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Scientific Article

Breast Reconstruction Complications After Postmastectomy Proton Radiation Therapy for Breast Cancer

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Purpose: Our purpose was to report complications requiring surgical intervention among patients treated with postmastectomy proton radiation therapy (PMPRT) for breast cancer in the setting of breast reconstruction (BR).

Methods and Materials: Patients enrolled on a prospective proton registry who underwent BR with immediate autologous flap, tissue expander (TE), or implant in place during PMPRT (50/50.4 Gy +/- chest wall boost) were eligible. Major reconstruction complication (MRC) was defined as a complication requiring surgical intervention. Absolute reconstruction failure was an MRC requiring surgical removal of BR. A routine revision (RR) was a plastic surgery refining cosmesis of the BR. Kaplan-Meier method was used to assess disease outcomes and MRC. Cox regression was used to assess predictors of MRC.

Results: Seventy-three courses of PMPRT were delivered to 68 women with BR between 2013 and 2021. Median follow-up was 42.1 months. Median age was 47 years. Fifty-six (76.7%) courses used pencil beam scanning PMPRT. Of 73 BR, 29 were flaps (39.7%), 30 implants (41.1%), and 14 TE (19.2%) at time of irradiation. There were 20 (27.4%) RR. There were 9 (12.3%) MRC among 5 implants, 2 flaps, and 2 TE, occurring a median of 29 months from PMPRT start. Three-year freedom from MRC was 86.9%. Three (4.1%) of the MRC were absolute reconstruction failure. Complications leading to MRC included capsular contracture in 5, fat necrosis in 2, and infection in 2. On univariable analysis, BR type, boost, proton technique, age, and smoking status were not associated with MRC, whereas higher body mass index trended toward significance (hazard ratio, 1.07; 95% CI, 0.99-1.16; $P = .10$).

Conclusions: Patients undergoing PMPRT to BR had a 12.3% incidence of major complications leading to surgical intervention, and total loss of BR was rare. MRC rates were similar among reconstruction types. Minor surgery for RR is common in our practice.

Introduction

Breast reconstruction (BR) after mastectomy for breast cancer is common and growing in use over time.[1] In an observational study of 20,560 women who underwent

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mastectomy for breast cancer, reconstruction use increased from 46% to 63% from 1998 to 2007.[2] Many women who elect to undergo BR will also require adjuvant therapy with postmastectomy radiation therapy (PMRT) to decrease the risk of cancer recurrence.[2-5] However, PMRT can increase the risk of complications to a reconstructed breast, such as capsular contracture, fat necrosis, and infection.[6] Complications of infection and contracture are more specific to tissue expander (TE) and implant reconstruction, and fat necrosis is more specific to autologous flaps. In some instances, these complications require surgical intervention to improve cosmesis or symmetry or to preserve the reconstruction. It has been estimated that there is a ~20% rate of surgical revision or major complication requiring removal of implant-based reconstruction after PMRT.[7]

The use of proton therapy in PMRT, or postmastectomy proton radiation therapy (PMPRT), limits exit dose and can improve sparing of the heart and lung, as cardiac exposure has been previously correlated with cardiac toxicity.[8-10] On the other hand, proton radiation has a higher linear energy transfer and relative biological effectiveness (RBE), which may result in differences in the normal tissue effects and range uncertainty, especially at the distal edge of the beam.[11] This has led to concern for toxicity to the BR with PMPRT, and a recent study suggests that PMPRT is associated with an elevated risk of surgical intervention for reconstruction complications compared with photon PMRT.[12] However, published data on BR complications with PMPRT are scarce, and the vast majority report on PMPRT to TEs and implants[12-15] and do not include immediate autologous flap reconstruction as a primary reconstruction strategy. In this report, we aim to report complications requiring minor or major surgical intervention among patients treated with PMPRT to implant, TE, and autologous flap reconstructions.

Methods and Materials

This was a single-institution study of women with breast cancer enrolled on a prospective registry of proton therapy at our institution who underwent PMPRT. We included patients who were treated with protons after mastectomy and BR with either passively scattered (PS) or pencil beam scanning (PBS) technique. We use 2 beams in our practice, a right anterior oblique and a left anterior oblique. For expander cases, multifield optimization is used.[16] All other reconstruction types are planned with single-field optimization.

