From Salvage to Prevention: A Single-Surgeon Experience with Acellular Dermal Matrix and Infection in Prepectoral Breast Reconstruction

Jeremy M. Powers, M.D.
Katherine D. Reuter Muñoz, M.D.
Jamie Parkerson, M.S.
Lauren C. Nigro, M.D.
Nadia P. Blanchet, M.D.

Royal Oak, Mich.; and Richmond and Norfolk, Va.

Background: Increasing amounts of acellular dermal matrix are being used with the adoption of prepectoral breast reconstruction. Postoperative infection remains a challenge in breast reconstruction, and the contribution of acellular dermal matrix type, processing, and sterility assurance level to risk of complications in prepectoral reconstruction is not well studied.

Methods: The authors performed a retrospective review of patients who underwent immediate prepectoral breast reconstruction from February of 2017 to July of 2020. Because of an increase in the rate of infection, the drain protocol was changed and acellular dermal matrix type was switched from AlloDerm (sterility assurance level, 10^{-3}) to DermACELL (sterility assurance level, 10^{-6}) in January of 2019. Demographic and surgical variables were collected, in addition to details regarding development and management of infection.

Results: Despite higher rates of direct-to-implant reconstruction and bilateral procedures and increased implant volumes, the rate of infection was significantly lower in patients who received DermACELL instead of AlloDerm [two of 38 (5.3 percent) versus 11 of 41 (26.8 percent); $p = 0.014$]. Drain duration was slightly longer in the DermACELL group, consistent with the change in drain protocol. Baseline demographic and clinical characteristics remained similar between the two groups.

Conclusions: With increased reliance on large amounts of acellular dermal matrix for prepectoral breast reconstruction, it directly follows that the properties of acellular dermal matrix with respect to incorporation, sterility, and implant support are that much more important to consider. There have been few studies comparing different types of acellular dermal matrix in prepectoral breast reconstruction, and further research is required to determine the contribution of acellular dermal matrix type and processing techniques to development of postoperative infection. (*Plast. Reconstr. Surg.* 148: 1201, 2021.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Over the past 15 years, the use of acellular dermal matrix in breast reconstruction has evolved, with changing trends in implant placement in relation to the pectoralis muscle. From an inferolateral sling in partial subpectoral placement, to full anterior coverage or total wrap with prepectoral implant placement, increasing amounts of acellular dermal matrix are being used in breast reconstruction.[1] Unfortunately, surgical-site infections remain a challenge despite extensive preventative measures adopted by most surgeons.[2,3] Even with optimal proactive management, infection of the implant pocket can still occur and may require implant removal, resulting in reconstructive failure or need for autologous reconstruction. Patient comorbidities that are known to contribute to infection risk include diabetes, smoking, obesity, neoadjuvant chemotherapy, and previous irradiation.[4–6] However,

From the Division of Plastic and Reconstructive Surgery, Department of Surgery, William Beaumont Hospital; Virginia Commonwealth University School of Medicine; Eastern Virginia Medical School; Division of Plastic and Reconstructive Surgery, Department of Surgery, Virginia Commonwealth University Health; and private practice.
Received for publication September 13, 2020; accepted April 13, 2021.

DOI: 10.1097/PRS.0000000000008519

Disclosure: *None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.*

the potential contribution of surgical technique, including implant location and use of acellular dermal matrix, is not as well studied, with no studies comparing experience with different types of acellular dermal matrix in prepectoral breast reconstruction.

The senior author transitioned from partial subpectoral to prepectoral breast reconstruction in 2017, recognizing the functional benefits of decreased pain and rates of capsular contracture, prevention of animation deformity, and potential aesthetic advantages of improved lower pole shape and natural ptosis.[7–9] Early experience with the technique proved these advantages; however, an increase in overall infection rate was noted. Quality improvement was undertaken at the hospital to investigate possible sources of an increased infection rate, with no cause identified. Although operative technique remained the same, eventually the drain removal protocol was changed followed 3 months later by a switch of the acellular dermal matrix type to a product with a 3-log further improvement in sterility assurance level. The primary objective of this study was to compare rates of infection after immediate prepectoral breast reconstruction with the use of two different acellular dermal matrices. Our secondary objective was to report our experience with management of these infectious complications with a novel diagnostic and therapeutic technique.

PATIENTS AND METHODS

Study Design

We undertook a retrospective review of patients who underwent immediate prepectoral breast reconstruction performed by a single plastic surgeon (N.P.B.) from February of 2017 to July of 2020. Data collected for each patient during chart review included type of reconstruction (direct-to-implant versus tissue expander); laterality of procedure; patient height, weight, and body mass index; diabetes; type of acellular dermal matrix; radiation therapy; chemotherapy; nipple-sparing versus skin-sparing mastectomy; type of acellular dermal matrix used; implant volume or initial tissue expander fill; time to drain removal; and development and management of infection.

