

## Brief Communication



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# Capsular Contracture After Postmastectomy Radiation in Implant-Based Breast Reconstruction: Effect of Implant Pocket and Two-Stage Surgery

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## ABSTRACT

Capsular contracture (CC) is a concerning issue for individuals undergoing postmastectomy radiation therapy (PMRT) with implant-based breast reconstruction. This study investigated whether the extent of CC and implant migration differs based on implant placement and the reconstruction stage. Insertion plane and stage of breast implants were investigated, and the presence and severe cases of CC and implant migration were analyzed. Among 195 participants, 83 were in the pre-pectoral group, and 112 were in the sub-pectoral group. Two-staged surgery was performed on 116 patients, while 79 underwent direct-to-implant (DTI). Notably, The occurrence of CC (prepectoral, 17 [20.48%] and subpectoral, 42 [37.50%];  $p = 0.011$ ), CC severity (prepectoral, 4 [4.82%] and subpectoral, 17 [15.17%];  $p = 0.021$ ), and implant upward migration (prepectoral, 15 [18.07%] and subpectoral, 38 [33.92%];  $p = 0.014$ ) significantly varied between the two groups. The incidence of CC was more common in the DTI group (odds ratio [OR], 2.283; 95% confidence interval [CI], 1.164–4.478). Furthermore, subpectoral placement was an independent risk factor for occurrence (OR, 2.989; 95% CI, 1.476–6.054) and severity of CC (OR, 38.552; 95% CI, 1.855–801.186) and upward implant migration (OR, 2.531; 95% CI, 1.263–5.071). Our findings suggest that pre-pectoral reconstruction and the two-stage operation benefit patients who may undergo PMRT. These approaches can help reduce the incidence of CC and abnormal implant migration following radiation, leading to improved aesthetic outcomes and greater patient satisfaction.

**Keywords:** Breast Implantation; Radiotherapy; Risk Factors

## INTRODUCTION

The development of radiation therapy to eradicate cancer cells in the target area has significantly improved oncologic prognosis [1-5]. The ability to selectively deliver radiation

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#### Conflict of Interest

The authors declare that they have no competing interests.

#### Data Availability

In accordance with the ICMJE data sharing policy, the authors have agreed to make the data available upon request.

#### Author Contributions

Conceptualization: Min K, Yun IS, Roh TS, Bae SJ, Jeong J, Ahn SG, Kim YS; Data curation: Moon S, Min K, Kim TH, Um JH, Kook Y, Baek SH; Formal analysis: Moon S, Min K, Kook Y, Baek SH, Ahn SG; Methodology: Yun IS, Roh TS, Bae SJ, Jeong J, Ahn SG, Kim YS; Resources: Kim TH, Um JH; Supervision: Yun IS, Roh TS, Bae SJ, Jeong J, Ahn SG, Kim YS; Visualization: Min K, Kim TH, Um JH, Kook Y, Baek SH; Writing - original draft: Moon S, Min K; Writing - review & editing: Moon S, Ahn SG.

has resulted in fewer side effects. However, there are still concerns about acute and delayed damage to normal tissue, leading to inflammation and fibrosis [1,6-11].

The rising popularity of breast reconstruction using prostheses post-mastectomy has sparked interest in the aesthetic outcomes of prosthesis insertion [12-15]. Immediate breast reconstruction followed by radiation increases the risk of severe capsular contracture (CC), thickening, or deformation of the capsule around the prosthesis due to tissue changes [16-20].

On the other hand, innovations in prostheses, acellular dermal matrix, and intra-operative indocyanine green angiography have prompted discussions on optimal implant placement [21-25]. Traditionally, implants were positioned submuscularly due to unpredictable mastectomy flap circulation and the need for precise pocket sizing [26]. However, these achievements challenge the continuation of submuscular placement, as it can result in animation deformity from pectoralis muscle contraction, reducing patient satisfaction and causing implant migration and malrotation [27]. Furthermore, animation deformity of the breast caused by the contraction of the pectoralis muscle becomes a factor that reduces patient satisfaction [28,29]. Moreover, muscle contraction can also lead to implant migration and malrotation.

