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Acellular Dermal Matrix in Immediate Expander/Implant Breast Reconstruction: A Multicenter Assessment of Risks and Benefits

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Abstract

INTRODUCTION—Acellular dermal matrix (ADM) has gained widespread acceptance in immediate expander/implant reconstruction due to perceived benefits, including improved expansion dynamics and superior aesthetic results. Although previous investigators have evaluated its risks, few studies have assessed the impact of ADM on other outcomes, including patient-reported measures.

METHODS—The Mastectomy Reconstruction Outcomes Consortium (MROC) Study used a prospective cohort design to evaluate patients undergoing post-mastectomy reconstruction from 10 centers and 58 participating surgeons between 2012 and 2015. The analysis focused on women receiving immediate tissue expander reconstruction following mastectomies for cancer treatment or prophylaxis. Medical records and PRO data, using the BREAST-Q and Numeric Pain Rating Scale (NPRS) instruments, were reviewed. Bivariate analyses and mixed-effects regression models were applied.

RESULTS—A total of 1,297 patients were evaluated, including 655 (50.5%) with ADM and 642 (49.5%) without ADM. Controlling for demographic and clinical covariates, no significant differences were seen between ADM and non-ADM cohorts in overall complications (OR=1.21, p=0.263), major complications (OR=1.43, p=0.052), wound infections (OR=1.49, p=0.118), or reconstructive failures (OR=1.55, p=0.089) at two years following reconstruction. There were also no significant differences between the cohorts in the time to expander/implant exchange (p=0.78). No significant differences were observed in PRO scores, including satisfaction with breast, psychosocial well-being, sexual well-being, physical well-being and postoperative pain.

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CONCLUSION—In our multicenter, prospective analysis, we found no significant ADM effects on complications, time to exchange or PRO in immediate expander/implant breast reconstruction. Further studies are needed to develop criteria for more selective use of ADM in these patients.

Introduction

Immediate breast reconstruction following mastectomy has become commonplace in patients undergoing mastectomies for breast cancer treatment or prophylaxis, with demonstrated psychosocial, body image and quality of life benefits (1, 2). While a range of reconstructive options is available to patients, two-stage tissue expander/implant (E/I) reconstruction remains the most widely used technique for restoration of breast contour, form and symmetry. According to the American Society of Plastic Surgeons, 77,219 procedures were performed in the United States in 2015, accounting for 72.6 percent of all reconstructions and reflecting a steady rise in the utilization of these procedures over the past decade (3, 4).

Since its introduction over a decade ago, acellular dermal matrix (ADM) has become an integral part of E/I reconstruction. Currently, ADM is used in over 75% of immediate tissue expander breast reconstructions (3). Marketed by a variety of manufacturers, this material is commonly placed as a sling between the inferior edge of the pectoralis muscle and the inframammary fold to provide support for the expander. Advocates of ADM in E/I reconstruction cite a number of purported benefits over traditional techniques, including the creation of aesthetically superior breast shapes by controlling implant position and improved tissue expansion dynamics, resulting in shorter expansion times and less patient discomfort (5–8). However, recent meta-analyses have reported greater risks of post-operative complications when ADM is used in E/I reconstruction, compared to total submuscular and dual plane techniques (9–11). These studies have noted higher rates of major infections, seromas and reconstructive failures with ADM. Given the additional cost associated with use of ADM in expander-based reconstruction, assessing the potential benefits and risks of these materials has become particularly important in today’s resource-conscious health care environment (12).

Despite the widespread use of ADM, there remains a paucity of high quality research to critically evaluate its effectiveness (13, 14). The majority of available studies have been limited by their small, single center and single surgeon patient populations, and by their retrospective designs. While advocates of ADM anecdotally report superior aesthetic results, there are few studies evaluating the effects of ADM on patient satisfaction and other patient-reported outcomes (PROs) in E/I reconstruction (15, 16).

Using the multi-center Mastectomy Reconstruction Outcomes Consortium (MROC), this study sought to prospectively evaluate the effectiveness of acellular dermal matrix in implant-based, post-mastectomy breast reconstruction, assessing associated risks and patient-reported outcomes.

Materials and Methods

Patients were recruited as part of the Mastectomy Outcomes Consortium (MROC) Study, a prospective cohort study funded by the National Cancer Institute, involving ten high volume breast reconstruction centers and 58 surgeons across the United States and Canada. Institutional Review Board approval was obtained at all sites. Eligible patients were enrolled between 2012 and 2015 and included those undergoing tissue expander placement for immediate unilateral or bilateral reconstruction following mastectomy for breast cancer treatment or prophylaxis. All patients subsequently underwent expander exchange for saline- or silicone-filled reconstructive implants. In this analysis, all participants had two year follow-up data from the time of expander placement. Excluded were all patients undergoing delayed reconstruction, direct-to-implant procedures, autologous tissue techniques, or bilateral reconstruction with only unilateral ADM placement.

