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ORIGINAL ARTICLE
Breast

Absorbable Biosynthetic Scaffolds in Place of Silicone for Breast Reconstruction: A 9-Year Experience with 53 Patients

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Background: Few series report on using fat grafting as the primary form of breast reconstruction. A 9-year experience with absorbable biosynthetic scaffolds, used in place of silicone implants, for breast reconstruction is reviewed.
Methods: A clinical quality improvement approach was used to evaluate real-world data on a single plastic surgeon's experience treating breast reconstruction patients over a 7-year period.
Results: Fifty-three patients had 74 breasts reconstructed, (following 51 therapeutic mastectomies and 23 prophylactic). Five of the 51 breasts (9.80 %) developed a local recurrence (mean follow-up of 4.5–5.5 years). This compared favorably with the practice's previous 6 years of silicone reconstructions. The most common complications were benign fat necrosis and oil cysts. More than 100 radiologic examinations were performed without interference by the absorbable implants. By 12–18 months post implantation, very little immune response was seen on histologic examinations of the biosynthetic scaffold constructs. Mature collagen and robust vascularity characterized the "mesh zone," whereas regenerated adipose tissue was seen in between and on top of the folded sheets of the implants. The average number of fat graft sessions in immediate reconstructions was 2.3, with a mean total fat graft volume of 551 mL, to restore an average mastectomy defect volume of 307 mL. Aesthetic outcomes were much better in the immediate reconstruction of nipple-sparing mastectomy group, which saw 68% achieve an A/B grade; 19%, C grade; and 13%, D/F on subjective grading.
Conclusion: This composite strategy, using biosynthetic scaffold and autologous fat grafting, yielded outcomes equivalent to flap reconstructions with the ease of implants.
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INTRODUCTION

We published an article in 2020 that described a novel approach to total breast reconstruction with an absorbable biosynthetic scaffold and serial fat grafting.[1] Over the last decade, the trend of de-escalation in mastectomy morbidity has been a rising tide that has lifted the results of all breast reconstructions. Our emphasis has been on immediate reconstruction and on nipple-sparing mastectomy (NSM), driven by anatomic dissection, specifically, excision of the corpus mammae (ectodermal origin) and preservation of the superficial fascia system (SFS) of fat and fascia (mesodermal origin) that surrounds the corpus (Fig. 1). The circum-mammary ligament (CML), an important part of the breast SFS, is a zone of adherence of superficial fascia to deep fascia of the chest wall and represents a corridor of vascular, lymphatic, and nerve conduction essential to a healthy breast skin envelope.[2]

We used three-dimensional soft tissue stents consisting of long-term absorbable mesh, in place of silicone, shaped in the operating room at the time of mastectomy.

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As our 2020 report detailed, the original cases were done with TIGR (Novus Scientific) mesh and SERI (Allergan) silk mesh. Once we switched to P4HB Phasix (BD) mesh on our fourth patient, we found the handling characteristics most favorable and performed all subsequent cases with P4HB mesh. Between February 2015 and December of 2021, we have implanted 53 patients with 74 long-term absorbable mesh constructs following 51 therapeutic and 23 prophylactic mastectomies.

METHODS

This work was conducted under the principles of Clinical Quality Improvement (CQI).[3] IRB oversight is not mandated for CQI studies. CQI work is not experimentation but an analysis of clinical practice with the goal of improving patient care. Hence, the work described in this article was not hypothesis-driven scientific research or a clinical trial. All patients were treated in the course of clinical practice with no fixed protocol for patient selection or technique. A formal review and designation of this project as CQI activity was obtained from CQ Insights, Knoxville, TN, before the 2020 publication in *Plastic and Reconstructive Surgery*. Federal guidance recognizes CQI, and consent from the patient is not required for de-identified evaluation, report, or publication of outcomes of nonresearch activities.[4] This review of process and outcomes followed all HIPAA requirements. Written consent was obtained before the use of patient photographs. Since starting this work, the manufacturer of the mesh has updated labeling for this product to include a precaution that the safety and effectiveness of surgical mesh in breast surgery, including in augmentation or reconstruction, has not been determined by the FDA (https://www.fda.gov/medical-devices/letters-health-care-providers/labeling-updates-bd-mesh-products-letter-health-care-providers?utm_medium=email&utm_source=govdelivery). All patients from the beginning of this series were given in-depth, verbal and written, informed consent about the off-label use of FDA approved mesh products and were given alternative options such as direct-to-silicone implantation or autologous flap surgery.

Takeaways

Question: Can a new hybrid approach to breast reconstruction safely improve outcomes?

Findings: We used a CQI paradigm to improve breast reconstruction with three-dimensional absorbable mesh scaffolds and serial fat grafting for immediate reconstruction following nipple-sparing mastectomy. All cases were treated as outpatient surgery, without mortality or serious morbidity, and with high-quality aesthetic results in two-thirds of cases.

Meaning: It is possible to safely achieve high-quality results, equivalent to autologous breast reconstruction, using serial fat grafting and three-dimensional, absorbable biosynthetic scaffolds in place of silicone implants.

