Porcine Acellular Peritoneal Matrix in Immediate Breast Reconstruction: A Multicenter, Prospective, Single-Arm Trial

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Background: Use of biological implants such as acellular dermal matrices in tissue expander breast reconstruction is a common adjunct to submuscular implant placement. There is a paucity of published prospective studies involving acellular matrices. The authors sought to evaluate a porcine-derived acellular peritoneal matrix product for immediate breast reconstruction.

Methods: A prospective, single-arm trial was designed to analyze safety and outcomes of immediate tissue expander–based breast reconstruction with a novel porcine-derived acellular peritoneal matrix surgical mesh implant. Twenty-five patients were enrolled in this industry-sponsored trial. Patient demographics, surgical information, complications, histologic characteristics, and satisfaction (assessed by means of the BREAST-Q questionnaire) were evaluated.

Results: Twenty-five patients (44 breasts) underwent mastectomy with immediate breast reconstruction using tissue expanders with acellular peritoneal matrix. Sixteen reconstructed breasts experienced at least one complication (36 percent). Seroma and hematoma occurred in one of 44 (2.3 percent) and two of 44 breasts (4.6 percent), respectively. Wound dehiscence occurred in four of 44 breasts (9.1 percent). Three subjects experienced reconstruction failure resulting in expander and/or acellular peritoneal matrix removal (6.8 percent); all failures were preceded by wound dehiscence. Histologic analysis showed cellular infiltration and product resorption. Results of the BREAST-Q demonstrated a level of postoperative patient satisfaction consistent with results in the available literature.

Conclusions: Prepared porcine-derived acellular peritoneal matrix is a safe adjunct in immediate two-stage tissue expander-based breast reconstruction. Further studies are required to determine efficacy compared to current commercially available acellular matrices. (*Plast. Reconstr. Surg.* 143: 10e, 2019.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

4
THERAPEUTIC

In the United States, one of eight women will be diagnosed with breast cancer.[1] Although breast conserving therapy is often considered, many women will undergo mastectomy for oncologic control. Following mastectomy, women may elect to undergo breast reconstruction with autologous or alloplastic procedures, and two-stage tissue expander–based surgery is the most common reconstructive technique.[2,3] Although complete submuscular coverage can be achieved through tissue mobilization, surgeons have the option to augment the inferior pole with commercially

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available products designed to act as a sling for implant support and cover.[4,5]

Currently, human-derived acellular dermal matrix is the most commonly used product in two-stage breast reconstruction, although other products are available. The purported advantages of using these products compared with total submuscular coverage include improved expander positioning, greater initial intraoperative fill volume, decreased pain, fewer postoperative office visits required for expansion, and ultimately improved aesthetic outcome.[5–7] Critics point to disadvantages, including higher reported risk of skin necrosis, infection, and seroma, although the risk of increased reoperation and implant failure is unclear.[8–11] In this industry-sponsored, prospective, multicenter, single-arm study, we evaluate a porcine-derived acellular peritoneal matrix product for immediate two-stage expander-based breast reconstruction. The main outcome was determination of safety, with secondary evaluation of patient-reported health satisfaction, handling, and histologic characteristics.

PATIENTS AND METHODS

Product

This novel porcine-derived acellular peritoneal matrix implant (Meso BioMatrix; DSM Biomedical, Exton, Pa.) is a nonperforated surgical matrix product designed to reinforce soft tissue. This acellular peritoneal matrix has a previously established biomechanical profile, with high tensile strength (40.65 ± 21.65 N/cm) and suture pull-through strength (9.12 ± 3.62 N). The implant is derived from porcine peritoneum that has been decellularized using proprietary methods involving a series of agitations in organic solvents, detergents, salt solutions, and enzymes with multiple rinses. After the final rinse, the implant is lyophilized, packaged in gas-permeable material, and terminally sterilized with ethylene oxide.[12] Figure 1 demonstrates the acellular peritoneal matrix after rehydration in saline and before implantation.

Study Design

The study was designed as a prospective, multicenter, single-arm feasibility trial of patients undergoing two-stage, tissue expander–based breast reconstruction. The trial was registered with ClinicalTrials.gov (NCT01823107).[13] Participating surgeons sought and obtained local institutional ethics board approval before enrolling patients in the study. In consultation with the U.S. Food and Drug Administration, a target enrollment of 25 patients was set to evaluate the safety of the device in humans. No sample size calculation was used. Ten U.S. Food and Drug Administration–approved institutions obtained local institutional review board approval. The first subject was enrolled on June 27, 2012, and the last on September 25, 2015. Follow-up was completed in June of 2017. All surgeons participating in the study were experienced with two-stage breast reconstruction using decellularized matrix products.

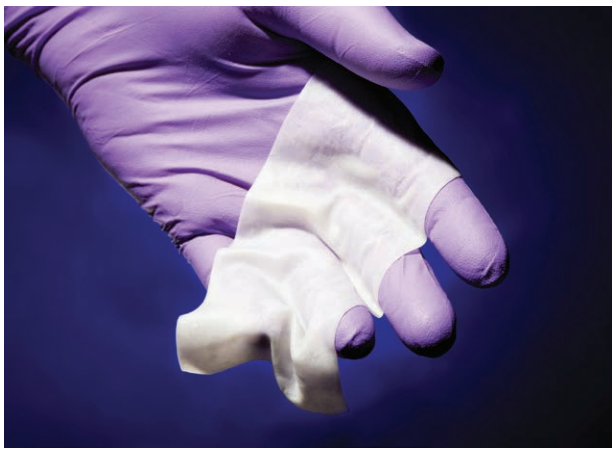

Fig. 1. Acellular peritoneal matrix following rehydration in saline.