Surgical-site infections were diagnosed when patients presented with breast erythema, swelling, drainage, and/or fevers/chills. Minor infections were those that were managed with oral antibiotics, whereas major infections were those that required intravenous antibiotics, operating room take-back, or explantation. This study was performed in accordance with the ethical principles outlined in the Declaration of Helsinki.

Surgical Technique

Preoperatively, patients underwent nasal swab cultures for methicillin-resistant *Staphylococcus aureus* screening and were decolonized if positive. Antibacterial soap was recommended for bathing both preoperatively and postoperatively for all patients.

The senior author consistently worked with the same four oncologic surgeons throughout the study period. After the completion of mastectomy, the skin was reprepared with 10% povidone-iodine and redraped with sterile surgical drapes over the previous drapes. The mastectomy pocket was irrigated copiously throughout the case with triple-antibiotic solution containing 1 liter of normal saline, 1 g of vancomycin, 80 mg of gentamicin, and 50,000 U of bacitracin (as of February of 2020, injectable bacitracin was no longer available on the market), mixed with 100 ml of 10% povidone-iodine. Indocyanine green angiography (SPY Elite; Stryker, Kalamazoo, Mich.) was used with an appropriate implant sizer in place and skin with poor perfusion was débrided. In cases of globally poor perfusion on SPY, reconstruction was delayed. Before permanent implant placement, the wounds were reprepared with povidone-iodine. A no-touch technique was used, with minimal handling of the permanent implant and use of an implant delivery device when appropriate.[10,11]

The senior author used AlloDerm SELECT (Allergan/AbbVie, Dublin, Ireland, and Chicago, Ill.) for anterior coverage of the tissue expander or implant from July of 2017 through December of 2018. One sheet of 16 × 20-cm ready-to-use product (or two smaller 8 × 20-cm sheets sewn together, depending on availability) was manually perforated on the back table. DermACELL (LifeNet Health, Virginia Beach, Va.) was used from January of 2019 through July of 2020 in a similar fashion, with the same product sizes. After rinsing and soaking in the antibiotic/povidone-iodine solution, 2-0 Vicryl suture (Ethicon, Inc., Somerville, N.J.) was used to anchor the acellular dermal matrix construct to the medial, superior, and lateral aspects of the mastectomy pocket. The implant was inserted through the remaining opening inferiorly, with excess acellular dermal matrix draped underneath the implant laterally and inferiorly to create a greater zone of adherence to mitigate inferior descent. Further 2-0

Vicryl sutures were used to anchor the folded edge of the acellular dermal matrix to the inferior chest wall to reestablish the inframammary fold. The same insetting technique was used with both acellular dermal matrix types. Before closure, a single, 15-French, round-channel drain was placed along the lateral, inferior, and medial aspects of the implant/acellular dermal matrix construct by means of a tendon-passer to obtain a long subcutaneous tunnel between the implant/acellular dermal matrix and the drain-exit site at the skin. Postoperatively, patients were prescribed cefadroxil (Duricef; Bristol-Meyers Squibb, New York, N.Y.) or doxycycline (for penicillin-allergic patients) as antibiotic prophylaxis until drain removal.[12] An occlusive dressing was maintained around the drain site.

With the change to the prepectoral technique, the senior author noticed an increase in postoperative infections to nearly one in four patients, compared to one in 26 patients when AlloDerm had been used with a subpectoral technique in previously published data.[13] This led to a quality improvement initiative at the hospital, in which the operating rooms were terminally cleaned and scrub/circulating staff were screened for methicillin-resistant *Staphylococcus aureus* colonization. Scrubbing, preparing, and draping were observed and evaluated to ensure that proper techniques and protocols were being followed. No deficiencies in these processes were identified. Three months before the change in acellular dermal matrix, one other change took place with respect to drain management in October of 2018. Before that time, drains were left in place until draining less than 25 ml/day for at least one 24-hour period. After that time, drain removal took place only after observing drainage less than 25 ml/day for 2 consecutive days.[14]

In afebrile patients without obvious fluid collections, if infection was suspected, antibiotics were administered with close clinical follow-up. In the presence of marked erythema, swelling, fluid collection, or fever, patients were admitted and treated with intravenous antibiotics, and samples were obtained by ultrasound guidance from the suspected infection site and cultured. When available, the fluid was submitted for quantitative polymerase chain reaction testing to identify bacterial organisms and antibiotic susceptibility within 48 hours, which were then used to inform antibiotic selection. If patients failed to improve on intravenous antibiotic therapy, those with the need for expedited upcoming chemotherapy or radiation therapy underwent primary explantation. If implant salvage was attempted, surgical technique involved liberal antibiotic irrigation of the breast pocket, removal and replacement of any unincorporated acellular dermal matrix, replacement of implant or expander, and placement of absorbable antibiotic beads (STIMULAN; Biocomposites US, Wilmington, N.C.) tailored to the quantitative polymerase chain reaction results with conservative excision of the previous mastectomy incision.[15,16]

