Application of Umbilical Cord Tissue Allografts in Sacral Decubitus Ulcers: A Case Study and Review of Literature

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Abstract

Each year, thousands of patients suffer from sacral decubitus ulcers, also known as pressure ulcers or sores. The current standard of care for sacral decubitus ulcer treatment is expensive and suboptimal. Treatments can range in cost from a $15 dollar tube of Neosporin Ointment to $240,000 dollars for a skin flap surgery. Most pressure sores are not addressed aggressively until the skin is broken. Late-stage pressure sores present a unique challenge to physicians, in particular when they are deep, tunneling, and have tendon or bone involvement, as is the case for the two patients in this case study.

At the time of consultation, both patients had wounds that were classified as Stage IV with tissue loss and involvement of bone or tendon, according to the National Pressure Ulcer Advisory Panel (NPUAP). Upon inspection at the final examination, both wounds had contracted over 90%.

Introduction

- Pressure ulcers are caused by a combination of shearing forces, friction, moisture, and prolonged pressure over a bony prominence
- It may take as little as 1-2 hours to develop a stage III or IV pressure sore
- 83% of bedridden patients develop decubitus ulcers within the first five days of hospitalization
- Pressure Sores are categorized into four stages
  - Stage 1 only affects the outer layer of the epidermis
  - Stage 2 ulcers are deeper into the dermis sometimes with an open wound or pus-filled blister
  - Stage 3 extends past the dermis into the subcutaneous tissue
  - Stage 4 deep and large wounds that can affect the muscles and ligaments with black skin resulting from tissue necrosis
  - Stages 3 and 4 almost always require surgical intervention to achieve closure
- Average hospital costs for a stage IV pressure sore may exceed $124,000 per occurrence
- 2.5 million new pressure ulcer cases each year
- approximately 60,000 patients die from pressure sore-related complications annually, the 8th most common cause of death
- Wharton's jelly contains fibrous collagen types I, III, V, hyaluronic acid, and other glycosaminoglycans

Patient History

Patient 1

- Sustained a gunshot wound in 1975, leaving her paralyzed
- Developed a pressure ulcer that became infected in 2016, resulting in the removal of the coccyx and surrounding fascial tissues (wound measurement 16cm x 8cm)
- Unable to receive VAC, treated with Stravix placental grafts and electrical therapy for a year
- At the time of referral to this study, the patient presented with a mid-sacral pressure sore with exposed tendon, bone, and tunneling lasting over ten years

Patient 2

- Suffered a fall in March 2020, resulting in paralysis
- Developed a dime-sized pressure ulcer while in nursing home
- Post care facility stay, the patient had a significant abscess that developed into a large ulcer
- Patient refused flap surgery
- Underwent surgical debridement including fascia and muscle down to the ischial bone in November 2021
- At the time of referral to this study, the patient suffered from an ischial pressure sore with exposed tendon, bone, and tunneling for 30 months.

Treatment

- Both patients exhausted conservative measures, oral and IV antibiotic treatment, and failed dehydrated amniotic membrane allograft placement
- After unsuccessful interventions, both patients received several applications of Wharton's jelly flowable tissue allografts to assist in wound closure.

