Original Article

Impact of radiation on immediate breast reconstruction: a retrospective single institution cohort study

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Background: While the trend towards immediate breast reconstruction is growing, data on the long-term outcomes of patients receiving irradiation afterwards are scarce. We retrospectively reviewed the long-term complication rates in patients who received adjuvant radiation therapy after immediate breast reconstruction in our institution.

Methods: We included 134 patients with breast cancer who underwent single-stage immediate breast reconstruction between January 2008 and December 2018. Sixty-eight patients received adjuvant irradiation and 66 patients did not. Autologous tissue, implant-based, and combined (implant and flap) reconstruction were performed in 40, 55, and 39 patients, respectively. Flap and implant complications data were collected. Baker's classification was used to assess capsular contracture.

Results: The average follow-up was 47 months. Both groups had similar baseline clinical characteristics and treatments received. The irradiated-group had a higher incidence of adjuvant chemotherapy (P<0.01) and a significantly higher rate of grade III/IV capsular contracture (42.1% *vs.* 26.9%; P=0.004) than that of the non-irradiated group. The median time to the development of capsular contracture was 37 *vs.* 41 months in the irradiated *vs.* the non-irradiated group, respectively. There were no differences in the incidence of flap complications between both groups. The only significant risk factor associated with grade III/IV capsular contracture was adjuvant post-mastectomy irradiation. The irradiated group had a higher risk of developing grade III/IV capsular contracture [odds ratio (OR), 4.35; 95% confidence interval (CI): 1.55–12.27].

Conclusions: Postmastectomy radiotherapy adversely affects implant-based immediate one-stage reconstruction by increasing the rate of moderate to severe capsular contracture but is not associated with flap complications.

Keywords: Immediate reconstruction; postoperative radiotherapy; breast cancer; breast reconstruction

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Introduction

Postoperative irradiation decreases locoregional recurrence and improves breast cancer-specific survival in patients with breast cancer. In the Early Breast Cancer Trialists' Collaborative Group's meta-analysis, post-mastectomy irradiation reduced locoregional recurrence by approximately 10.0% in 10 years (62.5% *vs.* 51.9%, P<0.00001) and decreased breast cancer mortality by 8.1% in 20 years (66.4% *vs.* 58.3%, P=0.001) (1). Studies have also demonstrated improved locoregional control and overall survival in high-risk patients after mastectomy irradiation (2-5). Postmastectomy radiotherapy (PMRT) is currently recommended for lymph node-positive, tumor stage III–IV, and resected margin-positive patients (6).

Increasing the overall survival and quality of life of breast cancer patients is possible due to advancements in systemic treatment and radiation technology and new treatment option availability. Patient satisfaction and quality of life are greatly enhanced when an attractive appearance is achieved. Breast reconstruction timing can be immediate (one-stage reconstruction with breast reconstruction in the same session as the mastectomy) or delayed (two-stage reconstruction at 6–12 months post-mastectomy) (7-9).

Compared to mastectomy alone, immediate reconstruction has no effect on oncologic safety and does not increase the incidence of local recurrence or distant metastases (10,11). Because the cost of surgery (mastectomy and reconstruction) is covered as a single operation, immediate reconstruction is more popular among Thai breast cancer patients; delayed reconstruction necessitates two operations, and the patient must cover the cost of the second operation.

Many studies have shown that capsular contracture or flap shrinkage is the most common long-term complication (12). The cause of capsular contracture is multifactorial. The majority of studies using a two-stage immediate reconstruction technique later reported capsular contracture (13,14).

In this study, we investigated the effect of radiotherapy in implant-based reconstruction in the Asian population, as well as the effects of radiotherapy on operative complications and cosmetic outcomes following immediate breast reconstruction. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-61/rc).

Highlight box

Key findings

- PMRT adversely affects implant-based immediate one-stage reconstruction but is not associated with flap complications
- There was no association between capsular contracture and the radiation techniques, radiation dose, radiation field, pocket plane, bolus material use, or adjuvant chemotherapy.

What is known and what is new?

