

Application of Umbilical Cord Tissue Allografts in Reduction Mammoplasty Wound: A Case Study

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Abstract:

Nearly 15 million patients undergo cosmetic surgery in the United States each year, with breast augmentations such as implants, lifts, or reductions being some of the most common procedures. The most common complications of these procedures are scarring and infection at the incision site, which often necessitates expensive corrective surgery.

After significant weight loss, the patient in this study underwent an elective lower body lift in conjunction with a breast reduction and nipple-areolar transplant. An autologous skin graft was used at the transplant donor site. The skin graft unfortunately necrosed, warranting the need for rapid wound closure to avoid further pain and infection. The patient was treated for eight weeks with conservative measures. After eight weeks of failed attempts to close her wound, she was referred for specialist care.

Upon initial examination, the donor site wound measured 3.5 cm x 3.5 cm with no sign of epithelialization. The patient received a single dose of Wharton's jelly flowable perinatal tissue allograft and five hyperbaric oxygen therapy treatments over seven weeks. Upon inspection at the final examination, the wound was closed entirely with 100% epithelialization overlying granulation tissue.

This case study demonstrates a precedent for the application of Wharton's jelly flowable allografts in complicated cosmetic post-surgical wounds. Future efforts will be directed at applying Wharton's jelly allografts on a preventative basis. Preventative applications could be in stage 2 pressure sores or intra-operatively to decrease potential patient suffering, prevent emotional distress, and reduce unnecessary healthcare expenses.

1. Introduction

Reduction mammoplasty, commonly known as a breast reduction, is a procedure in which the overall volumetric abatement of the breast is performed to assuage the painful symptoms and the emotional distress associated with macromastia (Purohit, 2008) (Dabbah, 1995). Reduction mammoplasty has increased in popularity by 49% in patients from 2020 to 2021. (Aesthetic Plastic Surgery National Databank 2020-2021) (ABPS). Breast reduction surgery is performed to mitigate issues for women experiencing negative symptoms from natural or cosmetic breast hypertrophy (Nava, 2017) (Lewin, 2014).

A study conducted in 2014, which examined the risk factors for complications within 30 days following breast reduction surgery in a group of 512 patients, found a 32% complication rate. The significant risk factors in this study included a long suprasternal notch-to-nipple distance, higher body mass index (BMI), diabetes, and smoking (Lewin, 2014). Minor surgical complications may include hematoma, wound infection, and delayed wound healing. Major

complications associated with breast reductions include wound dehiscence, flap necrosis, and nipple-areolar necrosis (Sachs, 2022). The risk of post-operative infections nearly tripled in surgeries lasting more than 120 minutes compared to operations lasting less than one hour (Kompatscher, 2003). Post-reduction skin grafts or flaps become imperative in larger necrotic areas where conservative methods cannot achieve epithelialization. Although skin grafts may be utilized to cover a wide area where skin loss is present, matching skin texture, color, and contour with the donor site makes grafting problematic and less ideal for aesthetic reconstructive measurements (Nomori, 2020).

The patient in this study received one Wharton's jelly (WJ) allograft application along with a total of eight HBOT treatments. Upon initial examination, the wound measured 3.5 cm in diameter and was wet and open. Upon examination at the final visit, the wound was entirely closed and completely epithelialized. While Wharton's jelly is known for its function as a micro-architectural framework or extracellular matrix, there have been reports of successful application in wound care (Arno, 2014). This case study demonstrates that the application of WJ allografts has the potential to accelerate wound closure time. Future non-randomized and randomized controlled trials may further establish standardized protocols for WJ application in wounds that are stage 2, intra-operative application to prevent post-operative wound dehiscence and to accelerate wound closure in deep or irregular cosmetic wounds that are not amenable to standard Dehydrated Amniotic Membrane Allograft application.

2. Case Presentation Section

2.1. Umbilical Cord Tissue Allografts

All methods were completed in compliance with the United States Food and Drug Administration (FDA) and American Association of Tissue Banks (AATB) standards.

