

Safety of CPX4 Breast Tissue Expanders in Primary Reconstruction Patients

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Background: In the United States, 2-stage expander-to-implant–based breast reconstruction accounts for more than half of all breast reconstruction procedures. Tissue expansion technology has undergone significant advancements in the past few decades. Previous reports suggest that the most common perioperative complications associated with breast tissue expanders are infection and skin flap necrosis. However, little clinical data are available for CPX4 Breast Tissue Expanders. The aim of the study was to measure real-world outcomes related to safety and effectiveness of the tissue expansion process, in patients who underwent primary breast reconstruction following the use of CPX4 Breast Tissue Expanders.

Methods: This was a single-arm retrospective cohort design looking at patients who underwent 2-stage, expander-to-implant–based primary breast reconstruction at a single site between April 2013 and December 2016 and who had a minimum of 2 years follow-up. Descriptive statistics were used to summarize baseline characteristics and safety outcomes.

Results: A total of 123 patients were followed for an average of 3.73 ± 0.94 years. At least 1 complication during the time of tissue expansion, before the permanent implant, was reported in 39/123 (31.7%) patients [51/220 implants (23.2%)]. The most frequently reported complications were delayed wound healing (13.8%) and cellulitis/infection (9.7%).

Conclusion: Analyses of real-world data from a single site provide further support for the safety and effectiveness of the CPX4 Breast Tissue Expander for women undergoing 2-stage expander-to-implant primary breast reconstruction. (*Plast Reconstr Surg Glob Open* 2021;9:e3425; doi: [10.1097/GOX.0000000000003425](https://doi.org/10.1097/GOX.0000000000003425); Published online 26 March 2021.)

INTRODUCTION

Breast cancer is estimated to comprise nearly one-fifth of all female cancers, with approximately 1 million new cases reported worldwide each year.¹ Following mastectomy for breast malignancies, many women undergo breast reconstruction. In the United States, 2-stage expander-to-implant breast reconstruction accounts for approximately 67% of all breast reconstruction procedures.² Tissue expansion technology has undergone significant advancements since the first clinical report published by Neumann in February 1957.³ CPX4 Breast

Tissue Expanders were approved by the US Food and Drug Administration in April 2013 for use in breast reconstruction after mastectomy, correction of an underdeveloped breast, scar revision, and tissue defect procedures, and are intended for temporary (≤ 6 months) submuscular or subcutaneous implantation. In an attempt to measure real-world safety outcomes associated with these devices, data were analyzed from consecutive patients who underwent primary breast reconstruction following use of CPX4 Breast Tissue Expanders by 2 surgeons at a single site. This study focuses on complications occurring during the tissue expansion period.

METHODS

This was a single-arm retrospective cohort design looking at data from patients who underwent 2-stage expander-to-implant primary breast reconstruction at a single site between April 2013 and December 2016, and had at least

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2 years of follow-up from final implant. Patients underwent tissue expansion with 1 of the 3 SILTEX CPX4 Breast Tissue Expanders [Style 8200 (Medium Height), Style 9200 (SILTEX with Suture Tabs, Medium Height), or Style 9300 (SILTEX with Suture Tabs, Tall Height)].

All patients were treated according to normal clinical practice, as described herein. All patients were counseled on delayed reconstruction, immediate reconstruction with expanders, and immediate direct-to-implant reconstruction with permanent implants. Ultimately, the decision was left to the patient. In some cases, expander or direct-to-implant procedures were encouraged. For example, use of a tissue expander may be more likely to result in optimal outcomes for higher BMI patients because it would enable use of a larger final implant than would a single-stage procedure. Following mastectomy by the operating breast surgeon, meticulous hemostasis was obtained throughout the mastectomy defect with electrocautery. The pocket was copiously irrigated with saline followed by a triple antibiotic solution. The breast pocket was recreated with an unfolded, trimmed acellular dermal matrix (ADM) anchored to the chest wall every 2–3cm with 2-0 Vicryl sutures. The ADM re-defined the inframammary fold inferiorly and breast border laterally, with at least 2cm overlap over the inferior border of the pectoralis muscle. The tissue expander was placed in a subpectoral position within the neo-pocket. Suturing of expander tabs occurred from a medial-to-lateral orientation. Mastectomy flaps, pectoralis muscles, and adjacent tissue were minimally dissected as needed to facilitate tension-free closure, but further dissection was not routinely performed. Plain or liposomal bupivacaine was injected in the surrounding parenchyma for analgesia before closure. Drains were placed in bilateral mastectomy defects to bulb suction. Closure was performed in three layers with 2-0 Vicryl, 3-0 Monocryl, and 4-0 barbed Monocryl sutures. Expanders were filled with saline following closure via percutaneous approach to a volume that did not blanch the skin. If closure did not facilitate expander filling, it was forgone until follow-up. Non-malignant reconstructions were performed in a similar manner but through a vertical mastopexy incision. Pre-pectoral reconstructions were not routinely performed. On expander exchange for permanent implant, an incision was made through the previous incision unless the tissue was thin. Where this was not possible, an inframammary or vertical incision was preferred. Capsulotomies were performed, hemostasis was obtained, and copious irrigation was again performed with saline, then triple antibiotic solution. Intrapocket bupivacaine was placed for analgesia.

