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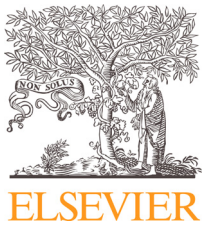

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Pre-operative Radiotherapy And Deep Inferior Epigastric Artery Perforator (DIEP) flAp study (PRADA): Aesthetic outcome and patient satisfaction at one year

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Summary *Introduction:* The optimal combination of radiotherapy and breast reconstruction has not yet been defined. Post-mastectomy radiotherapy (PMRT) has deleterious effects on breast reconstruction, leading to caution amongst surgeons. Pre-operative radiotherapy (PRT) is a growing area of interest, is demonstrated to be safe, and spares autologous flaps from radiotherapy. This study evaluates the aesthetic outcome of PRT and deep inferior epigastric artery perforator (DIEP) flap reconstruction within the **P**re-operative **R**adiotherapy **A**nd **D**eep Inferior Epigastric artery Perforator (DIEP) fl**A**p (PRADA) cohort.
Methods: PRADA was an observational cohort study designed to evaluate the feasibility and safety of PRT for women undergoing neoadjuvant chemotherapy and DIEP reconstruction. Panel evaluation of 3D surface images (3D-SIs) and patient-reported outcome measures (BREAST-Q) for a subset of women in the study were compared with those of a DIEP-PMRT cohort who had undergone DIEP reconstruction and PMRT.
Results: Seventeen out of 33 women from the PRADA study participated in this planned sub-study. Twenty-eight women formed the DIEP-PMRT cohort (median follow-up 23 months). The

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median (inter-quartile range [IQR]) 'satisfaction with breasts' score at 12 months for the PRADA cohort was significantly better than the DIEP-PMRT cohort (77 [72-87] versus 64 [54-71], respectively), $p=0.01$). Median [IQR] panel evaluation (5-point scale) was also significantly better for the PRADA cohort than for the DIEP-PMRT cohort (4.3 [3.9-4.6] versus 3.6 [2.8-4] $p=0.003$).
Conclusions: Aesthetic outcome for the PRADA cohort was reported to be 'good' or 'excellent' in 93% of cases using a bespoke panel assessment with robust methodology. Patient satisfaction at one year is encouraging and superior to DIEP-PMRT at 23 months. Switching surgery-radiotherapy sequencing leads to similar breast aesthetic outcomes and warrants further large-scale, multi-centre evaluation in a randomised trial.

Introduction

The optimal integration of radiotherapy and breast reconstruction surgery timing and techniques has not yet been defined. Heterogeneity between studies regarding both surgical and radiotherapy approach, follow-up, and primary end points make robust comparison challenging. Post-mastectomy radiotherapy (PMRT) is offered to women with higher risk of locoregional recurrence and results in improved local regional control and survival.[1] However, PMRT has deleterious effects on the reconstructed breast, leading to many women being advised against immediate reconstruction.[2]

It is now generally accepted that immediate reconstruction is preferable over delayed reconstruction mainly because of the superior aesthetic outcome achieved by maintenance of the natural skin envelope. While awaiting delayed reconstruction, women are affected by low emotional well-being, poor body image, and social distress.[3,4] Autologous breast reconstruction is reported to be, on balance, the technique of choice, given its lower rate of complications and reconstruction failure, acceptable flap survival rates,[5] and cosmesis. The reported deleterious effects of radiotherapy on autologous reconstruction are flap volume reduction (12.3% with radiotherapy versus 2.6% without) and higher rates of fat necrosis,[6] flap contracture,[7] and breast symptoms (including neo-breast pain, swelling, sensitivity, and skin changes).[8] Some women experience minimal PMRT reconstruction complications while others suffer major complications, some resulting in reconstruction failure; this unpredictability leads to caution among surgeons.

