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The Instructions for Authors can be accessed on this journal’s Web site at www.annalsplasticsurgery.com.
President's Introduction to the 2017 SESPRS Supplement

Walter L. Erhardt, MD, FACS

It is with pleasure that I introduce this Annals of Plastic Surgery featuring articles presented at the 59th Annual Meeting of the Southeastern Society of Plastic and Reconstructive Surgeons, which was held on June 11 to 15, 2016, at Disney World's Grand Floridian Resort and Spa. This supplement marks the latest of many years of collaboration through which the southeastern has had the honor of having many of the articles presented at our annual meeting accepted for publication in the Annals of Plastic Surgery.

The stated mission of the SESPRS is “advancing professional excellence, quality education, and regional collegiality,” and the Society's main educational endeavors, the Breast and Oculoplastic Symposia held annually in Atlanta in January and the Society's Annual Meeting held at a resort in the southeast each June, are 2 renowned plastic surgery educational events. Whereas the symposia focus on single anatomic regions, the annual meeting's content, developed in response to member input, covers the spectrum of plastic surgery. A combination of panels, lectureships (including MOC-approved presentations), member articles, and a robustly competitive resident article competition, the Annual Meeting format contains both aesthetic and reconstructive topics, as well as topics to aid our members in maintaining professional and efficient practices.

True to the scope of last year's meeting, the 19 articles included in this Annals of Plastic Surgery issue range from research to clinical and aesthetic to reconstructive. All of the abstracts were peer reviewed by the SESPRS Scientific Program Committee chaired by Dr. Braun Graham and formatted by the authors for inclusion in this issue. My thanks to the authors and to the Annals of Plastic Surgery editorial staff for their help in making this supplement possible. I hope you will find the following articles stimulating.
Neoadjuvant Therapy Combined With Oncoplastic Reduction for High-Stage Breast Cancer Patients

Justine S. Broecker, BA,* Alexandra M. Hart, MD,† Toncred M. Styblo, MD,‡ and Albert Losken, MD†

Objective: Oncoplastic surgery has been shown to be a good alternative to breast conservation surgery (BCS) alone for patients with breast cancer. Its role in patients with advanced disease is unclear. In this study, we evaluate the safety of oncoplastic BCS (OBCS) in patients who received neoadjuvant therapy (NT) for high stage breast cancer.

Methods: The oncologic outcomes of consecutive patients classified as high stage (>T2 or at least N1) who received NT followed by BCS at EUH by a single breast surgeon (T.M.S.) from September 2004 until June 2015 were compared with those who received BCS combined with an oncoplastic reduction. Patients were surveyed using the Breast-Q to determine their satisfaction after surgery.

Results: A total of 87 patients were included in this series. The mean initial tumor size (4.37 vs 2.56 cm), the weight of the surgical specimen, and the post-NT tumor size were all larger in the OBCS group as compared with BCS alone (1.54 vs 1.29 cm). The mean follow-up was 44 months. The average percent reduction in tumor size in response to NT was slightly greater in the OBCS group (61 vs 52%). Oncologic outcomes were similar for OBCS reduction and BCS groups, respectively: positive margin rate, reexcision rate, completion mastectomy rate, local recurrence rate, and 5-year DSS. Patient satisfaction was similar between the 2 groups.

Conclusions: The oncologic approach in high stage patients treated with neoadjuvant systemic therapy has been well established. Oncoplastic reduction can be further subdivided into volume displacement and volume replacement forms of reconstruction. Oncoplastic surgery (OBCS) can be further subdivided into volume displacement form of reconstruction at the time of lumpectomy. Oncoplastic techniques have evolved to broaden the indications for breast conservation therapy and to improve aesthetic results after BCT. Additional oncologic benefits of oncoplastic techniques compared with BCT alone have also been well established.

Oncoplastic techniques may broaden indications of BCT to include patients with breast cancer and address tissue defects, and has gained popularity as an alternative technique to breast conservation surgery (BCT) alone. Oncoplastic breast conservation surgery (OBCS) can be further subdivided into volume displacement and volume replacement forms of reconstruction. Oncoplastic reduction is defined as volume displacement form of reconstruction at the time of lumpectomy. Oncoplastic techniques have evolved to broaden the indications for breast conservation therapy and to improve aesthetic results after BCT. Additional oncologic benefits of oncoplastic techniques compared with BCT alone have also been well established.

The ability of the OBCS technique to preferentially treat larger tumors also makes it amenable to neoadjuvant chemotherapy, and the oncologic safety of neoadjuvant therapy (NT) combined with oncoplastic reduction has also been well established.

There has been limited evaluation of the oncologic safety of NT followed by oncoplastic reduction for higher stage breast cancer patients. The purpose of this report is to determine whether it is safe to perform NT followed by oncoplastic reduction in higher stage breast cancer patients.

METHODS

This is a retrospective review of all patients with a diagnosis of high stage breast cancer (>T1 or at least N1) who received NT before breast conservation therapy between September 2004 and June 2015. Patients were excluded from this study if they had metastasis (M1) at the time of diagnosis or did not adhere to the recommended standard treatment for their disease. Study approval was obtained from the institutional review board.

Patients were stratified into 2 groups based on surgical procedures received: those who underwent BCT followed by immediate oncoplastic reduction (group 1) and those who underwent BCT alone without any immediate reconstruction (group 2). All BCTs were performed by a single oncoplastic surgeon (T.M.S.) and all additional reconstruction was performed by a single plastic surgeon (AL). Clinical and pathologic variables evaluated included patient demographics, preoperative histology and clinical stage, NT received, details of BCT as well as oncoplastic reduction if received, postoperative histology, and clinical course after surgery. Patients were defined as high stage based on clinical stage before initiating NT (>T1 or at least N1). Intraoperative data evaluated included tumor size, specimen weights, nodal status, and specimen radiography when appropriate. In all cases, the tumor was excised by the surgical oncologist before submission for routine pathologic analysis. All patients having preoperative imaging guidance confirmed specimen adequacy with intraoperative specimen radiography. Both pre-NT and post-NT tumor size were determined by imaging (either ultrasound or magnetic resonance imaging) and percent change in tumor size in response to NT was then calculated between the 2 tumor sizes.

Outcomes of interest included positive surgical margins, surgical reexcision, progression to completion mastectomy, local recurrence, metastasis, and death. Before the 2013 SSO/ASTRO guidelines some patients received re-excision for margins 1 mm or less.

Patients from both groups were surveyed using the Breast-Q to determine patient satisfaction with their breast surgery. Surveys were mailed to patients or conducted over the telephone.

Statistical Analysis

General frequencies, chi-square and Kaplan-Meier statistical analysis were calculated using SPSS 23.0 (Armonk, NY: IBM Corp). Chi square analysis was performed to compare BCS and OBCS cohorts. Fischer’s exact test was used to calculate P values. Survival analysis was performed using Kaplan-Meier.

RESULTS

Demographic and Clinicopathologic Results

We included a total of 87 patients in our review who received NT followed by breast-conserving therapy (BCT) as shown in Table 1.
## TABLE 1. Demographic, Clinicopathologic, and Oncologic Results

<table>
<thead>
<tr>
<th></th>
<th>All Patients, 87</th>
<th>OBCS, 47 (53)</th>
<th>BCS, 40 (47)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age: mean (range), y</strong></td>
<td>57 (22–86)</td>
<td>53 (22–73)</td>
<td>61 (35–86)</td>
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</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
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<tr>
<td>White</td>
<td>43 (51)</td>
<td>21 (45)</td>
<td>22 (60)</td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>38 (45)</td>
<td>24 (51)</td>
<td>14 (38)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2 (2)</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (1)</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>BMI, mean (range)</strong></td>
<td>30.5 (18.5–53.7)</td>
<td>30.8 (22.0–44.7)</td>
<td>28.9 (19.5–43.1)</td>
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</tr>
<tr>
<td><strong>IDC</strong></td>
<td>73 (84)</td>
<td>36 (90)</td>
<td>37 (79)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>ILC</strong></td>
<td>12 (14)</td>
<td>4 (10)</td>
<td>8 (17)</td>
<td></td>
</tr>
<tr>
<td><strong>ER+/PR+</strong></td>
<td>48 (55)</td>
<td>26 (55)</td>
<td>22 (55)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Luminal A</strong></td>
<td>34 (39)</td>
<td>19 (30)</td>
<td>15 (38)</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>Luminal B</strong></td>
<td>14 (16)</td>
<td>7 (15)</td>
<td>7 (18)</td>
<td>0.97</td>
</tr>
<tr>
<td><strong>HER-2+</strong></td>
<td>29 (33)</td>
<td>17 (36)</td>
<td>12 (30)</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>Triple-negative</strong></td>
<td>22 (25)</td>
<td>9 (19)</td>
<td>13 (33)</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Pre-NT AJC stage:</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>2</td>
<td>66 (74)</td>
<td>35 (75)</td>
<td>31 (78)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21 (24)</td>
<td>12 (26)</td>
<td>9 (23)</td>
<td></td>
</tr>
<tr>
<td><strong>Preoperative T stage:</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>T1</td>
<td>19 (21)</td>
<td>6 (13)</td>
<td>13 (33)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>49 (55)</td>
<td>28 (60)</td>
<td>21 (53)</td>
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<td>T3</td>
<td>11 (12)</td>
<td>9 (19)</td>
<td>2 (5)</td>
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</tr>
<tr>
<td>T4</td>
<td>8 (9)</td>
<td>4 (9)</td>
<td>4 (10)</td>
<td></td>
</tr>
<tr>
<td><strong>Preoperative N stage:</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>N0</td>
<td>39 (44)</td>
<td>20 (43)</td>
<td>19 (48)</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>38 (43)</td>
<td>23 (49)</td>
<td>15 (38)</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>9 (10)</td>
<td>3 (6)</td>
<td>6 (15)</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td>1 (1)</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-NT tumor size: mean (range), cm</strong></td>
<td>3.58 (0.40–11.00)</td>
<td>4.37 (0.70–11.00)</td>
<td>2.65 (0.40–6.50)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Postoperative tumor size: mean (range), cm</strong></td>
<td>1.43 (0–5.2)</td>
<td>1.54 (0–4.4)</td>
<td>1.29 (0–5.2)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>% Reduction in tumor size, mean (range)</strong></td>
<td>57 (–80 to 100)</td>
<td>61 (–80 to 100)</td>
<td>52 (–40 to 100)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Response to NT:</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>Complete</td>
<td>32 (27)</td>
<td>17 (36)</td>
<td>15 (38)</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>44 (51)</td>
<td>26 (55)</td>
<td>18 (45)</td>
<td></td>
</tr>
<tr>
<td>Zero</td>
<td>3 (4)</td>
<td>0</td>
<td>3 (8)</td>
<td></td>
</tr>
<tr>
<td>Progression</td>
<td>8 (9)</td>
<td>4 (9)</td>
<td>4 (10)</td>
<td></td>
</tr>
<tr>
<td>Positive margin</td>
<td>6 (7)</td>
<td>3 (6)</td>
<td>3 (8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Reexcision</td>
<td>5 (6)</td>
<td>2 (4)</td>
<td>3 (8)</td>
<td>0.66</td>
</tr>
<tr>
<td>Reexcision positive margins</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
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<tr>
<td>Completion mastectomy</td>
<td>5 (6)</td>
<td>3 (6)</td>
<td>2 (5)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>NT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemo (Adria)</td>
<td>41 (47)</td>
<td>19 (40)</td>
<td>22 (55)</td>
<td>0.19</td>
</tr>
<tr>
<td>Chemo (Tax)</td>
<td>21 (24)</td>
<td>12 (24)</td>
<td>9 (23)</td>
<td>0.83</td>
</tr>
<tr>
<td>Herc/Per chem</td>
<td>19 (21)</td>
<td>12 (24)</td>
<td>7 (18)</td>
<td>0.42</td>
</tr>
<tr>
<td>Hormonal</td>
<td>6 (7)</td>
<td>4 (9)</td>
<td>2 (5)</td>
<td>0.36</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>5 (6)</td>
<td>2 (5)</td>
<td>3 (6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Metastasis</td>
<td>12 (14)</td>
<td>5 (11)</td>
<td>7 (18)</td>
<td>0.37</td>
</tr>
<tr>
<td>Time to local recurrence: mean (range), mo</td>
<td>23 (10–48)</td>
<td>19 (17–22)</td>
<td>29 (10–48)</td>
<td>0.69</td>
</tr>
<tr>
<td>Time to metastasis: mean (range), mo</td>
<td>34 (11–71)</td>
<td>29 (11–71)</td>
<td>38 (19–59)</td>
<td>0.43</td>
</tr>
<tr>
<td>Death</td>
<td>10 (11)</td>
<td>4 (9)</td>
<td>6 (15)</td>
<td>0.49</td>
</tr>
<tr>
<td>NED</td>
<td>69 (78)</td>
<td>40 (85)</td>
<td>29 (73)</td>
<td>0.50</td>
</tr>
<tr>
<td>Length of follow-up: mean (range), mo</td>
<td>44 (2–125)</td>
<td>44 (2–125)</td>
<td>43.4 (10–101)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

n/a indicates not applicable; NED, no evidence of disease.
Forty-seven patients underwent an oncoplastic reduction at the same time as BCT (group 1) and 40 patients received BCT alone (group 2). Patients in group 1 were younger (mean age, 53 vs 61; \( P = .002 \)).

Patients in group 1 had significantly larger initial tumor sizes before NT (4.37 cm vs 2.65 cm; \( P < .001 \)) and had a more advanced T stage (28% vs 15% T3/T4; \( P = .05 \)). The majority of patients in both groups were hormone receptor positive (either ER or PR positive or both) (55% vs 55%; \( P = 1.00 \)). There were similar rates of Her-2–positive breast cancer (36% vs 25%; \( P = .37 \)) but there was a slightly higher rate of triple negatives in the group 2 (23% vs 33%, \( P = .48 \)). Most patients received neoadjuvant chemotherapy in both groups. Most triple negative breast cancer patients received Adriamycin-based chemotherapy (60%) followed by taxol-based chemotherapy (40%). All eligible patients (by date) with HER-2neu amplification received herceptin or pertuzumab based induction, and a smaller percentage (7%) received hormonal NT. Response to NT was greater in group 1 compared with group 2 (average % reduction in tumor size, 61% vs 52%; \( P = .28 \)) (Figs. 1–4).

The mean weight of excised tumor was larger in group 1 (152.3 vs 70.2 g; \( P = .012 \)). The tumor size determined by imaging after NT and surgical excision was also larger in group 1 (1.29 cm vs 1.04 cm; \( P = .45 \)).

The majority of patients received adjuvant hormonal therapy (51% vs 60%) as well as radiation (96% vs 93%) after surgery (exceptions included completion mastectomy or patient and/or Medical Doctor choice).

### Oncologic Outcomes

Positive margin rate (6% vs 8%, \( P = 1.00 \)), re-excision rate (4% vs 8%, \( P = .66 \)), completion mastectomy rate (6% vs 3%, \( P = 1.00 \)), local recurrence rate (5% vs 6%, \( P = 1.00 \)), metastasis rate (11% vs 18%, \( P = .37 \)), and death rate (9% vs 15%, \( P = .49 \)) were similar between the 2 groups. The mean time to local recurrence was 23 months, and similar between the 2 groups (19 vs 29 months; \( P = .69 \)). Mean time to metastasis (29 months vs 38 months; \( P = .43 \)) was longer in the BCS group. Average length of follow up was 44 months for both groups combined (2–125 months) with similar rate of follow-up between the 2 groups. Five-year disease-specific survival (95% vs 100%, \( P = .64 \)) were similar between groups 1 and 2, respectively. At most recent follow-up, 85% of patients in group 1 and 73% of patients in group 2 were disease-free (no evidence of disease, \( P = .05 \)).

### Patient Satisfaction Results

A total of 30 patients completed a subset of questions from the postoperative BREAST-Q survey regarding satisfaction with their breast surgery. More patients from the OBCS reported to be very satisfied with the appearance (\( P = .03 \)). Also, patients in the OBCS group were more often satisfied with the size of their breast postoperatively (66% vs 50%, \( P = .63 \)) and how their breasts lined up with each other (53% vs 31%, \( P = .42 \)). Please refer to Figure 5 for results from the patient survey regarding their satisfaction with breast surgery. We also surveyed patients subjectively, and a common theme mentioned among several patients was that radiation changed the cosmetic result of their breast after surgery.

### DISCUSSION

Currently, there is a 12.4% lifetime risk of invasive breast cancer for women in the United States. Screening and management of breast cancer has evolved over the past few decades, resulting in an increased survival rate.\(^{15}\) Therefore, the surgical management of breast cancer has also shifted focus to reflect these changes in survival to enhance patient quality of life after breast cancer. Breast-conserving surgery was introduced in 1981\(^{16}\) and has continued to demonstrate comparable oncological outcomes to radical mastectomy with superior quality of life for the treatment of some breast cancers.\(^ {17,19} \) However, breast conservation surgery has limitations to the size of tumor that can be adequately removed without significant breast deformity. Oncoplastic breast conserving surgery (OBCS) was introduced into the literature in the mid-1990s\(^ {18} \) as a means to expand the benefit of breast conserving to include wider excisions while maintaining cosmesis.\(^ {1} \) There are a variety of OBCS techniques available depending on various tumor and patient characteristics\(^ {1} \) that are broadly divided into volume displacement, volume replacement and reduction.\(^ {21} \) Oncoplastic reduction combines lumpectomy with traditional breast reduction. Although OBCS including oncoplastic reduction has been developed with oncologic safety in mind and has often shown similar oncologic outcomes to breast conserving surgery alone, little is known about the indications for and oncologic safety of oncoplastic reduction for higher-stage patients who have a higher risk of mortality from breast cancer.
We reviewed 87 high-stage breast cancer patients who underwent breast conserving surgery after NT. Forty patients received breast conservation therapy alone and 47 received immediate oncoplastic reduction after their breast-conserving surgery. Our patient population reflects similar demographics and clinical characteristics to high-stage breast cancer patients diagnosed and treated in the United States and were relatively similar between the 2 groups. The mean age at time of surgery of our combined groups was 57 years, slightly younger than the median age of breast cancer diagnosis in the United States (61 years); and, the patients who had oncoplastic reduction were significantly younger than those who underwent breast conserving surgery alone (53 vs 61, \( P = 0.002 \)). This reflects a trend nationally in that younger women are more likely to pursue breast reconstruction compared to older women.

The average tumor size preoperatively was significantly larger for the OBCS group compared with the BCT group (4.36 cm vs 2.54 cm, \( P < 0.001 \)), and OBCS patients had a significantly more advanced T stage (28% vs 15%, \( P = 0.05 \)). The ability of oncoplastic surgery and immediate reconstruction to enable greater resections with breast conserving therapy as opposed to mastectomy has been well...
established. The OBS patients tended to have a greater response to NT with a slightly greater average percent reduction in tumor size (69.5% vs 48.5%, \( P = 0.26 \)), although, oncoplastic patients had larger resections (152.3 g vs 70.8 g, \( P = 0.012 \)) It is unclear why these patients may have responded to a greater degree despite similar molecular subtypes and treatment. As a result, tumor sizes were relatively similar between the 2 groups at the time of surgery (1.54 cm vs 1.29 cm, \( P = 0.28 \)).

Our results demonstrate similar oncologic outcomes for high-stage breast cancer patients treated with oncoplastic breast-conserving surgery as compared to breast conserving surgery alone. Positive margin rate, reexcision rate, completion mastectomy rate, local recurrence, metastasis and death rate were similar between the 2 groups. In addition, 5-year disease-specific survival was similar between the 2 groups. The oncologic safety of oncoplastic techniques has been well established for lower-stage breast cancers, but its safety among higher-stage breast cancer patients, particularly after NT, has been less well studied. Although we have a small study size, our results along with others suggest that oncoplastic reduction is a safe alternative after NT for high-stage breast cancer patients and should be further studied with larger sample sizes and longer follow-up.

One of the primary benefits of oncoplastic surgery is its demonstrated ability to improve patient cosmesis and satisfaction after surgical resection for breast cancer. Oncoplastic reduction in particular has the added benefit of reducing macromastia and because it is often performed bilaterally can retain breast symmetry after lumpectomy. Unfortunately, as has been well documented, radiation after BCT can significantly alter cosmetic results of breast reconstruction, and many of our patients noted that radiation similarly negatively impacted the cosmesis of their breast after either surgery through the development of skin fibrosis, arm lymphedema, and change in the size of the radiated breast. However, in general, based on the answers to the BREAST-Q, patients who underwent oncoplastic reduction appeared more likely to be satisfied with the comfort, appearance and size of their breast compared with the patients who underwent breast conservation therapy alone.

Our study is limited to a small, retrospective review of patients whose surgery was chosen based on Medical Doctor/patient preference rather than randomization. To further evaluate the impact of oncoplastic surgery oncologic outcomes, larger prospective randomized studies with longer follow-up are needed.

CONCLUSIONS

Our results suggest that oncoplastic surgery is an oncologically safe alternative to breast-conserving surgery alone with the potential for superior patient cosmesis and satisfaction for high stage breast cancer patients after NT. Furthermore, oncoplastic reduction paired with NT appears to be able to broaden the indication for breast-conserving surgery for higher-stage patients with larger tumor sizes who would otherwise require mastectomy.

REFERENCES

The Muscle-Sparing Latissimus Dorsi Flap for Breast Reconstruction: A Retrospective Review of 126 Consecutive Flaps

Jonathan Cook, MD,* Jessica Waughtel, DO,† Christopher Brooks, MD,‡ Dawn Hardin, RN,‡ Yin Kan Hjee, MD,‡ and Yoav Barnavon, MD†

Abstract: Our experience in the use of muscle-sparing latissimus dorsi (MSLD) flaps for breast reconstruction is presented. The procedure was performed on 83 patients by the senior author over an 8-year period. Of the 83 patients reviewed, a total of 126 MSLD flaps were done for immediate (26) or delayed (100) breast reconstructions. Preoperative and postoperative photographs were taken of all patients, and complications as well as ancillary procedures were recorded. The MSLD flap is shown to be a versatile option for breast reconstruction in a variety of clinical settings, with minimal complications and satisfactory aesthetic results.

Key Words: breast reconstruction, latissimus dorsi flap, myocutaneous flap, muscle-sparing, MSLD, thoracodorsal artery, descending branch

BACKGROUND

The latissimus dorsi (LD) musculocutaneous flap has been a reliable option for breast reconstruction since it was first described in 1906.1–3 In 1995, Angirigiani et al2 were the first to describe the thoracodorsal artery perforator flap. Schwabegger et al3 in 2003 reported the advantages of a “muscle-sparing” approach, harvesting a larger skin paddle carried by a relatively small segment of LD muscle. In 2008, Hamdi4 noted that this skin paddle could be oriented obliquely for improved contour. Saint-Cyr5 further refined this approach in 2009, emphasizing that a transversely oriented skin paddle with a pedicled descending branch muscle-sparing latissimus dorsi (MSLD) flap resulted in minimal functional deficits, a low incidence of donor-site seromas, and a cosmetically acceptable scar.

Considering the work done by previous authors, we aimed to determine whether these results are reproducible over a variety of clinical settings, having utility in an immediate and delayed fashion, and whether the MSLD flap could be utilized once other reconstructive procedures had failed. Whereas previous studies have reported on the efficacy, aesthetics, and complication rates of the MSLD flap, our study provides the largest retrospective review of the MSLD flap for breast reconstruction. Our surgical technique, as well as its success in multiple clinical settings, ancillary procedures, and associated complications, is reported here.

PATIENTS AND METHODS

A retrospective chart review of patients who underwent breast reconstruction with MSLD flaps from September 2008 to January 2016 was performed. Inclusion criteria were any patient who underwent MSLD flap reconstruction by our senior author during the defined study period and had a minimum of 3 months of follow-up. Patient demographics, body mass index (BMI), and breast reconstructive history were collected through careful review of the patients’ medical records. Patients were divided into 3 groups based on their indications for MSLD flap reconstruction: immediate reconstruction, delayed primary reconstruction, and salvage of previously failed breast reconstruction.

Out of 83 patients included in this study, there were a total of 126 flaps. Mean age at time of MSLD flap reconstruction was 56 years (range, 30–81 years). Mean BMI at the time of surgery was 30 kg/m² (range, 17.47 kg/m²). All patients were followed in the office for a minimum of 3 months postoperatively (range, 3 months to 5 years). Complications were recorded and included the presence of infection (defined as the presence of erythema, wound drainage, or positive wound cultures), clinical seroma, hematoma, and partial flap necrosis. Ancillary procedures were also recorded, including placement of breast implants and fat grafting.

Patient Selection

Preoperative photographs were taken upon initial consultation. The full range of operative choices was considered for all patients. When abdominally based reconstruction was not considered an option, or if patients were poor candidates for implant-based reconstruction, they were offered MSLD flap reconstruction. Patients were considered appropriate candidates for MSLD flap reconstruction if they desired autologous tissue reconstruction and if they were deemed unfit for an abdominally based procedure. The ideal patient was one whose upper back adipose tissue provided an approximate match for their premastectomy breast tissue volume.

Operative Technique

The skin flap and the anterior border of the LD muscle are marked preoperatively with the patient in the standing position. A pinch test of the transverse skin crease below the axillary fat pad is used to identify the widest portion of the transversely oriented flap. This crease is continuous with the inframammary fold (Fig. 1). The patient is positioned intraoperatively in the lateral decubitus position. An elliptical incision is made, beginning at the inframammary fold and extending towards the midline of the back, along the inferior margin of the skin flap. The native back skin is elevated from the LD muscle inferiorly, and the anterior muscle border is identified. The latissimus muscle is divided distal to the flap to create a 5-cm-wide muscle strip, and a retrograde dissection of the flap and overlying soft tissue paddle is performed. The anterior descending branch of the thoracodorsal artery identiﬁed with a Doppler probe, and muscle splitting is then further performed. When available, indocyanine green imaging is used to confirm adequate flap perfusion. The mastectomy defect is then prepared, if necessary, and the flap is transferred to the recipient bed. The back incision is closed in layers over a closed-suction drain. The patient is then discharged on the second postoperative day.
repositioned into the supine position on the operating room table, and the flap is partially deepithelialized before inset.

RESULTS

Eighty-three patients were included in this study, for a total of 126 flaps. Seventeen patients underwent immediate reconstruction, for a total of 26 flaps (21%). Sixty-six patients underwent delayed reconstruction, for a total of 100 flaps (79%). Delayed reconstruction was then subdivided into delayed primary (33%) and salvage reconstruction (46%) (Fig. 2).

The follow-up period ranged from 3 months to 5 years, and all patients were evaluated by the operating surgeon. Ancillary procedures were deemed necessary by assessing for symmetry, the presence of contour deformities, patient satisfaction, and ultimate goals (Table 1). Twenty-two patients (26.5%) underwent placement of breast implants as part of their reconstruction, and 52 patients (62.7%) had fat grafting.

Regardless of indication, there were a total of 39 flap-related complications (summarized in Table 2). The most common complication in our study was minor infection, with a rate of 11.1%. This was followed by fat necrosis (7.9%), donor-site seroma (5.5%), partial flap necrosis (4%), and hematoma (1.6%). There were no cases of complete flap loss.

Of the immediate primary MSLD flap group, there were 2 cases of minor infection (7.7%), including 1 case of an infected seroma diagnosed on culture of aspirated fluid and 1 case of seropurulent incisional drainage. Both cases were managed successfully with antibiotics alone. In addition, there was 1 case of donor-site seroma (3.8%), 2 cases of fat necrosis (7.7%), and 1 case of partial flap necrosis (3.8%). There were no hematomas or complete flap loss in the immediate primary group. The total complication rate for the immediate primary group was 23% (6 of a total of 26 flaps).

In the delayed primary group, there were 2 cases of minor infection (4.8%), 5 cases of donor-site seroma (11.9%), 1 hematoma (2.4%), 4 cases of fat necrosis (9.5%), and 4 cases of partial flap necrosis (9.5%). One case of infection was simple cellulitis, and the other was considered infected because of prolonged wound healing time, with subsequent resolution after antibiotics. The total complication rate in the delayed primary group was 38% (16 of 42 flaps).

In the salvage MSLD flap group, there was a similar rate of complications at 28% (16 of 58 flaps). There were 10 cases of minor infection (17.2%), 1 case of seroma (1.7%), 1 case of hematoma (1.7%), and 4 cases of fat necrosis (6.9%). These results are summarized in Table 3.

CASE REPORTS

Case 1

A 57-year-old patient presented status post left modified radical mastectomy and radiation therapy, with severe skin hyperpigmentation

<table>
<thead>
<tr>
<th>Flap-related Complication</th>
<th>No. Flaps (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complications</td>
<td>87 (69)</td>
</tr>
<tr>
<td>Infection</td>
<td>14 (11.1)</td>
</tr>
<tr>
<td>Seroma</td>
<td>7 (5.5)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Partial flap necrosis</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Fat necrosis</td>
<td>10 (7.9)</td>
</tr>
<tr>
<td>Total complications</td>
<td>38 (30)</td>
</tr>
</tbody>
</table>
and tissue contraction. She also had a past medical history of suction lipectomy of the abdomen. She was not a candidate for implant-based reconstruction. Her BMI was 31 kg/m$^2$. She underwent delayed left breast reconstruction with MSLD flap, subsequent fat grafting, and right mastopexy for symmetry (Fig. 3).

Case 2
A 53-year-old woman presented after having left modified radical mastectomy and radiation therapy. She desired breast reconstruction with autologous tissue but was fearful of abdominally based reconstruction. Her BMI was 29 kg/m$^2$. She underwent delayed left breast reconstruction with MSLD flap and subsequent fat grafting, nipple reconstruction, and nipple tattooing (Fig. 4).

Case 3
A 61-year-old female presented in consultation for possible immediate breast reconstruction. She was recently diagnosed with left breast multifocal ductal carcinoma in-situ. Her BMI was 35 kg/m$^2$. Her surgical history included bilateral reduction mammoplasty. She underwent immediate left breast reconstruction with MSLD flap with subsequent right mastopexy, fat grafting, and upper body lift (Fig. 5).

Case 4
A 55-year-old female presented with a diagnosis of right breast invasive ductal carcinoma (Fig. 6). Genetic testing was also completed given a strong family history of breast cancer. She was found to be positive for the $BRCA2$ mutation. Her BMI was 27 kg/m$^2$, and she had a history of bilateral breast mastopexy and abdominoplasty. Initially, the patient desired implant-based reconstruction, and she underwent bilateral skin-sparing and nipple-sparing mastectomies with placement of tissue expanders. Her postoperative course was complicated by partial flap necrosis. Tissue expanders were removed, and after 3 months, she returned to the operating room for bilateral MSLD flaps reconstruction. Her second recovery was uneventful. We were able to attain reasonable

<table>
<thead>
<tr>
<th>Flap-related Complication</th>
<th>Immediate (%)</th>
<th>Delayed (%)</th>
<th>Salvage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2 (7.7)</td>
<td>2 (4.8)</td>
<td>10 (17.2)</td>
</tr>
<tr>
<td>Seroma</td>
<td>1 (3.8)</td>
<td>5 (11.9)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>0 (0)</td>
<td>1 (2.4)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Fat necrosis</td>
<td>2 (7.7)</td>
<td>4 (9.5)</td>
<td>4 (6.9)</td>
</tr>
<tr>
<td>Partial flap necrosis</td>
<td>1 (3.8)</td>
<td>4 (9.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total complications</td>
<td>6 (23)</td>
<td>16 (42)</td>
<td>16 (28)</td>
</tr>
</tbody>
</table>
FIGURE 4. A 53-year-old female previously underwent left modified radical mastectomy and radiation therapy. Preoperative photographs (top row). Twenty-eight months after left MSLD flap and subsequent fat grafting (bottom row).

FIGURE 5. A 61-year-old female diagnosed with left breast multifocal ductal carcinoma in-situ desired autologous breast reconstruction. Her surgical history included bilateral reduction mammoplasty. Preoperative photographs (top row). After immediate left breast reconstruction with MSLD flap with subsequent right mastopexy, fat grafting, and upper body lift (bottom row).
We report our experience using the MSLD flap in a variety of settings for breast reconstruction in 83 patients (126 flaps). To our knowledge, this represents the largest series of MSLD flaps reported in the literature to date, it is not possible to draw definitive conclusions about specific outcomes or complications. Indeed, the incidence of complications reported in our series is higher than noted in previous studies.\textsuperscript{4,5} This could be explained in part by the relatively broad criteria in the literature. Based on our experience, we believe that the MSLD flap can reach as far medially as the anterior midline. This expands the surgeon’s options for flap placement and provides an opportunity to correct in future study through the use of standard definitions for postoperative complications.

Conclusions

This study reports our experience using the MSLD flap in a variety of settings for breast reconstruction in 83 patients (126 flaps). To our knowledge, this represents the largest series of MSLD flaps reported in the literature. Based on our experience, we believe that the MSLD flap can be considered a “workhorse” flap for breast reconstruction. We found

Symmetry and a good aesthetic outcome after bilateral MSLD flaps with fat grafting to bilateral breasts (Fig. 7).

**DISCUSSION**

Techniques for breast reconstruction using thoracodorsal artery based flaps have evolved over time, from the use of the entire LD muscle to the thoracodorsal artery perforator flap. Most recently, the pedicled descending branch MSLD flap was described by Saint-Cyr et al.,\textsuperscript{1} who recognized that a transverse skin paddle may be oriented with relative freedom in relation to the underlying perforator vessels. This enabled a more aesthetic outcome with minimal complications, when compared to earlier pedicle flap approaches.\textsuperscript{1,4,6} We report our experience using the MSLD flap for immediate primary, delayed primary, and salvage breast reconstruction in a series of 83 consecutive patients (126 flaps). We achieved excellent subjective and objective outcomes, with follow-up ranging from 3 months to 5 years.

One key feature of our technique is the utilization of a 5-cm–wide muscle strip of the anterior LD during flap harvest. Although this differs slightly from previous recommendations,\textsuperscript{1,3–5,7} we found that using a 5-cm muscle width allowed us to reliably include the anterior descending branch of the thoracodorsal artery and its muscular perforators.

This 5-cm strip typically constitutes less than 20% of the muscle by width and, we believe, is the minimum amount of muscle that should be harvested to ensure perfusion of the overlying skin paddle. By limiting the width of this muscle cuff, the transverse branch of the thoracodorsal artery and the main thoracodorsal nerve may be left in situ. Like previous authors, we believe that the muscle strip plays an important role in protecting the neurovascular pedicle and decreasing seroma formation.\textsuperscript{1,3,6}

Our study also highlights the versatility of the MSLD flap as a reconstructive tool in a variety of situations. One reason for the broad applicability of this flap is in the relatively forgiving relationship between the skin paddle and the underlying perforator.\textsuperscript{1,3} This enables the flap to be designed to accommodate a wide range of body habitus. Indeed, our patients’ mean BMI at the time of surgery was 30 kg/m\textsuperscript{2} (range, 17–47.2 kg/m\textsuperscript{2}).

We achieved highly satisfactory results using the MSLD flap for immediate primary breast reconstruction. This was an attractive option for patients who preferred not to have a breast implant as part of their reconstruction and who desired to maintain an active lifestyle (such as tennis-players, golfers, or bowlers).\textsuperscript{6} In patients whose mastectomies included resection of the nipple-areola complex, we were often able to utilize the MSLD skin paddle as the foundation for areola reconstruction in subsequent procedures. We found that the difference in skin color, turgor, and texture of the MSLD skin paddle provided an ideal contrast to the surrounding skin of the native breast flap (Fig. 8).

The MSLD flap was also particularly well-suited for the so-called salvage breast reconstruction (eg, after previous attempts at breast reconstruction surgery). In the irradiated or previously operated field, the MSLD flap provided the advantages of requiring a relatively simple dissection, with versatility in supporting a variety of flap orientations with respect to thoracodorsal artery perforator location.\textsuperscript{1,5} The anterior extent of the skin paddle dissection recruits additional volume to the flap and facilitates the creation of a conical shape for the breast mound. Coupled with a generous arc of rotation (up to 180 degrees), this flap can reach as far medially as the anterior midline. This expands the surgeon’s options for flap placement and provides an opportunity to inset in a way that enables increased breast projection along with more natural ptosis.