Donation and Collection. Human umbilical cords were obtained from consenting mothers following full-term Caesarian section deliveries. Prior to delivery, birth mothers underwent comprehensive medical, social, and blood testing. An independent certified laboratory tested all donations for infectious disease in accordance with Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 CFR part 493, and FDA regulations. Each birth mother was tested for Hepatitis B Core Antibody (HBcAb), Hepatitis B Surface Antigen (HBsAg), Hepatitis C Antibody (HCV), Human Immunodeficiency Virus Antibody (HIV-1/HIV-2 Plus O), Human T-Lymphotropic Virus Antibody (HTLV-I/II), Syphilis (RPR), Cytomegalovirus (CMV), HIV-1/HCV/HSV, NAT, and West Nile Virus (WNV). Each test was performed with an FDA-Approved testing kit. All test results were negative or non-reactive.

Preparation of Processed Umbilical Cord Tissue Samples Product. Wharton's jelly was aseptically dissociated from the rinsed umbilical cord. After dissociation, 100mg of Wharton's jelly was suspended in approximately 2mL of sterile Sodium Chloride 0.9% solution (normal saline). The sample was not combined with cells, tissues, or articles other than the exceptions outlined in 21 CFR Part 1271.10(a)(3) (Human Cells, Tissues, and Cellular and Tissue-Based Product Regulation).

Allograft Application. The patient had allograft application performed in a private medical setting. Prior to application, the skin around the wound was cleaned and dried, biofilm abatement was performed, and marks were made in 0.5 cm increments around the circumference of the wound. Two cc's of Wharton's jelly flowable allograft were applied in the dermal layer around the circumference of the wound at each mark, diluted in 1cc of preservative free normal saline.

2.2. Patient History

The patient in this case is a 43-year-old female who received an elective reduction mammoplasty after losing a significant amount of weight. The patient's nipple-areola complex was transplanted cephalad, and a skin graft was placed over the donor site. The autologous skin graft necrosed, leaving an open wound. The patient received one WJ allograft application and eight hyperbaric oxygen therapy treatments.

3. Results

The patient's wound closed with a combination of Wharton's Jelly allograft application and eight HBOT treatments in 7 weeks, following eight weeks of failed conservative measures evident in Figures 1 and 2. Upon application on September 2, 2022, the wound measured 3.50 cm x 3.50 cm. Upon the first follow-up on September 10, 2022, the wound measured 2.0 cm x 2.0 cm with 43% epithelialization. Upon final examination, the wound was entirely closed with some discoloration. These results demonstrate a significant, favorable clinical outcome compared to the prior eight weeks of failed conservative management. The application of Wharton's jelly proved a critical component in timely wound epithelialization and closure. Lateral and deep infectious involvement of the breast tissue was avoided.

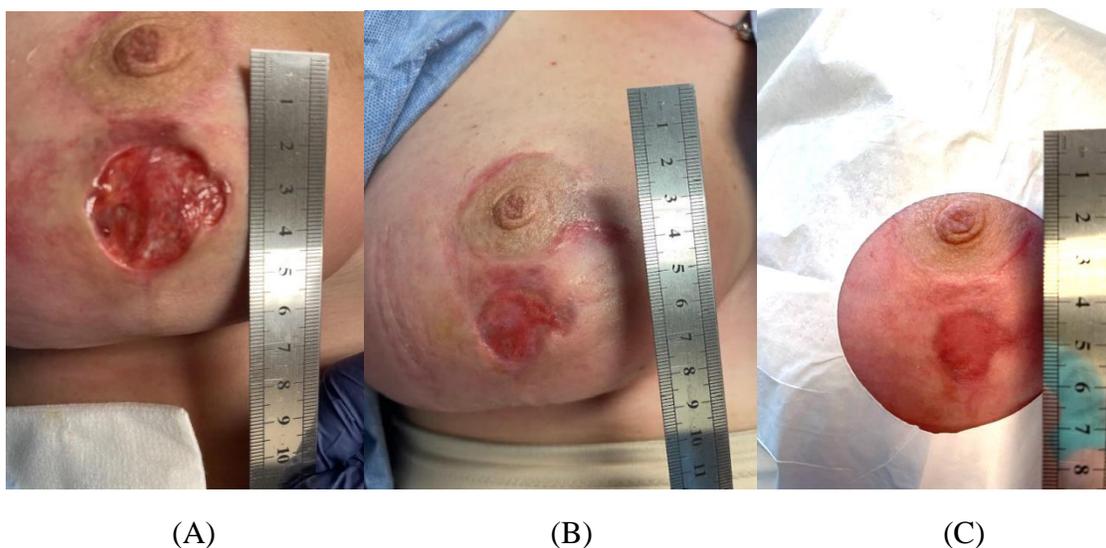


Figure 1. (A) First HBOT August 31, 2022, wound size 3.5 cm x 3.5 cm, no epithelialization (B) Follow up appointment on September 10, 2022, wound size 2 cm x 2 cm, 43% epithelialization (C) Second follow up on September 21, 2022, 100% epithelialization, completely healed, pigment discoloration