Previous studies explored the impact of postmastectomy radiation therapy (PMRT) on cosmetic outcomes based on implant placement (subpectoral or prepectoral) [30-32], but often overlooked factors like reconstruction method, use of acellular dermal matrix (ADM), and follow-up duration. These studies also did not investigate changes in implant position after PMRT. Given this context, our aim is to assess variations in CC severity and implant position changes following PMRT, based on the type of implant placement and operation (one- or two-staged).

## METHODS

### Patients

A retrospective review was conducted on patients who underwent implant-based breast reconstruction (IBR) at a single institution from January 2017 to September 2022. The study was approved by the Institutional Review Board, adhering to good clinical practice guidelines under the Declaration of Helsinki (3-2023-0208). Due to the retrospective study design, the requirement for written informed consent was waived.

Only unilateral reconstruction cases were included in the study to assess changes in the reconstruction site. Additionally, due to the shift of reconstruction from subpectoral plane-based breast reconstruction to prepectoral plane-based breast reconstruction over time, the follow-up period for patients was limited to a minimum of six months and a maximum of two years after PMRT to ensure sufficient completion of radiation effects on the tissue and to minimize bias due to differences in follow-up periods. Patients with a history of previous breast surgeries (augmentation, excision, breast-conserving operation) within two years before the follow-up period, as well as those who had explanted the breast implant within the 2-year follow-up period, were excluded from the study. The patients were divided into two groups: those in the prepectoral plane and those in the subpectoral plane. We also analyzed various IBR methods, including direct-to-implant (DTI) cases and two-stage cases.

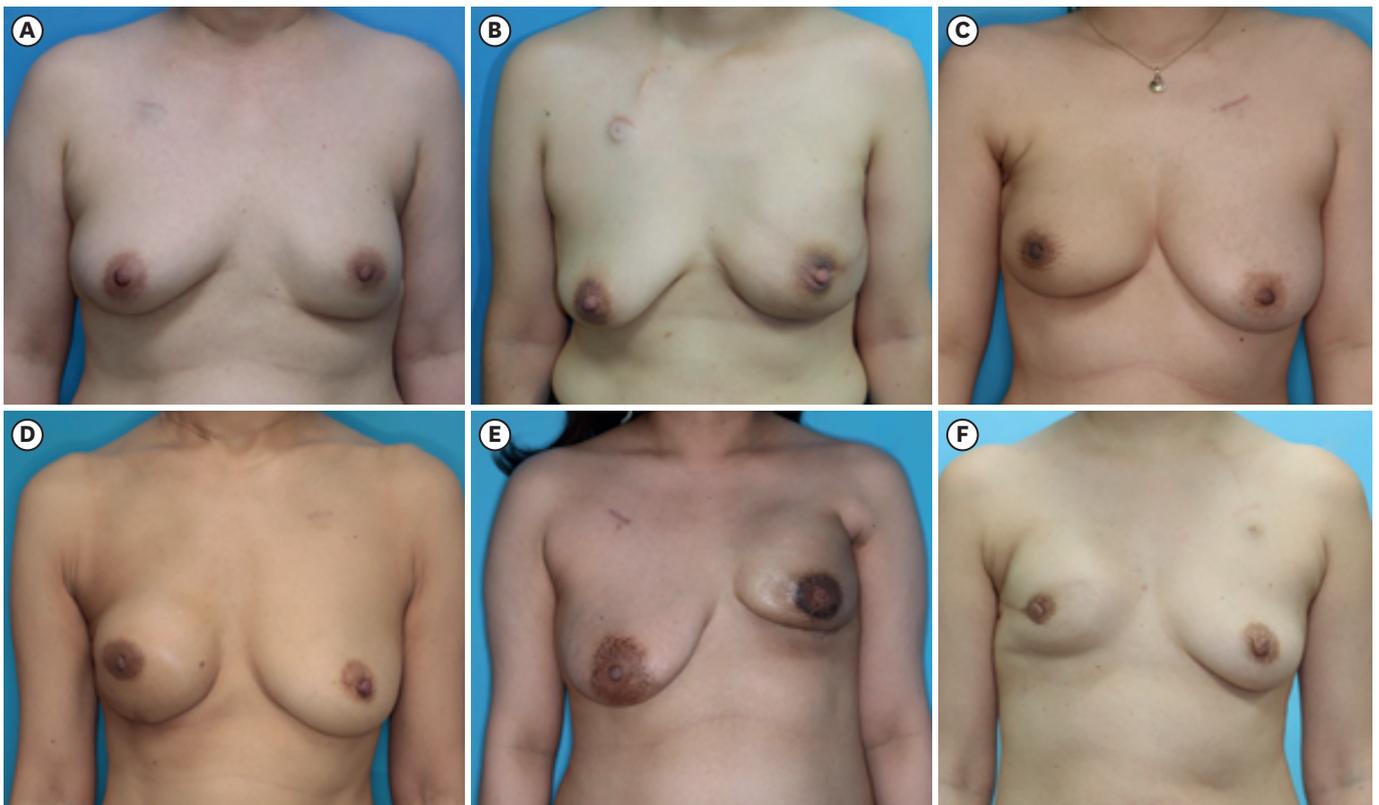
Basic patient characteristics such as age, body mass index (BMI), history of hypertension, diabetes, or smoking were recorded. Surgical information included reconstruction

