Comparing the Outcome of Different Biologically Derived Acellular Dermal Matrices in Implant-based Immediate Breast Reconstruction: A Meta-analysis of the Literatures

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Background: Acellular dermal matrices (ADMs) have been used extensively in implant-based breast reconstruction. It was reported that due to the different sources and processing methods, the outcomes of ADMs in implant-based breast reconstructions are expected to differ. We designed this study to statistically analyze and discuss the outcome of 3 commonly used ADMs, AlloDerm, Strattice, and Surgi-mend in implant-based breast reconstruction.

Methods: Comprehensive review of the literatures searched on electronic databases was done to identify studies published between 2006 and 2017 comparing the outcome of ADMs. Pooled random effect estimates for each complication and 95% confidence interval (CI) were calculated. One-way analysis of variance and Bonferroni test were used to compare statistical significance between and within groups, respectively. Multiple linear regression was done to include confounding factors and R statistic program for forest plot.

Results: Twenty-one studies met the inclusion with a total of 1,659, 999, and 912 breasts reconstructions in AlloDerm, Strattice, and Surgi-mend, respectively. Seven complications extracted including major and minor infection, seroma, implant loss, hematoma, capsular contracture, and localized erythema. Pooled total complication rates were 23.82% (95% CI, 21.18–26.47%) in Strattice, 17.98% (95% CI, 15.49–20.47%) in Surgi-mend, 16.21% (95% CI, 14.44–17.99%) in AlloDerm. Seroma rate was the highest in Strattice group (8.61%; 95% CI, 6.87–10.35%). There was no statistical significance between and within groups.

Conclusion: Although Strattice exhibited a higher overall pooled complication rate compared with AlloDerm and Surgi-mend, the incidence of individual complication varies between studies. A cost analysis of different ADMs may aid in choosing the type of ADMs to be used. (Plast Reconstr Surg Glob Open 2018;6:e1701; doi: 10.1097/GOX.0000000000001701; Published online 19 March 2018.)

INTRODUCTION

Acellular dermal matrices (ADMs) are biomaterials used extensively in the last decade in implant-based breast reconstructions with successful outcomes and acceptable complication rates.1,2 The approach of using this technique is attributable to the ability to perform skin-sparing or nipple-sparing mastectomies.3 First introduced in 2001, Salzberg et al.3,4 has successfully introduced its use to provide implant coverage at the inferolateral pole of the breast in implant-based breast reconstructions.

It was reported that due to the different source and processing methods, the outcomes in the use of ADMs in implant-based breast reconstructions are expected to differ. In this study, we will be discussing and analyzing 3 of the most commonly used ADMs in implant-based breast reconstructions, which are AlloDerm (LifeCell Corp., Branchburg, N.J.), Strattice (LifeCell Corp., Branchburg, N.J.), and Surgi-mend PRS (TEI, Biosciences, Inc., Boston, Mass.).

AlloDerm, the most commonly and widely investigated ADM, is a human-derived ADM commonly used in the...
United States and has not received the European Conformity (CE) marking for licensed use in Europe. Alloderm is an ADM with reduced antigenicity that is produced from the epidermis human cadaveric skin. Alloderm was described as an ADM that is able to incorporate with host tissue via new matrix formed from specialized stem cells, which allowed for tissue regeneration. Up until 2013, Alloderm, then known as Regenerative Tissue Matrix, was not terminally sterilized contrary to Strattice and Surgimend. The Ready-to-Use counterpart was terminally sterilized.

Strattice is a noncrosslinked porcine-derived xenogeneic ADM. It is derived from porcine fetal dermis. It became available at the end of 2008 and was licensed to use in Europe. Due to the limited availability in human cadaveric skin, Strattice has its advantages. The structure and collagen arrangement of Strattice is almost similar to human cadaveric ADMs. It has undergone processing to maintain the integrity of the extracellular matrix allowing Strattice to act as a scaffold for cellular regeneration and neovascularization with hopes of reduced xenogeneic rejection response.

SurgiMend, similar to Strattice, is a xenogeneic, noncrosslinked ADM, which is a fetal bovine-derived dermal collagen. Studies have shown that it is rich in collagen types I and II and described by manufacturers and study stating that it is rich is collagen type III. These may facilitate tissue regeneration by impeding scarring.

Manufacturing
The manufacturing steps behind an ADM largely govern its subsequent functional properties in situ. One ADM can vary from another by either its source and/or processing of the tissue. Independent of the source, the tissue undergoes a decellularization process in which the extracellular matrix is isolated. The method of isolation varies between different types of ADMs but can be largely categorized into mechanical and more commonly chemical or biological processing.

The primary purpose of decellularization is to reduce the immunogenicity of the scaffold material so that it is host-compatible. In general, decellularization helps to augment the reconstructive capabilities of surrounding tissues. The commonest methods of decellularization are chemical and biological including the use of trypsin/triton, sodium hydroxide (NaOH), sodium dodecyl sulfate, and sodium deoxycholate.