Patients with history of prior radiation to the ipsilateral chest wall (reirradiation) were excluded. However, PMPRT courses for recurrent breast cancer (eg, chest wall or axillary recurrence) who had a history of prior mastectomy with reconstruction without adjuvant radiation were included. Conventionally fractionated radiation therapy was delivered to an initial dose of 50 or 50.4 Gy RBE in 1.8 Gy daily fractions, with or without a chest wall boost, at the discretion of the treating physician. Chest wall boosts were either 10 Gy in 4 to 5 fractions or 16 Gy in 8 fractions, with proton, photon, or electron technique. Clinical target volumes included the chest wall, axilla, and supraclavicular nodes with or without coverage of the internal mammary nodes (IMN), at the discretion of the treating physician. Contours were in accordance with the Radiation Therapy Oncology Group atlas and/or RADCOMP atlas.[17] Organs at risk (OAR) were contoured and included the heart and lungs. Coverage parameters were set such that 95% of the dose covered 95% of the chest wall planning target volume. Patients were treated with 2 oblique anterior fields using single-field or multifield optimization where appropriate. Patients were treated supine with the ipsilateral arm up using a Vac-Lok bag (CIVCO) for immobilization. Deep inspiration breath hold was used at physician's discretion to reduce the dose to the heart and lungs in challenging anatomy. Daily kilovoltage images were taken for localization. Patients had at least 1 cone beam computed tomography (CT) or verification simulation for quality assurance of positioning and stability of the anatomy in comparison with the initial CT simulation after the start of radiation. Radiation was started a minimum of 4 weeks after the last surgery or after clearance from the plastic surgeon, whichever was later.

We reported the reconstruction type that was in place at the time of radiation: autologous flap, TE, or permanent implant. Surgical details of reconstruction type were extracted via chart review of operative notes and confirmed by CT images performed at the time of simulation. TE and implant reconstructions were further categorized as either prepectoral or postpectoral. Postpectoral (also known as "sub" or "retro-pectoral") reconstruction involves placing the TE or implant deep into the pectoralis muscle. Prepectoral reconstruction involves placing the implant or TE under the skin and overlying the pectoralis muscle. Autologous flap reconstructions were further categorized as muscle sparing free transverse rectus abdominis myocutaneous flap, deep inferior epigastric perforator flap, or transverse gracilis myocutaneous flap.

We included radiation-related complications that required surgical intervention only, which was determined by chart review of surgical notes and encounters. Similar to the methodology of Noaum et al,[12] surgical intervention was selected as the event of interest in order to avoid subjective variability inherent to toxicity grading. A major reconstruction complication (MRC) was defined as a radiation-related complication requiring surgical intervention to the reconstruction, with or without successful salvage/repair of the reconstruction (eg, radiation-related capsular contracture requiring surgery with capsulotomy and implant exchange). An absolute reconstruction failure (ARF) was defined as the subset of MRC where a complication leads to surgical removal of the

reconstruction (implant, TE, or autologous flap) without replacement reconstruction in place at the time of last available follow-up. The date of the surgical intervention for MRC or ARF was noted. For patients with ARF, if they had prior attempts at surgical revision that ultimately failed, only the last surgery date where the reconstruction was removed without replacement was used for analysis. The complication (eg, capsular contracture, fat necrosis, infection, etc) that prompted surgical intervention was noted. A routine revision (RR) or minor surgical intervention was defined as plastic surgeon–intended refinement of the cosmetic outcome of the reconstructed breast, not necessarily related to PMPRT toxicity. For example, fat grafting to improve the contours of an autologous flap or routine implant exchange of an old implant for a new implant coded as an RR not an MRC. For those who underwent a 2-stage reconstruction, the planned TE to permanent implant exchange was not counted as an event. Similarly, capsular contracture of a TE before permanent implant exchange was not counted as an event, given that capsular contracture is routinely addressed at the time of exchange to permanent implant. Thus, for those with TE in place at the time of radiation, MRC/ARF was only reported as an event if it occurred after exchange to permanent implant.

Descriptive statistics were used to summarize patient and treatment characteristics. Kaplan-Meier method, measured from date of first PMPRT fraction, was used to assess overall survival (OS), progression-free survival (PFS), freedom from distant metastasis, and freedom from MRC. Cox regression was used to assess predictors of MRC. Statistical analysis was performed using SAS OnDemand for Academics.

