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Considering the Optimal Timing of Breast Reconstruction With Abdominal Flaps With Adjuvant Irradiation in 370 Consecutive Pedicled Transverse Rectus Abdominis Myocutaneous Flap and Free Deep Inferior Epigastric Perforator Flap Performed in a Chinese Oncology Center

Is There a Significant Difference Between Immediate and Delayed?

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Purpose: There is an ongoing debate on the optimal sequence of radiation and breast reconstruction. The purpose of this article was to (a) assess the impact of radiation on autologous breast reconstruction and (b) analyze the best timing for autologous breast reconstruction in the setting of radiation in a Chinese population.

Methods: A retrospective review of patients undergoing breast reconstruction with autologous lower abdominal flaps between 2001 and 2014 in the Tianjin Medical University and Cancer Hospital was performed. Patients were grouped by their irradiation status (irradiated vs nonirradiated). The irradiated group was further stratified into 2 groups by the timing of irradiation (immediate breast reconstruction followed by radiation vs prior radiation and delayed breast reconstruction). The primary outcomes were early and late breast complications, secondary and revision surgeries to the reconstructed breast, whereas the secondary outcomes were aesthetic and psychological evaluations of the patients. Logistic regression was used to assess the potential association between irradiation, patient and treatment variables, and surgical outcomes.

Results: Three hundred sixty patients with 370 reconstructed breasts were included in the study. Two hundred seventy-eight cases were nonirradiated, of which 158 were immediate and 120 were delayed. Ninety-two cases were irradiated, of which 61 were immediate, and 31 were delayed. Three hundred thirty-two cases underwent pedicled transverse rectus abdominis myocutaneous flap, 38 had deep inferior epigastric perforator flap. The irradiated group had a significant increase in secondary surgery due to fat necrosis ($P < 0.001$) and in late complications ($P = 0.011$). A significant increase in flap contracture ($P = 0.043$) and an increasing trend in the severity of fat necrosis were observed when radiation was performed after breast reconstruction. However, radiation and its timing did not have an adverse impact on patients' aesthetic and psychological evaluations by the Breast-Q survey.

Conclusions: Radiation administered to the reconstructed breast mound increased the rate of late complications and the need for secondary surgery with increased abdominal flap shrinkage and contracture and the severity of flap fat necrosis. Irradiation on the reconstructed breast did not lead to worse aesthetic outcomes due to the generally different expectation in the Chinese female patients in that they were more focused on the breast shape when clothed. Immediate breast reconstruction followed by irradiated was a generally successful treatment sequence in the Chinese module.

Key Words: breast reconstruction, autologous, radiation, timing, Chinese population

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Radiation therapy is an essential treatment parameter for breast cancer patients with large tumor and/or lymph node invasion reducing local recurrence and improving disease-free survival as well as overall survival.[1,2] However, radiation treatment can have adverse effects on autologous tissues used in immediate breast reconstruction. Radiation can cause local edema, erythema, and desquamation in the short-term and significant tissue fibrosis and contracture in the long term.[3,4] For patients who wish to have autologous breast reconstruction, the effect of radiation and its timing is still controversial.[5–8] From an oncologic perspective, breast reconstruction before or after irradiation has similar survival benefits.[9] Although the National Comprehensive Cancer Network guideline suggests delaying breast reconstruction until 6 months after the completion of postmastectomy irradiation due to aesthetic considerations, some surgeons have argued that immediate breast reconstruction followed by irradiation can still achieve satisfactory outcomes and avoid the mental stress of an absent breast mound during adjuvant therapies, while maintaining cost-effectiveness.[10–13]

In this study, we performed a retrospective review of patients who had autologous breast reconstruction in our clinical oncology center to illustrate the impact of radiation on autologous breast reconstruction and analyze the best timing in our practice for autologous breast reconstruction in the setting of postmastectomy radiation.

PATIENTS AND METHODS

We retrospectively collected data of autologous breast reconstruction between May 2001 and June 2014 in Tianjin Cancer Hospital.