This study has several limitations. First, it is a retrospective study, and although it does provide the largest series of patients reported in the literature to date, it is not possible to draw definitive conclusions about specific outcomes or complications. Indeed, the incidence of complications reported in our series is higher than noted in previous studies.\textsuperscript{4,5} This could be explained in part by the relatively broad criteria we used in defining postoperative infection and seroma and could be corrected in future study through the use of standard definitions for postoperative complications.

Further investigation in the form of a well-controlled cohort study would be necessary to evaluate whether specific patient or operative factors are associated with different complications, as outlined by previous authors. Another area of future study would be in quantifying the differences in operative times between the MSLD and other autologous breast reconstructive procedures; we speculate that the relative ease of positioning the patient (initially in the lateral decubitus position and then supine for completion of flap insetting) provides for a particularly efficient operative approach. Finally, we plan to continue our study by quantifying patient satisfaction using a standardized instrument provided to patients during their postoperative reconstructive journey.

**CONCLUSIONS**

This study reports our experience using the MSLD flap in a variety of settings for breast reconstruction in 83 patients (126 flaps). To our knowledge, this represents the largest series of MSLD flaps reported in the literature. Based on our experience, we believe that the MSLD flap can be considered a “workhorse” flap for breast reconstruction. We found

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FIGURE 6. Preoperative imaging of a 55-year-old female with a history of bilateral breast mastopexy and abdominoplasty who was diagnosed with right breast intraductal carcinoma.
excellent aesthetic and functional results from the use of this flap for immediate breast reconstruction, as well as in the delayed reconstructive setting (after mastectomy) and for salvage after prior failed breast reconstruction. The MSLD flap is a versatile alternative to breast reconstruction using other fasciocutaneous flaps or free tissue transfer techniques.

REFERENCES

FIGURE 7. A 55 year-old-female after bilateral skin-sparing and nipple-sparing mastectomies and failed tissue expander reconstruction secondary to partial flap necrosis (top row). Fifteen months after bilateral MSLD flap reconstruction and fat grafting to bilateral breasts (bottom row).

FIGURE 8. Contrast between the skin paddle and native breast flap skin.
Background: Patients with a history of prior breast augmentation and newly diagnosed breast cancer represent a rapidly expanding and unique subset of patients. Prior studies have described changes in breast parenchyma and characteristic body habitus of previously augmented patients, as well as increased rates of capsular contracture associated with breast conservation therapy. In our current study, we aimed to study the risk factors contributing to morbidity and whether recurrence rates are higher in patients with prior breast augmentation undergoing lumpectomy or mastectomy for breast cancer and identify differences in complications between these 2 groups.

Methods: Retrospective analysis approved by institutional review board was performed on patients with prior breast augmentation undergoing lumpectomy (N = 52) and mastectomy (N = 64) for breast cancer.

Results: Patients with prior breast augmentation undergoing mastectomy had a higher rate of complications compared with those undergoing lumpectomy (20.3% vs 5.9% respectively, \( P = 0.031 \)), after adjusting for patient-specific factors including body mass index [odds ratio (OR), 0.242; 95% confidence interval (CI), 0.063–0.922; \( P = 0.0376 \)], tumor stage (OR, 0.257; 95% CI, 0.064–1.036; \( P = 0.0562 \)), smoking status (OR, 0.244; 95% CI, 0.065–0.918; \( P = 0.0370 \)), and chemotherapy (OR, 0.242; 95% CI, 0.064–0.914; \( P = 0.0364 \)). Four patients (7.7%) developed late complications in the lumpectomy group with 2 developing capsular contractures, 1 had fat necrosis and 1 needed complex reconstruction because of flattening of the nipple-areolar complex. There was no difference in recurrence or tumor margins between lumpectomy and mastectomy groups.

Conclusions: Patients with prior breast augmentation undergoing mastectomy have higher complication rates compared with lumpectomy even after adjusting for tumor stage. There appears to be no increased oncologic risk associated with either procedure given our current follow-up. Understanding these operative risks may help in patients’ decision-making process with regards to type of oncolgic surgery.

Key Words: implant-sparing, augmentation, lumpectomy, mastectomy, breast, reconstruction, submuscular, complications, recurrence

(Ann Plast Surg 2017;78: S269–S274)

 Patients with a history of prior breast augmentation and newly diagnosed breast cancer represent a rapidly expanding and unique subset of patients. Prior studies have described changes in breast parenchyma and characteristic body habitus of previously augmented patients, as well as increased rates of capsular contracture associated with breast conservation therapy. In our current study, we aimed to study the risk factors contributing to morbidity in patients with prior breast augmentation undergoing lumpectomy or mastectomy for breast cancer and identify differences in complications between these 2 groups.

Augmentation mammoplasty is one of the most common cosmetic procedures performed in the United States and continues to rise in frequency. Since 2000, there has been a 35% increase in the number of cosmetic augmentation performed annually with 286,000 augmentations performed in 2014.1 As these numbers continue to rise, it is not surprising that a unique population of patients with prior augmentation will develop breast cancer. There will be 231,840 predicted new diagnoses of breast cancer in females in 2015 occurring most frequently in those aged 55 to 64 years with a 5-year survival rate of roughly 89%.2

Previously augmented patients represent a difficult population for which to care. They have been previously documented as being younger and have lower body mass index (BMI) than women of similar age without augmentation.3 For these reasons, previously augmented patients discussing reconstructive options after a cancer diagnosis may have higher cosmetic demands that need to be considered preoperatively.

As more procedures, such as skin-sparing and nipple-sparing mastectomies, become more commonplace, patients may avoid a portion of the stigma associated with removing their breast by retaining anatomic units that are tied into the psychological aspect of having a breast. Patients continue to opt for implant-based reconstruction with over 80% of reconstructions in 2014 involving some form of breast prosthetic.1 Those undergoing expander-implant reconstruction have the benefit of no donor sites but at the expense of multiple office visits, more extensive surgery, and the associated stigma of an acquired breast absence.4 Patients with previously placed submuscular implants present an opportunity for both the reconstructive surgeon and the patient: the cancer can be dealt with as oncologically feasible, and the patient retains the soft tissue envelope necessary for further procedures.

The choice of oncologic surgery is decided between the patient and breast surgeon with well-documented efficacy and near equivalence in survival rates in mastectomy as well as breast conservation surgery.5 Although the literature is somewhat scarce in previously augmented patients undergoing breast cancer removal, it appears that sparing implants previously placed in a submuscular plane at the time of lumpectomy or mastectomy is a reasonable option.3,6–8 The complications associated with this procedure have been described, although patient-specific factors that cause these complications are lacking at this time. A recent study has demonstrated an increased risk of complications in previously augmented patients undergoing removal of implants with exchange to expanders versus those who undergo implant-sparing mastectomy.9 This lends support to the idea that reconstructive surgeons should consider leaving previously placed submuscular implants in place for both aesthetic and morbidity reduction purposes.

This study examines the largest cohort of patients with prior submuscular breast augmentation undergoing lumpectomy versus mastectomy through an implant-sparing technique with the hopes of identifying risk factors associated with increased complication...
METHODS

Patient Selection

An institutional board review–approved retrospective analysis was performed on patients with prior breast augmentation undergoing lumpectomy (N = 52) and mastectomy (N = 64) for breast cancer. Patients with previously placed subglandular implants undergoing mastectomy or lumpectomy were excluded.

Statistical Analysis

Patients were stratified into 2 groups for complication analysis: those having any postoperative complication and those who did not. The difference in recurrence and complication rates according to patients receiving mastectomy versus lumpectomy was assessed using a \( \chi^2 \) test and summarized as odds ratio (OR) along with 95% confidence intervals (CIs). Wilcoxon rank sum test with normal approximation was used to test difference in BMI between lumpectomy and mastectomy. Fisher exact test was used to test the difference in complication, tumor margins, and other clinical variables between lumpectomy and mastectomy patients. Multiple logistic regression was used to obtain adjusted ORs accounting for smoking status, BMI, chemotherapy, or tumor stage. Bonferroni correction was applied to adjust for multiple comparisons. All \( P \) values are 2-sided, unless otherwise stated, and considered statistically significant for at 0.05 for all comparisons. All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC).

RESULTS

Complications

Patients with prior submuscular augmentation mammoplasty undergoing implant-sparing mastectomy compared with implant-sparing lumpectomy had a statistically significant increased odds of complications (Table 1). The OR was 5.863 (95% CI, 1.255–27.378; \( P = 0.022 \)). The results remained unchanged in favor of lumpectomy compared with mastectomy when adjusted for BMI (OR, 6.013; 95% CI, 1.255–28.807; \( P = 0.025 \)), receipt of chemotherapy (OR, 5.840; 95% CI, 1.231–27.712; \( P = 0.026 \)), and smoking status (OR, 5.857; 95% CI 1.254–27.362; \( P = 0.025 \)). Four patients (7.7%) developed late complications in the lumpectomy group with 2 developing capsular contractures, 1 had fat necrosis and 1 needed complex reconstruction because of flattening of the nipple-areolar complex. There was no difference in recurrence or tumor margins between lumpectomy and mastectomy groups (Table 2).

CONCLUSIONS

Given the nature of breast implants remaining in place for a number of years in combination with the increasing number of cosmetic augmentations performed annually, it is not surprising that the largest numbers of patients with prior augmentation will present with new breast cancer diagnoses desiring reconstruction (Figs. 1, 2). These patients will be faced with a population of surgeons unfamiliar with how to handle their oncologic surgery. Performing a lumpectomy or mastectomy while preserving a previously placed subpectoral breast implant will become a more commonly performed procedure. The core desire is to provide a safe operation, but we should also endeavor to provide the least morbidity as well as superb cosmetic outcomes.

Implant-sparing lumpectomy or mastectomy is a safe procedure to perform and has the benefits of maintaining the breast mound after mastectomy, fewer office visits that forego the painful weekly expansion, avoiding the stigma associated with the mastectomy defect, and less strenuous recovery.4,8 Although delaying the reconstruction limits stress to mastectomy skin flaps, those patients desiring immediate single-stage reconstruction with incremental size changes of the implant can be considered. This works particularly well for a patient with

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>( P )</th>
</tr>
</thead>
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<tr>
<td>All complications</td>
<td>5.863</td>
<td>0.022</td>
</tr>
<tr>
<td>Adjusted for BMI</td>
<td>6.013</td>
<td>0.025</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>5.840</td>
<td>0.026</td>
</tr>
<tr>
<td>Smoking</td>
<td>5.857</td>
<td>0.025</td>
</tr>
</tbody>
</table>

When examining complication rates for patients undergoing implant-sparing lumpectomy versus mastectomy, we found, even after adjusting for comorbidities, a higher rate of complications associated with implant-sparing mastectomy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Lumpectomy N (%)</th>
<th>Mastectomy N (%)</th>
<th>( P )</th>
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<tbody>
<tr>
<td>Smoking</td>
<td>Current</td>
<td>10 (19.2)</td>
<td>7 (10.9)</td>
<td>0.455</td>
</tr>
<tr>
<td></td>
<td>Past</td>
<td>16 (30.8)</td>
<td>23 (35.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonsmoker</td>
<td>26 (50.0)</td>
<td>34 (53.1)</td>
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</tr>
<tr>
<td>Tumor stage</td>
<td>Tis</td>
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<td>8 (13.1)</td>
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<td>T0–T1</td>
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<td>33 (54.1)</td>
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<td>T2–T4</td>
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<td>61 (95.3)</td>
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<td></td>
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<td>4 (7.8)</td>
<td>3 (4.7)</td>
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<td>Tumor margins</td>
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<td>11 (22.9)</td>
<td>12 (20.0)</td>
<td>0.32</td>
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<td>31 (64.6)</td>
<td>45 (75.0)</td>
<td></td>
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<tr>
<td></td>
<td>Positive</td>
<td>6 (12.5)</td>
<td>3 (5.0)</td>
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</table>

When examining recurrence rates or tumor margins between implant-sparing lumpectomy versus mastectomy groups, we found no statistical differences.
implants placed in the remote past that desires immediate exchange because of concerns of the age of the implant. If a patient wants a significant size difference, consideration can be given to exchange of the submuscular implant to a standard 2-stage expander-implant–based reconstruction. However, we feel that the greatest strength of this technique lies in the ability to perform a safe oncologic procedure with an initial implant-sparing procedure, followed by exchange to a larger implant approximately 6 weeks later to achieve the desired size and shape.

Patients undergoing breast cancer surgery with previous augmentation have been shown to have less than 50% of their overall breast volume corresponding to native breast tissue. Although survival is the same, patients should be counseled on the adverse effects of radiation in the setting of retained prosthesis as well as the potential for cosmetic deformity given the small remaining native breast volume. Women with larger breast volumes may find this resultant deformity acceptable; however, the option always exists to use the implant as a static expander of the skin envelope that can later be converted to an autologous reconstruction.

At this time, having an informed discussion with a patient about the risks, benefits, and possible complications is limited by the small sample sizes for many studies examining patients undergoing implant-sparing mastectomy or lumpectomy. A new study reveals the difference in complications between previously augmented and non-augmented patients undergoing immediate reconstruction after mastectomy is

**FIGURE 1.** A, A 47-year-old female with 400 cm$^3$ submuscular saline implants. B, After implant- and nipple-sparing bilateral mastectomies with resection weight of approximately 380 g bilaterally. C, She was ultimately exchanged to 650 cm$^3$ silicone smooth round implants bilaterally.
higher in the previously augmented group, although it does not reach statistical significance. A prior study demonstrated the risk factors associated with complications in non-augmented patients undergoing expander-implant–based reconstruction. Although it is helpful to examine complications in the general population of expander-implant–based reconstruction, this provides a myopic view as the previously augmented population represents a unique subset that is typically younger with a lower BMI.

Our study demonstrates a higher early complication rate associated with implant-sparing mastectomies versus lumpectomies. This is not surprising given that the higher complication rates associated standard and modified radical mastectomies and breast conservation therapy via lumpectomy. Future studies are warranted to determine if these hold consistent for long-term complications.

Capsular contracture remains one of the most concerning complications facing patients undergoing implant-sparing techniques because it requires reoperation and can cause substantial psychosocial stress. Previous studies have reported on the risk of developing subsequent capsular contracture in the setting of retained protheses with rates approximately 60% quoted in each series. Two (3.8%) of our patients undergoing implant-sparing lumpectomy developed late capsular contracture, which is in contrast with the published literature and likely is an effect of short follow up at this time.

Limitations are present in any scientific study. As mentioned above, capsular contracture is a significant concern for any surgeon using implants. This is certainly a shortfall of our article in that any true long-term complication rates for capsular contracture are unable to be gleaned because of our relatively short follow-up as well as small cohorts owing to the relatively new nature of this procedure.

Future studies will aim to further elucidate whether long-term complications bear out any differences from those described above or with the radiation therapy associated with implant-sparing lumpectomies. We will also be considering the unique cohort of genetic carriers for increased breast cancer risk and the philosophy of performing breast augmentation in anticipation of planned bilateral prophylactic mastectomies (Fig. 3).

Our protocol typically involves preoperative collaboration between the breast and plastic surgeons to agree that the procedure is oncologically feasible as well as for preoperative markings. Patients then underwent implant-sparing lumpectomy or mastectomy, and the tissues were allowed to heal for 3 months, at which time the volume of the removed specimen and previously submuscularly placed implant

![Figure 2](image-url)

**Figure 2.** A, A 43 year-old female with history of 380 cm³ saline submuscular augmentation. B, She ultimately underwent unilateral right mastectomy with a 160-g resection specimen and was later exchanged to 480 cm³ saline implant.
The pool of literature that exists on patients with prior augmentation undergoing breast cancer surgery is steadily growing. Most studies describe all patients with implants and a new diagnosis of breast cancer including those placed in a subglandular position. In our experience, these patients are likely not candidates for an implant-sparing procedure. Our study is the largest to date describing a cohort of previous submuscular breast augmentation patients undergoing implant-sparing mastectomy or lumpectomy and the complication rates for them. Preoperative discussion of outcomes is critical in patients that demand superb aesthetic outcomes, and the attempt of this study was to begin qualifying and quantifying those factors associated with complications in this patient population. Understanding these operative risks may help in patients' decision-making process with regards to type of oncologic surgery.

REFERENCES

Unilateral Versus Bilateral Breast Reconstruction

Is Less Really More?

Lauren V. Kuykendall, MD,* Bugra Tugertimur, MS, † Corin Agoris, MS, † Sara Bijan, MS, †
Ambuj Kumar, MD, MPH, ‡ and Deniz Dayicioglu, MD* ‡

Objective: Over the recent years, there has been an increase in prophylactic mastectomies with an associated increase in bilateral breast reconstruction. We aimed to compare outcomes in terms of patient satisfaction with unilateral versus bilateral breast reconstruction after deep inferior epigastric perforator (DIEP) flap and implant-based reconstruction.

Methods: Patients who underwent breast reconstruction by a single surgeon between July 2011 and July 2015 were surveyed using the independently validated BREAST-Q questionnaire. Mean satisfaction scores between patients undergoing unilateral versus bilateral breast reconstruction were compared and stratified based on the type of reconstruction [eg, DIEP flap, tissue expander to implant (TE/I)]. Groups were further categorized by age (patients <55 years and ≥55 years of age) and body mass index (<24.9 and ≥24.9). Complications were recorded.

Results: Of the 308 patients included, 118 (38%) had unilateral reconstruction (42 TE/I and 76 DIEP) and 190 (62%) had bilateral reconstruction (124 TE/I and 66 DIEP). A total of 95 patient surveys were included (31% response rate). Overall, patients receiving unilateral reconstruction demonstrated increased satisfaction with outcome (P = 0.028), psychosocial well-being (P = 0.043), and sexual well-being (P = 0.002). Complication rates were similar between unilateral and bilateral reconstruction. No significant differences for satisfaction were found in the TE/I group (N = 58; unilateral, 10; bilateral, 48).

In the DIEP group (N = 37; unilateral, 20; bilateral, 17), those receiving unilateral reconstruction had higher satisfaction with outcome (P = 0.013) and sexual well-being (P = 0.014). Additionally, younger patients (<55 years) were more likely to undergo bilateral reconstruction (P = 0.018). Body mass index did not have a significant association with unilateral or bilateral reconstruction.

Conclusions: Patients undergoing DIEP flap reconstruction showed higher satisfaction with unilateral reconstruction, whereas patients receiving TE/I reconstruction, either unilateral or bilateral, were equally satisfied. Additionally, younger women were more likely to undergo bilateral reconstruction, which is consistent with current data trends. When considering surgical options, unilateral DIEP flap reconstruction may provide improved outcomes in terms of patient satisfaction when compared with bilateral reconstruction in select patients.

Key Words: breast reconstruction, implant-based reconstruction, DIEP flap reconstruction, patient satisfaction, unilateral versus bilateral reconstruction, BREAST-Q, patient reported outcomes

(Ann Plast Surg 2017;78: S275–S278)

Over the past decade, there has been an increase in contralateral prophylactic mastectomies in women with unilateral breast cancer with a concomitant increase in breast reconstruction.1–4 Since 2000, there has been a 35% increase in breast reconstruction procedures with more than 60% of these being bilateral reconstruction.5 In women with unilateral breast cancer, the annual incidence of contralateral breast cancer ranges from 0.5% to 0.75%, with a lifetime risk of 15%.4–6 Factors associated with increased risk of developing contralateral breast cancer include young age, family history of breast cancer, lobular type histology, multicentric breast cancer, previous chest radiation, and BRCA1/2 mutations.3,4,6,7 Women choose contralateral prophylactic mastectomy for many reasons, including fear of recurrence, anxiety about future risk of new cancer, and improvement in breast reconstruction outcomes.4,5,6 However, this rise in contralateral prophylactic mastectomy is most prevalent in women with early-stage disease for whom long-term cancer survival outcomes are equivalent between breast conservation and mastectomy.6 With comparable oncologic outcomes and survival rates, evaluations of patient-reported outcomes are helpful in facilitating the decision-making process and optimizing long-term health and satisfaction.9 Advocates of prophylactic mastectomy report improved sense of well-being because of decreased disease-related anxiety and the potential for improved aesthetic outcomes, psychosocial well-being, and overall satisfaction.5,10–14

Although studies have reported that patients undergoing post-mastectomy breast reconstruction have improved satisfaction with outcome, there are limited data regarding satisfaction levels when unilateral and bilateral reconstruction are compared.10,12,14 The demand for more rigorous outcome measures has led to increased studies focused on validated patient-reported outcomes.10 Patient-reported outcome measures provide a means of quantifying how the patient perceives their health and the impact treatments have on their quality of life.15 The BREAST-Q questionnaire was developed to provide reliable, valid, and clinically meaningful patient-reported outcomes data.15–17 This questionnaire has been validated in more than 15,000 patients and has been proven to help study and measure the impact and effectiveness of breast surgery from the patient’s perspective.15,16 Using this tool, we aimed to compare patient satisfaction with unilateral versus bilateral breast reconstruction after deep inferior epigastric perforator (DIEP) flap and implant-based reconstruction. We hypothesized that differences between unilateral and bilateral reconstruction would exist among the defined groups.

METHODS

Women who underwent breast reconstruction by a single surgeon between July 2011 and July 2015 were identified using operative case logs. Data were gathered from a retrospective chart review including patient demographics, type of reconstruction, and complications. All women were patients at H. Lee Moffitt Cancer Center and Research Institute, a National Comprehensive Cancer Center, under the care of the senior author. Patients were categorized based on unilateral versus bilateral reconstruction. Patients underwent either DIEP free flap or tissue expander to implant (TE/I) breast reconstruction. In the TE/I group, patients who underwent nipple-sparing mastectomy, delayed reconstruction, radiation therapy, additional flap reconstruction, and placement of acellular dermal matrix as well as those with incomplete...
data were excluded. In the DIEP flap group, those with incomplete data were excluded. Complications were defined as dehiscence, infection, hematoma, full-thickness skin loss, or flap loss requiring reoperation within 30 days.

A total of 308 patients were mailed postoperative satisfaction surveys using the independently validated BREAST-Q questionnaire [BREAST-Q Reconstruction Module (Postoperative) 1.0], and satisfaction scores were recorded on a scale of 0 to 100. The mean satisfaction scores between patients undergoing unilateral versus bilateral breast reconstruction were compared and stratified based on the type of reconstruction (eg, DIEP flap, TE/I).

Secondarily, we evaluated age and body mass index (BMI) in relation to the choice for unilateral versus bilateral reconstruction. Age groups were determined by median age of the patient population (patients <55 years and ≥55 years of age). Body mass index groups were determined by national criteria for normal and obese weight (BMI <24.9 and ≥24.9).

All analyses were performed using SPSS statistical analysis software (version 22; IBM SPSS Statistics, Inc). Difference in satisfaction scores was assessed using the independent sample t test and summarized as mean difference along with 95% confidence intervals. Association between categorical variables was summarized as odds ratio (OR) and 95% confidence interval, and difference was assessed using Fisher exact test. To adjust for multiple comparison, Bonferroni correction was applied. Statistical significant level was set at P < 0.05.

RESULTS

Of the 308 patients initially included, 166 (54%) underwent TE/I reconstruction and 142 (46%) underwent DIEP flap reconstruction. A total of 118 (38%) had unilateral reconstruction (42 TE/I and 76 DIEP), and 190 (62%) had bilateral reconstruction (124 TE/I and 66 DIEP) (Fig. 1).

Within the unilateral group, 58% were more than 55 years of age and 74% had a BMI of more than 24.9. Within the bilateral group, 57% of patients were under 55 years of age and 68% had a BMI of more than 24.9 (Fig. 1). Younger patients were significantly more likely to undergo bilateral reconstruction (OR, 1.812; P = 0.018), whereas BMI had no significant association (OR, 1.359; P = 0.319) (Fig. 2).

Complication rates were similar between the 2 groups (11% overall) with unilateral reconstruction having a 3% complication rate and bilateral reconstruction having an 8% complication rate (P = 0.229) (Fig. 2).

A total of 95 patients completed the BREAST-Q questionnaires (31% response rate). Of those patients who responded, 30 were unilateral and 65 were bilateral. Fifty-eight patients underwent TE/I reconstruction (10 unilateral and 48 bilateral). Thirty-seven patients underwent DIEP free flap reconstruction (20 unilateral and 17 bilateral) (Fig. 1).

Overall, patients receiving unilateral reconstruction demonstrated increased satisfaction with outcome (P = 0.028), psychosocial well-being (P = 0.043), and sexual well-being (P = 0.002). No significant differences for satisfaction were found in the TE/I group. In the DIEP group, those receiving unilateral reconstruction had higher satisfaction with outcome (P = 0.013) and sexual well-being (P = 0.014) (Fig. 3).

DISCUSSION

In recent years, there has been a growing trend toward contralateral prophylactic mastectomy given its ability to reduce the incidence of contralateral breast cancer by more than 90%. This increase in bilateral mastectomy has led to more women electing for bilateral breast reconstruction. Postmastectomy breast reconstruction can be a difficult decision for women given the wide array of surgical options from implant to various autologous-based reconstructions. To better understand...
these decisions, there has been a growing body of literature focusing on patient-reported outcomes and satisfaction following mastectomy and breast reconstruction. Recent data have demonstrated that, although cancer-related anxiety has improved, overall satisfaction following bilateral mastectomy and reconstruction has been less favorable. In this study, we utilized the independently validated BREAST-Q questionnaire to evaluate patient-reported outcomes in terms of satisfaction with unilateral versus bilateral breast reconstruction after DIEP flap and TE/I reconstruction.

We found that patients undergoing unilateral breast reconstruction compared with bilateral breast reconstruction demonstrated higher satisfaction in multiple categories including surgical outcome, psychosocial well-being, and sexual well-being. When patients were stratified into groups based on type of reconstruction, patients who underwent DIEP flap reconstruction demonstrated higher satisfaction with unilateral reconstruction, specifically with surgical outcome and sexual well-being. These findings reinforce current outcomes-based literature and might be attributable to better ability to recreate relative symmetry and shape of the native breast using autologous tissue. Additionally, bilateral autologous reconstruction may not provide adequate volume to replicate missing breasts in selected patients with the potential for increased donor site morbidity. A recent study found that patients who underwent unilateral mastectomy and reconstruction reported preservation of sensation as a reason for improved satisfaction. This may indicate that maintaining the contralateral breast contributes to improved sexual well-being and patient satisfaction.

Patients who underwent TE/I reconstruction demonstrated no significant difference in mean satisfaction scores between unilateral and bilateral reconstruction. These results differ somewhat from previous reports which found improved aesthetic outcome and patient satisfaction with unilateral and bilateral reconstruction. These results differ somewhat from previous reports which found improved aesthetic outcome and patient satisfaction.

FIGURE 2. Patient characteristics: age and BMI in unilateral versus bilateral reconstruction. Younger patients were more likely to undergo bilateral breast reconstruction (P = 0.018). Body mass index showed no significant association (P = 0.319). Complications were comparable (P = 0.229).

![Patient Characteristics](image)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
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<td><strong>Age (n)</strong></td>
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<td>Bilateral</td>
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<tr>
<td><strong>Complications(n)</strong></td>
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<td>9</td>
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</table>

FIGURE 3. BREAST-Q mean satisfaction scores. Overall, patients receiving unilateral reconstruction demonstrated increased satisfaction with outcome (P = 0.028), psychosocial well-being (P = 0.043), and sexual well-being (P = 0.002).
with bilateral implant reconstruction compared to unilateral. This was attributed to the fact that both breast contour and degree of ptosis are symmetrical and the reconstructed breasts age in a similar fashion.\textsuperscript{15,17} Notably, many of these early studies lacked validated patient reported outcome measures.

Of the patients in the TE/I group who responded to the questionnaire, 82\% underwent bilateral reconstruction. Patients undergoing bilateral as compared to unilateral reconstruction were younger and had higher BMI, although the latter finding did not reach statistical significance. A recent study looked closely at patients who opted for bilateral reconstruction and found them more likely to undergo immediate reconstruction, have reconstruction at a younger age, and have a prophylactic mastectomy. These patients were also less likely to undergo radiation and chemotherapy, which likely influences patient motivations and aesthetic standards.\textsuperscript{10,14}

The overall complication rate was 11\% and was comparable between unilateral and bilateral reconstruction (3\% vs 8\%, \textit{P} = 0.229). These rates are slightly less than previous reports, which is likely owed to the fact that only major complications requiring return to the operating room within 30 days were evaluated.

There are a number of limitations to our study. As all surveys were sent at the same time point, patients responded to the surveys at varying stages of their postoperative course. The surveys were sent postoperatively, and patients responded at intervals varying from approximately 6 months to 4 years. Additionally, as patients only responded once to the survey, there was no ability to assess how individual patient satisfaction evolved. Recent studies have demonstrated that satisfaction with breast reconstruction by procedure type may diminish over time. Yueh et al.\textsuperscript{14} reported that health-related quality of life and length of time since surgery significantly affected patient satisfaction, suggesting that older reconstructions are less satisfied than newer reconstructions. As in all survey-based studies, responder bias is inherent as patients at extremes of satisfaction or dissatisfaction are more likely to respond to the survey. Furthermore, the study was a retrospective study and recall bias may exist as patients try to remember details of their reconstruction. Finally, the response rate of the survey was 31\%, which is low compared with other current outcomes based studies. Since the data collection, we have started implementing preoperative and postoperative BREAST-Q questionnaires for all patients undergoing breast reconstruction that will help with future prospective studies where patients can be surveyed at predetermined times.

Despite the increasing trends in bilateral breast reconstruction, we found that patients undergoing unilateral breast reconstruction have higher satisfaction in several categories compared to bilateral reconstruction. In relation to type of reconstruction, we found that women with DIEP flap reconstruction have higher satisfaction with unilateral reconstruction whereas patients with TE/I reconstruction were equally satisfied. Patient-reported outcome measures have become increasingly important in improving quality of care, and further studies will continue to highlight the factors that lead to improved satisfaction for our patients.

\section*{REFERENCES}

Numerical Correlation of Levator Advancement in Preoperative Planning

Valeria Makeeva, BSc,* Sherry S. Collawn, MD, PhD,† Evelina N. Pierce, BA,* Mina S. Mousa, MD,* Jennifer H. Yang, MD,‡ Peter N. Davison, BA,* and Elodie C. Jospitre, BA§

Background: Several procedures have been proposed for the treatment of eyelid ptosis, and both levator advancement and levator plication are widely used to shorten the levator palpebrae superioris. The purpose of this study was to quantify perioperative lid measurements in patients undergoing bilateral levator aponeurosis advancements to aid in preoperative planning.

Methods: Between July 2014 and June 2016, the authors performed a retrospective analysis of all bilateral upper eyelid levator advancement procedures for ptosis performed by the senior surgeon. There are a total of 21 patients (6 men and 15 women) with a mean age of 63 years (range, 48–79 years). The average time at follow-up was 5.3 months, with a range of 1 to 26 months.

Results: In this retrospective study, we collected data on presurgical measurements including marginal reflex distance 1 (MRD1), surgical technique used (symmetrical/asymmetrical levator advancement) with millimeters of advancement used, and postsurgical measurements. We found that on average, an advancement of 4 mm led to an improvement in MRD1 of 2.26 mm (n = 14), and advancement of 5 mm led to an improvement in MRD1 of 2.74 mm (n = 15). Patients also reported improvements in their quality of life.

Conclusions: Our results may be used to guide clinicians in preoperative planning.

Key Words: levator advancement, levator plication, blepharoplasty, marginal reflex distance 1, eyelid ptosis

(Ann Plast Surg 2017;78: S279–S281)

Marginal reflex distance 1 (MRD1) as shown in Figure 1 is defined as the distance between the upper lid margin and the corneal light reflection at forward gaze with eyebrows remaining fixated to eliminate their contribution to lid elevation. It is influenced by the levator aponeurosis, sympathetic innervation to the Muller muscle, the skin and orbicularis muscle, and brow position.¹ Marginal reflex distance 1 was first described by Putterman and Urist² in 1975 to standardize upper eyelid ptosis measurements. Before the popularization of MRD1, clinicians measured the width of the palpebral fissure to determine eyelid elevation, a measure that was unreliable if lower eyelid level was abnormal.³ Normal MRD1 is classified as greater than 2.5 mm, whereas mild upper lid ptosis is classified as less than 2 mm.³

Multiple reports document preoperative and postoperative MRD1 increases after different blepharoplasty procedures including levator advancement.⁴–¹⁴ However, postoperative eyelid height is still cited as difficult to predict.⁵–¹⁵ Although previous reports address intertechnique differences in postoperative eyelid height, they rarely address the subject of predicting such intratechnique differences in postoperative eyelid height.

Intraoperative MRD1 has been suggested as a tool to investigate the relationship between preoperative and postoperative eyelid heights.⁵ However, swelling and weight of the anterior lamella of the eyelids may make intraoperative MRD1 measurements difficult.⁶ We propose an alternate method correlating differing degrees of levator advancement to change in MRD1 to help guide clinicians in preoperative planning.

SURGICAL TECHNIQUE

Levator shortening techniques were popularized in the 1970s and 1980s.²⁰ Jones et al²¹ further used the technique of external levator superioris aponeurosis repair using local anesthesia in 1975.

At our institution and in our report, all patients underwent bilateral levator superioris repair using local anesthesia in sterile fashion, local anesthesia was injected using 1% xylocaine, 2 mL, with 1/100,000 epinephrine. Eye shields were used for globe protection and were applied with topical tetracaine drops. Anesthesia was with monitored anesthesia care. An ellipse of skin was removed approximately 7 to 8 mm above the lash line in men and 8 mm in women. A 1-mm strip of orbicularis was removed, and the levator aponeurosis was then identified with deeper dissection. The tarsal plate was identified, and planned millimeters of advancement were marked on the levator aponeurosis. The levator aponeurosis was then incised over the tarsal plate, and the distal 1 mm of aponeurosis excised. Three horizontal 5–0 Nylon mattress sutures were used to attach the upper tarsal plate to the site marked on the aponeurosis. The amount of advancement was measured and recorded for each eyelid. The supratarsal fold was recreated with three 5–0 Vicryl sutures attaching the orbicularis down to the site of levator advancement.

METHODS

A retrospective review between July 2014 and June 2016 included 42 eyelids of 21 patients (6 men and 15 women) with blepharoptosis corrected by levator advancement technique performed by the senior surgeon. Patients underwent either 4- or 5-mm advancement, and less commonly 3-, 6-, 7-, and 8-mm advancement. The advancement distance was based on the expected elevation of the eyelid over the pupil. University of Alabama at Birmingham, Institutional Review Board for Human Use approval was obtained for review of eyelid ptosis patient records. The average age of the 21 patients included in this study was 63 years, ranging from 47 to 79 years.

Evaluation of preoperative parameters included age, sex, and preoperative eyelid measurements including MRD1. Postoperative data, such as eyelid measurements including MRD1 and length of follow-up, were recorded. Marginal reflex distance 1 measurements were collected using handheld ruler; a method cited as yielding reliable results in the hands of a skilled clinician.¹ In both preoperative groups, no intraoperative complications developed. No infections, hematomas, or other complications were noted postoperatively in either group.

Statistical analyses comparing preoperative and postoperative MRD1 measurements using paired t tests were performed. The average time at follow-up was 5.3 months, with a range of 1 to 26 months.

RESULTS

For 4-mm advancement (n = 14), the average preoperative MRD1 was 1.2 mm, with a range of 0 to 3.5 mm. The average postoperative MRD1 was 3.57 mm, with a range of 3 to 5 mm. It is important to note that postoperative MRD1 of less than 2 mm is classified as mild

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Conflicts of interest and sources of funding: none declared.

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DOI: 10.1097/SAP.0000000000001143
In conclusion, the percent effectiveness was 27%. In addition, we calculated the percent effectiveness of the procedure, which we defined as follows: the percent ratio of MRD1 improvement divided by the advancement distance. In the 4-mm patient population the procedure was 67% effective, whereas in the 5-mm population, it was only 48% effective. Preoperative and postoperative MRD1 improvements were above the 3.57 mm average with a range of 4 to 5 mm. There was a statistically significant difference between preoperative and postoperative MRD1 measurements ($P < 0.05$), with results considered statistically significant when $P$ is less than 0.05. Preoperative and postoperative measurements on patients who underwent 4-mm levator advancements are shown in Figure 2. Overall, based on our numbers, an advancement of 4 mm resulted in an average eyelid elevation of 2.26 mm.