4. Discussion

As observed in the present case study, the application of Wharton's jelly for the closure of wounds following reduction mammoplasty significantly improved wound closure time. After eight weeks of failed conservative measures, Wharton's jelly was administered to the wound. Prior work has demonstrated the role of WJ as an extracellular matrix analog, sharing comparative quantitative and qualitative structure to collagen structural tissue matrices in load-bearing joints, intervertebral discs, and dermis. The collagen seen in the extracellular matrix (ECM) of dermal tissue, as shown in Figure 2, has a homologous structure similar to WJ in the formation pattern as well as the diameter of fibers. In Figure 2, the scanning electron microscope (SEM) photo of native and acellular skin shows the entangled structure of collagen fibers, which is analogous to all other anatomical locations of ECM in the body, notably in articular cartilage and the fibers in WJ (Davis, 2022). The average diameter of the skin collagen fibers is about 60nm, and the average diameter of the WJ fibers is 65nm (Figure 2, 3). These similarities suggest that WJ may be a suitable allograft alternative for the repair of structural tissue defects in the dermis.

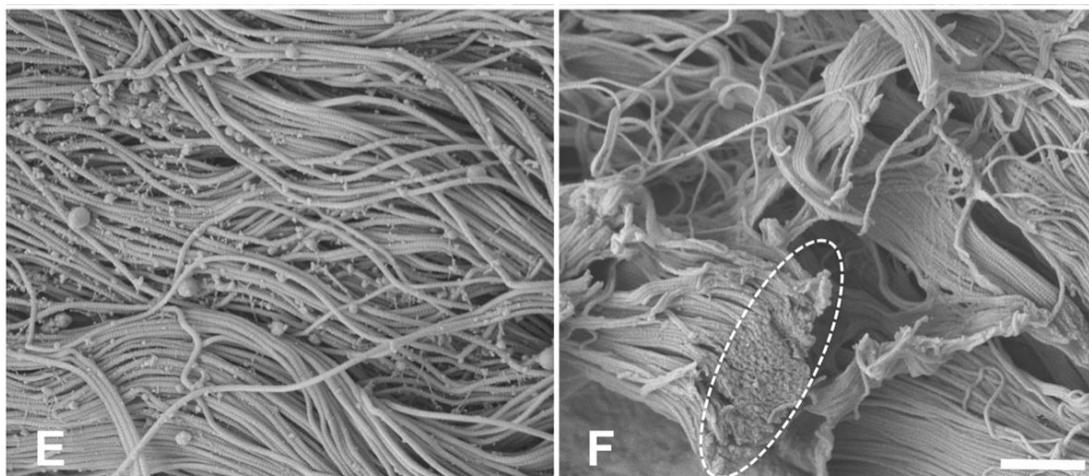


Figure 2. Scanning electron microscopy of E) native skin F) acellular skin. In the higher 10,000x magnification type I collagen clotting was observed (interrupted circles) accompanied by a loss of cross-linking collagens. Scale bar 1 μ m. The mean collagen fiber diameter from papillary and reticular dermis in normal skin was 56.2 \pm 2.5 nm and 62.8 \pm 4.3 nm respectively (<https://pubmed.ncbi.nlm.nih.gov/6699234/>)