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TABLE 1. Patient Characteristics and Treatment Variables by Radiation Status

	Irradiated (n = 92)	Nonirradiated (n = 278)	*P*
Age, y			0.178
<40	36 (36.1%)	92 (33.1%)	
40–50	40 (43.5%)	151 (54.3%)	
≥50	16 (17.4%)	35 (12.6%)	
BMI			0.226
≤25	65 (79.1%)	220 (79.0%)	
25–30	25 (27.2%)	52 (18.8%)	
>30	2 (2.2%)	6 (2.2%)	
Follow-up, mo	31.51 ± 19.45	28.72 ± 18.29	0.06
Smoking status	2 (2.2%)	3 (1.1%)	0.789
Comorbidities			0.367
Diabetes mellitus	0 (0%)	2 (0.7%)	
Hypercoagulation	7 (7.6%)	9 (3.2%)	
Hyperlipidemia	2 (2.2%)	4 (1.4%)	
Others	2 (2.2%)	8 (2.9%)	
Pathology			0.009*
In situ	1 (1.1%)	29 (10.4%)	
Invasive	90 (97.8%)	241 (86.7%)	
Others	1 (1.1%)	8 (2.9%)	
Lymph node invasion	73 (79.3%)	47 (16.9%)	<0.001*
Neoadjuvant chemotherapy	19 (20.7%)	14 (5.0%)	<0.001*
Adjuvant chemotherapy	85 (92.4%)	244 (87.8%)	0.221
Hormone therapy	61 (71.8%)	161 (67.6%)	0.482

*Occurs when a *P* value of <0.05 was found and considered statistically significant.

BMI, body mass index.

Patients were divided into irradiated and nonirradiated groups, and the irradiated group was further stratified into 2 groups according to the sequence of radiation and breast reconstruction. Patient demographics, pathological features, treatment variables, and surgical characteristics were analyzed.

The primary outcome included early and late breast complications, secondary and revision surgery to the reconstructed breasts. Early complications included impaired flap perfusion, flap necrosis, and delayed wound healing. Late complications referred to flap parenchymal changes, which included fat necrosis and flap contracture. The secondary outcomes were aesthetic and psychological evaluations completed by the individual patients.

Impaired flap perfusion was defined as arterial occlusion or venous congestion that leads to changes in flap turgor with noticeable dark skin color changes. Secondary surgery referred to surgical interventions to the reconstructed breasts to address any early complications and fat necrosis. Revision surgery referred to revisions of the reconstructed breasts to achieve better contour and shape and overall symmetry. Fat necrosis was defined as a palpable firm mass 1 cm or greater that persisted 3 months or longer clinically or any palpable mass diagnosed by imaging or pathology. The change of fat necrosis was described as any change in the firm/necrotic area inspected clinically or by imaging between clinical visits. Breast-Q[14] modules for breast reconstruction were adopted to evaluate aesthetic and psychological outcomes and contained a series of questions assessing breast symmetry, contour, softness, and psychological status.

Patients were followed up clinically at 3 months and at least 1 year postirradiation in the immediate breast reconstruction followed by irradiation group, or at 3 months and at least 1 year postoperatively in the remaining groups. This time interval was selected because radiation was usually initiated at 4 to 5 months postoperatively in our clinical center, and we aimed to record a baseline of complications and aesthetic evaluations at 3 months postoperation to better assess the subsequent influence of radiation on surgical outcomes.

The review board of Tianjin Oncology Hospital approved this study.

Statistical Analysis

χ^2 test was used to compare the differences for categorical variables, and Mann-Whitney *U* test was used to compare the differences for continuous variables.

Univariate and multivariate analyses were used to identify the potential association between irradiation, patient and treatment variables, and surgical outcomes. A *P* value less than 0.05 was considered significant. We performed the analysis in SPSS 21.0.

RESULTS

Three hundred sixty Chinese patients who underwent 370 cases of breast reconstruction were reviewed, 92 cases received radiation therapy, and 278 cases did not. The median patient age was 42 years, the median body mass index was 23.34, and the median follow-up duration was 21 months. Within the nonirradiated group, 158 cases had immediate reconstruction, and 120 cases had delayed reconstruction. Within the irradiated group, 61 cases had immediate breast reconstruction followed by radiation (IBR + XRT), 31 cases had prior radiation and delayed breast reconstruction (XRT + DBR).

External beam irradiation was used in all patients with a total dosage of 4000 to 5040 cGy, 20 to 28 fractions over a total of 4 to 5 weeks. Only 1 case had a 500-cGy boost to the tumor bed.