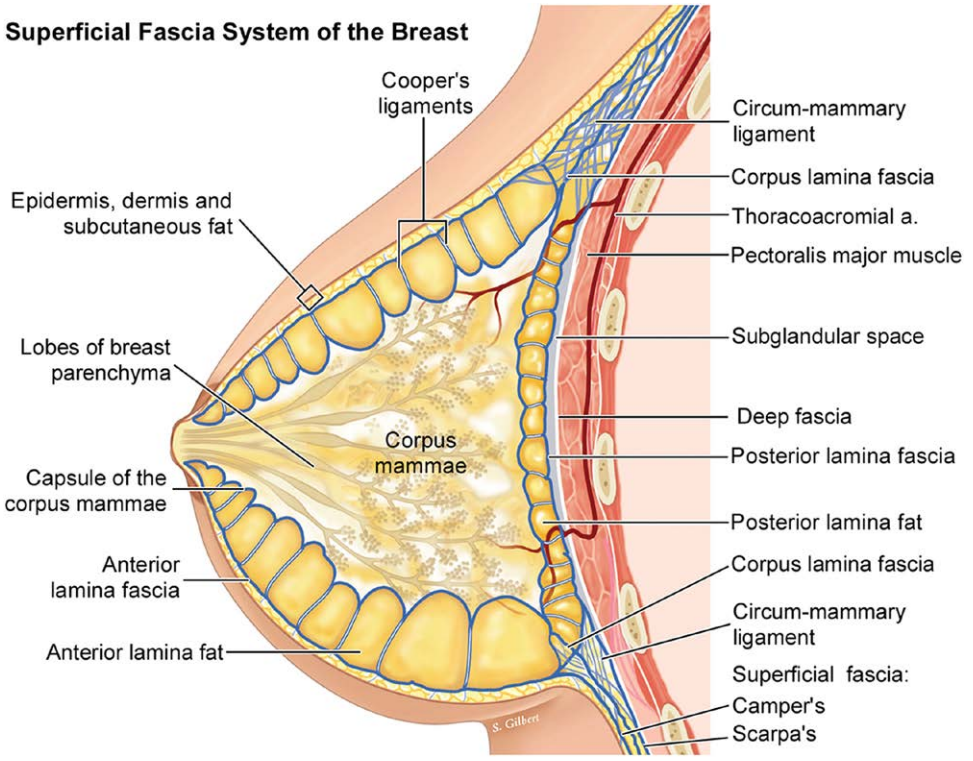

Fig. 1. Surgical anatomy of the breast illustrating the SFS (mesodermal origin), which surrounds the corpus mammae (ectodermal origin). Illustration by Susan Gilbert. Used with permission.

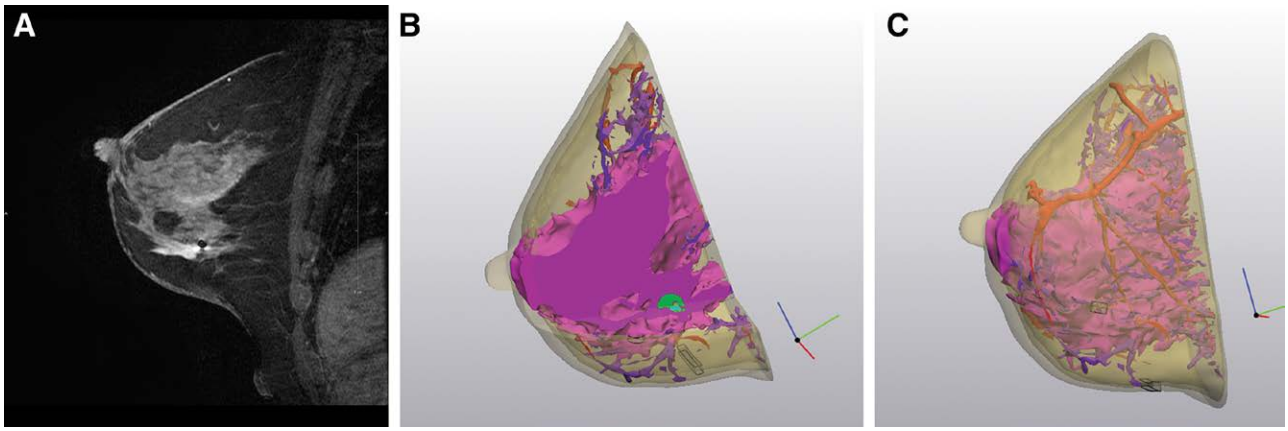

Fig. 2. Breast MRI and associated three dimensional model, for preoperative planning of nipple sparing mastectomy. A, MRI of preoperative patient with a 1-centimeter invasive ductal carcinoma in the lower, inner quadrant. B, Three-dimensional computer model with tumor in green and biopsy clip in blue. C, Computer model with second intercostal perforating artery, from the internal mammary artery, running through the anterior lamellar fat to the nipple.

All patients in this report were sequential referrals for breast reconstruction between February 2015 and December 2021. After informed consent, six additional patients, representing seven reconstructions, chose direct-to-silicone reconstructions. The following is a review of the results with biosynthetic absorbable mesh and a description of our learning curve.