Following decellularization, the dermal scaffolds then undergo terminal sterilization process by various methods including ultraviolet radiation, gamma radiation, and supercritical fluid techniques including use of CO₂. Before shipment, the matrix is stored in a hydrated form or lyophilized to dry; then rehydrated for usage.

METHODS
We have conducted a meticulous literature search on the databases Embase, Pubmed, and Medline, looking at literatures published from 2006 to 2017 in all 3 databases on the use of ADMs in implant-based immediate breast reconstruction. Search terms that were used include acellular dermal matrix, Acellular dermal matrices, ADMs, Breast reconstruction, breast implantation, breast implants, strattice, surgimend, alloderm, porcine, bovine, human ADM, complications, outcome, properties, collagen, seroma, infections, capsular contracture, hematoma, implant loss, explantation localized inflammation, localized erythema, and red breast syndrome.

Data Extraction
Primary outcome of interest for this meta-analysis was incidence of postoperative complications. Seven common complications associated with the use of ADMs in implant-based breast reconstruction were identified in the literatures, which were major infections classified as infections including cellulitis that were required readmission to theatre, minor infections classified as infections that were treated with oral or intravenous antibiotics that resolved without further complications, seroma, hematoma, implant loss, localized inflammation. Localized inflammation is erythema of the overlying skin in the absence of cellulitis or erysipelas or other skin infections and was not classified under complications in most studies. Figure 1 showed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart for the selection of articles.

The group of authors have also listed a series of inclusive criteria for the study, including all original studies on alloplastic/implant-based breast reconstruction with the use of ADMs, different biologically derived ADMs used in breast reconstruction, Alloderm, Strattice, and Surgimend. Additional data that were extracted were first authors; study institution; publication year; follow-up (mean/median); types of ADMs used, Alloderm, Strattice, and Surgimend; data for procedural characteristics; patient’s body mass index (BMI); confounding risk factors such as smoking, diabetes, neoadjuvant and adjuvant chemotherapy, and radiotherapy.

Fig. 1. Study attrition diagram.
Exclusion criteria were review articles, discussions, published abstracts, case reports, articles written in non-English language, and articles published before 2006.

Statistical Analysis
Pooled random effect estimates for each postoperative complication and 95% confidence interval (95% CI) were calculated using Microsoft Excel. Using IBM SPSS Statistics for Windows (Version 22.0. Armonk, NY: IBM Corp.), one-way analysis of variance (ANOVA) and Bonferroni test were used to compare statistical significance between and within 3 groups, respectively. Multiple linear regression was done to include confounding factors. Using the complication rate and 95% CI, findings were presented on a forest plot using R Statistics (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.).

Risk of Bias Assessment
Cochrane risk of bias tool was used for risk bias assessment (Table 1). Studies were assessed for performance outcome bias, selective reporting bias, attrition bias, and funding bias. Low, fair, and high outcome levels were ranked in each study based on the level of biasness.

RESULTS
A total of 58 publications were identified in the initial search on PubMed, Ovid, Medline, and Embase. Using predefined exclusion and inclusion selection criteria, 2 literatures were found to be duplicate, 16 literatures were not related to ADMs, 3 abstracts, 1 letter, 1 case report, and 14 reviews were excluded resulting in 211-5,7-11,19-29 studies that were eligible for this meta-analysis. Four of these studies were comparative studies of ADMs; therefore, we have stratified these data as individual studies5,9,10,19 making a total of 25 studies. All of these studies satisfied criteria for the study of ADMs used in implant-based immediate breast reconstruction.

Eight Alloderm studies, 11 Strattice studies, and 6 Surgimend studies were identified for our analysis. As described in Table 1, in the studies that were assessed using Cochrane Risk of Bias Tool, 12 studies had high risk, 5 studies had low risk, and 4 studies had fair risk of bias.

Patient demographics, risk factors, and indication for surgery were pooled together in Table 2. The total number of implant-based immediate breast reconstructions were 1,659 breasts, 999 breasts, and 912 breasts involving the use of Alloderm, Strattice, and Surgimend, respectively. Majority of the cases were indicated for invasive mastectomies, followed by prophylactic mastectomies with only a total of 1 revision and 7 delayed mastectomies as reflected in Table 2.

From the literatures that were investigated, the patients age range were 31.9–58.5 years. Only 6 studies reported the mean mastectomy weight and axillary node clearance surgery. All of the studies reported patients who had adjuvant chemotherapy and radiotherapy. Patient’s comorbidities, history of chemotherapy, radiotherapy, and axillary node clearance surgery may affect postsurgical outcomes, and this will be discussed further in discussion.

Six common complications associated with the use of ADMs in implant-based breast reconstruction were identified in the literatures. Pooled complication rates are listed in Table 3. This showed a higher overall complication rate (23.82%) in the Strattice group as compared with Surgimend (17.98%) and Alloderm (16.21%), which had the best overall outcome. Incidence of individual complications of each group were listed in Tables 5–7. The most common complication was major infections in Alloderm (3.80%; CI, 2.88–4.72%) and seroma in Surgimend (4.61%; CI, 3.24–5.97%) and Strattice (8.61%; CI, 6.87–10.35%). Strattice was also found to have the highest incidence of localized inflammation at 3.3% (95% CI, 2.2–4.41%) as seen in Table 8.