For the 5-mm advancement ($n = 15$), the average preoperative MRD1 was 0.857 mm, with a range of 0 to 2 mm. The average postoperative MRD1 was 3.6 mm, with a range of 3 to 4.5 mm. All patients resulted in postoperative MRD1s greater than 2 mm, indicating that the surgical procedure was successful. Of the 5-mm advancements, 8 postoperative MRD1 improvements were below the 3.6 mm average with a range of 3 to 3.5 mm and 6 were above with a range of 4 to 4.5 mm. The average postoperative improvement in MRD1 in all patients was 3.569 mm, with a range of 3 to 5 mm. There was a statistically significant difference between preoperative and postoperative MRD1 measurements ($P < 0.05$), with results considered statistically significant when $P$ is less than 0.05. Preoperative and postoperative measurements on patients who underwent 5-mm levator advancements are shown in Figure 3. Overall, based on our numbers, an advancement of 5 mm resulted in an average eyelid elevation of 2.74 mm.

Perioperative photographs of 2 patients who underwent levator advancement are shown in Figure 4.

In addition, we calculated the percent effectiveness of the procedure, which we defined as follows: the percent of MRD1 improvement divided by the advancement distance. In the 4-mm patient population the procedure was 67% effective, whereas in the 5-mm population, it was only 48% effective. Preoperative and postoperative MRD1 improvements were above the 3.57 mm average with a range of 4 to 5 mm. There was a statistically significant difference between preoperative and postoperative MRD1 measurements ($P < 0.05$), with results considered statistically significant when $P$ is less than 0.05. Preoperative and postoperative measurements on patients who underwent 4-mm levator advancements are shown in Figure 2. Overall, based on our numbers, an advancement of 4 mm resulted in an average eyelid elevation of 2.26 mm.

Future directions for study include further correlating preoperative and postoperative MRD1 measurements with higher powered investigations including a greater number of patients as one limitation of this study was a small number of patients, making definitive conclusions between measurements and outcomes difficult.

The timing of follow-up can also be a factor in determination of postoperative MRD1, because there is generally a lower amount of eyelid elevation less than 1 month postsurgery. Therefore, it is important to recognize the trend in data points between preoperative and postoperative MRD1 measurements.
Numerical Correlation of Levator Advancement

Ptosis has a diversity of etiologies including acquired and congenital causes. Other future areas for study will be examining levator advancement and perioperative MRD1 measurements will be necessary. Ptosis has a diversity of etiologies including acquired and congenital causes. Other future areas for study will be examining levator advancement and perioperative MRD1 measurements in those patients in whom such measurements may present challenges, such as those with deep eyes, brow ptosis, facial paralysis, or asymmetrical advancements.

ACKNOWLEDGMENT

The artist’s drawing in Figure 1 was by Matthew K. Collawn. Permission was obtained to use his artwork in this article.

REFERENCES

Dermal Autograft Using Donor Breast as Alternative to Acellular Dermal Matrices in Tissue Expander Breast Reconstruction

A Comparative Review

William Darden North, MD,* Christopher S. Kubajak, BS,*† Brad St. Martin, MPH,† and Brian Rinker, MD*

Background: Shifting preference for implant-based breast reconstruction has resulted in an increased use of acellular dermal matrix (ADM) in tissue-expander breast reconstruction. The benefits afforded by ADM must be weighed against a potential increased risk for postoperative complications. Dermal autograft–assisted breast reconstruction using autograft harvest from the lower abdomen has been shown to result in equivalent aesthetics and patient satisfaction compared with ADM at a lower cost, with fewer complications. The purpose of this study was to review a series of patients who underwent bilateral mastectomy and immediate dermal autograft–assisted tissue expander (TE) breast reconstruction using the non-cancerous breast as a donor site, comparing the outcomes with a concurrent cohort of patients undergoing ADM-assisted reconstruction to determine the relative safety, cost, and effectiveness of the 2 procedures.

Methods: The study population included all patients who underwent dermal autograft–assisted TE breast reconstruction, using the contralateral cancer-free breast as the source of dermal autograft, between 2010 and 2015. The ADM cohort consisted of patients who underwent bilateral mastectomy and immediate ADM-assisted TE breast reconstruction during the same period. Univariate analysis was performed for demographic data, complications, operative cost, and operative time. Data were compared using the Wilcoxon rank sum test for non-parametric data and χ2 analyses for continuous and categorical variables. Significance was defined as P value less than 0.05.

Results: Seventeen patients received dermal autograft using the non-cancerous breast donor site. Twenty-seven patients who underwent ADM-assisted reconstruction during the same period were identified. Significantly higher cost was demonstrated between groups (ADM, US $9999.87; autograft, US $3924.19; P = 0.0001). No significant difference existed operative time (autograft, 97 min; ADM, 120 min). No difference was found in wound healing complications (ADM, 14.8%; autograft, 23.53%; P = 0.47). No significant difference was found in major complications (ADM, 26%; autograft, 17.65%; P = 0.52) or infectious complications (ADM, 26%; autograft, 17.65%; P = 0.52).

Conclusions: Dermal autograft–assisted breast reconstruction using the contralateral non-cancerous breast as the source of dermal autograft harvest represents a lower cost alternative to ADM without increased risk of postoperative complications.

Key Words: dermal autograft, acellular dermal matrices, AlloDerm, tissue expander, breast reconstruction

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METHODS

Chart Review

The study was reviewed by and met the standards of the sponsoring institutional review board for studies involving human subjects. The study population included all patients who underwent dermal autograft–assisted TE breast reconstruction using the contralateral, cancer-free breast as the source of dermal autograft, between 2010 and 2015, inclusive. All operations were performed at one university medical center by one senior surgeon (B.D.R.). The ADM cohort

In 2016, an estimated 246,660 cases of invasive breast cancer will be diagnosed in the United States, many of which will require therapeutic mastectomy. In addition, there has been a trend in recent years for women to choose to undergo prophylactic mastectomy of the non-cancer-bearing contralateral breast. Breast reconstruction becomes a vital step in the recovery process for these women, with 41% of women electing to have some form of reconstruction. A paradigm shift has occurred in the last decade with a larger proportion of women choosing immediate implant-based reconstruction over autologous reconstruction.2,3

With the shift toward implant-based reconstruction, the use of acellular dermal matrix (ADM) in breast reconstruction has grown in popularity. In 2015, over half of women receiving implant-based breast reconstruction received ADM.2 The ability to create an inferior sling with ADM provides several distinct advantages over prior techniques, including improved lower pole coverage, enlargement of the subpectoral space, better control of the inframammary fold (IMF), and maintenance of medial implant position.4-12 However, ADM usage has been associated in multiple studies with increased rates of postoperative complications, including seroma, hematoma, infection, skin flap necrosis, and implant loss.13-18

The advantages of a lower pole sling are undeniable. Dermal autograft is a readily available, biocompatible, and inexpensive alternative to ADM. Dermal autograft–assisted tissue expander (TE) breast reconstruction using dermal autograft harvested from the lower abdomen has been previously described. The procedure has been shown to result in equivalent aesthetics and patient satisfaction rates as ADM-assisted reconstruction, at a lower cost and with fewer complications.19-21 A larger number of women are opting for bilateral prophylactic mastectomies or prophylactic mastectomy of their contralateral non-cancer-bearing breast. Many of these patients suffer from ptosis or macromastia, where a skin-reducing mastectomy is incorporated into the ablative and reconstructive plan. In these cases, the lower pole of the breast can be a potential donor site for dermal autograft harvest, thus, obviating the need for a separate abdominal donor site.

The purpose of this study was to review a series of patients who underwent bilateral mastectomy and immediate dermal autograft–assisted TE breast reconstruction using the non-cancerous breast as a donor site and to compare the outcomes with a concurrent cohort of patients undergoing ADM-assisted reconstruction, to determine the relative safety, cost, and effectiveness of the 2 procedures.
consisted of patients who underwent bilateral mastectomy and immediate ADM-assisted TE breast reconstruction, by the same surgeon during the same time period. Demographic data, body mass index, chemotherapy history, smoking status, and other comorbid factors were recorded. Wound healing complications were recorded for patients experiencing dehiscence, skin flap necrosis, and delayed wound healing. Infectious complications were recorded for patients experiencing cellulitis, breast abscess, and TE infection. Major complications were defined as any unplanned readmission or return to the operating room. Surgical logs were accessed for each patient to determine the total operative time from incision to closing. Operative cost was calculated using the product of operative time and the medical center's average cost per hour of operating time. In patients undergoing reconstruction using ADM, the cost per sheet of ADM was added to the operative cost calculation.

Operative Technique

Patients were classified into 2 groups: those receiving ADM for lower pole expander coverage (ADM group) and those receiving dermal autograft from the contralateral non-cancerous breast (autograft group). All patients in the ADM group received AlloDerm (LifeCell Corporation, Branchburg, NJ), with placement in each case using previously described techniques. For the autograft group, all patients had significant ptosis, with the entire nipple-areolar complex positioned inferior to the IMF when standing, and were candidates for a Passot-pattern horizontal skin-reducing mastectomy. In a standing position, the donor site was marked out as a horizontally oriented ellipse of skin on the lower pole of the contralateral non-cancerous breast, on the skin between the nipple-areolar complex and IMF. The horizontal and vertical dimensions of the graft were determined by the dimensions of the breast, but the width of the grafts measured between 22 cm and 30 cm and the height measured between 6 cm and 12 cm in the study period. The graft harvest began by scoring the perimeter of the graft with a scalpel (Fig 1). The graft was then de-epithelialized with long-handled Metzenbaum scissors and harvested in the subcutaneous plane with a scalpel. The graft was defatted with scissors on a back table and split into two halves. The autograft was then sutured internally, superficial side up, to the IMF, lateral mammary fold, and inferior border of the pectoralis major muscle, covering the inferior pole of the TE (Fig 2).

Data Analysis

SAS Enterprise Guide version 5.1 was used to perform all analyses. Univariate analysis was performed for all demographic data, complications, operative cost, and operative time. Data collected were
Medical comorbidities

<table>
<thead>
<tr>
<th></th>
<th>Autograft Group (%)</th>
<th>ADM Group (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>17</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>53 (46–59)</td>
<td>52 (41–61)</td>
<td>0.84</td>
</tr>
<tr>
<td>BMI</td>
<td>32 (28.5–36.6)</td>
<td>25 (22.3–29)</td>
<td>0.01</td>
</tr>
<tr>
<td>Obese</td>
<td>10 (58)</td>
<td>6 (22)</td>
<td>0.14</td>
</tr>
<tr>
<td>Smokers</td>
<td>6 (35)</td>
<td>7 (25)</td>
<td>0.51</td>
</tr>
<tr>
<td>Received chemotherapy</td>
<td>9 (53)</td>
<td>15 (56)</td>
<td>0.87</td>
</tr>
</tbody>
</table>

Medical comorbidities

- Diabetes: 3 (17.6) vs 3 (11.1), P = 0.54
- Hypertension: 6 (35.3) vs 10 (37), P = 0.91
- COPD: 3 (17.6) vs 3 (11.1), P = 0.54

Categorical variables reported as n (%).

Continuous variable median values reported with interquartile range.

Continuous variable median values reported with interquartile range.

Categorical variables reported as n (%).

Comparison of Treatment Groups

Seventeen patients (34 breasts) were identified who underwent dermal autograft-assisted TE breast reconstruction using the non-cancerous breast donor site during the study period. For historical control, 27 patients were identified who underwent ADM-assisted reconstruction during the same period. In the autograft population ages ranged from 37 to 68 years with a median age of 53 years. In the ADM population ages ranged from 26 to 71 years with a median age of 52 years. No statistical significance existed in respect to age between the 2 populations. No statistical significance was found between the 2 populations. No statistical significance was found between the 2 populations. No statistical significance was found between the 2 populations.

Operative time, min: 97 (1.4–2.77) vs 120 (1.5–2.5), P = 0.11

Operative cost, US $: 3924.19 (3573–4144) vs 9999.87 (5686–10681), P = 0.05

Table 1. Treatment Group Comparative Data

RESULTS

Comparison of Treatment Groups

No statistically significant difference was observed in wound healing complications between the ADM group (14.8%) and autograft (23.53%), P = 0.47. Neither major complications (26% for ADM vs 17.65% for autograft) nor infectious complications (26% for ADM vs 18% for autograft, P = 0.52) demonstrated significant difference (Table 2).

Outcomes

The average cost per patient was significantly higher in the autograft group. However, this difference was not statistically significant. No statistically significant difference was observed in wound healing complications between the ADM group (14.8%) and autograft (23.53%), P = 0.47. Neither major complications (26% for ADM vs 17.65% for autograft) nor infectious complications (26% for ADM vs 18% for autograft, P = 0.52) demonstrated significant difference (Table 2).

DISCUSSION

A paradigm shift has occurred in breast reconstruction in the United States, with implant-based breast reconstruction being favored over autologous reconstruction. With this shift has occurred a complementary increase in ADM-assisted TE breast reconstruction.2–4,23 The benefits of ADM must be weighed against a potential increased risk of infection, seroma, hematoma, and skin flap necrosis.13–18 As the number of women diagnosed with breast cancer continues to rise, so have the rates of mastectomy and breast reconstruction. In a climate of ever-increasing health-care costs, safe and cost-effective methods for breast reconstruction should be sought.

Dermal autograft harvest from the abdomen in tissue-expander reconstruction has been described previously, demonstrating an improved complication profile than the use of ADM.19–21 The aim of the present study was to describe a technique using the contralateral non-cancerous breast removed during prophylactic mastectomy as the source for dermal autograft to be used as an alternative to ADM in immediate TE reconstruction. This donor site is available only in women undergoing a bilateral procedure and with sufficient ptosis to require a sizeable skin-reducing mastectomy. We avoided using dermis from a known cancer-bearing breast, but using skin from such a breast is probably oncologically sound, if taken from a site distant to the tumor (Fig 3).

Our results demonstrate that for women with large ptotic breasts providing adequate tissue for dermal autograft harvest, operative cost can be significantly decreased over the use of ADM, without added operative time. This corroborates the findings of a recent published review of the cost-effectiveness of autologous dermal flaps compared with ADM.24 In addition, rates of wound healing and infectious complications showed no difference between the 2 groups, and no difference was found in the rate of major complications requiring unplanned re-admission or return to the operating room. There was no significant difference in complications between the 2 groups, despite the fact that there was a higher average BMI in the autograft group. In previous studies, BMI has been a strong predictor for postoperative complications.17,25,26 A previous study using dermal autograft harvested from the abdomen demonstrated improvements in infectious and wound healing complications as well as major complication rates for patients when compared with the use of ADM. Although our study was not able to demonstrate statistical significance, similar trends were seen for infectious and major complications in the dermal autograft group.

Table 2. Recorded Outcomes Assessment

Continuous variable median values reported with interquartile range.

Categorical variables reported as n (%).
The study is a retrospective cohort review, with the inherent limitations. Due to the relatively narrow indications for the procedure, the sample size was small. The treatment groups were not randomly assigned, but rather assigned based on availability of donor tissue and patient preference. In respect to operative time, investigators were limited to reviewing data from surgical logs, which used "incision" and "closing" for start and end time. This makes timing of various aspects of the procedure, such as autograft harvest, difficult to assess accurately, as the plastic surgery team and surgical oncology team work in concert at our institution. This potentially accounts for the trend toward decreased operative time in the autograft group compared with the ADM group, although no significant difference was found.

CONCLUSIONS

In this present study, we demonstrated that dermal autograft breast reconstruction using the contralateral non-cancerous breast as the dermal autograft donor site represents a lower cost alternative to ADM without increased risk of postoperative complications.

REFERENCES

Aesthetic vulvovaginal surgery has become the final frontier of cosmetic surgery. Accordingly, there has been an increased interest in plastic surgical procedures for the female genitalia. Labiaplasty is the most common among such procedures, and the number of practitioners and techniques has varied widely in the medical literature. This article will focus on the problems and pearls encountered by the author in treating enlargement of the labia minora and clitoral hood. The content will focus on the technical aspects of the labiaplasty surgery and ways to avoid common complications encountered during this procedure.

**Key Words:** labiaplasty, clitoral hood reduction, labia minora, clitoris, clitoral hood, aesthetic vaginal surgery, vaginal rejuvenation, female genitalia, aesthetic vulvovaginal surgery

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Aesthetic vulvovaginal surgery represents the “final frontier” of aesthetic surgery. There has been a growing interest in cosmetic procedures on the female genitalia, with 44% and 16% increases year over year in the number of labiaplasties performed since 2013. This interest is not limited to patients: a broad range of subspecialists have been drawn to the labiaplasty trend. Accordingly and with the adoption of any new procedure, there have been varied results following the use of 2 divergent labiaplasty techniques. This review aims to address the problems and pearls associated with labiaplasty surgery using modifications of the extended wedge technique, presenting the author's preferred approach for managing enlarged labia minora and prominence of the clitoral hood.

**MATERIALS AND METHODS**

Over a 3-year period, the author's technique evolved, combining the extended wedge approach defined by Dr Alter3,4 and the management of the clitoral hood described by Dr Hamori.5 A unified technique for a total vulvoplasty was defined based on contiguous circumferential recontouring of the labia minora and clitoral hood. This approach, termed the *horseshoe labiaplasty* because of the pattern of tissue resection (Video 1, http://links.lww.com/SAP/A225), allows for the management of both commonly associated anatomical findings of the hypertrophic female genitalia.

The labiaplasty procedure can be performed under a wide range of anesthetic options, from local to general anesthesia. Most cases are performed under intravenous sedation by an anesthesiologist. The first step is anesthetizing the most distal tip of the labia minora with a local anesthetic. The author's preference is to use .25% bupivacaine with epinephrine. Once this small infiltration has been achieved, a penetrating towel clip is used to grasp the tissues, and a pinch is performed to mark the amount of wedge resection. Markings are joined on the inner labial surface and extended cephalad in the sulcus between majora and minora, towards the clitoral hood. Here, a band of hood tissue can be included in the markings as needed based on the clitoral hood morphology, thus, completing the horseshoe. These areas are infiltrated, and after allowing for epinephrine effect, they are demucosalized only, maintaining the submucosal layer in its entirety as much as possible. Once hemostasis is achieved, closure is performed with a key “U” stitch at the labial margin using a 3-0 vicryl suture (Ethicon/Johnson & Johnson, Somerville, NJ), followed by interrupted, buried, submucosal 4-0 vicryl suture in 2 layers, on the medial and lateral aspects of the wedge resection. An additional 5-0 monofilament polyglycolic acid suture (Monocryl, Ethicon/Johnson & Johnson, Somerville, NJ) is run in subcuticular fashion on each side, beginning at the clitoral hood and ending in a through-and-through horizontal mattress suture at the labia minora edge. Antibiotic ointment and cold pack are then applied with an absorbable pad and mesh undergarment.

**RESULTS**

There are several problems that may be encountered in the labiaplasty procedure. One of the technical variety is in aligning the wedge after tissue resection. The ideal wedge location starts superiorly at the junction of the clitoral frenulum with the labia minora. This key point must be aligned with the lower wedge margin, which is more easily identified. This process is akin to aligning the white roll in cleft lip surgery, and ink markings or tattoos may be implemented to ensure alignment. The size of excision is similarly a challenge and is best measured with a pinch maneuver: when tension on the posterior fourchette

**FIGURE 1.** Preoperative appearance in lithotomy position of enlarged labia minora with labia reduplication (folds) and minimal clitoral hood excess.

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From the Oppenheimer Plastic Surgery, Orlando, FL.

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is visualized, the surgeon can be made aware that the planned resection may be too great.

The management of the clitoral hood is an additional problem, mostly diagnostic and not technical in nature. When clitoral hood enlargement is identified, a simple extension of each wedge across the hood can be performed to connect the 2 resection specimens. Because the procedure is a demucosalization/deepithelialization technique, the risk of nerve injury is as much as could be encountered in the harvest of a skin graft.

The most commonly encountered postoperative complications involving the extended wedge and horseshoe labiaplasty techniques are dehiscence at the labial margin. A variety of factors contribute to this, namely, friability of the delicate labial edge, moisture and friction, distal blood supply created by a wedge approach, yeast infections (no antibiotics are given pre- or perioperatively), repetitive trauma, over-aggressive wedge excision, and postoperative swelling. The use of the bidirectional barbed suture has drastically reduced the frequency of edge separation when compared to interrupted suture techniques used previously. The author has also implemented a vigorous regimen of ice and elevation postoperatively to manage edema, which can be striking, intimidating to the patient, and quite severe. Bed rest is recommended for a period of 2 to 3 days postoperatively.

Admittedly, the horseshoe extension across the hood inevitably interrupts some lymphatics, resulting in increased swelling and, therefore, tension on the wedge closure. One option in cases with severe hood redundancy is the “Edge-Wedge” approach as described by Dr Lara Devgan, MD, FACS (written communication, December 2016). This additional modification allows for a wedge or ellipse (or even connected “horseshoe”) to be taken from the hood and extending to the labia minora margin, while then performing an edge resection from the labia minora proper, extending from clitoral frenulum to the posterior fourchette. This resection pattern comes to a 3-point “T” on each side, much like the intersecting ellipses of a Wise pattern breast reduction. The risk of dehiscence is all but eliminated in this approach, although the scar burden is greater, extending along the entire labial edge.

CONCLUSIONS
The anatomical variation in the female genitalia is extraordinary, and therefore, the ease of a simple surgical approach is misleading. Much like the seemingly straightforward procedure of implant-based breast augmentation, individual anatomic differences—both between and within patients—largely dictate the outcome of a labiaplasty. It is paramount that the correct diagnosis is first made, namely, addressing the 2 related but distinct anatomical findings: labia minora hypertrophy and clitoral hood excess. Although the edge labiaplasty is more straightforward, the most common pitfall is leaving an untreated clitoral hood, when present. It is the author’s opinion that, although a edge labiaplasty may be suitable for some patients, an extended wedge labiaplasty with or without a “horseshoe” modification is suitable for all patients. Using the approach outlined above and the pearls described, many of the problems encountered during a labiaplasty procedure can be avoided, yielding high patient satisfaction and low complication rates, ultimately achieving the goal of the labiaplasty procedure: no labia minora or clitoral hood “show” on frontal view of the female genitalia (Figs. 1–4).

REFERENCES


Single Institution Review of Patients With Prior Breast Augmentation Undergoing Breast Conservation Therapy for Breast Cancer

Sangeetha Prabhakaran, MD,* Joshua B. Elston, MD,† Amina Lleshi, MPH,* Ambuj Kumar, MD,† Wei Hong Sun, MD,* Nazanin Khakpour, MD,* and Deniz Dayicioglu, MD*†

Background: Increasing number of patients with preexisting breast implants desire breast conservation therapy for breast cancer. There is paucity of comparative data on tumor margins and re-excisions in these patients. High re-excision rates up to 25% have been reported in breast conservation therapy patients; efforts to obtain cosmesis and avoid implant rupture might increase this further. We analyzed tumor margins, re-excision rates, and recurrence in previously augmented versus non-augmented patients undergoing lumpectomy for breast cancer. We preserved preexisting implants if feasible with oncologic clearance and cosmesis.

Methods: Institutional review board–approved retrospective analysis was performed on patients undergoing lumpectomy with history of prior breast augmentation (N = 52) and consecutively selected non-augmented patients (N = 51). Based on tumor distance to inked margin, we grouped margins as negative (≥2 mm), close (<2 mm), and positive. Patients were followed up clinically and with imaging in the outpatient clinic, and recurrences were documented.

Results: Patients in the non-augmented group were significantly more likely to have larger tumors (T2 and above; P = 0.05) compared with the augmented group. Although more patients in the augmented group had positive margins, this was not statistically significant (6 vs 3, P = 0.86). No difference was noted between re-excision rates among the augmented versus non-augmented groups (21.1% vs 19.6%, respectively; odds ratio, 0.91; 95% confidence interval, 0.35–2.37; P = 0.85); these remained unchanged even when adjusting for tumor stage (P = .75) and margins (P = 0.73). Although more patients in the augmented group recurred (4 vs 0), this was not statistically significant (P = 0.1).

Conclusions: Our results indicate that, from the oncological standpoint, patients with prior breast augmentation can undergo lumpectomy with equivalent tumor margins and re-excision rates. To the best of our knowledge, this is the first reported comparative study between these 2 groups.

Key Words: prior breast augmentation, breast conservation therapy, lumpectomy, breast cancer, augmentation mammoplasty, implants

(B)reast augmentation is the most prevalent surgical cosmetic procedure performed in the United States with close to 280,000 cases performed in the year 2015.1 With the increasing use of this procedure, it could be postulated that the number of women with breast cancer with history of prior augmentation is also likely to increase. These patients form a unique subset with several options available for surgical treatment of their breast cancer. Breast conservation therapy (BCT) includes breast-conserving surgery or lumpectomy followed by moderate-dose radiation therapy. The consideration of lumpectomy in women with prior breast augmentation is an increasingly popular option; however, this carries risk of radiation-induced contracture requiring reoperation, reported in some series as high as 65%.2

Women who have undergone implant placement, frequently also have small breast volumes, with resultant concerns about the ability to achieve negative margins after BCT. However, retrospective reviews have shown that BCT after implant breast augmentation achieved acceptable negative pathologic margins and, inclusive of radiotherapy, produced acceptable cosmetic results in about two thirds of the patients.3 In a series of 12 patients with prior breast augmentation who developed breast cancer, 6 patients underwent BCT; negative pathologic margins were obtained in all patients, 1 patient had local recurrence and 1 patient developed distant recurrence after initial surgery.4

In another series, among 20 women with prior augmentation who were treated with BCT, 3 had microscopically positive margins. No local recurrences were noted after a median follow-up of 3.9 years.5 High re-excision rates up to 25% have been reported in non-augmented patients undergoing BCT for breast cancer, and efforts to obtain cosmesis and avoid implant rupture in the presence of preexisting implants can potentially increase this number.6,7 The current evidence regarding tumor margins and re-excision rates in patients with prior breast augmentation is scant, mostly consisting of retrospective reviews and case series.

We wanted to review our single institutional experience of BCT in patients with prior breast augmentation and compare them with non-augmented patients with specific focus on tumor margins, re-excision rates, and recurrence.

METHODS

Institutional review board approval was obtained. We performed a retrospective analysis on 52 patients with prior breast augmentation and 51 consecutive non-augmented patients who underwent BCT for breast cancer at Moffitt Cancer Center. We analyzed tumor margins and re-excision rates in these patients. Based on tumor distance to inked margin, we grouped margins as negative when margins were greater than 2 mm, close (margins <2 mm), and positive (if tumor was present at the inked margin). Patients were followed up clinically and with imaging in the outpatient clinic, and incidence of tumor recurrence was noted.

Among patients with prior augmentation, the majority [33 (63.5%)] had submuscular implants and 18 (34.6%) had subglandular implants. We preferred to preserve preexisting implants if feasible with oncologic clearance and cosmesis. The association between the dependent and independent variables was assessed using the Fisher exact test. For all associations, the results were summarized as odds ratio (OR) and 95% confidence intervals (CIs). Statistical significance was set at 5% for all comparisons. To adjust for multiple comparisons, Bonferroni correction was applied. Statistical analyses were performed using SPSS v22 software.

RESULTS

Fifty-two patients with prior breast augmentation who underwent lumpectomy for breast cancer between December 2002 and November 2016 were identified. Of these, 35 (67.3%) patients were from the prior augmentation group and 17 (32.7%) were from the non-augmented group. The mean age of patients was 46±16 years and the mean age of breast cancer was 46±16 years. The median follow-up was 4.6 years (range, 0.2–18.1 years). The tumor characteristics of patients are presented in Table 1.

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TABLE 1. Comparison of Tumor Stage, Margins, and Re-excision Rates After Breast Conservative Surgery Between Patients With Prior Breast Augmentation and Non-augmented Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-augmented group (N = 51), N (%)</th>
<th>Augmented group (N = 52), N (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor stage</td>
<td>Tis (in-situ) 5 (9.8)</td>
<td>5 (9.6)</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>T1 28 (54.9)</td>
<td>36 (69.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T2 and higher 18 (35.3)</td>
<td>6 (11.5)</td>
<td></td>
</tr>
<tr>
<td>Margins</td>
<td>Negative 41 (80.4)</td>
<td>34 (65.4)</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>Close 7 (13.7)</td>
<td>9 (17.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive 3 (5.9)</td>
<td>6 (11.5)</td>
<td></td>
</tr>
<tr>
<td>Re-excision</td>
<td>Yes 10 (19.6)</td>
<td>11 (21.2)</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>No 41 (80.4)</td>
<td>41 (78.8)</td>
<td></td>
</tr>
</tbody>
</table>

There were 4 recurrences (7.7%) in the prior breast augmentation group. Three patients had locoregional recurrences, and 1 patient had both local and systemic sites of recurrence. Two patients were treated with mastectomy, 1 with axillary dissection and 1 with systemic therapy. None of these recurrences were noted in patients who had their implants removed (Table 2). Because the rate of recurrence in the non-augmented group was zero, we could not calculate a summary OR and 95% CI. However, the difference was statistically nonsignificant (P = 0.1; Table 3).

DISCUSSION

Breast conservation surgery is certainly feasible in patients with prior breast augmentation with preservation of implant. Figure 1 shows a patient who had prior breast augmentation and had 2 areas successfully excised using wire localization. One of these target areas was posterior to the implant and could not be visualized but was still successfully excised after wire localization. Figure 2 shows a patient with prior augmentation who developed a local recurrence after BCT and was subsequently treated with mastectomy. Our complication rate after BCT in the patients with prior breast augmentation was 3.8% (2/52), which reflects the safety of this procedure.

There is paucity of data in the literature on tumor margins, re-excisions, and recurrence rates in patients with preexisting implants who undergo BCT. We sought to study these variables in our patient population and compare them to non-augmented patients. Our results do not show any statistically significant differences in tumor margins, re-excision rates or recurrence between the 2 groups. Non-augmented patients have statistically significant larger tumors compared with the augmented group. The reason for this might be that patients with larger tumors might be preferably treated with mastectomy for oncologic clearance.

There were higher recurrences noted in the augmented group compared with the non-augmented group (4 vs 0), although this was not statistically significant. This might be owing to insufficient power due to smaller sample size, and we plan to continue this study in larger groups of patients.

It has also been noted that patients seeking cosmetic breast augmentation may have greater aesthetic expectations. No definitive

TABLE 2. Type of Recurrence Noted in Patients in the Prior Breast Augmentation Group who Recurred and Treatment Performed

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Type of Recurrence</th>
<th>Treatment of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Local recurrence</td>
<td>Mastectomy</td>
</tr>
<tr>
<td>2</td>
<td>Local + distant recurrence</td>
<td>Systemic therapy</td>
</tr>
<tr>
<td>3</td>
<td>Ipsilateral axilla</td>
<td>Axillary dissection</td>
</tr>
<tr>
<td>4</td>
<td>Local recurrence</td>
<td>Mastectomy</td>
</tr>
</tbody>
</table>

TABLE 3. Comparison of Tumor Recurrence Rates After Breast Conservative Surgery Between Patients With Prior Breast Augmentation and Non-augmented Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-augmented group (N = 51), N (%)</th>
<th>Augmented group (N = 52), N (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>No 51 (100)</td>
<td>47 (90.4)</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Yes 0 (0)</td>
<td>4 (7.7)</td>
<td></td>
</tr>
</tbody>
</table>

2014 were compared with 51 consecutive non-augmented patients who underwent lumpectomy between June 2010 and March 2011.

Median age of patients in the prior breast augmentation group at time of lumpectomy was 56.9 years (range, 34.7–72.7 years) and, in the non-augmented group, was 62.1 years (26.7–84.8 years). In the prior breast augmentation group, 36 (69.2%) had T1 stage versus 28 (54.9%) in the non-augmented group. More patients in the non-augmented group had T2 stage or higher compared with the prior breast augmentation group [18 (35.3%) vs 6 (11.5%), P = 0.05; Table 1]. The predominant tumor histology in the prior breast augmentation group was invasive ductal carcinoma [44 (84.6%)]. Although more prior breast augmentation patients had positive margins, 6 (11.5%) compared with 3 (5.9%) of the non-augmented group, this was not statistically significant (P = 0.86). There was thus no statistically significant overall difference in distribution of margins between these 2 groups (Table 1).

We compared re-excision rates between these groups. Eleven (21.2%) of patients in the prior breast augmentation group and 10 (19.6%) in the non-augmented group underwent re-excision of margins, but this was not statistically significant (P = 0.85; Table 1). The re-excision rate of 21.2%, in our prior breast augmentation group, was comparable to the currently reported re-excision rates in patients undergoing lumpectomy for breast cancer. The OR of re-excision was 0.91 (95% CI, 0.35–2.37; P = 0.85). These results remained unchanged when adjusted for tumor stage (OR, 0.85; 95% CI, 0.31–2.33; P = 0.75) and margins (OR, 0.84; 95% CI, 0.32–2.21; P = 0.73).

Two patients in the prior breast augmentation group developed complications. One had postoperative wound infection, and the other developed a systemic allergic reaction requiring readmission.

Six patients (11.5%) had implants removed in the lumpectomy group [2 prior to lumpectomy, 3 during lumpectomy (including 1 patient requested), and 1 prior to radiation]. Four of these implant removals were performed in patients with preexisting subglandular implants and 2 in patients with subsu-muscular implants.

Median period of follow-up in the prior breast augmentation group was 141 months (0.3–170.4 mo) and, in the non-augmented group, was 100.3 months (26.1–418.5 mo).
predictive factors for unfavorable cosmetic outcome have been identified in the literature because of the small numbers of patients analyzed in individual studies.9

Our study has some inherent disadvantages. It is a retrospective study with smaller number of patients and a relatively shorter period of follow-up. The impact of radiation causing problems such as capsular contracture has not been studied at this time, and we will monitor for this during long-term follow-up of these patients.

CONCLUSIONS

Use of BCT for management of breast cancer in patients with prior breast augmentation is safe and feasible. From the oncological standpoint, equivalent tumor margins and re-excision rates can be achieved in patients with preexisting implants undergoing BCT for breast cancer with implant preservation. Larger studies need to be performed to further confirm these results. Future efforts should also focus on understanding the long-term effects of radiation therapy in patients with prior augmentation undergoing BCT.

FIGURE 1. Postprocedure mammogram of a patient with prior breast augmentation. A, Postprocedure mammogram (right mediolateral oblique view). B, Post procedure mammogram (right craniocaudal view). These images represent the feasibility of performing lumpectomy in patients with prior breast augmentation. This patient had prior breast augmentation and had 2 areas successfully excised with wire localization. One of these target areas is posterior to the implant but was still successfully excised after wire localization.

FIGURE 2. Photographs of a patient with prior breast augmentation treated with breast conservative surgery subsequently treated with mastectomy for local recurrence.

REFERENCES


Use of Processed Nerve Allografts to Repair Nerve Injuries Greater Than 25 mm in the Hand

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Abstract: Processed nerve allografts (PNAs) have been demonstrated to have improved clinical results compared with hollow conduits for reconstruction of digital nerve gaps less than 25 mm; however, the use of PNAs for longer gaps warrants further clinical investigation. Long nerve gaps have been traditionally hard to study because of low incidence. The advent of the RANGER registry, a large, institutional review board–approved, active database for PNA (Avance Nerve Graft; AxoGen, Inc, Alachua, FL) has allowed evaluation of lower incidence subsets. The RANGER database was queried for digital nerve repairs of 25 mm or greater. Demographics, injury, treatment, and functional outcomes were recorded on standardized forms. Patients younger than 18 and those lacking quantitative follow-up data were excluded. Recovery was graded according to the Medical Research Council Classification for sensory function, with meaningful recovery defined as S3 or greater level. Fifty digital nerve injuries in 28 subjects were included. There were 22 male and 6 female subjects, and the mean age was 45. Three patients had a previous history of diabetes, and there were 6 active smokers. The most commonly reported mechanisms of injury were saw injuries (n = 13), crushing injuries (n = 9), resection of neuroma (n = 9), amputation/avulsions (n = 8), sharp lacerations (n = 7), and blast/gunshots (n = 4). The average gap length was 35 ± 8 mm (range, 25-50 mm). Recovery to the S3 or greater level was reported in 86% of repairs. Static 2-point discrimination (s2PD) and Semmes-Weinstein monofilament (SWF) were the most common completed assessments. Mean s2PD in 24 repairs reporting 2PD data was 9 ± 4 mm. For the 38 repairs with SWF data, protective sensation was reported in 33 repairs, deep pressure in 2, and no recovery in 3. These data compared favorably with historical data for nerve autograft repairs, with reported levels of recovery after PNA repairs of digital nerve injuries with gaps longer than 25 mm compare favorably with historical reports for nerve autograft repair but without donor site morbidity.

