Short-term Outcomes and Safety of Radiotherapy for Immediate Breast Reconstruction with Autologous Flap Transfer Following Breast-conserving Surgery

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Abstract

Background: The outcomes of immediate autologous breast reconstruction (IABR) after partial mastectomy followed by postoperative radiotherapy (RT) in terms of aesthetics, treatment-related complications, and local control are unclear. In this study, we evaluated the efficacy of IABR after partial mastectomy with or without breast RT, and thus the impact of radiation on autologous flap transfer.

Method: A retrospective cohort study involving consecutive breast cancer patients who underwent IABR after partial mastectomy between July 2011 and December 2017 at Shengjing Hospital was performed. Patients were divided into two groups based on whether or not they received RT after IABR. We compared aesthetic outcomes and changes in the flap size over the three-dimensional coordinates at various timepoints (pre-RT, 1, 6, and 12 months post-RT), as well as postoperative complications, survival, and recurrence rates between the two groups.

Results: No significant difference was found in the rate of regional recurrence between the two groups (3.13% vs. 3.85%, P=1.00), and no local recurrences occurred in either group. At the timepoints pre-RT, 1, and 6 months post-RT (approximately 4, 7, and 12 months after IABR, respectively), 77 (91.7%), 70 (83.3%), and 83 (98.8%) patients, respectively, had achieved very good or good cosmetic outcomes, and only changes in breast skin color at 1 month after RT (7 months after IABR) significantly differed between the RT and non-RT groups, with very good or good cosmetic result rates of 62.5% vs. 96.2%, respectively (P<0.001). No significant difference in the reduction of flap size was observed at any timepoint between the RT and non-RT groups. The flap size was significantly reduced at 4 months after IABR compared with the initial size during surgery, and then tended to be stable in both groups. There were no significant differences between the two groups in the rates of postoperative complications including necrosis of the flap, infection, hematoma, or seroma (all P>0.05). Finally, no grade 3 or greater RT-associated adverse events occurred during or after RT.

Conclusion: RT following IABR provides aesthetically satisfactory results without intolerable adverse complications and may safely be performed in patients who underwent IABR after partial mastectomy.

Introduction

Breast-conserving surgery (BCS) combined with postoperative radiotherapy (RT) has been commonly used in patients with early breast cancer [1, 2]. BCS is sometimes called lumpectomy, quadrantectomy, partial mastectomy, or segmental mastectomy depending on how much tissue is removed. Some selective breast cancer patients with larger tumor to breast ratio can undergo oncoplastic surgery after partial mastectomy, thus avoiding total mastectomy and obtaining better breast appearance [3-5]. Relational data have shown that the rate of positive margins in patients undergoing oncoplastic BCS was significantly lower than that of traditional BCS, and there were no differences in either overall survival rates or relapse-free survival rates between the two techniques [4]. Tissue-expander/implant and autologous tissue reconstruction are the two major surgical approaches to breast reconstruction. Previous studies have demonstrated that patients who received autologous tissue grafting are more satisfied with their breasts and attain higher levels of mental and sexual health than those who received implant-based reconstruction [6-8].

Various studies [9-13] have shown that immediate autologous breast reconstruction (IABR), including autologous fat grafting and myocutaneous flap transfer, is an alternative method for some patients who received BCS, with better aesthetic results and safety, lower rates of surgical complications, and higher overall survival rates.
compared with traditional BCS or implant-based reconstruction. Additionally, IABR has other advantages over delayed reconstruction such as a shorter total operative time, less scarring, and decreased psychological distress for the patients [14, 15].

However, the current indications for adjuvant RT after oncoplastic BCS still refer to the criteria for traditional BCS [16]. Importantly, it is unclear whether adjuvant RT after IABR following conserving surgery would have harmful effects on autologous tissue flaps, improve survival rates, or reduce local regional recurrence in patients who have undergone reconstructive surgery. Thus, the aim of this study was to observe the efficacy, aesthetic effect, changes in flap size, and complications of RT after IABR following conserving surgery.