Statistical Analysis

Patients were divided into two groups based on the type of acellular dermal matrix used to compare patient characteristics and rates of infection. Descriptive statistics were calculated, and comparisons were undertaken using the two-tailed t test to compare means/continuous variables and chi-square analysis or Fisher's exact test for proportions/categorical variables. A value of $p < 0.05$ was considered significant.

RESULTS

Patient demographic and surgical detail comparison by group is shown (Table 1). Group demographics were well matched, and rates of nipple-sparing mastectomy were comparable between the groups. There was a higher rate of bilateral and direct-to-implant reconstructions in the DermACELL group. Average initial fill volume was greater in the DermACELL group (486 ± 107 ml versus 375 ± 102 ml; $p < 0.001$). In addition, reflective of the change in drain protocol, the average drain duration was longer in the DermACELL group (9.6 ± 2.7 days versus 7.7 ± 3.1 days; $p = 0.006$). Consistent with the change

Table 1. Patient and Surgical Details

	AlloDerm (%)	DermACELL (%)	p
No. of patients	41	38	—
Average age, yr	49	45	0.121
Average BMI, kg/m^2	25.4	25.6	0.812
Diabetes	2 (4.9)	1 (2.6)	0.602
Chemotherapy	10 (24.4)	8 (21.1)	0.793
Radiation therapy	12 (29.3)	12 (31.6)	0.793
Nipple-sparing mastectomy	35 (85.4)	33 (86.8)	0.850
Bilateral	24 (58.5)	31 (81.6)	0.030*
Unilateral	17 (41.5)	7 (18.4)	—
Direct-to-implant	25 (61.0)	35 (92.1)	0.001*
Tissue expander	16 (39.0)	3 (7.9)	—
Average initial fill volume, ml	375	486	<0.001*
Average drain duration, days	7.7	9.6	0.006*
Presence of infection	11 (26.8)	2 (5.3)	0.014*
Average follow-up, mo	29.4	10.1	<0.001*

BMI, body mass index.
*Statistically significant.

in acellular dermal matrix in January of 2019 and the use of the AlloDerm group as the historical comparison, the follow up time in the AlloDerm group was significantly longer (29.4 ± 6.1 months versus 10.1 ± 5.4 months in the DermACELL group; $p < 0.001$).

The postoperative infection rate was significantly higher in the AlloDerm group compared with the DermACELL group [11 of 41 (26.8 percent) versus two of 38 (5.3 percent); $p = 0.014$] (Table 2). The first patient in the DermACELL group who was treated with antibiotics presented with right breast erythema on postoperative day 8 following nipple-sparing mastectomy and bilateral direct-to-implant reconstruction. She was placed on doxycycline without improvement in the erythema but remained afebrile with a normal white blood cell count. Because of persistence of the erythema, she was admitted to the hospital and placed on intravenous antibiotics. There were no fluid collections on ultrasound. After 2 weeks of antibiotic treatment, the erythema resolved and she did not require operative management. Of note, she had a history of lumpectomy and radiation therapy to the right breast 14 years previously and her direct-to-implant volume was 700 cc bilaterally, the largest in the series.

The second patient in the DermaCELL group who was treated with antibiotics initially underwent direct-to-implant reconstruction, with an implant volume of 500 cc. The drain was removed uneventfully on postoperative day 15. Two months after surgery, she presented to the clinic with a right-hand burn acquired while cooking and complicated by cellulitis. The erythema tracked up her arm and she also had a warm and erythematous right breast. She remained afebrile with a normal white blood cell count. She underwent wound care for the hand and was admitted to the hospital for intravenous antibiotic treatment overnight, then was discharged on Augmentin (GlaxoSmithKline, Research Triangle Park, N.C.) and doxycycline. She has since been seen in the clinic with resolution of upper extremity and breast erythema.

