Breast Surgery

Outcomes of Acellular Dermal Matrix for **Immediate Tissue Expander Reconstruction** with Radiotherapy: A Retrospective **Cohort Study**

Elizabeth S. Craig, MD; Mark W. Clemens, MD; John C. Koshy, MD; James Wren, BS; Zhang Hong, PhD; Charles Butler, MD; Patrick Garvey, MD; Jesse Selber, MD; and Steven Kronowitz, MD

15

5

10

Abstract

Background: Despite increasing literature support for the use of acellular dermal matrix (ADM) in expander-based breast reconstruction, the effect 20 of ADM on clinical outcomes in the presence of post-mastectomy radiation therapy (PMRT) has not been well described. **Objectives:** To analyze the impact ADM plays on clinical outcomes on immediate tissue expander (ITE) reconstruction undergoing PMRT. Methods: We retrospectively reviewed patients who underwent ITE breast reconstruction from 2004 to 2014 at MD Anderson Cancer Center. Patients were categorized into four cohorts: ADM, ADM with PMRT, non-ADM, and non-ADM with PMRT. Outcomes and complications were compared among cohorts. Results: Over 10 years, 957 patients underwent ITE reconstruction (683 non-ADM, 113 non-ADM with PMRT, 486 ADM, and 88 ADM with PMRT) with 1370 reconstructions. Overall complication rates for the ADM and non-ADM cohorts were 39.0% and 16.7%, respectively (P < 0.001). Within both 25 75 cohorts, mastectomy skin flap necrosis (MSFN) was the most common complication, followed by infection. ADM use was associated with a significantly higher rate of infections and seromas in both radiated and non-radiated groups; however, when comparing radiated cohorts, the incidence of explantation

was significantly lower with the use of ADM.

Conclusions: The decision to use ADM for expander-based breast reconstruction should be performed with caution, given higher overall rates of complications, including infections and seromas. There may, however, be a role for ADM in cases requiring PMRT, as the overall incidence of implant 80 failure is lower than non-ADM cases.

Level of Evidence: 3

35

30

Editorial Decision date: May 10, 2018.

40

45

50

Two-stage prosthetic breast reconstruction is currently the most common method of reconstruction for breast cancer patients worldwide, and over 68,000 tissue expander-based (TE) reconstructions were performed in the United States in 2016 alone.¹ The ability of ADM to assist with vascularized soft tissue coverage, increase intraoperative fill volumes, secure the pocket, improve breast ptosis, and reinforce the inframammary fold have led to its widespread use.²⁻⁹ ADM has gained popularity for its ability to provide optimal cosmetic results in implant-based reconstruction,^{10,11} but the

From the Department of Plastic and Reconstructive Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX. Dr Clemens is a Breast Surgery Section Editor for the Aesthetic Surgery Journal.

Corresponding Author:

Dr Mark Clemens, The University of Texas MD Anderson Cancer Center, 1400 Pressler St., Unit 1488, Houston, TX 77030, USA. E-mail: mwclemens@mdanderson.org

Presented in 2014 at the Texas Society of Plastic Surgeons Annual Meeting in San Antonio, TX.

Aesthetic Surgery Journal 2018, 1-11 © 2018 The American Society for Aesthetic Plastic Surgery, Inc. Reprints and permission: iournals.permissions@oup.com DOI: 10.1093/asj/sjy127 www.aestheticsurgeryjournal.com

UNIVERSITY PRESS

55

60

65

70

85 Therapeutic

90

95

aesthetic advantages have been tempered by the controversial data regarding seroma, infection, and other complication rates. 10,12-15

The beneficial impact that PMRT has on decreasing loco-re-105 gional recurrence in breast cancer patients has been well documented.¹⁶ In 2004, Kronowitz et al introduced the concept of "delayed-immediate" and "delayed-delayed" breast reconstruction, in an effort to preserve the breast footprint and skin envelope in cases in which the risk of PMRT is unknown.⁵ 110 However, this has posed a growing challenge to reconstructive surgeons, as the literature is replete with evidence illustrating the deleterious effects of PMRT on expander/ implant-based reconstruction, with complication rates as high as 58.8%.^{2,5,12,16-19} In addition, the literature has high-115 lighted the large proportion of patients in this population with unacceptable aesthetic results leading to expander/implant removal.¹⁹⁻²¹ While most reconstructive surgeons prefer autologous tissue reconstruction to expander/implant-based reconstruction in patients at risk for PMRT, it is not always feasible.

> As indications for PMRT continue to grow, understanding the outcomes of ADM in a radiated field becomes critical. The purpose of our study was to examine the impact of ADM with PMRT on clinical outcomes in ITE by performing a retrospective cohort study, which included ADM/non-ADM and PMRT/non-PMRT cohorts.