Key Words: digital nerves, nerve repair, nerve gap, processed nerve allograft

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Conflicts of interest and sources of funding: Funding for this research was provided by AxoGen, Inc. The authors receive research support from Axogen, Inc., and are members of the RANGER study group. Reprints: Brian Rinker, MD, FACS, Division of Plastic Surgery, University of Kentucky, Kentucky Clinic, K454 Lexington, KY. E-mail: brink2@email.uky.edu. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved. ISSN: 0148-7043/17/7806-S292 DOI: 10.1097/SAP.0000000000001037

Digital nerve injuries are among the most common conditions treated by hand surgeons. The conditions for a successful nerve repair are well known and consist of generous trimming of the nerve until healthy substance is observed, minimal handling, a tension-free coaptation, and maintaining a well-vascularized wound bed. 1 In many cases, however, the condition of a tension-free repair cannot be met. This occurs frequently in cases with a crushing or avulsing mechanism, with a wide zone of nerve injury. In these cases, the options include repairing under tension; positioning in flexion; or bridging the gap with a nerve autograft, processed nerve allograft, or conduit. Tension has been shown to inhibit axonal outgrowth and Schwann cell activity, likely through its effect on nerve microcirculation. 3,4 Positioning of the digits in flexion can lead to flexion contractures or can interfere with postoperative rehabilitation protocols.

Beginning in the 1940s, nerve autografts have been the mainstay of nerve gap repair. Autografts are readily available, inexpensive, and biocompatible. 5 However, they add time and operative complexity to the reconstruction and are associated with donor site sensory loss, which in some cases can be long-standing and debilitating. 6,7 To avoid these complications, surgeons have sought an alternative to autografting. Nerve conduits of various composition, including polyglycolic acid (PGA), collagen, and autologous vein, have been used in the clinical setting, with variable outcomes. 8–15 Processed nerve allografts are an alternative to nerve autografts and conduits, without donor site morbidity. They consist of human nerves which are prepared with enzymatic decellularization but with preservation of the epineurium and internal fascicular architecture. In experimental studies, they have been shown to revascularize rapidly, repopulate with host cells, and provide a supportive milieu for nerve regeneration. 16–18 Several large retrospective and prospective clinical studies have demonstrated levels of recovery after processed nerve allograft reconstruction of nerve gaps equaling or exceeding that reported for nerve autograft or conduit reconstructions. 19–23 However, most critical nerve gaps fall in the shorter end of the spectrum, between 5 and 15 mm, and most of the large retrospective series to date have contained a proportionately larger number of these shorter gaps. 8,9 Because of the relative scarcity of longer nerve gaps, it is harder to draw conclusions from the existing literature regarding the relative effectiveness of the available treatment modalities.

The RANGER Study registry, opened in 2007, is an institutional review board–approved, active database that collects data on the use and outcomes of processed nerve allografts using standardized collection methods. The registry pools data from a wide cross-section of patient demographics, nerve injury types, mechanisms, and practice settings. The advent of the RANGER processed nerve allograft registry allows investigators to specifically query outcomes in lower incidence subgroups. The purpose of this study was to review a large database of patients who underwent nerve reconstruction with processed nerve allograft to determine the degree of sensory recovery after repair of digital nerve injuries with critical gaps greater than 25 mm and to compare these results with historical controls for nerve autograft repairs.

METHODS

This investigation was performed with approval from our institutional review boards and in accordance with Good Clinical Practices.
All consenting subjects at least 18 years old and who had been implanted with processed allografts at participating sites were eligible for the study. Standardized case report forms were used for each subject to normalize chart information, and data were collected to the extent available in the medical records. Chart reviews were completed in an observational fashion to collect subject demographics, details of the nerve injury and repair(s), and concomitant injuries and treatments. Each center followed its own standard practices with regard to postoperative care, and functional outcomes data were collected in both a retrospective and prospective manner from all available follow-up evaluations. Additionally, information was collected on adverse experiences or complications related to the nerve graft occurring intraoperatively or postoperatively.

All collected data were entered into the centralized RANGER Study registry database. This database was queried for subjects presenting with digital nerve repairs of greater than 25 mm with quantitative follow-up data. Medical Research Council Classification (MRCC) for sensory function with meaningful recovery was defined as S3 or greater level. Outcomes were compared with historical data for nerve autograft.

RESULTS

Subject Demographic, Injury, and Operative Data
Twenty-two male and 6 female subjects were identified in the database presenting with 50 digital nerve repairs with gaps greater than 25 mm. The mean age was 45 ± 24 (22-78) years. Forty-two subjects reported no pertinent medical history that may affect the outcome of the repair. In the remaining 8 subjects, 5 reported hypertension, 1 reported diabetes, and 2 reported both hypertension and diabetes. Six subjects were active smokers. Mechanisms of injury included saw (n = 13), crushing injuries (n = 9), resection of neuroma (n = 9), amputation/avulsions (n = 8), sharp lacerations (n = 7), and blast/gunshots (n = 4). Injuries included all common and proper digital nerves in the hand with a majority also reporting concomitant bony, tendon, and/or vascular injuries. Table 1 shows the distribution of nerves repaired, and Table 2 summarizes the number of repairs with concomitant injuries. Most subjects were repaired acutely with the median time to repair at 6 (0-2514) days. The nerve gap injuries were reconstructed with an appropriately sized nerve allograft in a tensionless manner according to instructions for use. The average gap length was 35 ± 8 (27-50) mm.

Outcomes Data
Recovery to S3 or greater level was reported in 86% of repairs with 32 of these repairs reaching S3+ or S4 levels of recovery. These outcomes were found to be consistent across the entire gap range of up to 50 mm (Table 3). Static 2-point discrimination (2PD) and Semmes-Weinstein monofilament (SWF) were the most common completed quantitative assessments with a mean follow-up time of 11 months. Of subjects reporting 2PD, 92% reported return of s2PD with a mean of 9 ± 4 (4-15) mm. Of the subjects reporting SWF data (n = 38), protective sensation or greater was reported in 33 repairs, deep pressure in 2, and no recovery in 3. These data compared favorably with historical data for nerve autograft repairs, with reported levels of meaningful recovery of 60% to 88%. There were no reported adverse effects (Fig. 1).

DISCUSSION
Digital nerve injuries are among the most common condition treated by hand surgeons, but most digital nerve injuries are either amenable to direct suture or present with gaps shorter than 15 mm. Because of the relative scarcity of digital nerve injuries with gaps greater than 25 mm, there is a paucity of data on the relative effectiveness of the different modalities for reconstruction of these injuries, and it has been correspondingly difficult to make informed decisions about treatment.

In 1991, Frykman and Gramyk reported recovery to at least the S3+ level on the MRCC scale in 88% of 141 patients with digital nerve gaps treated with autografting. Patients with gap lengths up to 5 cm were included. In 1993, Kallio presented the results of a series of 254 digital nerve repairs in 95 patients, performed over a 16-year period. One hundred three nerve gaps in 37 patients were treated with nerve autografts, with gap lengths up to 5 cm. The source of autograft was either the antebrachial cutaneous or sural nerve. The size of the study group allowed subset analysis by gap length. Meaningful recovery, defined as recovery to the S3 or greater level, was observed in 100% of patients with gap lengths less than 21 mm, but this recovery rate fell to 67% for gap lengths between 21 and 49 mm and to 9% for gap lengths greater than 49 mm. A more recent study comparing results from autografting of digital nerve defects using either the posterior interosseous or medial antebrachial cutaneous nerve reported recovery of S3 or greater in 86% of 28 repairs, with a mean gap length of 22 mm.

### Table 1. Distribution of Repaired Nerves in the Hand

<table>
<thead>
<tr>
<th>Location</th>
<th>No. Repairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thumb</td>
<td>4 UDN/4 RDN</td>
</tr>
<tr>
<td>Index finger</td>
<td>5 UDN/6 RDN</td>
</tr>
<tr>
<td>Long finger</td>
<td>4 UDN/1 RDN</td>
</tr>
<tr>
<td>Ring finger</td>
<td>2 UDN/5 RDN</td>
</tr>
<tr>
<td>Small finger</td>
<td>6 UDN/4 RDN</td>
</tr>
<tr>
<td>Second Web Space</td>
<td>2</td>
</tr>
<tr>
<td>Third Web Space</td>
<td>5</td>
</tr>
<tr>
<td>Fourth Web Space</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location</th>
<th>No. Repairs</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>Ring finger</td>
<td>2 UDN/5 RDN</td>
</tr>
<tr>
<td>Long finger</td>
<td>4 UDN/1 RDN</td>
</tr>
<tr>
<td>Index finger</td>
<td>5 UDN/6 RDN</td>
</tr>
<tr>
<td>Thumb</td>
<td>4 UDN/4 RDN</td>
</tr>
<tr>
<td>Second Web Space</td>
<td>2</td>
</tr>
<tr>
<td>Third Web Space</td>
<td>5</td>
</tr>
<tr>
<td>Fourth Web Space</td>
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</table>

<table>
<thead>
<tr>
<th>Location</th>
<th>No. Repairs</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>Ring finger</td>
<td>2 UDN/5 RDN</td>
</tr>
<tr>
<td>Long finger</td>
<td>4 UDN/1 RDN</td>
</tr>
<tr>
<td>Index finger</td>
<td>5 UDN/6 RDN</td>
</tr>
<tr>
<td>Thumb</td>
<td>4 UDN/4 RDN</td>
</tr>
<tr>
<td>Second Web Space</td>
<td>2</td>
</tr>
<tr>
<td>Third Web Space</td>
<td>5</td>
</tr>
<tr>
<td>Fourth Web Space</td>
<td>1</td>
</tr>
</tbody>
</table>

UND indicates ulnar digital nerve; RDN, radial digital nerve.

### Table 2. Summary of Subjects With Concomitant Injuries

<table>
<thead>
<tr>
<th>Concomitant Injuries</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>2</td>
</tr>
<tr>
<td>Tendon</td>
<td>3</td>
</tr>
<tr>
<td>Fracture</td>
<td>4</td>
</tr>
<tr>
<td>Tendon and vascular</td>
<td>7</td>
</tr>
<tr>
<td>Fracture and vascular</td>
<td>4</td>
</tr>
<tr>
<td>Tendon and fracture</td>
<td>3</td>
</tr>
<tr>
<td>Vascular, tendon, and fracture</td>
<td>12</td>
</tr>
</tbody>
</table>

### Table 3. Distribution of MRCC Scores for Return of Sensory Function

<table>
<thead>
<tr>
<th>MRCC Score</th>
<th>Gaps 26–39 mm</th>
<th>Gaps 40–50 mm</th>
<th>Cumulative Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>S1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>S2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>S3</td>
<td>11</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>S3+</td>
<td>18</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>S4</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>MRCC ≥ S3</td>
<td>89%</td>
<td>86%</td>
<td>86%</td>
</tr>
</tbody>
</table>
In 2005, Battiston et al reported a se-
20 mm, but this level of recovery was
382. Unlike previous studies using autografts and syn-
–
Processed nerve allografts have many advantages in the clin-
This provides theoretical
the high level of recovery in this study was preserved, even
Nerve allografts did not
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Volume 78, Supplement 5, June 2017
Neurosurgery
Processed nerve
25 mm. More recently,
the use of the Avance Nerve Graft. It is an active database used by
gap resulting from resection of a sarcoma.
and autografts, dating to 1885 when Eduard Albert of Vienna used a
Lohmeyer et al reported recovery to the S3 or greater level in 9 (75%)
of digital nerve gaps using woven PGA conduits. Gaps ranged from 5 to
the series was 12.2 mm,
and no gap in the series was longer than 18 mm.
Nerve allografts have a history which exceeds that of conduits
surgery: the contribution of Gabriele Ferrara (1543-1627).
REFERENCES
Studies reporting results of long gap digital neve repairs using
synthetic conduits are rarer still. In 1990, Mackinnon and Dallon pre-
presented a series of 15 patients who underwent secondary reconstruction
digital nerve gaps using woven PGA conduits. Gaps ranged from 5 to
30 mm, with a mean of 17 mm. Recovery to the S3 or greater level was
observed in 86% of the repairs. In 2005, Battiston et al reported a se-
ries of 19 primary and secondary digital nerve reconstructions using
PGA conduits. The gap lengths ranged from 10 to 40 mm, with a mean of
20 mm. Recovery to the S3 level or greater was observed in 75% of
the 12 repairs with a gap length ≥ 20 mm, but this level of recovery was
seen in only 60% of the 5 repairs with a gap ≥ 25 mm. More recently,
Lohmeyer et al reported recovery to the S3 or greater level in 9 (75%)
of 12 patients who underwent repair of digital nerve gaps using a hollow
collagen conduit. The average gap length in this series was 12.2 mm,
and no gap in the series was longer than 18 mm.
Nerve allografts have a history which exceeds that of conduits and
autografts, dating to 1885 when Eduard Albert of Vienna used a
fresh allograft from an amputated limb to bridge a 3-cm median nerve
gap resulting from resection of a sarcoma.
Nerve allografts did not gain broad acceptance for more than a century, however, because of
the need for immunomodulatory therapy and the risk of disease trans-
mision. Techniques have been developed, such as irradiation, enzy-
matic treatment, cryopreservation, and detergent-processing, to render
allografts acellular, thus eliminating the need for immunosuppres-
sion.
Processed nerve allografts have many advantages in the clinical
setting. They are biocompatible, easy to use, and avoid a donor
site deficit. First made available in 2008, the Avance Nerve Graft is the
only processed nerve allograft approved by the US Food and Drug
Administration for clinical use in the United States. It undergoes a com-
bination of detergent and enzymatic processing, which is balanced to
mitigate cellular burden while maintaining the basal laminar proteins
and microarchitecture of the nerve, both of which are believed to be
critical in supporting nerve regeneration.
This provides theoretical
support for the superiority of processed allograft over other means of re-
construction of a long nerve gap. Additional support for this notion has
been provided by animal studies. In a rat sciatic nerve model, processed
erve allograft was found to be superior to nerve isografts and collagen
conduits in the reconstruction of a 10-mm gap. Processed nerve
allograft repairs resulted in improved functional recovery and higher
axon counts.
The RANGER registry was initiated in 2008 to capture data on the
use of the Avance Nerve Graft. It is an active database used by
multiple centers, across a wide cross section of geographic areas and
practice settings. Standardized entry forms are used, but each participat-
ing site follows its own standard of care for intraoperative and postop-
erative management. The large number of patients included in the
database allows for subset analysis with numbers in excess of that
which has previously been possible in peripheral nerve research. For
the present study, 50 nerve repairs were identified using processed
nerve allografts for digital nerve gaps between 25 and 50 mm length.
Of these, 36 (86%) resulted in measured recovery at the S3 or greater
level. These results compare favorably with historical data for autografts
and conduits. Unlike previous studies using autografts and syn-
thetic conduits, which showed a degradation in recovery at longer gap
lengths, the high level of recovery in this study was preserved, even in
the subset of patients with gap lengths between 40 and 50 mm (86% recovery).
The observed advantage of allografts over autografts may re-
late to the processing, which removes the cellular material, which is still
present in autografts, but must be removed through phagocytosis.
The observed advantage to conduits likely results from the presence of
intact nerve basal lamina or possibly growth factors, which
promote regeneration.
This study is not without limitations. It is retrospective in nature.
The patients were not randomized to treatment groups, but rather the
type of treatment was left to the surgeon’s discretion. Surgeons were
not held to standardized treatment protocols but rather followed the
standard of care for their treatment site; therefore, suture materials, su-
turing techniques, use of microscopy, and postoperative assessments
were not standardized. Surgeons and those performing the assessments
were not blinded. However, the registry remains ongoing and continues
to collect outcomes data. This should allow for an even more granular
subset analysis in the future. In addition, a multicenter, prospective ran-
donized study is underway to compare processed allograft repairs with
conduit repair, which should provide even more clarity to one of the un-
answered questions in hand surgery: the optimal treatment for a critical
erve gap. In the meantime, surgeons should feel confident using proc-
essed nerve allografts in injuries of the digital nerves, even for long
nerve gaps.


Fluorescein Isothiocyanate
A Novel Application for Lymphatic Surgery

Lisa Spiguel, MD,* Christiana Shaw, MD,* Adam Katz, MD,† Lifei Guo, MD, PhD,‡ Hung-Chi Chen, MD,§ Bernard T. Lee, MD,|| and Dhruv Singhal, MD†||

Abstract: The Lymphatic Microsurgical Preventing Healing Approach (LYMPHA) procedure entails performing a lymphovenous bypass (LVB) at the time of axillary lymph node dissection to reduce lymphedema risk. The two most common fluorophores utilized in LVB are blue dye and indocyanine green. We developed a novel application of fluorescein isothiocyanate for intraoperative lymphatic mapping. Our goal is to demonstrate the safety and efficacy of fluorescein isothiocyanate for this application. We reviewed a prospectively collected database on breast cancer patients who underwent LYMPHA from March to September 2015. Fluorescein isothiocyanate was used to identify arm lymphatic channels after axillary lymph node dissection to perform an LVB between disrupted lymphatics and axillary vein tributaries. Data on preoperative and intraoperative variables were analyzed. Thirteen patients underwent LYMPHA with intraoperative fluorescein isothiocyanate lymphatic mapping from March to September 2015. Average patient age was 50 years with a mean body mass index of 28. On average, 3.4 lacerated lymphatic channels were identified at an average distance of 2.72 cm (range, 0.25–5 cm) caudal to the axillary vein. On average, 1.7 channels were bypassed per patient. Eleven anastomoses were performed to the accessory branch of the axillary vein and 1 to a lateral branch. In 1 patient, a bypass was not performed due to poor lymphatic caliber and inadequate length of the harvested vein tributary. No intraoperative adverse events were noted. Fluorescin isothiocyanate is a safe and effective method for intraoperative lymphatic mapping. Fluorescein isothiocyanate imaging allows for simultaneous dissection and lymphatic visualization, making it an ideal agent for lymphatic mapping and dissection in open surgical fields, such as in the LYMPHA procedure.

Key Words: FITC, LYMPHA, lymphatic surgery

(Ann Plast Surg 2017;78: S296–S298)

In 2009, Dr. Campisi introduced a technique to prevent lymphedema termed the Lymphatic Microsurgical Preventing Healing Approach (LYMPHA).1 In this technique, lymphatics draining the arm are identified and bypassed into an axillary vein tributary at the time of axillary dissection. Dr. Campisi’s team has reported an unprecedented 5% lymphedema rate after axillary lymph node dissection (ALND) and LYMPHA over a four year follow-up.2 Historical rates of lymphedema after ALND are highly variable however usually are quoted between 20% and 40%3–6 and have been reported as high as 77%.7 The challenge of the LYMPHA procedure is visualizing healthy cut lymphatics lateral to the level 1 lymph nodes after an ALND. Dr. Campisi’s team was able to identify these lymphatics by injecting blue dye into the ipsilateral proximal upper arm. However, breast surgeons often prefer to use a dual tracer method including both blue dye and technetium sulfur colloid for sentinel lymph node (SLN) identification. This is especially important in cases where neoadjuvant chemotherapy has previously been administered.8,9 Therefore, a different dye was sought for arm lymphatic mapping to differentiate staining from arm versus breast lymphatics.

The most common method of lymphatic vessel mapping currently in use is indocyanine green (ICG). However, the challenge with ICG is that the dye is near-infrared and therefore excited in the nonvisible spectrum. This limits the usefulness of ICG for visualization and simultaneous dissection because the dye is displayed as a white signal on a black background and cannot be concurrently visualized through the binoculars of a microscope (Fig. 1A). Fluorescein isothiocyanate (FITC), on the other hand, is excited in the visible spectrum and routinely used in the operating room. Neurosurgeons inject this dye intravenously and use microscopes equipped with filter technology to visualize tumors while maintaining life-like color of the surrounding tissues allowing for simultaneous magnification and tissue dissection (Fig. 1B). This is a powerful property for the lymphatic surgeon. Although FITC has been used outside the operating room for lymphatic mapping in the skin,10–12 to our knowledge, it had never been used in the operating room for lymphatic mapping. More recently, a single case report was published from France where FITC was used to perform a lymphovenous bypass (LVB) in the superficial tissues of the arm in a patient with chronic lymphedema.13,14 We hypothesized that FITC would be a safe and highly effective dye for lymphatic mapping and dissection in open surgical fields, such as in the LYMPHA procedure.

METHODS

We reviewed our prospectively collected Lymphedema Repository data on all breast cancer patients who underwent the LYMPHA procedure from March to September 2015. All patients that underwent the LYMPHA procedure with FITC were included in the review, and the charts were reviewed for demographic information (age, body mass index) and perioperative data (number of lymphatic channels visualized and bypassed, distance of channels from axillary vein, name of targeted vein, and adverse events).

Surgical Technique

Immediately before the ALND, 2 mL of a modified 2% fluorescein solution are injected intradermally and along the muscle fascia of the ipsilateral upper arm (Fig. 2A). Our solution is modified from the stock AK-FLUOR 10% (Akorn Inc, Lake Forest, Ill) solution by diluting 2 cc with 7.5 cc of normal saline and 0.5 cc of AlbuRx5 (CSL Behring Inc, King of Prussia, Pa). The ALND is performed with careful attention to preserve a superficial accessory vein tributary which

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Conflicts of interest and sources of funding: none declared.


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longitudinally traverses the level 1 lymph nodes. The superior dissection of the level 1 axillary contents along the axillary vein is performed with identification of the accessory vein tributary which is typically found anterior to the thoracodorsal neurovascular bundle. The vein is then dissected free from the level 1 axillary contents and clipped distally to provide maximal length. Routine completion of the levels 1 and 2 ALND is then performed.

After completion of the axillary dissection, a Pentero 900D Microscope (Carl Zeiss Inc, Germany) equipped with the YELLOW 560 package is used to identify and map the cut lymphatic channels draining the arm. The harvested vein is prepared per standard microsurgical technique. Using 9–0 nylon suture, a “U” stitch is placed to capture the anterior wall of the vein and parachute in the lymphatic channels chosen for bypass.¹ (Fig. 2B) 10-0 nylon is then used to suture the

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**FIGURE 1.** Comparison of ICG and FITC Imaging. A, Image of an superficial circumflex iliac artery donor flap harvest site with reverse lymphatic mapping¹ of the abdomen with ICG. Residual lymphatics draining the abdomen are identified as a white signal on a black background. Of note, despite the microscope being equipped with ICG capabilities, this image cannot be visualized in real-time through the binoculars and instead is displayed on a secondary screen. B, FITC imaging demonstrating a spinal meningioma. Note the life like color of the surrounding tissues and ability to visualize the target through the binoculars of the microscope allowing for simultaneous magnification and dissection of the meningioma. (Figure 1B courtesy of Dr. Maryam Rahman, Neurosurgery, UF Health).

**FIGURE 2.** Schematic of the modified LYMPHA technique using FITC. A, Both blue and nuclear dyes are reserved for breast sentinel lymph node identification. FITC is injected in the proximal upper inner arm. B, After completion of the axillary dissection and removal of levels 1 and 2 lymph nodes, arm lymphatic channels, now “glowing” from the FITC injection, are identified and re-routed into an axillary vein tributary.
used commonly by our neurosurgery and ophthalmology colleagues with a high safety profile.15–17 No serious adverse reaction has ever been documented, to our knowledge, when injected intradermally. Moreover, FITC does not permanently stain surrounding tissues, as opposed to ICG and blue dyes, which facilitates dissection of the lymphatic channels. The primary advantage of FITC over ICG in lymphatic surgery is the ability to allow for simultaneous visualization and dissection of lymphatic channels because FITC is excited in the visible spectrum, making it an ideal dye to be used in open surgical fields. The limitations of FITC are that its depth of penetration is a quarter that of ICG (therefore, ineffective for transdermal visualization), and it does require specialized equipment for visualization. However, as we noted at our institution, this specialized equipment if often already readily available.

CONCLUSIONS

Fluorescein isothiocyanate is a safe and effective technique for lymphatic mapping in the LYMPHA technique. We encourage our colleagues to explore the power of FITC in open surgical fields to simultaneously visualize, magnify, and dissect lymphatic channels.

REFERENCES


TABLE 1. Advantages and Disadvantages of the 2 Most Commonly Used Fluorophores in Lymphatic Surgery (Blue Dye and ICG) in Comparison to FITC

<table>
<thead>
<tr>
<th>Dye</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue dye</td>
<td>Technical</td>
<td>Technical</td>
</tr>
<tr>
<td></td>
<td>✔Visualized through binoculars (live surgery)</td>
<td>✔No depth of penetration</td>
</tr>
<tr>
<td></td>
<td>✔No specialized equipment necessary</td>
<td>✔Permanent training</td>
</tr>
<tr>
<td></td>
<td>Safety</td>
<td>✔Adverse reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin necrosis (methylene blue)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaphylaxis (isosulfan blue)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✔Cross-reactivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sulfur drugs (isosulfan blue)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSRI (methylene blue)</td>
</tr>
<tr>
<td>ICG</td>
<td>Technical</td>
<td>Technical</td>
</tr>
<tr>
<td></td>
<td>✔Depth of penetration = 20 mm</td>
<td>✔Unable to visualize through binoculars (no live surgery)</td>
</tr>
<tr>
<td></td>
<td>Safety</td>
<td>✔Permanently stained</td>
</tr>
<tr>
<td></td>
<td>✔No adverse reactions (dermal)</td>
<td>✔Requires specialized equipment</td>
</tr>
<tr>
<td>FITC</td>
<td>Technical</td>
<td>Technical</td>
</tr>
<tr>
<td></td>
<td>✔Visualized through binoculars (live surgery)</td>
<td>✔Requires specialized equipment</td>
</tr>
<tr>
<td></td>
<td>✔Depth of penetration = 5 mm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✔No permanent staining</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Safety</td>
<td>✔No adverse reactions (dermal)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✔No cross-reactivities</td>
</tr>
</tbody>
</table>

SSRI, selective serotonin reuptake inhibitor.

RESULTS

Thirteen patients underwent LYMPHA with intraoperative FITC lymphatic imaging from March to September 2015. Average patient age was 50 years with a mean body mass index of 28. On average, 3.4 lacerrated lymphatic channels (range, 1–8) were identified at an average distance of 2.72 cm (range, 0.25–5 cm) caudal to the axillary vein. 1.7 channels were bypassed per patient (0–4). Eleven anastomoses were performed to the accessory branch of the axillary vein and 1 to a lateral branch. In 1 patient, a bypass was not performed due to poor lymphatic caliber and inadequate length of the vein tributary. No intraoperative or 30-day postoperative adverse events were noted. LYMPHA added an average of 67 minutes (45–120 minutes) to the oncologic procedure.

DISCUSSION

This study demonstrates that FITC is a safe and effective dye for the LYMPHA technique. In comparison to ICG and blue dye, FITC has many advantages. (Table 1) Fluorescein isothiocyanate is a safe dye
A Comparison of 4 Analgesic Regimens for Acute Postoperative Pain Control in Breast Augmentation Patients

Pamela Tan, MD,* Morgan Sparks Martin, MD,* Nina Shank, BA,* Leann Myers, PhD;† Emily Wolfe, MD,* John Lindsey, MD,* and Stephen Metzinger, MD*

Purpose: Patients undergoing breast augmentation are treated with multiple combinations of medications for pain control including ketorolac, liposomal bupivacaine, bupivacaine, and intravenous and oral narcotics. There is no current consensus on the optimal combination; therefore, all are used at the discretion of the surgeon.

Methods: This was a single-center, retrospective study. The total number of patients included was 132. Comparisons were made between 4 groups: bupivacaine only (B); bupivacaine and liposomal bupivacaine (BL); bupivacaine and liposomal bupivacaine plus intraoperative ketorolac (BLKi); and bupivacaine and liposomal bupivacaine plus postoperative ketorolac (BLkp). Average pain scores immediately postoperative and before discharge were recorded and correlated to percentage of patients who received narcotic in the post-anesthesia care unit (PACU). Additional end points noted were side effects including nausea and time spent in PACU postoperatively.

Results: Those receiving intraoperative ketorolac had the lowest pain on discharge (P < 0.0001) and the lowest percentage of patients receiving narcotics (P = 0.009) out of all 4 groups. There was no significant difference between the 4 groups in terms of time spent in PACU, pain immediately after the procedure, or amount of antiemetic given. No bleeding complications were noted for those who did or did not receive ketorolac.

Conclusions: When given options for pain control in breast augmentation, intraoperative ketorolac should be considered, because its inclusion was significant in decreasing use of narcotics and pain upon discharge. Addition of other costly drugs such as liposomal bupivacaine may not provide additional benefit in the immediate postoperative setting for procedures with a short recovery period such as breast augmentation.

Key Words: pain management, breast augmentation, ketorolac, bupivacaine, liposomal bupivacaine

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MATERIALS AND METHODS

Study Population

This was a single-center, retrospective study that analyzed patients who underwent elective outpatient surgery for breast augmentation. All patients were female and 18 years or older. Patients that underwent surgery for this procedure over a 7-year period were included (2009–2015). Those who did not receive a combination of bupivacaine and liposomal bupivacaine with or without ketorolac were excluded. Two surgeons performed all operations with similar techniques. Data were collected via a database located at the outpatient surgery center where the procedures were performed. This database held all scanned medical records pertaining to the perioperative care of the patient. The study was approved by the Biomedical Institutional Review Board of Tulane University New Orleans with waiver of consent.

Data Collection

For the purpose of this study, information was collected regarding type of analgesia used intravenously or intramuscularly by anesthesia and subcutaneously by the surgeon intraoperatively. These data were combined with the medications given intravenously and by mouth in the PACU. Timing of the narcotics given postoperatively was also analyzed.

Comparisons were made between 4 groups: bupivacaine only (B); bupivacaine and liposomal bupivacaine (BL); bupivacaine and liposomal bupivacaine plus postoperative ketorolac (BLkp).
B Group (n=59)

FIGURE 1. Patients in the B group were given a mean of 40 mL of bupivacaine with 0.25% epinephrine per patient, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection.

BL Group (n=26)

FIGURE 2. Patients in the BL group were given a mixture of 20 mL of bupivacaine, 20 mL of liposomal bupivacaine with 0.25% epinephrine, and 20 mL of 0.9% normal saline, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection.

Technique

Primary breast augmentation was performed in all patients in the subpectoral plane. Patients were first seen and marked preoperatively. After appropriate induction of anesthesia, skin prepping, and sterile draping, the operation was initiated with injection of local anesthetic into the incision and as an intercostal nerve block, specific to each group as detailed below. An incision was then made at the inframammary fold or periareolar. Dissection was performed such that a subpectoral plane was created using a dual plane technique with complete division of pectoralis origins along the inferior border. Once adequate hemostasis was achieved, injection of local anesthetic into the breast pocket was performed. After implant selection, pocket was irrigated, and permanent saline or silicone implants were placed. No drains were used.

The mean implant volume for the study population was 363 cc with a range of 175 to 550 cc. There was no difference in the mean volume of implant placed between the groups. All implants were round and smooth. Out of 132 patients, 68 (51.5%) had saline implants and 64 (48.5%) had silicone implants. Inframammary incisions were used in 100 (75.8%) out of 132 patients, and periareolar incisions were placed in 32 (24.2%) out of 132 patients.

The injection of local anesthetic for each group was as follows:

Patients in the B group (Fig. 1) were given a mean of 40 mL of bupivacaine with 0.25% epinephrine per patient, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection.

Patients in the BL group (Fig. 2) were given a mixture of 20 mL of bupivacaine, 20 mL of liposomal bupivacaine with 0.25% epinephrine, and 20 mL of 0.9% normal saline, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection.

Patients in the BLKp group (Fig. 4) were given a mixture of 20 mL of bupivacaine, 20 mL of liposomal bupivacaine with 0.25% epinephrine, and 20 mL of 0.9% normal saline, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection. In addition, ketorolac 30 mg intravenous (IV) and 30 mg intramuscular (IM) were given postincisionally but before the end of procedure.

Patients in the BLK group (Fig. 3) were given a mixture of 20 mL of bupivacaine, 20 mL of liposomal bupivacaine with 0.25% epinephrine, and 20 mL of 0.9% normal saline, and this was injected into 3 areas: (1) into the marked incision before incision, (2) intercostal nerve block before incision, and (3) into the breast pocket after dissection. In addition, ketorolac 30 mg IV and 30 mg IM were given at the end of procedure.

It should be noted that the use of liposomal bupivacaine as a regional nerve block is off-label and has not been approved by the Food and Drug Administration.

Statistical Analysis

For the continuous measures, data were analyzed using analysis of variance methods. When assumptions of normality were not met, results were verified by analysis with the Kruskal-Wallis test. For categorical measures, differences in frequencies were assessed using Pearson $\chi^2$ test. Subhypotheses were assessed using Bonferroni-adjusted $P$ values.
In addition, there are side effects such as headache, constipation, sleep disturbance, and altered mental status, as well as tolerance and abuse that often occur. To reduce use, other modes of analgesia such as nonsteroidal anti-inflammatory drugs (NSAIDs) and local anesthetics are advised.

Local anesthetics have the ability to limit central sensitization by limiting impulses to afferent fibers and diminishing spinal cord stimulation and pain processing.\(^8,16\) This can contribute to a significant pain-free period postoperatively. Bupivacaine has a half-life of 2.7 hours, and this duration is prolonged when combined with epinephrine.\(^3\) It is also comparatively inexpensive and can be used to obtain this pain-free period.\(^10,17\) An alternative that is even longer acting is liposomal bupivacaine. This liposomal formulation is administered intraoperatively and releases bupivacaine for up to 96 hours. This has been demonstrated in other studies as an advantageous addition to multimodal analgesia.\(^18\)–\(^22\)

Nonsteroidal anti-inflammatory drugs have the ability to work both centrally and peripherally. The local inflammatory response from injury is reduced, attenuating peripheral sensitization, which also decreases spinal nociceptive processing.\(^10\)

Centrally, they prevent spinal prostanoid synthesis. By reducing both peripheral and central sensitization, pain is reduced in the postoperative period, requiring fewer additional analgesics including decreased total dose of opioids even after major surgery.\(^8,16,23\) Nonsteroidal anti-inflammatory drugs are likely to be inadequate when used alone.\(^23\)–\(^25\)

Other studies have demonstrated that a combination of NSAIDs such as ketorolac with other modalities including local anesthetics is safe and superior than the use of each product alone.\(^23\)–\(^25\)

One study comparing intravenous ketorolac versus placebo for pain control after surgery found that NSAIDs combined with opioids resulted in not only less opioid consumption and better analgesia but also decreased postoperative nausea, vomiting, and sedation.\(^26\)–\(^28\) This gives NSAIDs an advantage over opioids in the perioperative period.\(^10\) Ketorolac has even been shown to provide similar analgesic effect to morphine.\(^29,30\) For mild to moderate postoperative pain, NSAIDs should be the drug of choice.\(^3\)–\(^13\)

Multimodal analgesia has become the standard in clinical practice in recent decades in attempts to prevent peripheral and central stimulation and control postoperative pain.\(^26\)–\(^31\)–\(^33\) This approach utilizes combinations of analgesic drugs to optimize pain relief. Drugs with different mechanisms of action can be used to target distinct origins of the pectoralis major muscle. In our study, we have aimed to demonstrate the best combination of drugs for optimal pain control in this patient population.