The use of pre-operative radiotherapy (PRT) or neoadjuvant radiotherapy is a growing area of interest in breast cancer treatment.[9] In the context of reconstruction, the change in sequence of treatment may mitigate some of the effects of PMRT on the reconstructed breast: by irradiating the breast prior to mastectomy and reconstruction, the autologous flap itself is spared radiotherapy, potentially reducing fibrosis and fat necrosis. PRT is consistently reported to be both oncologically and surgically safe.[10-15] Other potential benefits of PRT include reduced time for completion of the treatment,[16] improved access to immediate breast reconstruction,[16,17] and the ability to assess tumour response to radiotherapy which may prove to be a surrogate end point for local control, potentially improving the efficiency of knowledge-generating research and offering the opportunity for radiobiological studies.[17] Operative concerns regarding PRT were largely linked to radiation-related vascular injury leading to poor healing and necrosis of the skin flaps.[10,18] Outcomes pertaining to wound complications and skin necrosis rates from recent trials involving PRT, mastectomy, and breast reconstruction have, however, been reassuring.[15,19,20] An additional challenge was to define the timeline to enable resolution of acute inflammation and maximise tumour regression yet minimise fibrotic changes within the surgical field.

The aesthetic outcome after PRT and reconstruction is reported to be good to excellent in majority of the studies.[12,13,15,19] However, heterogeneity between surgical techniques, methods of assessment, scales for scoring cosmesis, and follow-up limits comparison between studies or a meta-analysis of results.

The **P**re-operative **R**adiotherapy **A**nd **D**eep Inferior Epigastric artery Perforator (DIEP) fl**A**p study (PRADA study) [NCT02771938] was a prospective cohort study to assess the surgical safety and feasibility of PRT in women with locally advanced breast cancer undergoing neoadjuvant chemotherapy (NACT), mastectomy, and DIEP flap reconstruction who were recommended PMRT. The primary end point was the presence of an open breast wound at 4 weeks post-surgery.[21] Secondary end points included aesthetic evaluation and patient satisfaction, and these are reported here.

Methods

The PRADA study recruited candidates at two major London centres performing a high volume of autologous breast reconstructions. All patients who were due to undergo NACT, mastectomy with DIEP flap reconstruction (either following unsuccessful breast conservation surgery or upfront selection), and PMRT were offered the alternative sequence of radiotherapy before skin-sparing mastectomy and DIEP reconstruction. In these patients, radiotherapy was delivered to the breast (+/- regional nodes) 2–6 weeks after completing NACT and 4–6 weeks before the surgery. The radiotherapy dosing schedule was either 40Gy in 15 fractions over 3 weeks or 42.72Gy in 16 fractions over 3.2 weeks. Thirty-three patients were recruited to the PRADA study between 2016 and 18, and the primary outcome measure was the presence of an open wound at 4 weeks. All participants were

invited to participate in three-dimensional surface imaging (3D-SI) at the baseline, 3 months, and 12 months postoperatively to enable aesthetic evaluation of the outcome. Only one of the three sites had 3D-SI capability; so, while all participants were invited to join the aesthetic outcome sub-study, only those who were able to travel to that site were included. At the same time points, participants also completed a BREAST-Q breast reconstruction questionnaire – a validated patient-reported outcome measure (PROM) used to measure health-related quality of life and patient satisfaction.[22]

Results from a previous study of aesthetic outcome after DIEP flap reconstruction and PMRT at the Royal Marsden were used for comparison and will henceforth be referred to as the DIEP-PMRT cohort.[23] The 28 participants in the DIEP-PMRT cohort underwent mastectomy and DIEP reconstruction, followed by PMRT between 2009 and 2014. A single 3D-SI and BREAST-Q were completed at a median follow-up of 23 (interquartile range [IQR] 17–38) months after treatment. Some women in the DIEP-PMRT cohort received a higher dose of radiotherapy than those in the PRADA group (Table 2). Propensity matching was not undertaken as the follow-up period did not overlap.

3D-SIs were acquired using VECTRA XT® capture system (Canfield Scientific, New Jersey, USA). Women were positioned with their hands on their hips and their elbows behind the mid-axillary line to optimise visualisation of the lateral aspect of the breast. The images were taken at the end-inspiratory pause during quiet breathing.