Patient Recruitment

Patient recruitment began in June of 2012. Women who were undergoing two-stage implant-based reconstruction for either unilateral or bilateral mastectomy defects were considered for enrollment. Inclusion and exclusion criteria are outlined in Table 1. Twenty-five patients were enrolled through September 25, 2015, at six of the approved sites. The remaining four sites were withdrawn from the study. Information regarding patient demographics, medical and breast history, and informed consent was obtained during the preoperative visit. The breast history was obtained for all breasts in recruited patients, regardless of surgical intent. The patients and providers were aware of the intended intervention, and no blinding was performed.

Surgical Procedure

Patients underwent either unilateral or bilateral mastectomy, with or without lymphadenectomy. The skin flaps were then assessed for viability before proceeding with tissue expander insertion either visually or with indocyanine green

Table 1. Inclusion and Exclusion Criteria for Patient Recruitment

Inclusion
Nonsmoker
Undergoing unilateral or bilateral two-stage tissue expander–assisted breast reconstruction
Life expectancy >18 mo
Able to return for required follow-up visits
Exclusion
Body mass index ≥35 kg/m^2
Prior reconstructive breast surgery, breast augmentation, mastopexy, or reduction mammaplasty
History of chronic corticosteroid use
Type 1 diabetes
History of radiation therapy to chest
Preoperative treatment with induction chemotherapy for breast cancer
Pregnancy
Participating in another investigational drug or device trial that has not completed the follow-up period

techniques at the surgeon's discretion. If the skin flaps were not adequately perfused on either clinical or indocyanine green examination, the reconstruction was deferred and the patient was not included in the trial. Tissue expanders were inserted in the subpectoral plane. Acellular peritoneal matrix was hydrated for 5 minutes immediately before insertion with either saline, antibiotic, or povidone-iodine solution, at the surgeon's discretion. The hydrated implant was then inset with the "rough" (nonperitoneal surface) side toward the skin flap at the inferior margin of the pectoralis major and sutured to the chest wall to suspend the tissue expander and create an inferior sling. The tension, suture material, and technique used was at the surgeon's discretion. The surgeon was then asked to rate acellular peritoneal matrix hydration, handling, strength, and suturability as "good," "average," or "poor." The tissue expander was then instilled with saline, and initial fill volume was recorded. Number of drains, type of drains, and plane of insertion were left to the discretion of the surgeon.

After the first-stage surgery and a period of healing determined by the surgeon, patients underwent tissue expansion, and the number of office visits and fill volume were recorded. Patients were asked to follow up at prescribed times in addition to expansion times arranged at the patient's and surgeon's discretion. At the completion of expansion, the patient underwent second-stage surgery, where the tissue expander was removed either through the initial mastectomy scar or through an inframammary fold incision. During the second-stage surgery, the surgeon collected 3-mm-diameter punch biopsy specimens from each reconstructed breast at the following locations: (1) the interface of acellular peritoneal matrix with the pectoralis major muscle, (2) the central area of acellular peritoneal matrix, (3) the interface of acellular peritoneal matrix with the chest wall at the inframammary fold, and (4) the capsule behind the tissue expander (patient tissue alone) as the control specimen.

When deviation from standard two-stage reconstruction occurred, such as in unplanned autologous reconstruction, these subjects were noted and the indication for deviation was recorded. Similarly, if the patient underwent secondary balancing procedures (e.g., reduction mammaplasty, augmentation, or mastopexy) these were also recorded.

Pathologic Analysis

The biopsy specimens were placed in separate containers in 10% formalin and shipped to PPD Global Central Labs (Highland Heights, Ky.) for sectioning, staining, and standardized pathologic analysis as described previously by Hoganson et al.[12] The pathologist analyzed the samples for the presence and extent of the following: encapsulation, inflammation, neovascularization, cellular infiltration, product resorption, and newly formed fibroconnective tissue. The pathologist graded the presence of the above variables as 0 (none), 1 (minimal), 2 (moderate), or 3 (extensive).

Questionnaire

Subjects were asked to complete the reconstructive module of the BREAST-Q (Memorial Sloan Kettering Cancer Center, New York, N.Y.), a standardized instrument measuring patient satisfaction and health-related quality of life.[14] The scales selected included the following: (1) Satisfaction with Breasts; (2) Satisfaction with Outcome; (3) Psychosocial Well-being; and (4) Physical Well-being: Chest. Scoring was performed using the Q-Score tool and recorded on a scale of 1 to 100, with higher scores indicating higher satisfaction.[15]

Reporting of Anticipated and Unanticipated Adverse Events

All adverse events were submitted to the study coordinators and the U.S. Food and Drug Administration medical monitor at the time of occurrence. All patients were evaluated for adverse events at all scheduled and unscheduled visits. The diagnosis of an adverse event was left to the discretion of the attending surgeon. Adverse events were classified as anticipated, unanticipated, and breast-related or systemic/non–breast-related.

Chronicity, severity, duration of time from procedure, action taken, and outcome were also recorded. There were no industry-led interventions in adverse events; clinical decision-making and management were at the discretion of the attending surgeon and affected patient. All serious adverse events were submitted to the medical monitor for consideration of early termination.

Study Endpoints

Study enrollment was terminated after the last patient was enrolled. Data acquisition was terminated after the last patient had her final 12-month postimplant exchange follow-up in June of 2017.

Statistical Analyses

Descriptive statistics were performed using Microsoft Excel 2016 (Microsoft Corp., Redmond, Wash.).

