TheraSkin® and TheraGenesis® Supported Wound Healing for Multiple Chronic Venous Leg Ulcers in a Single Patient: An Interim Report

CASE STUDY

Case(s) performed by: Srikanth Mahavadi, DPM
Co-author(s): Alyssa Cromer, BS CMW

INTRODUCTION

Chronic wounds, such as diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs), impose substantial treatment and cost burdens on global healthcare systems, representing an estimated 1 to 4% of total healthcare spending in developed countries.[1,2] A global increase in the prevalence of diabetes in recent years has led to a marked increase in chronic wounds and their associated social, economic, and physical burdens.[3] Annually, more than 9 million people worldwide are believed to suffer from DFUs, while in the United States alone, approximately 600,000 people experience VLUs.[2,4,5]

VLUs, primarily caused by venous hypertension, arise due to increased venous pressure and inflammation which leads to damage in the vein walls and surrounding tissues.[1,6] VLUs are typically hard to heal given that they can be resistant to treatment with a high recurrence rate of 50 to 70%.[6-8] Patients with a higher risk of developing VLUs include older and obese patients, among others.[6] Patients with such chronic wounds endure pain, disability, and loss of productivity, and are at increased risk for depression, social isolation, amputation, and death.[2,4,9] Current treatments for diabetic ulcers include wound dressing, hyperbaric oxygen, negative pressure wound therapy (NPWT), and, in advanced cases, amputation of the limb.[10-12] However, once amputation occurs, the patient's life expectancy significantly decreases.[13] As such, it is imperative to have efficacious treatments for these pernicious wounds.

Advanced treatment options for DFUs and VLUs involve the use of split-thickness human skin allografts and/or bilayer wound matrices, which have demonstrated efficacy in a variety of medical applications, including wound care.[14-17] These matrices have been shown to support cellular and vascular in-growth *in vitro* and *in vivo*.[18-21]

For example, TheraSkin® (LifeNet Health®, Virginia Beach, VA) is a split-thickness human skin allograft with retained living cells, endogenous growth factors, and a native extracellular matrix (ECM). The intact ECM provides a natural skin environment to enable several functions, including structural support, a substrate for cell movement, and direct interactions with the recipient cells to help facilitate healing.[19] The retained growth factors, cytokines, and living cells (e.g. viable fibroblasts and keratinocytes) can support angiogenesis and the healing of damaged or diseased skin.[15,22,23] Additionally, TheraSkin can be vascularized by the recipient following transplantation to support development of granulation tissue, which aids in epithelialization for wound closure.[15,22,23]

TheraGenesis® (LifeNet Health, Virginia Beach, VA) bilayer wound matrix, is a collagen-based wound dressing that consists of two layers: a porcine tendon-derived atelocollagen sponge layer and a silicone film layer. It also contains a non-adhesive gauze (TREX™) to reinforce the silicone film, and slits to aid in the drainage of exudate. The biodegradable collagen/silicone matrix provides a flexible scaffold to assist with cellular proliferation for cellular infiltration and capillary growth as demonstrated *in vitro* and *in vivo*.[20,21]

The following case presentation describes the combined use of TheraSkin and TheraGenesis to support the treatment of multiple large non-healing VLUs in a single patient. The patient provided consent for inclusion and the use of deidentified images.

CASE PRESENTATION

A 67-year-old female (BMI = 41.3) presented with chronic venous hypertension and 7 non-pressure VLUs on both lower extremities. These wounds had been persistent for over 10 years resulting in intermittent pain and swelling. Locations of the wounds were as follows: 3 on the lower right leg (anterior, lateral/posterior, and medial/posterior), 2 on the lower left leg (lateral and medial), and 2 on the dorsal side of the left and right feet. The wounds were large, with soft tissue calcifications and exposed bone on the right side and evidence of infection (total wound surface area: 638.9 cm^2; right side: 478.8 cm^2). Due to the severity of her condition and comorbidities including diabetes, hypertension, osteoarthritis, cellulitis/abscess of the right leg, sepsis, etc., the patient had a high risk for complications affecting wound healing.

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AUGUST 2023— At the patient's initial visit (Figure 1), she underwent excisional debridement of the multiple VLUs (total area of debridement: >600.0 cm^2) to remove devitalized tissue (fibrin, biofilm, slough and exudate), epidermis, dermis, subcutaneous tissue, muscle/fascia, and bone. The procedure resulted in minimal blood loss (5 ml), although the treatment was poorly tolerated by the patient due to significant procedural pain. Hemostasis was achieved by pressure and wound cleansers and dressings were applied. To rule out osteomyelitis (OM), a removed bone fragment was sent for pathology. No grafts were applied during this visit as preapproval was required prior to usage. Off-loading was not a requirement for this patient due to the location of the wounds.