Patients' characteristics, treatment variables, and surgical characteristics were similar between the irradiated and nonirradiated groups, with the exception that a higher percentage of patients in the irradiated group had invasive breast cancer ($P = 0.009$), lymph node invasion ($P < 0.001$), and received neoadjuvant chemotherapy ($P < 0.001$). Typically irradiated patients manifest larger invasive tumor size and/or more lymph node invasion with neoadjuvant chemotherapy performed to downgrade the tumor staging before mastectomy. More patients elected to undergo free flap reconstruction in the nonirradiated group ($P = 0.011$) (Table 1 and Table 2). Forty-two patients were missing

TABLE 2. Surgical Characteristics by Irradiation Status

	Irradiated(n = 92)	Non-radiated (n = 278)	*P*
Timing of reconstruction			0.109
Immediate	61 (66.3%)	158 (56.8%)	
Delayed	31 (33.7%)	120 (43.2%)	
Flap type			0.011*
Pedicled TRAM	89 (96.7%)	243 (87.4%)	
DIEP	3 (3.3%)	35 (12.6%)	
Pedicle type			0.262
Ipsilateral	3 (3.4%)	20 (8.2%)	
Contralateral	80 (89.9%)	211 (86.8%)	
Bilateral	6 (6.7%)	12 (4.9%)	
Zones			0.221
Hemi-flap	7 (7.6%)	34 (12.2%)	
Cross midline flap	85 (92.4%)	244 (87.8%)	

*Occurs when a *P* value of <0.05 was found and considered statistically significant.

during the follow-up, and patients' characteristics were similar between those who completed the follow-up and those who did not, except that a higher percentage of patients who were missing in the follow-up had invasive breast cancer and had single-pedicled transverse rectus abdominis myocutaneous flap (TRAM) flap reconstruction (Supplementary Table 1, http://links.lww.com/SAP/A199). Therefore, it was considered appropriate to only compare the surgical outcomes between irradiated and nonirradiated patients who had completed the follow-up.

Effects of Radiation on Surgical Outcomes

No significant differences were observed in early breast complications (Table 3); however, a significant increase was noted in late breast complications in the irradiated group ($P = 0.009$). The overall occurrence of fat necrosis was significantly higher (23.3% vs 13.6%, $P = 0.037$) in the irradiated groups. The severity of fat necrosis in terms of the size of the necrotic mass also increased significantly in the irradiated group ($P = 0.005$); however, the rates of new fat necrosis was similar between the 2 groups ($P = 0.606$). There was also a significant increase in flap contracture in the irradiated group ($P = 0.006$) (Table 4). Patients in the irradiated group had higher rates of secondary surgery to take out fat necrosis ($P < 0.001$). Secondary surgery that was not related to fat necrosis and revision surgery was similar between the 2 groups ($P = 0.057$, $P = 0.990$) (Table 3). Aesthetic and psychological evaluations were not significantly different between the 2 groups ($P > 0.05$) (Table 5). Figures 1 to 4 demonstrated examples of patients from different groups who expressed satisfactory results.

Effects of Timing of Radiation on Surgical Outcomes

To further investigate whether the timing of radiation has any effects on the reconstructed breasts, we evaluated the differences in surgical outcomes after patients were stratified by the sequence of radiation and breast reconstruction in the irradiated group. Patients in the IBR + XRT group had longer follow-up duration (34.03 ± 20.43 months vs 26.11 ± 16.19 months, $P = 0.029$), and fewer smokers (0% vs 6.5%, $P = 0.035$). Other patients' characteristics and treatment variables were similar between the 2 subgroups (Supplementary Table 2, http://links.lww.com/SAP/A199).

The incidence of early breast complications and secondary surgery was not significant between the subgroups ($P = 0.572$, $P = 0.475$). However, a significant increase in flap contracture ($P = 0.043$) and a trend of increased severity of fat necrosis ($P = 0.072$) were observed in the immediate breast reconstruction followed by irradiation. A higher percentage of patients in the delayed reconstruction group received revision surgery to the reconstructed breasts ($P = 0.003$) (Table 6 and Table 7). Patients' aesthetic and psychological evaluations were similar between the subgroups (Supplementary Table 3, http://links.lww.com/SAP/A199). Moreover, no significant change of aesthetic evaluation in the same patient was observed before and after irradiation in the IBR + XRT group (Table 8).