Patient Outcomes

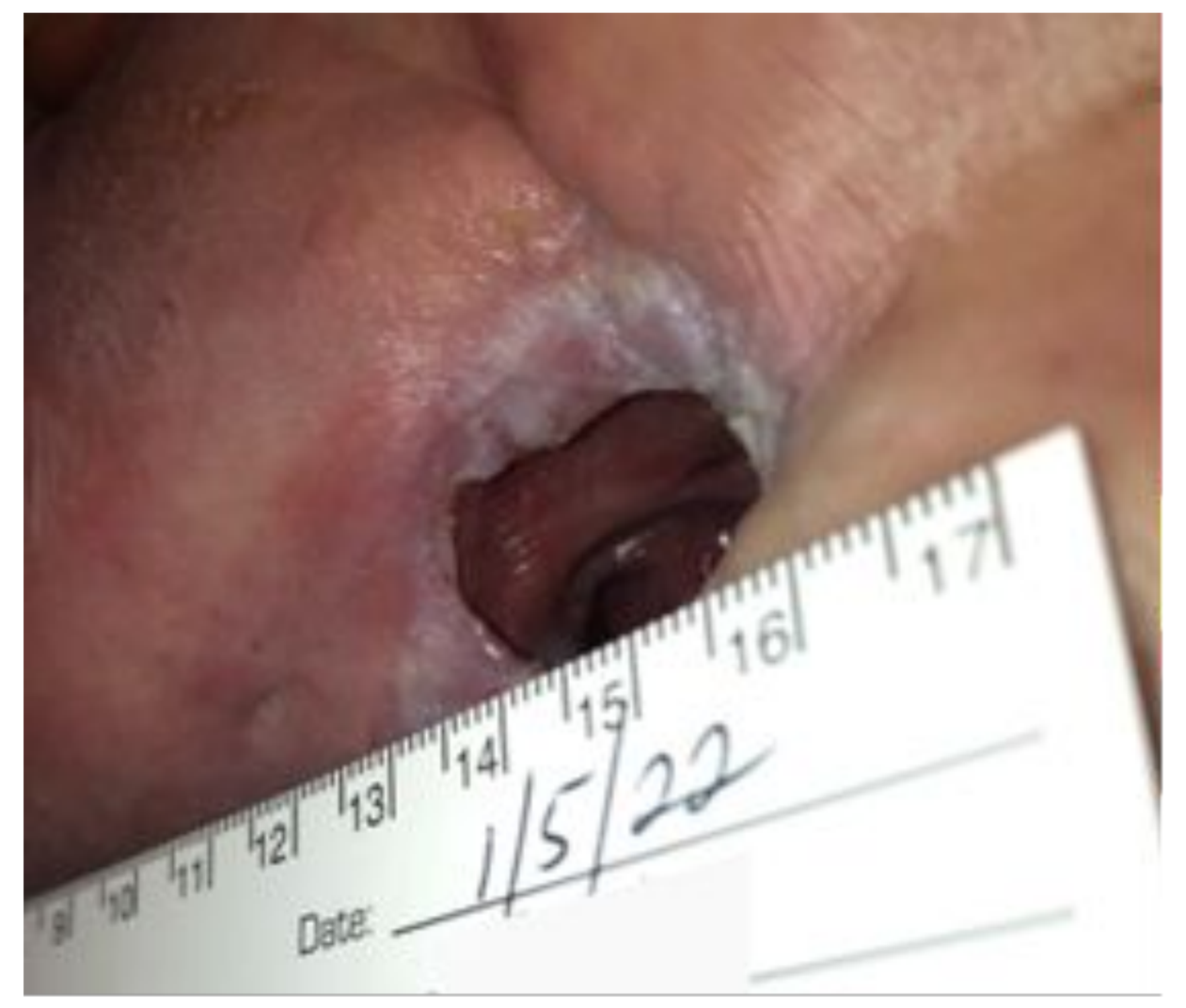

Figure 1. Patient 1, January 5, 2022
SDU size 3.00 cm x 3.00 cm x 2.00 cm

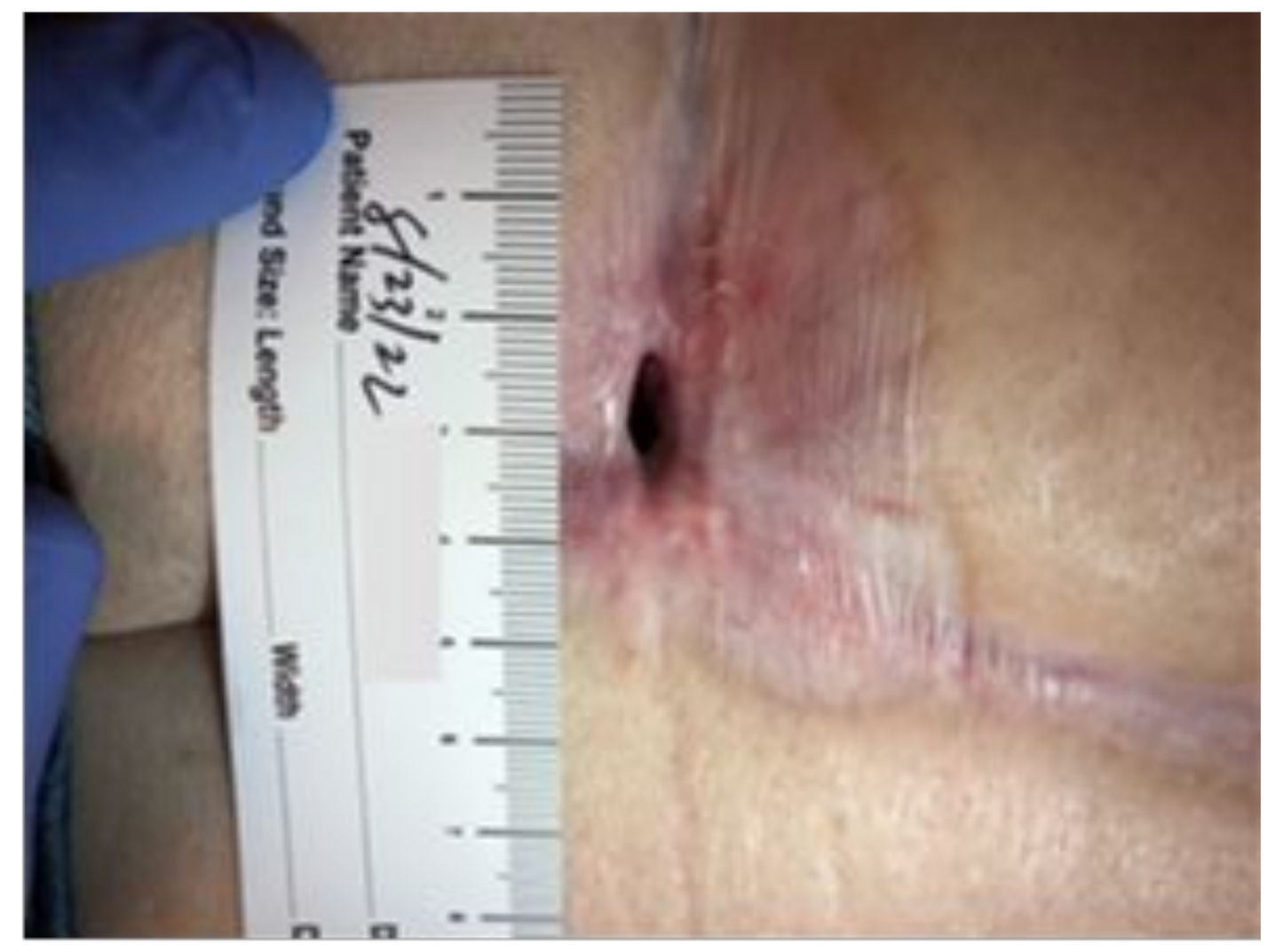

Figure 2. Patient 1, August 23, 2022
SDU size 1.30 cm x 0.45 cm x 1.00 cm

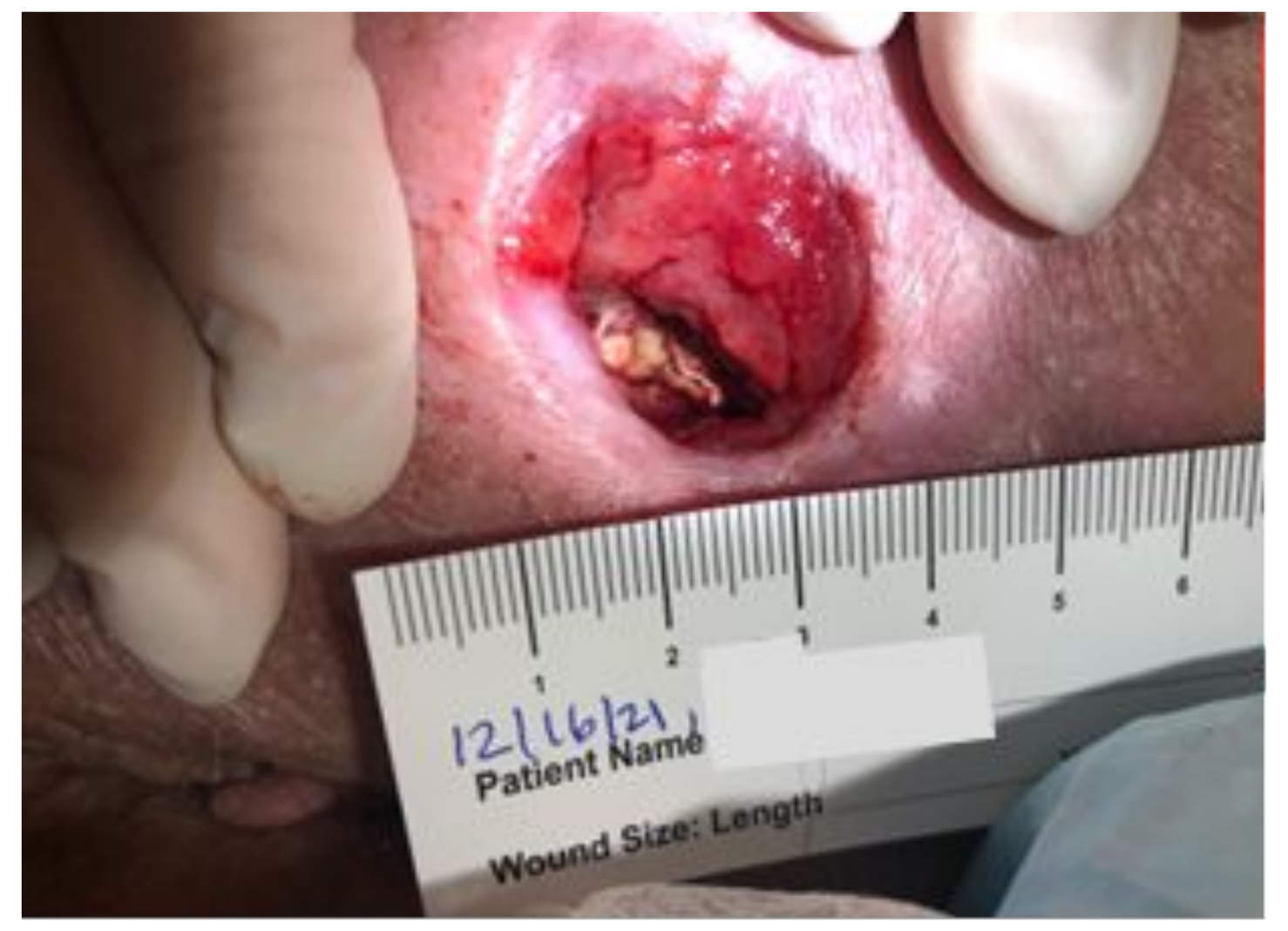

Figure 3. Patient 2, December 16, 2021
SDU size 3.00 cm x 2.30 cm x 2.50 cm

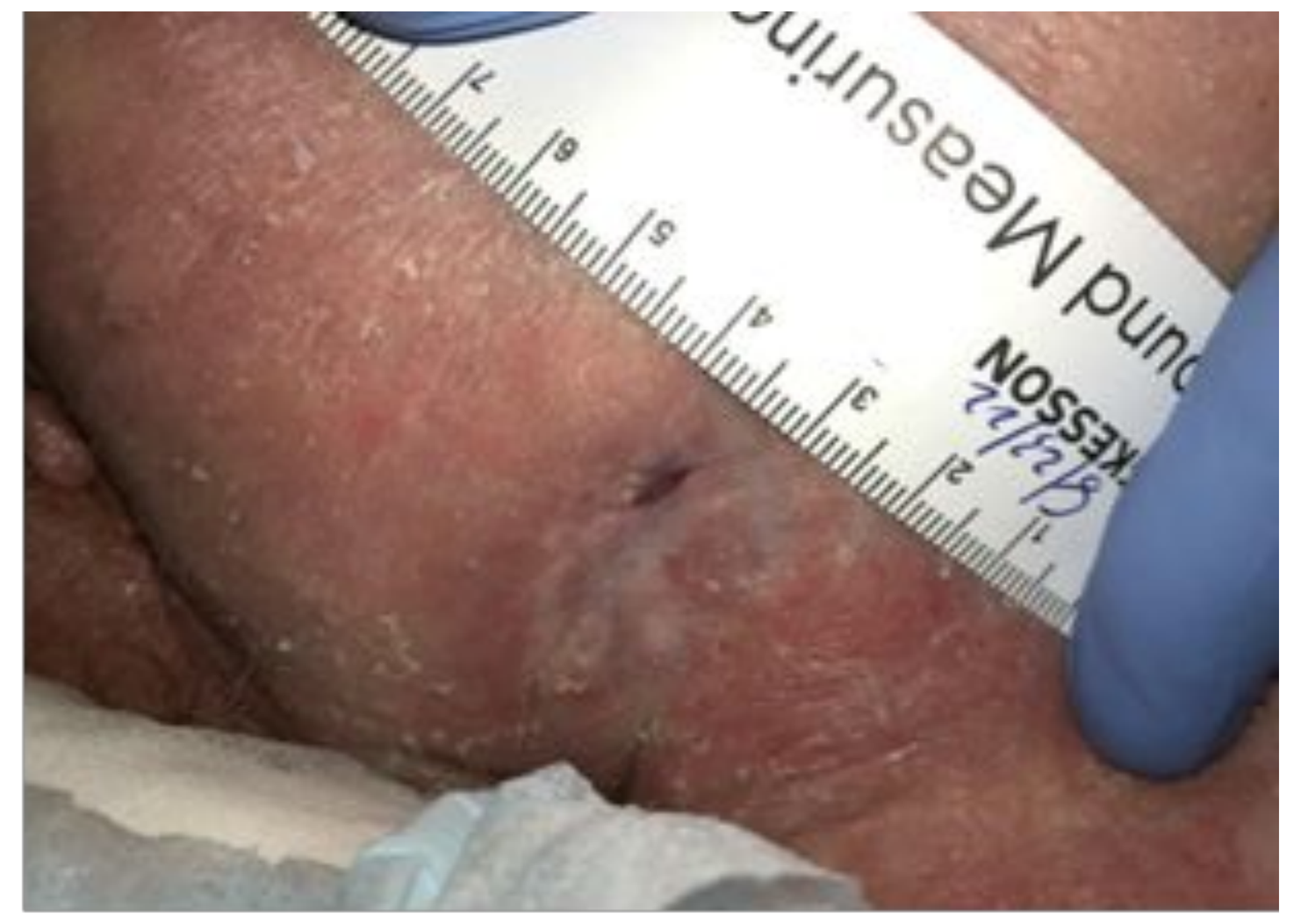

Figure 4. Patient 2, August 23, 2022
SDU size 0.60 cm x 0.10 cm x .8 cm

Methods and Materials

The allograft was applied in a private medical setting. For each application of Wharton's Jelly, 2cc's of Cryotext[TM] were administered via syringe to the tissue around the circumference of the wound. Dr. Lavor tracked the size of the wounds with the standard ruler method and a volumetric approach similar to the method by (Berg 1990). The skin around the wound was cleaned and dried, the patient was positioned so the ulcer was level. The wound was filled with sterile saline and the volume required to fill the wound was recorded. The edges of the sore were traced with a pen in order to obtain an accurate measure of the surface area.

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

Donation and Collection. Human umbilical cords were obtained from consenting mothers following full-term Cesarean 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 (HLTV-I/11), Syphilis (RPR), Cytomegalovirus (CMV), HIV-1/HCV/HBV, 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).

Data

Table 1. Progression of length, width, and depth measurements in Patient 1 SDU over six applications of cryopreserved Wharton's jelly allograft .