method (DTI or two-stage), mastectomy method (nipple sparing mastectomy, skin sparing mastectomy, or conventional total mastectomy), contralateral procedures (mastectomy, reduction, or augmentation), axillary lymph node dissection (ALND), mastectomy specimen weight, product and size of ADM, implant size, and total dose of post-mastectomy radiation. Oncologic data encompassed neoadjuvant chemotherapy, adjuvant chemotherapy, pathologic cancer stage, and the period between breast reconstruction and radiotherapy.

Mastectomy operations were conducted by three breast surgeons (Jeong J, Ahn SG, and Bae SJ), and the IBRs were conducted by two experienced plastic surgeons (Roh TS and Kim YS). All patients have used human allogenic acellular dermal matrix (DermACELL<sup>®</sup>; LifeNet Health, Virginia Beach, USA, or MegaDerm<sup>®</sup>; L&C Bio Inc., Seongnam, Korea), and breast implant insertion pockets were selected based on the thickness of mastectomy skin or skin perfusion observed using indocyanine green angiography. Generally, in cases where mastectomy skin thickness was thin, or there was a reduction in skin perfusion on angiography, the subpectoral plane was chosen. Conversely, when skin thickness was sufficient or there was adequate skin perfusion on angiography, the prepectoral plane was selected.

### CCs and upward migration

For CC, the presence of CC and severe CC (Baker grade III or higher) were investigated, and the occurrence of implant upward migration and rippling was evaluated by comparing photos taken before surgery and at least six months after PMRT. We included cases depicting various grades of CC in **Figure 1A-E**. Additionally, we incorporated the case showing implant upward migration (**Figure 1F**). Postoperative outcomes and complications were assessed, including



**Figure 1.** Capsular contractures based on the Baker's classification and implant upward migration. Cases of patients (A) without capsular contracture, (B-E) Baker's grade 1-4 contractures each, and (F) the case of implant upward migration.

drain maintenance period, presence of remnant seroma after drain removal within a week, hematoma, mastectomy skin flap necrosis, and infection cases.

### Statistical analysis

For comparisons between the previously classified groups, the  $\chi^2$  or Fisher's exact test was used for categorical variables, and the Student's *t*-test or Mann-Whitney test was used for continuous variables. Multivariate logistic regression analysis with the backward elimination method was performed to calculate risk factors and odds ratios (ORs) for variables that showed statistical significance in postoperative complications. These analyses were conducted using SPSS 26.0 (IBM Corp., Armonk, USA).

## RESULTS

### Demographics and surgical characteristics of a study population

A total of 195 patients underwent IBR followed by PMRT (Table 1). Among this cohort, 83 patients were in the prepectoral group, and 112 patients were in the subpectoral group.