Of the 51 biosynthetic mesh cases following a *therapeutic* mastectomy, 38 were immediate reconstructions, and 13 were delayed reconstructions; 23 *prophylactic* mastectomies/biosynthetic mesh reconstructions were performed, 15 were immediate reconstructions, and eight were delayed. The breast surgeon and plastic surgeon worked together as a team to strategically evaluate the preoperative mammogram, ultrasound, and, in most cases, magnetic resonance imaging (MRI) (Fig. 2). We began our experience with lateral or axillary radial incisions, but as our experience increased, we converted to incisions in the infra-mammary fold. In some larger-breasted patients, an inverted T incision or a Wise pattern was used.

Fig. 3. Photograph of a sixth generation absorbable biosynthetic mesh scaffold made in the operating room on the sterile back table, before the start of the operation.

SHAPING OF THE MESH SCAFFOLD

All implants were fashioned from the commercially available mesh scaffolds on the sterile back table (see Video from our 2020 article).[1] The design began in 2015 with simple stacked sheets of mesh, typically squares folded in half to achieve a rectangle of the desired breast base diameter, with a fixation suture centrally. The open ends of the folded square were turned upward, and the lateral edges were trimmed to achieve the desired contour. This was unfurled and fixed to achieve a hemispherical shape. Improvements were made over the 7-year period to the construct design aimed at increasing size and stability (Fig. 3).

SURGICAL TECHNIQUE

Primary incisions are made, and a separate small axillary incision is used for a sentinel lymph node biopsy, which also assists in the dissection of the axillary tail region. Sharp dissection along the white surface of the corpus mammae separates it from the yellow fat lobules of the SFS. Injection of tumescent anesthesia and monopolar electrocautery is used to maintain hemostasis. Extraction of the encapsulated corpus mammae is facilitated by traction and counter traction. The retraction forces should always move the corpus centrally to avoid undercutting the CML peripherally. The superficial dissection should move in circular whorls along the spiking Cooper's ligaments, which intersect with the grape-sized fat lobules of the anterior lamella fat. Posteriorly, the deep layer of laminated fat and fascia can be dissected away from the corpus with linear dissection, as here the corpus is flat. The peripheral margins of the corpus mammae, within the CML, make for a nodular, irregular disc and must be dissected accordingly.[5]

The reconstruction begins with a purse string suture threaded through the CML. This cinching suture (polypropylene, barbed suture- Quill or V-Lock) returns the base diameter of the breast back to its premastectomy dimensions, which greatly decreases the reconstructive volume. Next, the mesh construct is inserted into the defect and sutured to the CML at four to six spots. The incision is then closed in layers. Seventeen patients in the series had no drains placed, to preserve the postoperative inflammatory exudate bathing the mesh, but this resulted in seromas in some cases; the final compromise was to use one intermittent negative pressure closed system drain, for 5–7 days.

Patients underwent subsequent rounds of autologous fat grafting, using standard Coleman technique, beginning at 4 weeks postoperative. Fat grafts were injected into the subcutaneous and prepectoral planes on initial fat grafting. Subsequent sessions, four months apart, also included injection of fat into the intermediate zone and directly through the mesh region. Patients requiring adjuvant therapy begin it 2 weeks after the first fat graft and resume any additional fat grafting 6 weeks after it is concluded.

RESULTS

Fifty-three patients had 74 breasts reconstructed (see Table 1: patient data). Five of 51 therapeutic mastectomy/mesh fat graft reconstructions (9.80%) developed a local recurrence during a mean, per-patient, physician follow-up of 4.5 years, which was an average of 5.5 years since the date of mesh implantation surgery. Fifty-one biosynthetic reconstructions were following therapeutic mastectomy (85% invasive and 15% in situ cancers). Of the 23 prophylactic cases [two-thirds were high-risk (+gene mutation), and one-third were intermediate risk (+family history)], none developed a cancer following prophylactic mastectomy and reconstruction. This result compared favorably to our previous 6 years' experience with silicone reconstruction, which had five local/regional recurrences (13.16%) in 38 therapeutic mastectomies (mean follow-up 7.5 years). Metastatic disease was 5.7% versus 9.4% (biosynthetic scaffold/silicone), and breast cancer deaths were 3.8% versus 3.1%.

Table 1. Patient Data on 53 Total Breast Reconstruction Patients with Absorbable Biosynthetic Scaffold and Serial Fat Grafting, Comparing the Immediate Reconstruction Group with the Delayed Group

Data	Immediate	Delayed
No. patients	39	14
Mean age	58	60
Average BMI	27	25
Race	White: 37 African American: 2	White: 13 Hispanic: 1
History of smoking	Current: 15% Previous: 17.5%	Current: 0 Previous: 21%
Adjuvant chemo RX	18%	50%
Candidates for hormonal adjuvant RX	28/39 = 72%	7/14 = 50%
Candidates for hormonal adjuvant RX who received a full course of treatment	20/28 = 71%*	6/7 = 86%
Radiation RX	8/53 breast = 15.1%†	2/21 breasts = 9.5%
Four of the five immediate patients who had local recurrence refused any adjuvant therapies.		
53 patients (100%) were treated as outpatient surgery, including seven patients in their 70s.		