Breast reconstruction patients were seen weekly until expander filling was complete. After tissue expander exchange to permanent implant, patients were scheduled for in-office follow-up visits at 1 week, 2 weeks, 1 month, 2 months, 6 months, and 1 year postoperatively.

Additional phone and email follow-ups were performed for all patients at 2 years or more after their final implant, consisting of the following 3 questions, supplemented by specific descriptors: (1) Have you experienced any problems or complications (eg, hematoma, bleeding, pulmonary embolism, cellulitis, infection, abscess, hospitalization, hardening of breast, capsular contracture, late

seroma, new masses, or malignancies)? (2) Have you had any surgeries or breast procedures (eg, biopsies, implant exchange, explant, breast lift/mastopexy) at an outside practice? (3) What is your overall satisfaction with the appearance of your breasts? (This question excluded consideration of how the patient feels about the surgeon or practice team.) Patients were asked to elaborate and were provided with directed questioning if they indicated that a problem had occurred or if they had a satisfaction score of <8. In these communications, patients were asked about complications occurring during both tissue expansion and after implantation with the permanent device.

All data were de-identified by the site before analysis. De-identified data received in Excel format were imported into SAS data files for analysis. Tabulation of summary statistics, graphical presentations, and data analyses were performed using SAS/STAT software, version 9.4 (SAS Institute Inc., Cary, N.C.). Northside Hospital Institutional Review Board determined this project was exempt from IRB review according to federal regulations under 45 CFR 46.104(d).

RESULTS

Primary reconstruction patients (n = 123) were followed for an average of 3.73 ± 0.94 years with the tissue expansion process averaging 176.8 ± 107.6 days. Baseline characteristics/medical history and procedural data are presented in Tables 1 and 2, respectively.

The total number of patients experiencing a complication during the time of tissue expansion (before the permanent implant) was 39/123 (31.7%), and the total number of implants affected was 51/220 (23.2%). Complications related to tissue expansion are reported in Table 3. All correction methods for tissue expander complications are included in Table 4.

Table 1. Baseline Characteristics and Medical History

	n (%) or Mean ± SD
Total Patients	123 (100)
Demographics	
Age at first surgery	53.2 ± 11.9
History of smoking	27 (22.0)
Body mass index	25.6 ± 5.7
Medical history	
Antidepressant medication	37 (30.1)
Birth control medication	2 (1.6)
Hormone replacement therapy	5 (4.1)
No. children	1.9 ± 1.1
No. pregnancies	2.2 ± 1.0
Family history of breast cancer	63 (51.2)
Diabetes	13 (10.6)
Hypertension	35 (28.5)
Coronary artery disease	18 (14.6)
Hypothyroid	10 (8.1)
Other cancer*	3 (2.4)
Cancer treatment	
Chemotherapy	54 (43.9)
Radiation	
None	91 (74.0)
Before reconstruction	5 (4.1)
Concurrent with tissue expander use	14 (11.4)
After permanent implant	13 (10.6)

*Other cancer includes any type except basal cell and squamous cell skin cancers.