One-way analysis of variance test was computed on SPSS, and it was found that there were no significant statistical differences between all 3 groups. Bonferroni analysis was then done to compare the P value between groups, and there were no significant differences as depicted in Table 4. Further analysis of the outcome data by taking account for confounding factors, a multiple linear regression analysis was carried out. It was found that confounding factors did not significantly affect the outcome associated with the use of ADMs with the exception of minor infection rates in predictor group (d), which had a regression significance of P = 0.034 as seen in Table 9.

The occurrence of major infections was plotted in Figure 2, and it was statistically assumed that in 95% of these intervals intersection was at about 5.5%. Evgeniou et al.27 had much smaller number of cases; hence a larger CI had a much deviated and higher complication rate (23.8%; 95% CI, 5.59–42.02%) associated with the use of Strattice. In Figure 3, minor infection rates were significantly higher in study by Lardi et al.23 with the use of Strattice at 11.5% in 200 breasts (95% CI, 7.08–15.92%) and Liu et al.21 at 8.5% in 165 breasts (95% CI, 4.23–12.73%). Salzberg et al.3 reports a very small number of complication at 0.2% in 466 breast reconstructions (95% CI, -0.21% to 0.63%).

Seroma rate associated with the use of Strattice had the highest (8.61%) pooled complication. In Figure 4, Strattice studies, Dikmans et al.7 Hille-Betz et al.25 and Evgeniou et al.27 reported a complication rate of 20.9%, 20.4%, and 19%, respectively. In Alloderm group, pooled complication rates were the lowest at 3.07%. Glasberg and Light,19 Butterfield,18 and Gdaveitich et al.1 reported an individual seroma rate of 21.4%, 15.7%, and 10.4%, respectively. Surgimend group has a pooled seroma rate of 4.61%. A comparative study18 reported a lower seroma rate at 8.5% (95% CI, 5.62–11.47%) in 351 cases compared with Alloderm, which had a rate of 15.7% (95% CI, 8.17–23.29%) in 89 cases.

Implant loss rate associated with the use of Strattice was the highest (8.61%) pooled complication. In Figure 4, Strattice studies, Dikmans et al.7 Hille-Betz et al.25 and Evgeniou et al.27 reported a complication rate of 20.9%, 20.4%, and 19%, respectively. In Alloderm group, pooled complication rates were the lowest at 3.07%. Glasberg and Light,19 Butterfield,18 and Gdaveitich et al.1 reported an individual seroma rate of 21.4%, 15.7%, and 10.4%, respectively. Surgimend group has a pooled seroma rate of 4.61%. A comparative study18 reported a lower seroma rate at 8.5% (95% CI, 5.62–11.47%) in 351 cases compared with Alloderm, which had a rate of 15.7% (95% CI, 8.17–23.29%) in 89 cases.

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### Table 1. Risk Bias Study of the Literatures