Date of Examination	Patient 1 SDU Measurement (LxWxD)
1/5/2022	3.00 cm x 3.00 cm x 2.00 cm
2/23/2022	2.00 cm x 1.00 cm x 1.60 cm
8/23/22	1.30 cm x 0.60 cm x 1.80 cm

Table 2. Progression of length, width, and depth measurements in Patient 2 SDU over five applications of cryopreserved Wharton's jelly allograft
*2cm tunnels in two directions +Tunnels healed

Date of Examination	Patient 2 SDU Measurement (LxWxD)
12/16/2021	3.00 cm x 2.30 cm x 2.50 cm*
2/1/2022	1.20 cm x 1.50 cm x 1.50cm^{+}
8/23/22	0.60 cm x 0.10 cm x .8 cm

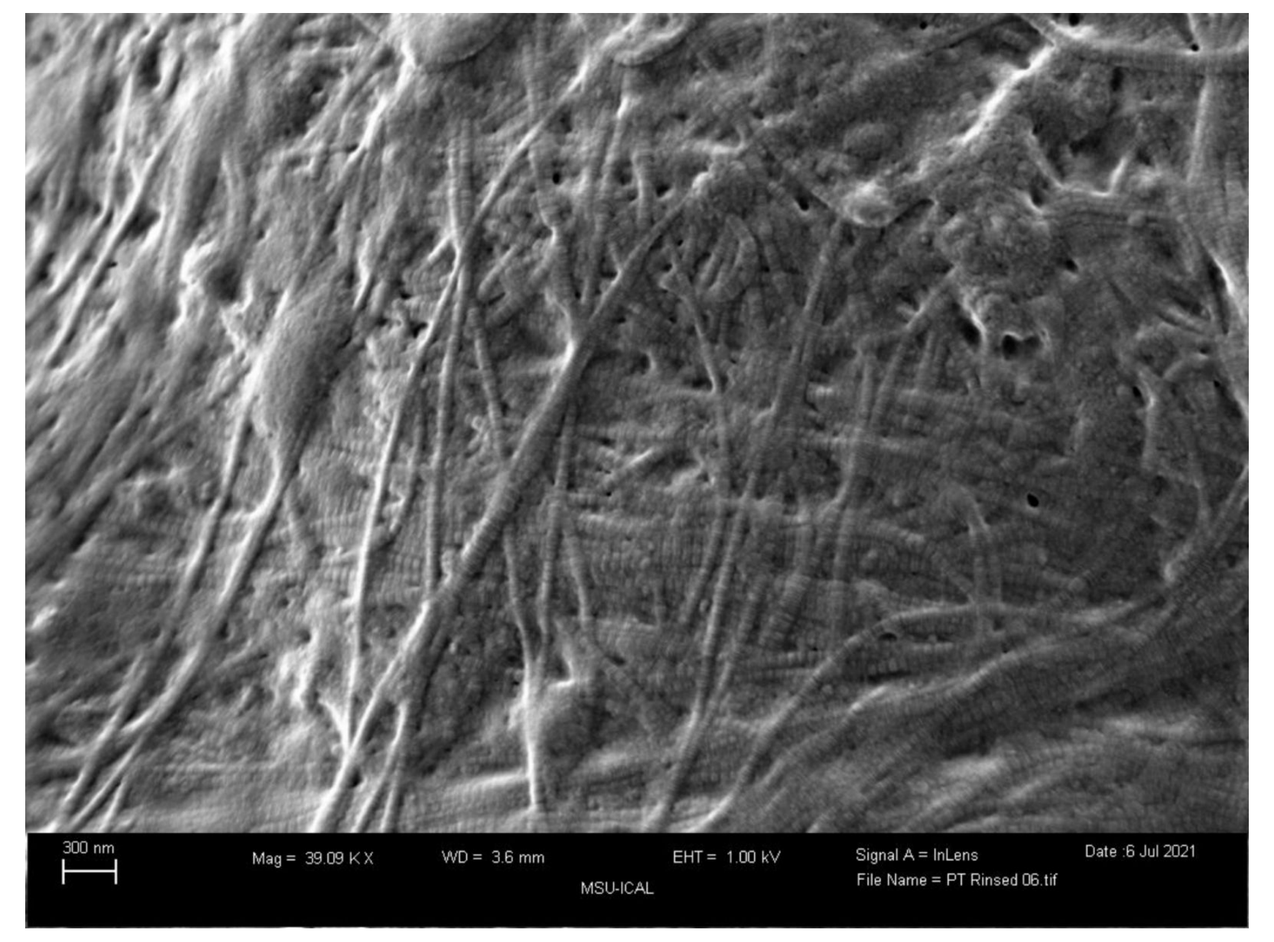

Figure 5. SEM micrographs of post-processed umbilical cord tissue samples. SEM image of preserved cross-linked collagen structures. (Scale bar: 300nm). Average fiber diameter, 65.4 nm.