Patients And Methods

Study population selection

We retrospectively reviewed clinical data of breast cancer patients who underwent partial mastectomy and IABR at Shengjing Hospital of China Medical University between July 2011 and December 2017. All enrolled patients underwent a wide tumor excision with negative margins and immediate reconstruction with a latissimus dorsi (LD) flap or free dermal fat graft (FDFG) All postoperative patients received primary systematic therapy including adjuvant chemotherapy, targeted therapy, and endocrine therapy, according to their clinicopathological staging and molecular classification. Breast RT or not depends on the indication of RT after BCS and surgical margin. In the early days of IABR in our center, surgeons generally allow patients with safety margin greater than 1 cm and lack of other RT indications to avoid RT. Patients were divided into two subgroups, the RT and non-RT groups, according to whether or not RT was given. Patients in the RT group received whole breast RT at approximately 4 months after surgery, with or without boost irradiation to the tumor bed. The radiation dose was scheduled as 50 Gy in 2-Gy per fraction for the whole breast RT phase, and 10 Gy in 2-Gy per fraction for the boost phase. All eligible patients underwent chest three-dimensional computed tomography (CT) scans at four timepoints: pre-RT (T0), 1 month post-RT (T1), 6 months post-RT (T6), and 12 months post-RT (T12) (corresponding to 4, 7, 12, and 18 months post-surgery, respectively), and the timepoint of IABR was defined T−4 (Fig. 1). All patients were followed up for more than 2 years after IABR. The study protocol was approved by the relevant institutional review committees, and all participants provided signed comprehensive informed consent forms to participate in the retrospective cohort study.

Data collection and main outcome measures

The data collected included age, performance status, tumor stage, histological and molecular classification, methods of breast reconstruction, extent of resection, adjuvant chemotherapy, adjuvant RT and RT doses, dates and sites of recurrences or metastases, date and cause of death, aesthetic outcomes, safety, and date of last follow-up.

The main outcome measures were aesthetic outcomes, the reduction in flap size compared with the initial implanted flap, and complications of surgery and/or RT. The cosmetic results after IABR, including breast scarring, shape, symmetry, skin color, and nipple position, were evaluated using the four point professional aesthetic assessment scale (very good, good, satisfactory, and poor) [17, 18] at the timepoints T0, T1, and T6. Flap size, including the longest and shortest diameters, and maximum thickness of the flap were measured
independently by one radiologist and one radiation oncologist based on three-dimensional CT scans performed at T−4, T0, T1, T6, and T12. The reduction of the longest diameter (LRi) was calculated by subtracting the longest diameter of the flap at T−4 (Lf) from longest diameter at the different timepoints (Li), i.e., LRi = Li−Lf. The reduction of shortest diameter (SRi = Si−Sf) and the reduction in maximum thickness (TRi = Ti−Tf) were calculated similarly.

Statistical analysis

All statistical analyses were performed using the SPSS statistical software version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation (SD) and were analyzed using the Student’s t-test. Survival curves of disease progression were drawn using the Kaplan–Meier method and compared using the log-rank test. The chi-square test and Fisher exact test were used for inter- and intra-group analyses, respectively. The accepted level of significance was P<0.05.