BASELINE VISIT—AUGUST 2023

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (anterior) | Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 1. Representative images of the initial presentation of the bilateral leg and foot ulcers prior to debridement. There was a total of 7 wounds with a total wound surface area of 638.9 cm^2, with deeper wounds on the right side (478.8 cm^2).

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SEPTEMBER 2023— The bilateral wounds did not improve, (Figure 2; total wound surface area: 656.3 cm^2**)** so further extensive debridement was required following the same method as before to promote wound healing. The patient had recently undergone IV antibiotic treatment for sepsis for her infected wounds, so the surgeon noted that the slough was easier to remove. Following debridement, dressings were applied, and plans were made for outpatient OR debridement and graft applications at the wound center following graft approval.

SEPTEMBER 2023

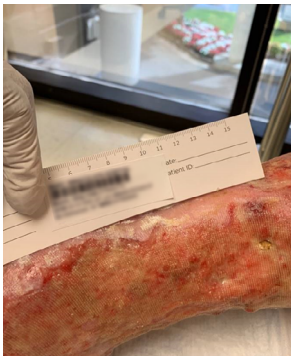
Left leg (lateral)

Left leg (medial)

Left foot (dorsal)

Right leg (anterior)

Right leg (lateral, posterior)



Right leg (medial, posterior)

Right foot (dorsal)

Figure 2. Representative pre-debridement images for the 7 wounds during the September 2023 follow up visit. Total wound surface area was 656.3 cm^2 with the right side measuring 491.7 cm^2.

NOVEMBER 2023— Approval was received in November 2023, so the patient was readmitted for treatment with graft applications. Total pre-debridement wound surface area measured 679.0 cm^2 with the right side measuring 525.0 cm^2. To prevent amputation and utilize all resources possible for limb salvage, the surgeon decided to use both TheraSkin and TheraGenesis grafts. The right anterior wound had healed following the patient's appointment in September, so these grafts were applied to the 6 remaining wounds following debridement to promote wound healing (Figure 3; graft measurements not reported).

NOVEMBER 2023—following graft approval

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 3. Representative images for each wound during the November 2023 follow-up after TheraSkin and TheraGenesis graft applications had been approved for use. Pre-procedural wound measurements were 679.0 cm^2 with the right side measuring 525.0 cm^2. The right anterior wound had healed following the patient's appointment in September, so TheraSkin and TheraGenesis grafts were applied to the 6 remaining wounds.

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DECEMBER 2023— Following the introduction of TheraSkin and TheraGenesis grafts at the last visit, there was approximately 25.0 cm^2 reduction in wound size with a total wound surface area of 653.7 cm^2 (right side: 503.3cm^2; Figure 4) for the 6 remaining wounds. Given this positive response to treatment, the surgeon performed further debridement for the entire area using the same method followed by applications of TheraSkin (39.0 sq cm) and TheraGenesis (dimensions not reported) which were secured with dressings. The procedure was well tolerated by the patient without significant pain.

DECEMBER 2023

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 4. Representative pre-debridement images for each wound during the December 2023 follow-up. Total wound surface area was 653.7 cm^2 (right side: 503.3 cm^2) for the 6 remaining wounds. Further debridement was performed followed by applications of TheraSkin (39.0 sq cm) and TheraGenesis (dimensions not reported) grafts secured with dressings.

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FEBRUARY 2024— Since the patient's last reported follow-up, she had received multiple outpatient treatments for her existing infection including antibiotics, but her condition worsened, leading to significant pain. The worsening of the patient's condition was not related to graft applications as the patient's condition was severe and she had various comorbidities that could affect wound healing. The patient was admitted to the ER as wound healing had stalled (Figure 5; total wound surface area: 728.8 cm^2; right side: 547.0 cm^2 whereby she underwent extensive wound debridement using a SonicOne® (LifeNet Health, Virginia Beach, VA) ultrasonic debridement device. The procedure involved thorough removal of necrotic tissue, deep debridement into the fascia, and some bone removal. Five TheraSkin grafts (116.0 cm^2) and 2 TheraGenesis grafts (8.2 x 6.0 cm), used at the deepest wound edges, wound surfaces, and wound matrix were applied to the wounds. All grafts were covered with nonadherent dressings and secured with a compressive bandage. Hemostasis was achieved.