Studies show that pain is triggered by sensitization of neurons in the pain pathway. This sensitization can be either central or peripheral.\(^5\) Placement of the implant into the retromuscular pocket has also increased pain associated with the procedure because of the partial detachment of the sternal and costal origins of the pectoralis major muscle. In our study, we have aimed to demonstrate the best combination of drugs for optimal pain control in this patient population.

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In our study, we looked at the effects of ketorolac on platelet function, which is crucial for surgical hemostasis. This has been demonstrated in animal studies with substantial results.16,43 It is commonly given near the end of surgery. This is a reversible inhibition of platelet aggregation causing prolonged bleeding times.30,48 This, however, does not conclude that ketorolac is unsafe for use. In patients who are not otherwise coagulopathic, it has even been demonstrated as safe with respect to bleeding in surgery patients including those undergoing spinal surgery.13,49-52

There is also a concern among the surgical community that ketorolac can cause acute kidney injury postoperatively. This is a rare event and occurs in approximately 1 in 1000 to 100,000.53 Its use does not significantly elevate serum creatinine levels and can be used safely.23,54 Some studies have shown that the transient fall in postoperative glomerular filtration rate and, thus, renal function is insignificant enough to warrant its use preoperatively.55

### TABLE 1. Summary of Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (n = 59)</th>
<th>BL (N = 26)</th>
<th>BLK (N = 34)</th>
<th>BLKP (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.8 9.9</td>
<td>31.9 9.3</td>
<td>32.1 8.4</td>
<td>28.1 6.9</td>
</tr>
<tr>
<td>BMI</td>
<td>21.7 2.7</td>
<td>22.5 4.4</td>
<td>22.3 3.0</td>
<td>20.8 2.3</td>
</tr>
<tr>
<td>Time PACU</td>
<td>90.9 18.7</td>
<td>93.8 23.7</td>
<td>86.4 16.9</td>
<td>96.9 12.9</td>
</tr>
<tr>
<td>Pain po (0–10)</td>
<td>0.56 1.74</td>
<td>0.23 1.18</td>
<td>0.53 1.94</td>
<td>0.00 0.00</td>
</tr>
<tr>
<td>Pain dc (0–10)</td>
<td>2.22 1.91</td>
<td>2.81 1.30</td>
<td>1.15 1.78</td>
<td>3.08 1.32</td>
</tr>
<tr>
<td>Time meds</td>
<td>33.9 19.5</td>
<td>38.6 37.2</td>
<td>24.6 12.1</td>
<td>41.4 23.2</td>
</tr>
<tr>
<td>Amount of meperidine given (mg) in PACU</td>
<td>37.1 18.9</td>
<td>34.2 18.6</td>
<td>34.0 32.0</td>
<td>23.2 8.6</td>
</tr>
<tr>
<td></td>
<td>N = 32</td>
<td>N = 19</td>
<td>N = 10</td>
<td>N = 7</td>
</tr>
<tr>
<td>Received meperidine</td>
<td>33 55.9</td>
<td>19 73.1</td>
<td>9 26.5</td>
<td>7 53.8</td>
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<tr>
<td>Received antiemetics</td>
<td>30 50.8</td>
<td>15 44.1</td>
<td>9 26.5</td>
<td>6 46.2</td>
</tr>
</tbody>
</table>

B group, bupivacaine only; BL group, bupivacaine and liposomal bupivacaine; BLKi group, ketorolac given intraoperatively plus bupivacaine and liposomal bupivacaine; BLKP group, ketorolac given postoperatively plus bupivacaine and liposomal bupivacaine. Variables listed above include age; BMI; time spent in the PACU; pain po, pain score immediately upon PACU arrival; pain dc, pain score upon discharge; time meds, timing of narcotic administration; amount of meperidine given (mg); patients receiving meperidine; and patients receiving antiemetics.

Numerous studies have shown that a multimodal regimen incorporating several different mechanisms of action has clear advantages over one that employs a single medication.7 In our study, we looked at 4 different pain regimens: group B, group BL, group BLKi, and group BLKP. Our study shows that intraoperative ketorolac with liposomal bupivacaine and bupivacaine (BLKi) performed the best in terms of lowering narcotic usage and pain scores upon discharge (Fig. 5).

Additionally, bupivacaine is much more cost-effective, because liposomal bupivacaine costs one hundred times more than standard bupivacaine.38

As discussed above, avoiding peripheral and central sensitization is an optimal method to decrease post-injury pain. Preventive analgesia utilizes this theory by using analgesia before the painful stimulus to decrease the intensity of the pain.19 This has been demonstrated in animal studies with substantial results.8 Because of NSAIDs demonstrating antinociceptive effects both on peripheral and central neurons, ketorolac is an optimal drug for use in preventive analgesia. Local anesthetic can be combined for additional local, peripheral nociceptor blockade to attenuate sensitization before the surgical stimulus.8,40

Based on the underlying principal of preemptive analgesia, ketorolac as well as local anesthetic should be given before incision for optimal pain prevention. Ketorolac should be given as preventive analgesia after primary hemostasis has been achieved.

Our study supports that the timing of ketorolac administration greatly influences outcomes. With regards to discharge pain scores and postoperative narcotic usage, our results suggest that intravenous ketorolac given systemically after surgery is less effective than ketorolac given intraoperatively, near the end of surgery. This is supported by a study in hand surgery. Here, preincisional use of both local anesthetics and NSAIDs as opposed to postincisional or postsurgical was superior for adequate pain control.41,42

Nonsteroidal anti-inflammatory drugs are still thought to be relatively contraindicated when used preincidentally because of the effect on platelet function, which is crucial for surgical hemostasis.10 Overall, it is accepted for use preincidentally in small procedures but is still unclear in larger more invasive procedures because of lack of sufficient evidence in its safety.16,43 In the neurosurgical population, it has been associated with higher risk for postoperative hematoma.44 Others have reported significant blood loss intraoperatively if ketorolac was given before “primary” hemostasis was achieved.45,46 There is currently no evidence to suggest any bleeding complications from use of ketorolac after hemostasis was achieved.37 It is commonly given near the end of surgery.11 In our study, ketorolac was used postincisional in breast augmentation with no bleeding complications. In both clinical and laboratory studies, bleeding has been demonstrated because of a reversible inhibition of platelet aggregation causing prolonged bleeding times.30,48 This, however, does not conclude that ketorolac is unsafe for use. In patients who are not otherwise coagulopathic, it has even been demonstrated as safe with respect to bleeding in surgery patients including those undergoing spinal procedure.53,49-52

There is also a concern among the surgical community that ketorolac can cause acute kidney injury postoperatively. This is a rare event and occurs in approximately 1 in 1000 to 100,000.53 Its use does not significantly elevate serum creatinine levels and can be used safely.23,54 Some studies have shown that the transient fall in postoperative glomerular filtration rate and, thus, renal function is insignificant enough to warrant its use preoperatively.55

FIGURE 5. Pain score at time of discharge. In pairwise comparisons, BLKi < BL, and BLKi < BLKP (all P < 0.05).
Studies have found that parenteral ketorolac is associated with upper gastrointestinal adverse effects including gastritis, duodenitis, peptic ulcers, and hemorrhage compared with nonuse.\textsuperscript{56} Ketorolac should be avoided in patients with malignancy and coagulopathies, as well as chronic kidney disease.

This study found no significant difference in postoperative nausea, vomiting, renal injury, or hemorrhage between these 4 groups.

CONCLUSIONS

Intraoperative ketorolac should be considered as part of the analgesic regimen for acute postoperative pain control in breast augmentation. Its inclusion was significant in decreasing patient use of narcotics and pain upon discharge. Other points to consider include its inclusion was significant in decreasing patient use of narcotics and pain upon discharge. Other points to consider include

REFERENCES


Clinical, Biomechanical, and Anatomic Investigation of Colles Fascia and Pubic Ramus Periosteum for Use During Medial Thighplasty

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Introduction: The medial thighplasty is a procedure where patients may attain superior mobility, hygiene, and cosmesis. Most surgeons use attachment of the superficial fascial system (SFS) of the thigh flap to the Colles fascia, whereas others attach the SFS to the pubic ramus periosteum. Because of a high complication profile, we aim to elucidate the clinical, biomechanical, and anatomic qualities of the Colles fascia versus the pubic ramus periosteum.

Materials and Methods: We performed a 17-year retrospective review documenting clinical complications, a biomechanical analysis of sutures placed in different tissue layers of the thigh, and a histologic analysis surrounding the ischiopubic ramus. Separate suture pull-out strength testing was conducted on cadaveric tissue using an Adirnet MTEST Quattro with no. 1 Vicryl suture and tissue grips at a displacement rate of 2.12 mm/s. Simultaneous displacement and force were acquired at 100 Hz and with measurements obtained at regular intervals between the pubic symphysis and the ischial tuberosity in both the Colles fascia and the deeper periosteal layers of the thigh. A histologic analysis was performed at 3 points along the ischiopubic ramus using paraffin-embedded large mount tissue sections stained with hematoxylin, eosin, and Gomori trichrome.

Results: Thirty-nine patients underwent medial thighplasty with a 46.16% complication rate. Suture pull-out force of the suspected superficial Colles fascia sites was, on average, 72.8% less than values from the deeper periosteal tissue. Anchor points in the Colles fascia elongated 17.4% further before failure than those in the periosteum. There was noticeable variability between anchor points and across samples. The histologic sections suggest that the Colles fascia from the different regions of the ischiopubic ramus varies considerably in both continuity and collagen fiber content with no discernible pattern. The periosteal and muscular fascial layers were more continuous histologically with direct attachments into the pubis and ischium.

Conclusions: Anchoring of the SFS to the periosteum did not improve our complication profile when compared with the literature. Both the biomechanical and histologic analyses demonstrate that the Colles fascia is highly variable in organizations with coincident variability in tissue strength. Our results require further study to identify the optimal surgical technique for medial thighplasty.

Key Words: medial thighplasty, body contouring, cosmetic, superficial fascial system, plastic surgery

Within the auspice of an obesity epidemic nationally, there has been increased popularization of bariatric surgery with a resultant need for postoperative body contouring.1–3 The massive weight loss achieved after gastric restrictive procedures produces severe skin laxity, lipodystrophy, and deformities best addressed through skin excision and reaproximation.4,5 On a psychosocial level, massive weight loss can negatively affect quality of life, self-esteem, and body image, while also exacerbating physical discomfort.6 First described by Lewis,7,8 medial thighplasty helps to improve mobility, hygiene, and aesthetics within the indicated patient population. This traditional technique, however, remained unpopular within the standard cosmetic plastic surgery clinic for many years because of scar migration, wound dehiscence, vulvar distortion, lymphatic disruption, and early recurrence of thigh ptosis.9

It was not until the notoriety of Lockwood10 and his description of the superficial fascial system (SFS), and its interconnectedness throughout the body, that the medial thigh lift was seen as a manageable and beneficial procedure. The SFS is thought to be widely distributed throughout the body because it is largely responsible for tethering the skin and fat to underlying tissues, creating many of the topographic landmarks in body-surface anatomy.11 Lockwood12–13 described a dense area of the Colles fascia at the junction of the perineum and medial thigh as the anatomic shelf—an idea that remained a standard throughout all future publications and medial thighplasty technique descriptions. Even today, the deep-tissue anchoring maneuver into Colles fascia is technically important in both horizontal and vertical thighplasty. Current practice still reflects this advancement but does not distinguish a difference between anchoring of the SFS to the superficial perineal fascia or the ischiopubic ramus to reinforce thighplasty and prevent scar migration.1 Figure 1 depicts an illustration of the Lockwood anatomic description of the medial thigh.

These anatomic and surgical advancements of the thigh lift as well as the addition of intraoperative liposuction have yet to appreciably decrease postoperative morbidity.14 Depending on study criteria, complication rates range from an average of 42.72% to as high as 74%, and most commonly include dehiscence, seroma formation, wound infection, or hematoma.6,15 Massive weight loss patients are predisposed to impaired wound healing and often have underlying comorbidities that may further complicate postoperative outcomes.16

Medial thighplasty remains a distinct challenge for even the most experienced plastic surgeon and holds distinct room for improvement. There is a paucity of literature surrounding the anatomic and biomechanical properties of Colles fascia compared with the periosteum of the inferior pubic ramus, even as key components to a successful repair. Noting a central lack of understanding and extreme complication profile, we attempt to distinguish a clinically relevant picture of the inner
thigh SFS, Colles fascia, and inferior pubic ramus periosteum using suture pull-out strengths and histologic mapping.

METHODS

Clinical Analysis

A 17-year retrospective chart review was conducted for all patients from our chief surgeon’s (J.L.) private practice who underwent medial thighplasty. Inclusion criteria included all patients older than 18 years who received medial thighplasty with anchoring to the inferior pubic ramus periosteum. Exclusion criteria were patients younger than 18 years. Demographic data such as age, sex, comorbid disease, and body mass index were tabulated. Complications were subdivided into major and minor criteria. Major complications were categorized as vulvar distortion, scar migration, hematomas, seromas requiring drainage, sepsis, death, and 3 or more minor complications. Minor complications included cellulitis, wound dehiscence, and seroma not requiring drainage. Institutional board review was acquired (protocol no. 9256).

Biomechanical Analysis

Uniaxial biomechanical parameters were tested on 2 unembalmed cadavers on separate occasions and included suture pull-out strength and displacement of tissue at load failure. Tissue pull-out strength and elongation were acquired using no. 1 Vicryl suture anchored at regular intervals between the pubic symphysis and the ischial tuberosity in both the superficial Colles fascia and the deeper periosteal tissue layers along the inferior ramus of the pubis (IRP). Case 1 used the left side of the pelvis to anchor 7 sutures into periosteal tissue along the IRP and the right side of the pelvis from the same specimen was used to anchor 7 sutures into the suspected Colles fascia. All anchor sites were placed at 1-cm intervals. Case 2 used 3 sites at 3-cm intervals with discrete anchor sites in the Colles fascia, the adductor fascia, and the deep periosteal layer along the IRP. The 3-site interval was used to reduce proximity effects when pulling adjacent sutures. In both cases, a single surgeon with more than 20 years of clinical experience placed all sutures to reduce variability due to clinician preference. An Admet MTEST Quattro mechanical test stand with specialized suture and tissue grips was used to hold and obtain data. Sutures were preloaded to less than 0.1 kg to remove slack in the tissue, and the system was then zeroed. All specimens were pulled at a displacement rate of 2.12 mm/s, and simultaneous displacement and force data were acquired at 100 Hz. All specimens were allowed to reach room temperature (68–70°F) before testing. Figure 2 depicts the Admet MTEST Quattro equipment usage during a suture-pull trial.

Histologic Analysis

A fresh female cadaver (age, 79 years) was acquired for the histologic evaluation of the SFS overlying the superior and inferior ischiopubic rami and the ischial tuberosity. Both the right and left ischial and pubis portions of the os coxae bones were removed with the soft tissues intact. The anterior margin of the removed specimen was the epidermis, and the posterior margin was the periosteum and soft tissue layers along the inferior ramus of the pubis (IRP). Case 1 used the left side of the pelvis to anchor 7 sutures into periosteal tissue along the IRP and the right side of the pelvis from the same specimen was used to anchor 7 sutures into the suspected Colles fascia. All anchor sites were placed at 1-cm intervals. Case 2 used 3 sites at 3-cm intervals with discrete anchor sites in the Colles fascia, the adductor fascia, and the deep periosteal layer along the IRP. The 3-site interval was used to reduce proximity effects when pulling adjacent sutures. In both cases, a single surgeon with more than 20 years of clinical experience placed all sutures to reduce variability due to clinician preference. An Admet MTEST Quattro mechanical test stand with specialized suture and tissue grips was used to hold and obtain data. Sutures were preloaded to less than 0.1 kg to remove slack in the tissue, and the system was then zeroed. All specimens were pulled at a displacement rate of 2.12 mm/s, and simultaneous displacement and force data were acquired at 100 Hz. All specimens were allowed to reach room temperature (68–70°F) before testing. Figure 2 depicts the Admet MTEST Quattro equipment usage during a suture-pull trial.

FIGURE 1. An illustration of the Lockwood anatomic description of the medial thigh. Oblique view of the pelvis including the muscles of the medial compartment of the thigh (red). The SFS (yellow) as described by Lockwood has been cut and reflected to display the clinically relevant anatomy of the medial thigh lift. The SFS of the medial thigh is continuous with the perineal fascia. The thick condensation or band of the Colles fascia is shown at the junction of the medial thigh and the perineum, overlying the inferior pubic ramus. This thick band continues cephalad toward the pubic symphysis. Not pictured: anteriorly, the SFS continues over the pubic symphysis as the Scarpa fascia of the abdomen. Posteriorly, the SFS is continuous with the urogenital diaphragm.
tissue structures attached to the bone. Care was given to restrict separation of the soft tissues from each other during the extraction process to ensure that the specimens remained as true to anatomic position as possible.

The specimens were decalcified over a 5-day period using Calex and then sliced using a cell path surgical knife at 1.5-cm intervals perpendicular to the long axis of the bone. Sections from 3 regions were chosen for anatomic investigation (Fig. 3). The tissue segments were paraffin embedded using a 3-day embedding process and sectioned at 6 μm using a Leica RM2125 microtome. The sections were then mounted on a 3 × 2-in glass microscope slide and stained with hematoxylin and eosin and Gomori trichrome. Photomicrographs were taken using a Nikon Eclipse Ni of 3 tissue segments labeled A to C (Figs. 4–6). These photomicrographs and microscope slides were visually analyzed for collagen continuity and organization by an expert histologist.

**RESULTS**

Thirty-nine patients underwent medial thighplasty with attachment of SFS to the periosteum and met the inclusion criteria for this study. Demographics included a mean age of 42 years and an average body mass index of 28.21, and the study group included 36 women and 3 men. Overall, there was a 46.16% complication rate, with 5 patients (12.6%) involving major complications and 13 patients (33.3%) involving minor complications. Primarily, patients experienced wound dehiscence (25.64%), cellulitis or erythema (20.5%), and seroma (2.56%). Notably, this population did not experience any scar migration, labial distortion, or severe complications such as sepsis or death.

Biomechanical analysis is reported on a case-specific basis.

**Case 1**

The Colles fascia showed a maximal load of 5.45 kg at a failure displacement of 52.33 mm at the site 1 cm from the ischial tuberosity. This was the highest load for any Colles site tested in either case specimen. Maximal load for all Colles sites ranged from a high of 5.45 kg to a low of 1.18 kg, and the displacement ranged from a high of 62.23 mm to a low of 22.82 mm (Table 1). In contrast, maximal load for the periosteal sites reached 20.56 kg at a failure displacement of 62.38 mm. Maximal load for all periosteal sites ranged from a high of 20.56 kg to a low of 2.37 kg, and the displacement ranged from a high of 62.38 mm to a low of 13.28 mm (Table 1). The difference in the maximal load for suture pull-out between the Colles site and the periosteal site was 73.5%, and at the minimal loads, the difference was 50.2%. The 2 highest loads were recorded at the periosteal site approximately...
1 and 2 cm from the symphyseal border. In contrast, the 2 lowest loads were recorded at the periosteal sites located 1 and 2 cm lateral and posterior to the high-load anchor sites (approximately 1 and 2 cm medial and anterior to the ischial tuberosity).

Case 2

Right Side

The Colles fascia showed a maximal load of 2.64 kg at a failure displacement of 26.94 mm at the site approximately 1.5 cm from the midline of the pubic symphysis. Maximal load for all Colles sites ranged from a high of 2.64 kg to a low of 0.91 kg, and the displacement ranged from a high of 26.94 mm to a low of 4.92 mm (Table 1). In contrast, maximal load for the periosteal sites reached 12.24 kg at a failure displacement of 55.83 mm. Maximal load for all periosteal sites ranged from a high of 12.24 kg to a low of 3.49 kg, and the displacement ranged from a high of 55.83 mm to a low of 9.01 mm (Table 1). The difference in the maximal load for suture pull-out between the Colles site and the periosteal site was 78.4%, and for the minimal loads, the difference was 73.9%. The 2 highest loads were recorded at the periosteal site immediately adjacent to the pubic symphysis and approximately 1 cm from the symphyseal border. In contrast, the lowest load was recorded at the periosteal site located 1.5 cm lateral and posterior to the high-load anchor site.

Left Side

The Colles fascia had a maximal load of 2.04 kg at a failure displacement of 34.99 mm at the site approximately 3.0 cm from the midline of the pubic symphysis. Maximal load for all Colles sites ranged from a high of 2.04 kg to a low of 1.56 kg, and the displacement ranged from a high of 34.99 mm to a low of 18.64 mm (Table 1). The maximal load for the periosteal sites reached 20.71 kg at a failure displacement of 42.81 mm. Maximal load for all periosteal sites ranged from a high of...
20.71 kg to a low of 6.92 kg, and the displacement ranged from a high of 44.68 mm to a low of 34.33 mm (Table 1). The difference in the maximal load for suture pull-out between the Colles site and the periosteal site was 90.1%, and at the minimal loads, the difference was 77.4%. The highest load was recorded at the periosteal site midway between the pubic symphysis and the ischial tuberosity. In contrast, the lowest load was recorded at the periosteal site located adjacent to the pubic symphysis.

In addition to the trials to determine suture pull-out loads in tissues, 2 unused sutures were tested using specifically designed yarn holders for the Admet MTEST Quattro to test for failure strength and were found consistent with manufacturer data. Based on manufacturer data, the maximal load was estimated at 12.1 kg at failure, which was similar to our trials that found loads of 12.71 kg, and 12.69 kg at failure.

The histologic microanatomy of the SFS in regions A to C was consistent on both the left and right sides of the cadaver.

A: The subcutaneous tissue had thick congruent bands of fibroelastic tissue spanning from the most superficial region of the hypodermis to the tendons inserting into the periosteum of the ischial tuberosity (Fig. 4). Most of the fibroelastic bands were composed of collagen and oriented in a direction that was parallel to the surface of the body. The ratio of collagen throughout the section was markedly increased compared with regions B and C.

B: The subcutaneous layer of these sections had thin interconnecting bands of fibroelastic tissue spanning from the most superficial region of the hypodermis to the superficial fascia of the underlying muscles and the crus of the clitoris (Fig. 5). There was a larger, more organized band of fibroelastic tissue superficial to the fascia of the gracilis muscle; however, this band was discontinuous throughout the entire specimen. Furthermore, the fibroelastic bands within the hypodermis were organized both parallel and perpendicular to the body’s surface.

The content of collagen versus elastic fibers within the hypodermis is also evidence to support the claim that the membranous layer of the SFS is not a continuous layer.24,25 The comparison of the microanatomy of regions A to C revealed that the fiber composition of these regions

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**DISCUSSION**

The SFS is anatomically variable in the area of the medial thigh in both biomechanical analysis and histologic observation. We also did not note a difference in complication rates within this series as compared with the literature. Because medial thighplasty continues to progress technically, a foundational understanding of the SFS must be a top priority. The ideal patient with localized skin excess and minimal adiposity of the thighs is often not the day-to-day reality of body contouring.17 Even with the addition of liposuction-assisted lifts improving postoperative thigh contour in both the bariatric and nonbariatric patients, complication rates remain unreasonably high.6,9,14,15,18

Massive weight loss from bariatric surgery creates an aesthetic sequelae of excess skin best corrected through body-contouring procedures such as medial thighplasty.19 Skin redundancies in the groin often cause dermatologic disease, which diminishes personal hygiene and the ability to exercise—severely hindering activities of daily living.2 Although medial thighplasty consistently demonstrates minor complications, patients receive a significant improvement in quality of life.19,20 Even outside of our country’s obesity epidemic, the westernization of diets in certain Asian countries has made body contouring more common in recent years.21 These questions and complications have global implications. Yet, the morbidity burden after medial thighplasty suppresses enthusiasm on the topic and often removes the procedure from a plastic surgeon’s armamentarium.

Although the importance of the SFS has been well documented in the plastic surgery literature, there is also evidence to suggest that the composition of the subcutaneous layer (SFS) may be anatomically variable on an individual basis and within certain body regions.22,23 There is also evidence to support the claim that the membranous layer of the SFS is not a continuous layer.24,25 The comparison of the microanatomy of regions A to C revealed that the fiber composition of these regions

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**TABLE 1. Biomechanical Experimental Data**

<table>
<thead>
<tr>
<th>Suture Location</th>
<th>Periosteum</th>
<th>Colles Fascia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Load, kg</td>
<td>Extension at Max Load, mm</td>
<td>Maximum Load, kg</td>
</tr>
<tr>
<td>Case 1</td>
<td></td>
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</tr>
<tr>
<td>Anterior at the symphysisal</td>
<td>10.98</td>
<td>23.24</td>
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<tr>
<td>surface</td>
<td>12.56</td>
<td>40.01</td>
</tr>
<tr>
<td>20.56</td>
<td>62.38</td>
<td>1.18</td>
</tr>
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<td>2.75</td>
<td>13.28</td>
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<td>2.37</td>
<td>25.34</td>
<td>3.60</td>
</tr>
<tr>
<td>4.88</td>
<td>36.60</td>
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<tr>
<td>Posterior at the ischial tuberosity</td>
<td>3.85</td>
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<td>Case 2—right pelvis</td>
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<td>52.76</td>
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<tr>
<td>surface</td>
<td>12.24</td>
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<td>Anterior inferior ramus</td>
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<td>4.92</td>
</tr>
<tr>
<td>Posterior at the ischial</td>
<td>3.49</td>
<td>9.01</td>
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<tr>
<td>tuberosity</td>
<td></td>
<td></td>
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<tr>
<td>Case 2—left pelvis</td>
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<td>Anterior at the symphysisal</td>
<td>6.92</td>
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<td>surface</td>
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<td>42.81</td>
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<tr>
<td>Medial at the inferior ramus</td>
<td>6.98</td>
<td>44.68</td>
</tr>
</tbody>
</table>

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varies according to location along the ischiopubic ramus. This observation has been seen in other regions of the body such as the abdomen and extremities.⁴²,⁴⁵ Although the distance between these regions is less than 2.5 cm, there are anatomic properties that likely affect the orientation of the fibroelastic bands that develop within the hypodermis. The muscle attachments change from all 3 of these regions. Section A is the attachment site for the adductor magnus and the obturator externus on the lateral aspect of the bone; section B is the attachment site for the gracilis, adductor brevis, and obturator externus laterally and the obturator internus on the internal aspect; section C is the attachment site for the adductor longus on the lateral aspect and the obturator internus on the internal aspect of the bone.⁴⁶ These differences may alter the stresses placed on the soft tissue structures surrounding these muscles and the composition of the hypodermis. In addition, because of the complex functionality of the perineal region, gravity itself places stress on the cutaneous and subcutaneous tissue layers because the remainder of the lower extremity draws the skin downward. Furthermore, the sitting position makes this region somewhat weight bearing. These factors most likely vary by individual and result in a subcutaneous anatomy that is also variable.

This study is not without limitations. Because of this being a single-surgeon, single-practice site literature review, we had limited number of patients for our clinical analysis. Retrospective reviews are inherently limited to relying on charting amenable to human error. Some surgeons also contend increased pain with periosteum attachment, although our clinical series could not prove this. As well, there are differences between fresh frozen cadaver specimen and animated tissue, which may affect both biomechanical and histologic interpretations.

CONCLUSIONS

Medial thighplasty remains a distinct challenge for plastic surgeons because of the high morbidity rate postoperatively and insufficient data driven agreement on technique. Our results preliminarily support the conclusion that there is anatomic variability of the SFS within the medial thigh region histologically and mechanically—although anchoring of the SFS to the inferior pubic ramus periosteum did not improve our complication profile in comparison with previous studies. A more in-depth evaluation of the anatomic and biomechanical properties within the thigh region may facilitate the design of optimal suturing techniques for individualized patient surgical plans.

ACKNOWLEDGMENTS

The authors thank Stephanie Preston for her contribution and creation of the artwork represented in Figure 1.

REFERENCES


Introduction: Correction of auricular deformities can be accomplished through splinting within the first few weeks of life. This is hypothesized to be due to retained circulating maternal estrogens decreasing the structural density of collagen; however, this has not been fully tested. Cartilage elasticity is dependent on the concentration of the proteoglycan aggregate, and hyaluronic acid, a constituent of proteoglycan aggregate, is increased by estrogens. Nonsurgical correction of these deformities in more developed patients has the potential to change clinical practice and eliminate surgical risks. Previous studies have demonstrated preliminary promise with the use of injectable estrogen to treat auricular deformities. For this study, we have validated an animal model and demonstrated the feasibility of a more therapeutically appropriate topical estrogen treatment in restoring neonatal plasticity of auricular cartilage.

Methods: Ears of 12 New Zealand rabbits were folded and splinted, and assigned an experimental group (estrogen, placebo, and untreated control) (n = 8 ears). Treatment ears received topical estrogen or placebo cream daily for 4 weeks, whereas controls received no treatment. The splints were removed following 2 additional weeks, and photographs were taken to calculate the retained fold angle. Biopsies were also taken for histologic analysis.

Results: The 8 control ears showed a statistically increased angle from a folded orientation of 46.6 degrees to return of ear position to a normal upright position of 151.2 degrees by the fourth day after splint removal. Both the estrogen-treated and placebo-treated ears responded to splinting with maintained folding (36.6 degrees and 32.5 degrees, respectively). Auricular cartilage thickness trended toward thicker in ears treated with estrogen, consistent with increased matrix components.

Conclusions: Estrogen and placebo treatment with splinting of ears lead to a significant change to the cartilage configuration, validating the model. The results of this study are very encouraging and provide the foundation for a noninvasive therapeutic approach for correcting auricular deformities. Future work will include a more detailed mechanistic study evaluating the dosing of estrogen and the efficiency of dermal penetration as well as evaluating the long-term outcomes and molecular mechanism-associated cartilaginous responses to estrogen.

Key Words: auricular deformities, nonsurgical correction, estrogen

Plasticity of Auricular Cartilage in Response to Hormone Therapy

Patrick S. Cottler, PhD, Matthew D. McLeod, MD, MPH, Jesse I. Payton, BS, Angela Pineros-Fernandez, MD, and Jonathan S. Black, MD

Cartilage elasticity has been shown to be dependent on the concentration of the proteoglycan aggregate, and hyaluronic acid, a constituent of proteoglycan aggregate, is increased by estrogens. The literature hypothesizes that remaining maternal estrogen within the first weeks of life increases hyaluronic acid and other extracellular components leading to a decrease in elasticity and an increase in cartilage malleability. This transient malleability of the auricular cartilage is the mechanism behind the early success of external molding. Though widely accepted, this hypothesis has not been fully tested, and there is limited literature on the topic. Previous studies have shown chemical component changes in the auricular cartilage matrix and ear appearance in response to the injections various steroid hormones including estrogen as well as increased malleability of ear cartilage in response to enzymatic treatment targeting hyaluronic acid and elastin. Though these studies provide the foundation for the hormonal treatment of auricular deformities, injection-based delivery limits the clinical relevance of this approach.

Nonsurgical correction of auricular deformities beyond the neonatal period has the potential to change clinical practice and eliminate surgical risks. The purpose of this study is to further validate an animal model to evaluate the efficacy and mechanisms of exogenous hormonal therapy to the external ear and to achieve plastic deformation of the auricular cartilage for effective ear recontouring. Topical estrogen was then investigated in this model as a potential agent to promote cartilage plasticity to test of the hypothesis that effective nonsurgical recontouring of auricular cartilage is due to circulating residual maternal estrogens. The results can be compared with previous reports of successfully altering auricular cartilage by increasing the hexosamine content in the chondromucoprotein compared with controls with intramuscular estrogen injection.

METHODS

Animal experiments were performed under a protocol approved by the University of Virginia Institutional Animal Care (Animal Welfare Assurance A3245-01) and Use Committee in accordance with the National Institutes of Health's Guide for the Care and Use of Laboratory Animals. Rabbits were housed in an Association for Assessment and Accreditation of Laboratory Animal Care-accredited facility. All procedures were performed under anesthesia, and all efforts were made to minimize pain or suffering.

Splint Placement

Twelve male New Zealand White Rabbits (2–2.5 kg) were used for this study due to their easily manipulated ears, the similarity of cartilage to human ears, and a similar previously described model. On the day of the procedure, animals were anesthetized to a surgical plane with inhaled isoflurane (2–2.5%), and each ear was shaved, depilated, and prepped for aseptic surgery with iodophor solution and 70% alcohol, and draped for surgery.

Each ear was folded 5 cm from its tip. A 2-0-Prolene suture (Ethicon, Somerville, NJ) was then passed through a cotton dental roll on the medial dorsal side of the ear, through the now adjacent proximal and distal ear, and then through another dental roll on the ventral side of the ear. The suture followed the reverse path on the lateral side of the ear and was tied so that the ear would retain a near linear configuration.
Splints were placed bilaterally on both ears on each animal (Fig. 1). Animals were then placed in soft Elizabethan collars for 2 to 3 days postprocedure to ensure the splints maintained position. Animals were given postoperative analgesics and allowed to fully recover from anesthesia.

**Topical Treatments**

The 12 animals were divided into 2 groups. The initial 4 animals (n = 8 ears) were used as an untreated control group. Splints were maintained for 6 weeks, and the ears did not receive any treatment. At the completion of the 6 weeks, animals were reanesthetized and the splints were removed and digital photographs were taken. Control ears were also photographed daily for 6 days after the removal of the splints. After the final photograph, animals were euthanized through an anesthetic overdose and 3-mm biopsies were then taken through the entire ear thickness at the medial and lateral aspect of the auricular cartilage of the fold of each ear and fixed in 10% formalin for histological processing.

The remaining 8 animals were prepped and received bilateral splints in the same fashion as described, and used to compare topical estrogen treatment to a placebo. 0.5 g of topical estrogen (Premarin [0.625 mg/g]; Pfizer NY, NY) was applied to the external surface of the left ear of each rabbit along the created fold just superior to its splint and gently massaged into the skin (n = 8 ears). Additionally, 0.5 g of a placebo cream with similar inert ingredients to Premarin (CVS Eczema Cream, CVS, Woonsocket, RI) was applied the created fold of the right in the same fashion (n = 8 ears). Both ears underwent daily application for 4 weeks. After 4 weeks of treatment, the splints were maintained for an additional 2 weeks without topical therapy. The 6 weeks of splinting is consistent with previously described successful splinting techniques in neonates. At the conclusion of 6 weeks, animals were reanesthetized, the splints were removed, digital photographs were taken, and animals were euthanized through an anesthetic overdose. Three-millimeter biopsies were then taken through the entire ear thickness at the medial and lateral aspect of the auricular cartilage of the fold of each ear and fixed in 10% formalin for histological processing.
Treatment Analysis

To determine the effect of the splinting and treatment, the angle of each ear was calculated by analyzing the digital images using ImageJ photo analysis software (Fig. 2). The fixed tissue biopsies were sectioned into 5 mm slices and stained with hematoxylin-eosin, and 20× images were obtained. The thickness of the cartilage was also calculated using ImageJ software.

RESULTS

Splints were successfully placed on all the ears of the 12 animals and were able to be maintained for 6 weeks (Fig. 1). All ears maintained an acute angle after splint removal without immediate rebound. At the time of splint removal, there was no statistical difference in the treatment arm between the untreated control ears (46.6 ± 10.8 degrees), the placebo-treated ears (32.5 ± 20.8 degrees), and the estrogen-treated ears (36.6 ± 11.4 degrees) (Fig. 3). The angle of the untreated control ears increased daily and returned to a presplinted orientation (151.2 ± 9.3 degrees) after 4 days (Fig. 4) with no additional change seen out to 7 days (data not shown).

The auricular cartilage in the rabbit ear thins as it transitions from the medial to the lateral aspect. To determine if the cartilage thickness was altered due to increased extracellular matrix deposition, measurements were taken at both the lateral and medial aspects of each ear. Though not statistically significant, the cartilage trended toward being thicker in the medial cartilage samples treated with estrogen (400.9 ± 147.4 μm), compared with the placebo-treated samples (292.0 ± 94.0 μm) and untreated control samples (261.2 ± 62.8 μm), as well as the lateral cartilage samples treated with estrogen (274.8 ± 99.7 μm), compared with the placebo-treated samples (213.3 ± 67.2 μm) and untreated control samples (204.8 ± 57.7 μm) (Fig. 5).

