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RESEARCH ARTICLE

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"Immediate versus delayed autologous breast reconstruction in patients undergoing post-mastectomy radiation therapy: A paradigm shift"

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Abstract

Background: While negative impacts of radiation on breast reconstruction have been well accepted, timing of autologous breast reconstruction in the setting of postmastectomy radiation therapy (PMRT) is still evolving. This study aims to address the dilemma of breast reconstruction timing in patients receiving PMRT.

Methods: A retrospective chart review was performed evaluating patients who underwent PMRT and autologous breast reconstruction. Postoperative complication and revision rates were compared.

Results: Thirty-six immediate (immediate breast reconstruction [IBR]) and 89 delayed reconstructions (delayed breast reconstruction [DBR]) were included with comparable patient characteristics between groups. Overall complication rates were not significantly different, or when separately assessing for surgical site infections, wound dehiscence, fat necrosis, or substantial volume loss. No free flaps were lost in either group. Revision rates were significantly lower in the IBR group ($p = 0.02$). DBR resulted in appreciably larger volumes of fat grafting to the therapeutically reconstructed breast ($p = 0.01$) and more contralateral mastopexies ($p = 0.02$). No significant difference was observed in fat necrosis excision, breast reduction, or need for secondary flap reconstruction or prosthetic use for volume loss.

Conclusions: IBR in the setting of PMRT does not result in higher rates of complications and requires fewer overall revisions, making it a compelling option for patients undergoing PMRT.

KEYWORDS
breast cancer, free flap, microsurgery

Presentations: Results presented at the Annual Meeting of the American Society of Reconstructive Microsurgeons in January 2022.

1 | INTRODUCTION

In the United States, breast cancer remains the most common form of cancer and the second leading cause of cancer death in women of all races and ethnicities.[1] Recent trends have demonstrated that not only are more women electing for mastectomy over lumpectomy in early-stage disease, but the number of women who choose to pursue postmastectomy breast reconstruction has also been on the rise.[2]

Postmastectomy radiation therapy (PMRT) continues to increase in prevalence among this patient population as it has been shown to decrease locoregional disease and improve overall rates of survival.[3] Current indications for PMRT include breast cancer patients with ≥4 positive axillary lymph nodes, primary tumor size ≥5 cm, disease extending to the skin or chest wall (T4), and positive or close margins.[4] However, radiation therapy is well known for its negative impacts on the wound healing process including degenerative changes, vascular thrombosis, atrophy, and fibrosis.[5]

Immediate breast reconstruction is preferred by most plastic surgeons given the enhanced aesthetic outcomes associated with preservation of the skin envelope, fewer number of revisions, and improved psychosocial well-being.[6–9] However, timing of autologous free tissue transfer for postmastectomy breast reconstruction remains a controversial topic in the setting of PMRT. Previous studies, including those by the senior author (DWC), have found significantly higher rates of late complications, including fat necrosis and contractures, associated with immediate autologous reconstruction in the setting of PMRT.[10–12] Due to these findings, many plastic surgeons still choose to delay autologous reconstruction to avoid direct radiation to the free flap and its subsequent consequences.

Nevertheless, with the advancement of radiation equipment and techniques over the last few decades, the dogma against immediate breast reconstruction for patients requiring PMRT is being challenged. Given the paucity of current data re-evaluating the timing of autologous reconstruction in the setting of PMRT, our study aims to address the dilemma of when to perform autologous breast reconstruction in patients undergoing PMRT.

2 | METHODS

Following approval by the Institutional Review Board (IRB19-0604), a retrospective chart review was performed to evaluate all patients who underwent autologous breast reconstruction at the University of Chicago Medicine from January 2015 through December 2019. Only patients who underwent PMRT were included in the analysis. Patients were separated into two groups: those who underwent autologous reconstruction before receiving PMRT, immediate breast reconstruction (IBR), and those who had PMRT before their autologous reconstruction, delayed breast reconstruction (DBR). Medical records were reviewed for patient demographics, comorbidities, cancer stage, treatment characteristics, timing of mastectomy, timing of autologous reconstruction, postoperative complications, and revisional surgeries performed under general anesthesia. Complications included OR takeback during the same admission, partial or total flap loss, pedicle thrombosis, mastectomy flap necrosis, surgical site infection, wound dehiscence, fat necrosis, and significant volume loss. Fat necrosis was diagnosed based on physician assessment. Significant volume loss was determined by the need for a second autologous flap reconstruction or external prosthesis use. Revisional surgeries included fat grafting, fat necrosis excision, mastopexy, breast reduction, liposuction, and subsequent flap reconstruction for volume loss. Minor revisions and nipple-areolar complex reconstruction performed under local anesthesia in clinic were not considered formal revisions. Statistical analysis was performed using the Student's *t* test to compare all continuous data and Fisher's exact test to analyze categorical data between the immediate and delayed reconstruction groups. A value of $p < 0.05$ was denoted as statistically significant.