Results

Patient characteristics

In total, 84 patients with stage I–III breast cancer who underwent BCS and IABR were included. Their mean age was 46 (range: 28-72) years. Among them, 57 patients underwent IABR with LD flaps and 27 underwent IABR with FDFG. There were 32 and 52 patients in the RT and non-RT groups, respectively. All patients in the RT group received whole breast RT at the median time of 4.1 (range: 1.0–7.5) months after IABR, among which 12 patients received boost irradiation to the tumor bed following whole breast RT. Clinical characteristics of patients in the two groups are summarized in Table 1. There were no significant differences between the two groups in terms of age, tumor size, stage, or the expression of progesterone receptor (PR), estrogen receptor (ER), and Her-2.
| Characteristic | RT group (n=32) | Non-RT group (n=52) | χ² | P value |
|---------------|----------------|---------------------|----|---------|
| Age (years)   |                |                     |    |         |
| ≥45           | 18             | 30                  | 0.17 | 0.897  |
| <45           | 14             | 22                  |    |         |
| Pathological stage |            |                     | 1.622 | 0.480 |
| I             | 13             | 28                  |    |         |
| II            | 15             | 40                  |    |         |
| III           | 4              | 4                   |    |         |
| T stage       |                |                     | 2.278 | 0.334 |
| pT1           | 24             | 32                  |    |         |
| pT2           | 7              | 18                  |    |         |
| pT3           | 1              | 1                   |    |         |
| N stage       |                |                     | 4.045 | 0.123 |
| pN0           | 18             | 40                  |    |         |
| pN1           | 10             | 9                   |    |         |
| pN2           | 4              | 3                   |    |         |
| ER            |                |                     | 0.526 | 0.468 |
| Positive      | 21             | 38                  |    |         |
| Negative      | 11             | 14                  |    |         |
| PR            |                |                     | 0.526 | 0.468 |
| Positive      | 21             | 38                  |    |         |
| Negative      | 11             | 14                  |    |         |
| Her-2         |                |                     | 0.348 | 0.555 |
| Positive      | 6              | 14                  |    |         |
| Negative      | 25             | 38                  |    |         |

Note: RT, radiotherapy; pT, pathological tumor stage

Aesthetic outcomes
The aesthetic outcomes for all patients are shown in Table S1 in the Supplementary Appendix. At T0, T1, and T6, the overall cosmetic results were considered to be very good or good in 91.7%, 83.3%, and 98.8% of cases, respectively, satisfactory in 7.1%, 15.5%, and 1.2% of cases, respectively, and poor in 1.2%, 1.2%, and 0% of cases, respectively. No significant difference in cosmetic effect was found between the RT and non-RT groups at the three timepoints, except for the breast skin color change at 1 month post-RT (Table 2). A lower rate of very good or good cosmetic results of skin color presented in the RT group compared with the non-RT group, but the difference had disappeared at T6.
Table 2
Cosmetic results of the RT group and non-RT group

| Cosmetic results, n (%) | pre-RT | P value | 1 month after RT | P value | 6 months after RT | P value |
|-------------------------|--------|---------|------------------|---------|------------------|---------|
|                         | RT     | Non-RT  | RT group         |          | Non-RT group     |          |
| Scar                    | 0.138  | 0.103   | 0.057            |         |                  |         |
| Very good               | 10 (31.2) | 9 (17.3) | 12 (37.5) | 11 (21.2) | 21 (65.6) | 23 (44.2) |
| Good                    | 22 (68.8) | 43 (82.7) | 20 (62.5) | 41 (78.8) | 11 (33.4) | 29 (55.8) |
| Satisfactory            | 0      | 0       | 0                | 0       | 0                | 0       |
| Poor                    | 0      | 0       | 0                | 0       | 0                | 0       |
| Shape                   | 0.209  | 0.192   | 0.198            |         |                  |         |
| Very good               | 10 (31.2) | 10 (19.2) | 13 (40.6) | 14 (26.9) | 20 (62.5) | 25 (48.5) |
| Good                    | 22 (68.8) | 42 (80.8) | 19 (59.4) | 38 (73.1) | 12 (37.5) | 27 (51.5) |
| Satisfactory            | 0      | 0       | 0                | 0       | 0                | 0       |
| Poor                    | 0      | 0       | 0                | 0       | 0                | 0       |
| Symmetry                | 0.356  | 0.094   | 0.239            |         |                  |         |
| Very good               | 11 (34.4) | 13 (25.0) | 15 (46.9) | 15 (28.8) | 19 (59.4) | 24 (46.2) |
| Good                    | 21 (65.6) | 39 (75.0) | 17 (53.1) | 37 (71.2) | 13 (40.6) | 28 (53.8) |
| Satisfactory            | 0      | 0       | 0                | 0       | 0                | 0       |
| Poor                    | 0      | 0       | 0                | 0       | 0                | 0       |
| Skin color              | 0.761  | <0.001  | 0.185            |         |                  |         |
| Very good               | 8 (25.0) | 10 (19.2) | 1 (3.1)  | 15 (28.8) | 23 (71.9) | 32 (61.5) |
| Good                    | 23 (71.9) | 41 (78.8) | 19 (59.4) | 35 (67.3) | 8 (25.0)  | 20 (38.5) |
| Satisfactory            | 1 (3.1)  | 1 (2.0)  | 12 (37.8) | 2 (3.9)  | 1 (3.1)   | 0        |
| Poor                    | 0      | 0       | 0                | 0       | 0                | 0       |
| Nipple position         | 0.454  | 0.082   | 0.075            |         |                  |         |
| Very good               | 8 (25.0) | 10 (19.2) | 12 (37.5) | 15 (28.8) | 20 (62.5) | 23 (44.2) |
| Class          | RT   | Pre-Op | T1    | T6    | T12   |
|----------------|------|--------|-------|-------|-------|
| Good           | 22   | 41     | 18    | 37    | 11    |
| (68.8)         | (78.8)| (56.3)| (71.2)| (34.4)| (55.8)|
| Satisfactory   | 1    | 1      | 2     | 0     | 1     |
| (3.1)          | (2.0)| (6.2)  |       |       | (3.1) |
| Poor           | 1    | 0      | 0     | 0     | 0     |
| (3.1)          |     |        |       |       |       |