RESULTS

Patient Demographics

Of 25 women who were enrolled in the study, 19 underwent bilateral mastectomy and six underwent unilateral mastectomy, for a total of 44 mastectomies. On medical history, there were no subjects with diabetes mellitus, six with hypertension, and eight with a history of smoking, although no subjects were active smokers. No subjects had previously undergone any breast surgery other than lumpectomy. The mean age of the patients was 49.4 ± 8.5 years (range, 32 to 67 years), and the mean body mass index was 25.0 ± 3.9 kg/m^2 (range, 20.4 to 30.9 kg/m^2), or overweight. The summary of patient demographics, breast history (for all breasts, regardless of surgical intent), and medical history is listed in Tables 2 and 3.

Table 2. Demographics and Medical History Summary of All Patients (*n* = 25) Undergoing Two-Stage Reconstruction with Acellular Peritoneal Matrix

Characteristic	Value (%)
Subject demographics	
Age at surgery, yr	
Mean ± SD	49.4 ± 8.5
Range	32–67
Sex (female)	25
Race	
White	24
Unknown	1
Ethnicity	
Non-Hispanic	24
Hispanic	1
BMI, kg/m^2	
Mean ± SD	25.0 ± 3.9
Range	20.4–30.9
Subject medical history	
Diabetes mellitus	0
Hypertension	6
Cancer outside the breast	2
Osteoarthritis	1
Rheumatoid arthritis	0
Autoimmune disease	0
History of smoking	8
Currently smoking	0
Family history of breast cancer	16
BRCA1 or *BRCA2* mutations	5

BMI, body mass index.

Table 3. Breast History Summary of All Patients (*n* = 25) Undergoing Two-Stage Reconstruction with Acellular Peritoneal Matrix*

Breast History	Right Breast	Left Breast
Degree of breast ptosis		
None	3	4
Mild	9	10
Moderate	9	5
Severe	2	2
Pseudo	1	1
Not assessed	1	3
Prior lumpectomy	3	2
Prior mastectomy	0	0
Prior reconstruction	0	0
Prior augmentation	0	0
Prior reduction mammaplasty	0	0
Prior mastopexy	0	0
Type of breast cancer		
None	15	11
Unknown	1	2
Infiltrating lobular carcinoma	3	3
Infiltrating ductal carcinoma	1	5
Ductal carcinoma in situ	4	3
Not available	1	1
Breasts undergoing planned mastectomy and reconstruction	23	21

*Describes all breasts separately, before surgery and regardless of surgical intent. Not all breasts underwent mastectomy and reconstruction (see Table 4).

Surgical Indications and First-Stage Reconstruction

Five subjects were *BRCA1/2*-positive, and 22 of 44 mastectomies were oncologically indicated, with the remainder being prophylactic. Of the 44 mastectomies, 12 were nipple-sparing, six were skin-sparing, 23 were total, and three were modified radical. Lymph nodes were resected in 20 of the mastectomies.

All patients underwent immediate breast reconstruction with acellular peritoneal matrix and tissue expanders after evaluation of skin flap perfusion. Before insertion, the acellular peritoneal matrix was hydrated in saline (14 of 44), antibiotic solution (28 of 44), or povidone-iodine solution (two of 44). The average tissue expander size at the time of reconstruction was 451.1 ± 121.7 cc (range, 250 to 700 cc) on the right and 444.0 ± 125.0 cc (range, 250 to 700 cc) on the left, with

initial fill volumes of 194.1 ± 106.9 cc (range, 50 to 450 cc) on the right and 183.8 ± 100.5 cc (range, 30 to 400 cc) on the left (Table 4).

Postoperative Management and Tissue Expansion

Patients were asked to follow up with their surgeon at 1 and 2 weeks after their first-stage surgery, with 25 of 25 subjects adhering to follow-up.

Table 4. Summary of First-Stage Surgical Procedure and Surgeon-Rated Handling of Acellular Peritoneal Matrix

	Right Breast	Left Breast
Mastectomy	23	21
Type of mastectomy		
Nipple-sparing	6	6
Skin-sparing	3	3
Total	12	11
Modified radical	2	1
Radical	0	0
Weight of breast tissue excised, g		
Mean ± SD	515.4 ± 293.8	497.1 ± 277.9
Range	143–999	145–988
Lymph nodes removed	9	11
First-stage reconstruction		
Immediate reconstruction	23	21
Skin flaps determined to be well-vascularized	23	21
Method of flap assessment		
Visual	22	20
Indocyanine green	1	0
APM hydrated in		
Saline	7	7
Antibiotic solution	15	13
Povidone solution	1	1
APM hydration (surgeon rating)		
Good	22	18
Average	1	3
Poor	0	0
APM handling (surgeon rating)		
Good	19	17
Average	4	4
Poor	0	0
APM suturability (surgeon rating)		
Good	19	17
Average	5	4
Poor	0	0
APM strength (surgeon rating)		
Good	19	17
Average	4	4
Poor	0	0
Tissue expander size, cc		
Mean ± SD	451.1 ± 121.7	444.0 ± 125.0
Range	250–700	250–700
Initial tissue expander fill volume (cc)		
Mean ± SD	194.1 ± 106.9	183.8 ± 100.5
Range	50–450	30–400

APM, acellular peritoneal matrix.

Of the initial 25 subjects, 24 proceeded with tissue expansion in an outpatient setting. The average fill volume per visit was 61.4 ± 45.5 cc (range, −75 to 125 cc) on the right and 66.6 ± 41.5 cc (range, −70 to 250 cc) on the left. The average number of tissue expansions visits per subject was 4.5 ± 1.7 (range, 1 to 9). Final fill volume averaged 453.2 ± 165.5 (range, 150 to 775 cc) on the right and 464.5 ± 172.8 cc (range, 150 to 775 cc) on the left (Table 5).