METHODS

120

125

We retrospectively reviewed a prospectively maintained 130 database of consecutive patients who underwent ITE breast reconstruction from June 2004 to December 2014 at The University of Texas MD Anderson Cancer Center. Patients were categorized into 4 cohorts: ADM, ADM with PMRT, non-ADM, and non-ADM with PMRT. Demographic information, 135 comorbidities, perioperative data, operative data, and complications were collected for comparison. The primary outcomes evaluated were seroma (clinically appreciable fluid collection requiring drainage), infection (cellulitis requiring antibiotic treatment), delayed wound healing (incision open-140 ing greater than 5 mm), and MSFN (including sloughing, desquamation, and full-thickness loss requiring bedside or operative debridement). The timing of complications was evaluated by comparing both ADM and non-ADM groups, as well as PMRT and non-PMRT groups. Patients were excluded 145 from the study if they received pre-mastectomy radiation therapy, or did not reach the endpoint of explantation or implant exchange and were lost to follow-up. This study was approved and carried out under the guidelines of the Institutional Review Board of MD Anderson Cancer Center. 150

Statistical Analysis

A univariate analysis was utilized to examine the associations between outcomes and patient characteristic. Patient

Table 1. Overall Demographic Information

Characteristic	Total			
	N = 957 patients			
Age in years, mean ± SD	49.3 ± 10.6 Range 28-72	16		
BMI, mean ± SD	26.6 ± 10.2 Range 14-51	100		
Smoker				
Active	64 (6.7)			
Previous	185 (19.3)	165		
Diabetes	58 (6.1)			
Peripheral vascular disease	2 (0.2)			

Overall demographic information of patients included in this study.

characteristics that were found to have both associations and *P* values less than or equal to 0.25 in the univariate analysis, were then included as independent variables in the multivariate generalized estimation model (GEE). The 175 final multivariate model was determined using a backward-selection algorithm. Multivariate GEE was used to assess the impact of various confounders on patient outcomes. The analyses were performed in SAS 9.2 (SAS Institute, Inc., Cary, NC). The timing of occurrence of 180 complications among the cohorts was compared using a 2-sided Wilcoxon rank sum test, with a P value less than 0.05 considered significant.

In order to rule out temporal bias, outcomes between the first and last 5 years of the study were compared, and 185 the rates of overall complications were found to be equivalent. In addition, plastic surgeons and breast surgeons were grouped by the number of cases performed and included in the multivariate analysis to evaluate surgeon technique or experience as potential confounders; however, these 190 were also not found to be significant.

Surgical Techniques

195 Tissue expanders were placed in the subpectoral pocket. Reconstructions without ADM involved either partial or total muscle coverage with standard elevation of the serratus anterior and/or rectus fascia. Reconstructions utilizing ADM were performed by securing a sheet of ADM to the inferior border of the pectoralis muscle once it had been released from the chest wall as a pectoralis muscle extension. Intraoperative tissue expansion was performed to tissue tolerance. Drains were placed according to surgeon preference. On average, the length of drains was 10 days 205 (range 7-22 days). Removal of drains was at the discretion of the attending physician and therefore was not standardized across all physicians. In general, drains were removed when output was less than 30 mL for 2 consecutive days.

155

.10	Characteristic	Non-Ra	adiated	Radia	ted	<i>P</i> values	265
		Non-ADM	ADM	Non-ADM	ADM		
		N = 683	N = 486	N=113	N = 88		
15	Age in years, mean ± SD	48.84 ± 10.6 Range 28-72	49.40 ± 10.7 Range 29-68	45.75 ± 10.0 Range 34-63	46.69 ± 9.4 Range 36-66	0.002	
	BMI, mean ± SD	26.66 ± 13.4 Range 18-42	26.34 ± 5.7 Range 14-51	26.26 ± 5.7 Range 19-49	26.29 ± 5.3 Range 20-38	0.96	270
	Smoker					0.83	
• •	Active	42 (6.1)	34 (7.0)	10 (8.8)	4 (4.5)		
20	Previous	133 (19.5)	90 (18.5)	23 (20.4)	15 (17.0)		275
	Diabetes	44 (6.4)	34 (7.0)	3 (2.7)	0 (0)	0.04	
	Peripheral vascular disease	0 (0)	3 (0.6)	0 (0)	0 (0)	NA	

5 Subgroup demographic information (radiated vs non-radiated and non-ADM vs ADM). Of note, data for 6 breasts had to be excluded from the ADM-radiated cohort because of missing radiation therapy information, resulting in 88 instead of 94 breasts in the radiated ADM cohort.