Study patients were divided into two cohorts: (1) those undergoing expander reconstruction with ADM, and (2) those receiving expander reconstruction without ADM. After obtaining informed consent, patient demographic and clinical information was gathered from electronic medical records (EMRs) by the site coordinators and included age, body mass index (BMI), laterality (unilateral vs. bilateral), indication for mastectomy (treatment vs. prophylactic), mastectomy type (nipple sparing, simple or modified radical), smoking status, diabetes, lymph-node management, adjuvant chemotherapy, and radiation.

At two years following initial tissue expander placement, site coordinators collected clinical data including complications, defined as adverse, surgery-related, postoperative events requiring additional treatment. Complications requiring re-hospitalization or re-operation were designated as “major”. Reconstructive failures, i.e., complications requiring implant removal, were also recorded. Finally, infections were subdivided into “all” and “major”, with former including all surgical site infections (based on Centers for Disease Control criteria) and the latter requiring intravenous antibiotics and/or re-operation.

Patient-reported outcomes were assessed using the previously validated BREAST-Q (18) and Numerical Pain Rating Scale (NPRS) (19), which were completed preoperatively and at one week, three months, one year and two years post-operatively. Domains of the BREAST-Q used for this analysis were Satisfaction with Breast, Physical Well-being, Psychosocial Well-being and Sexual Well-being. Each domain score was obtained by transforming the scale item responses using the Q-score software program. The transformed scores range from 0 to 100, with higher scores indicating greater satisfaction or quality of life. The NPRS score was reported on a scale from 1 to 10, with higher scores indicating greater levels of pain. The BREAST-Q Physical Well-being subscale and NPRS items were completed at all the five time points specified above. Items for all of the other domains for the BREAST-Q were completed preoperatively, and at one year and two years post-operatively. Patients who experienced reconstructive failure were excluded from the final PRO analysis.

Statistical Analysis

Clinical characteristics of patients were compared between ADM and non-ADM cohorts using Student’s t test for continuous variables and Chi-square tests for categorical variables.

Rates of overall and specific post-operative complications were calculated as the proportion of patients with complications by ADM use cohorts. Complications were considered as patient-level outcomes throughout the analyses.

For the comparisons of two-year complication between ADM use cohorts, separate mixed-effects logistic regression models were built for (1) any type of complication, (2) major complications, and (3) reconstructive failure. Each model included an indicator for ADM use, clinical characteristics, and random intercepts for centers (hospitals) and surgeons to account for between-center and between-surgeon variability. For the comparison of BREAST-Q Satisfaction with Breast, Psychosocial Well-being and Physical Well-being subscales, separate mixed-effects regression models were constructed, with dependent variables being the outcome measures at two years post-reconstruction. Each model included an indicator for ADM use, clinical characteristics, and baseline values of the outcome measures as covariates, and random intercepts for centers (hospitals) to account for between-center variability. For the BREAST-Q Physical Well-being subscale and NPRS, full longitudinal analyses were performed, with the dependent variables being the outcome measures collected across all the available time points. Each model included four time indicators (one week, three months, one year, and two years post-expander placement) and their interactions with ADM use. Clinical covariates, as well as three sets of random intercepts – one for centers (hospitals), one for surgeons nested within centers, and one for patients nested within surgeons – were also included. This allowed for comparison between the two cohorts on the longitudinal change of repeated PRO measures, while accounting for between-patient, between-surgeon, and between-center variability.

Patient-reported outcomes scores at the two year post-reconstruction time point were missing for approximately 40% of patients. To reduce potential bias, multiple imputations with chained equations were employed to create 10 complete imputed datasets. The regression models specified above were fit for each imputed data set. The results were then combined using Rubin's rule. We reported adjusted odds ratios (ORs) for complications and Beta coefficients for PROs, with 95% confidence intervals (CI) and corresponding p-values. All statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, NC), and statistical significance was set at 0.05.