**Table 1.** Demographics and surgical information according to type of implant placement

Variables	Prepectoral (n = 83)	Subpectoral (n = 112)	Total (n = 195)	p-value
Age (yr)	46.37 ± 8.12	47.29 ± 8.46	46.90 ± 8.306	0.450
BMI (kg/m <sup>2</sup> )	24.33 ± 3.84	23.36 ± 2.86	23.77 ± 3.334	0.045
Diabetes	4 (4.82)	8 (7.14)	12 (6.15)	0.504
Hypertension	9 (10.84)	12 (10.71)	21 (10.77)	0.977
Smoking	0 (0.00)	1 (0.89)	1 (0.51)	0.388
Reconstruction method				
DTI	46 (55.42)	33 (29.46)	79 (40.51)	
Two-stage	37 (44.58)	79 (70.54)	116 (59.49)	
Period between reconstruction and radiotherapy (day)	127.10 ± 79.16	138.35 ± 52.73	132.73 ± 65.95	0.541
Mastectomy method				0.010
Nipple-areolar sparing	50 (60.24)	43 (38.39)	93 (47.69)	
Skin sparing	18 (21.69)	35 (31.25)	53 (27.18)	
Total mastectomy	15 (18.07)	34 (30.36)	49 (25.13)	
Contralateral procedure (Mastopexy, reduction, augmentation etc.)	9 (10.84)	11 (9.82)	20 (10.26)	0.816
ALND	46 (55.42)	56 (50.00)	102 (52.31)	0.454
Mastectomy specimen weight (g)	506.33 ± 261.37	468.67 ± 220.53	484.7 ± 238.85	0.277
Implant size (cc)	327.95 ± 113.56	316.61 ± 115.58	321.44 ± 114.57	0.496
ADM				< 0.001
MegaDerm®	68	63	131	
DermACELL®	15	49	64	
Size of ADM (cm <sup>2</sup> )	233.66 ± 45.94	128.86 ± 15.01	173.47 ± 60.99	< 0.001
Neoadjuvant chemotherapy	55 (66.27)	66 (58.93)	121 (62.05)	0.297
Adjuvant chemotherapy	40 (48.19)	43 (38.39)	82 (42.56)	0.171
Pathological cancer stage				0.397
0	4 (4.82)	3 (2.68)	7 (3.59)	
1	17 (20.48)	24 (21.43)	41 (21.03)	
2	46 (55.42)	64 (57.14)	110 (56.41)	
3	16 (19.28)	19 (16.96)	35 (17.95)	
Radiation dose (Gy)	4415.77 ± 481.82	4471.58 ± 652.44	4437.96 ± 554.66	0.491
Subtypes				0.621
HR+/HER2-	37 (44.58)	41 (36.61)	78 (40.00)	
HR+/HER2+	8 (9.64)	11 (9.82)	19 (9.74)	
HR-/HER2+	22 (26.50)	37 (33.04)	59 (30.26)	
HR-/HER2- (TNBC)	16 (19.28)	23 (20.53)	39 (20.00)	

Values are presented as mean ± standard deviation or number (%).

BMI = body mass index; DTI = direct-to-implant; ALND = axillary lymph node dissection; ADM = acellular dermal matrix; HR+ = hormone receptor-positive; HER2- = human epidermal growth factor receptor 2-negative; HER2+ = human epidermal growth factor receptor 2-positive; HR- = hormone receptor-negative; TNBC = triple negative breast cancer.

Comparisons between the two groups revealed a slightly elevated mean BMI within the prepectoral group. Other factors, including underlying medical conditions, such as age, history of hypertension, and the interval between reconstruction and PMRT, demonstrated no significant distinctions.

Regarding surgical approaches, 55.40% of the prepectoral group underwent surgery with DTI method, whereas approximately 70.50% of the subpectoral received the two-stage operation ( $p < 0.001$ ). In terms of mastectomy type, nipple-areolar sparing mastectomy (NSM) was performed on 60.24% of the prepectoral group, compared to 38.39% of the subpectoral group ( $p = 0.010$ ). The size of ADM was different between the prepectoral group ( $233.66 \pm 45.94 \text{ cm}^2$ ) and the subpectoral group ( $128.86 \pm 15.01 \text{ cm}^2$ ,  $p < 0.001$ ), and surgical variables, including contralateral procedures, ALND, mastectomy specimens weight, implant size, and total radiation dose demonstrated no significant differences. Additionally, there were no differences in neo- and adjuvant chemotherapy rates, clinical staging, or breast cancer subtypes between the two groups.

The analysis then shifted towards comparing surgical complications between the two groups (Table 2). When evaluating the duration of drain maintenance post-implant-based breast reconstruction and PMRT, the prepectoral group exhibited an average of  $16.78 \pm 3.832$  days, whereas the subpectoral group averaged  $17.95 \pm 4.020$  days ( $p = 0.043$ ). Conversely, no notable distinction was observed between the two groups regarding acute complications, including seroma, hematoma, and infection.