FEBRUARY 2024

Left leg (lateral)

Left leg (medial)

Left foot (dorsal)

Right leg (lateral, posterior)

Right leg (medial, posterior)

Right foot (dorsal)

Figure 5. Representative pre-debridement images taken during the February 2024 follow up visit for each wound. Total wound surface area was 728.8 cm^2 with the right-side surface area measuring 547.0 cm^2. During this visit, the wounds were debrided and 5 TheraSkin grafts (116.0 cm^2) and 2 TheraGenesis grafts (8.2 x 6.0 cm), used at the deepest wound edges, were applied to the wounds.

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MARCH 2024— The size of the bilateral wounds had reduced following debridement and graft applications (Figure 6; total wound surface area: 699.0 cm^2; right side: 547.0 cm^2), but due to persistent pain and drainage, the patient was readmitted for treatment. After receiving IV antibiotics, the patient underwent further bilateral debridement and grafting for her legs and feet. The right leg's ulceration, extending into the fascia, required deeper debridement. Three 116.0 cm^2 TheraSkin grafts were applied to all wound surfaces, and one TheraGenesis graft (8.2 x 6.0 cm) was placed in the deepest part of the right leg ulceration. The grafts were secured, and the wounds were covered with nonadherent dressings and compression bandages.

MARCH 2024

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 6. Representative pre-debridement images for each wound during the March 2024 follow up visit.
Minor reduction in wound area was observed with the total wound surface area measuring 699.0 cm^2; right side: 547.0 cm^2.
Following debridement, 3 TheraSkin grafts (116.0 cm^2) and one TheraGenesis graft (8.2 x 6.0 cm) were reapplied to all wounds.

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JUNE 2024— Since the introduction of TheraSkin and TheraGenesis grafts and multiple debridement procedures, substantial reduction in wound surface area was observed in June 2024 whereby the total wound surface area was nearly 400.0 cm^2 smaller than the baseline measurement (Figure 7; total wound surface area: 263.9 cm^2; right side: 196.3 cm^2). To further promote healing, the patient underwent further debridement and grafting using the same method as described before. All ulcers were debrided, covering a total surface area of >200.0 cm^2, with minimal blood loss (5 ml). Hemostasis was achieved by pressure, and the procedure was well-tolerated, with no reported pain during or after the procedure. Both grafts were reapplied during this visit (dimensions not reported).

JUNE 2024

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 7. Representative images taken during the June 2024 follow up visit *(note: the right foot image is post-debridement as no pre-debridement picture was provided; all others are pre-debridement images)*. Significant reduction in wound area was observed with the total wound surface area measuring 263.9 cm^2; right side: 196.3 cm^2. Following debridement, TheraSkin and TheraGenesis grafts were reapplied (graft dimensions not reported).

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JULY 2024— Despite nearly 60% reduction in wound area (Figure 8; total wound surface area: 224.5 cm^2 right side: 167.5 cm^2) compared to baseline, the deepest ulcerations remained at the fascia level. Additionally, a superficial infection that was not attributable to the grafts was present at the time of surgery. Therefore, further debridement was required to evaluate the wound base and further promote healing. The SonicOne® debridement system was used to thoroughly perform bilateral debridement for the legs and feet, removing devitalized tissue and biofilm. A viable wound base with good granular tissue following debridement was observed. The deepest wounds, exposed with the tendon and fascia, were covered with 2 TheraGenesis grafts (4 x 3 cm) and the remaining areas of wounds were covered with TheraSkin (one 116.0 cm^2 and two 39.0 cm^2). The grafts were then covered with non-adherent dressings and compressive bandages. The patient tolerated the procedure well, with no complications, and was discharged with postoperative instructions.

JULY 2024

Left leg (lateral) | Left leg (medial) | Left foot (dorsal)

Right leg (lateral, posterior) | Right leg (medial, posterior) | Right foot (dorsal)

Figure 8. Representative pre-debridement images taken during the July 2024 follow up visit with the total pre-procedural wound surface area measuring 224.5 cm^2 (right side: 167.5 cm^2). Following debridement, the deepest wounds were covered with 2 TheraGenesis grafts (4.0 x 3.0 cm) and the remaining areas of wounds were covered with TheraSkin (one 110.0 cm^2 and two 39.0 cm^2).

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AUGUST 2024— The patient's most recent visit was in August 2024 whereby the total wound surface area was relatively larger compared to the month before (248.4 cm^2), likely as a result of the existent infection that was unrelated to the grafts. Despite the overall relative increase in wound size, the right side continued to improve, measuring 158.5 cm^2 at this visit (Figure 9). As the patient continues treatment, it is expected that the total wound surface area will continue its downward trend until full closure. At this visit, debridement was performed following the same method as described with additional applications of TheraSkin and TheraGenesis grafts to promote further wound closure (dimensions not reported).

