Tissue Expander Breast Reconstruction Using Prehydrated Human Acellular Dermis

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Introduction: Human acellular dermal matrices help facilitate immediate tissue expander-implant breast reconstruction by providing support to the inferolateral pole, improving control of implant position, and enhancing early volume expansion. Although several freeze-dried human acellular dermal products have demonstrated reasonable safety and efficacy in immediate tissue expander-implant breast reconstruction, no dedicated studies have evaluated clinical outcomes of prehydrated human acellular dermal matrix (PHADM) in breast reconstruction.

Methods: The outcomes of 121 consecutive tissue expander reconstructions performed by the senior author using PHADM were evaluated.

Results: Mean intraoperative tissue expander fill volume was 256.6 ± 133 mL, 60% of final expander volume. Patients required an average of 3.2 additional expansions prior to tissue expander-to-implant exchange. Mean follow-up period after reconstruction was 44 ± 26.5 weeks. Complications occurred in 20 (16.5%) breasts, including 9 (7.4%) soft-tissue infections, 8 (6.6%) partial mastectomy flap necroses, and 2 (1.7%) seromas. Eleven (9.1%) breasts ultimately required explantation. Patients receiving radiation demonstrated a strong trend toward greater complications (30.8% vs. 13.7%, $P = 0.0749$).

Conclusions: The outcomes and complication rates of PHADM tissue expander breast reconstruction are comparable to those reported with freeze-dried human acellular dermis.

Key Words: acellular dermis, breast reconstruction, FlexHD, tissue expansion

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Over 50,000 tissue expander-implant breast reconstructions are performed annually, accounting for approximately 60% of all postmastectomy breast reconstructions.[1] Of these, increasing percentage of surgeons are electing to use human acellular dermis to assist with tissue expander-based primary breast reconstruction.[2–12] In 2005, Breuing and Warren[2] reported the use of human acellular dermis in prosthetic breast reconstruction. Since then, several authors including Spear,[3] Salzberg,[4] Zienowicz and Karacaoglu,[5] Topol et al,[6] Bindingnavele et al,[7] Sbitany et al,[8,9] and Chun et al[10] have reported favorable outcome studies using freeze-dried human acellular dermis.[2–10] By disinserting the pectoralis muscle and recreating the lower pole with an acellular dermal "sling," surgeons can more precisely define the inframammary fold and place the expander in a more anatomically correct position vis-à-vis the natural soft-tissue shape of a normal, ptotic breast.[2–10] Furthermore, by producing a larger pocket free from the confines of the pectoralis muscle insertion inferiorly, acellular dermis permits greater intraoperative tissue expander fill volumes. This early and rapid expansion may help to improve the overall cosmetic outcome.[2,3,8,9]

Several human acellular dermal matrices are available, including Alloderm, Neoform, DermaMatrix, and FlexHD. Prehydrated human acellular dermal matrix (PHADM) by virtue of its prehydrated state may enhance operative efficiency by obviating a reconstitution phase. Although numerous studies on the outcomes and efficacy of freeze-dried acellular dermis-assisted breast reconstruction are present in the literature,[2–7,9–12] at the time of manuscript preparation, no PHADM-dedicated studies exist.

METHODS

Patients and Study Design

The institutional review board approved this study. A retrospective medical record review was performed on patients who underwent PHADM-assisted tissue expansion reconstruction by a single board-certified plastic surgeon (J.Y.S.K.).

Demographic information was collected, and efficacy measures included initial intraoperative tissue expander fill volumes, final tissue expander volume, number of serial expansions, and time to completion of reconstruction. Complications were reviewed and categorized as soft-tissue infection, mastectomy flap necrosis, seroma, hematoma, dehiscence or exposure and explantation.