3D-SIs from both cohorts were subject to panel evaluation using a scale developed through a Delphi consensus process specifically for breast reconstruction.[24] It consists of 5 sub-scales (symmetry, volume, shape, position of breast mound, and nipple-areola complex) in addition to a global scale. A 5-point Likert scale was used for each scale ranging from 'very poor' (1) to 'excellent' (5) (Table 3). Nine clinicians with at least 5 years of experience at consultant level comprised the panel: three oncoplastic surgeons, three plastic surgeons, and three radiation oncologists. To reduce bias, panellists were blinded to surgeon, radiation oncologist, and patient identity, as well as to the treatment received. A standardised sequence of 7 views of each 3D-SI was shown to the panel (right and left lateral and oblique, anteroposterior, cranial, and caudal). Images were viewed in one sitting, and panellists could ask for a patient sequence to be repeated if they required more time to give a score. Pre-treatment images were not scored. Discussion about the scores was not permitted. The panel was not shown benchmark images.

The BREAST-Q reconstruction module questionnaires were analysed using the Q-Score software. The resulting Q-score is from 0 to 100, with 100 being the best score. The results were compared with those from the DIEP-PMRT cohort. The minimal difference in the reconstruction BREAST-Q score which translates into clinical utility has been calculated at 4 points.[25]

Statistical Analysis

IBM SPSS Statistics 24 software was used to analyse the data. The mean global panel score from the 9 panellists was used for analysis. Simple descriptive statistics were used, with either mean and standard deviation or median and IQR according to the distribution of the data. The Mann–Whitney U test was used to describe the significance of between-group differences for panel and Q-scores.

Results

Seventeen out of 33 women from the PRADA study participated in the aesthetic evaluation. 3D-SI was completed by 15 women at baseline, 15 at 3-months, and 13 at 12-months of follow-up. BREAST-Q was completed by 14 women at baseline (pre-operative), 13 women at 3 months, and 12 women at 12 months. Completed BREAST-Q questionnaires were available for 27 of the 28 participants in the DIEP-PMRT cohort, and 3D-SI was available for all.

Demographics and clinical data are reported in Table 1. Operation dates for the DIEP-PMRT cohort ranged from October 2009 to September 2014 and for the PRADA cohort from April 2016 to March 2018. Median follow-up was significantly shorter in the PRADA group than the DIEP-PMRT cohort at 12 (IQR 12-12) and 23 (IQR 17-38) months, respectively ($p<0.01$). Mean (range) age was significantly lower in the PRADA cohort than the DIEP-PMRT cohort 49 (range 36-60) and 57 (range 42-72) ($p<0.01$). The body mass index was similar between cohorts. Median time from radiotherapy to surgery for the whole PRADA cohort was 20 days.

Patient satisfaction

The median (IQR) 'satisfaction with breasts' Q-score for the PRADA cohort was 48 (48-53), 73 (67-81), and 77 (72-87) at baseline, 3 months, and 12 months, respectively, and 64 (54-71) in the DIEP-PMRT cohort at a median follow-up of 23 (IQR 17-38) months (Figure 1). The Q-score for the PRADA cohort at 12 months was significantly higher than for the DIEP-PMRT cohort ($p = 0.01$). The Q-scores for the other BREAST-Q domains are illustrated in Table 4.

Panel assessment of aesthetic outcome

The median (IQR) global panel score for the PRADA cohort at 3 months was 3.9 out of 5 (3.8-4.4) and 4.3 out of 5 (3.9-4.6) at 12 months and for the DIEP-PMRT cohort was 3.6 out of 5 (2.8-4) at 23 months as illustrated in Figure 2. The panel score for the PRADA cohort at 12 months was significantly higher than for the DIEP-PMRT cohort at 23 months follow-up ($p = 0.003$). Figure 3 shows example 3D-SIs of participants from the PRADA and DIEP-PMRT cohorts with close to median panel scores.

Discussion

This is the first prospective study to report on aesthetic outcome using a validated scale after PRT and DIEP flap reconstruction. Good expert panel aesthetic scores were awarded to the PRADA cohort, with a median panel score of 4.3 out of a maximum of 5 points at 12-month of follow-up. This was

Table 1 Inclusion and exclusion criteria for the PRADA and DIEP-PMRT cohorts.