TABLE 3. Early Breast Complications, Secondary Surgery, and Revision Surgery of the Reconstructed Breasts by Irradiation Status

	Irradiated (n = 92)	Nonirradiated (n = 278)	P
Early breast complications			
Overall complications	15 (16.3%)	29 (10.4%)	0.131
Impaired perfusion	8 (8.7%)	17 (6.1%)	0.393
Partial necrosis	5 (5.4%)	6 (2.2%)	0.211
Delayed wound healing	9 (9.8%)	16 (5.8%)	0.182
Secondary surgery	17 (18.5%)	16 (5.8%)	<0.001*
Fat necrosis related	16 (17.4%)	11 (4.0%)	<0.001*
Non fat necrosis related	7 (7.6%)	7 (2.5%)	0.057
Revision surgery	4 (4.3%)	13 (4.3%)	0.990

*Occurs when a P value of <0.05 was found and considered statistically significant.

TABLE 4. Late Complications by Irradiation Status

	Irradiated (n = 86)	Nonirradiated (n = 242)	P
Overall late complications	23 (26.7%)	33 (13.6%)	0.009*
Overall Fat necrosis	20 (23.3%)	33 (13.6%)	0.037*
Change of fat necrosis between intervals			
Newly developed	2 (2.3%)	2 (0.8%)	0.606
Increased severity	4 (4.7%)	0 (0%)	0.005*
Flap Contracture	5 (5.8%)	1 (0.4%)	0.006*

*Occurs when a P value of <0.05 was found and considered statistically significant.

Factors Affecting Late Breast Complication Rates

We evaluated potential factors that were associated with late breast complications. Univariate and multivariate logistic regression analyses demonstrated that irradiation (odds ratio, 2.06; 95% confidence interval, 1.08–3.92; $P = 0.028$) and neoadjuvant chemotherapy (odds ratio, 2.58; 95% confidence interval, 1.07–6.19; $P = 0.034$) were significantly associated with late breast complications.

DISCUSSION

Laboratory studies revealed that radiation increased local sedimentation of collagen, affected angiogenesis of vascular beds, and therefore increased fibrosis in human tissues.[15] These, in theory, would lead to impaired perfusion and increased parenchymal changes in the reconstructed breasts. Since Spear et al[16] first clinically reported that irradiation had adverse effects on aesthetic outcomes and increased flap contracture in breast reconstruction in 2005, a handful of clinical studies have been conducted to illustrate this effect, but the results were inconsistent.[11,17–21] This study specifically focuses on the Chinese cohort to evaluate the potential radiation effect and find the best timing for radiation therapy.

TABLE 5. Patients' Aesthetic and Psychological Evaluations by Breast-Q Reconstruction Module by Irradiation Status

	Irradiated (n = 86)	Nonirradiated (n = 242)	P
Aesthetic evaluation 3 months postoperative	66.49 ± 16.40	66.68 ± 15.42	0.882
Aesthetic evaluation >1 year postoperative	66.40 ± 17.47	67.88 ± 15.86	0.595
Psychological evaluation	73.00 ± 25.20	76.44 ± 23.23	0.397

*Occurs when a P value of <0.05 was found and considered statistically significant.