3 | RESULTS

A total of 123 patients were included in the study with 36 immediate and 89 delayed autologous reconstructions. Two patients underwent prior unilateral right mastectomy and PMRT without autologous reconstruction, subsequently developed cancer in the contralateral left breast and underwent mastectomy with bilateral autologous reconstruction followed by PMRT of the left breast. These patients were included in both the immediate and delayed reconstruction groups. Patient demographics, including mean age at reconstruction (51.6 vs. 51.5 years, $p = 0.94$) and BMI (29.6 vs. 29.8 kg/m^2, $p = 0.91$), did not statistically differ between the IBR and DBR groups, respectively. No patients were actively smoking at the time of their reconstruction. However, 19.4% of the IBR and 27.0% of the DBR groups were former smokers ($p = 0.37$) that quit an average of 13.3 and 14.2 years before autologous reconstruction, respectively ($p = 0.88$). There were no diabetic patients in the IBR group, while 7.9% of the DBR group had a diagnosis of diabetes ($p = 0.19$) with a mean HbA1c of 6.7% (Table 1).

TABLE 1 Patient characteristics

	Immediate reconstruction *N* = 36	Delayed reconstruction *N* = 89	*p* value
Age (years)	51.6	51.5	0.94
BMI	29.6	29.8	0.91
Diabetes	0 (0%)	7 (7.9%)	0.19
HbA1c	–	6.7%	–
Tobacco use			
Current	0 (0%)	0 (0%)	–
Former	7 (19.4%)	24 (27.0%)	0.37
Years quit	13.3	14.2	0.88

Abbreviations: BMI, body mass index; HbA1c: hemaglobin A1c.

TABLE 2 Cancer characteristics

	Immediate reconstruction *N* = 36	Delayed reconstruction *N* = 89	*p* value
Cancer Stage			0.19
0	0 (0%)	2 (2.2%)	
IA	2 (22.2%)	1 (1.1%)	
IB	0 (0%)	0 (0%)	
IIA	8 (22.2%)	12 (13.5%)	
IIB	16 (44.4%)	16 (18.0%)	
IIIA	6 (16.7%)	26 (29.2%)	
IIIB	2 (5.6%)	5 (5.6%)	
IIIC	2 (5.6%)	5 (5.6%)	
Cancer side			0.5
Right breast	21 (58.3%)	39 (43.8%)	
Left breast	12 (33.3%)	48 (53.9%)	
Both	3 (8.3%)	2 (2.2%)	
Chemotherapy			*0.01*
Neoadjuvant	18 (50.0%)	28 (35.9%)	
Adjuvant	7 (19.4%)	46 (59.0%)	
Both	1 (2.8%)	4 (5.1%)	
Radiation dose (Greys)	50.1	50.9	0.11
Reconstruction			1.00
Unilateral	22 (61.1%)	54 (60.7%)	
Bilateral	14 (38.9%)	35 (39.3%)	

Cancer characteristics including cancer stage, side of malignancy, chemotherapy, and radiation therapy are summarized in Table 2. Cancer stage ($p = 0.19$) and side of malignancy ($p = 0.50$) were comparable between groups. Prior timing of chemotherapy significantly varied between the IBR and DBR groups with more patients in the IBR group undergoing neoadjuvant chemotherapy compared to more adjuvant chemotherapy in the DBR group ($p = 0.01$). Neoadjuvant chemotherapy was completed an average of 2.6 months (*SEM* = 0.72) before IBR, while adjuvant chemotherapy started 1.7 months (*SEM* = 0.31) following immediate autologous reconstruction. In the DBR group, all chemotherapy was completed before autologous reconstruction with a mean of 34.1 months (*SEM* = 7.69) between final chemotherapy treatment to DBR. In the IBR group, PMRT began an average of 2.0 months (*SEM* = 0.14) after autologous reconstruction or completion of adjuvant chemotherapy. An average of 19.0 months (*SEM* = 2.88) elapsed between the end of PMRT to delayed autologous reconstruction, and 41.4 months (*SEM* = 5.72) from the time of mastectomy to free flap reconstruction. The mean radiation doses were 50.1 Gy for the IBR and 50.9 Gy for the DBR groups ($p = 0.11$).