*Two of the five patients with local/regional recurrence refused full course of HRT.
†None of the five local/regional recurrence cases had radiation RX before recurrence.

Delayed reconstructions with this technique had poorer aesthetic outcomes and required more fat grafting sessions (2.3 versus 3.0). [**See table, Supplemental Digital Content 1,** which shows fat grafting data (immediate and delayed): ratio of mastectomy volume to total volume of grafted fat with body mass index, superficial fascia characteristics (1: worst; 5: best), and graded aesthetic outcomes. **http://links.lww.com/PRSGO/D211**.]

The most common complications were oil cysts and fat necrosis detected on physical examination (46.2% immediate group; 71.4% delayed group). Virtually all patients would have subclinical findings of cysts and fat necrosis, with combined mammography and ultrasonic examination following this type of reconstruction. One novel finding was seen in four immediate (10.3%) and four delayed patients (28.6%), which we have termed "fat graft cysts." They are benign macrocysts (1–4 cm.) containing flecks of fat graft globules that resemble a "snow globe" on ultrasound examination (Fig. 4). They have a regular border with no associated vascular signaling (Table 2). There were no cases of capsular contracture, chronic pain, erosion, or migration of mesh, and only one patient, out of 53, developed a late deep wound infection.

Twenty-nine of the 39 immediate reconstruction patients had radiologic evaluations postimplantation, accounting for 101 mammograms and/or ultrasounds and 15 MRIs. In no case did the presence of the mesh preclude a successful radiologic evaluation. Four of the five local recurrences were found by the plastic surgeon, during postoperative physical examinations (three subcutaneous and one chest wall); one additional recurrence was found on annual screening mammogram. In patients who had mammograms, the mesh zone was seen to have a radio-opaque appearance until 5 years post implantation, presumably due to the dense collagen that wraps around the mesh monofilaments. This radio dense region gradually disappears thereafter, as the collagen remodels (Fig. 5).

An IRB-approved needle biopsy study was performed on a group of nine volunteer patients between 1 and 5 years postimplantation of mesh. This IRB study is the focus of a separate article, but the general findings are included here. The innate immune cell response to the P4HB mesh fibers is characterized almost exclusively by a small number of macrophages that further decrease with time. These cells are typically scant in number by 13 months postimplantation and dispersed throughout

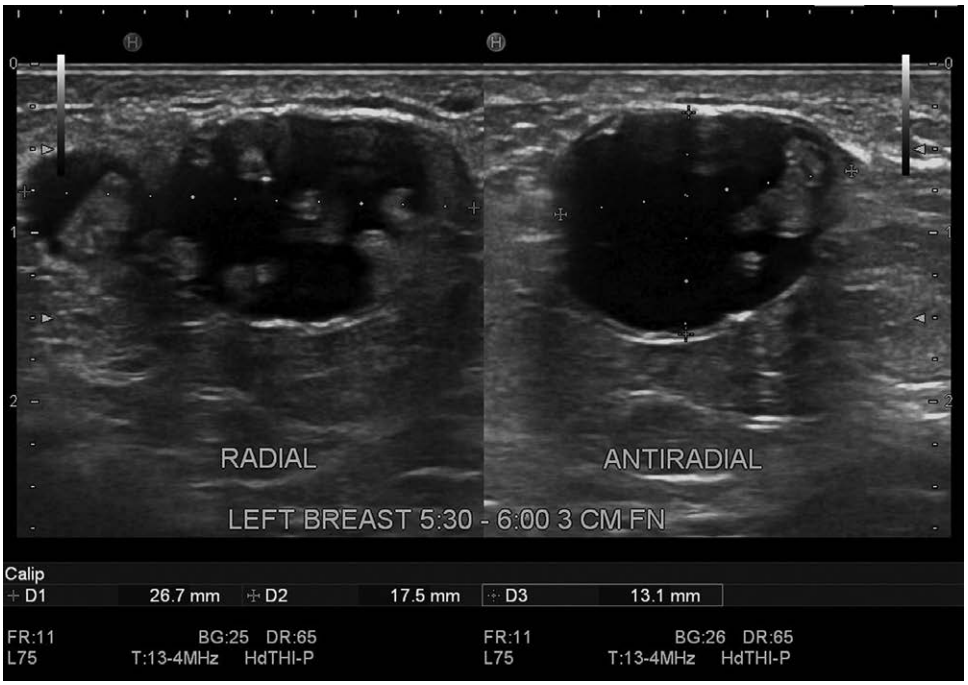

Fig. 4. Ultrasound of benign fat graft macrocyst, or snow globe cyst. Note the regular border and no associated vascular signal, with micro-lobules of fat unchanged from when they were injected.