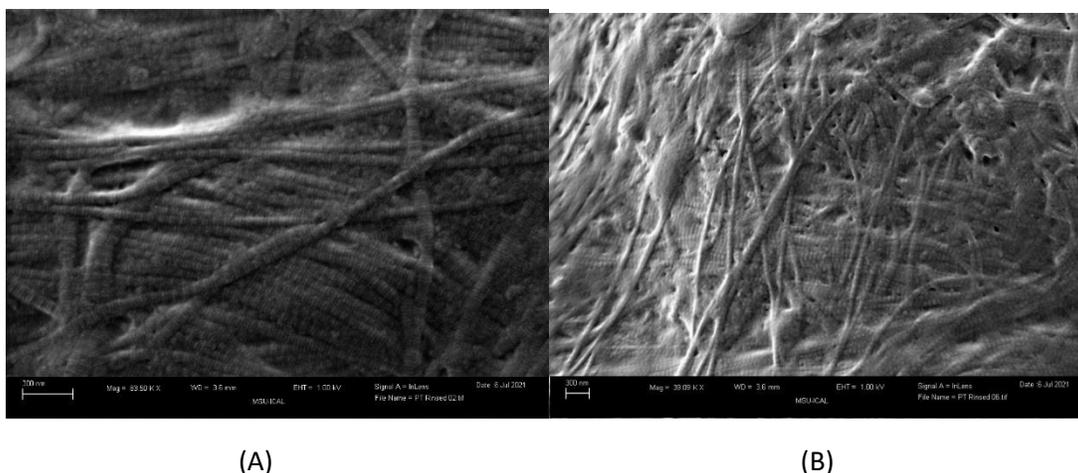


Figure 3. SEM micrographs of post-processed umbilical cord tissue samples. SEM image of preserved cross-linked collagen structures. (Scale bar: 300nm). Average fiber diameter, 65.4 nm.

The present case provides a foundation for the application of Wharton's jelly allografts for refractory wounds following reduction mammoplasties. WJ is comparable in cost to the standard of care for non-healing surgical wounds, which averages approximately \$6,931 for wound-related costs and \$20,752 for the total treatment cost (Joszt, 2021). Not only is the standard of care less effective, but when used alone, it may result in a prolonged length of stay and increased morbidity. In addition, expenses involved in treating non-healing surgical wounds, patient travel to and from a wound care clinic, wound care supplies not covered by insurance, lost wages from time off work, and caregiver fees are all out-of-pocket expenditures for patients.

5. Conclusions

The application of Wharton's jelly to improve the rate of cosmetic surgical wound closure demonstrated clinically favorable results. In the presented case, Wharton's jelly accelerated wound contracture and epithelization following eight weeks of failed conservative care. The use of Wharton's jelly allografts in combination with HBOT exponentially improved the overall closure rate of this surgical wound. Nonrandomized and randomized controlled trials can further define the frequency of flowable allograft application protocols and prevention-based protocols for stage 2 wound and intra-operative application of WJ.

The presented study aims to influence applications for the early, preventative use of Wharton's jelly allografts at the time of surgery to improve the current standard of care for intra-operative wound closure. Reduced hospital stay length, decreased surgical site infections rate, lower health care expenses from protracted post-operative wound care, and improved patient satisfaction and outcomes are all reasons to pursue alternative options for preventative wound care.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Institute of

Regenerative and Cellular Medicine (protocol code IRCM-2022-311 and approved on 12 January 2022).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement:

Data can be found in Appendix A

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Conflicts of Interest: John Shou, Naomi Lambert, Eric Vinke, and Tyler Barrett are associated with Regenerative Labs. Regenerative Labs was involved in the design of the study, data analysis, and writing. An independent physician performed the treatment and data collection at Advanced Regenerative Therapy. Regenerative Labs donated product for the present case and influenced the decision to publish.

Appendix A

Test Kits

1. HBcAb: Catalog number: 06P06, Abbott Laboratories, Abbott Park, IL, USA;
2. HbsAg: Catalog number: 06P02, Abbott Laboratories, Abbott Park, IL, USA;
3. HCV: Catalog number: 06P04, Abbott Laboratories, Abbott Park, IL, USA;
4. HIV1, HIV2, plus O: Catalog number: 06P01, Abbott Laboratories, Abbott Park, IL, USA;
5. HTLV-I/II: Catalog number: 06P07, Abbott Laboratories, Abbott Park, IL, USA;
6. RPR: Catalog number: 900025, Arlington Scientific, Springville, UT, USA;
7. HIV1, HCV, HBV, NAT: Catalog number: 303330, 303331, 303719, 303334, 303344;
8. WNV: Catalog number: 07001061190, Roche Diagnostics, Indianapolis, IN, USA.

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