Assessing a wound's neovascularization in real time using multispectral near-infrared imaging

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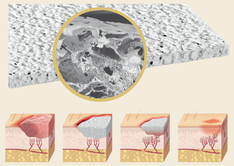
Background

Objective:

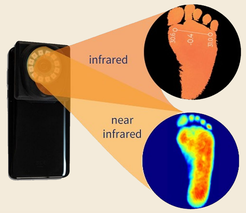
- To assess the wound bed of patients treated with **polylactic (PLA) wound closure matrices** using a novel multispectral near-infrared imaging device to monitor tissue oxygenation and temperature.

Background:

- Chronic wounds are characterized by being arrested in the inflammatory phase of healing, which causes impaired neo-angiogenesis, local hypoxia and low healing potential.
- There is mounting evidence of increased angiogenesis in chronic wounds treated with polylactic acid (PLA) dermal matrices because the **lactate** released by them 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**
- A novel **point-of-care wound imaging device** is capable of assessing tissue oxygenation via near-infrared spectroscopy, and temperature via long-wave infrared imaging, which are indicative of perfusion to the tissue.
- Therefore, we sought to determine whether the vascular changes in a wound bed induced by PLA matrices could be captured using the aforementioned imaging device.



PLA guided closure matrices have a highly porous structure that is designed to be used as a scaffold for tissue repair. However, as the material is degraded in an 8 to 12-week period, it is metabolized to lactate. This increases the local concentrations of lactate in the wound bed and triggers a pseudo-hypoxic reaction that in turn, upregulates VEGF expression and enhances the neo-angiogenesis of the wound bed.

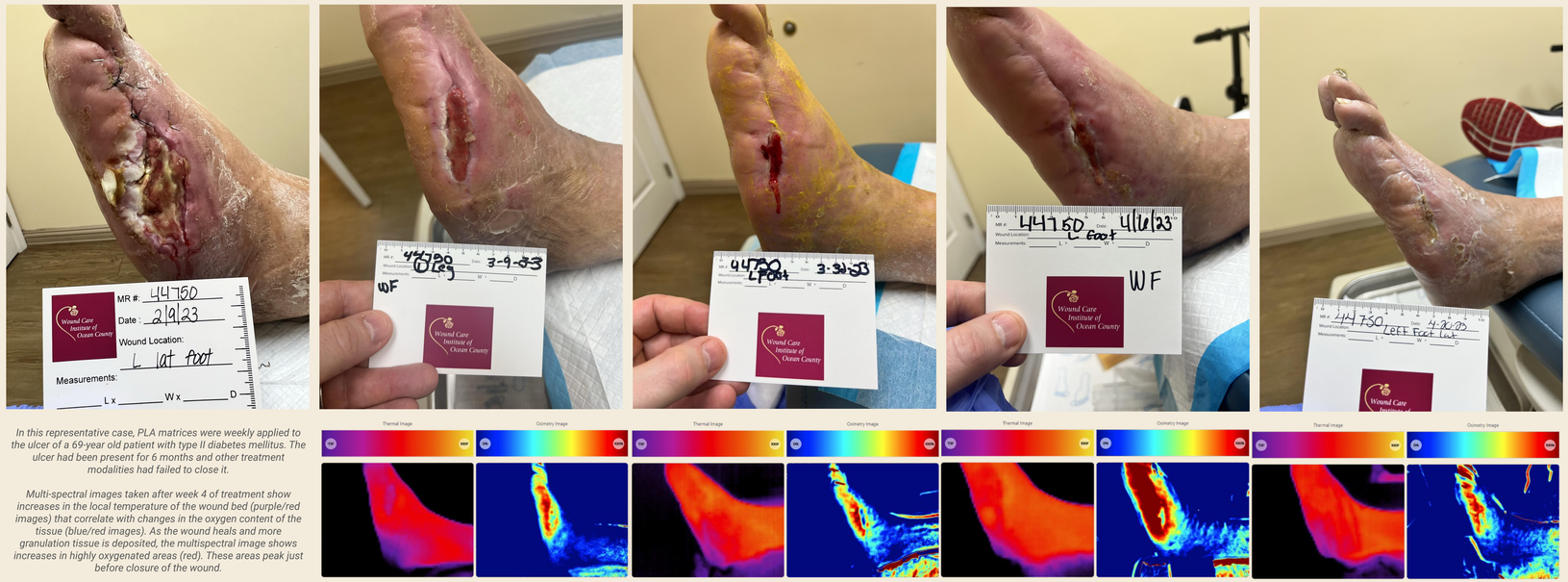


By using a combination of near-infrared spectroscopy and long-wave infrared thermal imaging, a novel handheld imaging device is capable of assessing the tissue oxygenation of the skin and wound beds.

Methods

- A series of 5 patients with chronic wounds received weekly applications of PLA matrices until healing. The **application protocol** was as follows:
  - **Wound bed preparation -** including debridement and hemostasis.
  - **PLA closure matrix application -** including the application of the matrix in intimate contact with the full wound surface, its fixation with a non-contact adhesive barrier, and the application of absorbent dressings and compressive bandages as needed.
- The **wound imaging protocol** consisted in the acquisition of images using the point-of-care device positioned at 20 to 30 cm from the wound bed, and 90° in respect to it, following its manufacturer's instructions.
- The matrices were left to integrate for 7 days. On every subsequent visit, an assessment of the wound was made visually and using a point-of-care multispectral near-infrared imaging device capable of quantifying tissue oxygenation level and temperature in the tissue and week-to-week changes were recorded and correlated with healing.
- A qualitative assessment of the images was performed by a trained user blinded to the treatment or time-points.

Results



In this representative case, PLA matrices were weekly applied to the ulcer of a 69-year old patient with type II diabetes mellitus. The ulcer had been present for 6 months and other treatment modalities had failed to close it.

Multi-spectral images taken after week 4 of treatment show increases in the local temperature of the wound bed (purple/red images) that correlate with changes in the oxygen content of the tissue (blue/red images). As the wound heals and more granulation tissue is deposited, the multispectral image shows increases in highly oxygenated areas (red). These areas peak just before closure of the wound.

- Following the application of PLA matrices, ulcer healing improved significantly in most patients.
- The matrices induced a robust healing response characterized by the deposition of large content of granulation tissue and the apparition of thick epithelial borders in the wound's edge.
- In line with these findings, the oxygen saturation of the wound bed increased over time, as well as the temperature of the peri-wound area.

Discussion

- Animal studies and limited human data have demonstrated that the lactate from the PLA matrices upregulates the production of VEGF, thereby inducing a potent neo-angiogenic response.
- However, in clinical practice, due to practical and ethical concerns, it is not always feasible to obtain tissue samples to assess this healing response.
- The use of novel multispectral near-infrared imaging devices capable of recording and measuring temperature as a proxy of perfusion and the oxygen saturation of a wound bed offers a powerful insight into the physiology of healing.
- These devices are predicted to have a significant impact on the wound treatment paradigms, as they offer non-contact, real-time, and low-cost physiological monitoring of healing tissue.

In summary, here, we confirm how the external administration of PLA into a wound bed leads to an increased angiogenic response that is critical for achieving healing.

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