Table 2. Surgical Complications in Immediate and Delayed Groups

Complications/Reconstruction Patients	Immediate, 39	Delayed, 14
Post fat graft nodule on physical examination	18 (46.2%)	10 (71.4%)
Open + ultrasound needle biopsy (to prove benign nodule)	5+8 (33.3%)	6+2 (57.1%)
Seroma	9 (25.1%)*	3 (21.4%)
Superficial wound infection (treated oral antibiotics)	8 (20.5%)	0
Deep wound infection (I&D, IV antibiotics)	1 (2.6%)	0
Explant of mesh construct	2 (5.1%)†	1 (7.1%)‡
Minor wound edge necrosis: debridement and closure	4 (10.3%)	0
Partial nipple areolar loss	2 (5.1%)	N/A
Minor hematoma which resolved without treatment	2 (5.1%)	0
Macro "fat graft cyst"	4 (10.3%)	4 (28.6%)
Capsular contracture	0	0
Erosion or migration of mesh	0	0
Chronic pain	0	0

*Seventeen immediate patients had no drains at mastectomy/immediate reconstruction.
†One secondary to sinus tract that developed after radiation therapy, and one partial (50%) removal of mesh after wound dehiscence and partial exposure of mesh.
‡One *removed* and *replaced* with larger mesh implant, as modified radical mastectomy skin envelop relaxed.

the implant site without concentration around the P4HB fibers. Unlike the classic foreign body response, there were only widely scattered multinucleated giant cells. The few remaining examples of innate immune cell response remained at this steady state for the duration of the biopsies available for examination. Fibroblasts were abundant in the early months post implantation and associated with the deposition of collagenous connective tissue between the mesh fibers. The collagen fibers were arranged in swarming bundles that appeared to mature and reached a steady state by 18–24 months. Neo-adipose tissue was present between the sheets of mesh within the open subsegments and on the mesh surface. Vascularity was robust and appropriate for the mature connective tissue that developed over time (Fig. 6). The space occupied by the P4HB monofilament fibers persists in the histologic tissue sections longer than we expected based on the known degradation profile of P4HB. In a porcine ventral hernia repair model in which the same P4HB bioscaffold was used, 85% of P4HB molecular weight had been lost by 12–18 months.[6] Among the patients who consented to needle biopsies, there were no identifiable differences between the surface or deep aspects of the P4HB scaffold.

Six employees of the plastic surgeon's practice were asked to assign aesthetic grades on a five-point scale. They anonymously graded each breast in before and after photographs. Graders were instructed to save "A" grades for after pictures that looked as if no surgery had been done, while the other end of the scale defined an "F" grade as a result that would have been better for the patient to have had an external prothesis. Results can be seen in Supplemental Digital Content 1 (**http://links.lww.com/PRSGO/D211**). To help lessen the subjective bias of the graders, we evaluated the overall results by combining A + B grades (68.0%) and D + F grades (12.7%), as it would be unlikely for anyone to confuse the two categories. This combination of grades left those in between, the "C"

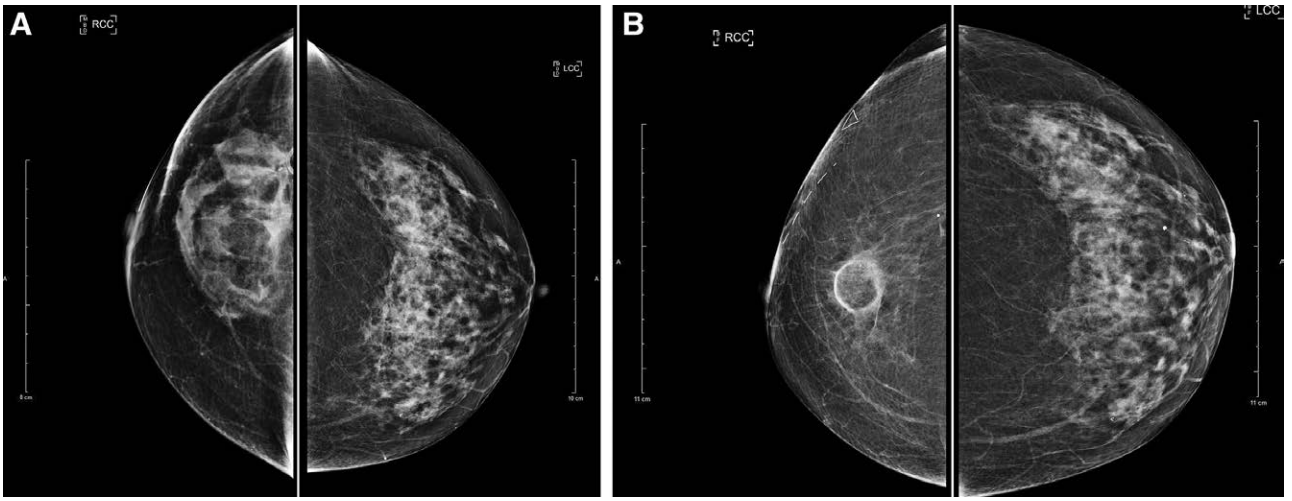

Fig. 5. Mammographic evidence of absorption of the biosynthetic mesh scaffold. A, Immediate patient 6, mammogram at one year post right mastectomy and implantation of biosynthetic mesh. B, Mammogram seven years post implantation. Note the appearance of the implant is gone and a benign, simple cyst at center with thin calcified rim.

