

Comparison of Two Dermal Matrices for Diabetic Foot Ulcer Closure

Jose L. Ramirez-Garcialuna, MD, PhD ^{1,2}, Christian Planck, MBA ², Max Froelich, MD, PhD ², Darren Doerr, MBA ²

¹ McGill University, Montreal, QC, Canada. ² PolyMedics Innovations, Woodstock, GA.



The Wound Healing Company

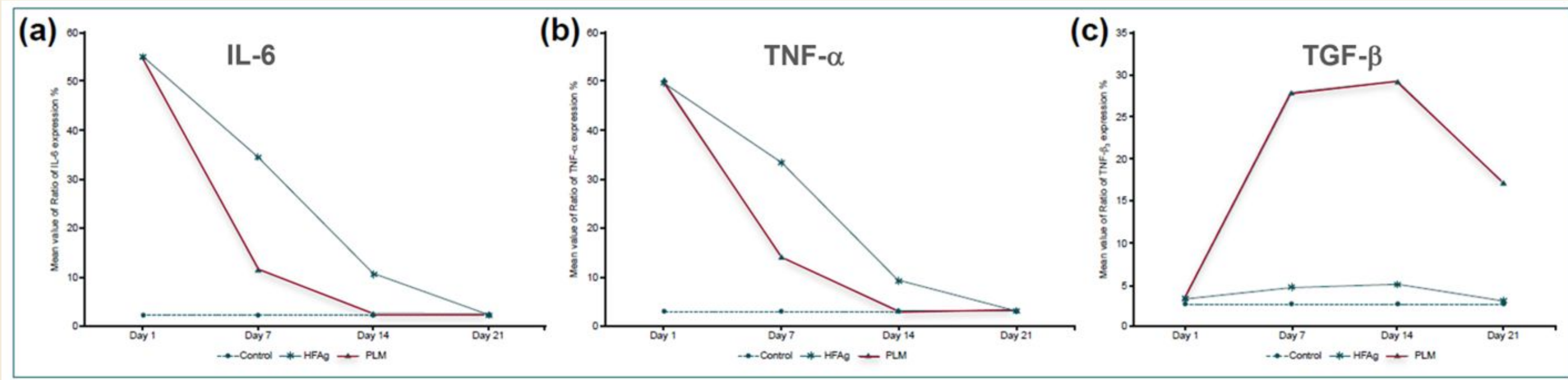
Background

Objective:

- To retrospectively compare the rate of wound closure by 12 weeks and the time needed to attain full closure of the wound of patients with diabetic foot ulcers who received **polylactic acid (PLA) synthetic closure matrices vs. fish skin xenografts**.

Background:

- Diabetic foot ulcers (DFUs) are usually refractive to traditional care and require advanced materials, such as dermal matrices, to promote healing.
- PLA has demonstrated excellent closure outcomes for patients with acute wounds such as burns.
- 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**
- Dermal closure matrices come from **different sources and exhibit different properties**, so it is still unclear whether there are advantages in using one type over others.
- Therefore, we sought to conduct a retrospective chart review to assess if there are significant differences between two matrices with known anti-inflammatory properties for **achieving DFU healing by 12 weeks**.



Modified from Ulus Travma Acil Cerrahi Derg. 2021 Jan;27(1):122-131.

Prior research by Demircan et al. demonstrated that PLA closure matrices exhibit potent anti-inflammatory effects in burns, as compared to active silver dressings, by reducing the local levels of IL-6 (panel A) and TNF-α (panel B), while upregulating those of TGF-β (panel C). Taken together, these results are associated with improved functional outcomes, such as reduced healing time and reduced scarring.

Legend: Control - negative control from cytokine analysis kit, HFAg - hydrofiber silver dressing, PLM - polylactic membrane

Methods

- This was a **retrospective study** of patients with DFUs of at least 12 weeks of age and >1 cm² without infection who received either PLA or fish skin dermal matrices as adjuncts to their standard of care.
- All patients were followed weekly for **12 weeks with applications of the matrices on every other visit**.
- All patients were treated in a **single high-volume center** by the same care team.
- The size of the wounds and the time until complete healing were recorded, as well as the rate of wound closure by the end of the follow-up period.
- The **end-points** of the study were:
 - The proportion of wounds achieving full closure by 12 weeks.
 - The odds of attaining closure by 12-weeks in the PLA group.
 - The time needed to achieve full closure of the wounds.
 - The presence of complications, including infection, amputation, or treatment failure.
- Analysis of the data was performed blindly by an independent researcher.