- Several studies have suggested that PMRT may have a negative impact on the aesthetic outcomes and increase the complication rates of immediate breast reconstruction, especially in implant-based reconstructions. However, some studies have reported no significant difference in the overall complication rate between the PMRT and non-PMRT groups. Our study focused specifically on immediate breast reconstruction and aimed to confirm the negative effect of PMRT on it.

What is the implication, and what should change now?

- The findings from the study will assist clinicians in discussing with patients who are indicated for PMRT and immediate implant-based breast reconstruction. It is essential that patients are informed preoperatively about the risks and potential complications.

Methods

Study population

The medical records of patients who underwent breast reconstruction surgery between January 2008 and December 2018 at King Chulalongkorn Memorial Hospital were retrospectively reviewed. All surgeries were performed by plastic surgeons. The study included all women aged >18 years who underwent mastectomy and immediate breast reconstruction using a one-stage, direct-to-implant (DTI) approach, autologous-based reconstruction, or a combination of both techniques. Patients who underwent conservative breast surgery and received previous radiotherapy were included in this study. Patients who underwent palliative surgery, cosmetic surgery (transgender patients), or reconstruction with a pedicled omental flap were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Research Ethics Committee of King Chulalongkorn Memorial Hospital (IRB approval number: 082/63) and the patients' consents were obtained before data recruitment.

Study design

This was a cross-sectional, retrospective study. Following

immediate breast reconstruction, the patients were divided into two groups: the irradiated and non-irradiated groups. Age, body mass index (BMI), smoking status, menopausal status, medical history of diabetes, and laterality were recorded. Tumor staging, histological characteristics, marginal status, axillary lymph node management, mastectomy techniques, and reconstruction techniques were documented. The outcomes and complications, including implant complications, such as capsular contracture, implant extrusion, and implant malposition, were analyzed. All flap complications, including partial skin flap necrosis, total skin flap necrosis, seroma, and mastectomy flap complications, such as infection or wound dehiscence, fat necrosis, donor site morbidities, and other perioperative complications, were also analyzed. Baker's classification was used to grade capsular contracture as follows: grade I (normally soft breast with a nonpalpable implant), grade II (breast slightly firm to touch that appears normal), grade III (breast firm to touch that appears distorted), and grade IV (breast hard and painful to touch that appears distorted) (15). To reduce potential bias, precise inclusion and exclusion criteria were followed, and data collection was carried out by two independent investigators.

Surgery

Implant-based reconstruction

At our center, we only used a one-stage approach (DTI). Before surgery, the patient's breast measurements and volume estimations were evaluated at an outpatient appointment. Two types of silicone implants are available: anatomic/round and textured/smooth. We discontinued the use of textured implants in late 2017 in response to case reports of breast implant-associated anaplastic large cell lymphoma in Thailand and elsewhere. Thereafter, we used only round, smooth implants in all subsequent cases. Implants were placed in the subpectoral plane, either with or without the serratus muscle or fascia flap.

Abdominal-based reconstruction [transverse rectus abdominis musculocutaneous (TRAM), deep inferior epigastric artery perforator (DIEP), or latissimus dorsi (LD) muscle flaps]

The type of reconstruction was determined by the patient's lifestyle, donor site availability, and expected donor morbidity. TRAM flaps were performed using the traditional method, muscle-sparing TRAM, and free TRAM. We primarily used the ipsilateral side with the breast defect and transposed it with a flip or rotation. To prevent abdominal bulkiness or hernia, we used polypropylene mesh in all patients with TRAM and DIEP flaps. The LD flap was harvested in this position and transposed to the breast defect via an axillary tunnel. Prior to transposition, thoracodorsal vessels were skeletonized and LD muscle insertion was divided, leaving only a cuff of muscle to protect the pedicle.

The combined technique involved the pedicled LD in conjunction with an implant. Depending on the surgeon's preference and the breast's soft tissue thickness, the pocket for the implant was prepectoral (below the LD muscle) or subpectoral. Concurrent or staged surgery on the contralateral side, such as breast reduction, mastopexy, augmentation, or subsequent nipple and areolar reconstruction, as well as nipple tattooing in skin-sparing mastectomies, was offered to patients to achieve the desired cosmetic outcomes and symmetry.