Table 2. Procedural Summary

Procedural Detail	n/N (%) or Mean \pm SD (N)
Procedure (per patient)	
Immediate breast reconstruction with TE	117/123 (95.1)
Delayed breast reconstruction with TE	6/123 (4.9)
Surgical approach (per patient)	
Submuscular	123/123 (100)
ADM used (per patient)	
Alloderm 132 cm ²	10/123 (8.1)
Flex HD 11 \times 20	21/123 (17.1)
Surgimend 10 \times 15	89/123 (72.4)
Unknown type	3/123 (2.4)
Tissue expander use (per breast)	
CPX4 (style 8200)	4/220 (1.8)
CPX4 (style 9200)	176/220 (80)
CPX4 (style 9300)	40/220 (18.2)
Follow-up after procedure	
Days to drain removal	27.2 \pm 18.6 (110)
Days to second stage surgery	176.8 \pm 107.6 (123)
No. expansions	3.9 \pm 2.2 (215)
TE fill volume, placement operation (cm ³)	247.8 \pm 120.4 (183)
Total TE fill volume (cm ³)	368.8 \pm 149.6 (215)

Table 3. Incidence of Complications during Tissue Expansion, before Permanent Implant

Follow-up Complications	Patients with the Complication (%)
Any one or more complications	39 (31.7%)
Delayed healing	17 (13.8%)
Cellulitis/infection	12 (9.7%)
Mastectomy flap necrosis	8 (6.5%)
Seroma	4 (3.3%)
Extrusion/exposure of implant	3 (2.4%)
Hematoma	2 (1.6%)
Nipple ischemia	1 (0.8%)
Red breast	1 (0.8%)

Patient-reported satisfaction scores at the last follow-up after placement of the permanent implant averaged 7.5 \pm 1.9 of 10, with a median of 8.

DISCUSSION

Two-stage, expander-to-implant breast reconstruction remains one of the most frequently utilized procedures for women undergoing breast reconstruction. The purpose of this analysis was to provide insights into the safety of CPX4 Breast Tissue Expanders during the expansion process in a real-world setting. Few

studies have focused on analyzing this stage of breast reconstruction.

CPX4 Breast Tissue Expanders offer significant enhancements over previous generations of tissue expanders (eg, CPX3), making this device a popular choice for 2-stage expander-to-implant breast reconstruction.⁴ CPX4 was designed for enhanced patient comfort by making the buffer zone more flexible and through use of a smooth injection dome. Stability and positional control are maximized through use of microtexture and suture tab fixation options, which help the surgeon to define and control the location of the reconstructed inframammary fold. The clinical benefits of these improvements are demonstrated in the current study.

The most common complications observed in this cohort were delayed healing (13.8%) and cellulitis/ infection (9.7%), similar to previous rates reported in the literature and discussed in more detail below. Considering that the majority of patients in this study underwent immediate breast reconstruction with tissue expansion (95.1%) and used ADM (100%), it is important to point out that there is an increased incidence of surgical site infection (8.9%) and seroma (14.1%) associated with immediate reconstruction and use of ADM⁵ reported in the literature.

There are certain factors that are also known to increase the complication rates in patients undergoing two-stage, expander-to-implant based breast reconstruction. For example, radiation concurrent with tissue expansion, applicable to 11.4% of the patients in this study, has been associated with complication rates as high as 60%, including poor wound healing, failed expansion, and poor projection.^{6,7} History of smoking, reported in 22.0% of patients, has been shown to increase risk of infection and poor wound healing, the 2 most common complications seen in the present analysis. The use of ADM, as in all cases of the present study, has been reported to lead to an increase in early complications such as hematoma, seroma formation, and infection.¹ It is therefore challenging to make comparisons with the current literature due to differences in characteristics of the women undergoing breast reconstruction, variations in surgeon experience and surgical techniques utilized, when the studies took place, and variations in inclusion and exclusion criteria.

Table 4. Correction Methods for Tissue Expander Complications

Complication	Correction Method	Count	%
Delayed healing	Medical*	8	47.1
	Surgical†	5	29.4
	Office procedure‡	4	23.5
Cellulitis/infection	Surgical†	5	41.7
	Medical (requiring admission/IV antibiotics)	4	33.3
	Medical*	3	25.0
Mastectomy flap necrosis	Surgical†	8	100.0
	Office procedure‡	3	75.0
Seroma	Surgical, with next stage of surgery	1	25.0
	Surgical†	3	100.0
Extrusion/exposure of implant	Surgical†	3	100.0
	Surgical†	2	100.0
Hematoma	Hyperbaric oxygen	1	100.0
	Office procedure‡ (fluid was aspirated/drained)	1	100.0

*Medical treatment performed in office.