There were no significant differences in overall complication rates between the IBR and DBR groups (61.1% vs. 71.9%, $p = 0.29$) (Table 3). In the IBR group, 3 patients (8.3%) were taken back to the OR postoperatively while no patients in the DBR group required immediate takeback ($p = 0.02$). One patient required reoperation for hematoma evacuation and 2 patients required reoperation for venous thrombectomy, however, there was no significant difference in the development of pedicle thrombosis between the groups ($p = 0.08$). There was no loss of free flaps in either study group. Partial flap necrosis occurred in 4 patients (4.5%) in the DBR group while none were observed in the IBR group ($p = 0.32$). All partial flap necrosis debridements were taken back to OR within 2–6 weeks from initial delayed flap reconstruction. Hematoma and seroma rates did not significantly differ (8.3% vs. 4.5%, $p = 0.41$). Notably more patients in the IBR group experienced mastectomy flap necrosis compared to the DBR group (13.9% vs. 3.4%, $p = 0.04$). Four DBR patients (4.5%) were diagnosed with a pulmonary embolism during the postoperative period compared to zero in the IBR group ($p = 0.32$). Surgical site infections (13.9% vs. 12.4%, $p = 0.78$), wound dehiscence (30.6% vs. 27.0%, $p = 0.67$), fat necrosis (36.1% vs. 31.5%, $p = 0.68$), and volume loss requiring secondary flap reconstruction or external prosthesis use on the radiated side (2.8% vs. 2.2%, $p = 1.00$) were comparable between the two study groups. One patient in each of the IBR and DBR groups eventually underwent a second latissimus dorsi flap reconstruction to improve breast volume, while another patient in the DBR group chose to continue use of an external prosthesis for volume loss to avoid further surgery.

Overall rates of revision were significantly less for the IBR group (47.2%, range: 1–4 revisions per patient) compared to the DBR group (69.7%, range: 1–6 revisions per patient, $p = 0.02$) (Table 4). Fewer patients required fat grafting to the radiated side in the IBR compared to the DBR group, however, this did not meet clinical significance (22.2% vs. 38.2%, $p = 0.10$). When further evaluating the difference in volume of fat grafting between the radiated breast relative to the contralateral breast, the IBR group required considerably lower total volumes of fat over time compared to the DBR group (mean 53 vs. 180 cc, $p = 0.01$). There were notably fewer contralateral breast mastopexies in the IBR compared to the DBR group (2.8% vs. 18.0%, $p = 0.02$). No significant difference was observed between the IBR and DBR groups with rates of contralateral breast reduction (8.3% vs. 15.7%, $p = 0.39$), contralateral liposuction (8.3% vs. 7.9%, $p = 1.00$), fat necrosis excision (19.4% vs. 15.7%, $p = 0.61$), or secondary flap reconstruction for volume loss (2.8% vs. 1.1%, $p = 0.58$). The mean length of follow up from time of reconstruction for DBR was 14.7 months (*SEM* = 1.23), while the mean length of follow up from reconstruction for IBR was 13.1 months (*SEM* = 1.55, $p = 0.44$) and from completion of PMRT post IBR was 9.9 months (*SEM* = 1.41, $p = 0.01$).

4 | DISCUSSION

Breast reconstruction is an essential component for many women undergoing breast cancer treatment. Immediate breast reconstruction following skin sparing or nipple sparing mastectomy is not only

TABLE 3 Postoperative complications

	Immediate reconstruction *N* = 36	Delayed reconstruction *N* = 89	*p* value
Rate of complications	22 (61.1%)	64 (71.9%)	0.29
OR takeback same admission	3 (8.3%)	0 (0%)	*0.02*
Pedicle thrombosis	2 (5.6%)	0 (0%)	0.08
Flap loss	0 (0%)	0 (0%)	–
Partial flap necrosis	0 (0%)	4 (4.5%)	0.32
Mastectomy flap necrosis	5 (13.9%)	3 (3.4%)	*0.04*
Surgical site infection	5 (13.9%)	11 (12.4%)	0.78
Wound dehiscence	11 (30.6%)	24 (27.0%)	0.67
Fat necrosis	13 (36.1%)	28 (31.5%)	0.68
Significant volume loss[a]	1 (2.8%)	2 (2.2%)	1.00

[a]Volume loss requiring second flap reconstruction or external prosthesis.