Importantly, in our center, all implant-based and combined technique reconstructions were performed without the use of acellular dermal matrix (ADM).

Materials

Smooth or textured round gel implants were used in all reconstructions (Mentor Worldwide LLC, Irvine, CA, USA).

Radiotherapy

PMRT was initiated 4–6 weeks after surgery or the completion of the last chemotherapy cycle. Computed tomography (CT) simulation (Philips Brilliance Big Bore, Phillips Medical Systems, Cleveland, OH, USA) was performed with 3–3.5 mm slices in the supine position. Breast-board immobilization with raised arms was used. Images were transferred to the planning system (Varian Eclipse, Varian Medical Systems, Palo Alto, CA, USA).

The ipsilateral chest wall with or without regional lymph nodes was included in the target volume. The radiation plan included two tangential photon beams for chest wall irradiation and an anteroposterior photon beam for supraclavicular region irradiation. Intensity-modulated radiotherapy (IMRT) and volumetric-modulated radiotherapy (VMAT) were also permitted. The prescribed dose was 50–60 Gy in 25–30 fractions, five days a week, with at least 95% of the planning target volume covered by the prescribed dose. The volume of tissue receiving >107% was minimized. If indicated, a bolus tissue compensator

was used. When a patient is diagnosed with T4-stage cancer (the disease involves skin or chest wall invasion) or inflammatory breast cancer, the radiation oncologist may consider increasing the radiation dose to 60 Gy. A radiation oncologist administered the PMRT at the King Chulalongkorn Memorial Hospital.

Statistical analysis

The sample size was calculated by the two independent proportions. Continuous variables were reported as mean ± standard deviation (SD) and compared using the paired *t*-test. Categorical data were analyzed using a two-tailed Fisher's exact test. For variables with less than 15% of missing variables, the missing data were imputed using means if they were normally distributed and with medians if they were not. Data with more than 15% of missing variables were analyzed using descriptive statistics only. The univariate logistic regression model was used to estimate the risk of capsular contracture based on clinical variables, odds ratio (OR), and 95% confidence intervals (CIs). All statistical analyses were performed using SPSS software version 20.0 (IBM, Chicago, IL, USA). P values <0.05 were considered statistically significant.

Results

Table 1 presents a comparison of the demographic information, clinical features, and results of the irradiated (n=68) and non-irradiated (n=66) groups. The mean follow-up in both groups (53.42±36.96 and 54.17±34.98 months, respectively; P>0.05) and patients' ages were comparable (44.81±8.96 and 45.27±7.41 years, respectively; P=0.51). All patients were non-smokers. There was no difference in BMI between both groups (22.31±3.56 and 22.02±3.24 kg/m^2, respectively; P=0.76) and no patient was obese (BMI ≥30 kg/m^2). There were no differences in operation time, laterality, or menopause status between the two groups. Modified radical mastectomy was more common in the irradiated groups, whereas conservative mastectomy, including skin-sparing (SSM) or nipple-sparing mastectomy (NSM) (modified radical mastectomy: 51.5% *vs.* 22.7%, SSM: 35.3% *vs.* 45.5%, and NSM: 10.3% *vs.* 30.3%; P=0.002), was more commonly performed in the non-irradiated group. Breast cancer staging was more advanced in the irradiated group, while most patients in the non-irradiated group had stage IA (36.4%) and IIA (25.8%) disease. The irradiated group had a higher prevalence of patients with positive margins, a primary indication for PMRT; a greater proportion of this group received adjuvant chemotherapy (79.4% *vs.* 51.5%; P<0.001) compared to the non-irradiated group. Only 7 (10.3%) and 4 (6.1%) patients in the irradiated and non-irradiated groups, respectively, underwent concurrent contralateral surgery.

