Using a Polylactic Acid Dermal Matrix for Achieving Wound Epithelialization in Patients with Pyoderma Gangrenosum

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PMI
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Background

Objective:

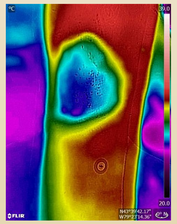
- Here, we present our experience using a **polylactic acid (PLA)** closure matrix to promote the **epithelization** of **pyoderma gangrenosum (PG) wounds** and achieve their closure.

Background:

- PG is an **inflammatory skin disorder** characterized by painful ulcerative lesions. Patients suffering this condition usually report wounds appearing after minor trauma and the increase of their size after debridement.
- Clinically, PG wounds are characterized by ruffled, hypertrophic borders, purple margins, and atrophic wound beds with extensive necrotic tissue and slough. Histopathologically, PG is characterized by neutrophil infiltration and tissue destruction by them.
- Diagnosis of PG wounds is challenging. However, under **infrared thermal imaging**, PG wounds appear **unusually cold**, which hints to the destruction of the wound's vasculature and lack of blood flow.
- Treatment of PG wounds is also challenging, as some wounds do not respond to anti-inflammatories and also respond poorly to traditional cellular and/or tissue products.
- PLA closure matrices are **fully synthetic** products that have demonstrated excellent closure outcomes for patients with challenging wounds by **restoring the interplay of the key elements of wound healing**.
- This is achieved because the **lactate** released by the PLA matrix acts as a paracrine agent (lactormone) with potent signaling effects that include:
  - **Hypoxia mimicking** and triggering of **neo-angiogenesis**
  - **Cell survival and proliferation**
  - **Anti-inflammation**
  - **Wound pH acidification**
- Here, we present our experience in achieving epithelization of hard-to-heal PG wounds after the administration of a novel PLA membrane that acts as **"a second skin"**.

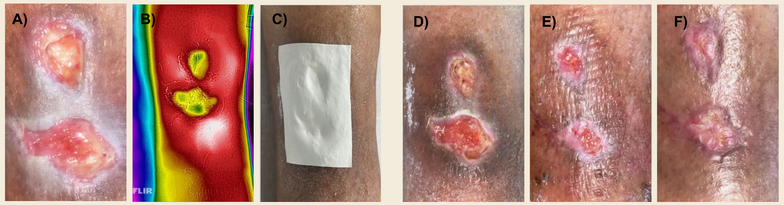
Diagnostic and Application Protocol

- Our diagnostic approach for PG ulcers is as follows:
  - Complete **clinical history** and wound history
  - Confirmation of the **absence of vascular pathology** by ABI or Doppler US
  - Confirmation of the **absence of bacterial contamination or infection** by auto-fluorescence and/or tissue biopsy
  - **Thermographic assessment**
  - Histopathological assessment if required
  - Clinical diagnosis of PG is made using the PARACELSUS score
- Our general treatment approach for refractive ulcers is:
  - Removal of all anti-inflammatory medications (as possible)
  - Wound maceration with zinc oxide paste
  - Weekly assessments until the ulcer is stable
- Once the PG wound is stable and necrotic tissue has been removed, PLA matrices were applied for 14 days.
- PLA matrices become translucent after application, so the wound bed can be monitored closely.



PG Thermogram
Thermography of PG wounds reveals unusually cold wounds with peri-wound inflammation. These wounds appear colder in the center and wherever there is necrotic tissue. In this case, the temperature difference between the wound bed and adjacent healthy skin was 6.5°C.

Case 1



Initial Presentation
After maceration and removal of necrotic tissue and slough , these wounds were considered stabilized and ready for the application of PLA closure matrices (A). Thermal imaging of the wound before treatment (B) showed a thermal asymmetry of -4.5°C between the wound beds and the contralateral leg area. Colder regions are apparent in this image as green spots, which correlate to the slough patches in the clinical image. A PLA matrix was applied to the wound bed and left untouched for 14 days (C). A few hours after application, the matrix becomes translucent, allowing the assessment of the wound bed on a weekly basis. A secondary alginate dressing was applied to the wound area above a layer of fatty gauzes and changed as often as needed.