Table 1 Demographics and clinical features

Characteristic	Median (range)
Age (y)	47 (25-66)
BMI	26.3 (18.2-49.8)
	N (%)
Diabetes (N = 68 patients)	4 (5.9)
Smoking status (N = 68 patients)	
Never smoker	50 (73.5)
Former smoker	16 (23.5)
Current smoker	2 (2.9)
Histology (N = 73 mastectomies)	
Ductal carcinoma/NOS	48 (65.8)
Lobular	23 (31.5)
Paget	1 (1.4)
Adenoid cystic/cribriform	1 (1.4)
Clinical group stage at diagnosis (N = 68 patients)	
0	5 (7.4)
1	19 (27.9)
2	20 (29.4)
3	23 (33.8)
4	1 (1.5)
Laterality (N = 68 patients)	
Left	43 (63.2)
Right	20 (29.4)
Bilateral	5 (7.4)

Abbreviations: BMI = body mass index; NOS = not otherwise specified.

Results

Between 2013 and 2021, 73 courses of PMPRT were delivered to 68 patients with BR after mastectomy for their breast cancer. The median follow-up time, measured from last fraction of PMPRT, was 42.1 months (95% CI, 32.3-50.1). The median age was 47 years (range, 25-66). Eighteen (24.7%) were treated for recurrent disease. Among those who were treated for recurrent disease, 12 had a history of prior mastectomy and reconstruction without adjuvant radiation. Table 1 shows a summary of demographics and clinical features.

Fifty-three courses (72.6%) had an initial dose of 50 Gy RBE/25 fractions, and 20 courses (27.4%) had an initial dose of 50.4 Gy RBE/28 fractions. PBS proton beam was used in 56 (75%) and PS proton beam in 17 (23.7%). Sixteen (21.9%) received a chest wall boost of 10 Gy RBE/4 to 5 fractions of 16 Gy RBE/8 fractions with a proton, photon, or electron technique. Table 2 shows a summary of treatment details.

Dosimetric data for the initial plans are listed in Table 3. Adequate mean clinical target volume (CTV) coverage (CTV D95% = 92.6%) and IMN coverage (IMN V90% = 98.5%) were achieved with acceptable doses to OARs. The average mean heart dose was 1.5 Gy and the mean lung V20 Gy was 12.4%. Mean heart dose was highest for bilateral chest wall courses (2.0 Gy, N = 8) and lowest for right chest wall courses (0.7 Gy, N = 22). Left chest wall courses had a mean heart dose of 1.9 Gy (N = 43).

Of 73 reconstructions, 29 had autologous flaps (39.7%), 30 implants (41.1%), and 14 TE (19.2%) in place at the time of PMPRT. Among the 30 permanent implants in place at the time of PMPRT, 10 were direct-to-implant reconstructions and 19 were 2-stage surgeries where an expander was placed before permanent implant placement (and permanent implant exchange occurred before the start of radiation). For 1 patient, details were not available to determine whether at the time of mastectomy there was an expander versus a direct-to-implant reconstruction. Table 4 shows additional reconstruction surgical details. There were 20 reconstructed breasts (27.4%) that

Table 2 Treatment characteristics

N = 73 courses	N (%)
Chemotherapy	
Neoadjuvant	13 (17.8)
Adjuvant	38 (52.1)
Both	2 (2.7)
None	20 (27.4)
Nodal evaluation	
Axillary lymph node dissection	50 (68.5)
Sentinel lymph node dissection	20 (27.4)
No nodal evaluation	3 (4.1)
Initial dose/fractionation (chest wall and regional nodes)	
50 Gy/25 fractions	20 (27.4)
50.4 Gy/28 fractions	53 (72.6)
Proton technique	
Passively scattered	17 (23.3)
Pencil beam scanning	56 (76.7)
Cone down dose/fractionation (chest wall)	
10 Gy/5 fractions	13 (17.8)
16 Gy/8 fractions	3 (4.1)
None	57 (78.1)
Cone down technique	
Protons	12 (16.4)
Photons (IMRT)	2 (2.7)
Electrons	2 (2.7)
IMN treated	62 (84.9)

Abbreviations: IMN = internal mammary nodes; IMRT = intensity modulated radiation therapy.