	Inclusion criteria	Exclusion criteria
PRADA Cohort[21] (PRT – DIEP)	>18 years Histopathological confirmation of breast cancer Require mastectomy for any reason Require adjuvant radiotherapy Suitable for DIEP flap reconstruction at the time of mastectomy	Inability to give informed consent MDM unable to recommend radiotherapy based on pre-operative histopathological and imaging findings Severe chemotherapy toxicity affecting treatment plan schedule
DIEP – PMRT cohort[23]	>18 years Histopathological confirmation of breast cancer Mastectomy and immediate DIEP reconstruction PMRT Operated between 2009-2014 at the Royal Marsden Hospital Able to attend for 3D-SI and complete BREAST-Q	Subsequent diagnosis of local recurrence, contralateral breast cancer, or metastatic disease Less than 1 year after the end of oncologic treatment Inability to answer the questionnaire or living outside the United Kingdom DIEP flap for chest wall resurfacing rather than breast reconstruction DIEP flap for non-breast cancer abnormality (e.g., sarcoma) DIEP flap for cosmetic failure of other reconstruction/breast conservation "Salvage" DIEP flap reconstruction i.e. failure of implant reconstruction to a flat chest wall and subsequent DIEP reconstruction.

Table 2 Demographics for the PRADA aesthetic cohort and the DIEP-PMRT cohort.

	PRADA cohort n=17	DIEP-PMRT cohort n=28	Significance
Age			
mean (range)	49 (36-60)	57 (42-74)	P<0.001
BMI			
mean (range)	27 (21-36)	27 (21-34)	P=0.57
Follow up in months			
median (IQR)	12 (12-12)	23 (17-38)	P=0.01
Axillary treatment (%)			
Surgery	9 (47)	9 (32)	P=0.29
SLNB	9 (47)	9 (32)	-
ALND	8 (53)	19 (68)	
Radiotherapy			
Axilla	2		
SCF	11		
IMC	1		
Symmetrising surgery (%)	4(24)	6(21)	P=0.869
Radiotherapy regime (%)			
50Gy 25#	0	7 (25)	P=0.09
40Gy 15#	13 (76)	13 (46)	
42.67Gy 16#	4 (24)	2 (7)	
Performed at a different centre	0	6 (21)	

significantly better than the scores awarded to DIEP-PMRT cohort. However, as PRADA was a surgery feasibility study, it was not powered for this specific end point. The wider IQR observed in the DIEP-PMRT cohort may reflect the variability of results with PMRT and potentially indicate more predictable results with PRT.

There are caveats to the comparison, in that the follow-up period for the DIEP-PMRT cohort is almost double that of the PRADA cohort; therefore, the effect of radiotherapy over time may not be fully appreciated. It is reported that two thirds of complications of PMRT occur within the first year and 80% within two years,[26,27] so although major differ-

Table 3 Likert scale used in the panel evaluation.

		Excellent 5	Good 4	Moderate 3	Poor 2	Very Poor 1
Shape	The global shape of the reconstructed breast/s	Shape symmetry out of bra achieved	Shape of operated breast is pleasing but ***not symmetrical***	Moderate difference in shape but does ***not*** detract from overall aesthetic result	Moderate focal deficits ***detracting*** from overall aesthetic result	Large focal deficits ***distorting contour*** significantly detracts from overall aesthetic result
Volume	Overall volume symmetry between breasts	Equal volume between breasts	Minor difference in Volume	Moderate difference in volume but does ***not*** detract from overall aesthetic result	Volume difference impacts overall aesthetic result	Major volumes mismatch significantly detracts from overall aesthetic result
Nipple Position	Nipple position in relation to the ipsilateral breast	Excellent symmetry between sides and nipple in an ideal position on reconstructed breast mound	Minor adjustments required to achieve excellence in nipple position	Noticeably suboptimal but does ***not*** influence overall aesthetic results	Nipple position slightly impacts overall aesthetic result	Nipple position significantly detracts from overall aesthetic result
Position of Breast Mound	In relation to chest wall and other breast	Equal to the other side ***and*** in an optimal position on chest wall	Minor asymmetry of position ***or*** symmetrical but suboptimal position	Asymmetry of position ***or*** symmetrical but suboptimal position ***not*** detracting from overall aesthetic result	Slightly impacts overall aesthetic result	Significantly detracts from overall aesthetic result
Symmetry	Comparison between breasts	Out of bra symmetry achieved	Mild asymmetry	Moderate asymmetry but does ***not*** detract from overall aesthetic result	Moderate asymmetry detracting from overall aesthetic result	Significant asymmetry detracting from overall aesthetic result
Global	Taking into consideration subscale evaluation what is your overall impression of the quality of the reconstruction	Excellent	Good	Moderate	Poor	Very Poor