Table 3. Patient Outcomes by ADM Group

230	Characteristic	Total	Non-Radiated		Radiated		<i>P</i> value	
		(N = 1	376 breasts)					285
			Non-ADM	ADM	Non-ADM	ADM		
	Complication	359 (26.1)	106 (15.5)	182 (37.4)	27 (23.9)	42 (47.7)	<0.0001	
235	Dehiscence	55 (4.0)	17 (2.5)	30 (6.2)	3 (2.7)	5 (5.7)	0.057	290
	Hematoma	25 (1.8)	13 (1.9)	7 (1.4)	2 (1.8)	3 (3.4)	0.83	
	Infection	108 (7.8)	25 (3.7)	56 (11.5)	13 (11.5)	14 (15.9)	<0.0001	
240	Necrosis	207 (15.0)	45 (6.6)	124 (25.5)	15 (13.3)	21 (23.9)	<0.0001	
	Seroma	97 (7.0)	26 (3.8)	53 (10.9)	6 (5.3)	12 (13.6)	<0.0001	295
	Explantation	119 (8.6)	40 (5.9)	46 (9.5)	23 (20.4)	10 (11.4)	0.0012	

245

Overall complication rates based on total number of patients included in this study, and based on subgroup.

Perioperative antibiotics were administered and, in general, continued postoperatively until all drains were removed.

One-thousand-three-hundred-seventy-six breast recon-

structions in 957 patients with ITE (574 reconstructions

performed with ADM, and 796 without ADM) met our

inclusion criteria (Table 1). The type of ADM used was

divided, as 24.7% of surgeons utilized Surgimend (TEI

Biosciences, Boston, MA) and 75.3% utilized Alloderm

(LifeCell Corporation, Bridgewater, NJ). The type of mesh

used in ADM reconstructions was analyzed against pri-

mary outcomes and found to have no influence. Fifteen

percent of the entire cohort received PMRT, 27% received

neoadjuvant chemotherapy, and 28% received adjuvant

250 **RESULTS**

255



chemotherapy. The majority of mastectomies (90.4%) utilized a skin-sparing technique; 6% were nipple sparing. The average follow-up was 210 days (range, 146-304).

Demographics were comparable among all groups (Table 2), with the following exceptions. Patients in the 305 ADM without PMRT cohort were older and had a higher incidence of diabetes than patients in the other cohorts (P = 0.002 and P < 0.001, respectively). Invasive disease and axillary dissections were statistically more prevalent in the cohorts who underwent PMRT than in those who did 310 not. Nipple-sparing mastectomies were statistically more prevalent within the ADM without PMRT cohort (8.8%, P < 0.0008). Reconstructions completed with ADM had higher initial TE fill volumes than did those in the non-ADM groups, despite having similar preoperative bra vol-315 umes (258 cc versus 152 cc, respectively, P < 0.001).

280

J



Figure 1. Postoperative complication rates between ADM and total muscle coverage (TMC) compared by timing of radiation therapy. Note that complication differences between ADM and TMC are mainly isolated to the early postoperative phase and more approximate in the long term.

	Table 4. Explantation							400
	Reasons for Explantation	Total	Non-Radiated		Radiated		<i>P</i> value	
250		N (%)	Non-ADM	ADM	Non-ADM	ADM		
350		N = 119	N = 40	N = 46	N = 23	N = 10		405
	Complication reason	101 (85%)	32 (80%)	45 (98%)	15 (65%)	9 (90%)	0.29]
	Necrosis	37 (30.9%)	11 (28%)	17 (37%)	6 (26%)	3 (30%)		
355	Infection	57 (46.0%)	19 (48%)	25 (54%)	9 (39%)	4 (40%)		
	Hematoma	2 (1.6%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)		410
	Over inflation	5 (4%)	0 (0%)	3 (6%)	0 (0%)	2 (20%)		
360	Non-complication reason	18 (15%)	8 (20%)	1 (2%)	8 (35%)	1 (12%)	NA]

Causes of explantation. The table is broken down into explantation due to a complication such as hematoma, etc. or, non-complication reasons such as pain, medical therapy, or patient choice. 415

Complications

Overall complication rate refers to all measured outcomes 365 with the exception of explantation, which we considered a "reconstructive failure" and, therefore, reported separately. The incidence of complications (MSFN, infection, hematoma/seroma, dehiscence, and explantation) was reviewed 370 within the cohorts and overall population (Table 3 and Figure 1). When analyzing the cohorts, data for 6 breasts had to be excluded from the radiated-ADM cohort due to incomplete radiation treatment data.

420 MSFN was the most common type of complication (Table 3). Higher preoperative bra volume, nipple-sparing mastectomy, PMRT, and the use of ADM were independent risk factors for necrosis. Active smoking was surprisingly not found to be an independent risk factor, but this was

345

425 **Table 5.** Multivariate Overall Complications

Characteristics	Multivariabl	Multivariable GEE model				
	OR (95% CI)	<i>P</i> value				
Smoking						
Never	Ref.	-				
Active	1.72 (0.97-3.02)	0.059				
Previous	1.30 (0.89-1.91)	0.18				
ADM	3.05 (2.33-4.22)	<0.0001				
PMRT	1.76 (1.22-2.56)	0.0027				
Number of cases done	before this surgery					
<50	Ref.	-				
>=50	0.72 (0.54-0.98)	0.036				

Multivariate analysis of all demographic variables as indepdnent predictors of overall complications.