Table 2. Infection Details

	AlloDerm (%)	DermACELL (%)
No. of patients	41	38
No. of infections	11 (26.8)	2 (5.3)
Minor infections	0	1
Major infections	11	1
Salvage with oral antibiotics	0	1/2 (50)
Salvage with intravenous antibiotics	2/11 (18.2)	1/2 (50)
Return to operating room	9/11 (81.8)	0
Explanted	3/11 (27.3)	0
Salvage with implant replacement/antibiotic beads	6/11 (54.5)	0

Among the 11 AlloDerm patients who developed infection, all were major infections treated with either intravenous antibiotics or return to the operating room. Two were able to be salvaged with intravenous antibiotics, whereas nine of 11 patients (81.8 percent) required operative intervention for either explantation to expedite chemotherapy/radiotherapy (three of nine) or attempt at salvage with implant replacement and quantitative polymerase chain reaction–tailored antibiotic beads. This protocol was successful in five of six patients, as one patient developed early skin breakdown and implant exposure (however, a second salvage attempt was successful). Of the other five patients, all healed uneventfully from their initial salvage procedure. However, one of these patients went on to receive radiation therapy that resulted in wound breakdown and implant removal, and the patient ultimately elected for autologous reconstruction.

DISCUSSION

With increased acceptance of acellular dermal matrix use, the prepectoral technique, which uses acellular dermal matrix for either full circumferential or anterior-only coverage of the implant, has emerged as a popular option because it has been suggested to improve aesthetic outcomes and to decrease postoperative pain, animation deformity, and capsular contracture.[17–22] Regarding animation, the senior author surveyed her subpectoral patients and found that over half would have been interested in a procedure not complicated by animation, provided there was minimal additional risk.[23] As such, her practice evolved to prepectoral breast reconstruction, as early reports in the literature were consistent with a low complication profile. However, when an alarming increase in infection was noted with the new technique, quality improvement was initiated, and changes were made in acellular dermal matrix type and drain management. The primary goals of this study were to quantify and compare rates of postoperative infection following immediate prepectoral breast reconstruction before and after a change in acellular dermal matrix and drain protocol, and report our experience with the management of postoperative infection in these patients.

The postoperative infection rate was found to be significantly decreased in patients who received DermACELL and a more stringent drain protocol compared with patients who received AlloDerm.

Despite a healthy, nonsmoking population with normal body mass index and minimal comorbidities in both groups, there was a significantly higher complication rate with use of AlloDerm. Furthermore, even with greater proportion of direct-to-implant reconstruction, bilateral procedures, and higher average initial implant volume in the DermACELL group, a lower rate and severity of infection was achieved.

Several factors could have contributed to lowering the infection rate. Experience was gained with prepectoral reconstruction over the course of the study, and a "learning curve" effect could have occurred, although in fact, surgical technique did not change. Alternatively, the more stringent drain protocol may have contributed to decreased seroma and better incorporation of acellular dermal matrix, potentially leading to a lower rate of infection. The change in drain protocol occurred 3 months before the change in acellular dermal matrix, yet two infections occurred in December of 2018—the same number of infections in the entire DermACELL group over nearly 2 years. Furthermore, the severity of infection was less in the DermACELL group, as the infections in this group did not require operative management. Certainly, the association between fluid collection/seroma and development of infection is a well-known principle of surgery. However, a direct linkage between drain output threshold for removal and drain duration and development of infection has not been established in the literature. Although there are no studies specifically correlating drain management and infection outcomes in prepectoral reconstruction, several large case series report differing removal protocols, from drain removal strictly at 7 days to drain removal after 2 consecutive days of less than 20 to 25 ml/day output,[14,21] whereas Antony and Robinson[24] and Sbitany[25] recommend in separate publications that drains remain in place for 2 to 3 weeks. Further study is required to determine the contribution of drain volume and duration to infection in breast reconstruction, particularly with the prepectoral technique. In conjunction with the change in drain protocol, the switch of acellular dermal matrix from AlloDerm (sterility assurance level, 10^{-3}) to DermACELL (sterility assurance level, 10^{-6}) may have played a role in the reduction in the rate of infection.

The use of acellular dermal matrix in breast reconstruction has been associated with higher rates of seroma and infection in some studies[26–34]; however, others have found equivalent complication rates with and without the use of acellular dermal matrix.[35–42] Industry funding of research involving acellular dermal matrix in breast reconstruction may compromise reliability of results, and as in all of medicine, negative findings may be underpublished, biasing the available literature.[43] Comparisons of different types of acellular dermal matrix in subpectoral reconstruction have demonstrated higher rates of seroma (12.7 percent) and red breast syndrome (26 percent) with use of AlloDerm.[38,44] Prior studies have specifically compared AlloDerm and DermACELL in the subpectoral reconstruction context and have not found differences in the rate of infection.[44,45] However, with the greatly increased amounts of acellular dermal matrix used in prepectoral reconstruction, it seems plausible that complication rates may increase proportionately.