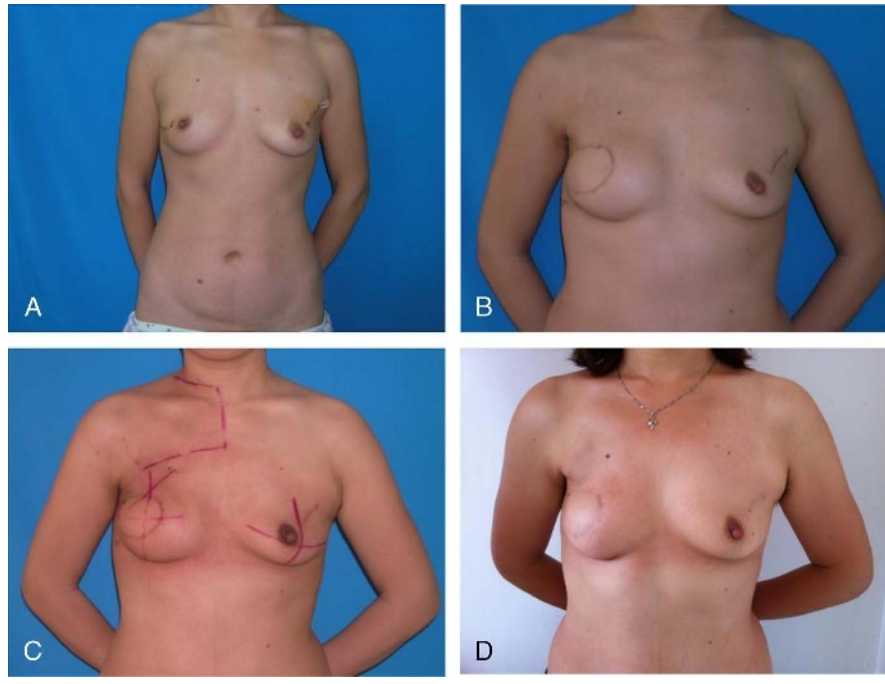

FIGURE 1. A, (above left) Preoperative photograph of a 38-year-old patient diagnosed with invasive ductal carcinoma in the right breast. She had right mastectomy and axillary lymph node dissection and immediate unilateral pedicled TRAM reconstruction followed by adjuvant chemotherapy, radiation and anti-Her2 therapy. B, (above right) 3 months postoperative. C, (below, left) 6 months postoperative, during radiation therapy. D, (below, right) 2 years postcompletion of radiation therapy.

In the meta-analysis reported by Kronowitz and Barry and Kell,[7,8] a significant increase in overall postoperative complications was observed in patients who underwent irradiation; Schaverien et al[5] reported, on the other hand, that the surgical complication rates were similar between irradiated and nonirradiated patients when fat necrosis was singled out from overall complications. It seemed confusing that some studies included donor and recipient site complications altogether as overall complications to investigate the impacts of irradiation when radiation was only conducted on the recipient site. Also, it was again confusing that most studies included fat necrosis and early wound healing complications together as early breast complications to investigate the effects of irradiation, but in our clinical settings, radiation therapy usually starts 4 to 5 months postoperation, and by that time, early wound healing complications might already have occurred and resolved. In our study design, we used late complications, which included fat necrosis and flap contracture, to denote parenchymal changes of the breast flap in the long term; and we also set 2 clinical assessment points, one before and one after radiation therapy in the IBR + XRT group to better demonstrate the impacts of irradiation on parenchymal changes and aesthetic result.

Our patient cohort demonstrated that irradiation did not have adverse effects on early breast complications; however, it did lead to significant parenchymal changes, especially the occurrence of flap contracture. Although Kelley et al[22] reported that the timing of irradiation did not affect postoperative complications, we did notice an increase in flap contracture when radiation was performed after immediate breast reconstruction, which was in accordance with the study by Berbers et al.[23] Our study also demonstrated that an increased rate

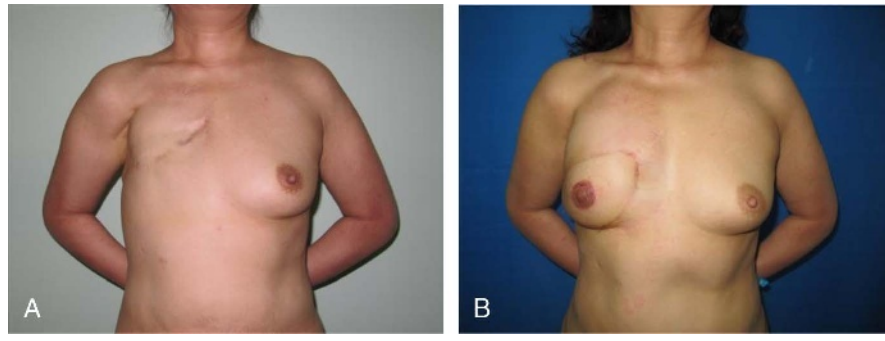

FIGURE 2. A, (left) Preoperative photograph of a 44-year-old patient who had previous right mastectomy and axillary lymph node dissection followed by adjuvant chemotherapy, radiation therapy, and hormonal therapy. She underwent unilateral pedicled TRAM reconstruction. B, (right) 2 years post delayed breast reconstruction.

