RESEARCH ARTICLE

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Long-Term Outcomes of Autologous Breast Reconstruction with or without Post-Mastectomy Radiotherapy

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Abstract

Background: The number of immediate breast reconstructions has significantly increased in recent years. Autologous breast reconstruction, in particular, offers superior long-term cosmetic outcomes and patient satisfaction. However, the effects of postmastectomy radiotherapy (PMRT) on autologous reconstructions remain a subject of debate. This study aims to evaluate the long-term outcomes of autologous breast reconstruction in patients who underwent PMRT compared to those who did not. **Methods:** Patients who underwent mastectomy and immediate autologous reconstruction between 2018 and 2023 were prospectively followed for complications and patient-reported outcomes. Patients were categorized into two groups: those who received PMRT (n = 43) and those who did not (n = 59). Patient-reported outcomes were assessed using the BREAST-Q questionnaire, while complications were analyzed based on clinical records. Statistical analysis included logistic regression to identify factors associated with complications and patient satisfaction. **Results:** The incidence of overall complications were significantly higher in the irradiated group (46.5%) compared to the unirradiated group (23.7%). PMRT was associated with a higher rate of fat necrosis (39.5% vs 8.5%) and flap fibrosis (9.3% vs 0%). The BREAST-Q scores for the physical well-being of the chest and satisfaction with breast reconstruction were significantly lower in the irradiated group. The psychosocial well-being scores did not differ between the two groups. Patients irradiated with the IMRT and VMAT techniques had lower complication rates and higher BREAST-Q scores compared to those treated with the 3D technique. **Conclusion:** While PMRT increases the risk of complications following autologous breast reconstruction, overall patient satisfaction remains high. The use of advanced radiotherapy techniques such as IMRT and VMAT may help mitigate some of the adverse effects associated with radiation therapy. Future research should focus on optimizing reconstruction techniques and refining patient selection criteria to enhance long-term outcomes.

Keywords: Breast reconstruction- autologous flap- TRAM flap- radiation therapy

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Introduction

The number of immediate breast reconstructions has significantly increased. Statistical data from the United States indicates that the rates of immediate reconstruction have escalated from 21% to 38% between 1998 and 2008 [1]. Immediate breast reconstruction offers several advantages, including reduced treatment costs, enhanced cosmetic outcomes, and improved psychological health benefits compared to delayed breast reconstruction [2]. Autologous reconstruction, in particular, creates more natural breast contours than prosthetic reconstruction. Women undergone autologous reconstruction tend to achieve better long-term cosmetic outcomes [3]. The lower abdomen is the most common donor site for autologous breast reconstruction due to its abundant tissue and reliable blood supply. The transverse rectus abdominis myocutaneous (TRAM) flap remains the preferred choice for pedicled flap breast reconstruction [4].

Recent studies have demonstrated that post-mastectomy radiotherapy (PMRT) effectively reduces local recurrence rates in patients with limited axillary lymph node metastasis or negative axillary nodes [5, 6]. This has led to an expansion in the indications for PMRT. However, PMRT is associated with a high incidence of complications. Earlier research has reported an increased risk of complications in patients undergoing both implant-based and autologous immediate reconstructive surgery post-radiotherapy [7]. More recent studies suggest that autologous flaps may tolerate radiotherapy better than previously indicated. The incidence and severity of complications are compared between immediate and delayed reconstruction in a post-mastectomy radiotherapy setting [8].

Technological advancements in radiation oncology have resulted in improved dose delivery and reduced normal tissue toxicity. Consequently, the impact of radiotherapy on immediate breast reconstruction with

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autologous flaps warrants re-evaluation.

The decision to choose a surgical method is influenced by factors beyond the risk of complications. Long-term aesthetic outcomes and patient satisfaction play a significant role. Long-term surgical results should be self-assessed by patients using specialized tools to ensure reliability. The BREAST-Q is currently considered the standard tool for assessing quality of life and patient satisfaction following breast surgery.