| References            | Study Design   | Type of ADM | Comparator ADM | Sample Size | Follow-up Stated | Outcome Reported                                                                 |
|-----------------------|----------------|-------------|----------------|-------------|------------------|-----------------------------------------------------------------------------------|
| Salzberg et al.¹      | 1. Retrospective cohort, nonrandomized | Alloderm     | Noncomparative  | 466 Breasts  | 28.9±21.3 mo     | 1. Total complication rate: 19 (4.1%)  
2. Types and incidence of complications associated with the use of Alloderm in immediate breast reconstruction.  
3. A comparison of complications in oncologic breasts and prophylactic breasts |
| Gdalevitch et al.²     | 1. Retrospective cohort, nonrandomized | Alloderm     | Noncomparative  | 164 Breasts  | Median 228 d    | 1. Total complication of 96 (58.5%)  
2. Types and incidence of complications associated with the use of Alloderm in immediate breast reconstruction  
3. Predictors of failures statistical measurement |
| Ricci et al.³         | 1. Retrospective cohort, nonrandomized | Alloderm     | Surginend      | 578 Breasts in Alloderm | Mean 587 d | 1. Total complication rate in Alloderm 174 (30.1%)  
2. Operative factors measured  
3. Multivariate analysis done |
|                       |                |             |                | 374 Breasts in Surginend | Mean 587 d | 1. Total complication rate in Surginend 68 (18.2%)  
2. Operative factors measured  
3. Multivariate analysis done |
| Spear et al.⁴         | 1. Prospective cohort, nonrandomized | Alloderm     | Noncomparative  | 58 Breasts   | 25.9             | 1. Total complication rate of 8 (13.8%)  
2. Mean intraoperative expander fill  
3. Incidence of complication in irradiated and nonirradiated breast |
| Liu et al.⁵           | 1. Retrospective cohort, nonrandomized | Alloderm     | FlexHD         | 165 Breasts in Alloderm | 6.4       | 1. Total complication rate of 47.3%  
2. Immediate versus delayed risk factors and complications  
3. Complications in ADM versus no ADM  
4. Multivariate analysis of complications |
| Gamboa-Bobadilla²⁸    | 1. Retrospective cohort, nonrandomized | Alloderm     | Noncomparative  | 13 Breasts   | 14               | 1. Total complication rate of 3 (25.1%)  
2. Complications related to the use of Alloderm  
3. Histological analysis |
| Butterfield²⁹         | 1. Retrospective cohort, nonrandomized | Alloderm     | Surginend      | 89 Breasts in Alloderm | 32.8±15.87 | 15.6±8.79                      | 1. Total complication rate in Alloderm versus Surginend (31.7% versus 44.2%)  
2. Patient demographic, risk factors, concurrent therapy for Surginend and Alloderm  
3. Uni- and multivariate analysis  
4. Cost analysis |
| Salzberg et al.¹      | 1. Retrospective cohort, nonrandomized | Strattice    | Noncomparative  | 105 Breasts  | 41.3 mo          | 1. Total complication rate in Salzberg breast reconstruction (8.6%)  
2. Types and incidence of complications associated with Strattice  
3. Histological analysis of implanted Strattice |
| Dikmans et al.²⁷      | 1. Randomized control trial          | Strattice    | One-stage IBBR with ADM (Strattice), Two-stage IBBR without Strattice Noncomparative | 91 Breasts | 24 mo | 1. Total complication (30.8%)  
2. Types and incidence of complications associated with 1-stage and 2-stage IBBR.  
3. Quality of life at 1 y. |
| Dikmans et al.²⁷      | 1. Retrospective cohort              | Strattice    | Noncomparative  | 110 Breasts  | 2010–2014        | 1. Total complication rate (2%)  
2. Types and incidence of complications.  
3. Reintervention rate.  
4. Arm mobility/function post surgery. |
| Reitsamer et al.²⁹    | 1. Prospective cohort                | Strattice    | Noncomparative  | 22 Breasts   | 6 mo             | (Continued) |

(Continued)
## Critical Appraisal

| Clear Inclusion Criteria | Blinded Outcome Assessors | Attrition Accounted for | Selective Outcome Reporting | Funding Bias | Ethical or IRB Approval | Power Calculation | Risk of Bias |
|--------------------------|---------------------------|-------------------------|------------------------------|--------------|------------------------|------------------|-------------|
| Clear inclusion. Patient evaluation flow chart provided. | No | Yes | No | No | Unclear | No | High |
| 11 Patients who underwent skin-sparing or nipple-sparing mastectomy followed by direct-to-implant single-stage immediate breast reconstruction in 2010 and 2011 at 3 university-affiliated centers were included | Yes | Yes | Yes | No | Unclear | No | Low |
| Clear inclusion. All patients who underwent ADM reconstruction. Consecutive patients. | No | Yes | No | No | No | Yes | Low |
| Clear inclusion. All the women undergoing immediate prosthetic breast reconstruction between March 2004 and June 2005 were included in the study. Patients undergoing delayed reconstruction were excluded, as were those who had undergone previous reconstruction. | Unclear | Unclear | No | Unclear | Unclear | Yes | High |
| Clear inclusions; patients who had undergone breast reconstruction using saline implant devices and HADM as tissue supplements from 2003 to 2004 | Unclear | Unclear | Yes | Unclear | No | No | High |
| Consecutive patients.; patients undergoing implant-based breast reconstruction with Alloderm or Surgimend between 2005 and 2010 | Unclear | Yes | Yes | No | No | Yes | Low |
| Clear inclusion- immediate single-stage or 2-stage implant-based breast reconstruction with the assistance of Strattice were included in this study | No | Not clear | Yes | No | Not stated | No | High |
| Clear inclusion. Eligible women were older than 18 y with breast carcinoma or a gene mutation linked with breast cancer who intended to undergo skin-sparing mastectomy and immediate IBBR | Yes | Yes | Yes | No | Yes | Yes | Low |
| No clear inclusion/exclusion. | No | Not stated | Yes | No | Not stated | No | High |
| No clear inclusion criteria. | Not stated | No | No | No | Not required | No | High |
Table 1. (Continued)

