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Breast

Implant-based Breast Reconstruction Outcomes Comparing Freeze-dried Aseptic Alloderm and Sterile Ready-to-use Alloderm

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Background: The use of acellular dermal matrix has revolutionized implant-based breast reconstruction in the 21st century. There have been a number of different dermal matrices introduced to clinical use and their equivalence has been debated. The purpose of this study is to examine a sequential series of acellular dermal matrix assisted implant-based breast reconstructions by a single surgeon and to compare the outcomes between a freeze-dried (FD) Alloderm cohort and a sterile ready to use Alloderm cohort.

Methods: After institutional review board approval, all consecutive implant-based breast reconstructions of a single surgeon (D.S.W.) from January 2009 to June 2016 were examined. Two hundred thirty-six patients received either FD Alloderm in the first 151 breasts reconstructed or sterile ready-to-use Alloderm in the last 227 breasts.

Results: The FD Alloderm patients had more tissue expander reconstructions performed and were all subpectoral placement. The ready-to-use Alloderm patients had more direct-to-implant procedures and some prepectoral placements. The complication rates were similar for seroma, hematoma, skin necrosis, and dehiscence. There were more infections, implant losses, and unexpected reoperations in the FD Alloderm group.

Conclusion: The rate of infection, explantation, and unexpected reoperation was lower in the sterile ready-to-use Alloderm group versus the FD Alloderm group.
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INTRODUCTION

The use of acellular dermal matrix (ADM) has revolutionized implant-based breast reconstruction allowing for greater initial fill volumes and shorter expansion times in tissue expander cases and the ability to go direct to implant more often in immediate reconstruction with evidence of decreased capsular contracture.[1] There have been a number of ADMs introduced to the market and the question of whether or not they are all equivalent has been debated. Although many studies have elicited the benefits of utilizing ADM, others have warned against its use noting higher rates of infections, seroma, explantation, and cost. The potential benefits of using ADM would appear to outweigh the risks, as matrix is now used in the majority of implant based post-mastectomy breast reconstructions.[2–4]

In 2006 LifeCell Corporation (Branchburg, NJ) introduced Alloderm for use in breast reconstruction. The product is human cadaveric dermis, processed in an aseptic manner to eliminate cellular and immunogenic components while preserving the dermal matrix structure. The product is freeze-dried (FD), packaged with cryopreservatives, and requires rehydration for 10–40 minutes before implantation. The product is aseptic, not sterile, and hence no sterility assurance level (SAL) can be given.

In about 2011 LifeCell introduced Alloderm ready to use (RTU) (ready-to-use), which is stored wet in preservative solution and terminally sterilized with gamma radiation. It can be used within a few minutes after package opening. Saline rinses to remove the preservative solution are recommended. Alloderm RTU has a SAL of 10^{-3}

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(probability of 1 per 1,000 sterilized items having a viable microorganism).

In 2014, perforated RTU was introduced to the market. This product is the same as Alloderm RTU from a preparation and sterility basis, but the contour shaped pieces are perforated.

The purpose of this study is to compare the postoperative complication rates in implant-based breast reconstruction between aseptic FD Alloderm and prehydrated, terminally sterilized RTU Alloderm.

METHODS

We performed a retrospective study of all consecutive post-mastectomy implant based breast reconstructions of a single surgeon (D.S.W.) from January 2009 to June 2016. Approval from the Institutional Review Board was obtained. Charts were reviewed to obtain demographic data, co-morbidities, oncologic management details, and specific surgical details on patients undergoing implant-based reconstruction. All patients had Alloderm utilized during this time period with prosthetic reconstructions. All breasts undergoing reconstruction with tissue expanders or permanent implants were included for analysis. Alloderm FD was used in the first 151 breasts, and then every patient received Alloderm RTU for the next 227 breasts. The primary outcomes of interest were infection, seroma, hematoma, skin necrosis, explantation, and unexpected reoperation.