Results

A total of 1,297 patients undergoing immediate breast reconstruction with tissue expanders met inclusion criteria for this analysis. Acellular dermal matrix was used in 655 patients (50.5%), while 642 patients (49.5%) did not receive ADM during expander placement. Demographic and clinical characteristics for the two cohorts are summarized in Table 1. Overall, average patient age was 48.4 (±10.4) years and BMI 25.7 (±5.3) kg/m^2, with no significant differences in these variables between the patient cohorts. There were also no significant group differences in laterality (unilateral versus bilateral reconstructions). The median time from tissue expander placement to exchange was remarkably consistent: 5.4 months for ADM patients, compared with 5.6 months for those without ADM (p=0.78). A greater proportion of ADM patients underwent mastectomies for prophylaxis, compared with the non-ADM group (14.0% versus 6.7%, respectively, p<0.001). Patients with ADM

underwent nipple sparing mastectomies more frequently, when compared to the non-ADM cohort (21.8% versus 12%, p<0.001). Fewer women with ADM had lymph-node staging procedures (p<0.001). The ADM cohort was less likely to undergo radiation therapy before or after reconstruction (p=0.02) and was less likely to receive adjuvant chemotherapy (p<0.001), compared with non-ADM patients.

Acellular dermal matrix was used in 10 MROC centers and by 58 participating surgeons. Interestingly, most surgeons fell into one of two practice patterns: 1) those using ADM in the vast majority of their patients, or 2) those rarely or never using ADM. Of the 58 participants, 23 surgeons (49.6%) used ADM in over 80 percent of their immediate tissue expander reconstructions, while 15 surgeons (25.8%) used ADM in less than 20 percent of their cases, and out of these, 11 surgeons did not use ADM at all. Only 20 surgeons (34.4%) relied on ADM more selectively, in 20 to 80 percent of their patients.

Two year postoperative complication rates are listed in Table 2. Although complication rates were generally higher in the ADM group, compared with the non-ADM cohort, these differences were not statistically significant for overall complications (27.9% versus 24.5%, respectively, p=0.18); major complications (22.4% versus 15.7%, respectively, p=0.052); wound infections (11.3% vs. 9.5%, p=0.11); or reconstructive failure (9.2% versus 5.8%, p=0.13). In terms of specific complications, a higher wound dehiscence rate was observed in the ADM group (3.4% versus 0.8%, p=0.02). The rate of wound infection requiring IV antibiotics or surgical intervention was also found to be higher in the ADM cohort (7.0% versus 4.5% for non-ADM patients, p=0.045).

Results of the mixed effects logistic regression analyses for complications are described in Table 3. Controlling for patient demographic and clinical variables, we observed no significant ADM effects on any (all) complications (OR=1.21, p=0.26), major complications (OR=1.43, p=0.052), wound infections (OR=1.49, p=0.12, or reconstructive failure (OR=1.55, p=0.09). While not statistically significant, the magnitude of the associated ORs suggests a trend towards higher risks within the ADM cohort for major complication and failure.

Unadjusted PRO scores are summarized in Table 4. Prior to reconstruction, ADM and non-ADM cohorts reported similar levels of satisfaction with breast, psychosocial well-being, physical well-being, and sexual well-being, and pain as measured by BREAST-Q and NPRS.

Mixed-effects regression models for two year PROs are described in Tables 5. Controlling for demographic and clinical covariates, ADM compared to non-ADM patients had similar scores on BREAST-Q Satisfaction with Breast (mean difference= −0.86, p=0.59), Psychosocial Well-being (mean difference= 0.31, p=0.85), and Sexual Well-being (mean difference= −1.72, p=0.26) at two years (Table 5).

The longitudinal analyses indicated that ADM had no significant effects on the change of BREAST-Q Physical Well-being or NPRS over time, as shown by the absence of significant interactions between time and ADM (results not shown here). The final models were fit without the interaction terms (Table 6) and showed that in both cohorts, physical well-being and pain increased significantly at one week post-surgery and gradually improved thereafter.

However, two years after reconstruction, both groups still experienced slightly higher pain and lower physical wellbeing, compared to their preoperative levels.

Discussion

Since its introduction over a decade ago, ADM has revolutionized immediate tissue expander breast reconstruction, often supplanting more traditional total submuscular or dual plane approaches (3, 20). While its proponents cite improved control of the implant pocket, accelerated tissue expansion dynamics, and superior aesthetic outcomes as rationale for its use, several studies have tempered this enthusiasm with reports of higher associated risks for postoperative complications compared with non-ADM techniques (21). However, there is a lack of high quality, prospective studies which comprehensively assess clinical outcomes. Few randomized controlled trials have been attempted, with the majority of published reports limited by retrospective designs and low patient numbers (22).

Among immediate tissue expander reconstruction patients, our analyses found that use of ADM had no significant effects on complications or patient-reported outcomes up to two years after the initial stage of reconstruction. This study used a multicenter prospective cohort design, enabling us to study 1,297 patients from 10 participating centers and 58 plastic surgeons across the United States and Canada. The prospective nature and large sample size allowed us to control for a variety of potential confounding variables through regression analyses. These features constitute the major strengths of this study and support the generalizability of its findings.