Given the ongoing debate regarding the effect of radiotherapy on the long-term outcomes of autologous breast reconstruction, this study aims to determine the impact of PMRT on complication risks, patient-reported outcomes, and health-related quality of life in the context of immediate breast reconstruction surgery with TRAM flap.

Materials and Methods

Patients and methods

This study included female patients diagnosed with stage I and II breast carcinoma, as classified by the American Joint Committee on Cancer (AJCC) 2018 guidelines. Eligible participants were between 18 and 65 years of age. All patients underwent mastectomy followed by immediate breast reconstruction utilizing the transverse rectus abdominis myocutaneous (TRAM) flap. Exclusion criteria included history of chest wall radiation, bilateral breast reconstruction, hybrid breast reconstruction (combines implant-based and autologous reconstruction), subsequent diagnosis of contralateral breast cancer, and incomplete post-treatment follow-up data.

The study was designed as a clinical investigation, enrolling all eligible patients. Clinical and paraclinical characteristics, including age, BMI, smoking, hypertension and diabetes status, and disease stage were recorded. The surgical procedure, consisting of mastectomy combined with immediate TRAM flap-based breast reconstruction, was performed following the standardized technical protocols at Vietnam National Cancer Hospital. Detailed documentation of the surgical process included the mastectomy technique and the volume of the reconstructed breast. Adjuvant therapy was administered in accordance with the treatment guidelines of Vietnam National Cancer Hospital. Patients requiring both chemotherapy and radiotherapy underwent chemotherapy first, followed by radiotherapy. Postmastectomy radiotherapy was delivered to the chest wall and reconstructed breast with or without the supraclavicular fossa. The used techniques included three-dimensional conformal radiation therapy (3DCRT), intensity-modulated radiation therapy (IMRT), or volumetric modulated arc therapy (VMAT). The used doses were 50 Gy in 25 fractions and 43.2 Gy in 16 fractions. A 10 Gy dose boost to the reconstructed breast and chest wall was used in cases with high risk features: close margins, lymphovascular space invasion (LVSI). Complications associated with the reconstructed breast were systematically documented during the postoperative period, throughout chemotherapy and radiotherapy, and during long-term follow-up. These complications included hematoma, seroma, wound infection, delayed healing, mastectomy skin flap/nipple necrosis, reconstructive flap necrosis, and fat necrosis. Major complications were defined as those necessitating corrective surgery (Dindo's classification, Level III) [9]. Reconstructive failure was defined as complete flap necrosis. Health-related quality of life was assessed using the Vietnamese version of BREAST-Q questionnaire (version 2.0). The assessment focused on three domains: psychosocial well-being, physical well-being of the chest, and satisfaction with the reconstructed breast. Patients interviews were conducted at least two years after reconstruction, either in person or via telephone. Scores were converted to a 100-point scale based on the standard BREAST-Q conversion table.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0. Descriptive statistics for qualitative variables were presented as frequencies and percentages, while quantitative variables were expressed as means and standard deviations. Proportions of patients in the irradiated group and the unirradiated group were compared using Chi-squared tests. The complication rates of each group were compared using the Fisher's Exact test. The effect of radiotherapy on the risk of complications was evaluated using a multivariate logistic regression model. Mean BREAST-Q scores between groups were compared using the Mann-Whitney U test. A two-sided significance level of $p < 0.05$ was considered statistically significant.

Ethical Consideration

This study adhered to the ethical principles outlined in the Declaration of Helsinki for biomedical research and was part of a larger study approved by the Biomedical Ethics Committee of Hanoi Medical University (Approval code: IRB-VN01.001/IRB00003121/FWA 00004148). Patients and their families were fully informed about the study's objectives and procedures. Participation was voluntary, and patients retained the right to withdraw from the study at any time.