Prior research supports the concept of greater risk of complications with greater surface area of acellular dermal matrix. Weichman and colleagues in 2012 found that AlloDerm surface area was larger in patients who experienced complications following partial subpectoral reconstruction.[29] Corroborating these findings, Selber et al. in 2015 found that the risk of seroma quadrupled as the surface area of acellular dermal matrix used in the reconstruction doubled.[30] Further supporting this relationship is the work of Hadad et al. in 2015, who describe the adoption of an acellular dermal matrix minimal use technique with a goal of reducing complications.[46] When they retrospectively compared their patients, they found a lower risk of complications, including infection, seroma, and explantation, in the minimal acellular dermal matrix group. Considered together, these studies strongly implicate acellular dermal matrix in complications after breast reconstruction, analogous to a "dose-response" relationship with respect to acellular dermal matrix surface area. These findings reflect the senior author's experience with transition to prepectoral reconstruction, increase in surface area of acellular dermal matrix used, and a concomitant increase in infectious complications.

With increased reliance on large amounts of acellular dermal matrix for the success of prepectoral techniques, it directly follows that the properties of the acellular dermal matrix with respect to incorporation, sterility, and implant support are that much more important to consider. In our study, two terminally sterile acellular dermal matrices were used. AlloDerm Ready-to-Use, with a sterility assurance level of 10^{-3}, represents a one in 1000 chance of an organism surviving in the product following sterilization,

whereas DermACELL and several other available acellular dermal matrices have a sterility assurance level of 10^{-6}, representing a one in 1 million chance. Although both products meet the U.S. Food and Drug Administration standard of sterility for allograft and biological materials, only acellular dermal matrices that have a sterility assurance level of 10^{-6} meet the standard used for implanted medical devices.[47,48] Histologically, acellular dermal matrix with a sterility assurance level of 10^{-6} has been observed to produce less inflammation, less granulation tissue, and less fibrosis than native tissue following breast reconstruction, although these data are limited by small sample size.[49] Although the contribution of acellular dermal matrix–processing techniques and sterility assurance level to in vivo performance of acellular dermal matrix has had some exploration in the context of subpectoral techniques,[50–53] it has not been well studied in prepectoral reconstruction with its associated larger amounts of acellular dermal matrix and deserves more attention. Whether or not a 3-log further reduction in sterility assurance level or another property of the acellular dermal matrix specifically led to decreased rates of postoperative infection/complication is not possible to correlate based on our study design; however, these results raise questions for future investigation.

Strengths of this study include consistent surgical technique and relatively healthy patient cohorts. Because of the high infection rate with AlloDerm, the senior author gained significant experience in managing infections, and absorbable antibiotic beads were a valuable resource and have been described.[15,16,54] Notably, patients whose reconstructions were salvaged with antibiotic beads did not seem to develop capsular contracture. Although there have been reports of the utility of antibiotic beads, the use of quantitative polymerase chain reaction to rapidly guide antibiotic selection in the clinical management of breast periprosthetic fluid collections has not been previously described in the literature. Quantitative polymerase chain reaction uses "next-generation" genetic sequencing technology to sequence the genome of any bacteria that may be present in the sample.[55] Individual genes lending antibiotic resistance are also identified. The advantage of quantitative polymerase chain reaction is timely identification (<2-day turnaround) of both organism and susceptibility, allowing for appropriate antibiotic selection for the absorbable beads. The downside is that the test has high sensitivity and may identify organisms that are nonpathologic (however, it could be argued that any bacteria isolated from a breast pocket represents a pathogen). Multiple recent studies are applying this technology to the study of capsular contracture,[56,57] but the clinical use of quantitative polymerase chain reaction in breast reconstruction represents a novel application of this diagnostic modality that deserves further study.

Limitations of the study include its retrospective nature, use of a historical comparator group, and relatively small sample size. The drain protocol and acellular dermal matrix switch occurred 3 months apart, and the study design is unable to determine the relative contribution of each of these measures to the reduction in rates of infection. In addition, the high rate of infection experienced with AlloDerm in our study deviates markedly from the low rates of infection in prior case series of prepectoral reconstruction,[14,21] and comparisons of subpectoral and prepectoral techniques have demonstrated similar rates of infection.[19,58–61] Patient characteristics and surgical technique were generally similar to these prior reports and it is unknown why such a high rate of infection was experienced with AlloDerm in our patients. Furthermore, the dose-response relationship of acellular dermal matrix and complications demonstrated by prior studies[29,30,46] are not reflected in the recent published comparisons of subpectoral and prepectoral reconstruction,[19,58–61] and these discrepancies in the literature deserve further exploration. Nonetheless, we believe the questions raised by this study's findings deserve well-designed follow-up investigations, which may either refute or corroborate this report with more solid evidence.