| References         | Study Design     | Type of ADM | Comparator ADM | Sample Size | Follow-up Stated | Outcome Reported                                                                 |
|--------------------|------------------|-------------|----------------|-------------|------------------|----------------------------------------------------------------------------------|
| Lardi et al.       | 1. Retrospective cohort, 2. Nonrandomized. | Strattice   | Noncomparative | 200         | 22.2 mo          | 1. Total complication rate (45.5%)  
2. Types and incidence of complications.                                           |
| Hille-Betz et al.  | 1. Retrospective cohort, 2. Randomized       | Strattice   | Immediate expander implant. Delayed expander-implant reconstructions Revision surgery for implant associated breast deformities. | 98          | 19.6             | 1. Total complication rate (34.7%)  
2. Potential impact of subsequent radiotherapy.                                     |
| Gunnarsson Gl et al. | 1. Retrospective cohort, 2. Nonrandomized. | Strattice   | Noncomparative | 76          | 326 d            | 1. Total complication rate (19.7%)  
2. Comparison of complication rate between smokers and nonsmokers; hypertensive and nonhypertensive patients.  
3. Effect of chemoradiotherapy on surgical reconstruction.                             |
| Evinenou et al.    | 1. Retrospective cohort                        | Strattice   | Noncomparative | 21          | 2009–2011        | 1. Total complication rate (95.2%)  
2. Types and incidence of complications.                                              |
| Glasberg and Light | 1. Retrospective cohort, 2. Nonrandomized     | Strattice   | AlloDerm       | 144 Breasts in Strattice | 18.2          | 1. Total complication rate (18.5%)  
2. Aesthetic outcome—patient reported.                                                  |
| Ball et al.        | 1. Retrospective cohort, 2. Nonrandomized      | Strattice   | 1. IBBR using Strattice, 2. IBBR using Surgimend Noncomparative | 110 (30       | 380 d            | 1. Total complication rate (25.8%)  
2. Types and incidence of complications between comparator groups.                    |
| Himsl et al.       | 1. Retrospective cohort                        | Strattice   | Noncomparative | 27 Breasts   | Median 19 mo     | 1. Total complication rate (34.7%)  
2. Types and incidence of complications between comparator groups                     |
| Eichler et al.     | 1. Retrospective cohort, 2. Nonrandomized      | Surgimend   | 1. IBBR using Surgimend, 2. IBBR using Epiflex | 63 Breasts    | 2008–2013        | 1. Total complication rate (17.5%)  
2. Types and incidence of complications between comparator groups.                    |
| Eichler et al.     | 1. Retrospective cohort, 2. Nonrandomized      | Surgimend   | 1. IBBR using Surgimend, 2. IBBR using Tutomedesh | 18 Surgimend  | 2014–2016        | 1. Total complication rate (11.1%)  
2. Types and incidence of complications between comparator groups.                    |
| Gaster et al.      | 1. Prospective cohort                           | Surgimend   | No comparators | 17          | 2009–2011        | 1. Total complication rate (5.9%)  
2. Types and incidence of complications.                                              |

Table 2. Patient Demographics, Risk Factors, and Indications for Surgery between ADM Groups

| Study Demographics | AlloDerm | Strattice | Surgimend |
|--------------------|----------|-----------|-----------|
| No. patients, n    | 983      | 691       | 617       |
| No. breasts, n     | 1,659    | 999       | 912       |
| Mean BMI (kg/m²)   | 25.8     | 24.35     | 23.9      |
| Smoking, n         | 91       | 112       | 56        |
| Diabetes, n        | 46       | 12        | 8         |
| Indications for surgery |        |           |           |
| Invasive           | 899      | 125 patients | 112 patients |
| Prophylactic       | 720      | 46 patients | 7 patients |
| Revision           | 1        | 0         | 0         |
| Delayed            | 1        | 0         | 6 patients |

| IRB, Institutional Review Board (IRB); IBBR, Implant-based breast reconstruction; IBR, Immediate breast reconstruction. |

Table 3. One-way ANOVA between ADM Groups

| Complications       | Surgimend (n = 912) | Strattice (n = 999) | AlloDerm (N = 1,659) | One-way ANOVA (P between Groups) |
|---------------------|---------------------|---------------------|----------------------|----------------------------------|
| Major (%)           | 3.51                | 2.10                | 3.80                 | 0.502                            |
| Minor (%)           | 4.17                | 4.69                | 3.48                 | 0.693                            |
| Seroma (%)          | 4.61                | 8.61                | 3.07                 | 0.279                            |
| Hematoma (%)        | 1.21                | 2.10                | 2.11                 | 0.580                            |
| Implant loss (%)    | 4.50                | 5.61                | 2.59                 | 0.343                            |
| Capsular (%)        | 0.00                | 0.80                | 1.21                 | 0.345                            |
| Total complications | 17.98               | 25.82               | 16.21                |                                  |

P of < 0.05 = significant difference in results. Italics indicates best outcome.  
Bold indicates worst outcome.
| Study Demographics | Comparator | Sample Size | Follow-up | Stated Outcome Reported |
|--------------------|------------|-------------|-----------|-------------------------|
| Surgimend          | Alloderm   | 27          | 2008–2013 | Total complication rate (19.7%) |
|                    |            | 76          |           | Types and incidence of complications |
|                    |            | 326         |           | Histological analysis of tissue specimens |
|                    |            |             |           | Aesthetic outcome—patient reported |
|                    |            |             |           | DISCUSSION |

**DISCUSSION**

ADM-assisted breast reconstruction provides better esthetic outcome when compared with the traditional subpectoral implant placement, in terms of creating a better inframammary fold definition and allowing for lower rate of capsular contracture. This meta-analysis, the performance of ADMs within in vivo models and how well this compared with human studies were also investigated.