Results

Baseline characteristics

A cohort of 102 patients diagnosed with stage I or II breast cancer who underwent mastectomy followed by immediate transverse rectus abdominis myocutaneous (TRAM) flap reconstruction between January 2018 and February 2023 was included in the analysis. All patients had a minimum follow-up period of 24 months. Among them, 43 patients (42.2%) received adjuvant radiotherapy, while 59 (57.8%) did not. Table 1 shows a detailed summary of the study population's characteristics.

The participants' age ranged from 31 to 60 years, with a mean age of 44 years. The mean body mass index (BMI) varied between 19.1 and 29.5, with an average of 22.6. There was one patient with diabetes and no patient smoking. The reconstructed breast volume ranged from 270 mL to 660 mL, with a mean volume of 386 mL. There were no statistically significant differences between the irradiated and unirradiated groups in terms of age, BMI, history of hypertension, mastectomy technique, or

reconstructed breast volume. However, the proportion of patients with stage II disease and those receiving neoadjuvant or adjuvant chemotherapy was significantly higher in the irradiated group.

Univariate and Multivariate Analysis

The overall complication rates were 46.5% in the irradiated group and 23.7% in the unirradiated group. Notably, no patient experienced total flap necrosis. Fat necrosis was the most common complication among irradiated patients, whereas seroma was the most prevalent complication in the non-irradiated group. The rates of infection, fat necrosis, and flap fibrosis were significantly higher in the irradiated group (Table 2).

The median interval from surgery to the initiation of radiotherapy was 5 (range: 3 - 6) weeks for patients who underwent neoadjuvant chemotherapy, and 28 (range: 17 - 38) weeks for those who did not receive neoadjuvant chemotherapy. A total of 21 patients (51.2%) were administered IMRT or VMAT. 5 patients (11.6%) received a radiation dose of 43 Gy. 8 patients (18.6%) were given a chest wall boost.

Table 3 details the risk of reconstructed breast complications, major complications, and fat necrosis in relation to radiotherapy indications and techniques. In both univariate and multivariate analyses, the overall complication rate, infection incidence, and fat necrosis were significantly higher in the irradiated cohort (Table 4). Furthermore, the overall complication rate and fat necrosis were significantly lower in patients who underwent intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) compared to those who received three-dimensional (3D) radiotherapy. No significant differences were observed in complication rates based on fractionation schemes or chest wall boost.

Satisfaction and Quality of Life

A total of 98 patients completed the BREAST-Q questionnaire, which assesses health-related quality of life and satisfaction with constructed breasts. Four patients with recurrence did not respond to the questionnaire.

Health-related quality of life was assessed using the BREAST-Q questionnaire, with mean scores for psychosocial well-being, physical well-being of the chest, and satisfaction with breast reconstruction reported as 82.4 ± 9.4, 82.4 ± 6.4, and 72.2 ± 9.3, respectively. Compared to the unirradiated group, patients in the irradiated group reported significantly lower scores for physical well-being of the chest and satisfaction with the reconstructed breast. Additionally, patients who underwent IMRT or VMAT reported significantly higher satisfaction with their reconstructed breast than those who received 3D radiotherapy (p = 0.003) (Figure 1).

Table 1. Characteristics of the 102 Subjects Enrolled in the Study

	Irradiated (n = 43) No (%)	Unirradiated (n = 59) No (%)	p value
Age, year			0.613*
< 40	10 (23.3)	19 (32.2)	
40 - 49	24 (55.8)	29 (49.2)	
≥ 50	9 (20.9)	11 (18.6)	
BMI, kg/m^2			>0.05**
≤ 24.9	37 (86)	50 (84.7)	
≥ 25	6 (14)	9 (15.3)	
Hypertension Stage	2 (4.7)	5 (8.5)	0.696**
I	3 (7.0)	39 (66.1)	<0.001**
II	40 (93.0)	20 (33.9)	
Mastectomy type			
MRM	14 (32.6)	18 (30.5)	0.201*
SSM	8 (18.6)	20 (33.9)	
NSM	21 (48.8)	21 (35.6)	
Reconstructed breast volume			
< 300 ml	6 (14.0)	8 (13.6)	0.847*
300 - 399ml	24 (55.8)	30 (50.8)	
≥ 400ml	13 (30.2)	21 (35.6)	
Neo/adjuvant chemotherapy	43 (100)	47 (79.7)	0.001**