Second-Stage Reconstruction and Secondary Procedures

Of the initial 25 subjects, 24 went on to have second-stage reconstruction. The average duration from the first to the second stage was 191.0 ± 68.8 days (range, 91 to 385 days). Of the initial 44 mastectomies, 40 underwent exchange with a permanent breast implant according to the study protocol (see below for study deviation) (Tables 6 and 7).

During the first-stage follow-up period, eight subjects underwent chemotherapy and three subjects underwent radiotherapy to the reconstructed breast. During the second-stage follow-up period, two subjects underwent chemotherapy.

For balancing procedures on the nonreconstructed breasts, three subjects underwent reduction mammaplasty and three underwent augmentation. Fat grafting was performed on 22 reconstructed breasts (Tables 6 and 7). All study subjects who underwent second-stage surgery followed up with their surgeon at 1 week, 1 month, 3 months, 6 months, and 1 year after reconstruction.

Table 5. Tissue Expansion Phase Summary

	No.	Right Breast	Left Breast
Tissue expansion visits			
Subject with at least one tissue expansion visit	24		
Subjects that completed tissue expansion	23		
No. of TE visits per subject			
Average ± SD	4.5 ± 1.7		
Range	1–9		
Tissue expander fill volume summary			
Fill volume per visit, cc			
Average ± SD		61.4 ± 45.5	66.6 ± 41.5
Range		−75–125	−70–250
Final fill volume, cc			
Average ± SD		453.2 ± 165.5	464.5 ± 172.8
Range		150–775	150–775

TE, tissue expansion.

Table 6. Second-Stage Surgical Summary

Characteristic	Value
No. of subjects that underwent second-stage reconstruction	24
Time from first- to second-stage procedure, days	
Mean	191.0 ± 68.8
Range	91–385
Chemotherapy	
During first-stage follow-up period	8
During second-stage follow-up period	3
Radiotherapy	
During first-stage follow-up period	3
During second-stage follow-up period	0

Table 7. Second-Stage Surgical Summary per Breast

	Right Breast	Left Breast
Reconstruction with a breast implant according to protocol	20	20
Incision location		
First-stage incision	11	12
Inframammary fold	9	8
Surgical adjustments to breast		
Sutures to adjust pocket location	8	5
Additional biological mesh	0	0
Capsulorrhaphy	2	3
Capsulotomy	1	2
Tissue excision	1	1
Capsule release (medial–inferior)	0	1
Breast implant type		
Saline	1	1
Silicone gel	19	19
Breast implant size, cc		
Average ± SD	516.8 ± 152.3	513.0 ± 156.8
Range	250–750	225–750
Reconstruction with autologous tissue flap (on reconstructed breast)		
DIEP flap	0	1
TRAM flap	2	0
Latissimus flap (with implant)	0	1
Secondary procedures (on contralateral, nonreconstructed breast)		
Breast augmentation	1	1
Reduction mammaplasty	2	1
Fat grafting	12	10

DIEP, deep inferior epigastric perforator; TRAM, transverse rectus abdominis myocutaneous.

Pathologic Analysis

A summary of results from the pathologic analysis is shown in Table 8. Of note, acellular peritoneal matrix resorption was graded as 1.79 ± 1.36 (range, 0 to 3), 2.00 ± 1.15 (range, 0 to 3), and 1.74 ± 1.33 (range, 0 to 3) at the pectoralis muscle interface, the central aspect, and the inframammary fold interface, respectively, with a grade of 2 representing moderate resorption. These pathologic samples were obtained an average of 184.28 ± 71.77 days (range, 70 to 385 days) after implantation. Newly formed fibroconnective tissue was graded as 1.73 ± 0.95 (range, 0 to 3), 1.85 ± 0.92 (range, 0 to 3), and 1.79 ± 1.03 (range, 0 to 3) at the pectoralis muscle interface, the central aspect, and the inframammary fold interface, respectively. Chronic inflammation was graded as 1.67 ± 0.78 (range, 0 to 3), 1.67 ± 0.68 (range, 0 to 3), and 1.71 ± 0.73 (range, 1 to 3) at the pectoralis muscle interface, the central aspect, and the inframammary fold interface, respectively. Figure 2 demonstrates hematoxylin and eosin–stained histologic slides from the central acellular peritoneal matrix and the control capsule (no acellular peritoneal matrix); the specimens were harvested 3 months after implantation at the second-stage surgery. Figure 2, *above*, shows grade 2/3 infiltration of patient cells into the acellular peritoneal matrix, with moderate product resorption and grade 2/3 chronic inflammation. Figure 2, *below*, shows similar grade 2/3 chronic inflammation, with no neovascularization. Figure 3 demonstrates a macroscopic view of the matrix while obtaining a punch biopsy from the central acellular peritoneal matrix during second-stage surgery.

Patient-Reported Health Outcomes and Final Aesthetic Assessment

Twenty-three patients completed the reconstruction module of the BREAST-Q at 6 months after second-stage surgery and 24 patients completed the module at 12 months after second-stage surgery (Table 9). Mean breast-specific satisfaction was 69.9 ± 17.2 (range, 42 to 100) at 6 months and 71.2 ± 15.5 (range, 39 to 100) at 12 months. Satisfaction with outcome (a measure of overall satisfaction) was 79.2 ± 19.35 (range, 35 to 100) at 6 months and 80.3 ± 17.53 (range, 35 to 100) at 12 months. Psychosocial well-being averaged 84.7 ± 17.48 (range, 49 to 100) at 6 months and 81 .6 ± 16.04 (range, 47 to 100) at 12 months and physical well-being: chest averaged 82.2 ± 19.51 (range, 13 to 100) at 6 months and 79.0 ± 15.74 (range, 50 to 100) at 12 months.