A known complication in implant-based breast reconstruction following skin-sparing mastectomy is skin necrosis. It ranges from simple epidermolysis to a full-thickness flap necrosis, and if severe enough, lead to implant exposure, and subsequent implant loss.

Although this outcome was not included in our study because...
ADMs do not directly cause skin/flap necrosis, this will be discussed further. Studies report various methods to improve cellular behavior through surface modifications of ADMs including chemical modification with L-arginine in bovine ADM\(^{31}\) and modification of porcine acellular dermal matrix PADM via dopamine self-polymerization/collagen immobilization.\(^{32}\) A recent in vivo rat study further showed chemical cross-linking Permacol, which is porcine-derived, with hexamethylene diisocyanate caused an increase in cellular density and penetration at 12 months postimplantation compared with noncrosslinked implants. Furthermore, it was suggested that a thorough assessment of postmastectomy skin flap viability is crucial to reduce the incidence of skin necrosis.\(^{23,27}\)

Capsular contracture is thought to be a local inflammatory response leading to excessive production of collagen by fibroblasts where they are in contact with the implant.\(^{33}\) The Baker Classification system is a subjective classification system based upon clinical findings in the patient. Studies have proven that the use of ADMs in implant-based breast reconstruction is associated with a lower rate of capsular contracture up to a 20-fold reduction.\(^{34}\) Basu et al.\(^{35}\) reported a significant reduction in granulation tissue formation, levels of vascular proliferation, chronic inflammatory changes, fibroblast cellularity and foreign body giant cell inflammatory reaction, when comparing acellular cadaveric dermis sample to native breast capsules. Cross correlation with cytotoxicity studies in animal models reveal similar results. The degree of inflammation caused by human ADMs at 4 weeks in an in vivo rabbit model for incisional hernia repair was not statistically different from that caused by the use of porcine ADMs.\(^{36}\) In both instance, the degree of capsular contracture up to a 20-fold reduction.\(^{37}\) Basu et al.\(^{38}\) reported a significant reduction in granulation tissue formation, levels of vascular proliferation, chronic inflammatory changes, fibroblast cellularity and foreign body giant cell inflammatory reaction, when comparing acellular cadaveric dermis sample to native breast capsules. Cross correlation with cytotoxicity studies in animal models reveal similar results. The degree of inflammation caused by human ADMs at 4 weeks in an in vivo rabbit model for incisional hernia repair was not statistically different from that caused by the use of porcine ADMs.\(^{36}\) In both instance, the degree of inflammation detected by histology was low grade (level 1). A further study looked at the inflammatory response induced by porcine ADMs that were prepared by ultrasonification and freeze-thawing. Inflammatory markers, Interleukin-2 (IL-2) and Interferon gamma (IFN-\(\gamma\)), were absent in both the PADM and human acellular dermal matrix group up to 48 hours postimplantation.\(^{37}\) These are produced by antigen-sensitized T-cells in the context of foreign body rejection,\(^{38}\) suggesting both were well tolerated. There may be a role for biopsy during a single-stage ADM breast reconstruction to ascertain local tissue inflammation through definitive histological analysis. This is especially necessary as capsular contracture itself can be influenced by other confounding factors.\(^{32,39}\)

Although pooled data showed that Surgimend has the highest incidence of infection (7.68%), when individualized, Alloderm has the highest rate of major infections (3.8%) when compared with Surgimend (3.51%) and Strattice (2.1%). Although the HADM, Alloderm is clas-

### Table 4. Bonferroni Statistical Analysis within Groups using SPSS

| Fixed Variable | Brand          | Dependant Variables | P Sig. | Minor Infection | P Sig. | Major Infection | P Sig. | Seroma | P Sig. | Hematoma | P Sig. | Implant Loss | P Sig. | Capsular Contracture | P Sig. |
|----------------|----------------|---------------------|--------|----------------|--------|-----------------|--------|--------|--------|----------|--------|--------------|--------|---------------------|--------|
| Strattice      | Alloderm       | 0.745               | 1      | 1              | 0.346  | 0.91            | 0.667  | 1      | 0.858  | 1        | 0.651  | 1            | 0.667  | 1              |
| Surgimend      | Strattice      | 0.745               | 1      | 1              | 0.346  | 0.91            | 0.667  | 1      | 0.858  | 1        | 0.651  | 1            | 0.667  | 1              |
| Alloderm       | Surgimend      | 0.745               | 1      | 1              | 0.346  | 0.91            | 0.667  | 1      | 0.858  | 1        | 0.651  | 1            | 0.667  | 1              |

\(P < 0.05 = \) significant difference in values. (Sig. = P value)

### Table 5. Surgimend Group Pooled Complication

| Complications | n  | p (%)   | SE  | 95% CI        |
|---------------|----|---------|-----|---------------|
| Major         | 32 | 3.51    | 0.0061 | 2.31–4.70     |
| Minor         | 38 | 4.17    | 0.0066 | 2.87–5.46     |
| Seroma        | 42 | 4.61    | 0.0069 | 3.24–5.97     |
| Hematoma      | 11 | 1.21    | 0.0036 | 0.50–1.91     |
| Implant loss  | 41 | 4.50    | 0.0069 | 3.15–5.84     |
| Capsular      | 0  | 0.00    |       |               |
| Total         | 164| 17.98   | 0.0127 | 15.49–20.47   |

p. Proportion; SE, standard error.