Several recent meta-analyses evaluating clinical outcomes in ADM-assisted breast reconstruction have reported higher overall complication rates with use of ADM in expander-based reconstruction. However, these studies have cited widely varying complication rates, ranging from 6 to 60 percent (21). This wide variation may be explained by differences in study designs and by different definitions of what constitutes a complication. In our analysis, we found overall complication rates of 27.9 percent in the ADM cohort and 24.5 percent in the non-ADM group, which are consistent with those of previous reports. Controlling for a variety of potential confounding variables, ADM had no significant effects on complications in the regression analyses. Since surgical practices vary across sites and can impact outcomes, controlling for center effects was another important strength of this study.

Surgeons using ADM have clear preferences for particular brands of these products. However, in the current data analysis, we did not attempt to differentiate between ADM types. A number of manufacturers supply a large variety of ADM options, which vary in sterile preparation, need for rehydration and shelf-lives. Several reports have attempted to assess differences in clinical complication rates among these products but have returned mixed results (23, 24).

Improved tissue expansion dynamics potentially resulting in accelerated rates of volume fill, fewer expansion procedures, and earlier exchange operations are among the commonly cited rationale for use of ADM in immediate breast reconstruction (25). Our analysis found that

the time period from expander placement to exchange did not differ significantly between the two study cohorts, suggesting that ADM use may not confer a major time saving. While this variable is arguably only a proxy measure of expansion rate and does not reflect actual differences in intraoperative fill volumes or numbers of expansion, it does indicate that ADM use may not facilitate faster completion times for reconstruction.

To date, the majority of published reports evaluating ADM-assisted breast reconstruction have focused on clinical outcomes, largely neglecting assessments of patient reported outcomes. Only four studies were found to have use validated instruments (8, 15, 22, 26). McCarthy and colleagues evaluated PROs using the BREAST-Q in a single center, randomized, controlled trial comparing AlloDerm-assisted immediate reconstruction with standard submuscular techniques (22). This study reported no significant differences between ADM and non-ADM patients in postoperative physical well-being or pain. While some studies have reported higher levels of satisfaction with the breast following reconstruction in ADM cohorts (16, 27), others have been unable to corroborate these findings (28).

The absence of significant ADM effects on expander-based reconstruction outcomes in our study raises an obvious question: Should we stop using ADM for these procedures? Given the number of studies supporting its use, our findings do not support abandonment of what many surgeons view as an extremely effective technique. However, these results do suggest that perhaps we need to be more selective in how and in whom we use ADM, given that it adds significantly to the cost of reconstruction. Previous authors have attempted to develop algorithms to identify patient populations in which ADM may prove beneficial (29), but there remains a paucity of evidence-based selection criteria for use of this material in implant-based breast reconstruction. For example, while not reflected in our analysis, the use of ADM in nipple sparing mastectomies might produce better outcomes. Additional prospective, multicenter research is needed to identify patient subgroups for which ADM may improve outcomes.

Despite its strengths, our study also has important limitations. As patients were not randomized to procedures with or without ADM, it remains conceivable that our results may be attributable to unknown demographic or clinical confounders. While a randomized, controlled trial (RCT) design might have controlled for these unknown confounders, surgeons appear to have strong preferences for or against use of ADM in breast reconstruction, thus making an RCT logistically challenging. In our analyses, there also remains a possibility of selection bias: Perhaps surgeons preferentially employed ADM for more difficult cases, thereby rendering a more conservative overall estimate of the effects of ADM. However, this latter possibility appears unlikely, given that the predominant number of surgeons in the study either used or avoided ADM in most or all of their cases.

Finally, non-response (drop-out) rates are almost always a challenge in survey studies. For MROC, we noted 40 percent nonresponse rate at two-years, despite systematic follow-up e-mails and phone calls from study staff to those with missing or incomplete surveys. While we employed multiple imputation statistical analyses to control for multiple variables, these methods were based on the assumption that missing data were independent of patient

outcome—i.e., that non-responders were no more or less likely to experience good or bad outcomes, compared to responders. Because we were unable to survey the non-responders, the possibility of selection bias cannot be entirely excluded.

Conclusion

Acellular dermal matrix has become an integral component of immediate tissue expander-based breast reconstruction. However, in a prospective, multicenter analysis comparing outcomes with and without ADM, we found no significant differences in postoperative complication rates. Furthermore, we did not observe any statistically significant ADM effects on patient-reported outcomes at two years. Given the costs of these materials, our results suggest a need for development of evidence-based selection criteria to identify patient subgroups which might benefit from use of ADM.