We adopted a broad definition of infection as follows: (1) purulent drainage with or without positive culture, (2) positive periprosthetic cultures with or without purulence or (3) any infection suspicion by the surgeon (for example cellulitis) for which antibiotics were prescribed whether oral or intravenous.[5] Seroma was defined as any recognized fluid collection after drain removal whether aspirated, re-drained, or not. Hematoma was any postoperative collection of blood, minor or major, whether evacuated or not. Mastectomy skin flap necrosis was defined as any evidence of ischemia from minor blistering to full thickness necrosis whether debrided or not. Dehiscence was defined as any wound edge separation whether associated with mastectomy skin flap necrosis or not, including thinning of the incision with impending device exposure, all of which were excised and tabulated both as dehiscence and unexpected reoperation. Unexpected reoperation included washouts and implant exchange for suspected infection, debridement of mastectomy skin flap necrosis or management of dehiscence or impending exposure, evacuation of hematoma, evacuation and drain replacement for seroma, or removal of device for infection (explantation). Management of capsular contracture was not included as an unexpected reoperation in this study. Expected reoperations included expander-to-implant second stage procedures, nipple areola procedures, and aesthetic revisions such as fat grafting and symmetry procedures.

During the 6-year study period, 238 women underwent implant-based breast reconstruction and Alloderm was routinely used. There were 378 breasts reconstructed during this time. In the majority of cases the tissue expander or implant was placed under the pectoralis major muscle with an inferior lateral Alloderm sling. In the later part of the study, there was a subset of patients who had prepectoral placement of the device utilizing 2 pieces of Alloderm RTU perforated contour pieces for total anterior implant coverage. Patient outcomes were recorded for at least 6 months after the definitive reconstruction, whether they were expander/second stage implant placement or direct to implant cases.

During the entire study period, closed suction drains were kept in place until drain output was <20 ml in 24 hours. Two drains were used in the majority of cases. In cases utilizing non-perforated Alloderm (both FD and RTU), one drain was placed in the sub-Alloderm periprosthetic space and one in the subcutaneous plane. In cases using perforated Alloderm RTU (the last 123 breasts), both drains were placed subcutaneously. All patients were treated with prophylactic oral antibiotics until the last drain was removed (doxycycline).

Every tissue expander was a Dermaspan textured surface device and every implant was a Mentor round, smooth surface silicone gel implant of varying profile.

Immediate intraoperative tissue expansion was performed routinely in the operating room as tolerated to fill the residual skin envelope without tension. Implants were chosen by considering desired base diameter and volume.

Bacitracin antibiotic irrigation was used from 2009 to 2013 and then the use of triple antibiotic (gentamicin, cephalexin, bacitracin) became the routine.

Analysis of each breast on the basis of age, BMI, co-morbidities, surgical indication, adjuvant/neoadjuvant chemotherapy, history of radiation, smoking history, initial tissue expander fill volume, and size of implant in the direct to implant cases was done.

Complications were evaluated on a per breast basis. Fischer's exact test was performed to compare outcomes among different types of Alloderm. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Between January 2009 and June 2016, 236 women underwent implant-based breast reconstruction with Alloderm. Of these 236 women, 94 underwent unilateral reconstruction and 142 bilateral reconstructions. The indication for mastectomy was cancer in 116 breasts and prophylaxis in 262 breasts. The mean patient age was 49.7 years. The mean BMI was 26.5. Additional details are displayed in Table 1.

A total of 378 breasts were reconstructed with ADM. FD Alloderm was used in 151 consecutive breasts and Alloderm RTU in 227 breasts. The mean follow-up was longer in the FD group. Patients in the FD group were also younger and their BMI lower. There were no other significant differences in the two cohorts' patient specific variables (Table 1).

The method of reconstruction was different in the 2 groups in that tissue expanders were more common in the FD group, direct to implant was more common in the RTU group and the pre-pectoral reconstructions were limited

Table 1. Patient Comorbidities

	Total	FD Alloderm	RTU Alloderm	*P*
No. breasts	378	151	227	
Smoking*	48	19	29	1.00
Hypertension	88	39	49	0.38
Diabetes	17	4	13	0.21

* Patients smoking within a year of initial presentation were considered smokers. All were required to quit and to pass a urine test for nicotine metabolites before undergoing breast reconstruction; hence, there were no active smokers in the series, to our knowledge.

to the RTU group. This distribution reflects the surgeons evolving preference for the type of implant-based reconstruction and was independent of the type of Alloderm decision (Table 2).

Complications were reported for the individual breast and are compiled in Table 3. Recorded complications of tissue expander reconstructions are representative of the first stage TE placement only. The rate of infection, implant loss, and unexpected reoperation were significantly higher in the FD group than the RTU group. The rates of seroma, hematoma, skin necrosis, and dehiscence were not different in the 2 groups. There was no difference in the rate of infection or implant loss with body mass index over 30 nor with the diagnosis of diabetes. Unexpected reoperation was due to hematoma in 7 patients, dehiscence or impending exposure in 8 patients, skin necrosis in 20 patients, and infection in 21 patients. Implant losses were all associated with infection.