Adverse Events

The summary of adverse events is shown in Tables 10 through 12. One patient withdrew from the study after experiencing wound breakdown before tissue expansion. Revision of the scar and further reconstruction was considered; however, the patient and surgeon made the decision to remove the implant and acellular peritoneal matrix after learning that the patient required chemotherapy and did not wish to delay treatment. Sixteen reconstructed breasts sustained

Table 8. Histologic Scoring Summary from Biopsy Specimens Obtained during Second-Stage Surgery*†

Variable	PM–APM Interface	Central APM	IMF–APM Interface	Control Biopsy Specimen
Interface encapsulation				
Mean ± SD	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Range	0–0	0–0	0–0	0–0
No.	40	39	40	15
Interface inflammation				
Acute				
Mean ± SD	0.23 ± 0.53	0.23 ± 0.61	0.12 ± 50	0.16 ± 0.53
Range	0–2	0–3	0–3	0–3
No.	43	43	43	43
Chronic				
Mean ± SD	1.67 ± 0.78	1.67 ± 0.68	1.71 ± 0.73	1.38 ± 0.62
Range	0–3	0–3	1–3	0–3
No.	43	43	42	42
Eosinophilic				
Mean ± SD	0.49 ± 0.67	0.47 ± 0.63	0.44 ± 0.67	0.30 ± 0.51
Range	0–2	0–2	0–2	0–2
No.	43	43	43	43
Neovascularization				
Interface				
Mean ± SD	1.28 ± 0.65	1.13 ± 0.47	1.27 ± 0.51	1.0 ± 0.59
Range	0–3	0–2	1–3	0–3
No.	39	38	37	29
Internal				
Mean ± SD	0.40 ± 0.87	0.41 ± 0.84	0.41 ± 0.98	1.69 ± 0.75
Range	0–3	0–3	0–3	1–3
No.	25	27	29	14
Cellular infiltration				
Interface				
Mean ± SD	1.59 ± 0.85	1.59 ± 0.68	1.87 ± 0.70	1.12 ± 0.54
Range	0–3	0–3	0–3	0–2
No.	39	37	38	27
Internal				
Mean ± SD	0.52 ± 0.92	0.70 ± 0.91	0.61 ± 0.96	1.92 ± 1.32
Range	0–3	0–3	0–3	0–3
No.	25	27	28	13
Product resorption				
Mean ± SD	1.79 ± 1.36	2.00 ± 1.15	1.74 ± 1.33	N/A
Range	0–3	0–3	0–3	N/A
No.	43	42	42	N/A
Newly formed fibroconnective tissue				
Mean ± SD	1.73 ± 0.95	1.85 ± 0.92	1.79 ± 1.03	1.18 ± 0.98
Range	0–3	0–3	0–3	0–3
No.	42	42	40	38

PM, pectoralis major; APM, acellular peritoneal matrix; IMF, inframammary fold.
*Mean duration from implant to biopsy specimen collection ± SD was 184.28 ± 71.77 days (range, 70 to 385 days).
†0 = none, 1 = minimal, 2 = moderate, and 3 = extensive.

at least one complication (36 percent). Seroma and hematoma occurred in one of 44 breasts (2.3 percent) and two of 44 breasts (4.6 percent), respectively. Wound dehiscence occurred in four of 44 breasts (9.1 percent). The total reoperation rate was seven of 44 (15.9 percent). Erythema requiring antibiotics was observed in four of 44 reconstructed breasts (9.1 percent), and all cases resolved without implant removal. Mastectomy flap necrosis occurred in one of 44 breasts (2.3 percent) and required débridement in the operating room. Capsular contracture was evaluated at the time of implant exchange and at each follow-up visit up to and including the final 12-month postoperative visit. There were no cases of capsular contracture identified. Eight of the listed complications met the definition of a serious adverse event (SAE),[16] seven of which were breast-related [seven of 44 (15.9 percent)]. Three subjects experienced reconstruction failure resulting in expander and or acellular peritoneal matrix removal (6.8 percent); wound dehiscence preceded all three failures (Table 13). One patient who underwent deep inferior epigastric perforator flap reconstruction of a failed immediate reconstruction also elected to undergo transverse rectus abdominis myocutaneous flap reconstruction of the contralateral reconstructed breast for