445

450

455

460

465

470

475

likely due to insufficient power, as only 6% of our patient population were active smokers.

The overall infection rate was 7.8%. Multivariate analysis identified higher bra volume, higher initial expander fill volume, PMRT, and the use of ADM as significant risk factors for infection. For every increase of 100 cc in the initial expander fill volume, the risk of infection increased by 2%. Patients who underwent PMRT were 2 times more likely to have an infection than those who did not. Overall, ADM AO1 was associated with an increased risk of infection compared with no ADM [odds ratio (OR) = 1.93, P = 0.01]. Among the patients who did not receive PMRT, the use of ADM increased the chance of having an infection 2 and a half times (OR = 2.48, P = 0.002). For patients reconstructed without ADM, the effect of PMRT alone increased their chance of infection 3 and a half times (Table 4). In contrast, PMRT appeared to have no significant impact on infection rate in patients reconstructed with ADM (P = 0.60).

Only 33% of the patients who developed infections had a history of seroma; conversely, 9% had infections prior to being diagnosed with a seroma, but the majority of infections appeared to occur de novo. Seven percent of the patients, overall, developed seromas. Patients reconstructed with ADM who received PMRT had the highest incidence of seroma, at 13.6%, followed by the cohort of patients with ADM but without PMRT at 10.9%. The use of ADM was found to be an independent risk factor for seroma formation (along with higher bra volume), and increased the chance of seroma by threefold (P < 0.0001). Smoking, PMRT, and initial expander fill volume were not contributing factors for incidence of seroma.

Explantation occurred in 119 patients or 8.6% of the cohort overall. Age, BMI, PMRT, bra volume, intraoperative TE fill volume, nipple-sparing mastectomy, axillary dissection, and invasive disease were significant risk factors for explantation in the univariate analysis. Neither ADM nor PMRT were found to be independent risk factors for explantation overall. However, for patients who underwent PMRT, ADM was associated with fewer explantations and lower odds of explantation when compared with non-ADM patients (OR = 0.38, P = 0.04). In fact, the highest rate of explantation occurred in the non-ADM with PMRT cohort (20.4%, P = 0.0012). Within the non-ADM group, PMRT increased the odds of explantation threefold (OR = 3.19, P = 0.002).

The main reason for explantation overall was infection (both overall and among cohorts), which occurred in 46% of the explantations, followed by mastectomy skin necrosis, which occurred in 30.9%. Reasons for explantation other than complications comprised only 15% of all explantations and included pain, unsatisfactory aesthetic outcome, TE rupture, and need for/interference with further treatment (Table 4).

Multivariate analysis was performed to evaluate the role of preoperative variables in contributing to complications, and identified older age, higher bra volume, smoking, PMRT, and the use of ADM as independent risk factors for overall complication rate (Table 5). Notably, neither the use of either neoadjuvant or adjuvant chemotherapy, nor initial fill was associated with increased overall complication or explantation rates. While controlling for these factors and others, including preoperative bra volume, type of mastectomy, BMI, and smoking status, we were able to note several relationships among ADM, radiation, and the occurrence of complications (Table 6).

The timing of these complications occurring did not dif-510 fer significantly between the ADM/non-ADM and PMRT/ non-PMRT groups. The only differences that were iden-AO2 tified were that radiated TEs were explanted much later than non-irradiated TEs (median 111.5 days vs 56.0 days; P value 0.02) and the timing of seromas (15.0 vs 29.0 days, 515 P value 0.001); mastectomy skin flap necrosis (15.0 vs 10.0 days, P value 0.01) was different between the ADM and non-ADM groups, although these differences are not clinically significant. There was no difference in radiated groups in terms of the timing of infection, seroma, or 520 necrosis, or differences between the ADM groups in terms of timing of explantation or seroma occurrence.