DISCUSSION

Surgical molding of auricular deformities involves invasive suturing methods combined with cartilage excision and/or scoring. These techniques provide reliable correction, but not until the ear is near adult size (age, 5–7 years). Surgery has numerous disadvantages beyond the delay of repair including infection, hematoma, and most commonly recurrence of the deformity. Cost is a significant concern as well because most insurance carriers classify repair as "cosmetic." The psychosocial consequences of severe deformities can be profound leading many parents to pursue correction. Earlier treatment in with non-invasive methods would address many of the surgical disadvantages. Nonsurgical molding of auricular deformities has reported success in the neonatal period. Remaining maternal estrogen is thought to be responsible for this plasticity but scientific data are scarce. Previous models exist documenting change in ear shape using intramuscular and direct estrogen injections. This demonstrates promise in altering the malleability of ear cartilage, but specifics regarding the animal models used are unclear. Additionally, these reports using an invasive injection of the treatment modality provide limited data as to the long-term efficacy. Though Oh et al used an ointment delivery of estrogen to ear deformities, it is unknown whether topical methods of delivery for these treatments would be efficacious and provide a clinically applicable long-term noninvasive approach.

The control arm of our study further clarified the animal model needed to study ear plasticity. At the end of 6 weeks of splinting, untreated control ears exhibited an immediate preservation of the acute splinting angle. However, there was not any long-term plastic recontouring,

FIGURE 3. The average angle of the ears for the control, placebo-treated, and estrogen-treated ears immediately after the splints were removed. There was not any statistical difference between the groups (P < 0.05).

FIGURE 4. Demonstration of the maintained elasticity of the nontreated control ears. Four days after the splints were removed, the ear angle was able returned to a more normal configuration. *Statistically significant increase in ear angle (P < 0.05).

FIGURE 5. The average thickness of the auricular cartilage trended toward being thicker in the cartilage samples treated with estrogen. No significant differences were seen (P < 0.05).
because this effect was temporary in the untreated control ears as they returned to a normal configuration by the fourth day after the splints were removed (Fig. 4). These data provide a clear foundation for the animal model for future study looking at lasting change to ear shape. Comparisons to treatments will provide evidence of their efficacy.

Both the estrogen-treated and placebo-treated ears demonstrated the acute effect from splinting. The ear angle from each treatment group was not statistically different from the control group immediately after splint removal (Fig. 3); however, it is unclear whether that effect is permanent. It is also unclear whether the placebo ears would demonstrate same shape as the treatment ears over time. It is possible that the estrogen application on one ear led to a systemic treatment effect on the placebo-treated ear. This potential systemic effect of estrogen needs to be further evaluated. Additionally, the dosing of the estrogen will need further investigation. To be a clinically relevant therapeutic approach, the application of estrogen would need to be topically applied; therefore, these future dosing studies will include more detailed evaluation of the dermal penetration.

Though the thickness of the cartilage was not statistically different between ears, the trend toward increased thickness in the estrogen-treated ears could indicate it is consistent with increased levels of extracellular matrix components such as hyaluronic acid as has been previously suggested.6,8,9

There were several limitations to this initial study evaluating a model to test treatments for postneonatal nonsurgical ear contouring. In efforts to determine the microscopic structure of the cartilage due to treatment, biopsies were taken immediately after the splints were removed. Therefore, the long-term effects of the treatments are still unclear. However, this study provides an excellent foundation for future mechanistic studies on auricular cartilage plasticity.

There is much promise in the use of estrogen to allow for increased ear malleability beyond the first weeks of life. We plan future study to evaluate the many possibilities we have seen in this pilot study. Using our validated animal model, we plan to evaluate the lasting effect of estrogen treatment on ear shape by following the animals over time without disruption of their ear architecture through tissue harvest. We plan to evaluate the ear cartilage and systemic blood for estrogen levels with a comparison to injectable estrogen. This would aid in determining systemic effect of estrogen and efficacy of topical application in dermal penetration.

CONCLUSIONS

We have presented an improved, validated animal model for the study of auricular molding through external approaches. Although the results are promising, further study is needed to determine the efficacy of dermal penetration of estrogen to the perichondrium and if the effect of estrogen is long lasting. The ability to extend the period of neonatal cartilage plasticity would provide exciting improvements to our knowledge of cartilage mechanics and better treatment options for children.

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Abdominal Wall Allograft
Preclinical Biomechanical Investigation of a Novel Reconstructive Adjunct

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Introduction: Acellular dermal matrices have revolutionized abdominal wall reconstruction; however, device failure and hernia recurrence remain significant problems. Fascia grafts are a reconstructive adjunct with increased tensile strength compared with acellular dermal matrices; however, clinical use is limited by insufficient donor material and donor site morbidity. To this end, we investigate the biomechanical properties of human abdominal wall allografts (AWAs) consisting of the anterior rectus sheath from xiphoid to pubis.

Methods: After cadaveric procurement of 6 human AWAs, the tissue was divided horizontally and a matched-sample study was performed with specimens randomized to 2 groups: fresh, unprocessed versus processed with gamma irradiation and decellularization. Specimens were evaluated for physical properties, DNA content, tensile strength, and electron microscopy.

Results: All AWA donors were male, with a mean age of 55.2 years (range, 35–74 years). Procured AWAs had a mean length of 21.70 ± 1.8 cm, width of 14.30 ± 1.32 cm, and area of 318.50 cm², and processing resulted in a 98.3% reduction in DNA content. Ultimate tensile strength was significantly increased after tissue processing, and after subcutaneous implantation, processed AWA demonstrated 4-fold increased tensile strength compared with unprocessed AWAs.

Conclusions: Acellular AWAs represent a novel reconstructive adjunct for abdominal wall reconstruction with the potential of replacing “like with like” without additional donor site morbidity or antigenicity.

Key Words: acellular, abdominal wall allograft, abdominal wall reconstruction, biomechanical properties

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Because they are derived from the dermis, ADMs have a structure and biomechanical profile different from that of abdominal wall fascia. Although ADMs have well-established benefits in resistance to infection and biocompatibility, the innate microstructure of dermis is not ideally suited to the functional stresses exerted on the abdominal wall, which include constant loading from intra-abdominal pressure as well as cyclical loading with respiration and during strenuous physical activity. The impact of these forces on the tensile durability of ADMs has been clinically borne out in multiple studies that document a substantial rate of hernia recurrence and abdominal wall laxity with use of ADMs in abdominal wall reconstruction.

Before the introduction of ADMs, there was a long history of abdominal wall reconstruction with fascia flaps.26–28 The indications for fascia flaps are similar to those for ADMs, including deficient autologous tissue and a contaminated surgical field.29–31 Animal models of abdominal wall reconstruction with fascia lata allografts have shown no decrease in tensile strength at 1 year, and human abdominal wall reconstruction with fascia lata allografts has been performed with no major signs of recurrence, laxity, or infection at a mean follow-up of approximately 2 years.32–34 With the goal of improving options and outcomes in abdominal wall reconstruction, we performed a preclinical biomechanical investigation of an acellular abdominal wall allograft (AWA). This novel reconstructive adjunct has the potential to not only reconstruct deficient tissue on a gross anatomic scale but also restore the structural properties that are essential to long-term durable function of the abdominal wall while avoiding the problems of antigenicity and donor site morbidity.
MATERIALS AND METHODS

AWA Procurement

Six AWAs were procured from organ donors according to guidelines for human cellular and tissue-based products. Briefly, the anterior rectus sheath fascia was isolated from the xyphoid to the pubis and laterally from semilunar line to semilunar line. The linea alba was preserved during isolation of the construct (Fig. 1). The constructs were then characterized for maximum length, maximum width, surface area, and weight in grams (Table 1). The constructs were then divided transversely perpendicular to the linea alba, and transferred to LifeNet Health on ice for proprietary tissue processing according to approved protocols (Fig. 1).

Experimental Groups and Tissue Processing

Two experimental groups were investigated—control AWAs (Fig. 1; right panel, top) and Matracell-processed acellular AWAs (Fig. 1; right panel, bottom). Both groups are handled in a similar fashion including freezing and gamma irradiation with the exception of Matracell tissue processing to directly compare the effects of tissue acellularization on the physical and mechanical properties of the AWA constructs. After cadaveric procurement of human AWAs, the tissue was sent on ice to LifeNet Health for tissue processing using gamma irradiation for sterilization as well as Matracell tissue processing, which is an efficient 2-day decellularization protocol, which demonstrates a more than 98% reduction in donor DNA with multiple disinfecting agents targeting both cellular and genetic components to produce a safe bio-implant. The protocol includes validated United States Pharmacopeia chapter 71 endpoint microbial testing and does not utilize any animal-derived reagents. The tissue processing protocol has been used previously for commercially available products for orthopedic, cardiac, and vascular procedures.

DNA Quantification of AWAs

The DNA reduction after tissue processing and acellularization were assessed on 1 × 1 cm sections of AWA constructs for DNA using the DNeasy kit (QIAgen). The DNA concentration was determined with a spectrophotometer and was normalized to AWA dry weight, as well as compared with the unprocessed and acellular AWA groups.

<table>
<thead>
<tr>
<th>TABLE 1. AWA Physical Properties</th>
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<td>Demographics of Donor Tissue</td>
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<td>After tissue processing</td>
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SEM, standard error of the mean.

Tissue Response to Implantation of AWA

Animal experiments were performed under a protocol approved by the University of Virginia Institutional Animal Care (Animal Welfare Assurance No. A3245-01) and Use Committee in accordance with the National Institutes of Health's Guide for the Care and Use of Laboratory Animals. Rats were housed in a facility accredited by Association for Assessment and Accreditation of Laboratory Animal Care. All procedures were performed under anesthesia, and all efforts were made to minimize pain or suffering. Abdominal wall allograft specimens, processed and unprocessed, were thawed in room temperature phosphate buffered saline (1 x), and three 1.0 × 5.5 cm samples of each specimen were sharply cut perpendicular to the linea alba of the donor and placed into an iodophor solution. Three female Sprague-Dawley rats (250–300 g) were utilized for this portion of the study. Animals were anesthetized and maintained under inhaled isoflurane (2%–2.5%). Once anesthetized, the animals were positioned supine, shaved, depilated, and prepared for aseptic surgery with iodophor scrub followed by 70% alcohol and iodophor solution, and then draped for surgery. A 4 cm midline skin incision was created in the mid abdomen and the dissection proceeded through the panniculus carnosus muscle to expose...
The abdominal wall fascia and linea alba. Samples of human AWA (1.0 × 5.5 cm²) that had been soaking in iodophor solution for 10 minutes and rinsed with sterile water were placed longitudinally on the anterior surface of the abdominal wall and secured proximally and distally 4-0 Vicryl in interrupted fashion at the cranial and caudal ends. Unprocessed AWA samples were placed into the animals' right side, and processed AWA samples were placed into the in animals' left side. After implantation, the skin flaps were reapproximated in a tension free manner overlying the implanted AWAs and secured with 4–0 Prolene sutures and the animal was circumferentially bandaged. Animals were also given a subcutaneous injection of buprenorphine (0.5 mg/kg) for pain, recovered and returned to their cages. Female animals were utilized to allow for ease of urination with the bandaging. One week after implantation, the bandages and sutures were removed. Three weeks after implantation, the animals were reanesthetized with inhaled isoflurane (2%–2.5%) and the midline was reopened and the skin was carefully dissected and retracted to expose the AWA implants. The implants were sharply excised. A 2- to 3-mm strip was sharply dissected from the short axis and placed into 10% formalin for histology and scanning electron microscopy. The remainder of the specimen was utilized for material strength testing. Animals were then euthanized with an anesthetic overdose of Euthasol.

Characterization of the Effect of Mode of Tissue Processing on AWA Tensile Strength

The AWA constructs were subjected to repeat baseline characterization after tissue processing, and then, they were dissected into 1 cm by 5 cm strips perpendicular to the linea alba but not including the linea alba in the specimen. Mechanical tensile strength testing was performed on an Instron mechanical tester (Model No. 5943) equipped with a 100-N load cell (Model No. 2530-427) and 1 kg screw action clamps (Norwood, Mass). The AWA strips were loaded onto a 4 × 2 cm² sheet

**FIGURE 2.** Processed and unprocessed AWAs were subjected to mechanical strength testing. Processed AWAs demonstrated a significant increase in ultimate tensile strength (P < 0.05, n = 6 per group).

**FIGURE 3.** Processed and unprocessed AWAs were subjected to scanning electron microscopy to determine the effect of tissue processing on ultrastructural architecture and collagen cross-linking. Processed AWAs demonstrated a notable increase in collagen cross-linking with a significant increase in the number of collagen branch points as well as an increase in the density of collagen fibers per high-power field. Representative images depict the collagen ultrastructure at 500x and 5000x, respectively.
of 100-grit sandpaper pretreated with cyanoacrylate. The AWA strips within the clamp segments were covered with cyanoacrylate followed by sandpaper folded over to ensure solid clamp contact. The AWA strips were loaded into mechanical clamps with a gauge length of 20 mm and clamp length of 15 mm for the studies before tissue implantation. For studies performed after subcutaneous implantation in a rat model, because of tissue availability, samples were loaded with a 1-cm clamp length and 20 mm gauge length. Specimens were prestretched with 10 cycles of 5 mm strain at 10 mm/s and then pulled to failure at 100 mm/min to ensure a midsubstance tear. End of test was determined by 80% decrease from peak load or maximum 10 cm of extension. Primary outcomes include maximum load (N), tensile stress at maximum load (MPa), and elastic modulus.

Scanning Electron Microscopy for Ultrastructural Characterization

Samples of unprocessed and processed AWAs before and after implantation were evaluated through scanning electron microscopy to evaluate the microscopic structure. After the AWA samples were fixed in 10% formalin for 5 days, they were washed (3 × 10 min) with 0.1 M cacodylate buffer and then treated with 2% osmium tetroxide for 60 min. After 2 × 10 min washes with 0.1 M cacodylate buffer and distilled H2O, the samples were dehydrated in a series of 10-minute ethanol treatments (30%, 50%, 70%, 95%, and 100%). Samples were then placed into a critical point dryer with a 15-minute purge time and then mounted on microscope stubs with carbon stickers and sputter coated with gold, 200 seconds at 60 mA. Once coated, the samples were imaged on a Zeiss Sigma HD scanning electron microscope at a voltage of 3.0 kV and a working distance of 13.4 mm.

Histologic Characterization of AWA

AWA constructs (1 × 1 cm sections) were formalin fixed and embedded in paraffin. Sections with a concentration of 5 μM were subjected to staining with hematoxylin and eosin to cellular infiltration after implantation and compared with the unprocessed and acellular AWA groups. Cell counting and quantification were performed using ImageJ software.

Statistical Analysis

All values recorded are presented as mean ± standard error of the mean from independent experiments from given n sizes. Statistical significance of multiple treatments was determined by analysis of variance followed by the Bonferroni post hoc test when appropriate. Statistical significance between 2 groups was determined by using the 2-tailed Student t test. P values of less than 0.05 are considered significant.

RESULTS

All AWA donors were male, with a mean age of 55.2 years (range, 35–74 years). Physical data for Matracell-processed acellular AWAs are presented in Table 1. Procured AWAs had a mean length of 21.70 ± 1.8 cm, width of 14.30 ± 1.32 cm, and area of 318.50 cm². The average weight before and after decellularization was 41.26 g and 22.42 g, respectively. There was a 98.3% reduction in DNA after the Matracell processing of the AWAs.
Mechanical testing was performed on matched unprocessed and processed AWAs before soft tissue implantation (Fig. 2). The maximum load was 4.72 ± 1.80 kgf in the unprocessed AWA group and 6.8 ± 0.74 kgf in the processed AWA group, which demonstrates a significant increase in ultimate tensile strength after tissue processing ($P < 0.05$, $n = 6$ per group) (Fig. 2A). Young modulus was 31.39 ± 17.82 mPA for the unprocessed AWA group and 38.25 ± 25.76 mPA for the processed AWA group (Fig. 2B). Maximum extension at failure was 5.91 ± 1.84 mPA for the unprocessed AWA group and 11.46 ± 3.91 mPA for the processed AWA group, which also demonstrated a significant increase after tissue processing ($P < 0.05$, $n = 6$ per group) (Fig. 2C).

Collagen ultrastructure was assessed at baseline to assess the effect of tissue processing on the composition of the AWAs with scanning electron microscopy (Fig. 3). Processed AWAs demonstrated a notable increase in collagen cross-linking with an increase in the number of collagen branch points as well as an increase in the density of collagen fibers per high-power field (Fig. 3).

Mechanical strength testing was then performed after subcutaneous implantation of the AWAs in a rat model as described. After tissue implantation, the maximum load at failure was 0.66 ± 0.15 kgf in the unprocessed AWA group and 2.64 ± 0.54 kgf in the processed AWA group, which demonstrates a significant increase in ultimate tensile strength in the processed group ($P < 0.05$, $n = 6$ per group) (Fig. 4). Both groups experienced a decrease in maximal tensile strength after 3 weeks of subcutaneous implantation; however, the effect was significantly decreased in the processed AWA group.

After abdominal wall implantation, the processed and unprocessed AWAs were procured and were subjected to scanning electron microscopy to determine the effect of tissue processing on ultrastructural architecture. Processed AWAs demonstrated a notable increase in surface cellularity (Fig. 5). Collagen architecture is maintained in both groups after 4 weeks of implantation. Representative images depict the collagen ultrastructure at 500x and 5000x, respectively ($n = 3$).

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After abdominal wall implantation, the processed and unprocessed AWAs were procured and were subjected to scanning electron microscopy to determine the effect of tissue processing on ultrastructural architecture. Processed AWAs demonstrated a notable increase in surface cellularity (Fig. 5). Collagen architecture is maintained in both groups after 3 weeks of implantation. To further confirm the findings of increased surface cellularity, histologic analysis was performed after 3 weeks of subcutaneous implantation. After abdominal wall implantation, processed AWAs demonstrate a significant increase in cellularity in both the center of the construct (0.59 ± 0.28% and 2.34 ± 0.77% for unprocessed AWA and processed AWA, respectively) and the AWA-host tissue border zone (3.53 ± 1.61% and 11.61 ± 4.31% for unprocessed AWA and processed AWA, respectively) ($P < 0.05$, $n = 3$); however, both groups demonstrated the presence of basophilic cells throughout the construct (Fig. 6).
DISCUSSION

Given the substantial problem posed by hernia recurrence, with rates approaching 40% in the literature, advances in the field of abdominal wall reconstruction have the potential to impact the care of thousands of patients annually. The availability of suitable autologous tissues with the tensile and cellular properties necessary to facilitate healing of the abdominal wall repair and withstand the forces applied to the abdominal wall during the recovery period is generally deficient. This fact is often compounded by a patient population with multiple comorbidities and previous operative procedures, which further compromise available tissues, leading to a postoperative major complication rate approaching 20%. Acellular dermal matrices serve as a regenerative biomaterial scaffold to support cell host integration and collagen remodeling and are used in a variety of reconstructive surgical applications. Acellular dermal matrices have been processed to render the tissues sterile and acellular to facilitate biocompatibility and revascularization. The ADMs for abdominal wall reconstruction have revolutionized the management of complex abdominal wall defects with the provision of an ample tissue source when autologous tissues are insufficient. However, ADMs are derived from dermis and, therefore, have mechanical properties disparate from that of native abdominal wall fascia. In search of a way to replace abdominal wall fascial defects in “like with like” fashion, a variety of autologous approaches using expendable donor fascia through separation of components for local abdominal wall fascia have been proposed. However, these techniques are technically demanding, are associated with increased donor site morbidity, and are not always sufficient to restore fascial continuity to the abdominal wall. To this end, we describe and provisionally characterize the utility of human abdominal wall, which consists of the anterior rectus sheath from semilunar line to semilunar line and from xiphoid to pubis, and subjected to tissue processing to render it sterile and acellular. We have demonstrated that our tissue processing technique results in increased tensile strength compared with unprocessed fascia, which is substantiated ultrastructurally with the presence of increased collagen cross-linking. We have performed preclinical characterization in a rat subcutaneous implantation model and have demonstrated that processed acellular AWAs retain tensile strength to a greater degree than unprocessed AWAs and, despite the increased collagen cross-linking and preserved tensile strength, these constructs allow cellular penetration and bio-incorporation. This study is intended to serve as an initial preclinical evaluation of the bioethical characteristics of AWAs as a potential alternative to other adjuncts available for abdominal wall reconstruction. The tissue procurement and processing described herein result in the procurement of abdominal wall fascial grafts of significant size, 318 cm² in surface area, and relatively uniform thickness. The tissue processing described herein, is analogous to tissue processing used for commercially available ADMs (DermACELL, LifeNet Health, Inc, Virginia Beach, Va) with similar reduction in total DNA content and alterations in collagen ultrastructure. Future studies will elucidate the potential of this construct for abdominal wall reconstruction in animal and human models of abdominal wall hernia to determine its bio-incorporation properties, suture pullout strength, and mechanical failure strength before clinical applications.

Limitations of the AWA approach include difficulty associated with processing the abdominal wall without the creation of fascial defects, in contrast to ADM, which can be procured with the use of a mechanical dermatome. Furthermore, donors must be appropriate as all abdominal walls are not created equal. History of previous abdominal hernia or bulge, history of intra-abdominal surgery, or obesity should be considered contraindications to abdominal wall procurement. The size of the abdominal wall is also limited by the size of the donor, and more importantly, the thickness of the construct is limited by the thickness of the abdominal wall, in contrast to ADM, which can be procured in thicker or thinner fashion to meet specific reconstructive needs. Furthermore, the procurement of AWA fascia is not practical in donors intended for solid intra-abdominal organ donation, because procurement of the fascia would delay procurement of liver, kidney, or pancreas tissues by the organ procurement team.

CONCLUSIONS

Acellular ADWs have potential to serve as a novel reconstructive adjunct for abdominal wall reconstruction with the potential of replacing “like with like” without additional donor site morbidity or antigenicity. There was a decrease in maximum load at failure seen after implantation. Therefore, further testing is required in a clinically relevant model of abdominal wall repair to assess its biomechanical properties after implantation in comparison with existing modalities for abdominal wall reconstruction.

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The authors wish to thank LifeNet Health for harvesting and processing the abdominal wall fascia samples used during this study. We would also like to thank Lisa Sallowek, LVT, RLATG, for the excellent care given to all the animals used during this study.

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Identifying Risk Factors Leading to Unanticipated Postoperative Readmission

Peter A. Felice, MD,* David T. Kerekes, BS,† and Bruce A. Mast, MD*

Introduction: Unanticipated postoperative readmissions are a grading metric directly linked to both the quality of patient care and physician reimbursement. However, little data exist to define factors responsible for these readmissions in the plastic surgery patient population. This study aims to identify patient risk factors contributing to unanticipated postoperative readmissions to optimize perioperative patient care and mitigate negative financial impact upon providers.

Methods: We present an institutional review board-approved study retrospective review of 819 plastic surgery patients undergoing operative procedures performed at our institution between January 1, 2013, and December 31, 2014. All unanticipated readmissions within 30 days of an operation were identified and subjected to statistical analysis in an effort to determine whether these readmissions were associated with identifiable patient risk factors.

Results: One hundred forty-nine (18.1%) of the 819 investigated patients underwent readmission, reoperation, or both within 30 postoperative days. Seventy-four (9%) patients required hospital readmission, alone; 55 (6.7%) underwent readmission with operative intervention; and 20 (2.4%) required outpatient operative intervention without readmission. Readmitted patients were significantly more likely to have a positive smoking history (P = 0.009), hypertension (P = 0.0008), congestive heart failure (P = 0.0015), chronic obstructive pulmonary disease (P = 0.023), a higher mean age (P = 0.0001), and a higher Charlson Comorbidity Score (P = 0.0001).

Conclusions: These results identify risk factors associated with unanticipated postoperative readmissions specific to a plastic surgery patient population. With this information, practitioners can allocate appropriate perioperative resources and planning for patients at increased risk for readmission, thereby improving delivery of patient care and satisfying quality metrics linked to provider reimbursement.

Key Words: postoperative readmission, unanticipated readmission, hospital readmission reduction program, quality metric, physician reimbursement, plastic surgery patient

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Results

Of the 819 patients investigated in this study, 149 (18.1%) patients experienced unanticipated readmission, reoperation, or both within the 30-day postoperative period. 74 (9.0%) patients were readmitted for nonsurgical issues requiring nonoperative management, alone, while 55 (6.7%) were readmitted and underwent operative intervention during that same readmission. Lastly, 20 (2.4%) patients underwent outpatient operative procedures but did not require a hospital readmission. This breakdown of our study population is summarized in Figure 1.

Several risk factor variables pertaining to both patient demographic and health history information were chosen for statistical analysis (Fig. 2). When comparing these variables for readmitted and non-readmitted patients, we discovered that a positive smoking history (P = 0.009), hypertension (P = 0.0008), congestive heart failure (P = 0.0015), and chronic obstructive pulmonary disease (P = 0.023) were significantly elevated in our population of readmitted plastic surgery patients. Additionally, the mean age for readmitted patients was 52.4 years, a value significantly higher than the mean age of non-readmitted patients at 38.3 years (P = 0.0001). Readmitted patients also had a significantly higher mean Charlson Comorbidities Index score at 0.94 than did non-readmitted patients at 0.39 (P = 0.0001). No...
statistically significant differences were noted between readmitted and non-readmitted patients for any of the other variables investigated.

**DISCUSSION**

Quality metrics are a prominent component in how physicians are evaluated and gauge overall practitioner performance and reputation. Furthermore, readmission rates have become a quality indicator used to determine practitioner reimbursement from the Centers for Medicare and Medicaid Services. These metric assessments and practitioner reviews are readily available through performance-based websites, social media postings, and patient-sponsored internet surveys, which are all increasingly used by patients when it comes to choosing a surgical provider. This attention to outcome-based and quality-based measures and the direct link both have to physician reimbursement places a considerable onus on the practitioner to provide optimal patient care.

Many studies investigate patient risk factors associated with unanticipated readmissions for various general surgery patient populations. Although their findings may translate to various other medical and surgical subspecialties, we set out to determine exactly which risk factors were responsible for compromising the postoperative course of the plastic surgery patient population. We evaluated various patient demographic and health history data points based on previously published data as well as our authors' own prediction that significant medical comorbidities would contribute to a complicated postoperative course. When comparing these variables in our statistical analysis of readmitted and non-readmitted patients, we observed that readmitted patients were significantly more likely to be tobacco users, hypertensive, and have a previous diagnosis of congestive heart failure or chronic obstructive pulmonary disease. Additionally, advanced age and a higher health severity score calculated by the Charlson Comorbidities Index (CCI) put patients at a significantly greater risk for 30-day readmission. The CCI is calculated using age, albumin level, history of myocardial infarction, cerebrovascular disease, as well as other systemic disease processes, and was a relevant variable to include because it reinforced many of the other individual risk factor variables evaluated in our study population. In addition to defining the risk factors associated with readmission, just as enlightening was the discovery of which risk factors were not. For instance, patients with a history of radiation administration, cancer history, immunosuppressed conditions, and greater travel distances to access care centers, factors we assumed would lend to unanticipated readmissions, were not significantly different between the readmitted and non-readmitted patient populations.

Our study has some limitations we are currently working to improve. We are expanding the number of subjects and incorporating...
additional categorical variables to bolster study power and statistical significance. We also plan on exploring whether distinctions exist between readmitted and non-readmitted patients based on the type and complexity of plastic surgery procedures performed. It may also be useful to parse out whether significant readmission differences are seen between ambulatory and inpatient operative settings, as well as when comparing procedures performed by junior or senior attending physicians. Future project aims include initiating a prospective study to determine whether the risk factors defined by this investigation are in fact associated with future readmissions. Additionally, we are in the process of constructing a Postoperative Readmission Risk Calculator to quantitatively predict the percentage likelihood of 30-day postoperative readmissions based on known patient demographics and risk factors.

Ultimately, our vision is that this information be used at the time of the initial consultation between physicians and patients and be reiterated frequently throughout the perioperative course. Practitioners and patients can work together to ameliorate modifiable patient risk factors and have a free and open dialogue where anticipated risks, benefits, and expectations of an operative procedure are fully disclosed. With this exchange and understanding, the patient and physician both take ownership of, and responsibility for, the challenges and goals of the postoperative course to arrive at an optimal result.

CONCLUSIONS

This study identifies specific risk factors responsible for unanticipated postoperative readmissions in a plastic surgery patient population. With this information, our goal is to further optimize patient care by providing appropriate perioperative resources and planning for patients with characteristics that place them at an increased risk for postoperative complication and readmission. In addition, application of this information can help satisfy quality-directed metrics linked to reimbursement for institutions and individuals responsible for patients' care.

REFERENCES

Goals: The aims of this discussion were to inform the medical community about the American Board of Cosmetic Surgery's ongoing attempts in Louisiana to achieve equivalency to American Board of Medical Specialties (ABMS) member boards so that its diplomates may use the term “board certified” in advertising and to ensure public safety by upholding the standards for medical board certification.

Background: In 2011, Louisiana passed a truth in medical advertising law, which was intended to protect the public by prohibiting the use of the term “board certified” by improperly credentialed physicians. An American Board of Cosmetic Surgery diplomate petitioned the Louisiana State Board of Medical Examiners to approve a rule that would establish a pathway to equivalency for non-ABMS member boards, whose diplomates have not completed training approved by the Accreditation Council for Graduate Medical Education (ACGME) in the specialty they are certifying. Physicians and physician organizations representing multiple specialties (facial plastic and reconstructive surgery, otolaryngology [head and neck surgery], orthopedic spine surgery, pediatric neurosurgery, dermatology, and plastic surgery) urged the Louisiana State Board of Medical Examiners to clarify its advertising policy, limiting the use of the term “board certified” to physicians who have completed ACGME-approved training in the specialty or subspecialty named in the certificate.

Discussion: The public equates the term “board certified” with the highest level of expertise in a medical specialty. When a certifying board does not require completion of ACGME or American Osteopathic Association (AOA)-accredited training in the specialty it certifies, the result is an unacceptable degree of variability in the education and training standards applied to its diplomates. Independent, third-party oversight of certifying boards and training programs is necessary to ensure quality standards are upheld. Any system that assesses a non-ABMS or non-AOA-certified board for equivalency approval must ensure that the training and qualifications required by the non-ABMS or AOA board are equivalent in scope, content, and duration to those required by the ABMS and AOA. This issue must not be misconstrued as a fight between physicians of 2 competing specialties. Preserving the legitimacy of board certification is incumbent upon all medical specialties and subspecialties. This argument is a truthful, principled defense of the legitimacy of board certification.

Key Words: board certification, plastic surgery, ABMS, ACGME, ASPS, ABPS, truth in advertising, facial plastic surgery, state medical board, Louisiana, cosmetic surgery

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Among the general public, the term “board certified” denotes the highest level of achievement in medical training and expertise. When individuals seek medical care, the knowledge that their doctor is board certified assures them that they are engaging a physician with significant direct training and demonstrated skill in the specialty certification advertised. Third-party regulatory oversight of medical boards and residency programs is necessary to ensure that high standards for quality education and training are upheld.

The national standards for independent oversight of medical specialty boards are the American Board of Medical Specialties (ABMS) and the American Osteopathic Association (AOA). All 24 ABMS member boards require their diplomates to successfully complete residency training programs supervised by the Accreditation Council for Graduate Medical Education (ACGME) in the specialty that the board is certifying. Graduates are then required to pass rigorous examinations to obtain initial board certification and to participate in accredited Maintenance of Certification programs for the duration of their medical careers. This exacting system was developed to ensure that board-certified physicians have undergone the appropriate scope, content, and duration of training and that they have developed the validated skills necessary to practice safely and competently.

By June 30, 2020, the ACGME will be the single graduate medical education accreditation system in the United States. The single accreditation system allows graduates of allopathic and osteopathic medical schools to complete their residency and/or fellowship education in ACGME-accredited programs and demonstrate achievement of common milestones and competencies. Accreditation Council for Graduate Medical Education accreditation is overseen by a residency review committee made up of volunteer specialty experts from the field that set standards and provide peer evaluation of sponsoring institutions and specialty and subspecialty residency and fellowship programs.

Patients have a right to know about their physician’s qualifications, education, and training. When physicians advertise themselves to the public as “board certified,” the public cannot be expected to differentiate between a legitimate medical board and a standard one. Louisiana Act 337, signed into law in 2011, was designed to protect the public by prohibiting physicians from using the term “board certified” in advertising unless the board meets any of the following criteria:

1. The board is an ABMS member board or an AOA certifying board.
2. The board has been approved by the Louisiana State Board of Medical Examiners (LSBME).
3. The board requires an ACGME- or AOA-approved postgraduate training program that provides complete training in that specialty or subspecialty.

In cases where the LSBME considers a non-ABMS member board for equivalency approval, the state medical board must ensure that the training and qualifications required by the non-ABMS or AOA board are equivalent in scope, content, and duration to those required by the ABMS and AOA. The ACGME- and AOA-approved residency programs require specific standards in regard to instructor qualifications, a minimum number and variety of types of procedures performed, and progressive patient care responsibility. When a certifying body does not require completion of ACGME- or AOA-accredited training in the specialty it certifies, the result is an unacceptable degree of variability in the education and training standards applied to its diplomates.

The American Board of Cosmetic Surgery (ABCS) is not an ABMS member board and does not have an ACGME training program. As such, the only criteria of Louisiana’s truth in advertising law the ABCS can potentially meet is number 2—approval by the LSBME.
In April 2015, an ABCS diplomate, an otorhinolaryngologist who has expanded his scope of practice to include cosmetic surgery of the breast, trunk, and extremities, petitioned the LSBME to enact a rule that would establish a pathway for non-ABMS member boards to be recognized as equivalent to ABMS- and AOA-approved boards. This request was modeled after a rule approved by the Texas Board of Medical Examiners on April 12, 2013, through a non-transparent process, which allowed for the issue to be voted on as one of numerous “consent agenda” items. No public notice of a meeting or hearing of the Ad Hoc Committee on Advertising can be found in the public record. The rule was passed without a public hearing or discussion of the public safety, training, and expertise issues related to board certification. Section A2e of the rule reads as the following: Requires all physicians seeking certification to have satisfactorily completed postgraduate training that is accredited by the ACGME or the AOA and that provides substantial and identifiable supervised training of comprehensive scope in the specialty or subspecialty certified.

A reasonable person would interpret this as requiring all physicians seeking certification to complete ACGME postgraduate training in the specialty being certified. In contrast, the cosmetic surgeons contend that this requirement consists of 2 independent clauses, the first of which is met by the completion of any previous ACGME-approved training, such as general surgery or obstetrics and gynecology (OB/GYN). The second stipulation of the clause, they assert, is met by non-ACGME-accredited training from a cosmetic surgery fellowship or apprenticeship.

It is irrelevant whether a cosmetic surgeon has undergone previous ACGME residency training in general surgery or OB/GYN because neither of these residencies provides complete training in cosmetic surgery.

The leadership of the Texas Society of Plastic Surgeons wrote a letter to the LSBME, urging them to “(1) maintain the highest level of standards and qualifications when awarding the use of ‘board certified’ to physicians, (2) that any and all discussions and/or votes regarding the use of the term ‘board certified’ be done in the ‘light of day’ with proper and timely notice to the public and all interested physicians and parties, and (3) that the LSBME employ a stakeholder process that includes all interested parties when considering the use of the term ‘board certified’.”

Independent, third-party regulatory oversight of a medical training program is necessary to ensure high-quality education and training. To secure this necessary oversight, physicians from multiple specialties (plastic surgery, facial plastic surgery, orthopedic spine surgery, pediatric neurosurgery, and dermatology), representing multiple state and national organizations, have urged in spoken and written testimony that the LSBME strike the previously mentioned language in section A2e of the proposed rule and replace it with the following:

Requires successful completion of a postgraduate training program accredited by the ACGME or the AOA that provides complete training in the specific specialty or subspecialty named in the certificate.