Assessment after PLA Applications
After the first 2-week application, the wound bed looked mature and without macerated borders (D). The wound size recorded was 2.45 cm², representing a 15% reduction in size. After the second application, the wound size was reduced by 75% and the wounds showed a thick epithelial border and lack of slough or necrotic tissue (E). Finally, after a third application, the wound bed was fully epithelialized with minimal scarring and contracture of the surrounding tissue (F).

- Patient 1 was a 52-year-old female with a history of asthma, atopic dermatitis, and two ulcers in the right leg for the past 2-years.
- After wound stabilization, PLA matrices were applied bi-weekly, leading to full closure after 3 applications.

Case 2

Initial Presentation
On initial presentation, this ulcer was characterized by excruciating pain. Thermography showed a homogeneously cold wound bed, with a thermal asymmetry of -6.5°C and peri-wound inflammatory changes.

First PLA Application
After the first 2-week application of a PLA matrix, the wound bed appeared remodeled, with raised borders, and a discrete epithelial border. The thermographic assessment of the wound bed showed an increase in the wound's temperature, particularly in its lower regions, which correlated with the area with a thicker epithelial border.

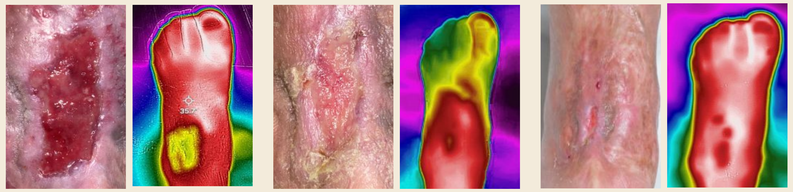
Second PLA Application
After a second 2-week PLA application, the wound size was drastically reduced. Epithelial borders were patent around the lesion. Thermographic assessment showed a lack of inflammatory changes in the peri-wound area and a minimal thermal asymmetry of the wound bed.

- Patient 2 was a 68-year-old diabetic and overweight female with an ulcer on the right external malleolus for the past 8 months. Her medical history was otherwise unremarkable.
- The patient had been unsuccessfully treated with compression therapy and collagen grafts.
- After wound stabilization, two rounds of PLA matrices administration led to the epithelization of >90% of the wound area.
- Progressive thermal changes in the wound bed correlated with wound closure. Our previous research has demonstrated that restoration of a wound bed's thermal asymmetry is correlated with increased angiogenesis.

Case 3

Initial Presentation
This wound had undergone a series of failed healing attempts, which left scarred and contracted tissue. Thermographic assessment of the wound bed showed a cold ulcer and distal hyperaemia.

Third Assessment
After the third administration of a PLA matrix, significant improvement was found. Epithelial borders and thermal changes are compatible with wound healing. The decision to leave the PLA matrices for longer periods of time was made thus.



12-Weeks
After 12-weeks of treatment and 5 rounds of PLA matrices, the wound bed has been completely filled with granulation tissue.

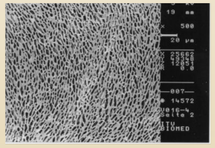
18-weeks
After 18-weeks of treatment, the wound size has been reduced by >60% and its depth is negligible. Thermal asymmetry is <3°C.

24-weeks
The wound has almost completely healed. The healing tissue looks less scarred than the previous healing attempts. The temperature distribution in the foot is almost homogeneous.

- Patient 3 is a 56-year-old female with a history of a non-healing ulcer for the past 5-years following a tendon repair. The wound had been treated by multiple care teams and surgical procedures, including skin grafting had previously failed.
- After histopathological confirmation of PG and wound bed preparation, repeated rounds of PLA matrices were performed, which led to full closure of the wound bed.
- In this patient, the PLA matrices were left for 21 to 28 days undisturbed.

Discussion

- PLA closure matrices induce a healing response in PG wounds characterized by modulation of the local inflammation, neo-vascularization, and advancement of epithelial borders.
- These matrices have small pores (3 to 30 µm) that prevent cell invasion, thus acting as a synthetic epidermis.
- The healing observed can be explained by PLA's properties, which induce an anti-inflammatory, pro-angiogenic, and pH-stabilizing effect in the tissue.



PLA Matrix Electron Microscopy
PLA matrices show a random pore distribution under the electron microscope. Pores range from 3 to 30 µm in diameter

References

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