DISCUSSION

While the literature is replete with data regarding the risks and benefits of ADM in ITE reconstructions, we performed the largest retrospective cohort study specifically aimed at assessing the impact of ADM in the setting of PMRT. As expected, the overall complication rate, as well as the incidence of infection and seroma, appeared to be higher in patients undergoing ITE with ADM; however, there were

525

54

54

55

555

560

565

570

575

580

AO3

	No	n-Radiated	Irrac	liated		
	Non-ADM	ADM	Non-ADM	ADM	Irradiated vs Non-Irradiated ADM	Non-ADM Radiated vs ADM Radiated
Overall complication	Ref	3.16 (2.28-4.39)	1.95 (1.19-3.19)	4.61 (2.72-7.83)	OR = 1.52 (0.92-2.53)	OR = 2.36 (1.23-4.55)
		P < 0.0001	P = 0.008	P < 0.0001	<i>P</i> = 0.10	<i>P</i> = 0.009
Dehiscence	Ref	2.46 (1.23-4.93)	1.07 (0.31-3.66)	2.26 (0.78-6.59)		
		P = 0.01	P = 0.91	P = 0.13	0.83	<i>P</i> = 0.33
Infection	Ref	2.68 (1.54-5.06)	3.23 (1.61-7.22)	3.67 (1.82-8.84)		
		P = 0.0015	P = 0.002	<i>P</i> = 0.0017	<i>P</i> = 0.60	<i>P</i> = 0.77
Necrosis	Ref	4.99 (3.28-8.03)	2.76 (1.47-5.60)	4.01 (2.15-8.42)		
		P=<0.0001	P = 0.002	P < 0.0001	<i>P</i> = 0.48	<i>P</i> = 0.37
Seroma	Ref	3.19 (1.85-5.52)	1.59 (0.61-4.57)	4.17 (1.85-9.40)		
		P < 0.0001	P = 0.337	<i>P</i> = 0.0006	<i>P</i> = 0.57	<i>P</i> = 0.08
Explantation	Ref	1.90 (1.03-3.51)	3.19 (1.49-6.52)	1.22 (0.45-3.29)	OR = 0.64 (0.26-1.59)	OR = 0.38 (0.11-0.96)
		<i>P</i> = 0.04	P = 0.002	<i>P</i> = 0.69	<i>P</i> = 0.34	<i>P</i> = 0.04

Table 6. Multivariate Everything

Multivariate analysis examining the role of ADM and radiation on overall complications, dehiscence, infection, necrosis, seroma, and explantation. Odds ratios (OR) were not performed if statistical significance was not present. The non-ADM and non-radiated cohort was used as a point of reference for OR determinations. OR reported as OR (95% Cl).

fewer expander failures in the PMRT who utilized ADM. In fact, the use of ADM appeared to play a protective role in preventing re-operation and explantation in patients undergoing PMRT (Figure 2).

The overall complication rate of 26% in our study is slightly higher than that reported in the literature; however, this is likely due to the significantly larger sample of irradiated patients, a known risk factor for negative outcomes.^{22,23} Similar to previous reports, we found a higher complication rate in the ADM cohort than in the non-ADM cohort. In addition to age, BMI, PMRT, and smoking, risk factors previously reported in the literature, bra volume was found to be an independent risk factor for complications. While both BMI and bra volume were found to be significant variables in the univariate analysis, only bra volume was found to be significant in the multivariate analysis. Bra volume may, therefore, be a more specific indicator for breast-related outcomes, as a large BMI does not always correspond with large breast size.^{5,24}

The MSFN rate in both ADM and non-ADM patients is greater than that reported in the literature.^{10,22,23} However, it should be noted that for a given bra volume, both ADM cohorts (irradiated and non-irradiated) had intraoperative fill volumes that were 100 cc higher on average than those of the non-ADM cohorts. While ADM allows for a greater intraoperative fill volume, this advantage can place additional pressure on thin, ischemic flaps, contributing to higher rates of MSFN. Judicious clinical assessment of skin viability, and perhaps the use of SPY can offer additional assistance in determining tissue tolerance to fill volumes. PMRT was also found to be a significant risk factor for MSFN, and this may be secondary to more aggressive mastectomies being performed in the setting of advanced disease (as indicated by the need for PMRT). Other contributing risk factors to mastectomy skin necrosis—bra volume and the nipple-sparing technique—are fixed variables and should therefore be included in preoperative discussions with the patients.

Both PMRT and ADM were found to be significant risk factors for infections; however, other factors may have either over- or underreported the true incidence of infection. It should be noted that we have a "red breast clinic" at our institution where patients with suspected infections undergo immediate ultrasonographic evaluation, an infectious disease consult, and drainage of any fluid collection by interventional radiology as part of a standard protocol. Our approach to diagnosing and treating cellulitis with intravenous antibiotics likely differs from that of other practices and might lead to the overestimation of the true incidence of infection, particularly in our ADM patients. However, given that infection is the leading cause of explantation, it is possible that our aggressive approach might also increase our ability to salvage reconstructions.