### Table 6. Strattice Group Pooled Complications

| Complications | n  | p (%)   | SE  | 95% CI        |
|---------------|----|---------|-----|---------------|
| Major         | 21 | 2.10    | 0.0045 | 1.21–2.99     |
| Minor         | 48 | 4.60    | 0.0045 | 3.30–5.90     |
| Seroma        | 86 | 8.61    | 0.0089 | 6.87–10.35    |
| Hematoma      | 21 | 2.10    | 0.0045 | 1.21–2.99     |
| Implant loss  | 56 | 5.61    | 0.0073 | 4.18–7.03     |
| Capsular      | 8  | 0.80    | 0.0028 | 0.25–1.35     |
| Total         | 238| 23.82   | 0.0155 | 21.18–26.47   |

p. proportion; SE, standard error.

### Table 7. Alloderm Group Pooled Complication

| Complications | n  | p (%)   | SE  | 95% CI        |
|---------------|----|---------|-----|---------------|
| Major         | 63 | 3.80    | 0.0047 | 2.68–4.72     |
| Minor         | 57 | 3.44    | 0.0034 | 2.56–4.31     |
| Seroma        | 51 | 3.07    | 0.0042 | 2.24–3.90     |
| Hematoma      | 35 | 2.11    | 0.0035 | 1.42–2.80     |
| Implant loss  | 43 | 2.59    | 0.0039 | 1.83–3.36     |
| Capsular      | 20 | 1.21    | 0.0027 | 0.68–1.73     |
| Total         | 269| 16.21   | 0.0090 | 14.44–17.99   |

p. proportion; SE, standard error.

### Table 8. Incidence of Localized Inflammation between ADMs

| Types of ADMs | Breast, n (%) | SE  | 95% CI        |
|---------------|---------------|-----|---------------|
| Surgimend     | 10 (1.10)     | 0.0034 | 0.0042–0.0177 |
| Strattice     | 33 (3.3)      | 0.0057 | 0.022–0.0441  |
| Alloderm      | 37 (2.2)      | 0.0036 | 0.0152–0.0294 |
| Total         | 80 (2.24)     |       |               |

SE, standard error.
Table 9. Regression Analysis of Outcome and Confounding Effects on All ADM Groups using SPSS

| Complications       | Regression Significance (P) |
|---------------------|-----------------------------|
|                     | a   | b   | c   | d   | e   | f   | g   | h   | i   |
| Major infection     | 0.966 | 0.991 | 0.973 | 0.973 | 0.821 | 0.876 | 0.869 | 0.926 | 0.957 |
| Minor infection     | 0.346 | 0.072 | 0.065 | 0.034 | 0.063 | 0.116 | 0.191 | 0.249 | 0.234 |
| Seroma              | 0.168 | 0.385 | 0.228 | 0.339 | 0.28 | 0.211 | 0.546 | 0.578 | 0.696 |
| Hematoma            | 0.247 | 0.358 | 0.241 | 0.308 | 0.428 | 0.303 | 0.426 | 0.33 | 0.65 |
| Implant loss        | 0.315 | 0.594 | 0.473 | 0.547 | 0.558 | 0.54 | 0.625 | 0.693 | 0.787 |
| Capsular contracture| 0.535 | 0.669 | 0.647 | 0.802 | 0.863 | 0.8 | 0.842 | 0.909 | 0.717 |

P < 0.05 indicates statistical significance. Bold indicates statistical significance p<0.05

a, Predictors: (Constant), Brand; b, Predictors: (Constant), Brand, Smoking; c, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus; d, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus, Age; e, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus, Age, Neoadjuvant_Chemo; f, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus, Age, Neoadjuvant_Chemo, Adjuvant_Chemo; g, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus, Age, Neoadjuvant_Chemo, Adjuvant_Chemo, Preop_radiotherapy; h, Predictors: (Constant), Brand, Smoking, Obesity, Diabetes_Mellitus, Age, Neoadjuvant_Chemo, Adjuvant_Chemo, Preop_radiotherapy, Postop_radiotherapy;

Fig. 2. Forest plot estimating the proportion of the incidence of major infection among Alloderm, Surgimend, and Strattice groups.