At the time of submission, this report was one of the first studies to compare infection outcomes associated with varying acellular dermal matrix type in prepectoral breast reconstruction, although results from a randomized trial comparing acellular dermal matrices in prepectoral reconstruction will be forthcoming.[62] It is our view that acellular dermal matrix is an additional variable in implant-based reconstruction and that it is only reasonable to think that it may contribute to increased postoperative complications; furthermore, the significantly larger amounts that are used in prepectoral reconstruction place this technique in a different category of study. It is important to ensure that prepectoral reconstruction and increased use of acellular dermal matrix do not result in increased rates of complications. In an otherwise higher risk population in terms of direct-to-implant, bilateral procedures, and implant fill volumes, a reduction

in infection risk was observed with change of acellular dermal matrix and drain protocol. As such, careful product selection and postoperative drain management are critical to successful patient outcomes. Further research is required to determine the relative contribution of acellular dermal matrix processing techniques and level of sterility to rate of incorporation and development of postoperative infection. Larger prospective clinical trials of different acellular dermal matrices are needed to determine the true role acellular dermal matrix type and processing play in postoperative complications and outcomes following breast reconstruction with a prepectoral technique.

Nadia P. Blanchet, M.D.
9210 Forest Hill Avenue, Suite B1
Richmond, Va. 23235
nadia@nadiablanchet.com

ACKNOWLEDGMENTS

The authors would like to acknowledge Lisa Simmons and Fay Townes for their assistance with data collection.