AUGUST 2024

Left leg (lateral)

Left leg (medial)

Left foot (dorsal)

Right leg (lateral, posterior)

Right leg (medial, posterior)

Right foot (dorsal)

Figure 9. Representative pre-debridement images taken during the August 2024 follow up visit with pre-procedural total wound surface measuring 248.4 cm^2 (right side: 158.5 cm^2). The total wound surface area was relatively larger compared to the month before likely as a result of the existent infection that was unrelated to the grafts. The patient is still undergoing treatment.

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The patient is currently continuing treatment, and as such, the results presented herein are part of an interim report. The results are promising with an approximately 61% reduction in wound area following the introduction of TheraSkin and TheraGenesis grafts and extensive debridement procedures with the use of SonicOne (Figures 10 and 11). A more comprehensive analysis will be provided when the full course of treatment is completed.

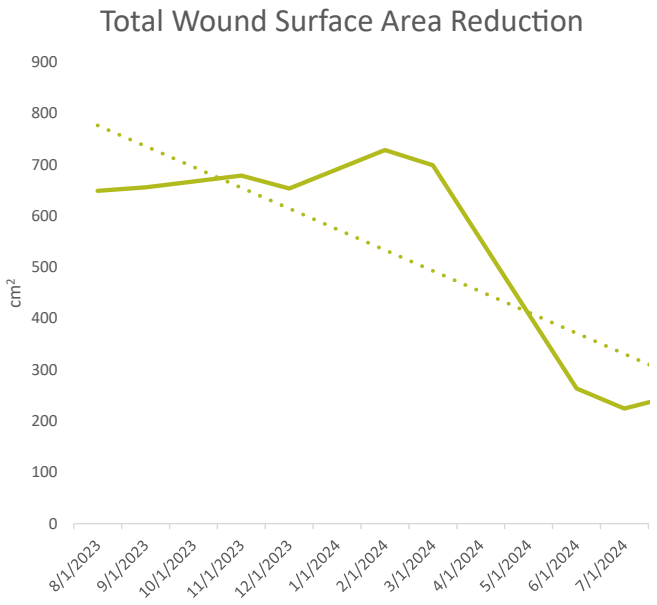

Figure 10. Total wound surface area over time with resulting trendline. Substantial ~400.0 cm^2 reduction in total wound surface area from August 2023 to August 2024 following debridement and applications of TheraSkin and TheraGenesis. Baseline total wound surface area was 649.4 cm^2 while the total wound surface area for the latest follow-up was 248.4 cm^2. Total wound surface area is expected to continue this downward trend until closure as the patient is still undergoing treatment.

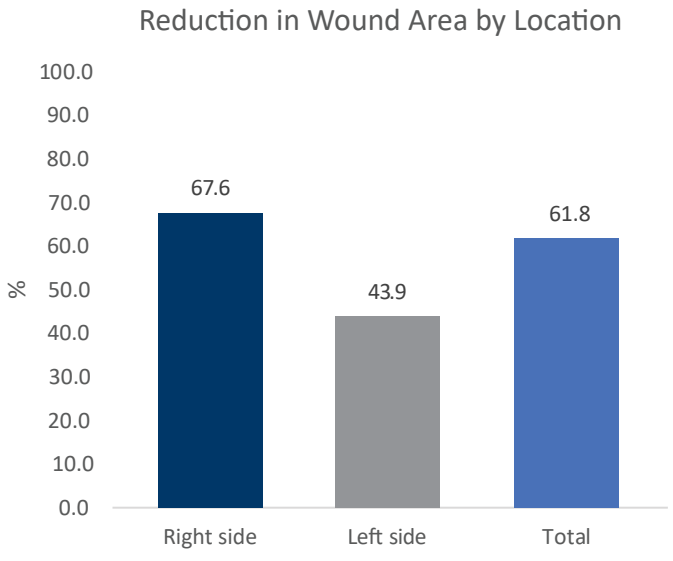

Figure 11. Reduction in wound area (%) for each side for this interim report. Total reduction in wound area from baseline was 61.8%. Note that the right side contained the deepest wounds with exposed fascia and bone.

SUMMARY

This interim case presentation report demonstrates a novel and successful use of TheraSkin, TheraGenesis, and SonicOne debridement to support wound closure for this patient with challenging comorbidities that can impede healing when other treatments have failed. Although the patient is still undergoing treatment, there was evidence of significant reduction in wound size following the introduction of these grafts and extensive debridement. Therefore, these results support the clinical advantages of TheraSkin and TheraGenesis. Although a case study cannot be used to predict how TheraSkin and TheraGenesis will behave in other patients, these results demonstrate a versatile and successful use of these grafts to support wound closure.

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Results from case studies are not predictive of results in other cases. Results in other cases may vary.

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