### CCs and upward migration

A total of 59 (30.26%) individuals were diagnosed with CCs of all grades during the course of the study. Notably, severe contractures (grade 3 and 4) were identified in 21 patients (10.77%). The presence of CC yielded statistically significant disparities, with 17 patients (20.48%) from the prepectoral group and 42 patients (37.50%) from the subpectoral group ( $p = 0.011$ ; Figure 2A). Similarly, the occurrence of severe CC displayed a trend, with 4 patients (4.82%) from the prepectoral group and 17 patients (15.18%) from the subpectoral group ( $p = 0.021$ ).

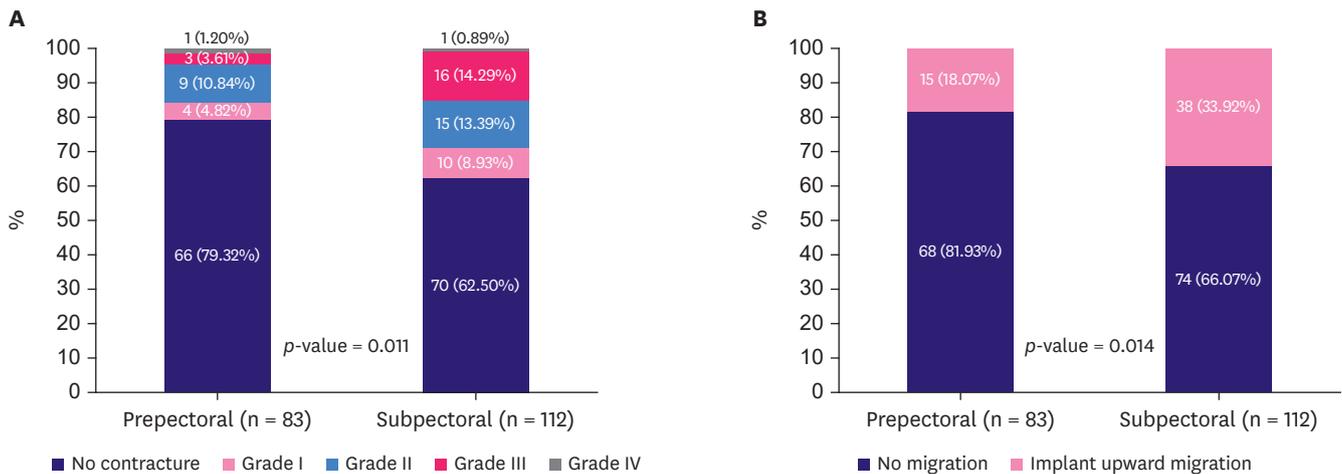
Furthermore, implant upward migration affected 53 patients (27.18%). Notably, the prepectoral group exhibited this phenomenon in 15 patients (18.07%), whereas the subpectoral group experienced it in 38 patients (33.92%), signifying a statistically significant difference ( $p = 0.014$ ; Figure 2B).

**Table 2.** Surgical complications according to type of implant placement

Variables	Prepectoral (n = 83)	Subpectoral (n = 112)	Total (n = 195)	p-value
Drain maintenance (day)	16.78 ± 3.832	17.95 ± 4.020	17.37 ± 3.926	0.043
Presence of complication	22 (26.51)	20 (17.86)	40 (21.54)	0.315
Complications				
Seroma	4 (4.82)	1 (0.09)	5 (2.56)	0.086
Hematoma	2 (2.41)	3 (2.68)	5 (2.56)	0.906
Skin flap necrosis	7 (8.43)	5 (4.46)	10 (5.13)	0.254
Infection	1 (1.20)	0 (0.00)	1 (0.51)	0.244
Rippling	8 (9.64)	11 (9.82)	19 (9.74)	0.966
Presence of CC	17 (20.48)	42 (37.50)	59 (30.26)	0.011
CC ≥ 3	4 (4.82)	17 (15.18)	21 (10.77)	0.021
Implant upward position	15 (18.07)	38 (33.92)	53 (27.18)	0.014

Values are presented as mean ± standard deviation or number (%).

CC = capsular contracture.