Table 4 Reconstruction surgical details

N = 73 reconstructions	N (%)
Implant	30 (41.1)
Prepectoral	1
Postpectoral	27
Unknown insertion location	1
Expander	14 (19.2)
Prepectoral	4
Postpectoral	9
Unknown insertion location	1
Autologous flap type	29 (39.7)
DIEP	9
MSFTRAM	19
TMG	1

Abbreviations: DIEP = deep inferior epigastric perforator; MSFTRAM = muscle sparing free transverse rectus abdominis myocutaneous; TMG = transverse gracilis myocutaneous.

underwent 1 or more RR. There were 9 (12.3%) MRC: 5 implants (6.8%), 2 flaps (2.7%), and 2 TEs (2.7%). Three (4.1%) of these MRC were also ARF. Table 5 shows complication details. Median time from start PMPRT to MRC was 29.1 months (range, 7.8-43.2). Complications leading to MRC included capsular contracture in 5 (6.9%), fat necrosis in 2 (2.7%), and infection in 2 (2.7%).

Specifically among the 12 patients who were treated for recurrent disease and also had a history of prior mastectomy and reconstruction without adjuvant radiation, 11 had surgical excision of the recurrent disease before PMPRT. The reconstruction types included 2 deep inferior epigastric perforator flaps and 10 implants. For this patient population, the median time between reconstruction

Table 3 Dosimetric data

Dosimetric Measure	Mean	SD	Min	Max
Prescription		Initial: 50-54 Gy RBE/20-25 fractions (N = 73) Cone down: 10-16 Gy RBE/4-8 fractions (N = 16)		
Max dose (Gy)	58.5	4.8	53.3	79.4
CTV D95% (%)	92.6	7.9	71.8	102.1
IMN V90% (%)	98.5	3.6	79.6	100.6
Lung V20 Gy (%)	12.4	4.3	2.2	25.7
Ipsilateral lung V20 Gy (%)	23.9	6.5	5.8	35.0
Heart mean dose (Gy)	1.5	0.9	0.0	3.3
Contralateral breast V5 Gy (%)	0.5	1.6	0.0	10.9

Abbreviations: CTV = clinical target volume; IMN = internal mammary nodes; max = maximum; min = minimum; RBE = relative biologic effectiveness; V = volume.

Table 5 Reconstruction complications

Patient	Reconstruction type	Proton technique	Total dose (Gy)	Time from RT start −MRC/ ARF surgery (mo)	MRC +/- ARF	Reason for complication	Revision surgery details
1	Expander (prepectoral)	PBS	50.4	35.2	MRC	Capsular contracture	Capsulotomy and implant exchange
2	Expander (prepectoral)	PBS	50	29.5	MRC	Capsular contracture	Capsulotomy and implant exchange with latissimus muscle transposition flap to cover new implant
3	Implant (postpectoral)	PS	66.4	29.0	MRC	Capsular contracture	Capsulotomy and implant exchange with breast fat grafting
4	Implant (postpectoral)	PBS	50.4	43.2	MRC	Capsular contracture	Capsulotomy and implant exchange
5	Implant (postpectoral)	PS	50.4	7.8	MRC	Infection	Implant exchange; this was followed by a free flap reconstruction due to failure of the implant exchange 14 mo radiation start, which was intact at last follow-up
6	Implant (postpectoral)	PS	50.4	22.2	MRC with ARF	Capsular contracture	Implant removal without implant replacement
7	Implant (postpectoral)	PBS	60	36.9	MRC with ARF	Infection	Implant removal, debridement without implant replacement
8	MSFTRAM flap	PBS	50	12.4	MRC with ARF	Fat necrosis of flap and skin necrosis of lower pole of mastectomy	Removal of entire breast reconstruction after failed partial debridement with poor wound healing
9	MSFTRAM flap	PBS	50.4	25.4	MRC	Fat necrosis	Excision of fat necrosis

Abbreviations: ARF = absolute reconstruction failure; MRC = major reconstruction complication; MSFTRAM = muscle sparing free transverse rectus abdominis myocutaneous; PBS = pencil beam scanning; PS = passively scattered; RT = radiation.