| Class          | RT   | Pre-Op | T1    | T6    | T12   |
|----------------|------|--------|-------|-------|-------|
| Very good      | 6    | 7      | 0     | 11    | 7     |
| (18.8)         | (13.5)|       | (21.1)| (21.9)| (28.8)|
| Good           | 22   | 42     | 20    | 39    | 24    |
| (68.8)         | (80.8)| (62.5)| (75.0)| (75.0)| (71.2)|
| Satisfactory   | 3    | 3      | 11    | 2     | 1     |
| (9.3)          | (5.7)| (34.4)| (3.9) |       | (3.1) |
| Poor           | 1    | 0      | 1     | 0     | 0     |
| (3.1)          |     |        | (3.1)|       |       |

Overall        | 0.441| <0.001 | 0.424 |

Note: RT, radiotherapy

**Flap size changes**

The data of flap size reduction after surgery in the three-dimensions of longest diameter, shortest diameter, and maximum thickness for the whole group are summarized in Table 3. There were no significant differences in the reduction in any of the three dimensions at T1, T6, or T12 (P>0.05). However, there were significant differences in each of these indices at all three timepoints when compared to T0 (all P<0.05, Fig. 2A).
Table 3
Changes in flap size among all patients

| LR     | Mean ± SD (cm) | P value | SR     | Mean ± SD (cm) | P value | TR     | Mean ± SD (cm) | P value |
|--------|----------------|---------|--------|----------------|---------|--------|----------------|---------|
| LR₀    | 0.1202±0.08437 | 0.004   | SR₀    | 0.1094±0.07072 | 0.016   | TR₀    | 0.0518±0.03527 | <0.001 |
| LR₁    | 0.0951±0.01942 |         |        |                |         | TR₁    | 0.0481±0.03759 |        |
| LR₀    | 0.1202±0.08437 | 0.002   | SR₁    | 0.0924±0.02886 |         | TR₀    | 0.0518±0.03527 | 0.036  |
| LR₆    | 0.0927±0.01839 |         |        |                |         | TR₆    | 0.0495±0.04077 |        |
| LR₀    | 0.1202±0.08437 | 0.004   | SR₀    | 0.1094±0.07072 | 0.002   | TR₀    | 0.0518±0.03527 | 0.017  |
| LR₁₂   | 0.0946±0.02284 |         |        |                |         | TR₁₂   | 0.0489±0.04033 |        |
| LR₁    | 0.0951±0.01942 | >0.05   | SR₁₂   | 0.0871±0.01905 |         | TR₁    | 0.0481±0.03759 | >0.05  |
| LR₆    | 0.0927±0.01839 |         |        |                |         | TR₆    | 0.0495±0.04077 |        |
| LR₁₂   | 0.0946±0.02284 |         |        |                |         | TR₁₂   | 0.0489±0.04033 |        |