BMI, body mass index; MRM, modified radical mastectomy; SSM, skin-sparing mastectomy; NSM, nipple-sparing mastectomy; * Pearson Chi-Square test; ** Fisher's Exact test

Discussion

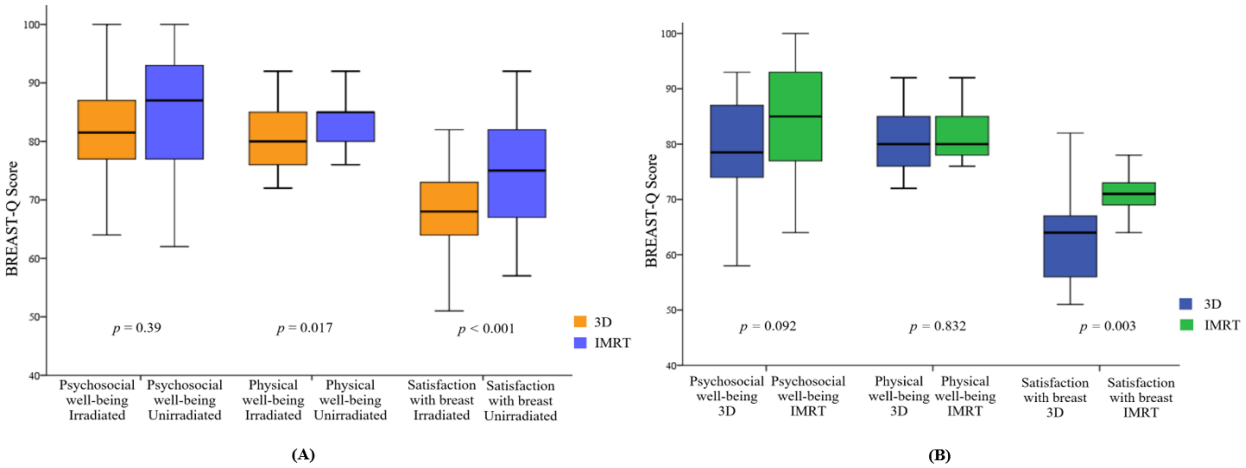
The expanding indications for adjuvant radiotherapy following mastectomy present significant challenges for immediate breast reconstruction surgery, particularly in managing complications and maintaining patient satisfaction. The impact of radiotherapy on autologous reconstruction remains a topic of debate. Through long-term follow-up of 102 cases of immediate TRAM flap breast reconstruction, our study found that the complication rate was significantly higher and satisfaction with the reconstructed breast was lower in patients who received adjuvant radiotherapy.

Among irradiated patients, the most common complications included delayed wound healing, infection,

Table 2. Complications at Reconstructed Breast in the Two Groups

	Irradiated (n = 43) No (%)	Unirradiated (n = 59) No (%)	p value
Hematoma	1 (2.3)	2 (3.4)	>0.05
Infection	6 (14.0)	1 (1.7)	0.04
Seroma	6 (14.0)	7 (11.9)	>0.05
Wound healing delayed	0 (0)	2 (3.4)	0.507
Mastectomy flap skin/nipple necrosis	2 (4.7)	4 (6.8)	0.463
Flap necrosis	6 (14.0)	4 (6.8)	0.315
Fat necrosis	17 (39.5)	5 (8.5)	<0.001
Flap fibrosis	4 (9.3)	0	0.028
Major complication	4 (9.3)	5 (8.5)	>0.05

p, Fisher's Exact test



p: Mann-Whitney U test

Figure 1. Two Years Postoperative BREAST-Q Scores by Radiation Indication (A) and radiation technique (B)