**Figure 2.** Capsular contractures and upward migration of implant between the prepectoral and subpectoral groups.

(A) The presence of CC showed significant differences: 17 (20.48%) in prepectoral vs. 42 (37.50%) in subpectoral ( $p = 0.011$ ). Severe cases were lower in prepectoral ( $n = 4$ , 4.82%) vs. subpectoral ( $n = 17$ , 15.17%) ( $p = 0.021$ ). (B) Upward implant migration occurred more in the subpectoral group experienced ( $n = 38$ , 33.92%) than in the prepectoral ( $n = 15$ , 18.07%) ( $p = 0.014$ ). CC = capsular contracture.

### A subgroup of DTI cases

To minimize the influence of the stage of surgery, we performed subgroup analyses in each group of either DTI or two-stage surgery groups. In the DTI group, 79 were included. Among them, 46 patients were in the prepectoral group, and 33 patients were in the subpectoral group. In the comparison between the two groups, there was a significant difference in BMI, with the prepectoral group showing a mean BMI of  $24.02 \pm 3.13$  kg/m<sup>2</sup> and the subpectoral group showing a mean BMI of  $22.69 \pm 2.58$  kg/m<sup>2</sup> ( $p = 0.049$ ). There was no difference between the two groups in terms of mastectomy method ( $p = 0.934$ ), underlying medical conditions, ALND, chemotherapy, and pathologic cancer stage. There was a significant difference in the implant size used during surgery, with the prepectoral group having a mean size of  $279.89 \pm 95.77$  cc and the subpectoral group having a mean size of  $235.61 \pm 96.23$  cc ( $p = 0.047$ ). The size of ADM was different between the prepectoral group ( $243.61 \pm 41.61$  cm<sup>2</sup>) and the subpectoral group ( $125.58 \pm 9.90$  cm<sup>2</sup>,  $p < 0.001$ ; **Supplementary Table 1**).

When comparing the drain maintenance period, the prepectoral group had a mean of  $16.67 \pm 3.88$  days, and the subpectoral group had a mean of  $17.18 \pm 5.09$  days, but there was no statistical significance ( $p = 0.616$ ). The overall incidence of complications was higher in the prepectoral group, with 12 (26.09%) compared to 6 (18.18%) in the subpectoral group, which did not show a statistical difference ( $p = 0.135$ ; **Supplementary Table 1**).

The presence of CC (prepectoral group: 13 patients [26.26%] vs. subpectoral group: 16 patients [48.48%],  $p = 0.066$ ) showed marginal significance. The occurrence of severe CC (prepectoral group: 3 patients [6.52%] vs. subpectoral group: 6 patients [18.18%],  $p = 0.108$ ) and implant upward migration (prepectoral group: 10 patients [21.74%] vs. subpectoral group: 13 patients [39.39%],  $p = 0.088$ ) did not show statistically significant differences (**Supplementary Table 1**).

### A subgroup of two-stage surgery

A total of 116 patients who received two-stage-based reconstruction and PMRT were included. Among them, 37 patients were in the prepectoral group, and 79 patients were in the subpectoral

**Table 3.** Multivariable analysis for the presence of capsular contracture

Variables	Presence of capsular contracture		Severe capsular contracture	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Reconstruction method		0.016		0.267
Two-stage operation	Ref.		Ref.	
DTI	2.283 (1.164–4.478)		2.978 (0.434–20.435)	
Implant position		0.002		0.018
Prepectoralis	Ref.		Ref.	
Subpectoralis	2.989 (1.476–6.054)		38.552 (1.855–801.186)	

OR = odds ratio; CI = confidence interval; DTI = direct-to-implant.

group. There was a marginal statistically significant difference in the implant size used during surgery, with the prepectoral group having a mean size of  $390.95 \pm 106.88$  cc and the subpectoral group having a mean size of  $349.62 \pm 107.18$  cc ( $p = 0.055$ ). (Table 3). In addition, the size of ADM was different between the prepectoral group ( $221.30 \pm 48.58$  cm<sup>2</sup>) and the subpectoral group ( $130.23 \pm 16.55$  cm<sup>2</sup>,  $p < 0.001$ ; Supplementary Table 2).

When comparing the drain maintenance period after PMRT, the prepectoral group had a mean of  $16.57 \pm 3.33$  days, and the subpectoral group had a mean of  $18.39 \pm 3.64$  days, showing statistical significance ( $p = 0.011$ ). On the other hand, there was no difference in complications ( $p = 0.532$ ; Supplementary Table 2).