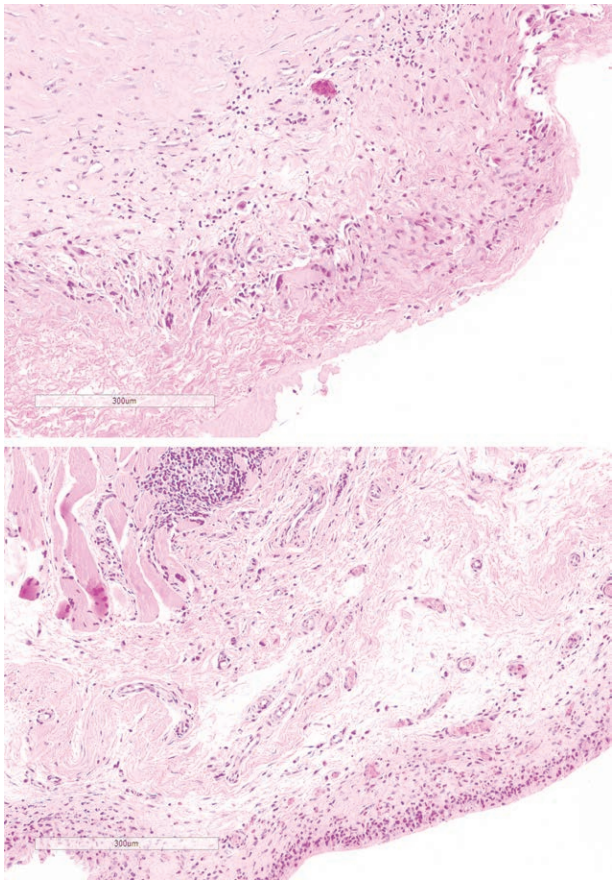

Fig. 2. (*Above*) Hematoxylin and eosin–stained histologic slide from the central acellular peritoneal matrix harvested 6 months after implantation at the second-stage surgery. There is grade 2/3 infiltration of patient cells into the acellular peritoneal matrix and grade 2/3 chronic inflammation. Product resorption was grade 2/3, or moderate. (*Below*) Hematoxylin and eosin–stained histologic slide from the control capsule (containing no acellular peritoneal matrix) harvested 3 months after implantation at the second-stage operation. The native capsule shows grade 2/3 chronic inflammation with no neovascularization.

balancing. This alteration was not attributable to a breast-related adverse event and therefore did not fit the U.S. Food and Drug Administration definition of reconstructive failure. Similarly, another patient underwent a transverse rectus abdominis myocutaneous flap of an immediate reconstruction that was healing well; in this case, the decision to abandon the expander before the second stage was made because of the unanticipated need for radiotherapy. Again, this did not fit the definition of reconstructive failure. We excluded both of these patients from subsequent analysis of the second-stage surgery. The remainder of adverse events were considered minor. No complications were directly attributed to the implanted acellular peritoneal matrix by the study monitor.

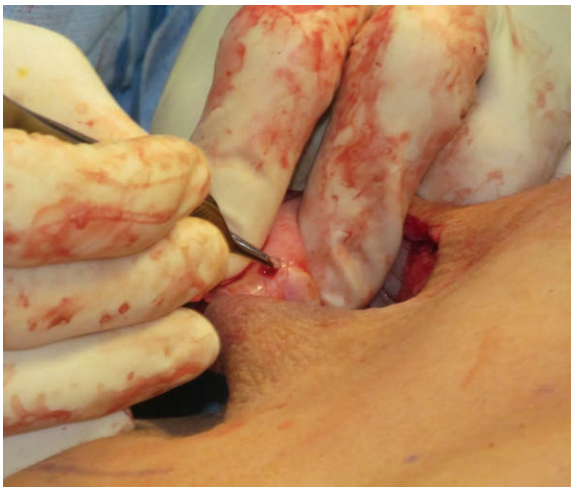

Fig. 3. Macroscopic view of the implant capsule during second-stage surgery (at 160 days after implantation). The matrix is well adhered, and a punch biopsy specimen is being obtained from the central acellular peritoneal matrix.

Table 9. Summary of Mean BREAST-Q Scores Obtained at 6 and 12 Months Postoperatively

Variable	6 Mo after Second Stage	12 Mo after Second Stage
No.	23	24
Satisfaction with Breasts		
Mean ± SD	69.9 ± 17.2	71.2 ± 15.5
Range	42–100	39–100
Satisfaction with Outcome		
Mean ± SD	79.2 ± 19.35	80.3 ± 17.53
Range	35–100	35–100
Psychosocial Well-being		
Mean ± SD	84.7 ± 17.48	81 .6 ± 16.04
Range	49–100	47–100
Physical Well-being: Chest		
Mean ± SD	82.2 ± 19.51	79.0 ± 15.74
Range	13–100	50–100

Table 10. Summary of Adverse Events Experienced during the Reconstruction Period

Adverse Events	Breast-Related	Non–Breast-Related
No. of subjects with AE	12/25	11/25
No. of breasts experiencing AE	16/44	—
Duration from procedure to AE, days		
Mean ± SD	126.1 ± 171.8	83.8 ± 108.9
Range	0–586	0–316

AE, adverse event.

Surgeon Rating of Acellular Peritoneal Matrix

The surgeon-rated opinion of acellular peritoneal matrix is summarized in Table 4. Surgeons rated hydration of the implant as good in 40 of 44 reconstructions, and average in four of 44.

Table 11. Total Adverse Events Experienced during the Reconstruction Period

Adverse Event	No.
Reconstructed breasts ($n = 44$)	
Dehiscence	4
Erythema	4
Breast pain	3
Hematoma	2
Seroma	1
Flap necrosis	1
Fever	1
Excoriation	1
Nodule	1
Implant malposition	1
Capsular contracture	0
Per subject ($n = 25$)	
Rash	3
Neck pain	1
Chest wall pain	1
Vomiting	1
URTI	1
UTI	1
PE	1
Urinary retention	1
Drug reaction	1
Nephrolithiasis	1

URTI, upper respiratory tract infection; UTI, urinary tract infection; PE, pulmonary embolus.

Table 12. Summary of Adverse Events Experienced during Reconstruction Period

	Breast-Related	Non–Breast-Related
Severity		
Mild	5	7
Moderate	10	7
Severe	7	1
Association		
Related to right breast	13	0
Related to left breast	9	0
Related to right APM	0	0
Related to left APM	0	0
Systemic/non–breast-related	0	15
Action taken		
None	4	3
Concomitant medication	7	7
Concomitant procedure	9	0
Other	2	5
Outcome		
Recovered without sequelae	20	15
Recovered with sequelae	0	0
Not yet recovered	1	0
Unknown	1	0
Permanent impairment	0	0
Serious adverse events	7	1
Seroma	1	0
Fever	0	1
Dehiscence	4	0
Hematoma	1	0
Flap necrosis	1	0
Reconstruction failure	3	—

APM, acellular peritoneal matrix.