Table 3. Complication Risk by Irradiation Indications and Techniques

	Overall complication OR (95%CI)	p	Infection OR (95%CI)	p	Fat necrosis OR (95%CI)	p
Radiation	2.79	0.02	9.41	0.04	7.06	<0.001
	(1.2-6.53)		(1.09-81.29)		(2.35-21.24)	
Technique						
3D	5.33	0.015	2.35	0.412	7.31	0.005
IMRT	(1.45-19.67)		(0.38-14.47)		(1.81-29.54)	
Dose						
50 Gy	4	0.351	NS	NS	2.91	0.633
43 Gy	(0.41-39.17)				(0.3-28.55)	
Chest wall boost	0.64	0.704	NS	NS	0.17	0.119
	(0.13-3.07)				(0.02-1.53)	

p, Fisher's Exact test

fat necrosis, and flap fibrosis or volume loss. Our findings indicate that infection and fat necrosis rates were significantly higher in the irradiated group compared to the unirradiated group. However, the majority of complications observed were classified as grade I or II according to the Dindo classification. These results align with those of Carlson et al., who reported higher rates of fat necrosis and overall complications, as well as poorer aesthetic outcomes, in irradiated patients following TRAM flap breast reconstruction [10]. Similarly, a systematic review by Liew et al. concluded that the risks of fat necrosis (RR = 1.91) and flap volume loss (RR = 8.16) were significantly increased in patients undergoing adjuvant radiotherapy [11].

Radiation-induced vascular damage is considered the primary mechanism underlying many of the complications observed in irradiated reconstructed breasts. Various surgical modifications have been proposed to improve flap perfusion and mitigate these risks, including the bipediculed TRAM flap, the supercharged pedicled TRAM flap, and the free TRAM flap. Jeong et al found that fat necrosis rates were lower in patients who underwent free TRAM flap reconstruction compared to those who received pedicled TRAM flaps [12].

When analyzing the subgroup of irradiated patients, we observed that both the overall complication rate and the incidence of fat necrosis were significantly lower in those treated with IMRT/VMAT compared to those receiving conventional 3D radiotherapy. Additionally, satisfaction with the reconstructed breast was significantly higher in the IMRT/VMAT group. A study by Lee et al., which analyzed 202 patients who underwent immediate breast reconstruction and received adjuvant radiotherapy, found that IMRT significantly reduced the risk of major complications ($p < 0.001$) and reconstruction failure ($p = 0.002$) compared to conventional radiotherapy, without compromising local recurrence rates or overall survival [13]. The key advantage of advanced radiotherapy techniques such as IMRT and VMAT lies in their ability to minimize radiation hot spots and reduce skin dose exposure, thereby lowering the incidence of grade II–III acute skin complications while preserving aesthetic and survival outcomes [14].

The clinical benefit of a dose boost to the tumor bed following breast-conserving surgery is well established in enhancing local disease control. However, this comes at

Table 4. Adjusted Odds Ratio Estimates of Reconstructed Breast Complications

	Overall complication		Infection		Fat necrosis	
	OR (95%CI)	p*	OR (95%CI)	p*	OR (95%CI)	p*
Radiation	5.03	0.01	10.87	0.06	9.03	0.001
	(1.48-17.06)		(0.91-130.06)		(2.37-34.44)	
BMI						
≤ 24.9 (ref)	1		1		1	
≥ 25	3.89	0.105	6.5	0.284	0.965	0.968
	(0.75-20.15)		(0.21-200.39)		(0.18-5.38)	
Hypertension	7.94	0.091	1.93	0.733	0.31	0.42
	(0.72-87.74)		(0.05-83.18)		(0.02-5.38)	
Mastectomy type		(0.451)	NS	NS		(0.841)
MRM (ref)	1				1	
SSM	2.25	0.207			1.27	0.724
	(0.64-0.93)				(0.34-4.73)	
NSM	1.36	0.675			1.62	0.573
	(0.33-5.63)				(0.3-8.7)	
Reconstructed breast volume		(<0.001)		(0.088)		(0.011)
< 300ml (ref)						
300 - 399ml	1		6.4	0.189	1	
	14.33	<0.001	(0.4-101.94)		8.27	0.044
≥ 400ml	(2.37-86.57)		18.56	0.031	(1.06-64.57)	
	28.1	0.004	(1.31-263.34)		8.95	0.004
	(6.37-123.99)				(2.06-39.02)	
Chemotherapy	2.92	0.338	NS	NS	NS	NS
	(0.33-26.07)					

p* value for each category compared with the reference; p value from a global test of the variable (shown in parentheses).