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Table 1

Clinical Characteristics of Patients Overall and by ADM Usage

Characteristics	Overall N=1297	ADM usage		p-Value
		ADM used N=655	ADM not used N=642	
Age, mean (SD)	48.4 (10.4)	48.8 (10.5)	48.1 (10.2)	0.205
BMI, mean (SD)	25.7 (5.3)	25.7 (5.5)	25.6 (5.1)	0.778
Months to exchange, median (range)[1]	5.5 (26.7)	5.4 (25.7)	5.6 (25.1)	0.775
Laterality				
Unilateral	490 (37.8%)	250 (38.2%)	240 (37.4%)	0.771
Bilateral	807 (62.2%)	405 (61.8%)	402 (62.6%)	
Indication for mastectomy				
Therapeutic	1162 (89.6%)	563 (86.0%)	599 (93.3%)	0.000
Prophylactic	135 (10.4%)	92 (14.0%)	43 (6.7%)	
Mastectomy type				
Nipple sparing	220 (17.0%)	143 (21.8%)	77 (12.0%)	0.000
Simple or modified radical	1077 (83.0%)	512 (78.2%)	565 (88.0%)	
Smoking status				
Non-smoker	864 (67.2%)	454 (70.1%)	410 (64.4%)	0.089
Previous smoker	391 (30.4%)	181 (27.9%)	210 (33.0%)	
Current smoker	30 (2.3%)	13 (2.0%)	17 (2.7%)	
Diabetes (NIDDM and IDDM)				
Yes	37 (2.9%)	19 (2.9%)	18 (2.8%)	0.916
No	1260 (97.1%)	636 (97.1%)	624 (97.2%)	
Lymph node management				
None	241 (18.6%)	158 (24.1%)	83 (12.9%)	0.000
SLNB only	636 (49.0%)	295 (45.0%)	341 (53.1%)	
ALND with or without SLNB	420 (32.4%)	202 (30.8%)	218 (34.0%)	
Radiation				
Before reconstruction	61 (4.7%)	25 (3.8%)	36 (5.6%)	0.024
During reconstruction[2]	192 (14.8%)	105 (16.0%)	87 (13.6%)	
After reconstruction	69 (5.3%)	25 (3.8%)	44 (6.9%)	
None	975 (75.2%)	500 (76.3%)	475 (74.0%)	
Chemotherapy				
During or after reconstruction	440 (33.9%)	193 (29.5%)	247 (38.5%)	0.001
Not during or after reconstruction	857 (66.1%)	462 (70.5%)	395 (61.5%)	

Abbreviations: ADM, acellular dermal matrix; BMI, body mass index; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; SD, standard deviation.

[1] Defined as the number of months between the initial placement of tissue expander and exchange for final implant; based on non-failure patients who underwent exchange.

[2] Defined as radiation received after the placement of tissue expander but before the exchange for final implant.

Table 2

Two-Year Postoperative Complication Rate Overall and by ADM Usage

Complication	Overall N=1297	ADM used N=655	ADM not used N=642	p-Value[1]
Any complication	340 (26.2%)	183 (27.9%)	157 (24.5%)	0.184
Major complication	248 (19.1%)	147 (22.4%)	101 (15.7%)	0.052
Wound infection	135 (10.4%)	74 (11.3%)	61 (9.5%)	0.112
Reconstructive failure	97 (7.5%)	60 (9.2%)	37 (5.8%)	0.126
Hematoma	43 (3.3%)	17 (2.6%)	26 (4.0%)	0.147
Wound dehiscence	27 (2.1%)	22 (3.4%)	5 (0.8%)	0.020
Wound infection requiring IV antibiotics or reoperation	75 (5.8%)	46 (7.0%)	29 (4.5%)	0.045
Wound infection requiring oral antibiotics	66 (5.1%)	32 (4.9%)	34 (5.3%)	0.523
Mastectomy skin flap necrosis	78 (6.0%)	44 (6.7%)	34 (5.3%)	0.228
Capsular contracture	22 (1.7%)	11 (1.7%)	11 (1.7%)	0.758
Implant malposition	12 (0.9%)	8 (1.2%)	4 (0.6%)	0.916
Seroma	41 (3.2%)	21 (3.2%)	20 (3.1%)	0.970
Implant leakage, rupture or deflation	17 (1.3%)	10 (1.5%)	7 (1.1%)	0.665

[1]For the comparison of two-year postoperative complication rates between ADM and no ADM group, adjusting for sites (hospitals) and surgeons.

