin as an OAR in breast cancer can significantly reduce the radiation dose to the skin. However, reducing the skin dose in breast cancer does not significantly decrease the incidence

of acute skin reactions of grade 2 or higher. This indicates that reducing the skin dose in breast cancer does not provide significant benefits to the patients.

Disclosure statement

The authors declare no conflict of interest.

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