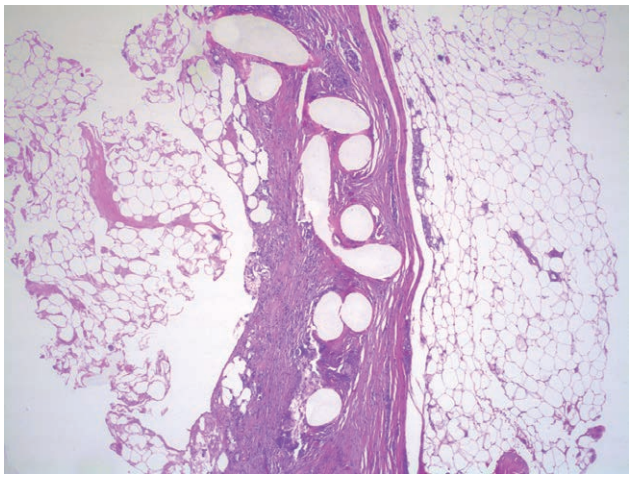

Fig. 6. Histology slide of scaffold and regenerated tissue from excisional biopsy, obtained when revision to the reconstruction required exposure of the mesh zone, 10 months post implantation.

grades, at just over 19%. Figure 7 shows a case from the immediate group: before and after photographs; a video of reconstructed adipose tissue, after the bioscaffold is gone, is at https://youtu.be/dHcRw35WAh0?feature=shared. Additional before and after results can be found in Video 1. [**See Video 1 (online),** which shows information on procedures performed, specimen estimated volumes, number and volumes of fat transfers and postoperative years of results.]

DISCUSSION

We now use absorbable bioscaffold reconstructions with fat grafting for cases of immediate reconstruction at the time of nipple-sparing mastectomy. Delayed reconstruction of failed silicone and non–skin-sparing mastectomies have loss of tissue and wound contracture, which make expansion with fat grafting difficult. We believe the novel use of a folded, three-dimensional, absorbable mesh device with autologous fat grafting to be helpful in making immediate breast reconstructions possible. The average number of fat graft procedures per immediate patient was 2.3, with volumes of fat grafted just under two times the mastectomy specimen volume. This fat grafting protocol compares favorably with the BRAVA experience reported by Khouri et al of 3.2 procedures per breast[7] and the four procedures reported by Homsey et al for total breast reconstruction with fat grafting and no expander.[8]

We now exclude patients who are underweight (BMI < 18.5). Also, patients with a history of very little breast development should have reconstruction with silicone-based expanders, which are forceful enough to expand the undeveloped breast soft tissue envelope. Age did not seem to be a factor, but significant multiple medical problems or poorly controlled chronic diseases are relative contraindications to this technique. Additionally, patients who are unable or unwilling to undergo serial fat grafting sessions are better served with direct-to-silicone implant-based reconstructions. Finally, patients with aggressive cancers will likely require chemotherapy and radiation and are at a higher risk for local/regional recurrence. They should be considered relative contraindications for the bioscaffold procedure, especially in the presence of other complicating factors.

Large volumes (300 mL–800 mL) were reconstructed immediately, with as little as two fat grafting operations. Histologic evaluation reveals that dense, well-vascularized collagen connective tissue develops with time, which is covered and infiltrated with mature adipose tissue. In preclinical swine models, the P4HB fibers degrade and absorb by approximately 12–18 months.[6] These findings are consistent with our observations of patients at 1 year (Fig. 8). The spaces occupied by the monofilament fibers persist in a partially disrupted state for several years post-implantation (Fig. 9), most likely becoming part of the

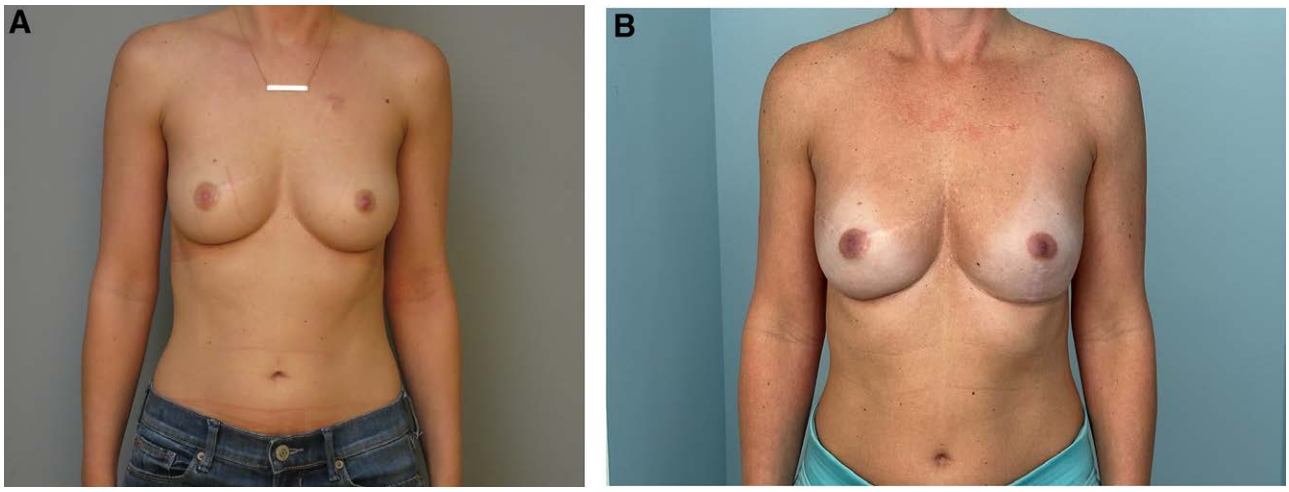

Fig. 7. Photographs of immediate patient 11. A, Before bilateral mastectomy. B, Six years post reconstruction with biosynthetic implant. Additional before and after results can be found in Video 1 (online).