TABLE 4 Breast revisions

	Immediate reconstruction *N* = 36	Delayed reconstruction *N* = 89	*p* value
Patients requiring revisions	17 (47.2%)	62 (69.7%)	*0.02*
Fat grafting	8 (22.2%)	34 (38.2%)	0.10
Mean grafted volume difference (cc)[a]	53	180	*0.01*
Fat necrosis excision from radiated breast	7 (19.4%)	14 (15.7%)	0.61
Contralateral mastopexy	1 (2.8%)	16 (18.0%)	*0.02*
Contralateral reduction	3 (8.3%)	14 (15.7%)	0.39
Contralateral liposuction	3 (8.3%)	7 (7.9%)	1.00
Second flap reconstruction for volume loss	1 (2.8%)	1 (1.1%)	0.49

[a]Grafted volume difference = volume of fat grafting to cancer side − volume of fat grafting to contralateral side.

oncologically safe when evaluating for local recurrence and overall survival, but is more esthetically advantageous, and associated with enhanced psychosocial well-being.[6–9] With preservation of the skin envelope, the immediate autologous flap can be buried with a small skin paddle for monitoring that may be repurposed for future nipple reconstruction (Figure 1). In the ideal situation with nipple sparing mastectomies, a thin skin paddle may be hidden in the inferior mammary fold and later easily excised under local anesthesia for the most aesthetic outcome. Once the pliable skin envelope has been lost through scarring and radiation, a much larger skin paddle is required with delayed autologous reconstructions (Figure 2), often leading to unfavorable aesthetic outcomes and additional revisions.

Modern radiation techniques have vastly evolved over the last few decades. PMRT has transitioned from a two-dimensional field to three-dimensional computed tomography planning with improved precision and reduced risk for side effects compared to less sophisticated historical techniques.[13] However, many surgeons still prefer delayed reconstruction to prevent direct radiation to the free flap in hopes of avoiding higher rates of complications as seen with immediate reconstruction in older studies.[10–12] Our research challenges this previous paradigm and found the overall complication rates to be comparable between the IBR and DBR groups. While our complication profile reinforces the findings reported in a systematic review and meta-analysis performed by Hershenhouse et al.,[14] this study further investigates the details of revisions following autologous breast reconstruction in the setting of PMRT, which has not been well reported in the current literature.

Although mastectomy flap necrosis was expectedly higher in the immediate reconstruction group, there were no significantly increased rates of pedicle thrombosis, partial flap necrosis, or total flap loss between the two groups. These findings were similarly demonstrated in the early complication profile seen by Tran et al. in

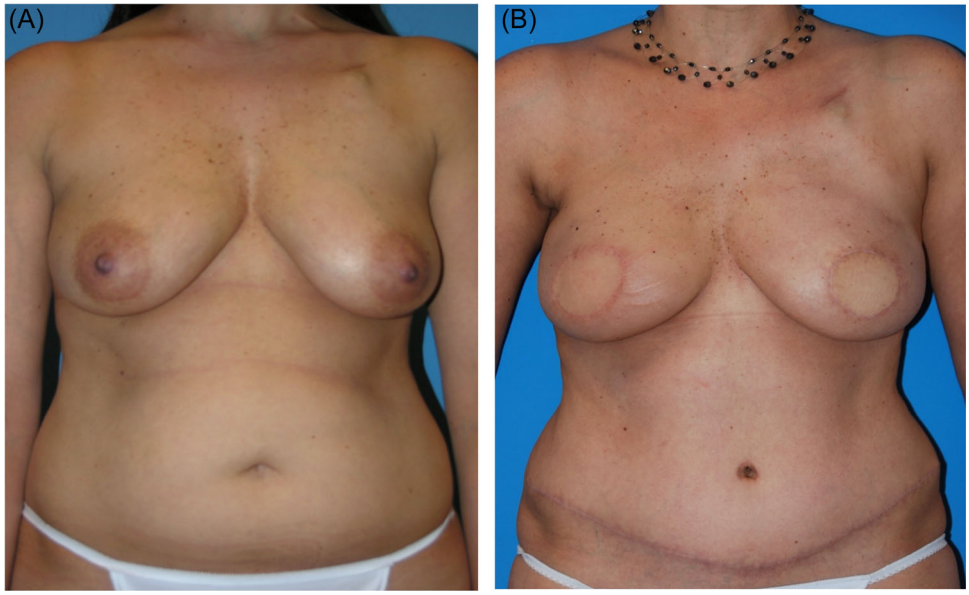

FIGURE 1 (A) Preoperative photo of native breasts with right sided malignancy. (B) Six months postradiation to the right reconstructed breast following bilateral skin sparing mastectomies with immediate autologous reconstruction