Under this language, non-ABMS or AOA boards can still be deemed equivalent. For example, diplomates of the American Board of Facial Plastic and Reconstructive Surgery (ABFPRS), the American Board of Pain Medicine, the American Board of Pediatric Neurosurgery, and the American Board of Spine Surgery all certify in an ACGME-recognized specialty that provides complete ACGME-approved training in the subspecialty named in the subspecialty certificate.

A central argument of the ABCS’s case for board equivalency in Louisiana is that the ABCS is analogous to other certifying bodies that have rightly been deemed equivalent to ABMS or AOA boards, specifically, the ABFPRS.

Equivalency is measured by scope, content, and duration of training of a related ABMS specialty. To become a diplomate of the ABFPRS, one must first successfully complete an ACGME-approved otolaryngology residency, which provides complete training in facial plastic surgery.

Board-certified otolaryngologists who have completed an additional 1-year fellowship in facial plastic surgery are eligible to take the certifying examination for the ABFPRS. A facial plastic surgery fellowship is a focused continuation of subspecialty training that was received in ACGME- or AOA-approved otolaryngology residency programs. Diplomates of the ABFPRS have already received complete training in facial plastic surgery during their ACGME-supervised otolaryngology residencies.

Comparably, the American Board of Spine Surgery certifies orthopedic surgeons and neurosurgeons who have received complete training in spine surgery while in their ACGME-approved orthopedic surgery or neurosurgery residencies. The additional 1-year fellowship these surgeons undertake is a focused continuation of the spine surgery training they receive in their ACGME-approved residencies.

Two of the three common ACGME residency pathways for certification by the ABCS—general surgery and OB/GYN—do not contain case requirements for the breadth of cosmetic surgical procedures. The third, otolaryngology, provides ACGME approved training in cosmetic surgery within the head and neck but not cosmetic surgery of the breast, trunk, and extremities. Otolaryngologists who complete a 1-year general cosmetic surgery fellowship have not undergone ACGME-approved training in cosmetic surgery of the breast, trunk, or extremities.

Unlike a facial plastic surgery, spine surgery, or pediatric neurosurgery fellowship, a cosmetic surgery fellowship is not a focused continuation of ACGME-approved residency training in the same specialty. A cosmetic surgery fellowship charts an entirely new course. There is no foundation of ACGME training in cosmetic surgery on which to focus or upon which to build.

Increasing government regulations, decreasing insurance reimbursement, and various economic and lifestyle pressures have caused some physicians to change or expand their area of practice, a phenomenon known as “practice drift.” The Federation of State Medical Boards’ policy states that patients should seek information about prospective physicians, including the level of expertise they have with particular procedures, their education (especially graduate medical education), and any board certifications held. The Federation of State Medical Boards also recommends that physicians should be prepared to provide information about their qualifications and any additional training undertaken that has prepared them to provide treatment that falls outside their original area of practice and should provide this information to patients as part of the informed consent process.

Louisiana is currently experiencing the scenario that occurred in California in 2008, which was decided at the appellate court level.

“This case involves an 11 year effort by the ABCS, to gain specialty board approval by the Medical Board of California, so that physicians certified by the ABCS may advertise themselves as board certified in cosmetic surgery.”

The state medical board enlisted an independent expert, Dr. Ronald Tompkins, to review ABCS fellowship programs. He concluded, “because of the . . . wide variations in prerequisites for, and scope and content of, the training programs of the American Board of Cosmetic Surgery, it is not possible for this reviewer to assign equivalency to an ABMS board or to a non-ABMS board approved in California.”

The California medical board denied the petitioner’s application after determining that the ABCS’s requirements were not equivalent to those of an ABMS member board. Dissatisfied, the ABCS filed a discrimination lawsuit against the California Medical Board.
The appellate court’s 2008 decision from The American Board of Cosmetic Surgery versus the Medical Board of California states, “Since the record reflects the reasons for the Board’s decision, the reasons are rationally related to the regulatory requirements and are supported by ample evidence, we conclude that the Medical Board did not abuse its discretion by denying the American Board of Cosmetic Surgery’s application.”

On April 26, 2016, Georgia enacted a truth in advertising law similar to Louisiana’s, but it closed the pathway of allowing the state medical board to recognize a non-ABMS member board whose diplomates do not undergo ACGME training in the specialty named in the certificate as equivalent.8

In a press release response to Georgia’s truth in advertising law, the American Board of Cosmetic Surgeons attempts to undermine the legitimacy of board certification by physician leaders from 2 competing specialties. Preserving the legitimacy of board certification is incumbent upon all medical specialties and subspecialties. This argument is a truthful, principled defense of the legitimacy of board certification by physician leaders from multiple specialties, representing multiple state and national medical societies.

The Louisiana Society of Plastic Surgeons trusts that the LSBME will affirm the committee’s findings and codify the necessity of completing ACGME-accredited training in the specialty or subspecialty named in a certifying board’s certificate.

Lessons we have learned or reaffirmed in Louisiana from this process are the following:

1. Public safety is the core issue and of paramount importance.
2. The legitimacy of board certification must be preserved and protected.
3. Independent, third-party oversight of certifying boards and training programs is necessary and must be mandatory.
4. Board certification in a specialty or subspecialty must require completion of an ACGME-accredited training program in that specialty and/or subspecialty named in the certificate, followed by successful completion of a certifying examination in that specialty.
5. Any system that assesses a non-ABMS member or non–AOA-certified board for equivalency approval must ensure that the training and qualifications required by the non-ABMS or AOA board are equivalent in scope, content, and duration to those required by the ABMS and AOA.
6. This issue must not be misconstrued as a “turf battle” between physicians of 2 competing specialties. Preserving the legitimacy of board certification is incumbent upon all medical specialties and subspecialties. This argument is a truthful, principled defense of the legitimacy of board certification by physician leaders from multiple specialties, representing multiple state and national medical societies.

REFERENCES

Purpose: This study aims to compare engineered nerve conduits constructed from porcine-derived urinary bladder matrix (UBM) with the criterion-standard nerve autografts, for segmental loss peripheral nerve repairs.

Methods: Forty-eight Sprague-Dawley rats were divided into 2 groups. All underwent a 10-mm sciatic nerve gap injury. This was repaired using either (1) conventional suture (Ethicon) — the 10-mm cut segment was oriented 180 degrees and used to coapt the proximal and distal stumps or (2) UBM conduit—the 10-mm nerve gap was bridged with UBM conduit. Behavior assessments such as sciatic function index and foot fault asymmetry scores were performed weekly. At 3- or 6-week time endpoints, the repaired nerves and bilateral gastrocnemius/soleus muscles were harvested from each animal. Nerves were evaluated using immunohistochemistry for motor and sensory axon staining and with diffusion tensor imaging. The net wet muscle weights were calculated to assess the degree of muscle atrophy.

Results: The UBM group demonstrated significantly improved foot fault asymmetry scores at 2 and 4 weeks, whereas there was no difference in sciatic function index. The net muscle weights were similar between both groups. Motor axon counts proximal/inside/distal to the conduit/graft were similar between UBM conduits and reverse autografts, whereas sensory axon counts within and distal to the conduit were significantly higher than those of the autograft at 6 weeks. Sensory axonal regeneration seemed to be adherent to the inner surface of the UBM conduit, whereas it had a scattered appearance in autografts. Diffusion tensor imaging parameters between groups were similar. Conclusions: Urinary bladder matrix conduits prove to be at least similar to nerve autografts for the repair of peripheral nerve injuries with a short gap. The UBM group demonstrated significantly improved foot fault asymmetry scores at 2 and 4 weeks, whereas there was no difference in sciatic function index. The net muscle weights were similar between both groups. Motor axon counts proximal/inside/distal to the conduit/graft were similar between UBM conduits and reverse autografts, whereas sensory axon counts within and distal to the conduit were significantly higher than those of the autograft at 6 weeks. Sensory axonal regeneration seemed to be adherent to the inner surface of the UBM conduit, whereas it had a scattered appearance in autografts. Diffusion tensor imaging parameters between groups were similar.

Clinical Relevance: In a clinical setting, UBM may eliminate the donor site morbidity and increased operative time associated with nerve autografting.

Key Words: conduit, diffusion tensor imaging, extracellular matrix, peripheral nerve, urinary bladder matrix

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Bridging the Gap
Engineered Porcine-derived Urinary Bladder Matrix Conduits as a Novel Scaffold for Peripheral Nerve Regeneration

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Purpose: This study aims to compare engineered nerve conduits constructed from porcine-derived urinary bladder matrix (UBM) with the criterion-standard nerve autografts, for segmental loss peripheral nerve repairs.

Methods: Forty-eight Sprague-Dawley rats were divided into 2 groups. All underwent a 10-mm sciatic nerve gap injury. This was repaired using either (1) conventional suture (Ethicon) — the 10-mm cut segment was oriented 180 degrees and used to coapt the proximal and distal stumps or (2) UBM conduit—the 10-mm nerve gap was bridged with UBM conduit. Behavior assessments such as sciatic function index and foot fault asymmetry scores were performed weekly. At 3- or 6-week time endpoints, the repaired nerves and bilateral gastrocnemius/soleus muscles were harvested from each animal. Nerves were evaluated using immunohistochemistry for motor and sensory axon staining and with diffusion tensor imaging. The net wet muscle weights were calculated to assess the degree of muscle atrophy.

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Clinical Relevance: In a clinical setting, UBM may eliminate the donor site morbidity and increased operative time associated with nerve autografting.

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(Month Year [Volume]: pages)
Behavioral Testing

Postoperatively, foot fault (FF) asymmetry and sciatic functional index (SFI) behavioral assessments were performed at weekly intervals. To prevent possible bias, behavior testers were blinded to the surgical protocols of each animal.

Foot Fault
Animals were allowed to roam freely on a wire mesh grid measuring 45 × 30 cm, with square openings measuring 2.5 × 2.5 cm. The grid was elevated 2 cm above a solid base. Trials of 50 total steps per hind limb were recorded for each animal. A full fault was recorded if the animal’s hind limb fell through the opening in the grid and touched the floor, whereas a partial fault was recorded if the foot did not touch the floor. An FF asymmetry score was calculated using the following equation: composite FF score = \( \frac{n \text{ partial faults}}{n \text{ full faults}} + \frac{n \text{ full faults}}{n \text{ total number of steps}} \times 100\% \), FF asymmetry score = %FF (normal hind limb) − %FF (surgical hind limb).

Sciatic Functional Index
Before surgery, habituation trials were performed for animals to navigate an inclined beam into their home cage without hesitation.\(^\text{14}\) Each hind limb was inked, and animals walked the beam until 6 consecutive (3 from each limb) foot prints were recorded. Print measurements include the following: normal print length (NPL), normal toe spread (NTS), normal intermediary toe spread (NIT), experimental print length (EPL), experimental toe spread (ETS), and experimental intermediary toe spread (EIT). Sciatic functional index scores were the calculated using the following formula: SFI = −38.3[(EPL − NPL)/NPL] + 109.5[(ETS − NTS)/NTS] + 13.3[(EIT − NIT)/NIT] − 8.8.\(^\text{15,16}\)

Sciatic Nerve and Gastrocnemius/Soleus Muscle Harvest

When the animals reached their final time endpoint, they were euthanized with Euthasol (Virbac AH, Fort Worth, Tex) intracardiac injections. The full length of the nerve was harvested and distributed equally to undergo either DTI processing or histology via IHC staining. The gastrocnemius and soleus muscles were then dissected from each hind limb and weighed (in grams) to obtain net wet weights for each animal.

Histology
Immunohistochemical staining for motor and sensory axons was performed as previously described using commercial antibodies specifically directed against carbonic anhydrase II (Abcam, Cambridge, Mass) and choline acetyltransferase (Millipore, Temecula, Calif).\(^\text{17}\) For carbonic anhydrase II, primary antibody was used at 1:200 overnight. For choline acetyltransferase staining, primary antibody was used at 1:200 for 1 hour. Digital images of stained sections were acquired using Image-Pro Plus 7.0 software (Media Cybernetics, Bethesda, Md) with an Olympus C-35AD-4 microscope at low magnification (10×). Digital images were loaded on ImageJ (Wayne Rasband, National Institute of Mental Health, Bethesda, Md); however, axon counts were obtained by manual count of the entire nerve area.

Diffusion Tensor Imaging
Tissue Sample Preparation
After nerve excision, reverse autografts were incubated in 4% glutaraldehyde/0.5% paraformaldehyde in phosphate-buffered saline (PBS) at 4°C and nerves repaired with a UBM conduit were incubated in 4% glutaraldehyde/2% paraformaldehyde in PBS at 4°C for better penetration of the conduit material. After a minimum of 24 hours of postfixation, excised nerves were placed in PBS + 2 mM gadolinium diethylene triamine pentaaetic acid (Magnevist, Bayer HealthCare, Wayne, NJ) at 4°C for at least 24 hours before imaging. For imaging, excised nerves were placed in glass capillary tubes (3-mm outer diameter) filled with a perfluropolyether liquid (Fomblin, Solvay Solexis, Thorofare, Nj) for susceptibility matching, preventing tissue dehydration, and a signal-free background. For higher throughput, 6 nerves in a hexagonal arrangement were imaged simultaneously.
Diffusion Tensor Magnetic Resonance Imaging

Magnetic resonance imaging was performed on a 4.7-T Agilent Direct Drive scanner (Agilent Technologies, Santa Clara, Calif) for reverse autografts and a 9.4-T Agilent Direct Drive scanner for conduit-repaired nerves. Diffusion tensor imaging data were acquired using a 3-dimensional diffusion-weighted spin-echo sequence with repetition time/echo time of 170/23.0 ms, 12 signal averages, and field of view of $9.6 \times 9.6 \times 14.4$ mm$^3$ for reverse autografts and repetition time/echo time of 160/23.0 ms, 10 signal averages, and field of view of $9.6 \times 9.6 \times 18.0$ mm$^3$ for conduit-repaired nerves. The nominal resolution for both groups was $100 \times 100 \times 450$ μm$^3$ (450 μm along the nerve). Diffusion weighting was achieved with $\delta/\Delta = 4/12$ ms, a prescribed $b$ value of 2000 s/mm$^2$, and 6 directions. One $b = 0$ image was acquired for a total of 7 images in a scan time of approximately 12 hours.

DTI Post-processing and Analysis

Image data reconstruction was performed using in-house written code in MATLAB (MathWorks, Natick, Mass), and DTI analysis was implemented using ExploreDTI.18 Three-dimensional image volumes were zero-padded 2 in each direction during reconstruction from k-space data. Diffusion tensors were estimated voxel-wise using a linear least-squares approach. From the diffusion tensor, fractional anisotropy (FA), axial diffusivity (AD), and radial diffusivity (RD) were computed on a voxel-wise basis and DTI tractography was performed.

Statistical Analysis

Statistical significance was determined using nonparametric Mann-Whitney U test and designated a $P$ value of less than 0.05.

RESULTS

Behavioral Evaluations of Sciatic Nerve Function

Animals repaired with a UBM conduit significantly performed better in FF than the reverse autografts in the 2-week and 4-week time point (Fig. 2). When evaluating SFI scoring, the UBM conduit had behavior results comparable with the reverse autograft at all time points (Fig. 3).

Gastrocnemius/Soleus Net Wet Weights

There was no statistically significant difference in net muscle weight between the UBM conduit and autografts at 3 weeks or 6 weeks (Fig. 4).

![Image of Foot Fault Score](image-url)

**FIGURE 2.** Foot fault scoring. $^*P < 0.05$, statistically significant. A more negative score indicates worse impairment.

![Image of Sciatic Function Index](image-url)

**FIGURE 3.** Sciatic function index scoring. A more negative score indicates worse impairment.

Nerve Histology With IHC

When harvesting the injured nerves, the UBM conduit segment in the 6-week endpoint group seemed more similar in size to the proximal and distal ends of the sciatic nerve than the 3-week conduits. The 3-week conduits seemed bulkier. This was accounted for by partial biodegradation of the conduit in 6-week group compared with the 3-week animals. No samples demonstrated evidence of neuroma formation.

After staining with choline acetyltransferase for motor axons and carbonic anhydrase II for sensory axons, cross sections proximal to, within, and distal to the conduit/graft were evaluated. There was no significant difference in motor axon counts proximal to, within, and distal to the conduit/graft in UBM conduits and autografts in the 6-week time point (Fig. 5a). However, the UBM conduit had greater sensory axons within the conduit ($455 \pm 31$ vs $140 \pm 34$, $P < 0.01$) and distal to the conduit ($253 \pm 27$ vs $77 \pm 14$, $P < 0.01$) in comparison with the autograft group at 6 weeks (Fig. 5b).

Within the 3-week time point, UBM conduits had similar axon counts to the reverse autografts in both motor and sensory axons proximal and within the conduit/graft. However, it is important to note that 2 samples in the 3-week UBM conduit group had uncharacteristically lower sensory counts compared with the other 3-week UBM samples (but similar to autografts) because of collapse, which resulted in a loss of statistical significance. Because of uncleared cellular debris from Wallerian degeneration in the distal end at 3 weeks, axon counts at those segments for both study groups were deemed unreliable and, thus, were not included in this study.

![Image of Gastrocnemius/Soleus Muscle Net Wet Weight](image-url)

**FIGURE 4.** Gastrocnemius/soleus muscle net wet weight.
basement membrane complex also helps regulate cell growth, differentiation, and migration during tissue development and reconstruction.7,8 The beneficial regenerative aspects of UBM scaffolds were demonstrated in this study because we found improved sensory axon numbers in comparison with the autograft. Uniquely, sensory axons also seemed adherent to the inner surface lining of the UBM conduit. Although the mechanism in which sensory axons favor growth along the conduit is unknown, structural proteins (ie, laminin, fibronectin, collagen) known to be present in ECM may be responsible. In vitro assays on human fetal sensory neurons have shown that laminin enhances Schwann cell response and antibodies to laminin suppress sensory neurite growth.20–22 Similarly, fibronectin has been shown to act as a chemoattractant for migrating Schwann cells and provide a direct substrate for adhesion and outgrowth of regenerating sensory axons.23–25 The UBM conduit basement membrane may possess more of these ECM structural proteins that support Schwann cell and sensory axon infiltration over autografts; however, further studies would need to be performed to identify the causative factor. Additionally, motor axon growth was not significantly different between groups at both 3- and 6-week time points. In relation to motor axon regeneration, UBM conduits presumably have a similar structural milieu to autografts to augment axonal outgrowth.

Although histomorphological parameters give information regarding nerve regeneration on a microscopic level, it is important to translate this information to functional recovery as histological evaluation after repair is not possible in humans. The FF scoring system has historically been used to determine the sensorimotor function in animals.23 The improved FF score at 2 and 4 weeks within the UBM conduit could be explained by higher sensory axon counts, in which animals may have more sensory feedback for the next step and grip the rung of the grid with fewer faults. However, despite a more robust sensory axon count, there is question of the accuracy of the FF at 2 weeks postoperatively, as axons are unlikely to have made complete functional connections.25 De Medinaceli et al15 had described difficulty in evaluating sensory function because of overlapping innervation and indirect measurements. Therefore, SFI scoring is regarded as a more reliable and reproducible quantitative method for the assessment of functional outcome in the recovery of the sciatic nerve in rats.14,15,22–28 In this study, we found that UBM conduits performed no worse than that of autografts in SFI at any time point.

The gastrocnemius net weight was similar between both groups, demonstrating likely similar degrees of muscle reinnervation. As expected, there was greater muscle atrophy in the injured limb in comparison with its control limb. Martins et al29 described that one must consider that not all regenerated fibers are viable and misdirected axon growth can lead to aberrant muscle reinnervation. This consideration, in addition to the time it takes regenerating axons to reach the motor end plate, explains the difference in the degree of atrophy between the experimental and the control limb.

This study is the first to monitor the efficacy of a nerve conduit in nerve regeneration using DTI technology. DTI is an advanced neuroimaging tool with the ability to evaluate peripheral nerves noninvasively, objectively, and quantitatively. Parameters yielded by DTI, such as FA, AD, and RD, reflect the anisotropic diffusion of water molecules along and perpendicular to the axon bundles, which provide valuable information on axonal regeneration and degeneration.27–29 The UBM conduits performed equally in all parameters of DTI in comparison with autografts demonstrating similar axonal integrity in all time periods. Diffusion tensor imaging can further be expanded to create tractography images, which allow visualization of the longitudinal extent of nerve regeneration. This study demonstrated track formation proximally to distally in the UBM conduit similar to reverse autografts. However, because of partial collapse found in some UBM samples, further experiments will need to be performed with less deformable models.

Motor axons in both groups seemed to be uniformly distributed in all segments (Fig. 6a). Interestingly, the sensory axons within the UBM conduit seemed to grow adherent to the inner lining of the conduit and then demonstrated a scattered appearance once they reached the distal segment. Sensory axons in the reverse autografts seemed to be scattered in both the graft and distal segments (Fig. 6b).

**Diffusion Tensor Imaging**

Diffusion tensor imaging of excised sciatic nerves was evaluated in 3 regions of interest: 1.5 mm proximal to the proximal graft site, the middle of the conduit/autograft, and 1.5 mm distal to the distal graft site. Fractional anisotropy, AD, and RD were measured for each region of interest. Within the 3- or 6-week UBM group, there was no difference in FA, AD, and RD, in all segments compared with the autografts (Table 1). Some UBM conduit samples had evidence of partial or near complete collapse without visualization of distal tracks. Figure 7 shows tractography demonstrating proximo-distal axonal growth at 6 weeks for noncollapsed UBM conduits and reverse autografts.

**DISCUSSION**

With advances in understanding nerve regeneration pathophysiology, tissue engineering research has focused on developing anisotropic ECM scaffolds that augment axonal regeneration and Schwann cell migration.14 In this study, we evaluate ECM derived from porcine bladder matrix to serve as a novel scaffold. In comparison with other xenogeneic ECM, porcine UBM has demonstrated fewer invasions of fibroblasts because of its intact basement membrane complex on its surface, thereby decreasing scar tissue formation.5 The advantage of an intact

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**FIGURE 5.** A, Motor axon count at 6 weeks. B, Sensory axon count at 6 weeks. *P < 0.05, statistically significant.*
The timing of outcome assessment in animal studies is critical to recognizing the true differences between study groups. Rodents have been described to have rapid neuroregenerative capacity compared with humans and higher mammals. Studying outcomes at earlier time points can provide insights into the regenerative capabilities of different species.

**TABLE 1.** Diffusion Tensor Imaging Parameters in Each Segment Between UBM Conduit and Reverse Autograft at 6 Weeks

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Proximal</th>
<th>SEM</th>
<th>P</th>
<th>Within</th>
<th>SEM</th>
<th>P</th>
<th>Distal</th>
<th>SEM</th>
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<tbody>
<tr>
<td>FA, μm²/ms</td>
<td>0.57</td>
<td>0.019</td>
<td>0.57</td>
<td>0.022</td>
<td>1.00</td>
<td>0.481</td>
<td>0.010</td>
<td>0.593</td>
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<tr>
<td>UBM conduit</td>
<td>0.524</td>
<td>0.016</td>
<td>0.562</td>
<td>0.014</td>
<td>0.545</td>
<td>0.018</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Reverse autograft</td>
<td>0.910</td>
<td>0.037</td>
<td>0.098</td>
<td>0.054</td>
<td>0.890</td>
<td>0.079</td>
<td></td>
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</tr>
<tr>
<td>AD, μm²/ms</td>
<td>0.57</td>
<td>0.08</td>
<td>0.08</td>
<td>0.054</td>
<td>0.791</td>
<td>0.020</td>
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<tr>
<td>UBM conduit</td>
<td>0.082</td>
<td>0.026</td>
<td>0.800</td>
<td>0.038</td>
<td>0.440</td>
<td>0.037</td>
<td></td>
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</tr>
<tr>
<td>Reverse autograft</td>
<td>0.360</td>
<td>0.029</td>
<td>0.488</td>
<td>0.053</td>
<td>0.363</td>
<td>0.015</td>
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<tr>
<td>RD, μm²/ms</td>
<td>1.00</td>
<td>0.08</td>
<td>0.08</td>
<td>0.053</td>
<td>0.440</td>
<td>0.037</td>
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<tr>
<td>UBM conduit</td>
<td>0.387</td>
<td>0.021</td>
<td>0.357</td>
<td>0.028</td>
<td>0.363</td>
<td>0.015</td>
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<tr>
<td>Reverse autograft</td>
<td>0.360</td>
<td>0.029</td>
<td>0.488</td>
<td>0.053</td>
<td>0.363</td>
<td>0.015</td>
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*P < 0.05, statistical significance.*

**FIGURE 6.** A, Motor axon histomorphology at 6 weeks. Motor axons seem to be uniformly distributed in all segments in both groups. B, Sensory axon histomorphology at 6 weeks. Sensory axons within the conduit seem to grow adherent to the inner lining of the UBM conduit.
At 6 weeks, Wallerian degeneration is complete, yet axonal regeneration is still ongoing, providing the ability to more accurately compare recovery differences between both groups. Therefore, this time point strengthens the validity of improved sensory axons at least early in the nerve recovery process when utilizing the UBM conduit. Further studies with later time points would need to be performed to ascertain if this still remains true when axonal regeneration is considered complete.

In comparing gross appearance of 3- and 6-week conduits groups, the latter conduits revealed that the conduit had partially degraded over time. A conduit resorption rate that mirrors the speed of nerve regeneration would be ideal as this would provide stability of the conduit walls for nerve regeneration, while being degradable to provide rapid behavioral recovery after ablation of sciatic nerve segments. Processing, analyzing, and visualizing diffusion MR data. Diffusion tensor imaging tractography at 6 weeks demonstrated to be at least similar to nerve autografts for the repair of peripheral nerve injuries. The matrix perhaps serves as a scaffold to augment sensory nerve growth. In a clinical setting, these promising results may eliminate the donor site morbidity and increased operative time associated with nerve autografting.

ACKNOWLEDGMENTS
We would like to thank Nancy Cardwell, Justine S. Kim, and Ravinder Bamba for their help with this study. We would also like to acknowledge the Animal Care staff and Amy Nunally for their assistance in animal care.

REFERENCES


Effects of Collagenase Digestion and Stromal Vascular Fraction Supplementation on Volume Retention of Fat Grafts

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Objective: The use of autologous fat as a soft tissue filler has increased over the past decade in both reconstructive and aesthetic surgeries. Enhancement of autologous fat grafts with the addition of the stromal vascular fraction (SVF) has been reported to improve long-term volume retention. Stromal vascular fraction is most commonly isolated using enzymatic digestion, but it is unknown what effect the digestion process has on the adipocytes and SVF cells that comprise the graft. Some clinicians have reported use of enzymatically digested fat grafts to alter the physical properties of the tissue in specialized applications. We have previously reported that increasing collagenase digestion duration adversely affects the viability of adipocytes and SVF cells. Here, we aimed to determine if collagenase digestion of adipocytes before grafting is detrimental to long-term graft retention and if SVF supplementation can ameliorate these potential deleterious effects.

Methods and Results: We used a published xenograft model in which human lipoaspirate was implanted into the scalp of immunocompromised mice to study the effects of collagenase digestion on in vivo graft survival after 12 weeks. We used 4 experimental groups: grafts composed of collagenase-digested and nondigested adipocytes (50-minute digestion) and grafts with and without SVF supplementation. We used microcomputed tomography to serially and noninvasively quantify graft volume, in conjunction with hematoxylin-eosin staining of histological cross-sections of implanted excised grafts to assess overall tissue viability. We found that adipocytes that were collagenase-digested before implantation had significantly lower retention rates at 12 weeks and poorer tissue health, which was assessed by quantifying the number of intact adipocytes, the number of cystic formations, and by scoring the degree of inflammation and fibrosis. Further, we found that SVF supplementation of the digested grafts improved graft survival, but not to the level observed in undigested grafts.

Conclusions: We conclude that collagenase digestion adversely affects the long-term volume retention of fat grafts, but that graft retention is improved by SVF supplementation. These experimental results can serve as an initial framework to further elucidate the reported efficacy and safety of using collagenase-digested fat grafts and SVF in the clinical setting.

Key Words: fat grafting, collagenase, stromal vascular fraction, adipose-derived stem cells

(Ann Plast Surg 2017;78: S335–S342)

Fat grafting is a technique used to achieve soft tissue volume augmentation and contour improvement. There are nearly 50 000 fat grafting procedures performed per year in the United States, with another 400 000 performed globally.1 Autologous fat has the advantages of being plentiful and innately biocompatible without the risk of foreign body reaction or allergic reaction.2

Harvesting, preparation or injection.1 Although the use of autologous fat in the clinical realm is rising, challenges in optimizing long-term fat graft volume retention continue to drive research and innovation.

Although the mechanism(s) responsible for fat graft survival remain unclear, proper vascularization and subsequent sufficient oxygen/nutrient delivery appear to be critical to fat graft survival.18–21 Clinicians and scientists have aimed to improve the long-term retention rate of fat grafts, and these approaches have been the subject of many published studies. Central to many recent studies is the "enhancement" of fat grafts with the stromal vascular fraction (SVF), or cultured and serially passaged SVF, which is described in the field as adipose-derived stem cells (ASCs).22–24 The SVF, composed of adipose-resident stromal cells that are easily isolated from lipoaspirate, is thought to include progeny adipocytes, ASCs, endothelial progenitor cells, macrophages, and vascular cells.25–20 It is believed that the progenitor and stem cells within the SVF are responsible for the enhanced fat graft retention after implantation by providing a source for new adipocytes, vascular cells, and support cells in the grafted tissue.27–28 The SVF is most commonly isolated from the adipose tissue using an enzyme such as collagenase, or an enzymatic “cocktail” which contains various collagenases (i.e., Liberase Blendzyme).26–31 Other techniques used to isolate SVF include centrifugation, mechanical isolation via vigorous shaking, and decanting after density gradient separation.32–34 Herein, we focus on fat grafting techniques that use enzymatic digestion, specifically collagenase, to harvest SVF and enhance fat grafts before grafting.

Previous studies have reported the use of enzymatic digestion of lipoaspirate material as a means to separate the SVF from adipocytes before using both the SVF and adipocytes as part of the autologous graft. Typically, the enzymatically isolated SVF is added to adipocytes that have not been enzymatically digested (reserved portion of lipoaspirate), but reports have described the use of collagenase-digested adipocytes as part of the graft.22,25,35 In their practice using collagenase-digested adipocytes to surgically correct infraorbital dark circles, Youn et al37 cite that collagenase digestion of the adipose tissue improved the contouring ability of the fat graft by making it a "more liquid filler," and they reported safe and efficacious results. Although the use of SVF/adipocytes harvested from collagenase-digested lipoaspirate is not currently approved for use by the United States Food and Drug Administration (FDA), collagenase has gained acceptance in the treatment of Dupuytren contracture and Peyronie disease.38,39 Furthermore, with the increasing use of enhanced fat grafting, specifically in large volume reconstructions and in cases with patients who have...
minimal adiposity, it will be important to study the effect of collagenase digestion on the adipocytes. In such circumstances, it may be necessary to use all of the fat harvested from the patient, including that used to obtain SVF, to have adequate volume for grafting. Future studies conducted on collagenase-digested adipocytes and SVF may provide grounds for FDA approval of collagenase-isolated SVF and adipocytes in fat grafts.

In our previously published research we reported the in vitro effect of collagenase digestion on adipocytes and SVF for both human and murine adipose tissue. We found that increasing the duration of collagenase digestion is detrimental to both the SVF and the adipocytes, causing decreases in the viability of both interstitial cells (which comprise the SVF compartment) and adipocytes. Collagenase digestion affected both adipocyte and interstitial cell viability in a dose- and time-dependent manner. For human tissue, the viability of adipocytes and SVF was significantly decreased when collagenase digestion times exceeded 50 minutes. Although our in vitro studies were the first to indicate the potentially detrimental effects of collagenase digestion on SVF and adipocytes, it is imperative to consider the effect of collagenase digestion on in vivo graft survival. To our knowledge, no studies to date have examined the effect of collagenase digestion on in vivo graft survival.

In this study, we adopted a previously published xenograft model in which human fat grafts were implanted in the scalps of immunocompromised mice to study the effects of collagenase digestion on in vivo graft survival. We used microcomputed tomography (micro-CT) to noninvasively monitor the volume of implanted fat grafts over the course of 12 weeks. The micro-CT data was coupled with hematoxylin-eosin (H&E) staining to provide information about the overall tissue health and viability.

A better understanding of the impact of collagenase digestion on in vivo graft survival is of importance to clinicians and will help clarify the efficacy of using digested adipocytes/SVF during autologous fat grafting. This study builds on our in vitro findings and aims to determine the potential detrimental effects of collagenase digestion on in vivo graft retention.

METHODS

Human Adipose Tissue Harvest

All procedures were performed in accordance with the University of Virginia Institutional Review Board. At the time of elective liposuction, human adipose tissue was obtained from the abdomen, flank and thigh using the Coleman technique. Briefly, through a small incision, a mixed tumescent solution (0.5% lidocaine with 1:200,000 of epinephrine in Lactated Ringer solution) was infiltrated into the donor site using a blunt Lamis infiltrator (Byron Medical, Inc., Tucson, Ariz.). The solution was infiltrated at a ratio of 1 mL of solution per cubic centimeter of fat graft to be harvested. The fat grafts were harvested through the same incisions made previously. The harvesting cannula (3 mm diameter) was connected to a 10-mL Luer-Lok syringe. Gently pulling back on the plunger of a 10-mL syringe, with suction generated by no more than 1 to 2 mL of pull on the plunger, provided gentle negative pressure while the cannula was advanced and retracted through the harvest site. After filling the syringe with harvested tissue, the cannula was disconnected from the syringe. A Luer-Lok plug was twisted onto the syringe to seal the Luer-Lok aperture, the plunger was removed from the barrel of the syringe and the body of the filled syringe was placed into a centrifuge (Byron Medical) and spun at 3000 rpm for 3 minutes. After centrifugation, the oil layer (upper level) was decanted and the aqueous layer (lower level) was also drained out of the syringe. The middle layer, composed predominantly of adipose tissue was used for subsequent studies. The fat graft was stored in a sterile container with phosphate-buffered saline (PBS) and transported to the University of Virginia Plastic Surgery Laboratory.

Isolation of Adipocytes From Collagenase-Digested Human Adipose Tissue

The human adipose tissue was digested in a collagenase-containing digestion buffer as described in our previous studies. Briefly, human tissue was digested at a concentration of 1 g tissue/mL of collagenase-containing digestion buffer consisting of 0.1% (weight/volume) collagenase Type I (Worthington Biochemical Corporation, Lakewood, NJ), 2.5% (weight/volume) bovine serum albumin (Jackson ImmunoResearch, West Grove, Pa.), 20 mM HEPES (Life Technologies, Grand Island, NY), 200 mM adenosine (Sigma, St. Louis, Mo), 1.2 mM KH2PO4 (Sigma), 1.2 mM MgSO4·7H2O (Sigma), 120 mM NaCl (Sigma), 4.7 mM KCl (Sigma), 1.3 mM CaCl2·2H2O (Fisher Scientific, Pittsburgh, Pa). The human adipose tissue was incubated in a 37°C water bath under constant agitation for 50 minutes. After digestion was complete, the samples were washed with PBS 3 times for 5 minutes each wash to remove residual collagenase. After PBS washes, samples were centrifuged at 1100 RPM for 5 minutes and the adipocytes were isolated using a micropipette. These adipocytes were termed collagenase-digested adipocytes and were stored in sterile microcentrifuge tubes at room temperature until use. All procedures were performed in a biosafety cabinet.

Isolation of Adipocytes From Untreated Human Adipose Tissue

Adipocytes were also derived from undigested adipose tissue in the same way as above, but the samples were incubated in collagenase-free buffer for 50 minutes. After incubation in the collagenase-free buffer, samples were washed 3 times with PBS as stated above and were centrifuged at 1100 RPM for 5 minutes. The untreated adipocytes were isolated using a micropipette and were stored in sterile microcentrifuge tubes at room temperature until use. All procedures were performed in a biosafety cabinet.