Note: SD, standard deviation; LR, reduction in longest diameter; SR, reduction in shortest diameter; TR, reduction in maximum thickness; LR₀,₁,₆,₁₂, LR of the flap at the timepoints pre-radiotherapy (RT); 1 month after RT, 6 months after RT, and 12 months after RT, respectively; SR₀,₁,₆,₁₂, SR of the flap at the timepoints pre-RT, 1 month after RT, 6 months after RT, and 12 months after RT, respectively; TR₀,₁,₆,₁₂, TR of the flap at the timepoints pre-RT, 1 month after RT, 6 months after RT, and 12 months after RT.

The data of flap size reduction in the RT and non-RT groups are summarized in Table 4. No significant difference in the reduction of flap size was found between the two groups at any timepoint (P>0.05). Furthermore, no significant difference in the reduction of flap size was found at T₁, T₆, or T₁₂ within each group. However, in both groups, the reduction of flap size along the longest diameter, shortest diameter, and maximum thickness at T₁, T₆, and T₁₂ were significantly different from those at T₀ (P<0.05, Fig. 2B).
## Table 4
Changes in flap size within the two groups

| Items     | Flap size changes, Mean ± SD (cm) | P value |
|-----------|-----------------------------------|---------|
|           | RT group (n=32)                   | Non-RT group (n=52) |         |
| LR<sub>0</sub> | 0.1294±0.08658                    | 0.1146±0.08332 | 0.440   |
| LR<sub>1</sub> | 0.0909±0.02022                    | 0.0977±0.01864 | 0.122   |
| LR<sub>6</sub> | 0.0894±0.01777                    | 0.0948±0.01863 | 0.190   |
| LR<sub>12</sub> | 0.0897±0.02321                   | 0.0977±0.02228 | 0.119   |
| SR<sub>0</sub> | 0.1038±0.08809                    | 0.1129±0.05822 | 0.568   |
| SR<sub>1</sub> | 0.0959±0.04110                    | 0.0902±0.01777 | 0.379   |
| SR<sub>6</sub> | 0.0863±0.01827                    | 0.0925±0.01835 | 0.133   |
| SR<sub>12</sub> | 0.0850±0.01566                   | 0.0885±0.02090 | 0.422   |
| TR<sub>0</sub> | 0.0500±0.03910                    | 0.0529±0.03304 | 0.718   |
| TR<sub>1</sub> | 0.0431±0.04269                    | 0.0512±0.03417 | 0.371   |
| TR<sub>6</sub> | 0.0453±0.04458                    | 0.0521±0.03847 | 0.461   |
| TR<sub>12</sub> | 0.0438±0.04346                   | 0.0521±0.03837 | 0.359   |

Note: RT, radiotherapy; SD, standard deviation; LR<sub>0,1,6,12</sub>, reduction of the longest axis of the flap at the time points pre-RT, 1 month after RT, 6 months after RT, and 12 months after RT, respectively; SR<sub>0,1,6,12</sub>, reduction of the shortest axis of the flap at the time points pre-RT, 1 month after RT, 6 months after RT, and 12 months after RT, respectively; TR<sub>0,1,6,12</sub>, reduction in the maximum thickness of the flap at the time points pre-RT, 1 month after RT, 6 months after RT, and 12 months after RT.