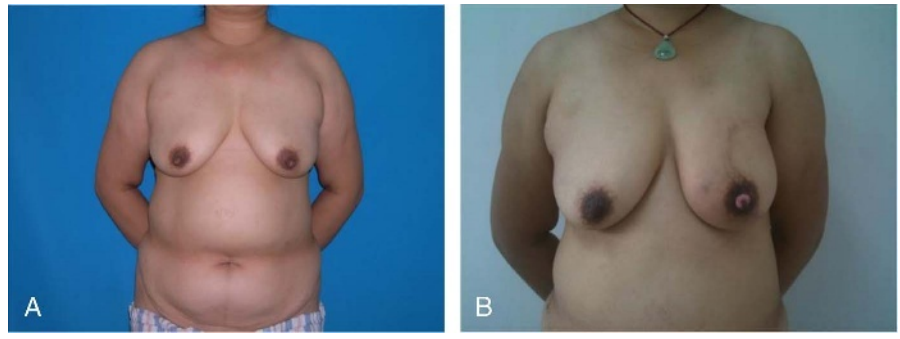

FIGURE 3. A, (left) Preoperative photograph of a 41-year-old patient diagnosed with invasive ductal carcinoma in the left breast. She underwent left nipple sparing mastectomy, axillary lymph node dissection, and immediate pedicled TRAM breast reconstruction followed by chemotherapy and hormonal therapy. B, (right) 2 years postoperative.

of overall fat necrosis affected the need for secondary surgery in the irradiated patients.

It was interesting to notice a trend that irradiation on the reconstructed breast had adverse effects on fat necrosis in that it increased the severity of fat necrosis already present rather than increasing the chance of newly developed fat necrosis. We therefore recommended surgical intervention to resolve the palpable firm mass in the reconstructed breasts with pathological confirmation before radiation in order to decrease the potential subsequent impact of radiation which could adversely affect the breast shape and final outcome. It was to argue when would be the best timing of this surgery, as chemotherapy would have adverse effect on the wound healing process and increase the risk for infection.[24] And the radiologists would be concerned with the delay in the initiation of radiotherapy would affect oncological outcomes. Early studies[25–27] revealed that an interval of more than 12 weeks between the surgery and the start of adjuvant therapy would cause oncological concerns. In the Memorial Sloan-Kettering algorithm[28] for immediate tissue expander and implant reconstruction for stage II and stage III breast cancer patients that underwent mastectomy and axillary lymph node dissection, the time for permanent implant replacement occurred at a median of 4 weeks after the completion of adjuvant chemotherapy. A median treatment interval of 8 weeks between the end of chemotherapy and the start of radiotherapy enabled acceptable 5-year locoregional control, distant metastasis-free survival, and overall survival. Therefore, in our later practice, we suggested the patients to resolve the fat necrosis 2 to 3 weeks after the last cycle of chemotherapy at which time the effect of chemotherapy on the peripheral blood count usually had worn away, and the extent of fat necrosis would most possibly be steady; and the patients continued to have radiation therapy 4 to 5 weeks after the completion of chemotherapy. Further observations will be needed to evaluate this treatment sequence, and further studies will be conducted to reveal the best timing for this

FIGURE 4. A, (above left) Preoperative photograph of a 40-year-old patient with previous right mastectomy and axillary lymph node dissection. She had adjuvant chemotherapy and hormonal therapy and underwent DIEP reconstruction. B, (above right) 8 months post-DIEP reconstruction. C, (below left): 1 year and 9 months post-DIEP reconstruction.

TABLE 6. Early Breast Complications, Secondary Surgery, and Revision Surgery of the Reconstructed Breasts Stratified by Timing of Radiation in Irradiated Patients

	IBR + XRT (n = 61)	XRT + DBR (n = 31)	*P*
Early breast complications			
Overall complications	9 (14.8%)	6 (19.4%)	0.572
Impaired perfusion	3 (4.9%)	5 (16.1%)	0.081
Partial necrosis	2 (3.3%)	3 (9.7%)	0.216
Delayed wound healing	7 (11.5%)	2 (6.5%)	0.429
Secondary surgery	10 (16.4%)	7 (22.6%)	0.475
Fat necrosis related	10 (16.4%)	6 (19.4%)	0.725
Non fat necrosis related	4 (6.6%)	3 (9.7%)	0.600
Revision surgery	0 (0%)	4 (12.9%)	0.003*

*Occurs when a *P* value of <0.05 was found and considered statistically significant.

kind of operation to obtain the best wound healing while maintaining oncological safety.