Fig. 3. Forest plot estimating the proportion of the incidence of minor infections among Alloderm, Surgimend, and Strattice groups.
classified as aseptic, histologic studies have reported neovascularization and inflammatory cell penetration into both sterile and aseptic ADMs⁴⁰ Nahabedian⁴¹ has demonstrated that Alloderm was able to revascularize, recellularize and following tissue integration, able to tolerate mild-to-moderate infections. AlloDerm showed greater microvascular density and soft-tissue ingrowth.⁴²

With regard to high incidence of seroma rate in Strat-tice group, Hille-Betz et al.⁴⁵ report that there was no antibiotic irrigation intraoperatively in their study, whereas the study by Dikmans et al.⁷ stated that there was a lack of registration on the use of antibiotics. In the study by Butterfield 2012,¹⁰ Surgimend had a much lower seroma rate as compared with Alloderm. The author reported that the number of drains inserted and whether the ADM is fenestrated or unfenestrated should be taken into consideration. Lardi et al.⁴³ have also suggested that the rate or seroma could potentially be reduced by lowering the drain removal threshold to around < 20 cc/24 h. Multiple studies have suggested that with the use of antibiotics for a period of time, 2 bulb suction drains, and by reducing the dead space between implant/expanded with skin, the incidence of seroma formation could potentially be reduced.⁴³

**Fig. 4.** Forest plot estimating the proportion of the incidence of seroma among Alloderm, Surgimend, and Strattice groups.

| Study                  | Types of ADM | Seroma | Total number of cases |
|------------------------|--------------|--------|----------------------|
| Butterfield JL 2013    | Alloderm     | 14(15.7%) | 89                   |
| Glasberg SD, Light D 2012 | Alloderm   | 27(21.4%) | 126                  |
| Gdolewicz P et al 2014 | Alloderm     | 17(10.4%) | 164                  |
| Rocci JA et al 2016    | Alloderm     | 12(2.2%)  | 578                  |
| Spear et al 2008       | Alloderm     | 1(1.7%)   | 58                   |
| Liu et al 2014         | Alloderm     | 5(3.0%)   | 165                  |
| Gamboa-Bobadilla, G. M. et al 2006 | Alloderm | 1(7.7%) | 13                   |
| Eicher C et al 2015    | Surgimend    | 1.6%     | 63                   |
| Butterfield JL 2013    | Surgimend    | 30(8.5%)  | 351                  |
| Rocci JA et al 2016    | Surgimend    | 7.1(1.9%) | 374                  |
| Ball et al 2017        | Surgimend    | 4(4.5%)   | 89                   |
| Ball et al 2017        | Strattice    | 3(10%)    | 30                   |
| Glasberg SD, Light D 2012 | Strattice | 9(6.25%) | 144                  |
| Dikmans et al 2016     | Strattice    | 23(20.9%) | 110                  |
| Hille-Betz et al 2015  | Strattice    | 20(20.4%) | 98                   |
| Lardi et al 2014       | Strattice    | 21(10.5%) | 200                  |
| Salzberg et al 2013    | Strattice    | 2(1.9%)   | 105                  |
| Gunnarsson GI et al 2013 | Strattice | 2(2.6%) | 76                   |
| Evgeniou, E. et al 2012| Strattice    | 4(8.8%)   | 21                   |
| Hnisl I et al 2012     | Strattice    | 2(4.1%)   | 27                   |

**Fig. 5.** Forest plot estimating the proportion of the incidence of implant loss among Alloderm, Surgimend, and Strattice groups.
Localized inflammation or erythema is also known as red breast syndrome, whose etiology is still poorly understood. It was thought to be a delayed hypersensitivity reaction to ADMs in breast reconstruction, causing redness to the skin overlying the ADMs. Salzberg et al. have reported that there is no evidence of true rejection response on histological analysis.

Multiple studies suggested that the main factors leading to an increase in complication rate are age older than 50 years, smoking status, mastectomy weight of > 600 g, and BMI > 30. A couple of articles also showed that breast irradiation postoperatively is related to a higher rate of complication, including wound dehiscence, higher rate of infections, and possibly capsular contraction. However, as discussed, there were no significant difference when adjusting for confounding factors. Inevitably, due to the lack of individual data from each study during extrapolation of data, we are unable to be completely advocate these accuracy as it might lead to a bias in results.

There were some limitations in this study. One of the main weaknesses is the low level of evidence in the studies included. We were only able to include 1 randomized controlled trial and 3 prospective cohort studies. It was also difficult to compare statistical differences in the indication for surgery as there were a few studies that re-

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**Fig. 6.** Forest plot estimating the proportion of the incidence of hematoma among AlloDerm, SurgiMend, and Strattice groups.

**Fig. 7.** Forest plot estimating the proportion of the incidence of localized inflammation among AlloDerm, SurgiMend, and Strattice groups.
corded the number of patients instead of the number of breasts. In quite a few studies, we were not able to extract data on patient’s comorbidities such as smoking and diabetec status. We also acknowledge that most of our studies have high risk of bias as reported in Table 1.

From the thorough analysis, Strattice exhibited a slightly higher overall pooled complication rate compared with Alloderm and Surgimend. However, the incidence of individual complication varies between studies. Potential learning curve effects of using ADMs may affect the outcome. A cost analysis and a large prospective study of different ADMs may aid in choosing the type of ADMs to be used.

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