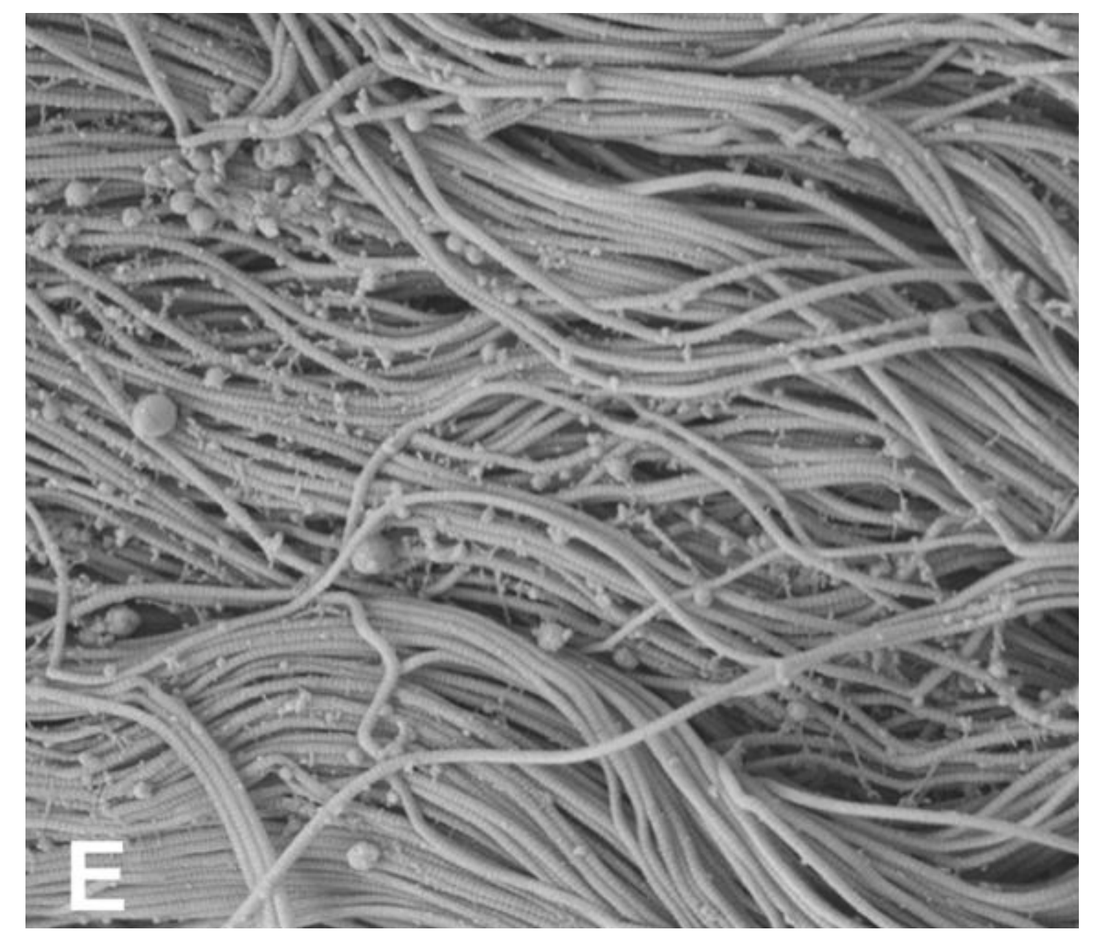

Figure 6. Scanning electron microscopy of native skin. In the higher 10,000x magnification type I collagen clotting was observed (interrupted circles) accompanied by a loss of cross-linking collagens. Scale bar 1 μm. The mean collagen fiber diameter from papillary and reticular dermis in normal skin was 56.2 +/- 2.5 nm and 62.8 +/- 4.3 nm respectively (https://pubmed.ncbi.nlm.nih.gov/6699234/)