Our data found an increased rate of revision surgery when radiation was performed before rather than after breast reconstruction; however, no statistical difference was observed between irradiated and nonirradiated patients. Because more patients with delayed breast reconstruction were willing to accept revision surgery in our cohort, we attributed this difference to the timing of reconstruction rather than the impact of irradiation.

It is generally accepted that postoperative irradiation has adverse effect on breast aesthetics, especially in the spectrum of breast symmetry.[6,16] Some authors argued that radiation before or after breast reconstruction had substantially similar aesthetic results.[12,18] In our cohort, the aesthetic and psychological evaluations by the patients were not affected by irradiation or its timing. Moreover, the aesthetic outcome was also similar before and after irradiation in patients who had immediate breast reconstruction followed by radiation therapy. Our 3 examples were typical of the patients from the different groups, which had similar Breast-Q ratings, although the aesthetic outcomes may be different in the eyes of the surgeons. We attributed this to the following aspects: our Chinese cohort of female breast cancer patients may well have different expectations than western patients in general, in that most of our patients would focus on the appearance of breast shape when clothed rather than unclothed. Although Breast-Q has been widely used in the western society, this survey put an emphasis on breast aesthetics unclothed, so we could argue that a different result might be reached provided that the aesthetic outcomes were evaluated by a third blind party of surgeons, or a more appropriate survey could be designed specifically for Chinese female patients. There was a possibility that the improvement in radiation precision might also reduce the adverse impact on autologous tissues because 85.2% of the patients in the IBR + XRT group received either 3-dimensional conformal radiotherapy or intensity-modulated radiation therapy; furthermore, either irradiation on internal mammary regions or tumor bed boost was rarely used. It was also worth mentioning that contrary to western practices, the mastectomy and breast reconstruction were performed by the same breast surgeons in our center, which could lead to different expectations, whereas the patients might hold higher aesthetic expectations typically held for the plastic surgeons. Although we failed to establish that immediate breast reconstruction had any aesthetic advantages over delayed breast reconstruction in our study, we did notice a slight benefit in psychological status in immediate breast reconstruction ($P = 0.049$, Supplementary Table 4, http://links.lww.com/SAP/A199).

Contrary to western practices, a relatively large fraction (40.8%) of our cohort received delayed breast reconstruction because the breast surgeons would advise patients with locally advanced breast cancer delay their breast reconstructions, and because we had a large number of patients with referrals. It was plausible to understand that although this delayed group of patients would have some lowered expectations, but perhaps more would want the best results possible because they were more prepared to undergo a series of revision surgery after breast reconstruction, and because delayed breast reconstructions were not covered by health insurance in China.

In our clinical center, both the pedicled TRAM and the deep inferior epigastric perforator flap (DIEP) were used for autologous breast reconstruction. Although the DIEP flap has gained popularity in the recent decades, because it uses dominant blood supply of the lower abdomen, can reduce abdominal morbidity, there is still the perspective that the DIEP flap cannot completely replace the pedicled TRAM because it increases the potential flap failure, increases operative time, and demands meticulous skill for flap dissection.[29–32] There is no clinical evidence to date that the pedicled TRAM has worse recipient site outcomes compared with other free flaps in the setting of irradiation.[33–35] In our cohort, 89.7% of the cases were reconstructed with pedicled TRAM, whereas 10.3% with DIEP, and more pedicled TRAM patients received irradiation ($P = 0.011$); however, the rates of fat necrosis and flap contracture were not statistically different ($P = 0.931$, $P = 0.264$, Supplementary Table 5–6, http://links.lww.com/SAP/A199) as well as the aesthetic and psychological evaluation by Breast-Q (Supplementary Table 7, http://links.lww.com/SAP/A199). Pedicled TRAM still can be a feasible option that tolerates irradiation well in breast reconstruction. Although some western literatures[32,36,37] suggested that pedicled TRAM flap was more prone to develop fat necrosis compared with DIEP, there was a wide range of occurrence of fat necrosis of pedicled TRAM (11.4%–58.8%) that could be attributed to surgeon and/or patient selection difference. There was a limited data comparing these 2 types of flap in the Chinese population. In a matched-pair analysis by Tan et al[38] in a single Singaporean institution, no significant difference in fat necrosis was noted between pedicled

TABLE 7. Late Complications Stratified by Timing of Radiation in Irradiated Patients

	IBR + XRT (n = 58)	XRT + DBR (n = 28)	*P*
Overall late complications	16 (27.6%)	7 (25.0%)	0.799
Overall fat necrosis	13 (22.4%)	7 (25.0%)	0.791
Change of fat necrosis between intervals			
Newly developed	2 (3.4%)	0 (0%)	0.206
Increased severity	4 (6.9%)	0 (0%)	0.072
Flap Contracture	5 (8.6%)	0 (0%)	0.043*

*Occurs when a *P* value of <0.05 was found and considered statistically significant.