Handling was reported as good in 36 of 44 cases and average in eight of 44. Strength was noted as good in 36 of 44 cases.

DISCUSSION

In the United States, two-stage implant-based reconstruction with tissue expansion is the most commonly used breast reconstruction technique.[17] The use of acellular matrix products for creation of a partial submuscular implant pocket is a common procedure, with the aim of increasing initial fill volumes and improving breast contour.[3,6,10,18] Prepared products may be of human, porcine, or bovine origin, with human-derived AlloDerm (LifeCell Corp., Branchburg, N.J.) the most extensively studied in the literature.[11,19]

The present study examined the use of a porcine-derived peritoneal matrix implant for two-stage tissue expander–based breast reconstruction. The primary outcome was safety of the implant, with secondary outcomes including handling, strength, histologic characteristics, and patient-reported satisfaction.

Implant Safety

Although acellular surgical mesh products have gained widespread acceptance in breast reconstruction, concerns remain that their use may increase the risk of postoperative complications, including infection, seroma, and implant failure.[8,10,20] The risk of complications occurring following acellular surgical mesh implantation in immediate breast reconstruction varies widely in the literature.[18] In a prospective, randomized, controlled trial comparing two human-derived acellular dermal matrix products [AlloDerm and DermaMatrix (Synthes, Inc., West Chester, Pa.)], seroma rates of 6.1 percent and 3.1 percent, respectively, were observed. The same study had a diagnosed infection rate of 13.9 percent and 16.3 percent, and tissue expander removal was required in 5 percent and 11.2 percent in AlloDerm and DermaMatrix, respectively.[21] In a study comparing two xenogenic acellular dermal matrix products [porcine-derived Strattice (LifeCell) and bovine-derived SurgiMend (TEI Biosciences, Boston, Mass.)], an overall seroma rate of 8.6 percent was observed, with no significant difference between the two products in terms of reoperation or reconstructive failure.[22] A recent meta-analysis comparing the use of acellular dermal matrix products with standard submuscular techniques found that use of acellular dermal matrix increased the risk of infection, seroma, and mastectomy flap necrosis, but did not increase the risk of implant loss or reoperation.[23] Capsular contracture is a purported benefit of decellularized matrix product use in breast reconstruction; the present study

Table 13. Causes and Sequelae of Reconstruction Failure

Subject	Stage	Serious Adverse Event	Action Taken	Outcome	Further Procedures
1	First	Right breast wound dehiscence	TE and APM removal	Recovered	Unknown; patient withdrawn
2	First	Right breast wound dehiscence	TE and APM removal	Recovered	Implant and LD flap
3	First	Left breast wound dehiscence	TE removal	Recovered	DIEP flap

TE, tissue expander; APM, acellular peritoneal matrix; LD, latissimus dorsi; DIEP, deep inferior epigastric perforator.

did not identify any cases of contracture through 12 months after implant exchange. Longer trials would be required to determine the long-term capsular contracture risk in immediate breast reconstruction using acellular peritoneal matrix. There are very few prospective single-arm or randomized controlled trials in the literature examining the complication profiles of matrix products. Although there is some suggestion that certain products may yield lower complication rates, this is not demonstrated on meta-analyses.[18,24,25]

The present study demonstrates a complication profile consistent with previously described immediate breast reconstruction using acellular matrix tissue.[23] Given the small sample size of this feasibility study and lack of randomization, comparative judgments between this product and other commercially available products cannot be made. Further prospective comparison studies with larger sample sizes are required to determine the overall efficacy of porcine-derived acellular peritoneal matrix.

Histologic Characteristics

A pathologist analyzed the biopsy specimens obtained during the second-stage procedure for signs of inflammation, neovascularization, cellular infiltration, and product resorption as described previously.[26–28] Analysis demonstrated that chronic inflammatory changes predominated at the host-matrix interface, with minimal acute inflammation at an average collection time of 6 months after implantation. Interface cellular infiltration, product resorption, and new fibroconnective tissue all demonstrated moderate changes (Fig. 2, *above*).

These histologic characteristics suggest that following a stage of inflammatory changes, product resorption occurs with concurrent replacement of xenogeneic graft material with host fibroconnective tissue.[27] The long-term fate of the matrix material is unknown—extended histologic studies are difficult, as there are no standardized operations beyond the implant exchange. Randomized comparison trials are required to evaluate the histologic differences between this matrix and other commercially available options.

Surgeon Rating and Patient-Reported Health Outcomes

Investigating surgeons found the porcine peritoneum to handle well, with good strength and suturability (Table 4). Further comparative studies are indicated to evaluate the handling characteristics and favorability between acellular peritoneal matrix and other commercially available materials.

The BREAST-Q was chosen to evaluate patient-reported satisfaction following tissue expander–based reconstruction using acellular peritoneal matrix. The questionnaire provides an objective and validated way of evaluating the impact of breast reconstruction.[29,30] Patient responses indicate that mean BREAST-Q scores in the domains measured at 6 months and 12 months postoperatively are consistent with previously reported scores for satisfaction after alloplastic reconstruction (Table 9).[31] Representative preoperative and postoperative (12 months after implant exchange) photographs are demonstrated in Figure 4.