Surgical Procedure

The pectoralis muscle is first disinserted, and a 6 × 16 cm thick category piece of PHADM (Flex HD, Musculoskeletal Transplant Foundation, Edison, NJ) is secured to the ensuing lower pole defect using 3-0 Vicryl suture (Ethicon Inc., Somerville, NJ) (Figs. 1A, B). The inferior aspect of the PHADM is sutured to the inframammary fold while the lateral aspect is sutured to the serratus muscle-fascia directly. A tissue expander (Mentor CPX3, Mentor, Santa Barbara, CA or 133 MV Biodimensional Expander, Allergan, Irvine, CA) is then placed in the submuscular and subgraft space (Fig. 1C). Once the muscle and graft interface is secured, two 7-mm clot stop drains (Axiom, Torrance, CA) are placed in the inferior space between the mastectomy flap and the graft and in the axillary and superior subcutaneous planes (Fig. 1D, Fig. 2). Antibiotic irrigation is used to rinse the operative pocket and the implants during the procedure. After complete muscle and graft coverage of the expander have been accomplished, the expander is judiciously inflated according to the degree of skin excess. Postoperatively, the drains remain in place until the output is less than 30 mL in 24 hours, a period typically lasting 7 to 10 days. Routine perioperative antibiotic prophylaxis is given.

Serial expansions of the tissue expander were initiated in patients after their incisions healed. Intervals and volumes of serial tissue expansions were determined on a per patient basis. After

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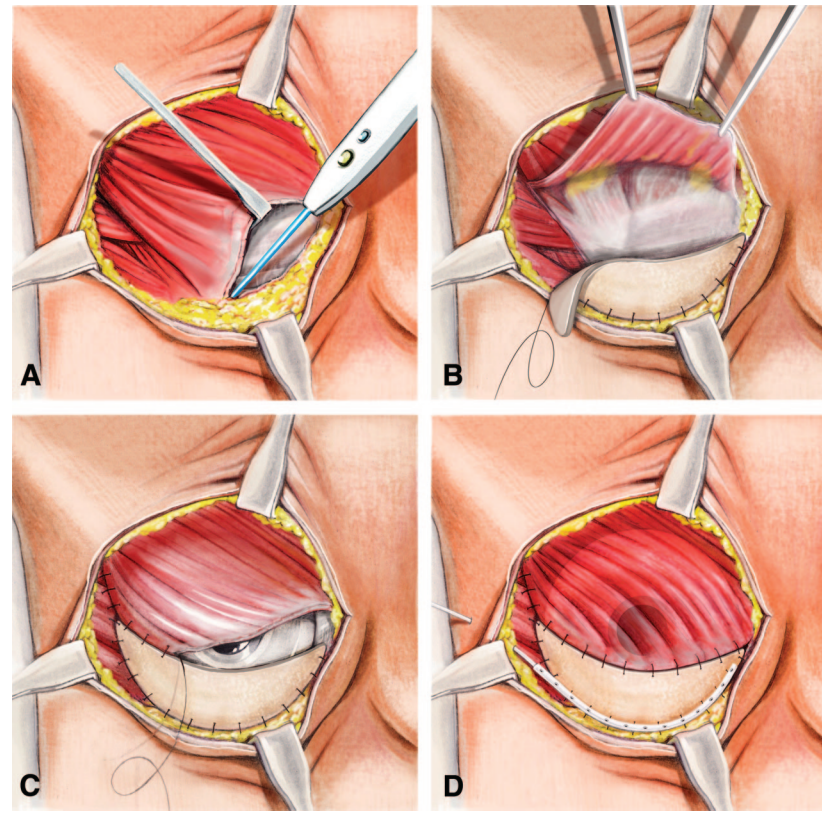

FIGURE 1. A, Disinsertion of the lower border of pectoralis major with bovie electrocautery. B, Intraoperative placement of the FlexHD prehydrated human acellular dermal matrix. Inferiorly, the prehydrated human acellular dermal matrix is secured to the chest wall to recreate the inframammary fold. C, Laterally, the prehydrated human acellular dermal matrix is secured directly to the serratus muscle to create the lateral portion of the mammary fold. The disinserted pectoralis major muscle is secured inferiorly to the prehydrated human acellular dermal matrix and laterally to the serratus muscle to provide complete coverage of the tissue expander or implant. D, The tissue expander is placed in the submuscular and subgraft plane and the opposing muscle and graft are secured with suture. A drain is placed in the space between the graft and the mastectomy flaps (another drain—not shown—is placed in the axillary and superior subcutaneous plane.

completion of adjuvant therapy and tissue expansion, Stage II reconstructions with tissue expander to implant exchange were performed as previously described by Spear.[3] Procedures for contralateral symmetry were also performed at the time of Stage II reconstruction when appropriate.