Implant-based reconstruction was performed in 61.8% of the irradiated group cases, compared to 78.8% in the non-irradiated group (P=0.097). Autologous reconstruction was performed in 38.2% and 21.2% of the irradiated and non-irradiated groups, respectively. Seventeen (25.0%) and 22 (33.3%) patients in the irradiated and non-irradiated groups, respectively, underwent combined techniques, with all autologous tissue harvested from ipsilateral pedicled LD flaps. All implants were placed in the subpectoral plane during implant-only reconstruction. Occasionally, implants were placed in the prepectoral plane under the LD muscle flap, depending on the surgeon's preference and the breast's soft tissue thickness. Only two cases of autologous reconstruction using microsurgical techniques have been reported: one DIEP flap and one supercharged vein. We frequently used either a pedicled LD flap or a pedicled TRAM flap for autologous reconstruction. As shown in *Table 2*, there were no clinically significant differences in the types of reconstruction between both groups.

Patients who received PMRT with implant-based reconstruction experienced a higher rate of severe capsular contracture (grade III–IV) than non-irradiated patients (42.1% *vs.* 26.9%; P=0.004). In the irradiated group, there was one case of implant extrusion in a patient who previously underwent conservative breast surgery and irradiation. She underwent a modified radical mastectomy, and we performed a one-stage breast reconstruction using only an implant (textured, round, 250 mL). The wound was dehiscent, necessitating the removal of the silicone implant. The results was shown in *Table 3*.

We compared the postoperative flap complications between the two groups: 25 patients (36.8%) in the irradiated group had flap complications compared to 16 (24.2%) in the non-irradiated group (P=0.195). The following complications were observed: partial skin flap loss (2.6% *vs.* 9.1%; P=0.323), total skin flap necrosis (2.6% *vs.* 0%; P=0.373), seroma (13.2% *vs.* 9.1%; P=0.749), fat necrosis (4.4% *vs.* 1.5%; P=0.616), and one major complication, post-operative myocardial infarction resulting in perioperative myocardial infarction. The irradiated and non-irradiated groups were followed up for a median of 47.15 and 50.57 months, respectively. At the time of last

Table 1 Demographic characteristics of the patients

Characteristic	RT (N=68)	Non-RT (N=66)	P value
Age (years)	44.81±8.96	45.27±7.41	0.51
BMI (kg/m^2)	22.31±3.56	22.02±3.24	0.76
Operative time (min)	316.90±144.31	287.82±136.68	0.165
Implant	188.24±95.68	164.89±51.35	
Autologous	389.29±104.86	375.30±102.15	
Combined	409.37±110.67	398.18±90.57	
Diabetes mellitus	3 (4.4)	0	0.087
Smoking status			–
Non-smoker	68 (100.0)	66 (100.0)	
Previous smoker	0	0	
Menopausal status			0.851
Premenopausal	47 (69.1)	44 (66.7)	
Postmenopausal	20 (29.4)	21 (31.8)	
NA	1 (1.5)	1 (1.5)	
Laterality			0.372
Left	37 (54.4)	28 (42.4)	
Right	29 (42.6)	35 (53.0)	
Both	2 (2.9)	3 (4.5)	
Histology			0.014
IDC	59 (86.8)	47 (71.2)	
ILC	3 (4.4)	1 (1.5)	
DCIS	1 (1.5)	11 (16.7)	
Other	5 (7.4)	7 (10.6)	
Lymphovascular invasion			0.053
Present	23 (33.8)	12 (18.2)	
Absent	31 (45.6)	37 (56.0)	
NA	14 (20.6)	17 (25.8)	
Margin status			0.007
Positive	7 (10.3)	1 (1.5)	
Negative	59 (86.8)	65 (98.5)	
NA	2 (2.9)	0	
Staging			<0.001
0	1 (1.5)	11 (16.7)	
I	12 (17.6)	25 (37.9)	
II	26 (38.2)	21 (31.8)	
III	22 (32.4)	2 (3.0)	
IV	1 (1.5)	0	
NA	6 (8.8)	7 (10.6)	

Continuous variables are presented as mean ± SD and categorical data are presented as n (%). RT, radiotherapy; BMI, body mass index; NA, not applicable; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; SD, standard deviation.