2001.[11] However, while Tran et al.[11] reported a significantly higher rate of secondary flap reconstruction or use of external prosthesis for contour and volume correction in the IBR group (28%), the findings of our study demonstrated equally low rates between the IBR (2.8%) and the DBR groups (2.2%). Our fat necrosis rates also differed from previously published data and was found not to be significantly different between the immediate and delayed groups, affecting about one-third of each study population. Additionally, despite receiving adjuvant chemotherapy following autologous reconstruction in the IBR group, there were no increased rates of wound dehiscence or surgical site infections compared to the DBR group, where chemotherapy was completed a mean of 34.1 months before reconstruction.

More notably, our evaluation of breast revisions following autologous reconstruction demonstrated significantly more surgery required by patients in the DBR group following initial reconstruction. Although the percentage of patients requiring eventual fat grafting did not remarkably vary, when looking at the difference in total quantity of fat grafted between the radiated and the nonradiated sides, the DBR group required threefold the volume of fat grafting over time compared to the IBR group. This data not only speaks toward the idea that volume loss following radiation is not as significant in the IBR group as previously believed, but that DBR requires more fat grafting over time to correct for its associated contour irregularities. As another way of capturing volume loss of the reconstructed breast, we looked at contralateral symmetry procedures including breast reduction, liposuction, and mastopexies performed. Our data did not demonstrate any increased rates of these contralateral procedures in the IBR compared to DBR groups to signify volume loss associated with radiation of the reconstructed breast.

Two-thirds of patients undergoing IBR were able to start PMRT within the optimal timing of 8 weeks after reconstruction or within 7 months for those requiring adjuvant chemotherapy.[15] Of the 10 patients with a delay in PMRT, 7 had complications including wound dehiscence, surgical site infection, or mastectomy flap necrosis that resulted in a postponement of treatment. Radiation dates were not available for the remaining 2 patients in the IBR group. No recurrences have been documented for the patients with delayed PMRT during the follow up period assessed. While our study does not asses long-term outcomes, Baek et al.[16] looked at adjuvant chemotherapy and radiation therapy following IBR and found no significant impact on survival outcomes.

Patients with delayed reconstruction waited a mean of 3.4 years from their initial mastectomy before undergoing an autologous reconstruction. Some patients had previously undergone tissue expander and/or implant-based reconstruction, however, ultimately chose to convert to autologous tissue. Given the known postmastectomy effects on psychosocial well-being including depression, lowered self-esteem, diminished sense of wholeness and femininity,[7] the delay in final reconstruction is not an insignificant factor to consider in overall quality of life.

There are several limitations of this study including the single center retrospective analysis and lack of patient-reported outcomes. Additionally, our institution was primarily performing delayed reconstructions until 2018 when immediate reconstructions became a more regular practice, thus resulting in a smaller sample size for the IBR group. While total time from reconstruction did not notably differ between the study groups, a shorter follow up period from completion of PMRT in the IBR group may contribute to lower rates of late complications, however, this would not be expected to affect the outcomes seen in early complication rates.

We believe that immediate autologous reconstruction is a compelling option for breast cancer patients undergoing PMRT and warrants