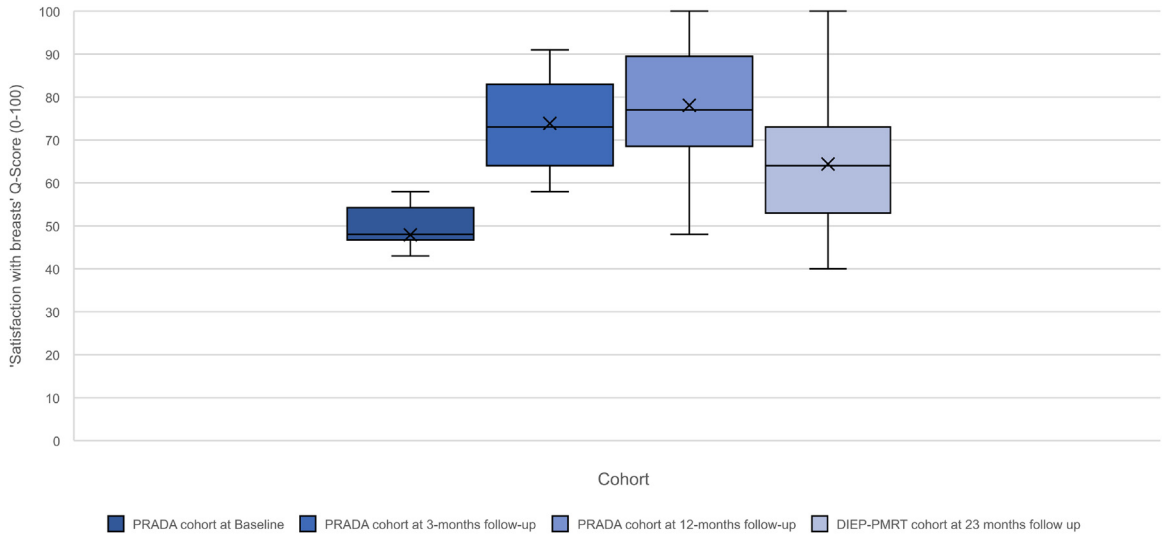

Figure 1 Box and whisker plot comparing the median Q-score for the BREAST-Q reconstruction module for the PRADA cohort at baseline, 3 months, and 12 months and the DIEP-PMRT cohort (median follow-up 23 months). Q-score of 100 is the maximum achievable.

Table 4 Summary of Q-score for the BREAST-Q reconstruction module for the PRADA cohort at baseline, 3 months, and 12 months post-surgery and the DIEP-PMRT cohort (median follow-up 23 months). Q-score of 100 is the maximum achievable.

Measurement timepoint	Satisfaction with breasts	Satisfaction with outcome	Psychosocial well-being	Physical well-being (chest)	Physical well-being (abdomen)	Sexual well-being
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
PRADA cohort baseline n=14/17	48 (48-53)	-	60 (53-79)	77 (70-91)	92 (83-100)	48 (40-60)
PRADA cohort at 3 months n=13/17	73 (67-81)	100 (75-100)	79 (67-82)	63 (58-78)	70 (67-84)	54 (49-67)
PRADA cohort at 12 months n=12/17	77 (72-87)	100 (83-100)	76 (62-92)	83 (80-93)	79 (70-100)	57 (42-93)
Historic control n=27/28	64 (54-71)	75 (67-100)	70 (62-86)	74 (66-85)	89 (75-89)	49 (44-66)