Explantations occurred in 8.6% of our patient population, the majority of which was in irradiated patients treated without ADM. Radiation is a known risk factor for



Figure 2. Example of prosthetic reconstruction of the radiated breast with acellular dermal matrix. Patient is a 41-year-old
female who required bilateral skin-sparing mastectomy and tissue expander reconstruction with ADM as a pectoralis major
extension for soft tissue support. (A, B, C) Appearance of skin 6 months following 3D conformal 50 gy external beam radiation
therapy with incision and internal mammary boost. Patient received device exchange and one round of autologous fat grafting.
(D) Appearance of incisions (E) at 1 month of the right non-radiated breast (F) and slower healing of the left radiated breast.
Implant choice was a shaped gel extra projection 650 mL implant on the right breast and a 700 mL implant on the left breast.
Postoperative course was uncomplicated with no further revisions, (G, H, I) appearance at 2 years postoperatively and (J) by
3D surface imaging (taken with 3dMD LLC Camera Systems, Atlanta, GA).



Figure 2. Continued

infection, but its impact on ADM is relatively unknown.²³ The effect of radiation on patients reconstructed without ADM was profound, increasing the infection rate 3 times. Similarly, the explanation rate of patients reconstructed without ADM who underwent PMRT was 3 times higher

than that of non-ADM patients who did not undergo PMRT (20.4% vs 5.9%, respectively). In contrast, patients reconstructed with ADM experienced no difference in infection or seroma rate in response to radiation. Radiation therapy is a known risk factor for complications in non-ADM



815

820

825

830

835

840

845

850

Figure 2. Continued

reconstructions; however, studies are just beginning to report the effects of radiation on ADM reconstructions. An evidence-based review performed by Clemens and Kronowitz suggests a potentially protective effect of ADM in the setting of PMRT, with decreased cellular infiltrates and decreased capsular contracture rates.^{6,15,19,21,25,27-32} Seth et al published a case-control series in 2012 with 592 ITE reconstructions and found no significant increase in complication rate following PMRT in patients reconstructed with ADM.³³ This is in contrast to the observed threefold increase in complication rate experienced by the non-ADM group following PMRT (P = 0.003). Unfortunately, a contrast analysis was not performed between the irradiated ADM and non-ADM groups to evaluate how ADM reconstructions behave with respect to traditional techniques in the setting of radiation. In addition, the ADM and non-ADM cohorts had varying demographic profiles that may have confounded their outcomes. While this study lends support to previously reported data, questions still remain regarding the true impact of PMRT on ADM in breast reconstruction, how this compares to traditional techniques, and how this influences patient selection criteria.

Our data support the conclusions by other authors that ADM plays a protective role in irradiated patients by limiting explantation.^{23,26} Among these, our study is the largest study to date using cohort comparisons to illustrate the impact of ADM on patients undergoing PMRT.³⁴⁻³⁸ We theorize that ADM has a higher infection and seroma rate prior to its incorporation. Use of antibiotics, aggressive treatment



of "red" breasts, and prolonged use of drains are imperative for promoting incorporation. Once incorporated, the ADM may serve as an additional vascularized layer over the TE, protecting it from bacterial contamination. Patients without ADM do not experience an "incorporation period," and therefore have initially lower infection and seroma rates. However, in the setting of radiation, non-ADM patients do not have the advantage of an additional vascularized ADM layer and are thus more susceptible to bacterial contamination, leading to higher explantation rates.

In 2012, Nahabedian published the following indications for ADM: women with A to D cup size breasts, regardless of age, who are not morbidly obese, have not had prior radiation, and are not active smokers.¹⁴ Similarly, Ganske et al described changes in their patient selection criteria and postoperative management that played a critical role in the success of their implant-based reconstructions with ADM.⁴ Intraoperative tailoring of the ADM to eliminate folding and dead space, aggressive mastectomy skin flap excision and debridement, and more conservative drain removal thresholds successfully decreased their complication rates to those equivalent to their non-ADM reconstructions.¹²

We recognize that our study has limitations. This is a 905 retrospective review and is subject to type II error. Capsular contracture rates were not included in our study or data collection because it was reported in a subjective and inconsistent manner. Our incidence of PMRT may be low compared to other studies; however, this may in part be 910 explained by the relatively high incidence of prophylactic

880

885

890

895

900

915

920

925

930

935

940

945

950

955

960

Disclosures

CONCLUSIONS

Dr Patrick Garvey was a consultant for LifeCell Corporation. Dr Jesse Selber was a consultant for TEI Biosciences and Mentor Worldwide. The other authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

mastectomies (31.4%). In addition, the non-ADM group

comprised both partial and total muscle coverage. One

could argue that partial muscle coverage places patients at

greater risk for bacterial contamination and explantation

as compared to total muscle coverage. However, only a

few patients had partial muscle coverage and are believed

to not have significantly impacted this group as a whole. In

addition, there was some variability in the timing of drain

removal and duration of antibiotics in our group practice

that could potentially impact seroma and infection rates,

although with 1367 reconstructions, we believe these

small differences were likely inconsequential. Patients who

completed PMRT at outside institutions were included in

this study, allowing some variability in radiation dosing

treatments. Again, the majority of patients received their

treatment at our institution, making any patients treated

The key to success in breast reconstruction is patient selec-

tion and patient education. With the introduction of ADM,

we now have another tool to consider and evaluate its util-

ity in each patient. The data presented in the current study

can be used to further guide patient selection, and educate

patients about their risk profile for complications when

using ADM. The decision to use ADM for expander-based

breast reconstruction should be performed with caution,

given higher overall rates of complications, including

infections and seromas. There may, however, be a role for

ADM in cases requiring PMRT, as the overall incidence of

implant failure is lower than non-ADM cases. The choice

to use ADM should be individualized, with particular

attention paid to the risk factors presented in our study.