Limitations

This study has limitations. As a feasibility trial, total enrollment was low. Patients were comparatively healthy, with a low body mass index, and were nonsmokers, with minimal medical comorbidities—all factors that could affect complications. Surgeons and patients were not blinded to the treatment. Variability in perioperative management, including administration of antibiotics, variations in expansion protocol, drain placement, and drain duration, could have an had effect on outcomes. There was some ambiguity in the diagnosis of adverse events, including wound dehiscence and skin necrosis. These diagnoses were at the discretion of the attending surgeon, and may have reflected the variability in provider terminology in the general plastic surgery community. It is important to recognize that use of surgical mesh products in breast reconstruction comes with a learning curve. That the investigating surgeons tend to have more experience with these products might prevent these results from

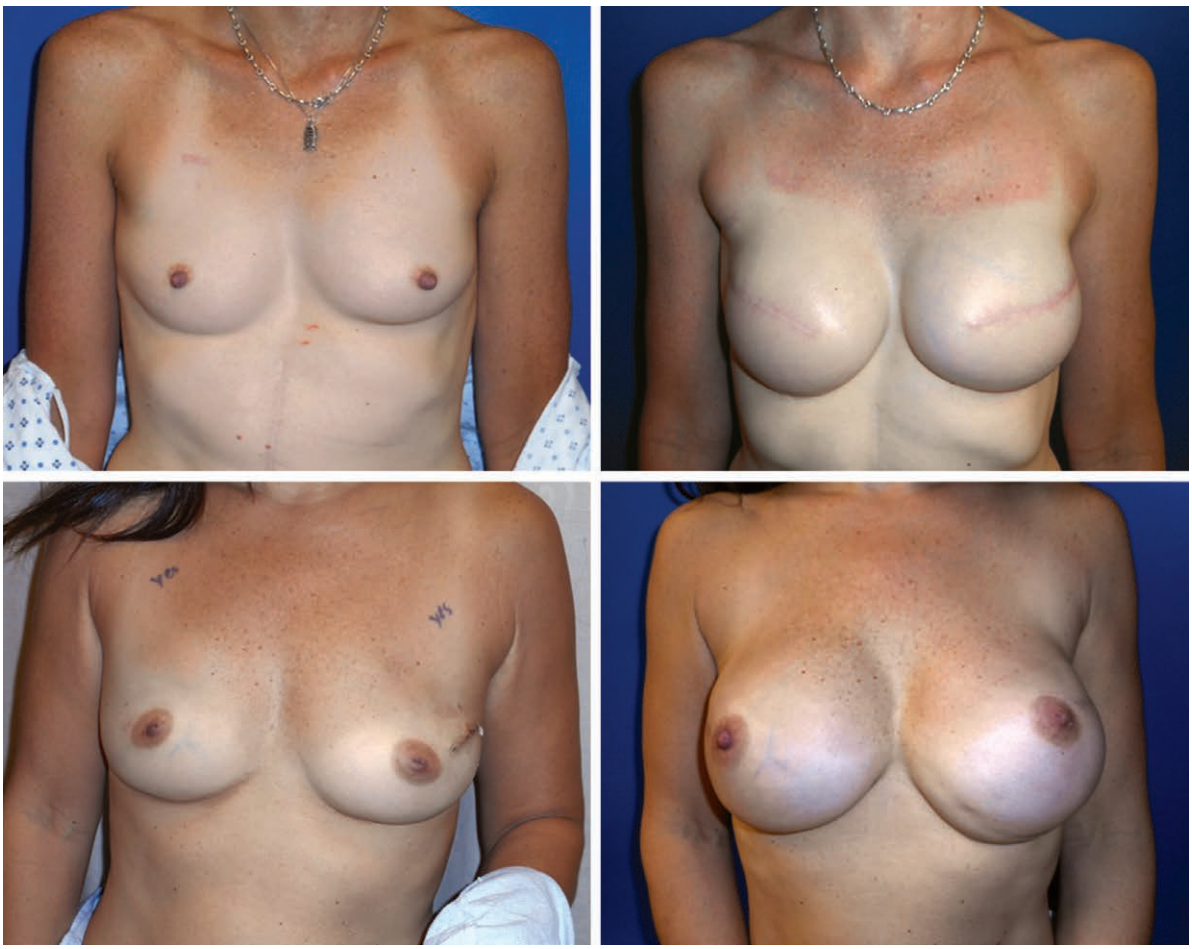

Fig. 4. (*Above*, *left*) Preoperative photograph of a patient who underwent bilateral simple mastectomy and immediate two-stage reconstruction with tissue expanders and acellular peritoneal matrix. (*Above*, *right*) Postoperative photograph of the same patient at the final study follow-up 12 months after implant exchange. (*Below*, *left*) Preoperative photograph of a patient who underwent bilateral nipple-sparing mastectomy and immediate two-stage reconstruction with tissue expanders and acellular peritoneal matrix. A biopsy scar is visible on the left lateral breast. (*Below*, *right*) Postoperative photograph of the same patient at the final study follow-up 12 months after implant exchange. She subsequently underwent correction of nipple asymmetry.

being generalizable to all surgeons. Because of the small sample size and lack of multiple treatment arms, we cannot determine any advantages or disadvantages of this matrix compared to existing matrix products. Lastly, although writing of the manuscript and interpretation of the data were performed without industry involvement or approval, it is prudent to recognize that this trial was industry-initiated and industry-sponsored.

CONCLUSIONS

This prospective single-arm trial evaluated the safety of a novel porcine-derived acellular peritoneal matrix product for two-stage tissue expander–based breast reconstruction. The results suggest that acellular peritoneal matrix has an acceptable safety profile for use in this patient population. In terms of secondary outcomes, patient satisfaction was high, and surgeons reported favorable handling characteristics. Histologic changes to this xenograft matrix occurred with a degree of chronic inflammation and graft resorption. Future prospective comparative studies are required to evaluate the efficacy, complications, and cost-effectiveness of porcine-derived acellular peritoneal matrix compared to currently available products.

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