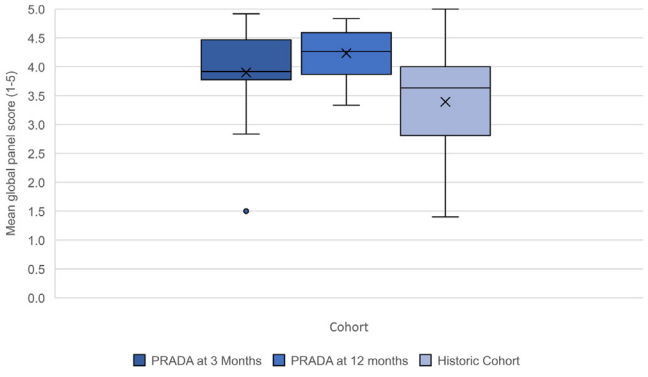

Figure 2 Box and whisker plot comparing median panel scores for the PRADA group at 3 and 12 months post-operatively and the DIEP-PMRT cohort (median post-radiotherapy follow-up 23 months). DIEP: deep inferior epigastric artery perforator flap; PRADA: pre-operative radiotherapy and DIEP flap reconstruction study; PMRT: post mastectomy radiotherapy.

ences are unlikely to have been missed, long-term follow-up is required to examine degradation of aesthetic results over time in both cohorts to truly appreciate the potential differences between PRT and PMRT on DIEP flap reconstruction aesthetic outcomes. There were also differences in the radiotherapy dose between groups with a proportion (although not statistically significant) in the DIEP-PMRT cohort receiving higher dose which may confound aesthetic outcomes.

Patient satisfaction with breasts

A 13-point difference in 'satisfaction with breasts' score was observed between the PRADA aesthetic cohort at 12 months and the DIEP-PMRT cohort at 23 months, and while this suggests better aesthetic outcome after PRT, we may not observe such a difference in a randomised study where the groups are more closely matched. Scores improved between 3 and 12 months, and one hypothesis is that post-operative discomfort or physical limitation, oedema, and scarring improve over this time frame. An alternative hy-

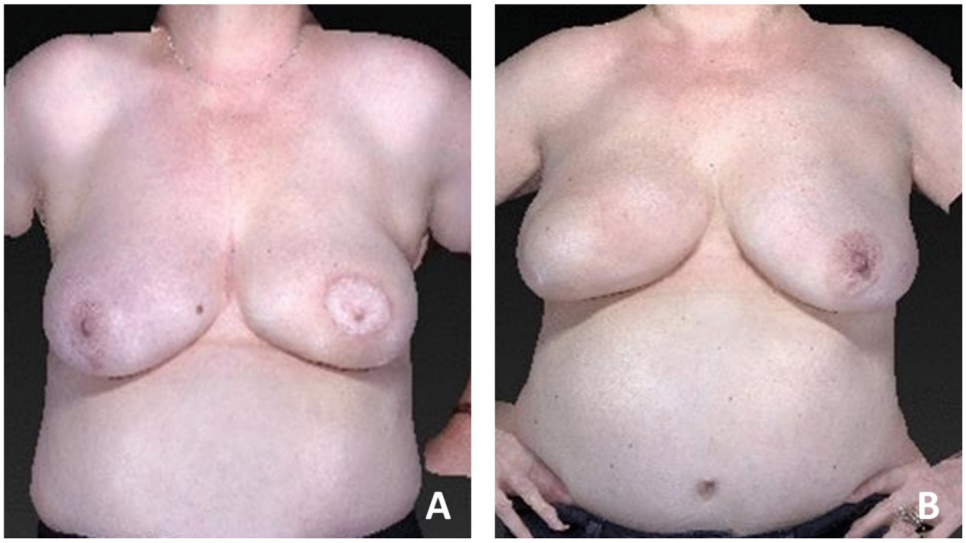

Figure 3 3D-SIs to represent median panel score from both cohorts. The panel assessed rotating 3D images. (A) 3D-SI from the PRADA cohort with a panel score of 4.3 and 'satisfaction with breasts' score of 85 (PRADA cohort median panel and BREAST-Q scores 4.3 and 77). (B) 3D-SI from the DIEP-PMRT cohort with a panel score of 3.6 and 'satisfaction with breasts' score of 69 (DIEP-PMRT cohort median panel and BREAST-Q scores 3.6 and 64). Both participants had unilateral surgery with no symmetrisation.