The presence of CC was observed in 4 patients (10.81%) in the prepectoral group and 26 patients (32.91%) in the subpectoral group, showing statistical significance ( $p = 0.011$ ). In terms of implant upward migration, the prepectoral group had 5 patients (13.51%), and the subpectoral group had 25 patients (31.65%), showing a statistical difference ( $p = 0.038$ ; Supplementary Table 2).

### Risk factors for contractures and upward migration

A multivariable analysis was conducted to ascertain risk factors for both CCs and implant upward migration. For all grades of CC, subpectoral implant placement and DTI were identified as significant risk factors (subpectoral: OR, 2.989; 95% confidence interval [CI], 1.476–6.054 and DTI: OR, 2.283; 95% CI, 1.164–4.478). In cases of severe CC (grade 3 or 4), only an implant placement was a significant risk factor (Table 3). Additionally, the subpectoral placement was a significant risk factor for the upward migration of the implant (Supplementary Table 3).

## DISCUSSION

Our study demonstrates that employing a pre-pectoral implant placement strategy and a two-stage surgical procedure is a superior approach for mitigating CC in individuals undergoing implant-based IBR followed by PMRT. Furthermore, positioning the implant above the pectoralis major muscle notably diminishes the risk of implant migration. These results underscore the importance of optimizing the surgical approach, particularly in patients eligible for PMRT during IBR planning, to effectively address concerns related to CC and implant migration.

Researchers have become curious about whether CC differs depending on the implant insertion plane [30–32]. Sobti et al. [30] investigated whether there was a difference in the incidence of CC between subpectoral and prepectoral DTI patients. They found that the

subpectoral plane had a more than four-fold higher risk of CC than the prepectoral plane. They also claimed that skeletal muscle fibrosis caused by PMRT in subpectoral implant reconstruction leads to superolateral displacement of the nipple-areolar complex, crease formation in the soft tissue envelope, flattening of the inferior pole, and crease formation in the axillary fold [30]. Sinnott et al. [32] compared the subpectoral and prepectoral planes in 79 breasts that underwent immediate breast reconstruction and PMRT. They reported that the subpectoral plane had a 52.20% incidence of CC compared to 16.10% for the prepectoral plane.

In addition, previous reports have suggested that the use of ADM in implant-based reconstruction reduces the incidence of CC in patients who receive PMRT [33-38]. Lee et al. [34] conducted an animal study using mice in which silicone implants were wrapped with ADM and radiation was applied. The study observed a lower number of inflammatory cells in the mice that underwent radiation with ADM wrapping. Clinically, Kim et al. [35] compared the thickness and expression of alpha smooth muscle actin, transforming growth factor beta 1, and platelet-derived growth factor beta in ADM capsules sampled during an expander-to-implant exchange after PMRT and non-PMRT in two-stage reconstruction patients [35]. The results showed that the areas where radiation was applied to the muscle had thicker ADM and higher expression levels of various factors, whereas the tissue with inserted ADM showed no significant difference in thickness compared to non-PMRT cases and had lower expression levels. Similar results were also reported by Tevlin et al. [37]. Given that the implant completely interfaces with ADM upon placement above the pectoralis major muscle, the prepectoral method provides an extra benefit in minimizing CC when contrasted with the subpectoral approach, wherein the implant is only partially covered by ADM.

Several studies have been conducted to examine the impact of PMRT on DTI or two-stage IBR [31-33]. Among them, Du et al. [33] conducted a meta-analysis of 22 studies published over a period of 26 years. The results showed that the incidence of CC after PMRT was higher in IBR with rates of 17.01% for DTI, 15.49% for IBR, and 10.60% for two-stage reconstruction (PMRT after implant), and 14.58% for two-stage reconstruction (PMRT before implant), all of which were statistically significant compared to non-PMRT cases. Recently, two-stage reconstruction is known to have the disadvantage of requiring regular outpatient visits for skin expansion after mastectomy and additional expander-to-implant changes under general anesthesia. However, according to the results of our findings, it provides an advantage to patients who need PMRT by allowing manipulation of the capsule through a second-stage operation. Therefore, considering two-stage reconstruction in patients who are certain to undergo PMRT after surgery is necessary.