DISCUSSION

ADM is now utilized by the majority of plastic surgeons for implant-based breast reconstruction.[2–4] Greater initial fill volumes and shorter expansion times in tissue expander cases and the ability to go direct to implant more often in immediate reconstruction with the use of ADM has been demonstrated. Capsular contracture rates have decreased and the routine use of ADM has improved the ease and quality of immediate breast reconstructions.[6]

Table 2. Method of Reconstruction

	FD Alloderm	RTU Alloderm
Delayed tissue expander subpectoral	30	42
Immediate tissue expander subpectoral	102	40
Immediate direct-to-implant subpectoral	19	127
Immediate direct-to-implant prepectoral	0	18

Table 3. Summary of Complications

	Freeze-dried Alloderm N = 151	RTU Alloderm N = 227	*P*
Infection	**26 (17%)**	**18 (7.9%)**	**0.0083**
Seroma	14 (9.3%)	19 (8.4%)	0.85
Hematoma	3 (2.0%)	4 (1.8%)	1.00
Skin necrosis	10 (6.6%)	21 (9.3%)	0.45
Dehiscence	8 (5.3%)	7 (3.1%)	0.29
Implant loss	**14 (9.3%)**	**8 (3.5%)**	**0.02**
Unexpected reoperation	**34 (22.5%)**	**22 (9.7%)**	**0.001**

Boldface values indicate statistically significant *p* values: <0.05.

There has been significant concern in the literature about infection rates in breast reconstruction with the use of dermal matrices. Weichman et al found a difference in infection rates between FD Alloderm and RTU Alloderm.[7] Their prospective study compared RTU Alloderm, total submuscular coverage, and FD Alloderm and found no difference in the infection rate between RTU and total submuscular coverage. They found diabetes, seroma, mastectomy skin flap necrosis, and aseptic FD Alloderm were all independent predictors of infectious complications. Lewis et al[8] found overall significantly less complications in RTU versus FD group. Hanson et al[9] found a higher failure rate in the FD group versus RTU. Parikh et al[10] found a higher explantation rate with FD versus RTU.

Conversely in a 2014 study, Yuen et al[11] reported that there was a clinically higher complication rate in the RTU group versus a control group using FD but there was a significantly higher BMI in the RTU group as well confounding the findings.

On the other hand, Buseman et al[12] found no difference in infection rates when comparing FD Alloderm with RTU Alloderm. Marcarios et al[13] did a meta-analysis of 2 studies comparing FD with RTU and determined there were no differences in any complications between the 2 groups. These 2 studies were the Weichman and the Yuen studies both of which had found differences in the FD and RTU groups originally.

Uniquely, our present study is a sequential comparison of aseptic FD Alloderm to sterile RTU Alloderm by a single surgeon. An issue with most previous studies has been the failure to account for the inevitable variability between plastic surgeons and between institutions. Our intraoperative technique and protocol changed little over the 6½-year period except with the switch from bacitracin irrigation to triple antibiotic irrigation. The patient populations were similar. There was an evolution from primarily subpectoral tissue expanders to mostly subpectoral direct to implant and then direct to implant prepectoral over the study period. We recognize that this is also an inherent limitation of the study in that the type of reconstruction was not controlled for. Finally, the senior surgeon began routine use of FD Alloderm in 2007 and used it consistently until 2011 when Alloderm RTU was introduced and he switched immediately and completely to utilizing the RTU product.

We have a complication rate that is decreasing over time with the routine use of Alloderm in implant-based breast reconstruction with a decreasing infection rate and a rising success rate. Over time, we have gained experience, decreased our operating times, improved our aesthetic results, and transitioned from subpectoral tissue expander 2 stage reconstructions to primarily one stage, prepectoral direct to implant reconstructions. We have recently broadened our inclusion criteria to include more ex-smokers, diabetics, and obese patients with larger mastectomy volumes and implant sizes.

CONCLUSION

Our data demonstrate that the use of ADM is associated with falling complication rates despite our broad and

inclusive definition of the relevant complications. We find that the rate of infection, the rate of explantation, and the rate of unexpected reoperation is lower in the sterile Alloderm RTU group versus the aseptic FD Alloderm group.

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