Table 3

Mixed-effects Logistic Regression Model for Two-Year Postoperative Complication

Covariate	Any Complication			Major Complication			Wound infection			Reconstructive Failure		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.02	(1.01, 1.03)	0.008	1.02	(1.01, 1.04)	0.008	1.01	(0.99, 1.04)	0.150	1.02	(0.99, 1.04)	0.125
BMI	1.04	(1.01, 1.06)	0.004	1.04	(1.02, 1.07)	0.002	1.06	(1.03, 1.10)	0.001	1.08	(1.04, 1.12)	<.001
ADM usage												
ADM not used		-Reference-			-Reference-			-Reference-			-Reference-	
ADM used	1.21	(0.86, 1.70)	0.263	1.43	(1.00, 2.05)	0.052	1.49	(0.90, 2.44)	0.118	1.55	(0.93, 2.58)	0.089
Laterality												
Unilateral		-Reference-			-Reference-			-Reference-			-Reference-	
Bilateral	1.49	(1.11, 1.99)	0.008	1.62	(1.16, 2.25)	0.004	1.23	(0.81, 1.86)	0.327	1.38	(0.84, 2.27)	0.200
Indication for mastectomy												
Therapeutic		-Reference-			-Reference-			-Reference-			-Reference-	
Prophylactic	0.71	(0.39, 1.29)	0.265	0.74	(0.38, 1.46)	0.389	0.49	(0.19, 1.26)	0.138	0.49	(0.14, 1.66)	0.251
Mastectomy type												
Simple or modified radical		-Reference-			-Reference-			-Reference-			-Reference-	
Nipple sparing	1.37	(0.92, 2.05)	0.125	1.09	(0.69, 1.73)	0.703	0.97	(0.52, 1.82)	0.925	1.67	(0.82, 3.41)	0.155
Smoking status												
Non-smoker		-Reference-			-Reference-			-Reference-			-Reference-	
Previous smoker	1.13	(0.84, 1.51)	0.412	1.06	(0.76, 1.47)	0.729	1.03	(0.69, 1.56)	0.871	1.40	(0.86, 2.27)	0.179
Current smoker	1.77	(0.80, 3.89)	0.158	3.19	(1.44, 7.10)	0.004	1.44	(0.50, 4.15)	0.498	7.24	(2.62, 20.00)	<.001
Diabetes												
No		-Reference-			-Reference-			-Reference-			-Reference-	
Yes	0.95	(0.41, 2.20)	0.914	0.98	(0.40, 2.42)	0.965	0.56	(0.15, 2.09)	0.390	0.98	(0.28, 3.44)	0.979
Lymph-node management												
None		-Reference-			-Reference-			-Reference-			-Reference-	
SLNB only	0.80	(0.50, 1.28)	0.355	0.81	(0.48, 1.37)	0.423	0.70	(0.37, 1.34)	0.282	0.60	(0.27, 1.34)	0.212
ALND with/without SLNB	0.57	(0.33, 0.97)	0.039	0.63	(0.35, 1.15)	0.132	0.45	(0.21, 0.95)	0.035	0.75	(0.33, 1.73)	0.500
Radiation												
None		-Reference-			-Reference-			-Reference-			-Reference-	

Covariate	Any Complication			Major Complication			Wound infection			Reconstructive Failure		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Before reconstruction	1.87	(1.05, 3.34)	0.034	1.96	(1.04, 3.72)	0.039	2.35	(1.12, 4.92)	0.023	4.38	(1.83, 10.50)	0.001
During reconstruction[1]	2.71	(1.81, 4.06)	<.001	2.90	(1.89, 4.46)	<.001	3.28	(1.92, 5.63)	<.001	6.32	(3.52, 11.34)	<.001
After reconstruction	3.14	(1.72, 5.74)	<.001	3.43	(1.81, 6.49)	<.001	1.85	(0.81, 4.23)	0.146	2.74	(1.03, 7.30)	0.044
Chemotherapy												
None		-Reference-			-Reference-			-Reference-			-Reference-	
During/after reconstruction	1.31	(0.96, 1.79)	0.090	1.39	(0.98, 1.97)	0.066	1.51	(0.98, 2.35)	0.064	1.57	(0.93, 2.65)	0.092

Abbreviations: ADM, acellular dermal matrix; BMI, body mass index; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; OR, odds ratio; CI, confidence interval.

[1]Defined as radiation received after the placement of tissue expander but before the exchange for final implant.