SVF Isolation

After the collagenase-digested adipocytes were removed via micropipette as stated above, the remaining portion of the sample was used to isolate the SVF for subsequent studies. After centrifugation, the sample stratifies into 3 layers based on densities—the top layer consisted of adipocytes (used as stated above), the middle layer is the tumescent fluid and washing fluid, and the bottom layer contains the SVF and blood cells. The adipocytes (top layer) were removed for use and the middle layer was aspirated leaving the bottom pellet containing the SVF. One milliliter of DMEM/F12 media (ThermoFisher Scientific, Waltham, Mass) was added to the pellet and gently mixed by pipetting. The solution was centrifuged at 1100 RPM for 5 minutes and 500 μL was removed from the sample. 1 mL of erythrocyte lysis buffer (eBioscience, San Diego, Calif) was added and the solution was gently vortexed to resuspend the pellet. The sample was incubated for 5 minutes at room temperature, which was followed by the addition of 1.5 mL of DMEM/F12. This solution was sterile filtered through a 40-μm centrifuge tube mesh and centrifuged at 1100 RPM for 5 minutes. After centrifugation, the supernatant was removed, and the pellet was resuspended in 1 mL of DMEM/F12. The cells were counted using a hemocytometer and were resuspended in sterile PBS into a known volume for the concentration desired for the subsequent studies.

Preparation of Adipose Grafts

Four separate groups were used for these studies: (1) undigested adipocytes without SVF supplementation, (2) undigested adipocytes with SVF supplementation, (3) digested adipocytes without SVF supplementation, and (4) digested adipocytes with SVF supplementation (Fig. 1A). All implanted adipose tissue grafts were 250 μL, and those grafts with SVF supplementation contained 12,500 SVF cells/250 μL.
Grafts were prepared based on the groups above and were loaded asphyxiation. The skin above the scalp was shaved and depilated. After depilation, the scalp was sterilized with 70% ethanol and 2% isoflurane and the hair on the top of head and around the ears was removed. SCID mice (Charles River, Washington, Mass) were anesthetized with 2% isoflurane and the hair on the top of head and around the ears was removed. Mice were anesthetized with 2% isoflurane and the hair on the top of head and around the ears was removed. Mice were anesthetized with 2% isoflurane and the hair on the top of head and around the ears was removed. Mice were anesthetized with 2% isoflurane and the hair on the top of head and around the ears was removed.

Animals. Mice were housed in an AAALAC-accredited facility. All procedures were performed under anesthesia, and all efforts were made to minimize pain or suffering.

Implantation of Adipose Grafts

Mouse experiments were performed under a protocol approved by the University of Virginia Institutional Animal Care and Use Committee (Animal Welfare Assurance A3245-01) in accordance with the National Institutes of Health’s Guide for the Care and Use of Laboratory Animals. Mice were housed in an AAALAC-accredited facility. All procedures were performed under anesthesia, and all efforts were made to minimize pain or suffering.

A xenograft adipose tissue graft model was modified in which adipose grafts were implanted in the scalp of recipient mice. NOD-SCID mice (Charles River, Washington, Mass) were anesthetized with 2% isoflurane and the hair on the top of head and around the ears was shaved and depilated. After depilation, the scalp was sterilized with 3% ethanol and povidone-iodine wipes. A small access incision as made at the base of the skull and a subcutaneous tunnel was created for implantation of the fat graft. 250 μL of isolated fat was injected with a 1-mL syringe through a 16-gauge Teflon cannula in a linear retrograde fashion. The incision was closed with 5-0 nylon sutures and the animal was recovered, monitored postoperatively, and returned to the animal vivarium.

Microcomputed Tomographic Imaging

A Scanco vivaCT 40 micro-CT instrument (Scanco Medical, Brütisellen, Switzerland) was used to scan recipient mice at various time points after implantation of human adipose tissue grafts as depicted in Figure 1B. Micro-CT scanning allowed for noninvasive quantification of the graft volume and provided topographical information of the adipose graft. Mice were anesthetized with 2% isoflurane before and during the entirety of the scanning procedure. Settings used on the micro-CT instrument were as follows: tube voltage, 55 kV; tube current, 145 pA; power, 8 W; integration 1 week postimplantation, 2 weeks postimplantation, 4 weeks postimplantation, 8 weeks postimplantation, and 12 weeks postimplantation (Fig. 1B).

Volumetric Analysis of Micro-CT Scans

Fiji, an image processing package based on ImageJ (National Institutes of Health, Bethesda, Md), was used to process the DICOM files generated from the micro-CT scans. “Segmentation Editor,” a plug-in within Fiji, was used to analyze the DICOM files and to quantify the graft volume. The DICOM files were imported into Fiji as an “Image Sequence” and converted to 8-bit grayscale (Fig. 2A). The imported stack of images was loaded into “Segmentation Editor” and the freehand tracing tool was used to outline the adipose graft on each fifth slice until the adipose graft was no longer visualized (Fig. 2B). The adipose graft was distinct from the surrounding skin based on the color and contrast of the image. After tracing every fifth slice, interpolation was performed to create selections/traces for slices between the previously traced slices. A 3D projection of these slices was constructed, and the volume of the adipose tissue graft was calculated after setting the voxel size for scaling purposes (Figs. 2C, D).

H&E Staining and Scoring

After fixation, adipose grafts were processed for paraffin embedding, and 5 μm samples were cut and stained with H&E. Individual 100X images were acquired using an EVOS XL microscope (ThermoFisher Scientific) and montages were made of the entirety of the adipose graft for analysis. An established and widely applied scoring system was used to assess histologic parameters as follows: presence of intact and nucleated fat cells; presence of cysts and vacuoles; inflammation, as evidenced by infiltration of lymphocytes and macrophages; and the presence of fibrosis and other components of connective tissue. Each of these parameters were graded on a scale of 0 to 5 by evaluation of the presence of the histologic parameters as follows: 0 = absence, 1 = minimal presence, 2 = minimal to moderate presence, 3 = moderate presence, 4 = moderate to extensive presence, 5 = extensive presence. Montaged images were scored by 3 blinded, trained observers. Representative examples of fibrosis, cysts/vacuoles, and inflammation are depicted in Figure 3A-C as well as average scores in Figure 3D.

RESULTS

Collagenase Digestion of Adipocytes Before Implantation Decreases Volume Retention, But SVF Supplementation Aids in Volume Retention of Collagenase-Digested Grafts

To determine the effect of collagenase digestion on the volume retention of the fat grafts, we used micro-CT to calculate graft volumes postimplantation. Calculation of adipose graft volumes from 3D projections revealed that collagenase digestion of adipocytes before grafting significantly reduced volume retention post-implantation. The graft volume of the collagenase treated group with SVF supplementation (group 4, 83.90 mm$^3$) was roughly one third of the initial grafted volume (250 mm$^3$) 1 week after implantation (Fig. 2D). The group that was collagenase digested without SVF supplementation (group 3) was
nearly undetectable via micro-CT scanning after 1 week, with an average volume of only 0.87 mm$^3$. The groups containing adipocytes that were not collagenase digested before implantation (group 1 and 2) had much higher volumes immediately postimplantation (Fig. 2D). The group with undigested adipocytes without SVF supplementation (group 1) had an average volume of 192.06 mm$^3$, whereas the group with undigested adipocytes with SVF supplementation (group 2) had an average volume of 163.21 mm$^3$ (Fig. 2D).

This decrease in graft volume for digested adipocytes was observed for all time points postimplantation up to 12 weeks. At the terminal time point of 12 weeks, the collagenase-digested group without SVF (group 3) was undetectable and the collagenase-digested group with SVF supplementation (group 4) had an average volume of 4.98 mm$^3$. The undigested group without SVF had an average volume of 109.69 mm$^3$, whereas the undigested group with SVF had an average volume of 86.01 mm$^3$ (Fig. 2D).

These masses were also consistent with the trends of the graft volumes at 12 weeks and the 40% to 50% volume retention rate observed for all time points postimplantation. The unsupplemented grafts that were collagenase digested before implantation (group 3) were undetectable at 12 weeks and not harvested (Fig. 3E). Consistent with the graft volumes determined using micro-CT scanning, the collagenase digested grafts with SVF supplementation (group 4) had an average mass of 0.017 g (Fig. 3E). Taken together, these data corroborate that this level of collagenase digestion is detrimental to graft survival and that SVF supplementation of digested grafts aids in volume retention.

Terminal Adipose Graft Masses Are Consistent With Graft Volumes

After 12 weeks, the adipose grafts were harvested and weighed to calculate the terminal graft volume. The masses of the undigested groups without SVF and with SVF were 0.116 and 0.104 g, respectively (Fig. 3E). The initial graft was assumed to be 0.225 g (0.9 g/mL density of adipose tissue), this equated to roughly 40% volume retention rate after 1 week, which is consistent with the literature. These masses were also consistent with the trends of the graft volumes at 12 weeks and the 40% to 50% volume retention rate (above). The unsupplemented grafts that were collagenase digested before implantation (group 3) were undetectable at 12 weeks and not harvested (Fig. 3E). Consistent with the graft volumes determined using micro-CT scanning, the collagenase digested grafts with SVF supplementation (group 4) had an average mass of 0.017 g (Fig. 3E). Taken together, these data corroborate that this level of collagenase digestion is detrimental to graft survival and that SVF supplementation of digested grafts aids in volume retention.
Collagenase Digestion Decreases Overall Tissue Health as Evidenced by H&E Scoring Metrics

After harvest, we scored the overall health of the fat grafts by using H&E staining and previously published protocols. The collagenase-digested grafts (group 3 and 4) had, on average, higher scores for inflammation, cysts/vacuole presence, and fibrosis when compared with grafts that had not been collagenase digested before implantation (group 1 and 2) (Fig. 3D). Because there were no grafts remaining at week 12 for group 3 (collagenase digested, no SVF supplementation), H&E scoring was not performed on this group. There was a significant increase in the amount of inflammation present, the number of cysts/vacuoles observed, and the amount of fibrosis in collagenase-digested when compared to undigested grafts (Fig. 3D). There was also a striking difference in the membrane integrity of the groups. The undigested grafts (group 1 and 2) had much more uniform, intact adipocytes than the collagenase-digested group (Fig. 3D). There were no statistically significant differences between group 1 and 2 for any metric, suggesting that SVF supplementation did not have an impact on the overall tissue health. These are in agreement with volume retention outcomes and suggest that collagenase digestion is detrimental to graft retention and overall tissue health.

DISCUSSION

The use of autologous fat grafting to address soft tissue defects has gained widespread acceptance in plastic surgery over the past decade. Autologous fat is biocompatible, easy to harvest, and allows clinicians to avoid the use of synthetic or foreign implant materials. Long-term resorption rates of autologous fat grafts range from 25% to 80% and are unpredictable, which has prompted clinicians and scientists to develop strategies to combat this adverse resorption process. Clinicians have started to "enhance" fat grafts by supplementing with the SVF that is most commonly isolated from lipoaspirate using enzymatic digestion (ie, collagenase digestion). Although other techniques can be used to isolate the SVF (mechanical, centrifugation, and so on), our current studies focused on fat grafting techniques that utilize enzymatic
digestion, specifically collagenase, before fat grafting. Many fat grafting studies have reported the use of enzymatic digestion to isolate the SVF and subsequent supplementation of the adipocyte portion with enzymatically isolated SVF.\textsuperscript{22,35,37} Additionally, other groups have used the collagenase-digested adipocyte portion as part of the graft without having a thorough understanding of the effect of digestion on the viability of adipocytes.\textsuperscript{38} In our previous study, we found that increasing the duration of collagenase digestion decreased the viability of adipocytes and the interstitial cells within the adipose tissue.\textsuperscript{40} In the present study, we examined the effect of collagenase digestion on adipocytes and the impact of digestion on in vivo graft survival. We modified a published xenograft model and implanted human lipoaspirate as a fat graft and then serially evaluated volume retention and tissue health over a 12-week time course.\textsuperscript{41} We found that collagenase digestion before grafting significantly decreased the long-term volume retention of the implanted adipose tissue, as evidenced by noninvasive micro-CT, and decreased the overall tissue health, as determined by H&E staining. Further, we found that SVF supplementation of collagenase-digested grafts slightly improved the volume retention, but not to the level observed using undigested grafts.

Collagenase digestion of the adipocytes before implantation not only adversely affected the long-term volume retention and overall tissue health, but micro-CT scans and volume calculations revealed rapid resorption of collagenase-digested adipose at the earliest time point (1 week). The collagenase-digested grafts were nearly undetectable, and the collagenase digested grafts with SVF supplementation retained only 40% of their initial volume. The H&E evaluation revealed an overall decrease in tissue health for collagenase-digested grafts, with the adipocytes having lower membrane integrity scores (more fragmented adipocytes), higher levels of inflammation/fibrosis, and a more significant presence of cysts and vacuoles when compared to adipocytes that were not collagenase digested. The mass of the collagenase-digested grafts was also significantly lower at the terminal time point. Taken together, these findings suggest that this level of collagenase-digestion before grafting is detrimental to the long-term volume retention of fat grafts.

Currently, it is unclear why the collagenase digestion of adipocytes before implantation/grafting decreases the volume retention, but previous studies may provide some insight. In our previous in vitro studies, for example, we observed that increasing durations of exposure to collagenase had an increasingly adverse effect on human adipocytes and interstitial cell viability.\textsuperscript{40} Our previous in vitro experiments suggest that in the present study, the collagenase-digested grafts had reduced viability at the onset of grafting. In another study conducted by Ruan et al,\textsuperscript{54} isolation of primary adipocytes from murine epididymal fat pads via collagenase digestion increased several genes that encoded several proinflammatory mediators. Specifically, Ruan et al reported a significant increase in TNF-α expression by primary adipocytes that were isolated using collagenase digestion. Based on these findings, we speculate that collagenase digestion of the adipocytes before grafting induces an inflammatory environment within the graft via TNF-α secretion that leads to increased resorption of the graft. In support of this theory, Thompson et al\textsuperscript{35} showed that IL-6 levels are also altered in adipocytes during collagenase digestion and that varying collagenase concentrations/rotational speeds during digestion modulates the IL-6 expression. IL-6 and TNF-α have been linked to obesity-related inflammation and are generally considered pro-inflammatory cytokines.\textsuperscript{16,55} Therefore, future studies investigating the effects of collagenase on adipose tissue retention should examine levels of these two pro-inflammatory cytokines as a function of digestion time as well as in the tissue after graft implantation.\textsuperscript{58}

Both preclinical and clinical studies have reported significant improvements in fat graft volume retention by “enhancing” or supplementing the fat grafts with SVF before implantation. We observed an improvement in volume retention for SVF-treated grafts that were collagenase-digested before implantation. Indeed, supplementation of collagenase-digested grafts with SVF before implantation delayed the resorption and increased the volume of the graft at each time point. Our findings are consistent with many other groups that have reported increased volume retention and delayed resorption after the supplementation of grafts with SVF.\textsuperscript{24,33} It is also possible that the collagenase digestion “striped” the adipose tissue graft of the interstitial cells, and supplementing the adipose graft with SVF cells “repopulated” the interstitial cell compartment, which appears to be necessary for graft survival. We have previously reported that increasing collagenase digestion decreases the number of interstitial cells within adipose tissue.\textsuperscript{39} This “striping” of the interstitial cell compartment may also provide further explanation as to why collagenase digestion negatively impacts graft retention.

Interestingly, SVF supplementation of grafts that were not collagenase digested had no effect on the overall volume retention for the experimental time points. This finding differs from what has been reported in the literature, which is that SVF supplementation improves volume retention.\textsuperscript{59} The cell dosage that we used (12,500 SVF cells for each 250 μL fat graft) was based on a similar study conducted by Paik et al.\textsuperscript{60,61} where the concentration of SVF cells within adipose tissue was titrated to achieve an optimal effect.\textsuperscript{24} They reported that concentrations of SVF cells above a certain threshold (10 million cells/mL) decreased tissue health and caused greater lipodegeneration in a similar xenograft model. Paik et al. further reported that 50,000 SVF cells/mL adipose tissue was an ideal concentration, and hence this was the SVF concentration used in our study. However, this concentration is much lower than concentrations demonstrated in other studies to significantly increase volume retention. For example, Gentile et al. supplementation of clinical fat grafts with 250,000 SVF cells/mL and reported less volume loss over 18 months.\textsuperscript{59} Studies which supplement grafts with ex vivo expanded ASCs have also used much higher concentrations of cells per volume of adipose tissue, with concentrations as high as $20 \times 10^6$ ASCs/mL fat.\textsuperscript{2} Because we did not conduct a dose-response study, we cannot draw conclusions about whether higher (or lower) doses of SVF might yield an improvement in fat graft volume retention in this murine model.

There are several other caveats to our study. First, we examined the effect of collagenase digestion on in vivo graft retention by using a single digestion duration (50 minutes). This digestion duration was based on our previous study in which we found that 50 minutes was the threshold beyond which adipocytes and interstitial cells demonstrated decreased viability.\textsuperscript{46} In future work, it will be important to evaluate both shorter and longer collagenase digestion times to more fully elucidate the effects of collagenase digestion on in vivo graft survival. Indeed, it is possible that shorter collagenase digestion times (eg, less than 50 minutes) may be beneficial to graft survival without jeopardizing the viability of the adipocytes within the graft. Short digestion durations may, in fact, benefit graft survival by increasing the surface area-to-volume ratio (eg, smaller parcels of fat), which could promote more rapid revascularization. Another important consideration in our work is the fact that all studies were conducted in immunocompromised mice (NOD-SCID mice), which lack a complete immune system. Although the xenograft model allows for the grafting of human adipose tissue into a mouse without rejection, the lack of a complete immune system omits a significant factor in the grafting and inflammatory process. Specifically, these mice have defective T and B cell development and have deficient natural killer cell function, and it is possible that these cell types play a significant role in the resorption process.\textsuperscript{60,61} Despite these caveats, this study constitutes an important follow-on to our previous in vitro experiments, and builds on those results by highlighting what could be a clinically important drawback of collagenase digestion that is only partially combatted by supplementation with SVF.
CONCLUSIONS

This study extends our previous in vitro finding, that collagenase digestion is detrimental to adipocyte and interstitial cell viability, to a clinically relevant in vivo model. The current study suggests that collagenase digestion of adipose grafts before implantation adversely affects the long-term in vivo retention over the course of 12 weeks. Further, we show that supplementing collagenase-digested fat grafts with SVF enhances volume retention and delays the resorption process. Our initial preclinical findings begin to help to clarify the safety and efficacy of using enzymatically digested adipocytes and SVF during autologous fat grafting. Further, this study helps to define the risks and benefits that different adipose treatments pose and may guide protocols for processing and preparing fat grafts in the clinical setting.

REFERENCES

12. Erdim M, Tezel E, Numanoglu A, et al. The effects of the size of liposuction fat grafting. Further, this study helps to define the risks and benefits that different adipose treatments pose and may guide protocols for processing and preparing fat grafts in the clinical setting.

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A Formula for Planning and Predicting Postoperative Mammoplasty Results

Mary G. Smithson, BS, * Sherry S. Collawn, MD, PhD, † Mina S. Mousa, MD, ‡ and Carly M. Bramel, PA-C §

Purpose: For women with macromastia, reduction mammoplasty is a safe and effective solution to increasing quality of life through alleviating pain and improving aesthetics. This study developed a way to combine a surgeon’s view of breast measurement (volume) with a patient’s view of breast measurement (distance between nipple and notch, inframammary fold, or midline) to provide patients with a better understanding of expected surgical outcomes after breast reduction with a medial superior pedicle.

Patient and Methods: An institutional review board approved retrospective chart review was performed on all medial superior pedicle reduction mammoplasties performed by a single surgeon at a university medical center from 2008 to 2016, and a total of 133 patients were identified. Measurements of interest for this study were nipple to sternal notch (N-S), nipple to inframammary fold (N-I), nipple to midline (N-M), and breast diameter (BD). The average bilateral change per measurement was calculated for each patient in centimeters. Change was averaged for left and right breasts for N-S, N-I, N-M, and BD per patient. Grams removed for left and right breasts were also averaged. Each measurement of average change was divided by the gram average and multiplied by 100 to obtain centimeter change per 100 grams. Individual patient measurements per type of measurement were averaged to achieve a final improvement reported in centimeters per 100 g tissue removed per breast.

Results: The average change in the N-S distance was calculated to be a decrease of 1.5 ± 0.8 cm/100 g of breast tissue removed. The average change in N-I was calculated to be an overall decrease of 0.7 ± 0.5 cm/100 g. The average change in N-M was calculated to be a decrease of 0.1 ± 0.3 cm/100 g. Finally, the average change in BD was calculated to be 0.0 ± 0.4 cm/100 g.

Conclusions: A surgeon’s expression of breast measurements in terms of volume can be difficult for a patient to understand and visualize. This study determined the impact volume has on length of typical breast measurements to increase patients’ understanding of expected outcomes. In summary, patients can be told to expect to see a nipple elevation of 1.5 cm per 100 grams of breast tissue removed using this medial superior pedicle technique.

Key Words: macromastia, medial superior pedicle reduction, surgical outcomes, volume and breast measurements, nipple to sternal notch (N-S), nipple to inframammary fold (NI), nipple to midline (N-M), and breast diameter (BD), nipple sensation, nipple elevation

For women with macromastia, reduction mammoplasty is a safe and effective solution to increasing quality of life through alleviating pain and improving aesthetics.4 Breast reductions have been shown to improve cervical and lumbar lordosis, thoracic kyphosis, and lumbar scoliosis as well as decreasing patient neck, back, and lumbar pain and reverting skeletal disturbances.2,3 Mammoplasty techniques were first described by Lötsch and Dartigues in 1923 and 1924, respectively, and were later reintroduced in 1970 by Lassus, using a vertical approach.4,5 The vertical approach led to a cascade of new techniques including Marchac and de Olarte’s inverted T-incision in 1982, Lejour’s introduction of liposuction in the 1990s, Hammond’s SPAR* technique in 1998, the Hall-Findlay technique in 1999, and the SPEAR** technique, which combines Hammond’s skin incision with Hall-Findlay’s utilization of the superomedial dermoglandular pedicle, in 2003.5 Whereas the inverted T-incision or Wise pattern closure with the inferior pedicle has been preferred for large breast reductions,6 the SPEAR technique has commonly been used for mild to moderate reductions,7 but the superomedial pedicle vertical scar breast reduction can also be used for larger reductions.8 After our review of the literature, quantitative measurements of change per volume have yet to be identified when using a technique similar to the Spear technique, and we will now present our measurements.

Quantitative measurements are important not only for the surgeon but also for the patient. Volume removed is the norm for quantifying and discussing reductions among surgeons and is how expectations are communicated to patients.8–11 However, follow-up and outcomes are typically measured using patient satisfaction surveys.12 Although surgeons feel comfortable with this, many patients cannot envision results before surgery based on volume alone and are forced to rely on past patient subjective satisfaction surveys. This is important because,
although many patients are happy with their results, there is a subset that would like either smaller or larger breasts. One way to alleviate this unhappiness with the results experienced by some patients is to provide a better way for patients to understand and envision their outcomes. This study developed a way to combine a surgeon’s view of breast measurement (volume) with a patient’s view of breast measurement (distance between nipple and notch, fold, or midline) to provide patients with a better understanding of expected outcomes.

PATIENTS AND METHODS

An institutional review board-approved retrospective chart review was performed on all mammoplasties performed by a single surgeon at a university medical center from 2008 to 2016. A total of 133 patients undergoing reduction mammoplasty using a medial superior pedicle technique with suture suspension of the medial superior pedicle to the pectoralis fascia (Fig. 1) were identified. The median weight of tissue excised per breast was between 400 and 500 g, with a range of 200 to 1000 g per breast. Skin closure was done using vertical approach in 40% of patients, inverted-T in 40%, and short-L in 20%.

Measurements of interest for this study were nipple to sternal notch (N-S), nipple to inframammary fold (N-I), nipple to midline (N-M), and breast diameter (BD) (Fig. 2). Only 31 of the 133 patient charts included both preoperative and postoperative measurements for at least one of the measurements of interest. All 31 patients had preoperative and 4-week postoperative measurements of N-S, 25 of 31 had preoperative and postoperative measurements of N-I, 16 of 31 had preoperative and postoperative measurements of N-M, and 14 of 31 had preoperative and postoperative measurement of BD. Patients were also asked about bilateral nipple sensation pre-op and post-op with 27 of the 133 reporting either an increase, decrease, or the same nipple sensation as before surgery. Figure 3 demonstrates a patient undergoing breast reduction with this technique.

The average bilateral change per measurement was calculated for each patient in centimeters. Change was averaged for left and right breasts for N-S, N-I, N-M, and BD per patient. Figure 4 shows the changes in N-S measurements. Grams removed for left and right breast were also averaged. Each measurement of average change was divided by the gram average and multiplied by 100 to obtain centimeter change per 100 g. Individual patient measurements per type of measurement were averaged to achieve a final improvement reported in centimeters per 100 g of tissue removed per breast.

RESULTS

For the 31 patients with preoperative and postoperative measurements of N-S, the average change in N-S per patient ranged from an increase of 0.3 cm/100 g to a decrease of 4.1 cm/100 g. Individual patient averages were combined and averaged to obtain an overall decrease of 1.5 ± 0.8 cm/100 g. Twenty-five patients had preoperative and postoperative measurements of N-I. The average change in N-I per patient ranged from no change (0.0 cm/100 g) to a decrease of 1.5 cm/100 g. Patient averages were averaged to obtain an overall decrease of 0.7 ± 0.5 cm/100 g. Sixteen patients had preoperative and postoperative measurements of N-M. The average change in N-M per patient ranged from an increase of 0.4 cm/100 g to a decrease of 0.6 cm/100 g. Patient averages were averaged to obtain an overall decrease of 0.1 ± 0.3 cm/100 g. Fourteen patients had preoperative and postoperative measurements of BD. The average change in N-M per patient ranged from an
which may have already resolved in other patients. A way to mitigate patients may have had falsely low numbers because of residual swelling, surgery and length of postoperative edema in an individual. Some patients were recorded. This does not account for individual responses to measurements. Another limitation is the fact that only 4-week measurements were accurate. Another idea would be to compare other reduction mammoplasty techniques to the SPEAR technique to see if other techniques have different average changes or any difference in N-M and BD.

**Future Studies**

One idea for future studies would be attempting to determine if actually knowing the measurements beforehand has a positive effect on patient satisfaction and if predication is correct. Patients undergoing this technique could be split into 2 groups: one given the average measures beforehand and the other just receiving traditional volume lingo. Patients would take a survey asking about overall satisfaction and if measurements were accurate. Another idea would be to compare other reduction mammoplasty techniques to the SPEAR technique to see if other techniques have different average changes or any difference in N-M and BD.

**CONCLUSIONS**

A surgeon’s expression of breast measurements in terms of volume can be difficult for a patient to understand and visualize. In this study, we established the impact volume has on length of typical breast measurements to increase patients’ understanding of expected outcomes.

**ACKNOWLEDGMENTS**

The artist’s drawing in Figure 1 was by Matthew K. Collawn. Permission was obtained to use his artwork in this paper.

**REFERENCES**


Background: Reduction mammaplasty is one of the most commonly performed plastic surgery operations. For a majority of techniques, the most common long-term complication is pseudoptosis. It has previously been proposed that upper breast suspensory ligaments (SL) are weaker than lower breast SL. We tested this hypothesis through anthropometry of the proxies for upper and lower SL strength: the sternal notch-nipple (SN-N) distance and the nipple-inframammary fold (N-IMF) distance, respectively.

Methods: An institutional review board–approved retrospective review of patients undergoing reduction mammaplasty in an academic faculty practice between 2008 and 2015 was conducted. Patient demographics included age, race, and body mass index (BMI); patient comorbidities included smoking status, diabetes, and hypertension. Breast anthropometric measurements included SN-N and N-IMF. Sternal notch-nipple was used as the primary metric of the upper SL strength, whereas N-IMF was used as the primary metric of the lower SL strength. Intraoperative details included reduction technique and resection mass. Postoperative complications were recorded, including nipple areola complex necrosis and hematoma. Linear regression analysis was performed with the primary endpoint of the relationship between SN-N and N-IMF distance in macromastia.

Results: Data from 208 patients, totaling 400 individual breast measurements, were collected. The mean SN-N length was 35.1 cm, mean N-IMF length was 16.0 cm, and mean resection weight was 1094 g. Linear regression found that N-IMF distance could be predicted as 45% of the SN-N distance (N-IMF = 0.454 * SN-N). This was a strong relationship, demonstrated by univariate analysis of SN-N and N-IMF (R, 0.624; P < 0.001). A Wise pattern was used in 89.9% of cases; an inferior pedicle was used in 83.7% of cases. Nipple areola complex necrosis occurred in 15 breasts (3.75%). Sternal notch-nipple (R, 0.127; P = 0.011) and N-IMF (R, 0.119; P = 0.017) were both predictive of nipple areola complex necrosis (Table 4).

Conclusions: In our series, the N-IMF distance increased 0.45 cm for every 1 cm increase in the SN-N distance. This relationship strengthens our primary hypothesis that the lower pole ligaments stretch at a significantly slower rate than the upper pole ligaments. Taking this into consideration, we suggest that surgeons seeking to minimize pseudoptosis rates should favor techniques that minimally disrupt the lower SL.

Key Words: macromastia, mammaplasty, reduction mammaplasty, suspensory ligaments, Cooper ligaments, breast ligaments, breast anthropometry, sternal notch-nipple, SN-N, nipple-inframammary fold, N-IMF, breast ptosis, pseudoptosis, bottoming out

(Part Plast Surg 2017; 78: S347–S350)
account for asymmetry and because outcomes in bilateral breasts were not necessarily the same.

RESULTS

During the study period, a total of 422 patients undergoing reduction mammaplasty were identified. The procedures were performed at 5 institutions by 7 academic plastic surgeons. After manually filtering the data to exclude 111 duplicate procedures and 103 patients with incomplete, incorrect, or absent measurements, a total of 208 patients (400 individual breasts) who received reduction mammaplasty ultimately met the selection criteria (Fig. 2).

The mean age at time of resection was 38 years; mean BMI was 34.1 (Table 1A). A total of 163 patients (78.4%) self-identified as African-American, 41 patients (19.7%) as Caucasian, and 2 patients each (0.96%) as Hispanic and Middle Eastern (Table 1B). In regards to medical comorbidities, 20 patients (9.6%) had a diagnosis of diabetes mellitus, 48 patients (23.1%) had a diagnosis of hypertension, and 27 patients (13.0%) identified as everyday smokers at the time of preoperative assessment.

Mean SN-N length was 35.1 cm, mean N-IMF length was 16.0 cm, and mean resection mass was 1094 g (Table 1A). Sternal notch-nipple distances and N-IMF distances were then linearly regressed, and a predictive formula was derived: the N-IMF distance increases 0.45 cm for every 1 cm increase in SN-N distance (N-IMF = 0.454 * SN-N, Fig. 3).

In all patients, only one reduction technique was performed per patient. One hundred seventy-four reductions used an inferior pedicle, and 34 reductions used a superomedial pedicle. Of the 174 inferior pedicle reductions, 161 (92.5%) of these implemented a Wise pattern incision and 13 (7.5%) used a Boston modification of Robertson technique pattern. In an independent t test, the mean SN-N length was 35.7 cm in breasts undergoing inferior pedicle reductions and 32.7 cm in superomedial pedicle reductions (P < 0.001, Table 2). Of the 33 superomedial pedicle

![FIGURE 1. Visualization of true ptosis (first, second, and third degree) compared to pseudoptosis.](image1)

![FIGURE 2. Patient exclusion criteria.](image2)

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<th>Variable</th>
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reductions, 25 (75.8%) used a Wise pattern incision and 8 (24.2%) used a vertical pattern incision.

In a univariate analysis, the N-IMF distance demonstrated no significant correlation with age, BMI, diabetes mellitus, hypertension, or smoking status. However, as one might assume, there is a positive correlation between N-IMF and SN-N distance and also between N-IMF distance and resection mass (Table 3).

Nipple areola complex necrosis occurred in 15 individual breasts (3.75%). Two patients experienced bilateral NAC necrosis. Postoperative hematoma occurred in 5 total breasts. In a univariate analysis (Table 4), a significant association was observed between NAC necrosis and resection mass ($P = 0.001$), N-IMF distance ($P = 0.017$), and SN-N distance ($P = 0.011$). There was no significant difference in N-IMF distance, resection mass, and rates of NAC necrosis between the 2 pedicles. However, with only 33 reductions based on a superomedial pedicle, this study is not sufficiently powered to make a definitive conclusion.

**DISCUSSION**

A primary objective of reduction mammoplasty is a long-lasting, aesthetically pleasing breast shape. Unfortunately, breast shape in the immediate postoperative period still varies unpredictably from the final breast shape. Pseudoptosis, or “bottoming out,” remains a too-common long-term complication of all reduction mammoplasty techniques. In the most commonly performed reduction technique, the Wise pattern with an inferior pedicle, pseudoptosis occurs in 50% of patients. In the technique with the lowest rates, the vertical pattern with a superomedial pedicle, pseudoptosis still occurs in 20% of patients. A critical barrier to further reducing the pseudoptosis rate is the absence of a known pathogenic mechanism. This is reflected in the diversity of methods that have been proposed to combat pseudoptosis, including placing the NAC below the traditional location of Pitanguy point, the use of acellular dermal matrix as an internal brassiere, muscle flaps, and fascial suspension. None have proven to be efficacious in preventing pseudoptosis.

In this study, we show a differential rate of stretch in macro-mastia: for every 1 cm increase in upper SL length (SN-N distance), the lower SL length (N-IMF distance) increases by 0.45 cm. This quantitative relationship is very similar to that reported by Jackson et al in a smaller cohort of patients. We hypothesize that this relationship is owing to weaker SL in the upper breast versus the lower breast. Chalekson et al argued that the decreased rate of pseudoptosis in the modified Robertson technique is owing to preservation of N-IMF parenchyma and the lower SL. Furthermore, an anatomic basis for this differential may exist: Würinger described a horizontal ligamentous septum of dense connective tissue that originates at the level of the fifth rib and divides the breast at the level of the nipple into cranial and caudal segments. This division may signify a transition point in SL strength.

On this basis, we propose that techniques such as the BMRT should be preferred by surgeons seeking to avoid pseudoptosis. The BMRT combines a broad-based inferior pedicle encompassing the entire inframammary fold with a superior apron flap to conceal the transverse scar along the inferior portion of the breast. Resection occurs in a bell-shaped pattern superior, medial, and lateral to the NAC. One criterion for selection of this technique is NAC transposition of higher than 5 cm, indicating that this technique is appropriate for moderate-large reductions. Movassaghi et al reports that the BMRT demonstrates decreased postoperative hematoma formation when compared to the Wise pattern reduction (0% vs 10%, $P = 0.016$) and also subjectively reports minimal to no postreduction pseudoptosis, although further scrutiny is necessary. Both Movassaghi et al and Chalekson hypothesize that the undisturbed dermis and breast tissue in the N-IMF region are the primary factor for prevention of pseudoptosis. Other advantages of the BMRT include decreased operative time and elimination of the “triple point,” the most common site of postoperative dehiscence.

Our study has several limitations. First, as an anthropometric pilot study, our data did not include pseudoptosis and other complications. The rates of these complications should be studied as a multicentered, randomized, controlled prospective trial. Second, our study was unable to biomechanically and histologically examine the

![FIGURE 3. Linear regression of SN-N and N-IMF distance shows a positive correlation.](image)

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<td>Age</td>
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<td>Diabetes</td>
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<td>Hypertension</td>
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NS, not significant.
upper and lower SL of the breast. This should be performed as either a cadaver study or a study of discarded specimens from prophylactic mastectomies. Lastly, our patient population differed demographically from the average United States population, thus, limiting the generalizability of our results. Our patients were more obese (mean BMI, 34.1), predominantly African American, and had more severe macromastia (mean resection mass, 1094 g per breast) than most studies of macromastia.22–26

**CONCLUSIONS**

In conclusion, this study demonstrates that N-IMF distance increases 0.45 cm for every 1 cm increase in SN-N distance. This relationship strengthens our primary hypothesis that the lower pole SL stretch at a significantly slower rate than the upper pole SL. Taking this into consideration, we suggest that surgeons seeking to minimize pseudoptosis rates should favor techniques that minimally disrupt the lower SL.

**REFERENCES**