Histologic Analysis

During the Stage II procedure, a 1 × 1 cm tissue sample was obtained from the PHADM and surrounding soft tissues from 3 patients who consented to tissue donation for research purposes. Tissues were treated with hematoxylin and eosin stain. Immunohistological analyses were also performed using antibodies against the endothelial cell CD31 and CD34 antigens (Mouse anti-Human, Zymed, 1:100 dilutions, San Francisco, CA) to confirm neovascularization. Specimen slides were reviewed by a pathologist.

Statistical Analysis

All statistical analyses were performed using SPSS Statistical Analysis Software (SPSS, Version 17.0, Chicago, IL). Independent 2-tailed *t* test or Fisher exact test were used where appropriate.

RESULTS

The senior author completed 121 consecutive tissue expander-implant breast reconstructions in 84 patients. All breasts were reconstructed using PHADM by the technique described. The mean age of patients at the time of Stage I reconstruction was 50.2 years (range, 26–81 years). Of the total, 47 reconstructions (38.8%) were unilateral and 74 reconstructions (61.2%) were bilateral. Therapeutic mastectomies were performed in 90 breasts (74.4%), whereas prophylactic mastectomies were performed in 31 breasts (25.6%). Ten breasts (8.3%) received nipple-sparing mastectomies, 3 breasts (2.5%) received neoadjuvant radiation therapy, and 23 breasts (19%) received adjuvant radiation therapy between Stage I and Stage II

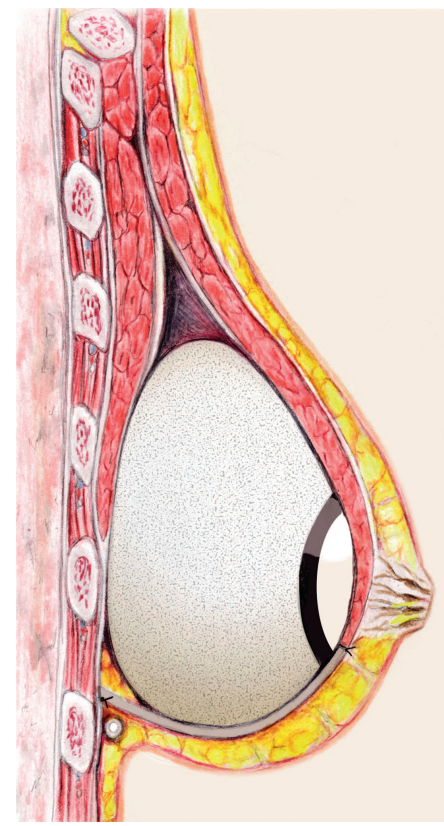

FIGURE 2. Lateral view of expander beneath the muscle and graft.

procedures; 49 patients (58.3%) received chemotherapy. Mean follow-up time after Stage II expander-implant exchange procedure was 44 ± 26.5 weeks. Mean initial intraoperative tissue expander fill volume was 256.6 ± 133 mL, resulting in a mean intraoperative fill percentage of 60% final volume. The mean number of expansions was 3.2 for all patients. During the second-stage exchange, all but 1 patient was found to have adherent PHADM.[13]

Overall, complications occurred in 20 breasts (16.5%) (Table 1). In total, there were 9 (7.4%) soft-tissue infections, 8 (6.6%) partial mastectomy flap necroses, 2 (1.7%) seromas, 8 (6.6%) implant exposures, and no hematomas. Eleven expanders (9.1%) ultimately required removal. Five of these patients were salvaged using a pedicled latissimus dorsi flap.

Patients receiving radiation demonstrated a trend toward greater complications; however, this difference did not reach statistical significance (Table 1). The overall incidence of complications in irradiated breasts was 30.8%, compared with 13.7% in nonirradiated breasts ($P = 0.0749$). Individually, radiation did not significantly increase the incidence of seromas (0.0% vs. 2.1%, $P = 0.999$), soft-tissue infection (11.5% vs. 6.3%, $P = 0.402$), mastectomy flap necrosis (15.4% vs. 4.2%, $P = 0.064$), or wound dehiscence and implant exposure (15.4% vs. 4.2%, $P = 0.064$).

Clear differences in collagen staining density were apparent between the PHADM and surrounding soft tissues (presumably collagen of a forming breast capsule) demonstrating evidence of robust revascularization and incorporation of the PHADM into native soft tissue. There were no giant cell foreign body reactions noted (Fig. 3). Neovascularization was confirmed by immunohistological staining against CD31 and CD34 endothelial cell markers (Fig. 4). Figures 5 and 6 are examples of acceptable outcomes in patients who underwent breast reconstruction using PHADM.