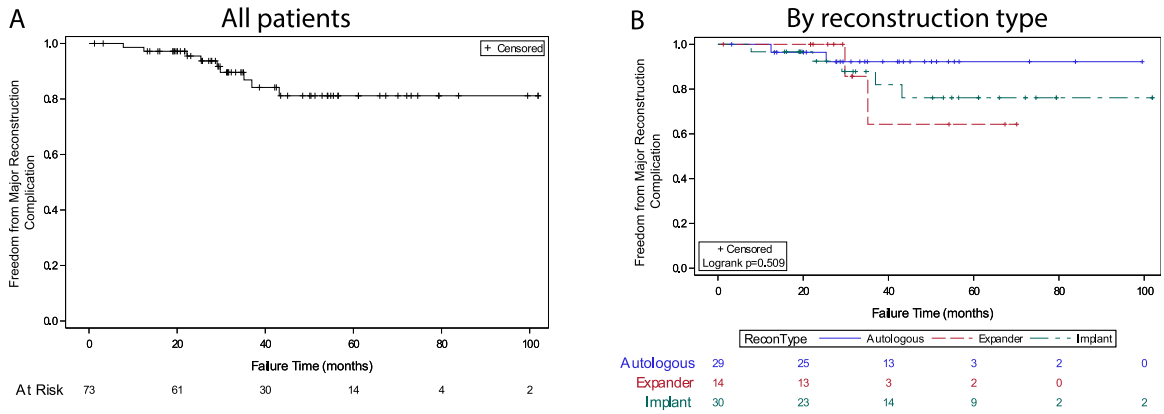

Figure 1 (A) Freedom from major reconstruction complication for all patients. (B) Freedom from major reconstruction complication for all patients separated by reconstruction type with autologous flap, expander, or implant.

surgery and the first fraction of PMPRT was 67 months (range, 20-240). Three of the 12 had MRC because of post-pectoral implant contracture. Time from start of PMPRT to MRC for these 3 patients was 22, 29, and 43 months.

On univariable analysis, reconstruction type, axillary nodal evaluation, boost, PBS/PS technique, age, and smoking status were not associated with MRC, whereas higher body mass index trended toward significance (hazard ratio, 1.07; 95% CI, 0.99-1.16; P = .10; Table E1). The 3-year freedom from MRC was 86.9% (95% CI, 73.9%-93.7%) and did not significantly differ by reconstruction type (Fig. 1).

Disease outcomes were as follows: 1- and 5-year locoregional control was 98.6% and 92%, respectively. Four-year OS and PFS were 91.5% and 77.1%, respectively. One- and 4-year distant control was 91.5% and 79.6%, respectively.

Discussion

For patients undergoing mastectomy with reconstruction for breast cancer, the risk of reconstruction complications due to adjuvant radiation with conventional photon PMRT is well documented[6]; however, it is unclear whether this risk is modified with proton therapy. In our study, 12% of patients experienced MRC. Here, we demonstrate that it is uncommon for a radiation-related reconstruction complication to lead to surgery compared with prior published reports. Permanent loss of the implant is very uncommon, with only 4% of patients experiencing ARF. Routine revision, however, was frequent in our practice, with 27% of patients undergoing a plastic surgery procedure intended to refine the cosmetic outcome of the reconstruction after PMPRT.

A recent study by Naoum et al[12] reported complications after implant-based reconstruction after PMRT and found that the "overall reconstruction failure," which aligns with our definition of MRC, was strongly associated with protons compared with photon PMRT, with an odds ratio of 5.56 (95% CI, 1.72-18.5; P = .004). Proton technique was also associated with increased odds of capsular contracture, with 47% of the proton patients experiencing contracture requiring surgical intervention. They hypothesized that the inherent high energy deposition at the end of a proton beam path may cause more contracture and lead to reconstruction failure. It is noted that Naoum et al[12] used a single proton field, compared with 2 fields in our study and routine in our practice. Their study was limited by the number of patients treated with the proton technique, representing 17 of the total 309. Other published data of proton PMRT complications demonstrate a smaller incidence of MRC, ranging from 22% to 29%. Table 6 compares the current study to others that report on PMPRT reconstruction complications. These represent single-institution experiences and are retrospective, with the exception of the phase 2 proton RT study reported by Jimenez et al.[13]

To our knowledge, the current study represents the largest published experience of PMPRT after BR, with 73 courses, and a substantial median follow-up time of 42 months to capture early and late events. Our data show that MRC occurs late, with a median time from PMPRT to MRC of 29 months (2.4 years). We also demonstrate the lowest incidence of MRC, 12.3%, compared with other known PMPRT series (Table 6).[12-15] Although exploratory, some possible explanations compared with other series include the use of 2 anterior oblique fields compared with a single anterior oblique field in other clinical or relatively high use of PBS (over three-quarters of patients) compared with other studies that may mitigate skin toxicities and improve dose conformity.