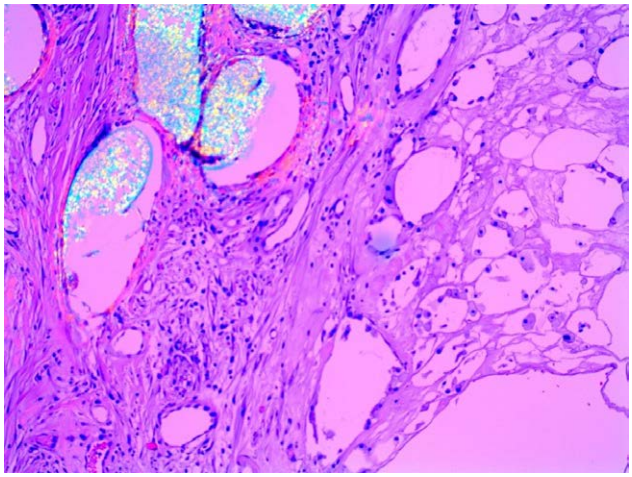

Fig. 8. Histology with polarizing filter demonstrating the partial absorption of the P4HB monofilament, knitted mesh fibers during the first year.

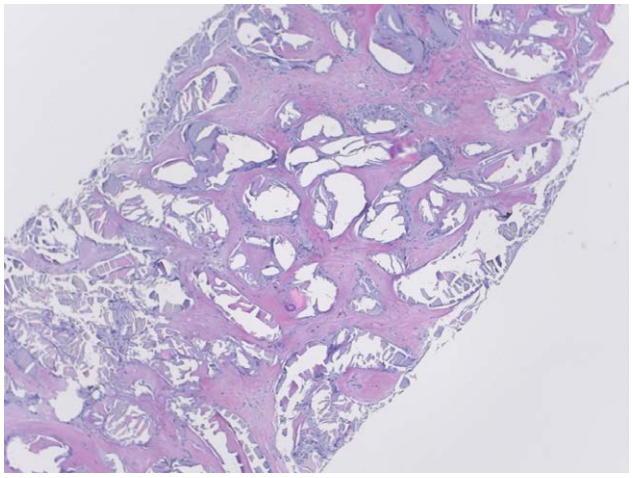

Fig. 9. Histology of needle biopsy of scaffold region at five years post implantation, showing the absorption of mesh material and partial collapse of the "mesh space."

fascial interstitium (Fig. 10). The remodeled tissue is well vascularized and lacks any active inflammatory immune response. From a clinical perspective, the tissue remodels over several years to become softer and assumes the compliance and movement of normal tissue. The vertical retinacula, characteristic of normal superficial fascia adipose tissue, forms and can be seen traveling from the chest through the mesh on MRI (Fig. 11). Procedures with complications, such as seroma requiring placement of drains, can develop tight, contracted vertical retinacula. Such retinacula will require rigotomy procedures at the time of fat grafting to achieve the release and expansion of skin and soft tissue envelope.[9] No matter the circumstances and cosmetic outcome, all patients showed improved results with additional fat graft surgery and time.

Despite five patients having a local/regional recurrence, there was no increase in cancer activity when compared with the historical experience in our practice with silicone-based reconstructions. The follow-up time of 5 years in our series of 74 total breast reconstructions was well beyond the time expected for the mesh to degrade and absorb (1–2 years).

Biological effects elicited by the degradation products of P4HB include immunomodulation and the upregulation of antimicrobial peptide production by macrophages.[10–12] An example of immunomodulation is the suppression of the proinflammatory (M1-like) macrophage phenotype and promotion of a regulatory, pro-remodeling (M2-like) phenotype.[13] Innate immune cells, especially macrophages, have been shown to exhibit remarkable plasticity within an extraordinarily broad spectrum.[14] The specific phenotype is dependent upon the microenvironmental milieu within which the macrophage is exposed. The earliest findings of macrophage phenotypic plasticity were in the context of tumor biology, and it was found that certain phenotypes were tumor-permissive.[15] Clearly, based on our