pothesis is that the women who did not provide a response to the questionnaire at 12 months were less satisfied. Two of the five women who did not respond at 12 months did respond at 3 months. Their scores were below the group's median for both 'satisfaction with breasts' and 'psychosocial well-being'. This reinforces the need for a larger, ideally randomised trial.

Panel assessment of aesthetics

Ninety-two percent of patients in the PRADA cohort received a good/excellent panel score (score of 4 or 5). Comparison with other PRT/reconstruction studies is challenging not only because of methodological differences between panel evaluations but also because of numerous other differences between studies.

In 2010, Giacalone et al reported aesthetic outcomes for 18 patients who received neoadjuvant chemoradiotherapy, skin-sparing mastectomy, and immediate latissimus dorsi (LD) reconstruction and 54 patients who received mastectomy, adjuvant radiotherapy, and delayed reconstruction at a mean follow-up of 4.7 years (without explicit reporting of the difference in follow-up between the two groups). Seventy-eight percent of the neoadjuvant chemoradiotherapy and immediate reconstruction group were awarded a good or excellent score by physicians versus 87% for the delayed reconstruction group.[19] The investigators employed the Gerber scale which includes 6 domains each with a maximum of 2 points (volume, shape, symmetry, ipsilateral and contralateral scars, and infra-mammary fold),[28] and two physicians rated the outcome either in person at a follow-up visit or using photographs. Although certain domains are similar to those used in the PRADA study, the methodology is different on a number of levels (blinding, number of raters, views, and 2D versus 3D photography). In addition, the comparison is drawn between a group with PMRT and delayed reconstruction limiting the relevance of the comparison.

A German group, also using the Gerber scale, reported good or excellent aesthetic outcome in 6 of 9 patients who underwent PRT, mastectomy, and immediate breast reconstruction.[13] This study had a small sample size, and the type of reconstruction included implant-based reconstruction (with acellular dermal matrix (ADM), LD, or implant alone), DIEP flap, and transverse rectus abdominis myocutaneous flap (TRAM) which may lead to different results after radiotherapy because of more muscle fibrosis/atrophy. The median follow-up was at 30 months (again without explicit statement that it was equal for the two groups). The median time from radiotherapy to surgery was 47 days which is longer than for the PRADA cohort (20 days) with a wider range (26-162 versus 12-39 days). The radiotherapy dose was also higher than that for PRADA (50.4Gy versus 40-42.72Gy).

A Canadian group published a retrospective review in 2012 of 30 women who received PRT and autologous reconstruction and reported good or excellent results in two-thirds of them.[12] A 4-point scale described by Kroll was used for shape and symmetry, where 3 points equated to a good score and 4 points an excellent score.[29] The senior author of the paper evaluated the outcome leaving the results open to bias. The median follow-up was longer than PRADA (3.5 years); the types of reconstruction used were LD, TRAM, or a combined method rather than DIEP reconstruction, the median time from radiotherapy to surgery was longer at 6.9 weeks (range 2.7-12.9), and the dose of radiotherapy was higher for most participants, 50Gy for 60% and hypofractionated for 40% (2.5Gy per fraction over 3.5 weeks).