TABLE 8. Comparison of Patients' Aesthetic Evaluation Before and After Irradiation in the IBR + XRT Group

	3 mo Postoperative	≥1 y Postradiation	*P*
IBR + XRT (n = 58)	68.67 ± 16.85	67.63 ± 17.44	0.432

*Paired sample *t* test.

TRAM and DIEP flaps (25% vs 18.8%, $P > 0.05$). In our data, the occurrence of fat necrosis in pedicled TRAM and DIEP was 16.2% and 15.6%, respectively. It could be attributed to the reason that a low proportion of our patients were smokers (1.4%) or obese (2.2%). There was still a possibility that our results were biased because pedicled TRAM was the major type of reconstruction in our patient group, and by the retrospective nature of our study.

Based on our results, although IBR + XRT increased the occurrence of flap contracture and developed a tendency toward more severe fat necrosis when comparing with XRT + DBR, we failed to establish that XRT + DBR had aesthetic advantages over IBR + XRT in Chinese population, as opposed to the National Comprehensive Cancer Network guidelines. Similarly, satisfactory aesthetic outcomes were reported by surgeons performing immediate breast reconstructions followed by irradiation.[5,19] We consider IBR + XRT a generally successful treatment sequence in that it reduces the number of surgical procedures; however, the patients are to be informed of higher chances of flap contracture, and specifically for patients who may initially demonstrate flap fat necrosis within the flap in the IBR + XRT module, surgical intervention to excise the fat necrosis is recommended before the initiation of radiation.

Early studies pointed out neoadjuvant chemotherapy did not increase early postoperative complication rates or reoperation rates[39]; however, it was associated with skin complications in irradiated patients.[40] In our patient database, logistic regression analysis found irradiation and neoadjuvant chemotherapy to be risk factors associated with late breast complication. Due to the retrospective nature of this study, we were unable to separate these 2 factors as more irradiated patients received neoadjuvant chemotherapy in our cohort. Further prospective and randomized studies are needed to clarify the effect of each factor and their interactions. A more objective method and detailed quantification of fat necrosis and flap contracture are suggested in the future to better assess the effects of irradiation. Furthermore, due to the relatively small sample size of the study, we were unable to assess the effects of different radiation technology, fractionation, radiation field, regional boost, and so on. More high-level evidence is required to shed light on these issues and to help surgeons devise the optimal algorithm for breast reconstruction patients in the setting of irradiation.

CONCLUSIONS

Irradiation causes tissue damage by increasing the severity of fat necrosis and rates of flap contracture in reconstructed breasts. However, contrary to our anticipation, perhaps due to different expectations by Chinese female patients, irradiation on autologous reconstructed breast had similar long-term aesthetic and psychological outcomes as delayed breast reconstruction after irradiation. Contrary to the western conception, Breast-Q may not be the optimal module for Chinese female patients who are more focused on the breast shape when clothed. We do believe that there are variables that may contribute to the aesthetic difference in the Chinese population, although we were unable to identify them in this study. We are now in the process of adapting the Breast-Q into a more population specific form.

Comparing with delayed breast reconstruction after radiation, immediate breast reconstruction followed by irradiation can be a successful treatment sequence for the Chinese population because it reduces the number of surgical procedures, avoids the loss of breast mound, while still maintaining a similar aesthetic grading by the patients. Nevertheless, for patients who have already developed fat necrosis, prompt surgical intervention is advocated before the initiation of radiation therapy. Chinese breast cancer patients who need postoperative radiotherapy may potentially benefit from the treatment sequence of immediate breast reconstruction followed by irradiation. Careful patient selection, evaluation, and informed consent are suggested to mitigate the possible physical as well as psychological effects of irradiation associated with breast reconstruction.

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