TABLE 1. Complication Rates in 121 Consecutive Prehydrated Human Acellular Dermis-Assisted Prosthetic Breast Reconstructions Stratified According to Radiotherapy Status

	Nonirradiated n = 95	Irradiated n = 26	Total n = 121	*P*
Overall complications	13.7%	30.8%	16.5%	0.0749
Soft-tissue infection	6.3%	11.5%	7.4%	0.402
Flap necrosis	4.2%	15.4%	6.6%	0.064
Seroma	2.1%	0.0%	1.7%	0.999
Exposure	4.2%	15.4%	6.6%	0.064

DISCUSSION

The utility of human acellular dermis as a soft-tissue replacement has been demonstrated throughout the body including pelvic, abdominal, and chest wall reconstruction[14–16]; hand surgery[17]; urethral reconstruction[18]; dural repair[19]; and breast reconstruction.[2–12] Prior studies have demonstrated the efficacy and relative safety of freeze-dried human acellular dermis in breast reconstruction.[2–12] To our knowledge, this is the first study to evaluate a dedicated series of PHADM in the setting of tissue expander-implant breast reconstruction.

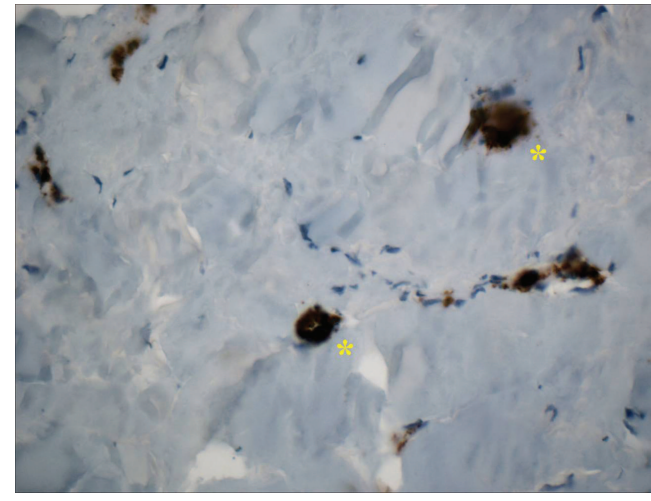

FIGURE 4. Endothelial cell-specific immunohistochemistry of FlexHD prehydrated human acellular dermal matrix. Specimen taken 3 months after PHADM placement during Stage II tissue expander to implant exchange and shown at 60× magnification after immunohistochemical labeling to endothelial cell CD31 markers. At 60× magnification, the lumens of blood vessels can be appreciated (asterisks).

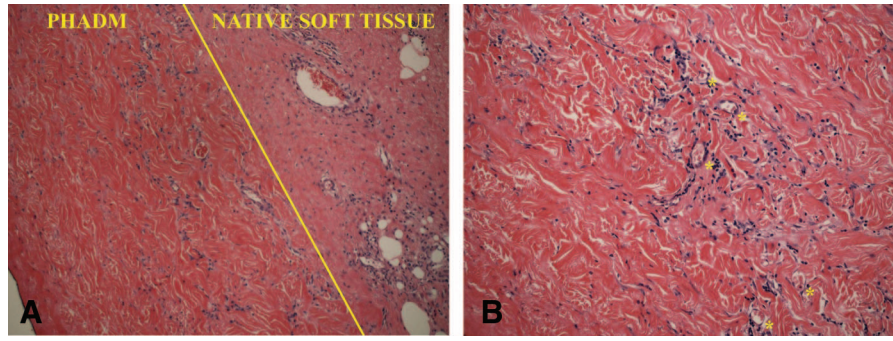

FIGURE 3. Histologic incorporation of prehydrated human acellular dermal matrix. Specimen taken 3 months after placement during Stage II tissue expander to implant exchange shown at 10× (A) and 40× (B) magnification with hematoxylin and eosin. At 10× magnification, a clear distinction (emphasized by the superimposed line) in collagen staining density is apparent between the prehydrated human acellular dermal matrix and native soft tissue. At 40× magnification, prehydrated human acellular dermal matrix is visibly populated with fibroblasts indicating integration of the dermal matrix into soft tissues. Also, numerous red blood cells are apparent in blood vessels (asterisks) within the prehydrated human acellular dermal matrix demonstrating neovascularization. There is no evidence of giant cell reaction that would signify overt rejection of the graft.