Of note, our study includes a large proportion of immediate autologous flap reconstructions (40%), which is underrepresented in other PMPRT studies. Apart from the current study in Table 6, there is a single flap reconstruction in the study by Luo et al.[14] Our data show that immediate autologous flap reconstruction has a low incidence of MRC (7%, 2 of 29 flaps) after PMPRT. Photon PMRT data also demonstrate a low rate of complications

Table 6 Comparison of studies reporting complications after PMPRT

Study first author, institution	Total number of PMPRT courses	Reconstruction type at time of PMPRT	Years treated	Median follow-up (mo)	Follow-up time measured from	MRC crude incidence* N (%)
Current study	73	30 implants, 14 expanders, 29 flaps	2013-2021	42	Date of PMPRT start	9 (12.3)
Current study (implant/expander only)	44	14 expanders, 30 implants	2013-2021	42	Date of PMPRT start	7 (15.9)
Smith, Mayo Clinic[15]	51	51 expanders	2015-2017	16	Date of PMPRT end	11 (21.6)
Luo, Memorial Sloan Kettering[14]	26	25 implants, 1 flap	2013-2015	35	Date of PMPRT end	7 (26.9)
Naoum, Mass General Hospital[12]	17	14 implants, 3 expanders	2000-2019	84	Date of diagnosis	9 (52.9)
Jimenez, Mass General Hospital[13]	49	(38 implants, 11 expanders)	2011-2016	55	Date of PMPRT start	14 (28.6)

Abbreviations: MRC = major reconstruction complication; PMPRT = postmastectomy proton radiation therapy.

* Studies have varying definitions and terminology to describe MRC. We applied our definition of MRC to the data available in each study for the purpose of comparison. Studies also had varying inclusion criteria. This table includes courses of PMPRT where there was either implant, expander, or flap in place at the time of PMPRT delivery. It does not include patients who had radiation reconstruction complications before undergoing PMPRT or patients who had no reconstruction at the time of PMPRT.

with flap reconstruction: In a systematic literature review evaluating the morbidity associated with autologous flap reconstruction and chest wall irradiation, there was a low total flap loss rate of 4% among the pooled 426 patients who had reconstruction followed by PMRT.[18] Likewise, we found a low incidence of total flap loss (or ARF), with 1 event among 29 flap reconstructions (3.4%). A separate meta-analysis found an unplanned reoperation rate of 7.6% among the pooled 729 patients who had flap reconstruction followed by PMRT.[19] Again, our data demonstrate similar findings, with 2 events of MRC among 29 flap reconstructions (6.9%). Prior study has found that autologous flap reconstruction may result in fewer complications and improved patient satisfaction compared with implant-based reconstruction.[6,20] Our analysis did not find a statistically significant association between reconstruction type and MRC; however, the incidence of MRC for flap reconstructions was lower than for radiation to the implant (2.7% vs 6.8%). It is possible that the small number of events did not provide the power to detect a statistically significant difference between reconstruction types. Also of note, among the 7 implants/expander cases of MRC, 5 were caused by capsular contracture (the other 2 due to infection). This suggests that capsular contracture is the dominant etiology of MRC for implant-based reconstructions. The 2 flap reconstruction MRCs were caused by fat necrosis, which is specific to a tissue-based reconstruction.

If the high proportion of autologous flaps contributed to the reconstruction success rate in our study, it is possible that the low proportion of TE reconstruction (19%) at the time of PMPRT in our cohort may have also played a role. There are PMRT data to suggest that radiation to a TE may result in a higher risk of reconstruction complications than radiation to a permanent implant.[12,21,22] For example, in the Naoum et al[12] analysis of their entire cohort of 309 patients (who mostly received photon PMRT), they found that radiation to the expander had significantly higher odds of overall reconstruction failure compared with radiation to the implant, with a hazard ratio of 2.11 ($P = .02$)[12]. Again, although we did not find a statistically significant difference in MRC between implant and expander, the low number of MRC events may have prevented the analysis from detecting small differences.