### Complications of IABR and safety of RT

The incidence rates of postoperative complications from IABR were 1.2% for partial necrosis of the flap, 1.2% for infection, 3.6% for hematoma, and 1.2% for seroma. There were no significant differences in the overall rate of complications (9.4% vs. 5.8%; relative risk [RR] =1.345, 95% confidence interval [CI]: 0.574-3.148; P=0.670) or in the rate of each complication between the RT and non-RT groups (Table 5).
Table 5
Postoperative complications in the RT and non-RT groups

| Items       | Complications, n (%) | P value |
|-------------|----------------------|---------|
|             | RT group (n=32)      | Non-RT group (n=52) |       |
| Partial necrosis | 1 (3.1)           | 0 (0)   | 1.00   |
| Infection   | 0 (0)                | 1 (1.9) | 0.62   |
| Hematoma    | 1 (3.1)              | 2 (3.8) | 1.00   |
| Seroma      | 1 (3.1)              | 2 (3.8) | 0.38   |
| Total       | 3 (9.4)              | 3 (5.8) | 0.67   |

Note: RT, radiotherapy.

No grade 3 or greater RT-related adverse events (AEs) occurred during or after RT. The most common AEs were grade 2 or less radiation pneumonitis (25%), radiation dermatitis (37.5%), and leukopenia (3.1%). Five (15.6%) and three (9.4%) cases experienced grade 1 and 2 radiation pneumonitis, respectively, within 3 months after RT; 12 (37.5%) patients who received a tumor bed boost experienced grade 1 radiation dermatitis during RT. The grade 1 leukopenia occurred in only one patient during the first week of RT.

Survival and recurrence
At a median follow-up time of 33.3 months (95% CI: 29.1–37.5), all 84 cases were alive, and the median disease-free survival had not been reached (Fig. 3). Four cases experienced distant or regional metastases, but no patients developed local recurrence. In the RT group, one patient experienced distant metastases and another experienced regional recurrence at 6.9 and 26.7 months after surgery, respectively. In the non-RT group, two cases experienced regional recurrence at 12.1 and 27.4 months after surgery, respectively. No significant difference was found in the regional recurrence rate between the RT and non-RT groups (3.13% vs. 3.85%; RR=0.871, 95% CI: 0.172-4.419; P=1.00).

Discussion
IABR plays a vital role for breast cancer patients in terms of preserving anatomical landmarks, minimizing scar fibrosis, reducing the total number of operations, and improving patient satisfaction and psychological outcomes. This is primarily because the long-term success and aesthetic satisfaction of autologous reconstruction are superior to delayed or alloplastic reconstruction [19-21]. However, there are scant data on the effect of RT on autologous flaps. In this cohort study, we focused on assessing the efficacy and safety of IABR with or without RT. The results showed that subsequent RT was well tolerated by patients who received IABR after BCS, and that patients were satisfied with the aesthetic outcomes, suggesting that RT had no serious effects on autologous tissue flaps.
Recently, autologous grafting has become much more widely used in breast cancer patients who need breast reconstruction because of its improved oncological outcomes and reconstruction quality [22, 23]. Additionally, surgeons are increasingly inclined to perform immediate breast reconstruction for patients who need adjuvant RT [24]. Studies have shown significantly improved aesthetic outcomes of grafted autologous flaps after mastectomy [25, 26]. However, aesthetic outcomes of RT following IABR have been contradictory [27]. Several previous studies [28-30], which included a total of 96 patients, evaluated aesthetic outcomes of reconstructed breasts after mastectomy by quartile scores based on patients’ self-evaluation; roughly 77.1% of the cases reported very good or good outcomes after RT. In our study, the rate of aesthetic outcomes being considered very good or good was the lowest for the RT group (62.5%) at 1 month after RT (T1) but reached 96.9% at 6 months after RT (T6), which was higher than previously reports. The differences might be caused by different radiation technique, methods of breast tumor resection, and/or breast reconstruction. In our study, 90.6% (29/32) of patients in the RT group underwent intensity modulated RT (IMRT) rather than 2- or 3-dimensional conformal RT for whole breast irradiation. IMRT could improve the dose distribution of treatment fields in the breast; thus, it might result in superior breast cosmesis and less palpable induration [31]. Additionally, all patients in our study retained partial breast tissue and needed a small transfer flap rather than replacement of the whole breast tissue with a flap, which provided restoration with a natural texture, shape, and volume of the breast.