REFERENCES

1. Rebowe RE, Allred LJ, Nahabedian MY. The evolution from subcutaneous to prepectoral prosthetic breast reconstruction. *Plast Reconstr Surg Glob Open* 2018;6:e1797.
2. Ooi ASh, Song DH. Reducing infection risk in implant-based breast-reconstruction surgery: Challenges and solutions. *Breast Cancer (Dove Med Press)* 2016;8:161–172.
3. Khansa I, Hendrick RG Jr, Shore A, Meyerson J, Yang M, Boehmler JH IV. Breast reconstruction with tissue expanders: Implementation of a standardized best-practices protocol to reduce infection rates. *Plast Reconstr Surg.* 2014;134:11–18.
4. Kato H, Nakagami G, Iwahira Y, et al. Risk factors and risk scoring tool for infection during tissue expansion in tissue expander and implant breast reconstruction. *Breast J.* 2013;19:618–626.
5. Long C, Sue GR, Chattopadhyay A, Huis In't Veld E, Lee GK. Critical evaluation of risk factors of infection following 2-stage implant-based breast reconstruction. *Plast Reconstr Surg Glob Open* 2017;5:e1386.
6. Piper ML, Roussel LO, Koltz PF, et al. Characterizing infections in prosthetic breast reconstruction: A validity assessment of national health databases. *J Plast Reconstr Aesthet Surg.* 2017;70:1345–1353.
7. Cattelani L, Polotto S, Arcuri MF, Pedrazzi G, Linguadoca C, Bonati E. One-step prepectoral breast reconstruction with dermal matrix-covered implant compared to submuscular implantation: Functional and cost evaluation. *Clin Breast Cancer* 2018;18:e703–e711.
8. Manrique OJ, Banuelos J, Abu-Ghname A, et al. Surgical outcomes of prepectoral versus subpectoral implant-based breast reconstruction in young women. *Plast Reconstr Surg Glob Open* 2019;7:e2119.
9. Kim JYS, Qiu CS, Chiu WK, et al. A quantitative analysis of animation deformity in prosthetic breast reconstruction. *Plast Reconstr Surg.* 2019;144:291–301.
10. Wilson HB. Early results show reduced infection rate using no-touch technique for expander/ADM breast reconstruction. *Plast Reconstr Surg Glob Open* 2015;3:e317.
11. Wilson HB. "No-touch" enhancement significantly reduces the risk of infection-related failure in immediate breast reconstruction. *Ann Plast Surg.* 2019;82(Suppl 5):S410–S416.
12. Clayton JL, Bazakas A, Lee CN, Hultman CS, Halvorson EG. Once is not enough: Withholding postoperative prophylactic antibiotics in prosthetic breast reconstruction is associated with an increased risk of infection. *Plast Reconstr Surg.* 2012;130:495–502.
13. Martinovic ME, Pellicane JV, Blanchet NP. Surgical delay of the nipple-areolar complex in high-risk nipple-sparing mastectomy reconstruction. *Plast Reconstr Surg Glob Open* 2016;4:e760.
14. Jones G, Antony AK. Single stage, direct to implant pre-pectoral breast reconstruction. *Gland Surg.* 2019;8:53–60.
15. Sherif RD, Ingargiola M, Sanati-Mehrizy P, Torina PJ, Harmaty MA. Use of antibiotic beads to salvage infected breast implants. *J Plast Reconstr Aesthet Surg.* 2017;70:1386–1390.
16. Gorvetzian JW, Kunkel RP, Demas CP. A single center retrospective evaluation of a surgical strategy to combat persistent soft tissue wounds utilizing absorbable antibiotic beads. *Adv Wound Care (New Rochelle)* 2019;8:49–57.
17. Reitsamer R, Peintinger F. Prepectoral implant placement and complete coverage with porcine acellular dermal matrix: A new technique for direct-to-implant breast reconstruction after nipple-sparing mastectomy. *J Plast Reconstr Aesthet Surg.* 2015;68:162–167.
18. Becker H, Lind JG II, Hopkins EG. Immediate implant-based prepectoral breast reconstruction using a vertical incision. *Plast Reconstr Surg Glob Open* 2015;3:e412.
19. Sbitany H, Piper M, Lentz R. Prepectoral breast reconstruction: A safe alternative to submuscular prosthetic reconstruction following nipple-sparing mastectomy. *Plast Reconstr Surg.* 2017;140:432–443.
20. Vidya R, Iqbal FM. A guide to prepectoral breast reconstruction: A new dimension to implant-based breast reconstruction. *Clin Breast Cancer* 2017;17:266–271.
21. Highton L, Johnson R, Kirwan C, Murphy J. Prepectoral implant-based breast reconstruction. *Plast Reconstr Surg Glob Open* 2017;5:e1488.
22. Nahabedian MY. Current approaches to prepectoral breast reconstruction. *Plast Reconstr Surg.* 2018;142:871–880.
23. Nigro LC, Blanchet NP. Animation deformity in postmastectomy implant-based reconstruction. *Plast Reconstr Surg Glob Open* 2017;5:e1407.
24. Antony AK, Robinson EC. An algorithmic approach to prepectoral direct-to-implant breast reconstruction: Version 2.0. *Plast Reconstr Surg.* 2019;143:1311–1319.
25. Sbitany H. Important considerations for performing prepectoral breast reconstruction. *Plast Reconstr Surg.* 2017;140(Prepectoral Breast Reconstruction):7S–13S.
26. 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;125:429–436.
27. Kim JYS, Davila AA, Persing S, et al. A meta-analysis of human acellular dermis and submuscular tissue expander breast reconstruction. *Plast Reconstr Surg.* 2012;129:28–41.
28. Liu AS, Kao HK, Reish RG, Hergrueter CA, May JW Jr, Guo L. Postoperative complications in prosthesis-based breast reconstruction using acellular dermal matrix. *Plast Reconstr Surg.* 2011;127:1755–1762.
29. 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;129:1049–1058.
30. Selber JC, Wren JH, Garvey PB, et al. Critical evaluation of risk factors and early complications in 564 consecutive two-stage implant-based breast reconstructions using acellular dermal matrix at a single center. *Plast Reconstr Surg.* 2015;136:10–20.
31. Jordan SW, Khavanin N, Fine NA, Kim JYS. An algorithmic approach for selective acellular dermal matrix use in immediate two-stage breast reconstruction: Indications and outcomes. *Plast Reconstr Surg.* 2014;134:178–188.