When a patient has a particularly challenging case because the desire for optimal target coverage and concerns for potential toxicity to critical organs compete, protons may offer a way to both optimize cancer control and minimize adverse events. Most of the PMPRT courses in our analysis had risk factors for increased incidental dose to the heart and lungs; over 70% were either treated to the left chest wall or bilaterally, and 62% of courses included treatment of the IMN region. Despite these treatment characteristics, our dosimetric data demonstrate that PMPRT meets CTV coverage goals while maintaining low

Table 7 Comparison of disease outcomes among studies of PMPRT with breast reconstruction

Study first author, institution	Actuarial time point	Overall survival (%)	Local control (%)	Progression-free survival (%)	Distant metastasis-free survival
Current study	4 y	91.5	At 1 y, 98.6	77.1	79.6
Smith, Mayo Clinic[15]	Disease outcomes not reported				
Luo, Memorial Sloan Kettering[14]	3 y	97.2			84.1
Naoum, Mass General Hospital[12]	5 y	Not reported	95.3 for RTE; 97.7 for RTI	Not reported	
Jimenez, Mass General Hospital[13]	5 y	91	Not reported	Not reported	86

Abbreviations: PMPRT = postmastectomy proton radiation therapy; RTE = radiation to expander; RTI = radiation to implant.

dose to OAR: the average mean heart dose (MHD) in our study was 1.5 Gy RBE, and the lung V20 was 12.4%. To put this into the context of historical literature, in a systematic review of 167 breast cancer radiation studies published between 2003 and 2013, the average MHD was 5.2 Gy, which increased to an average of 8.5 Gy for a subset of patients treated to the left side and to the IMN region.[23] With contemporary radiation techniques, heart doses have steadily decreased, and in a Michigan registry study of photon radiation after lumpectomy, in the year 2015, the median MHD was 1.85 Gy for left sided cases that included nodal fields.[24] For lung metrics, reducing the ipsilateral lung V20 to less than 30% has been shown to decrease the rate of pneumonitis.[25] Considering the potential benefits to the heart and lung with proton technique, combined with high locoregional control and the 12.3% incidence of MRC in our study, PMPRT may be a favorable option among patients desiring BR.

Disease outcomes were favorable with PMPRT. Four-year OS was 91.5%, and PFS was 77.1% among our patient population, where over 60% were treated with chemotherapy, and our patient population was fairly evenly distributed between clinical stage 1, 2, and 3 breast cancer (Table 1 shows demographics). Table 7 shows a comparison of disease outcomes among studies of PMPRT with breast reconstruction.

Our study had certain limitations. It was a retrospective analysis of patients prospectively enrolled on a proton registry study. Although there was significant uniformity of practice over the study years within this single institution experience, the specific proton dose and technique were not prospectively controlled over the 8 years of the study period. By limiting the study period to 2021, we ensured that the median follow-up was longer than the median time to complications and that the majority of the patient cohort had a minimum follow-up of 2 years. We did not report complications that did not require surgery, such as dermatitis, which is a common toxicity of PMRT. Prospective reporting of complications that do not require surgery, as well as patient reported outcomes, are the subject of future work. We also did not report on aesthetic outcome, which is challenging to quantify in a standardized manner and capture retrospectively; however, it remains a central component of the success of a BR. Reirradiation and hypofractionated regimens were not included, and there was no comparison to photon PMRT. There was a low event rate overall of MRC, which may have hindered our ability to detect statistically significant associations.

Conclusion

In conclusion, the current study represents the largest known published data set of PMPRT with reconstruction and includes the largest cohort with autologous flap reconstruction. Patients undergoing PMPRT with a reconstruction with autologous flap, implant, and TEs had a low incidence of complications leading to surgical intervention, and reconstruction loss was very rare. MRC rates were not significantly different among reconstruction types. Routine revisions after PMPRT are common in our practice. PMPRT provides excellent locoregional control and favorable dosimetry to critical organs such as the heart and lung.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2023.101385.

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