Although a few studies have reported data of aesthetic results after RT for patients who received IABR after BCS, aesthetic evaluations at different timepoints after RT and a comparative analysis between aesthetic results for patients with and without RT are still lacking. One early study [17] that included 34 patients who underwent RT at 4 to 6 weeks after IABR reported that the proportion of very good or good cosmetic outcomes was only 88.2%, which was lower than that of our study (96.9%). This difference might be due to the higher proportion of unaesthetic scars (8.9%) and marked fibrosis (2.9%) caused by the surgical methods used in that study. Unlike that study, we used LD flaps or FDFG to fill the defect through the primary incision so that an additional incision was avoided. Additionally, heterogeneity in the timepoints at which aesthetic outcomes were evaluated may be another reason. In our study, we evaluated cosmetic outcomes at different timepoints before and after radiotherapy and IABR. Additionally, the cosmetic outcomes of patients in the non-RT group were evaluated at the same timepoints. Thus, we observed that compared with the non-RT group, the addition of radiotherapy in the RT group did not affect cosmetic outcomes, indicating that RT might be a feasible option for breast cancer patients undergoing IABR after BCS because of durable cosmetic outcomes.

Postoperative flap volume changes are usually used to assess how much of the flap volume will ultimately remain. There is still a paucity of literature on flap volume changes following autologous flap breast reconstruction. Kimura et al. [32] described a maximum decrease in fat volume of 75.1% at 1 year after the operation, while Wilting et al. [33] showed a final overall flap volume decrease of 88.9% after 6 months. Rochlin et al. [27] found the incidence rate of flap volume loss events to be 16.9% among patients who received radiotherapy following IABR after mastectomy, but data on the impact of RT on flap volume changes are lacking. In this study, we assessed the changes of flap size in the three dimensions instead of volume changes, and our findings indicated that the size of the flap decreased slowly and tended to stabilize at the T1, T6, and T12 timepoints regardless of RT. Thus, RT had no adverse effect on flap size compared with the non-RT group. It is noteworthy that the flap size decreased obviously at an average of 4 months, which was shorter than what has been reported in previous studies [33, 34]. This may be related to the relatively smaller flap size required for BCS than for mastectomy, differences in patient populations or flap donor sites, baseline measurement times,
measurement techniques used to evaluate flap size, and host conditions. Currently, there are no reports on the factors that affect the initial flap size after autologous reconstruction, but the reduction in flap size may be partially due to early postoperative factors such as apoptosis [35], postoperative edema, and inflammation. Flap denervation and ischemic changes caused by transient ischemia may also contribute to this reduction.

In our study, the common postoperative complications were partial necrosis of the flap, infection, hematoma, and seroma, the incidence rates of which were between 1.2% and 3.6%, which were lower than the 2.9% to 14.7% reported in previous studies [10, 17, 23, 36]. Different patient populations, excision extensions, flap sizes, and donor sites might lead to this difference. Patients from Western countries or who undergo mastectomy usually need larger flaps and more quantity of fat grafting to balance the esthetic and oncological aspects of the larger breast size, which can easily lead to impaired blood supply in the grafting site. In contrast, due to the small- to medium-sized breasts in the Asian population, all patients in our study underwent BCS followed by IABR with smaller flaps, which can avoid the local unsatisfactory blood supply. Additionally, most of the patients (57/84) in our study underwent IABR with LD flaps, so few patients experienced the risk of fat necrosis or liquefaction, which was commonly seen in the above studies. Nevertheless, there is still controversy regarding whether RT could increase the risk of postoperative complications [37]. By summarizing the data of 11 retrospective studies that included 316 patients who received RT following IABR after mastectomy, Rochlin et al. [27] concluded that postoperative complications of fat necrosis and contracture could be increased to 16.9% and 35.4%, respectively, by RT. However, our study showed that RT did not increase the risk of any postoperative complications for patients who underwent IABR following BCS when compare with the non-RT group. No patients experienced contracture or fat necrosis in either group, and only one patient in the RT group (1.2%) experienced partial necrosis. This is likely because the scope of surgical resection in our study was smaller than that of mastectomy, and retained some neurovascular function, which relatively reduced RT-related complications.