Table 2 Operative and adjuvant characteristics of the patients

Characteristic	RT (N=68)	Non-RT (N=66)	P value
Surgery			0.002
MRM	35 (51.5)	15 (22.7)	
SSM	24 (35.3)	30 (45.5)	
NSM	7 (10.3)	20 (30.3)	
BCS	2 (2.9)	1 (1.5)	
Lymph node dissection type			<0.001
SLND	58 (85.3)	35 (53.0)	
ALND	7 (10.3)	22 (33.3)	
None	3 (4.4)	9 (13.6)	
Concomitant contralateral surgery	7 (10.3)	4 (6.1)	0.571
Reconstruction type			0.097
Implant	42 (61.8)	52 (78.8)	
Autologous	26 (38.2)	14 (21.2)	
Combined approach	17 (25.0)	22 (33.3)	0.664
Pocket plane			0.195
Prepectoral	8 (19.0)	16 (30.8)	
Subpectoral	34 (81.0)	36 (69.2)	
Adjuvant chemotherapy	54 (79.4)	34 (51.5)	<0.001
Adjuvant hormonal therapy	30 (44.1)	22 (33.3)	0.116

Categorical data are presented as n (%). RT, radiotherapy; MRM, modified radical mastectomy; SSM, skin-sparing mastectomy; NSM, nipple-sparing mastectomy; BCS, breast-conserving surgery; SLND, sentinel lymph node dissection; ALND, axillary lymph node dissection.

Table 3 Complications of the treatment

Characteristic	RT (N=68)	Non-RT (N=66)	P value
Event of complications from autologous	10 (38.5)	9 (64.3)	0.12
Event of complications from implant only	23 (92.0)	19 (63.3)	0.02
Event of complications from combined reconstruction	15 (88.2)	7 (31.8)	0.001
Implant complications	N=38	N=26	0.004
Capsular contracture grade I–II	21 (55.3)	19 (73.1)	
Capsular contracture grade III–IV	16 (42.1)	7 (26.9)	
Extrusion/malposition	1 (2.6)	0	
Flap complication			0.195
Yes	25 (36.8)	16 (24.2)	
No	42 (61.8)	49 (74.2)	
NA	1 (1.5)	1 (1.5)	
Follow-up time (months)	53.42±36.96	54.17±34.98	>0.05
Median time to complication (months)	36	41	<0.05
Last follow-up status			0.031
Disease free and alive	47 (69.1)	57 (86.4)	
Alive with locoregional recurrence	6 (8.8)	3 (4.5)	
Alive with distant metastasis	1 (1.5)	2 (3.0)	
Dead	11 (16.2)	1 (1.5)	
Loss to follow-up	3 (4.4)	3 (4.5)	

Continuous variables are presented as mean ± SD and categorical data are presented as n (%). RT, radiotherapy; NA, not applicable; SD, standard deviation.

follow-up, 11 patients (16.2%) in the irradiated group died, compared to 1 patient (1.5%) in the non-irradiated group (P=0.031). The higher death rate in the irradiated groups was due to higher cancer staging (33.8% *vs.* 3.0%; P<0.001) and histology of invasive ductal carcinoma (86.8% *vs.* 71.2%; P=0.014). Only three patients were lost to follow-up in each group.

As shown in *Table 4*, we conducted subgroup analyses of the implant-based reconstruction group to identify aggravating factors affecting severe capsular contracture. PMRT was the only factor associated with grade III–IV capsular contracture (47.5% *vs.* 30.4%; P=0.004). There was no association between capsular contracture and the radiation type, radiation dose (>50 *vs.* 50 Gy), radiation field, pocket plane, bolus material use, or adjuvant chemotherapy.

A univariate logistic regression model was used to estimate the effect of PMRT on severe capsular contracture (*Table 5*). Patients who had PMRT had a significantly increased risk for severe capsular contracture (OR: 4.35, 95% CI: 1.55–12.27; P=0.005). The dose of radiation (50 *vs.* >50 Gy, OR: 1.38, 95% CI: 0.17–11.15), the radiation field (chest wall only, OR: 0.5, 95% CI: 0.3–7.99; breast and boost, OR: 0.71, 95% CI: 0.14–3.55), and the pocket (subpectoral or prepectoral, OR: 1.79, 95% CI: 0.63–5.09) were not associated with severe capsular contracture. There were 20.5% of radiotherapy patients and 14.6% of non-radiotherapy patients who received capsular contracture treatment.