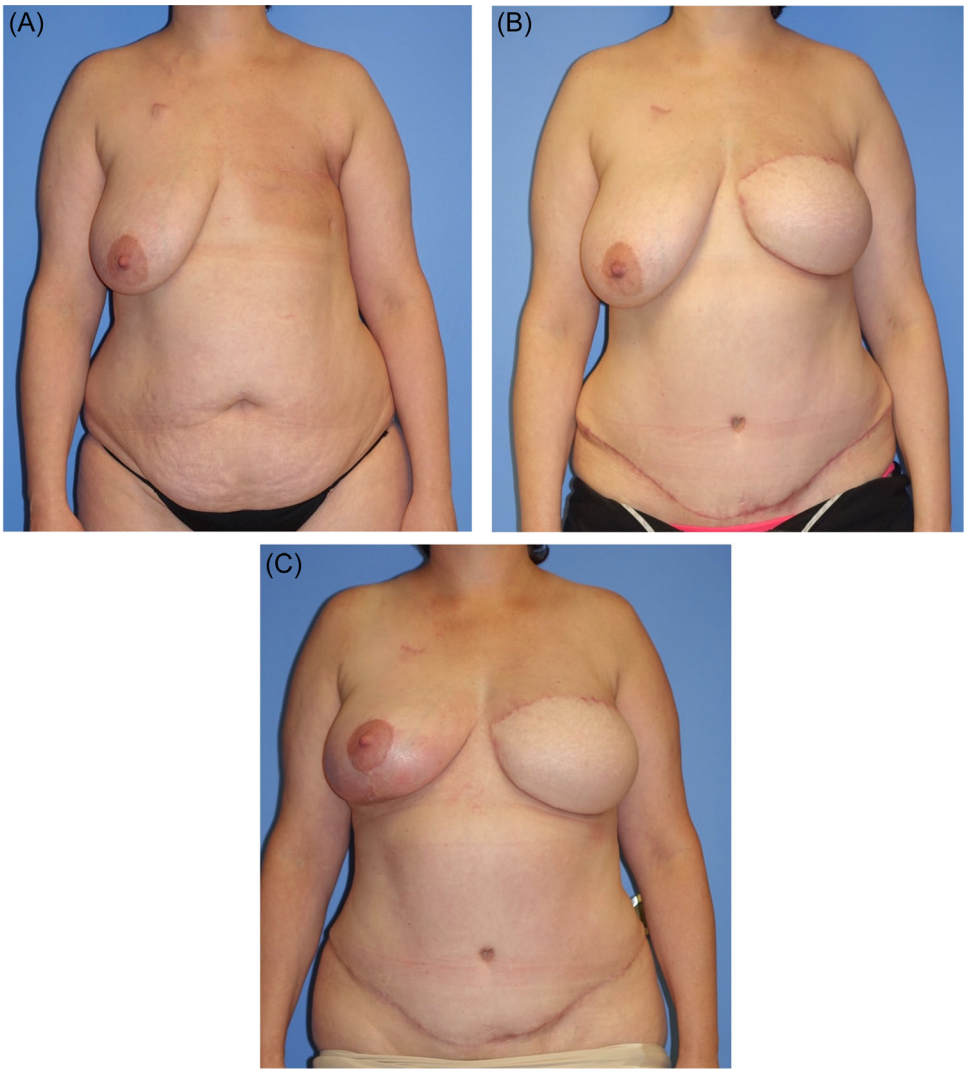

FIGURE 2 (A) Preoperative photo following left simple mastectomy and postmastectomy radiation therapy. (B) Postoperative photo after delayed autologous left breast reconstruction. (C) Following revisional surgery including fat grafting to the left reconstructed breast and mastopexy of the right breast

further research, especially as radiation therapy and technology continue to evolve. Given the variability of radiation protocols between institutions, a multi-institutional, prospective investigation would be beneficial to determine wider applicability of immediate breast reconstruction. Moving forward, patient-reported outcomes should also be evaluated to further address immediate versus delayed breast reconstruction in the setting PMRT. In addition, evaluation between immediate and delayed-immediate reconstruction in patients undergoing PMRT would be an interesting area of future research given preservation of the skin envelope with both reconstructive techniques.

5 | CONCLUSION

The results of this study support immediate autologous breast reconstruction as a viable option in the setting of PMRT, demonstrating a comparable complication profile and an overall decreased need for revisional surgeries when compared to delayed autologous reconstruction.

AUTHOR CONTRIBUTIONS

Mimi Y. Wu Young: is a Plastic and Reconstructive Surgery Resident at the University of Chicago Medicine. She contributed to the design of this study, performed the data collection, analysis, and composition of this manuscript. **Rebecca M. Garza**: is an Assistant Professor of Surgery in the Section of Plastic and Reconstructive Surgery at the University of Chicago Medicine. She contributed to the design of this study and provided guidance with data collection and revisions. **David W. Chang**: is Chief of the Section Plastic and Reconstructive Surgery and Director of the Microsurgery Fellowship at the University of Chicago Medicine. As the PI for this project, he provided clinical knowledge and played a significant role in the design, interpretation, revisions, and approval of this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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