Heterogeneity in study populations may reflect wide variations in clinical practice and changing trends in breast reconstruction. Internationally, over the past two decades, uptake of immediate breast reconstruction has increased (twofold in the UK between 1996 and 2012).[30] Implant-based

breast reconstruction remains the most popular reconstruction method (2015 data); there has been a decline in the popularity of LD-based reconstruction and an increase in DIEP flap reconstruction, most notably at specialist and academic centres.[30] At one of the institutions involved in the PRADA study, rates of LD-assisted reconstruction fell from 54% to under 1% of total immediate breast reconstruction from 2004 to 2013. Conversely, DIEP flap reconstruction rose from 1% to 38% over the same period.[30]

Patient-reported outcome measures (PROMs)

The PRADA cohort median 'satisfaction with breasts' Q score at 12 months follow-up was 77 [IQR 72-87], 13 points superior to those of the DIEP-PMRT cohort at 64 [IQR 54-71]. Disparity in follow-up may be a confounder. Complications associated with radiotherapy and breast reconstruction in the adjuvant or neoadjuvant setting can develop over a number of years; therefore, longer term PROM comparison between PRT and PMRT groups is required.[31] Participants in the PRADA cohort may also have had a perception of improved reconstructive quality owing to the theorecital benefits of 'sparing' the reconstruciton from the effects of radiotherapy.

The literature on patient-reported evaluation of reconstruction followed by PMRT has many limitations, with heterogenous populations and methods. However, it would appear that the 'satisfaction with breasts' Q-score for the PRADA population is also higher than in other studies of PMRT. Q-scores for irradiated implant-based reconstruction range from 40 to 58[32-34] and for irradiated autologous reconstructions from 44 to 66.[7,34] A study comparing 'satisfaction with breasts' in all types of breast cancer surgery (conservation, mastectomy only, and mastectomy and reconstruction [implant and autologous]) reported a Q-score of 71 for autologous reconstruction of which only 21% were irradiated.[35]

A Chinese study compared Q-scores after autologous reconstruction (TRAM or DIEP) with (n=86) and without (n=246) PMRT at >1-year follow-up. At 12 months the 'satisfaction with breasts' and 'psychosocial well-being' Q-scores for the unirradiated cohort were 68 and 76, respectively,[7] which are comparable to the PRADA cohort at one year (77 and 76, respectively). Lagendijk et al. report Q-scores for psychological, physical, and sexual well-being for 83 autologous reconstruction cases (78, 76, and 62, respectively), of which 22% were irradiated,[35] which is similar to the PRADA cohort score for the respective domains (76, 83, and 57, respectively). In contrast, a number of studies have failed to show a difference in patient-reported satisfaction for autologous reconstruction with or without PMRT.[7,8] While mindful of the aforementioned caveats limiting between-study comparisons, these observations may suggest that patients could be just as satisfied with their aesthetic outcome with PRT as they are in the absence of radiotherapy.

Studies reporting PROMs after PRT are scarce. Giacalone et al. used the Gerber scale and reported excellent or good aesthetic outcome in 89% of participants.[19] In a retrospective series of 111 patients who received PRT with LD reconstruction (+/- implant), an average patient satisfaction score of 17 out of 20 (85%) was reported at a median follow-up of 31 months.[15] The questionnaire used was not validated, so interpretation of results is challenging, but nonetheless encouraging. Other studies of neoadjuvant radiotherapy and breast reconstruction either do not evaluate aesthetic outcome at all[10,11,36] or do not describe their methods.[14] Given that all of the PRADA patients had locally advanced breast cancer and received radiotherapy, both of which have a negative impact on patient satisfaction, these early results from the feasibility study are encouraging.[37-39]

Within the limitations of this feasibility study, the PRADA treatment sequencing gives similar breast aesthetic outcomes and warrants further large-scale, multi-centre evaluation in a randomised trial.

Conclusion

The PRADA cohort represents one of the first prospective cohorts of PRT and DIEP flap reconstruction using validated aesthetic evaluation measures. Aesthetic outcome is reported as good or excellent in 92% of the cases using a bespoke panel assessment with robust methodology. Patient satisfaction at one year is encouraging and superior to DIEP and PMRT at 23 months. Heterogeneity in study design and methodology precludes reliable comparisons with the published literature.

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Compliance with Ethical Standards

There are no conflicts of interest.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standard. The protocol was reviewed and passed by London-Riverside NRES committee 15/LO/0010. The study is registered on a publicly accessible database, clinicaltrial.gov, NCT02304614.

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