the cost of increased acute toxicity to the irradiated area. In our study, high-risk patients received a dose boost to the chest wall, and initial findings suggested that this did not increase complication rates. Conversely, a study by Naoum et al. reported that chest wall dose boosts in reconstructed breast patients did not confer additional local disease control benefits but significantly increased the risk of complications [15]. The role of dose boosts in post-mastectomy radiotherapy remains controversial and warrants further investigation.

The ultimate objective of breast reconstruction is to improve patient quality of life without compromising oncologic outcomes. The expansion of adjuvant radiotherapy indications has the potential to elevate complication rates, thereby impacting patient satisfaction and overall quality of life. While the negative effects of radiotherapy on implant-based reconstruction are well documented, its impact on autologous reconstruction remains inconsistent across studies. In our analysis, patients in the radiotherapy group reported significantly lower scores for chest physical well-being and satisfaction with the reconstructed breast, while psychosocial well-being scores did not differ between groups (Figure 1). This aligns with findings from Steele et al., who reported significant differences in patient-reported outcomes among 412 autologous reconstruction patients ($p < 0.01$) [16]. Similarly, O'Connell et al. observed a significant reduction in satisfaction among irradiated patients undergoing immediate deep inferior epigastric perforator (DIEP) flap reconstruction ($p = 0.008$) [17]. However, a comprehensive review by Liew et al., which analyzed 21 studies involving 3,817 patients, concluded that self-reported aesthetic satisfaction and overall satisfaction rates were comparable between irradiated and non-irradiated groups [11].

A key limitation of this study, as with other research examining the effects of radiotherapy on breast reconstruction, is the inherent challenge of patient selection. The need for adjuvant radiotherapy complicates the implementation of random sampling, introducing potential selection bias. Additionally, this study focused exclusively on immediate breast reconstruction using TRAM flaps. Future research incorporating a broader range of flap techniques, such as latissimus dorsi (LD) flaps, free TRAM flaps, superficial inferior epigastric artery (SIEA) flaps, and DIEP flaps, would provide a more comprehensive understanding of the impact of radiotherapy on various autologous reconstruction methods. This, in turn, would assist both surgeons and patients in selecting the most appropriate reconstructive approach when post-mastectomy radiotherapy is anticipated.

In conclusion, post-mastectomy radiotherapy is associated with increased complication rates and lower satisfaction with breast reconstruction in patients undergoing immediate TRAM flap reconstruction.

While complications such as infection, fat necrosis, and flap fibrosis are more prevalent in irradiated patients, psychosocial well-being remains unaffected. This study underscores the need for continued research to refine reconstruction techniques and optimize outcomes for patients receiving PMRT. Additionally, advancements in radiotherapy, particularly IMRT and VMAT, demonstrate potential in reducing complication rates and enhancing patient satisfaction. Ultimately, the decision-making process for autologous breast reconstruction must carefully consider the potential effects of PMRT to ensure the best possible functional and aesthetic outcomes while maintaining oncologic safety.

Author Contribution Statement

Huy Cong Nguyen conceptualized and designed the study, collected and analyzed the data, and drafted the manuscript; Quang Hong Le supervised the study, provided essential materials, visualized several key data and critically revised the manuscript; Huy Le Trinh assisted in designing the study, data interpretation, and critically revised the manuscript; Dang Van Nguyen contributed to design the study and critically revised the manuscript. All authors reviewed and approved the manuscript before submission.

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Availability of data

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Conflict of Interest

All authors declare no conflict of interest.

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