Results

For both patients, wound diameter decreased from the initial allograft application to the final application shown in Table 1. Upon initial examination in January, the wound on patient 1 measured 3.00 cm x 3.00 cm and 2.00 cm deep, approximately 18 mL volume. Patient 2 also experienced similar wound size and diameter reduction success from the initial allograft application to the final application as shown in Table 2. Upon initial examination in December, the wound measured 3.00cm x 2.30cm x 2.5cm. Both had the total thickness of skin and tissue loss, visible tunnels, bone, and tendon were showing, classifying the wound as Stage IV. At the most recent examination in August, patient 1's wound measured 1.30 cm x 0.45 cm x 1.00cm, patient 2's wound measured 0.60 cm x 0.45 cm x 1.00 cm. The most noticeable component of healing being epithelization, with no tunnels, tendon, or bone visible. Throughout the UCT allograft applications, the epithelization of the SDU provided protection essential to mitigating wound infection and pathogens during the healing process. These are significant results compared to the 30 months before application when the patient did not have any epithelization advancements or wound closure. Ergo, the application of UCT allografts was essential in augmenting the healing process of the SDU.

Discussion

As observed in the present case study, the application of UCT allografts for chronic sacral decubitus ulcers augmented the time to wound closure in a significant manner. UCT allograft applications were applied over eight months after all conservative measures had been exhausted. As shown in Figures 1 and 2, both patient's wounds started at an overall volume of approximately 18mL. Steady volumetric reduction in the wound capacity is shown over time in Tables 1 and 2 and Figures 1 and 2. The most recent exam in August for patient 1 showed a 91% decrease in surface area and a 92% decrease in volume from the initial visit in January. For patient 2, there was a 99% decrease in volume and surface area from the initial visit in December to the most recent in August.

Wharton's Jelly provides a novel clinical application option for chronic ulcers with its ability to aid in repairing the extracellular matrix (ECM) damaged within the dermal tissue of a pressure ulcer. The collagen seen in dermal tissue (Figure 4) has a similar fibrous structure to WJ (Figure 3) in formation pattern as well as the diameter of fibers. The average diameter of the skin collagen fibers is about 60 nm, and the average diameter of the WJ fibers is 65nm (Figure 3,4). These similarities make WJ a suitable supplement for the repair of structural tissue damage in the dermis.

This case study provides a foundation for future research in applying Wharton's Jelly UCT allografts for refractory, complex tunneling SDUs. It is comparable in cost to the standard of care, which averages about USD 75,000-150,000 per patient (Padula, 2019). Not only is the standard of care for pressure ulcers less effective, but when used alone, it results in a prolonged length of stay and increased mortality. As of the 2008 passage of reduced payments, CMS refuses to reimburse hospitals for the costs associated with pressure ulcers acquired during inpatient services (Padula, 2015). When accounting for the expenses involved in treating SDUs, 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 for home care nurses or aids are all out-of-pocket expenditures for patients. Extending wound closure rates by weeks or even months may result in medical bankruptcy for patients and their families.

Conclusions

- The utilization of WJ allografts in the closure of decubitus ulcers produces favorable results and is consistent with current medical literature.
- WJ allografts augmented the ulcer's structural repair process for the patients in this study
- WJ allografts aided in the overall closure of two-year-old and ten-year-old stage 4 wounds that had previously failed conservative measures
- Non-randomized and randomized controlled trials can further define protocols and prevention-based strategies in less severe wounds
- WJ allografts, along with the current standard of care for decubitus ulcers, present a novel opportunity to reduce long-term morbidity and fatal septic infections

Future Directions

This case study demonstrates a precedent for applying Wharton's jelly flowable perinatal tissue allografts in late-stage sacral decubitus ulcers with associated tunneling. Future efforts will be directed at standardizing the preventative application of Wharton's jelly tissue allografts in Stage II pressure ulcers to decrease patient suffering and health care expenses associated with all pressure ulcers.

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).

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Acknowledgements

The authors would like to thank Saguaro Surgical for their collaboration in data collection.