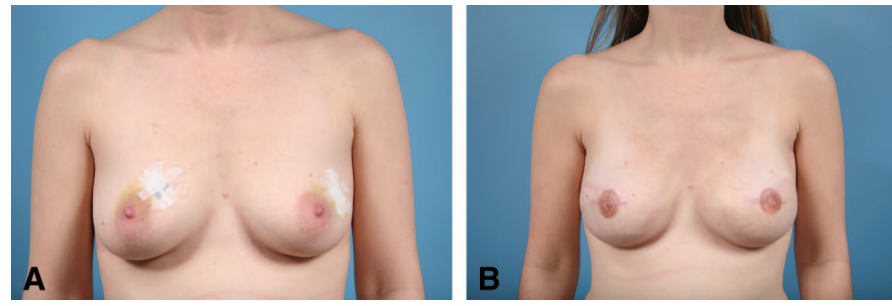

FIGURE 5. FlexHD acellular dermis-assisted 2-stage bilateral breast reconstruction. A 35-year-old woman underwent bilateral mastectomy. Preoperative view (A) and final result after completion of reconstruction (B).

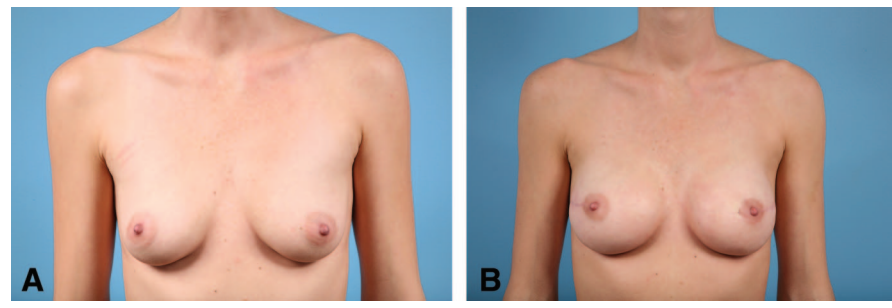

FIGURE 6. FlexHD Acellular dermis-assisted single-stage bilateral breast reconstruction. A 33-year-old woman underwent a prophylactic bilateral nipple-sparing mastectomy. Preoperative view (A) and final result 1 month after breast reconstruction (B).

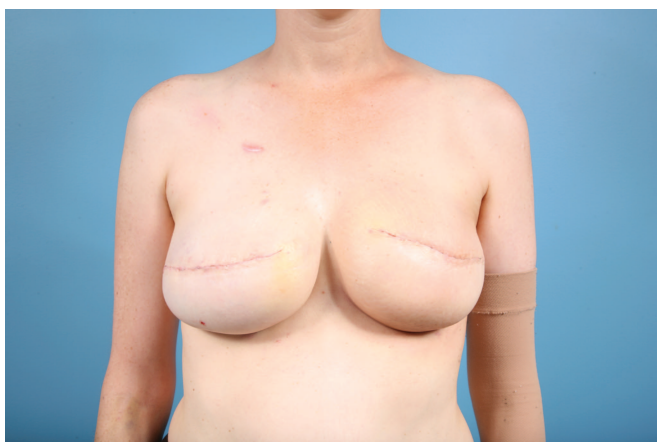

FIGURE 7. Example of a patient with bilateral FlexHD acellular dermis-assisted tissue expander reconstruction. Notice the robust volume and reasonable degree of symmetry in the shape of the irradiated side (left breast) vis-à-vis the right side.

The ability to better control expander-implant positioning with pectoralis disinsertion ("dual plane" technique) as described by Breuing and Warren, and Spear improve aesthetic outcome.[2,20] The addition of acellular dermis may further improve cosmetic outcomes by accelerating volume expansion and allowing surgeons to take advantage of excess mastectomy skin flaps.[2,3,8,9]

In this series, PHADM use allowed for significant initial intraoperative tissue expander fill which, on average, was 60% of the final tissue expander fill volume. This value is similar to the 66.1% initial tissue expander fill volume reported by Spear.[3] Although differences in tensile strength may exist between PHADM and other human acellular dermal matrices, PHADM was fully able to expand to a safe requisite volume in line with other studies. Indeed, in a standard mastectomy where the nipple and skin are excised, excessive tension on the mastectomy skin flaps due to overexpansion can promote vascular compromise of the flaps themselves. It is possible that the combination of thin mastectomy flaps and overexpansion contributed to the low but finite mastectomy flap necrosis seen in both our study and a study by Spear. This restriction is obviated when there is no vertical skin defect as in the case of a nipple-sparing approach.