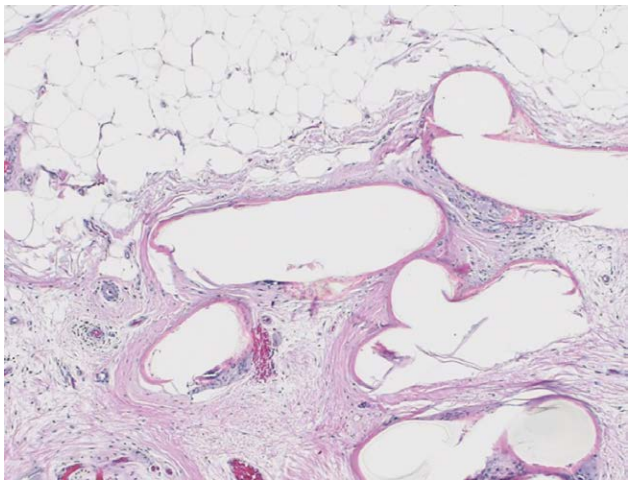

Fig. 10. Histology of specimen, 6 months postimplantation, showing empty monofilament space communicating with the interstitium, characterized by acellular stacked retinaculum of collagen fibers surrounding both vascular spaces and mesh spaces. Mature adipose tissue lies on top of these layers of interstitium surrounding the scaffold space.

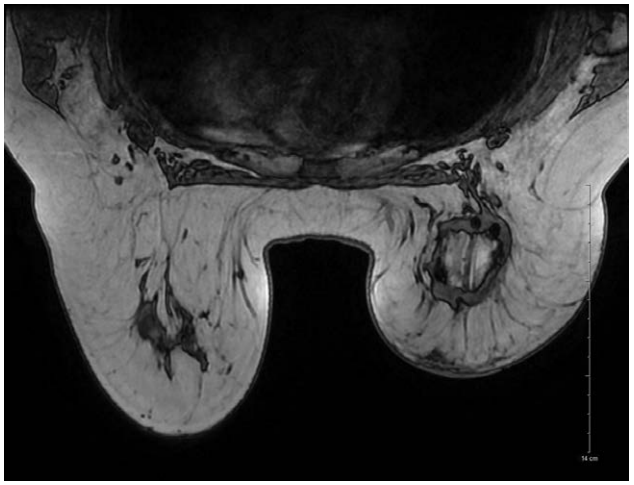

Fig. 11. MRI of immediate patient 7, at 6 months postimplantation. Note the absence of the corpus mammae in the right reconstructed breast but the presence of vertical retinaculum, or Cooper's ligaments, running as they should, from the posterior lamellar fascia through the mesh zone into the overlying skin.

experience reported in this article, the macrophage phenotype promoted by the P4HB mesh is not among this tumor-permissive group, which is also supported by the lack of increased incidence of neoplasia among the large number of patients who have been implanted with the P4HB mesh (Phasix) for hernia repairs.

Any recommendations regarding screening examinations following mastectomy should be considered carefully in each patient's circumstances. We now recommend avoiding routine screening radiologic examinations, which had a high rate of false positive findings following fat grafting, resulting in additional radiologic exams and needle biopsies. We now recommend that patients with low risk for local/regional recurrence (negative nodes and estrogen/progesterone positive), who agree to be compliant with adjuvant therapy, have monthly self-examinations and biannual breast examinations by the surgeon for surveillance of recurrence. This recommendation is consistent with our policy on radiologic examinations for our silicone reconstruction patients. When a physical examination identifies a suspicious or questionable finding, we agree with Smith's group, who published their experience with fat grafting for reconstruction in 2012. They recommend a focused ultrasound evaluation on patients with questionable findings on physical examination and biopsy of masses that have ultrasounds showing uncircumscribed margins in the presence of vascular internal blood flow signals. This had a 100% positive predictive value in their series.[16]

Finally, the P4HB biologic mesh scaffold mechanically initiates and facilitates the process of constructive tissue remodeling when it stents the mastectomy dead space and allows the superficial fascia remnants of the skin envelope to fall into the subsegments of the mesh construct. Bi et al have shown that regenerative macrophages from the superficial fascia promote angiogenesis and adipogenesis in fat grafting.[17] An earlier article from this same group showed external volume expansion, applied to SFS surgical wounds, created mechanical forces that led to the CXCL12/CXCR4 pathway mediated recruitment of circulating mesenchymal stromal cells to participate in adipose regeneration in a rat model.[18] We believe the three-dimensional mesh implant in our human patients maintains a spatial opportunity within the mastectomy wound, for the regeneration of fascial tissue fueled by serial fat grafting.

P4HB is a natural polymer made through fermentation using recombinant DNA technology in *E. coli*, making it a biosynthetic mesh.[19] Wolf et al published a study in 2019 that showed a regenerative wound environment stimulated by biological mesh had a unique macrophage population (differing from cancer-associated macrophages) and may have tumor-suppressive characteristics.[20] Ultimately, more experience will be needed to repeat our results in other centers and verify this novel technique's safety and effectiveness.

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DISCLOSURES

Dr. Rehnke is a paid consultant for Becton Dickinson (BD) and has sold intellectual property on absorbable implants to BD. Dr. Rehnke is also a paid consultant for Ricoh, USA, related to their three-dimensional modeling technology, used in preoperative planning for surgical treatment of patients with breast cancer. Dr. Badylak has received research funding from BD. Drs. Clarke and Goodrum have no financial interest to declare in relation to the content of this article. This work received no outside private or public funding.

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