In this cohort study, patients who received IABR and RT did not experience any grade ≥3 RT-associated AEs. Notably, compared with no radiation dermatitis cases among patients who only received whole breast irradiation, 12 patients (37.5%) with boost irradiation to the tumor bed experienced grade 1 radiation dermatitis during RT, but the dermatitis gradually disappeared after radiotherapy. A previous report [38] showed that the tumor bed could be markedly replaced with flaps during reconstruction following BCS. Although tumor bed boosted radiotherapy following whole breast irradiation can reduce local recurrence rates, researchers have found no evidence of a benefit for other oncological outcomes among BCS patients [39]. In light of this, it is necessary to conduct multidisciplinary discussions with breast surgeons, oncologist, and radiotherapists to accurately determine the location of the tumor bed and decide whether to perform tumor bed boosting during radiotherapy.

The introduction of oncoplastic techniques into clinical practice has the potential to reduce the risk of positive margins and ultimately the risk of local recurrence [40]. In our study, to ensure negative margins, we often performed a safer edge in the range of 1.5–3 cm, which is between the traditional BCS and mastectomy. RT was conducted in 38.1% of patients due to large tumors, lymph node metastases, or other high-risk factors. At a median follow-up of 33.3 months, all 84 analyzable patients remain alive, and median disease-free survival time has not been reached. In total, 3.57% of patients had regional recurrences (3.13% in the RT group and 3.85% in the non-RT group). No patient experienced local recurrence in the subsequent 33.3 months of follow-up. This benefit for patients who underwent IABR may come from both RT and safer surgical margins.
However, there are also some limitations to this study. The inherent limitations of the study are its small sample size and retrospective nature. Additionally, the follow-up time is insufficient to definitively evaluate long-term outcomes. Some RT-associated late complications like fibrosis need further follow-up.

**Conclusion**

This retrospective cohort study from our single-center showed that additional RT after IABR had no negative impact on aesthetic outcomes or flap size, and did not increase postoperative complications. Thus, adjuvant RT might be safely given to patients undergoing IABR following partial mastectomy. Further studies are needed to evaluate the long-term effects of RT on IABR.

**Abbreviations**

IABR: Immediate autologous breast reconstruction; RT: Radiotherapy; BCS: Breast-conserving surgery; LD: Latissimus dorsi; FDFG: Free dermal fat graft; CT: Computed tomography; SD: Standard deviation; PR: Progesterone receptor; ER: Estrogen receptor; AEs: Adverse events; IMRT: intensity modulated radiotherapy.

**Declarations**

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None

**Authors’ contributions**

Conception: CBH; Design of the work: SLZ and JTM; The acquisition and analysis: JS and YRW; Interpretation of data: SLZ, YJG, JZZM, and LS; Writing - Drafting the work or substantively revising it: SLZ, LTH, JTM and CBH. All authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

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**Availability of data and materials**

Not applicable.

**Conflict of interest**

The authors declare no conflict of interest.
Ethical approval and consent to participate

This study was approved by the Institutional Review Board of Shengjing Hospital of China Medical University (Approved number: 2016PS161J). All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figure 1

The relative timepoints for the RT and non-RT groups. RT, radiotherapy; IABR, immediate autologous breast reconstruction;
Figure 2

The reduction of flap size along the longest diameter, shortest diameter, and maximum thickness at pre-RT (4 months after surgery), 1 month post-RT (7 months after surgery), 6 months post-RT (12 months after surgery), and 12 months post-RT (18 months after surgery) for all patients (a), and for patients in the two groups (b). T0, pre-RT; T1, 1 month post-RT; T6, 6 months post-RT; T12, 12 months post-RT; *P<0.05; **P<0.01. RT, radiotherapy; LR, reduction in longest diameter; SR, reduction in shortest diameter; TR, reduction in maximum thickness.
Figure 3

Kaplan-Meier curve of disease-free survival for all the patients (a), and for RT group versus non-RT group (b). RT, radiotherapy.

Supplementary Files

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- TableS1.docx