Discussion

Our findings revealed that PMRT patients had a higher rate of grade III–IV capsular contracture than non-irradiated patients. PMRT, on the other hand, had no effect on flap complications. These findings support the data reported by Barry *et al.* (16) and Lambert *et al.* (17). In our study, there

Table 4 Treatment-related factors associated with capsular contracture grades

Factors	Grade I–II (n=40)	Grade III–IV (n=23)	P value
Radiation			0.004
No	19 (47.5)	7 (30.4)	
Yes	21 (52.5)	16 (69.6)	
Median time after IBR to RT			0.5
<3 months	4 (19.0)	4 (25.0)	
≥3 months	17 (81.0)	12 (75.0)	
RT techniques			0.370
2D	4 (19.0)	1 (6.3)	
3D	16 (76.2)	15 (93.7)	
IMRT	–	–	
Unknown	1 (4.8)	–	
RT dose			0.936
50 Gy	18 (85.7)	13 (81.3)	
>50 Gy	3 (14.3)	3 (18.8)	
Radiation volume			0.954
Chest wall only	4 (19.0)	4 (25.0)	
Breast + tumor bed boost	2 (9.5)	1 (6.3)	
Chest wall/breast + RNI	14 (66.7)	10 (62.5)	
Unknown	1 (4.8)	1 (6.3)	
Bolus use			0.767
Yes	9 (45.0)	6 (40.0)	
No	11 (55.0)	9 (60.0)	
Pocket			0.271
Prepectoral	14 (35.0)	8 (34.8)	
Subpectoral	26 (65.0)	15 (65.2)	
Adjuvant chemotherapy	37 (92.5)	17 (73.9)	0.305
Adjuvant hormonal therapy	27 (67.5)	12 (52.2)	0.605

Categorical data are presented as n (%). IBR, implant-based reconstruction; RT, radiotherapy; IMRT, intensity-modulated radiation therapy; RNI, regional lymph node irradiation.

Table 5 Univariate capsular contracture grade III–IV and risk estimates

Factors	No. of patients/ at risk	Odd ratio (95% CI)	P value
Radiation			
No	7/48	Ref	
Yes	16/38	4.35 (1.55–12.27)	0.005
RT dose			
50 Gy	10/31	Ref	
>50 Gy	2/4	1.38 (0.17–11.15)	0.413
Radiation volume			
Chest wall/breast + RNI	10/24	Ref	
Chest wall	4/8	0.5 (0.3–7.99)	0.624
Breast + tumor bed boost	1/3	0.71 (0.14–3.55)	0.681
Pocket			
Subpectoral	15/70	Ref	
Prepectoral	6/25	1.79 (0.63–5.09)	0.275

CI, confidence interval; Ref, reference; RT, radiotherapy; RNI, regional lymph node irradiation.

were no obese patients or smokers who underwent breast reconstruction using any technique. Obesity is linked to an increased risk of complications in both implant-based and autologous breast reconstruction procedures (18). Autologous flaps are typically needed when reconstructing a previously radiated field. It has the potential to bring distant healthy tissue to the irradiated field, resulting in a more aesthetically pleasing outcome (19,20).

In our study, 11 patients had failed conservative breast surgery and a history of chest radiation. Two months after the implant-only reconstruction, one patient experienced implant extrusion. According to Lee *et al.* (21), prior irradiation significantly increased the risk of complications in patients who underwent prosthetic reconstruction, and an autologous flap or combination techniques may be considered when reconstructing previously irradiated breasts. Although not all cases were candidates for autologous reconstruction, we recommend autologous reconstruction or a combination technique to suitable patients. Autologous reconstruction was associated with a lower risk of complications than implant-based reconstruction at two years (OR: 0.47, 95% CI: 0.27–0.82; P=0.007) in irradiated patients; no difference was found in non-irradiated patients (22).