outside the institution negligible in such a large cohort.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

- 1. American Society of Plastic Surgeons. 2016 Plastic Surgery Statistics Report. American Society of Plastic Surgeons website, 2016. https://www.plasticsurgery.org/documents/ News/Statistics/2016/2016-plastic-surgery-statisticsreport.pdf. Accessed September 1, 2017.
- 2. Antony AK, McCarthy CM, Cordeiro PG, et al. Acellular human dermis implantation in 153 immediate two-stage tissue expander breast reconstructions: determining the

incidence and significant predictors of complications. 965 *Plast Reconstr Surg.* 2010;125(6):1606-1614.

- 3. Basu CB, Leong M, Hicks MJ. Acellular cadaveric dermis decreases the inflammatory response in capsule formation in reconstructive breast surgery. Plast Reconstr Surg. 2010;126(6):1842-1847.
- 4. Berry T, Brooks S, Sydow N, et al. Complication rates of radiation on tissue expander and autologous tissue breast reconstruction. Ann Surg Oncol. 2010;17:202-210
- 5. Brooks S, Djohan R, Tendulkar R, Nutter B, Lyons J, Dietz J. Risk factors for complications of radiation ther-975 apy on tissue expander breast reconstructions. Breast J. 2012:18(1):28-34.
- 6. Chun YS, Verma K, Rosen H, et al. Implant-based breast reconstruction using acellular dermal matrix and the risk of postoperative complications. Plast Reconstr Surg. 2010;125(2):429-436.
- 7. Clemens MW, Kronowitz SJ. Acellular dermal matrix in irradiated tissue expander/implant-based breast reconstruction: evidence-based review. Plast Reconstr Surg. 2012;130(5):27S-34S.
- 8. Colwell AS, Tessler O, Lin AM, et al. Breast reconstruction 985 following nipple-sparing mastectomy: predictors of complications, reconstruction outcomes, and 5-year trends. Plast Reconstr Surg. 2014;133(3):496-506.
- 9. Cordeiro PG, Snell L, Heerdt A, McCarthy C. Immediate tissue expander/implant breast reconstruction after salvage mastectomy for cancer recurrence following lumpectomy/ 990 irradiation. Plast Resconstr Surg. 2010;129(2):342-350.
- 10. Cowen D, Gross E, Rouannet P, et al. Immediate post-mastectomy breast reconstruction followed by radiotherapy: risk factors for complications. Breast Cancer Res Treat. 2010;121(3):627-634.
- 11. Forsberg CG, Kelly DA, Wood BC, et al. Aesthetic outcomes of acellular dermal matrix in tissue expander/ implant-based breast reconstruction. Ann Plast Surg. 2014;72(6):S116-S120.
- 12. Ganske I, Verma K, Rosen H, Eriksson E, Chun YS. Minimizing complications with the use of acellular dermal matrix for immediate implant-based breast reconstruction. Ann Plast Surg. 2013;71(5):464-470.
- 13. Glasberg SB, Light D. AlloDerm and Strattice in breast reconstruction: a comparison and techniques for optimizing outcomes. *Plast Reconstr Surg.* 2012;129(6):1223-1233.
- 14. Gurunluoglu R, Gurunluoglu A, Williams SA, Tebockhorst S. Current trends in breast reconstruction: survey of American Society of Plastic Surgeons 2010. Ann Plast Surg. 2013;70(1):103-110.
- 15. Hanna KR, DeGeorge BR Jr, Mericli AF, Lin KY, Drake DB. Comparison study of two types of expander-based breast 1010 reconstruction. Ann Plast Surg. 2013;70(1):10-15.
- 16. Ho A, Cordeiro P, Disa J, et al. Long-term outcomes in breast cancer patients undergoing immediate 2-stage expander/implant reconstruction and postmastectomy radiation. Cancer. 2012;118(9):2552-2559.
- 17. Ho G, Nguyen TJ, Shahabi A, Hwang BH, Chan LS, Wong AK. A systematic review and meta-analysis of complications associated with acellular dermal matrix-assisted breast reconstruction. Ann Plast Surg. 2012;68(4):346-356.