Table 4

Summary of Patient-Reported Outcomes (PROs) by ADM Usage

PROs	ADM used N=595		ADM not used N=605		p-Value for baseline PRO[2]
	n[1]	Mean (SD)	n[1]	Mean (SD)	
BREAST-Q: Satisfaction with breast					
Baseline	593	64.1 (21.4)	602	63 (21.6)	0.398
Two years post-op	399	64 (18.1)	303	63.3 (17.5)	
BREAST-Q: Psychosocial well-being					
Baseline	592	72.1 (18.4)	600	71.6 (16.7)	0.645
Two years post-op	396	75.1 (19.4)	299	72.9 (18.2)	
BREAST-Q: Physical well-being					
Baseline	592	80 (14.4)	603	80.2 (14.3)	0.764
One week post-op	504	56 (12.1)	545	55.9 (12.6)	
Three months post-op	466	68.7 (12.9)	443	68.5 (14.5)	
One year post-op	439	75.6 (14.1)	380	77.2 (15.2)	
Two years post-op	393	76.6 (14.1)	299	78 (14.2)	
BREAST-Q: Sexual well-being					
Baseline	579	57.8 (20)	589	59.7 (17.8)	0.087
Two years post-op	379	53.2 (21)	292	53.9 (20.5)	
NPRS					
Baseline	544	1 (1.6)	545	1 (1.7)	0.941
One week post-op	459	4 (2)	496	4 (2.1)	
Three months post-op	429	1.7 (1.8)	401	2 (2.1)	
One year post-op	415	1.1 (1.6)	361	1.2 (1.7)	
Two years post-op	371	1 (1.5)	282	1.1 (1.6)	

[1] Denotes the number of patients with complete PROs.

[2] For the comparison of baseline PROs between ADM and no ADM groups.

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Table 5

Mixed-effects Regression Model for Two-Year Postoperative PROs: Satisfaction with Breast, Psychosocial Well-being and Sexual Well-being

Covariate	Satisfaction with Breast			Psychosocial Well-being			Sexual Well-being		
	Beta	95% CI	p-Value	Beta	95% CI	p-Value	Beta	95% CI	p-Value
Baseline outcome	0.11	(0.05, 0.17)	0.001	0.40	(0.34, 0.45)	<.001	0.36	(0.29, 0.43)	<.001
Age	−0.09	(−0.23, 0.05)	0.207	0.16	(0.03, 0.28)	0.013	0.21	(0.06, 0.35)	0.005
BMI	−0.26	(−0.53, 0.01)	0.058	−0.19	(−0.49, 0.12)	0.214	−0.35	(−0.67, −0.04)	0.027
ADM usage									
ADM not used		- Reference -			- Reference -			- Reference -	
ADM used	−0.86	(−4.02, 2.31)	0.588	0.31	(−2.98, 3.61)	0.846	−1.72	(−4.71, 1.28)	0.258
Laterality									
Unilateral		- Reference -			- Reference -			- Reference -	
Bilateral	3.78	(1.09, 6.47)	0.007	−0.30	(−2.59, 1.99)	0.796	2.60	(−0.47, 5.66)	0.095
Indication for mastectomy									
Therapeutic		- Reference -			- Reference -			- Reference -	
Prophylactic	2.37	(−3.03, 7.77)	0.382	6.78	(1.74, 11.82)	0.009	3.49	(−1.99, 8.97)	0.209
Mastectomy type									
Simple or modified radical		- Reference -			- Reference -			- Reference -	
Nipple sparing	−0.65	(−3.54, 2.25)	0.661	2.43	(−0.44, 5.29)	0.096	5.85	(1.41, 10.28)	0.011
Smoking									
Non-smoker		- Reference -			- Reference -			- Reference -	
Previous smoker	−2.28	(−5.15, 0.59)	0.117	−1.40	(−4.83, 2.03)	0.409	−1.99	(−4.80, 0.82)	0.163
Current smoker	−7.67	(−16.00, 0.67)	0.071	−2.71	(−10.86, 5.45)	0.513	−1.92	(−18.29, 14.44)	0.807
Diabetes									
No		- Reference -			- Reference -			- Reference -	
Yes	3.89	(−2.89, 10.68)	0.259	7.06	(−0.46, 14.58)	0.065	4.20	(−3.65, 12.05)	0.291
Lymph node management									
None		- Reference -			- Reference -			- Reference -	
SLNB only	−0.97	(−5.05, 3.11)	0.637	1.41	(−2.73, 5.55)	0.498	0.21	(−3.93, 4.36)	0.920
ALND with/without SLNB	−1.02	(−5.82, 3.78)	0.671	0.79	(−3.22, 4.79)	0.699	1.81	(−4.56, 8.18)	0.566
Radiation									