PHADM (FlexHD) is recovered from cadaveric donors and processed in accordance with American Association of Tissue Banking and USP71 standards.[21] Specifically, cadaveric cutaneous tissue is decellularized in a hypertonic bath using aseptic technique. The product is sterilized with detergents and disinfectant prior to storage and packaging in a 70% ethanol solution. Moreover, like other human acellular dermal matrices, PHADM appears to readily incorporate into soft tissues.[22]

Overall, the use of PHADM had an acceptable complication rate of 16.5%. This complication rate is within the range of other reported studies with human acellular dermis products. In recent larger studies, complication rates evaluating the use of Alloderm have ranged from 12.1% to 18%.[2,8,9] Few authors have argued against the overall safety of acellular dermis based reconstruction,[10] however, a majority of studies have reported improved aesthetic outcomes with acceptable complication rates that are not statistically different than traditional subpectoral or dual-plane prosthetic breast reconstruction.[3,8]

There is a decision-making point that occurs intraoperatively: to optimize the added benefit of acellular dermis-based breast reconstruction, a relative excess of skin must coexist with reasonably vascular mastectomy flaps. The presence of both conditions allows for the full potential of the technique to be realized with robust and safe intraoperative volume expansion. It could be argued that the sequela of overexpansion with compromised mastectomy flaps is a predisposition to flap necrosis.

Several technique descriptions utilizing acellular dermis are present in the literature. The author's preferred technique includes suturing the lateral aspect of the acellular dermal matrix to the serratus fascia. Concomitantly, the superolateral aspect of the expander is secured by shifting the lateral border of the pectoralis to the serratus. On a technical note, careful suturing of the acellular dermis to the fascia and muscle is critical—folds or inversions of the

acellular dermis can create granulomas.[23] Additionally, PHADM exhibits polarity and must be inserted with the fenestrated surface opposing the soft tissue and the smooth surface facing the tissue expander or implant. Failure to place the dermis correctly may predispose to inflammatory processes that mimic frank cellulitis—a condition the senior author terms "red breast syndrome."[13] The clinical findings include early erythema over the lower pole of the breast (superimposed over the anatomic extent of the acellular dermis) without systemic signs of infection such as fever and leukocytosis and without any radiographic evidence of seroma or abscess. A potential etiology for this syndrome may be mechanical or physiologic—the natural incorporation of graft can be retarded by a fluid barrier or by the relative poor porosity of inverted dermal-epidermal orientation. This in turn, may prevent revascularization and force the host immune system to treat the acellular dermis as a foreign body with consequent triggering of an inflammatory response and the "red breast." Indeed, this same phenomenon may be seen when thicker HADM or PHADM is used: the revascularization from already thin mastectomy flaps may be further challenged by the deeper penetration required of these thicker grafts and the prolonged integration attempts may itself stimulate a host inflammatory response. Clearly, further studies evaluating the role of graft composition vis-à-vis the revascularization potential of mastectomy flaps (and concomitant host response) are needed.

The effects of radiation merit discussion: in this series, the overall complication rate in irradiated breasts was 30.8% (compared with 13.7% in nonirradiated breasts, $P = 0.0749$). Despite this higher rate of complication, we agree with Spear and Maxwell that acellular dermis-assisted tissue expander reconstruction seems to resist radiation effects more than plain tissue expander reconstructions (Fig. 7). (Spear S, Maxwell P; Personal communication, 2010.) This amelioration of contracture may result from some barrier effect of the acellular dermis–perhaps in combination with some stretch effect from the rapid and early expansion. Future studies will help to confirm this phenomenon and elucidate the underlying physiological processes.

In conclusion, despite differences in hydration and processing, PHADM yields outcomes comparable to published reports using nonhydrated human acellular dermis in expander-implant based breast reconstruction.

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