32. Ivey JS, Abdollahi H, Herrera FA, Chang EI. Total muscle coverage versus AlloDerm human dermal matrix for implant-based breast reconstruction. *Plast Reconstr Surg.* 2019;143:1–6.
33. Smith JM, Broyles JM, Guo Y, Tuffaha SH, Mathes D, Sacks JM. Human acellular dermis increases surgical site infection and overall complication profile when compared with submuscular breast reconstruction: An updated meta-analysis incorporating new products. *J Plast Reconstr Aesthet Surg.* 2018;71:1547–1556.
34. Craig ES, Clemens MW, Koshy JC, et al. Outcomes of acellular dermal matrix for immediate tissue expander reconstruction with radiotherapy: A retrospective cohort study. *Aesthet Surg J.* 2019;39:279–288.
35. Boustany AN, Elmaraghi S, Agochukwu N, Cloyd B, Dugan AJ, Rinker B. A breast prosthesis infection update: Two-year incidence, risk factors and management at single institution. *Indian J Plast Surg.* 2018;51:7–14.
36. 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;71:464–470.
37. Nahabedian MY. AlloDerm performance in the setting of prosthetic breast surgery, infection, and irradiation. *Plast Reconstr Surg.* 2009;124:1743–1753.
38. Glasberg SB, Light D. AlloDerm and Strattice in breast reconstruction: A comparison and techniques for optimizing outcomes. *Plast Reconstr Surg.* 2012;129:1223–1233.
39. 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(Suppl 2):57S–66S.
40. Sorkin M, Qi J, Kim HM, et al. Acellular dermal matrix in immediate expander/implant breast reconstruction: A multicenter assessment of risks and benefits. *Plast Reconstr Surg.* 2017;140:1091–1100.
41. 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;128:403e–410e.
42. Ibrahim AMS, Shuster M, Koolen PGL, et al. Analysis of the National Surgical Quality Improvement Program database in 19,100 patients undergoing implant-based breast reconstruction: Complication rates with acellular dermal matrix. *Plast Reconstr Surg.* 2013;132:1057–1066.
43. Swanson E, Brown T. A discussion of conflicts of interest in plastic surgery and possible remedies. *Plast Reconstr Surg Glob Open* 2018;6:e2043.
44. Pittman TA, Fan KL, Knapp A, Frantz S, Spear SL. Comparison of different acellular dermal matrices in breast reconstruction: The 50/50 study. *Plast Reconstr Surg.* 2017;139:521–528.
45. Zenn MR, Salzberg CA. A direct comparison of AlloDerm-Ready to Use (RTU) and DermACELL in immediate breast implant reconstruction. *Eplasty* 2016;16:e23.
46. Hadad I, Liu AS, Guo L. A new approach to minimize acellular dermal matrix use in prosthesis-based breast reconstruction. *Plast Reconstr Surg Glob Open* 2015;3:e472.
47. Tipnis NP, Burgess DJ. Sterilization of implantable polymer-based medical devices: A review. *Int J Pharm.* 2018;544:455–460.
48. Nahabedian MY. Prosthetic breast reconstruction and red breast syndrome. *Plast Reconstr Surg Glob Open* 2019;7:e2108–e2108.
49. Yu D, Hanna KR, LeGallo RD, Drake DB. Comparison of histological characteristics of acellular dermal matrix capsules to surrounding breast capsules in acellular dermal matrix-assisted breast reconstruction. *Ann Plast Surg.* 2016;76:485–488.
50. Lewis P, Jewell J, Mattison G, Gupta S, Kim H. Reducing postoperative infections and red breast syndrome in patients with acellular dermal matrix-based breast reconstruction: The relative roles of product sterility and lower body mass index. *Ann Plast Surg.* 2015;74(Suppl 1):S30–S32.
51. Klein GM, Nasser AE, Phillips BT, et al. Is sterile better than aseptic? Comparing the microbiology of acellular dermal matrices. *Plast Reconstr Surg Glob Open* 2016;4:e761.
52. Klein GM, Singh G, Marquez J, et al. Acellular dermal matrix sterility: Does it affect microbial and clinical outcomes following implantation? *Plast Reconstr Surg Glob Open* 2019;7:e2355.
53. Parikh RP, Brown GM, Sharma K, Yan Y, Myckatyn TM. Immediate implant-based breast reconstruction with acellular dermal matrix: A comparison of sterile and aseptic AlloDerm in 2039 consecutive cases. *Plast Reconstr Surg.* 2018;142:1401–1409.
54. Kenna DM, Irojah BB, Mudge K, Eveler K. Absorbable antibiotic beads prophylaxis in immediate breast reconstruction. *Plast Reconstr Surg.* 2018;141:486e–492e.
55. Gu W, Miller S, Chiu CY. Clinical metagenomic next-generation sequencing for pathogen detection. *Annu Rev Pathol.* 2019;14:319–338.
56. Bachour Y, Poort L, Verweij SP, et al. PCR characterization of microbiota on contracted and non-contracted breast capsules. *Aesthetic Plast Surg.* 2019;43:918–926.
57. Cook J, Holmes CJ, Wixtrom R, Newman MI, Pozner JN. Characterizing the microbiome of the contracted breast capsule using next generation sequencing. *Aesthet Surg J.* 2021;41:440–447.
58. Antony AK, Poirier J, Madrigrano A, Kopkash KA, Robinson EC. Evolution of the surgical technique for "breast in a day" direct-to-implant breast reconstruction: Transitioning from dual-plane to prepectoral implant placement. *Plast Reconstr Surg.* 2019;143:1547–1556.
59. Wormer BA, Valmadrid AC, Ganesh Kumar N, et al. Reducing expansion visits in immediate implant-based breast reconstruction: A comparative study of prepectoral and subpectoral expander placement. *Plast Reconstr Surg.* 2019;144:276–286.
60. Manrique OJ, Kapoor T, Banuelos J, et al. Single-stage direct-to-implant breast reconstruction: A comparison between subpectoral versus prepectoral implant placement. *Ann Plast Surg.* 2020;84:361–365.
61. Mirhaidari SJ, Azouz V, Wagner DS. Prepectoral versus subpectoral direct to implant immediate breast reconstruction. *Ann Plast Surg.* 2020;84:263–270.
62. Parikh RP, Tenenbaum MM, Yan Y, Myckatyn TM. Cortiva versus AlloDerm Ready-to-use in prepectoral and submuscular breast reconstruction: Prospective randomized clinical trial study design and early findings. *Plast Reconstr Surg Glob Open* 2018;6:e2013.