Covariate	Satisfaction with Breast			Psychosocial Well-being			Sexual Well-being		
	Beta	**95% CI**	**p-Value**	**Beta**	**95% CI**	**p-Value**	**Beta**	**95% CI**	**p-Value**
None		- Reference -			- Reference -			- Reference -	
Before reconstruction	−2.89	(−9.98, 4.19)	0.412	−2.03	(−7.72, 3.67)	0.481	−1.83	(−9.23, 5.58)	0.621
During reconstruction[1]	−8.44	(−12.10, −4.78)	<.001	−5.61	(−9.28, −1.94)	0.003	−4.00	(−9.07, 1.07)	0.119
After reconstruction	−14.62	(−21.21, −8.04)	<.001	−6.27	(−13.04, 0.49)	0.068	−8.26	(−16.03, −0.48)	0.038
Chemotherapy									
None		- Reference -			- Reference -			- Reference -	
During or after reconstruction	−0.67	(−3.22, 1.88)	0.606	−2.59	(−5.29, 0.11)	0.060	−3.50	(−7.18, 0.18)	0.061

Abbreviations: ADM, acellular dermal matrix; BMI, body mass index; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; CI, confidence interval.

[1]Defined as radiation received after the placement of tissue expander but before the exchange for final implant.

Table 6

Mixed-effects Regression Model for PROs: Physical well-being and NPRS

Covariate	Physical well-being			NPRS		
	Beta	**95% CI**	**p-Value**	**Beta**	**95% CI**	**p-Value**
Age	0.07	(0.01, 0.13)	0.032	−0.01	(−0.02, −0.00)	0.030
BMI	−0.28	(−0.40, −0.16)	<.001	0.04	(0.03, 0.05)	<.001
PRO assessment time						
Baseline		- Reference -			- Reference -	
One week post-op	−24.20	(−25.13, −23.35)	<.001	2.96	(2.82, 3.10)	<.001
Three months post-op	−11.90	(−12.90, −10.97)	<.001	1.01	(0.88, 1.15)	<.001
One year post-op	−4.54	(−5.67, −3.42)	<.001	0.27	(0.14, 0.40)	<.001
Two years post-op	−3.44	(−4.42, −2.46)	<.001	0.20	(0.07, 0.32)	0.003
ADM usage						
ADM not used		- Reference -			- Reference -	
ADM used	−0.70	(−2.04, 0.63)	0.300	−0.01	(−0.16, 0.13)	0.851
Laterality						
Unilateral		- Reference -			- Reference -	
Bilateral	−1.08	(−2.29, 0.13)	0.081	0.19	(0.04, 0.35)	0.016
Indication for mastectomy						
Therapeutic		- Reference -			- Reference -	
Prophylactic	3.57	(1.24, 5.90)	0.003	−0.38	(−0.65, −0.10)	0.008
Mastectomy type						
Simple or modified radical		- Reference -			- Reference -	
Nipple sparing	0.38	(−1.26, 2.03)	0.646	−0.19	(−0.39, 0.00)	0.051
Smoking						
Non-smoker		- Reference -			- Reference -	
Previous smoker	−1.53	(−2.83, −0.22)	0.022	0.09	(−0.06, 0.24)	0.262
Current smoker	0.64	(−3.81, 5.09)	0.777	0.19	(−0.33, 0.71)	0.473
Diabetes						
No		- Reference -			- Reference -	
Yes	−1.96	(−5.81, 1.90)	0.318	0.65	(0.19, 1.11)	0.006

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Covariate	Physical well-being			NPRS		
	Beta	95% CI	p-Value	Beta	95% CI	p-Value
Lymph node biopsy						
None		- Reference -			- Reference -	
SLNB only	1.65	(−0.26, 3.57)	0.090	−0.12	(−0.35, 0.11)	0.299
ALND with/without SLNB	1.36	(−0.80, 3.53)	0.217	−0.15	(−0.42, 0.12)	0.271
Radiation						
None		- Reference -			- Reference -	
Before reconstruction	−1.52	(−4.28, 1.24)	0.280	−0.06	(−0.41, 0.28)	0.725
During reconstruction[1]	−3.43	(−5.28, −1.58)	0.000	0.36	(0.11, 0.60)	0.004
After reconstruction	−2.62	(−5.48, 0.23)	0.072	0.21	(−0.14, 0.56)	0.244
Chemotherapy						
None		- Reference -			- Reference -	
During or after reconstruction	−0.59	(−2.00, 0.81)	0.407	0.06	(−0.11, 0.23)	0.501

Abbreviations: ADM, acellular dermal matrix; BMI, body mass index; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; CI, confidence interval.

[1]Defined as radiation received after the placement of tissue expander but before the exchange for final implant.

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