995

970

AO4

980

1000

1005

- 18. Hubenak JR, Zhang Q, Branch CD, Kronowitz SJ. Mechanisms of injury to normal tissue after radiotherapy: a review. *Plast Reconstr Surg.* 2014;133(1):49e-56e.
 - Israeli Ro, Feingold R. Acellular dermal matrix in breast reconstruction in the setting of radiotherapy. *Aesthet Surg J.* 2011;31(7S):51S-64S.
- 1025 20. Jhaveri JD, Rush SC, Kostroff K, et al. Clinical outcomes of postmastectomy radiation therapy after immediate breast reconstruction. *Int J Radiat Oncol Biol Phys.* 2008;72(3):859-865.
 - Kim JY, Davila AA, Persing S, et al. A meta-analysis of human acellular dermis and submuscular tissue expander breast reconstruction. *Plast Reconstr Surg.* 2012;129(1):28-41.
 - 22. Komorowska-Timek E, Oberg KC, Timek TA, Gridley DS, Miles DA. The effect of AlloDerm envelopes on periprosthetic capsule formation with and without radiation. *Plast Reconstr Surg.* 2009;123(3):807-816.
- 1035 23. Kronowitz SJ. Current status of implant-based breast reconstruction in patients receiving postmastectomy radiation therapy. *Plast Reconstr Surg.* 2012;130(4):513e-523e.
 - 24. Kronowitz SJ, Hunt KK, Kuerer HM, et al. Delayedimmediate breast reconstruction. *Plast Reconstr Surg.* 2004;113(6):1617-1628.
 - 25. McCarthy CM, Lee CN, Halvorson EG, et al. The use of acellular dermal matrices in two-stage expander/implant reconstruction: a multicenter, blinded, randomized controlled trial. *Plast Reconstr Surg.* 2012;130(5):57S-66S.
 - Lam TC, Hsieh F, Boyages J. The effects of postmastectomy adjuvant radiotherapy on immediate two-stage prosthetic breast reconstruction: a systematic review. *Plast Reconstr Surg.* 2013;132(3):511-518.
 - 27. Moyer HR, Pinell-White X, Losken A. The effect of radiation on acellular dermal matrix and capsule formation in breast reconstruction: clinical outcomes and histologic analysis. *Plast Reconstr Surg.* 2014;133(2):214-221.
 - Nahabedian MY. Acellular dermal matrices in primary breast reconstruction: principles, concepts, and indications. *Plast Reconstr Surg.* 2012;130(5S-2):44S-53S.

- 29. Nahabedian MY. AlloDerm performance in the setting of prosthetic breast surgery, infection, and irradiation. *Plast Reconstr Surg.* 2009;124(6):1743-1753.
- Parks JW, Hammond SE, Walsh WA, Adams RL, Chandler RG, Luce EA. Human acellular dermis versus no acellular dermis in tissue expansion breast reconstruction. *Plast Reconstr Surg.* 2012;130(4):739-746.
- 31. Rawlani V, Buck DW 2nd, Johnson SA, Heyer KS, Kim JY. Tissue expander breast reconstruction using prehydrated human acellular dermis. *Ann Plast Surg.* 2011;66(6):593-597.
- 32. Sbitany H, Sandeen SN, Amalfi AN, Davenport MS, Langstein HN. Acellular dermis-assisted prosthetic breast reconstruction versus complete submuscular coverage: a head-to-head comparison of outcomes. *Plast Reconstr Surg.* 2009;124(6):1735-1740.
- 33. Seth AK, Hirsch EM, Fine NA, Kim JY. Utility of acellular dermis-assisted breast reconstruction in the setting of radiation: a comparative analysis. *Plast Reconstr Surg.* 2012;130(4):750-758.
- Spear SL, Parikh PM, Reisin E, Menon NG. Acellular dermis-assisted breast reconstruction. *Aesthetic Plast Surg.* 2008;32(3):418-425.
- 35. Spear SL, Seruya M, Rao SS, et al. Two-stage prosthetic breast reconstruction using AlloDerm including outcomes of different timings of radiotherapy. *Plast Reconstr Surg.* 2012;130(1):1-9.
- 36. Vardanian AJ, Clayton JL, Roostaeian J, et al. Comparison of implant-based immediate breast reconstruction with and without acellular dermal matrix. *Plast Reconstr Surg.* 2011;128(5):403e-410e.
- 37. Weichman KE, Wilson SC, Weinstein AL, et al. The use of acellular dermal matrix in immediate two-stage tissue expander breast reconstruction. *Plast Reconstr Surg.* 2012;129(5):1049-1058.
- Zienowicz RJ, Karacaoglu E. Implant-based breast reconstruction with allograft. *Plast Reconstr Surg.* 2007;120(2):373-381.

1060

1065

1030

1040

1045

1050