Therefore, this study aimed to compare the incidence of CC after PMRT and the degree of implant position changes based on the difference in implant insertion planes in a relatively large cohort of 195 ipsilateral immediate breast reconstruction patients, including 83 DTI and 112 two-stage reconstruction patients. To best of our knowledge, our study has a largest number of patients who underwent IBR with implant followed by PMRT. We also analyzed the incidence of CC based on its occurrence, grade, and severe cases (grade 3 or above) to obtain more specific results.

The results showed a higher incidence of CC than previously reported in the literature, indicating that mild forms of CC, which are not frequently reported, occur more often. In addition, the study reaffirms that PMRT induces fibrosis of the pectoralis major muscle, significantly increasing the risk of subsequent contracture. Notably, the subpectoral plane

has been identified as a significant risk factor for severe CC, classified as Baker grade 3 or higher, with a markedly high odds ratio. This suggests that implant reconstruction in the subpectoral plane under PMRT conditions may exhibit a negative synergic effect.

A noteworthy point is that the DTI group had a higher incidence of CC compared to the two-stage group, especially in the subpectoral plane. In two-stage reconstruction process, patients received regular infusions of normal saline. It may exert a tissue-stretching force opposite to that of contracture and potentially help control the thickness of the capsule and mitigate contracture phenomena.

On the other hand, in the DTI group, the size of the ADM was marginally statistically significant in reducing the risk of CC. This result indicates a potential for ADM size to mitigate the incidence of CC following PMRT. However, when analyzing risk factors for severe CC, a larger ADM size emerged as a risk factor, with statistical significance. Therefore, further research is needed to accurately determine the impact of ADM size on both the occurrence and severity of CC.

Regarding implant upward migration, the subpectoral insertion had a higher incidence than the prepectoral insertion. Moreover, although statistical comparisons were not performed, it was observed that the incidence of implant migration was lower in both the prepectoral and subpectoral planes for two-stage reconstruction compared to DTI reconstruction. This is probably attributed to the reposition the inframammary fold during the second stage of the operation. Despite this, the proportion of implants in an upward position was 31.65% in the two-stage subpectoral plane reconstruction group, which was significantly higher compared to 13.51% in the prepectoral plane reconstruction group ( $p = 0.038$ ). This suggests that the pectoralis muscle has a substantial impact on implant positioning.

Interestingly, the incidence rate of implant migration was similar to the incidence rate of CC grade 3 or above. This means that implant migration can occur even without severe CC and requires special attention due to its frequent occurrence.

Our study has several limitations. Firstly, it lacks classification of breast shape before the patient's surgery. Although the BMI and inserted implant volume in the prepectoral group tended to be larger than those in the subpectoral group, it does not fully explain breast ptosis. In this study, human-derived ADM was utilized, specifically from products of two different companies. The use of particular products under specific conditions was not standardized. Although previous research has not demonstrated differences in implant-based reconstruction outcomes based on ADM thickness or variations between ADM manufacturers, standardizing ADM products could significantly enhance the reliability of the analysis results [39-41]. Therefore, future studies should control for such variables to ensure more accurate and reliable findings. Additionally, this study did not quantitatively analyze the extent of implant upward migration. Although differences were observed in the incidence rate of migration, a quantitative analysis using a universally accepted landmark would be more helpful in understanding the changes in breast shape caused by PMRT. Lastly, this study used three different mastectomy methods. Although no statistical significance was observed in the comparison between groups, unifying these variables and conducting research would lead to more reasonable conclusions.

In summary, among patients undergoing implant-based IBR and PMRT, DTI on the subpectoral plane showed the highest incidence rate and severe case rate of CC,

while two-stage reconstruction on the prepectoral plane had the lowest occurrence of CC. If a patient is diagnosed the preoperative clinical stage demanding the necessity of PMRT, two-stage reconstruction could be considered. This approach can minimize the occurrence of CC and abnormal migration of the implant after radiation, ultimately leading to increased aesthetic satisfaction.

## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

Demographics, surgical information, and complications by the type of surgery (one-stage)

### Supplementary Table 2

Demographics, surgical information, and complications by the type of surgery (two-stage)

### Supplementary Table 3

Multivariable analysis for upward migration of the implant

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