Generally, two main types of implant-based reconstruction techniques are the one-stage approach, DTI,

and the two-stage approach. In the one-stage approach, the surgeons create the pocket, either subpectorally or prepectorally, with ADM or adjacent tissue and place the permanent implant at the same time after mastectomy. In the two-stage approach, the surgeons apply the tissue expander at the first stage and then change to a permanent implant in the second stage. In our institute, we use subpectoral DTI. This procedure requires only one stage, has fewer outpatient visits, shorter operative times, better aesthetic outcomes, and lower complication rates. Some patients returned with animation deformities that were easily corrected by changing the prosthesis to the prepectoral plane, resulting in good aesthetic outcomes and patient satisfaction. However, the key to success is patient selection. Most of our patients had small- to medium-sized breasts, good skin quality, and a thin structure. In recent years, DTI has grown in popularity among plastic surgeons. With the introduction of ADM and newer surgical techniques, prepectoral DTI may outperform the two-stage procedure (23,24).

Sinnott *et al.* discovered that among implant-based reconstruction patients who received PMRT, the subpectoral plane had a 3-fold increased rate of severe (Baker grade III–IV) capsular contracture compared to the prepectoral plane (25). In our study, we were unable to replicate these results. In the implant-based reconstruction group, the prepectoral plane had an OR of 1.79 (95% CI: 0.63–5.09; P=0.275) for the development of grade III–IV capsular contracture. This discrepancy may be due to the different techniques used. In prepectoral implant placement, we used LD muscle to cover the implants while Sinnott used ADM. ADM reduced myofibroblasts, vascularity, fibroblasts, and EndoMT in capsule tissues, as reported by Kim *et al.* Furthermore, ADM use reduced macrophages, which are key regulators of tissue fibrosis, as well as TGF-1 and PDGF-B expression (26). Recent studies have shown that ADM prevent the development of capsular contracture in implant-based reconstruction (27,28). ADM was first used as an adjunct tissue to cover breast prostheses in the lower lateral pole in conjunction with the pectoralis muscle in cosmetic surgery nearly a decade ago (29). However, with more covered implants, ADM wrapping around the entire implant has recently become more popular. According to Naoum *et al.* (30), single-stage DTI reconstruction had significantly lower complication rates than tissue expander/implant reconstruction with and without PMRT but was not significantly different from autologous complication rates with PMRT. However, in this study, we did not directly compare the rates of autologous and implant complications.

Surgical complications from breast reconstruction may delay the start of PMRT but do not affect overall survival (31). We compared capsular contracture rates in those who received PMRT less than and >3 months after reconstruction; the rates were comparable (P=0.5). The median time to complication was shorter in the irradiated group than in the non-irradiated group (36 *vs.* 41 months). Santosa *et al.* (32). also discovered no differences in complications when radiation was administered after expander placement in the first stage or after the change to permanent implants for two-stage implant-based reconstruction.

Radiation-related factors, such as total dose and chest wall or incisional boosts can impact surgical complications. Naoum *et al.* (33). recently demonstrated that chest wall boost radiotherapy provided no therapeutic benefit in local tumor control and risk of complications. Because of the smaller sample size, our study was unable to replicate the same results. In our study, all of our patients were non-smokers with a BMI <30 kg/m^2. The significant amount of severe capsular contracture is found in both preoperative and postoperative radiation exposure. Our advice is that implant-based breast reconstruction should be avoided in patient who has to treat with radiotherapy.

There were some limitations to our study. First, our study had a small sample size. Second, although it is very difficult to assess the toxicity in patients with combined approach reconstruction, in our analysis, there was no significant difference in terms of grading of capsular contracture in implant-only and combined reconstruction groups. Third, this was a non-randomized, retrospective study and selection bias may have been associated with the reconstruction techniques. Although randomization would avoid the drawbacks of observational studies, the patient's preference, the surgeon's experience, and institutional practices strongly affect the reconstruction procedure. Nevertheless, in our study, the demographic data between both groups were comparable, all reconstruction types were available, and we had longer follow-up times with a low loss to follow-up, which minimized the biases.

Conclusions

Patients who underwent PMRT had a significantly higher incidence of grade III–IV capsular contracture after implant-based reconstruction. The rates of autologous complications were not significantly different between those

who did and did not receive PMRT.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-61/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-61/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Research Ethics Committee of King Chulalongkorn Memorial Hospital (IRB approval number: 082/63) and the patients' consents were obtained before data recruitment.

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