†Debridement/procedure performed in operating room, under general anesthesia.

‡Debridement/procedure performed in office, under local anesthesia.

Heterogeneity among women undergoing breast reconstructions is also an important consideration in understanding the range of rates reported in the literature. For example, in a study assessing immediate breast reconstruction using tissue expansion replaced with a permanent implant between 50 days and 16 months (average 6 months), a complication rate of 37.5% over a follow-up period ranging from 6–48 months (average 31 months) was reported among 56 patients.⁸ In this same study, patient satisfaction was reported to be 7.8 on a 0–10 scale. Another study of tissue expansion with immediate breast reconstruction following mastectomy for cancer in 50 women undergoing 56 mastectomies found that early complications (within the first 30 days of surgery) occurred in 15/56 cases (27%) with an overall complication rate of 35.7% (follow-up range 6–28.5 months, average 13 months).⁹ On the lower end, a retrospective review of 2-stage reconstruction performed by a single surgeon between July 1992 and June 2004 (n = 1522 reconstructions in 1221 patients) reported a complication rate of 8.5% after tissue expander insertion with native skin flap necrosis (3.6%) and infection (3.1%) being the most commonly reported complications.¹⁰ On the higher end, a multi-center study (n = 326 patients available for analysis) looking at complication data collected from hospital records, office records, and telephone interviews 2 years after reconstruction reported a complication rate of 52% for immediate 2-stage breast reconstruction.¹¹ It is important to acknowledge that some of these rates, although referred to as early complications, included complications occurring after the placement of the permanent implant, making comparisons with rates previously reported in the literature less meaningful.

During the FDA's General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee, it was noted that the FDA has not approved any ADM surgical mesh for use in breast reconstruction, although ADM has previously been approved for alternate indications such as soft tissue coverage. Nonetheless, ADM is commonly used in breast reconstruction procedures, and has been for the past 20 years.¹² It offers many advantages, such as improved aesthetic outcomes, improved utilization of native mastectomy skin, preservation of implant location, and reduction in incidence of capsular contracture and explantation.^{12,13} A 2015 Plastic Surgery Statistics Report by the American Society of Plastic Surgeons estimated that ADM is used in more than two thirds of immediate tissue expander breast reconstruction.¹⁴ In the Mastectomy Reconstruction Outcomes Consortium Study, Sorkin et al focused on patient-reported outcomes in patients undergoing immediate 2-stage breast reconstruction, with (n = 655) and without ADM (n = 642).¹⁵ While no significant differences were observed in patient-reported outcomes, time to exchange, or complication rates for the 2 groups, this study did not differentiate between ADM types. The authors note that their findings could not be considered conclusive on the use of ADM. Instead, they suggested additional investigation into the patient population subgroups for whom the use of ADM might improve outcomes.

This analysis is not without limitations. Because the study was conducted retrospectively, we were not able to

capture patient-reported outcomes specific to the tissue-expansion period. There was no control arm; so only descriptive statistics were used; CPX4 devices were not compared with other devices such as CPX3. Because the number of patients was relatively low and from a single site, it was not possible to draw generalized conclusions. Finally, because smooth tissue expanders were not available until 2018, only data on textured tissue expanders were included in the analysis.

Additional studies are needed to analyze complications related to devices that incorporate novel tissue expansion technology (eg, smooth tissue expanders),¹⁶ optimization of lower pole expansion, patient-directed tissue expansion, dual port expanders, or other technologies that have demonstrated benefits compared with the technology used in the present analysis.³ However, these results demonstrate that the use of CPX4 Breast Tissue Expanders are a safe and efficacious option for women undergoing 2-stage, expander-to-implant based primary breast reconstruction.

CONCLUSION

The current analysis of real-world data from a single site provides support for the safety and effectiveness of the CPX4 Breast Tissue Expander for women undergoing two-stage, expander-to-implant primary breast reconstruction.

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