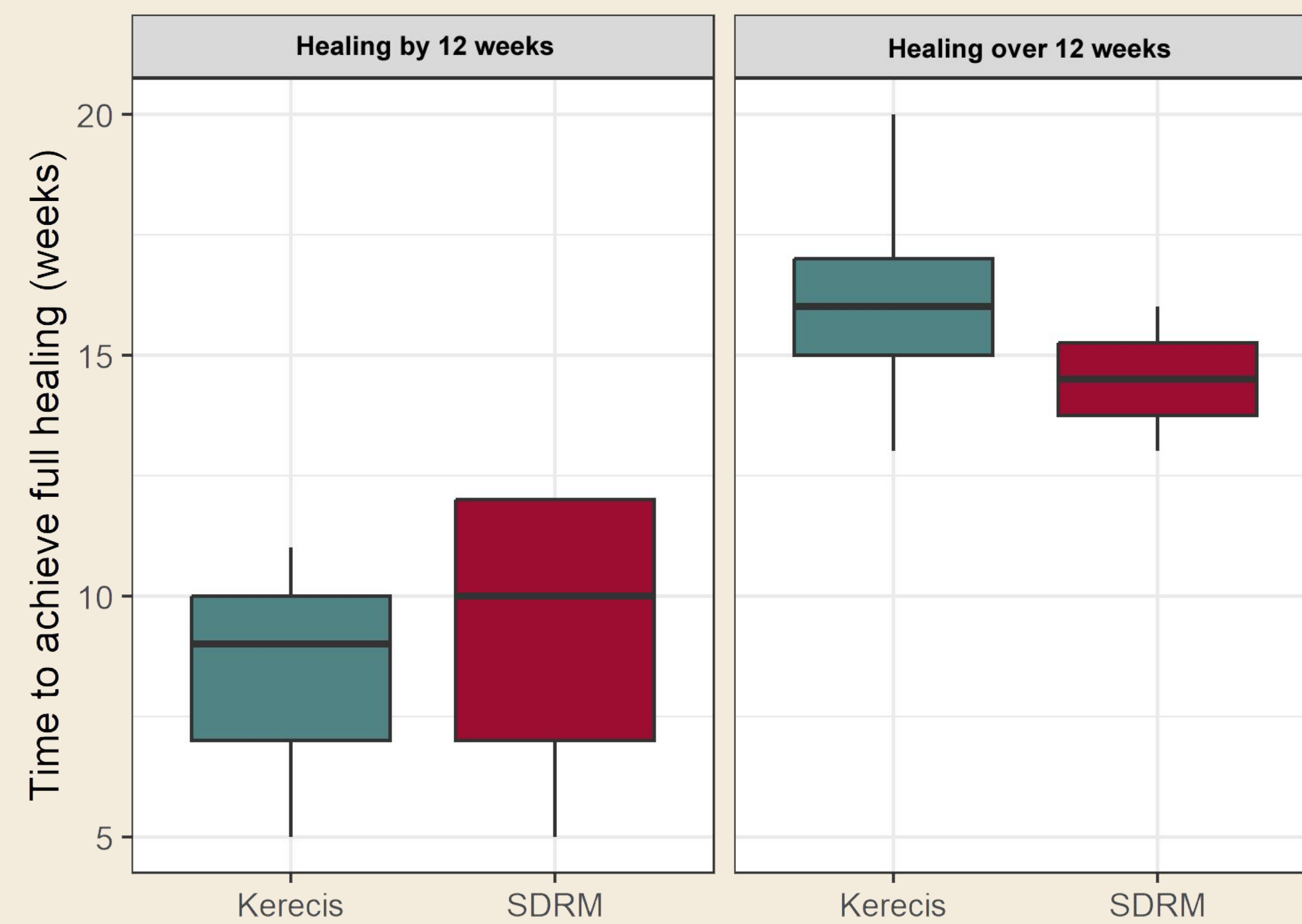
Results

- No significant differences between patient groups were found at baseline:

	Kerecis (N=24)	SDRM (N=22)	Total (N=46)	p-value
Age (years)				0.351 ¹
Mean (SD)	65.083 (6.865)	67.318 (9.152)	66.152 (8.028)	
Range	52.000 - 75.000	47.000 - 80.000	47.000 - 80.000	
Gender				0.404 ²
Female	7 (29.2%)	9 (40.9%)	16 (34.8%)	
Male	17 (70.8%)	13 (59.1%)	30 (65.2%)	
Location of the Wound				0.843 ²
Dorsum	5 (20.8%)	4 (18.2%)	9 (19.6%)	
Heel	4 (16.7%)	6 (27.3%)	10 (21.7%)	
Plantar	8 (33.3%)	7 (31.8%)	15 (32.6%)	
Toe/Metatarsal Head	7 (29.2%)	5 (22.7%)	12 (26.1%)	
Wound Size (cm ²)				0.281 ¹
Mean (SD)	7.626 (4.462)	6.217 (4.266)	6.952 (4.379)	
Range	1.430 - 15.980	1.300 - 12.300	1.300 - 15.980	

1. Linear Model ANOVA
2. Pearson's Chi-squared test

Time to Heal

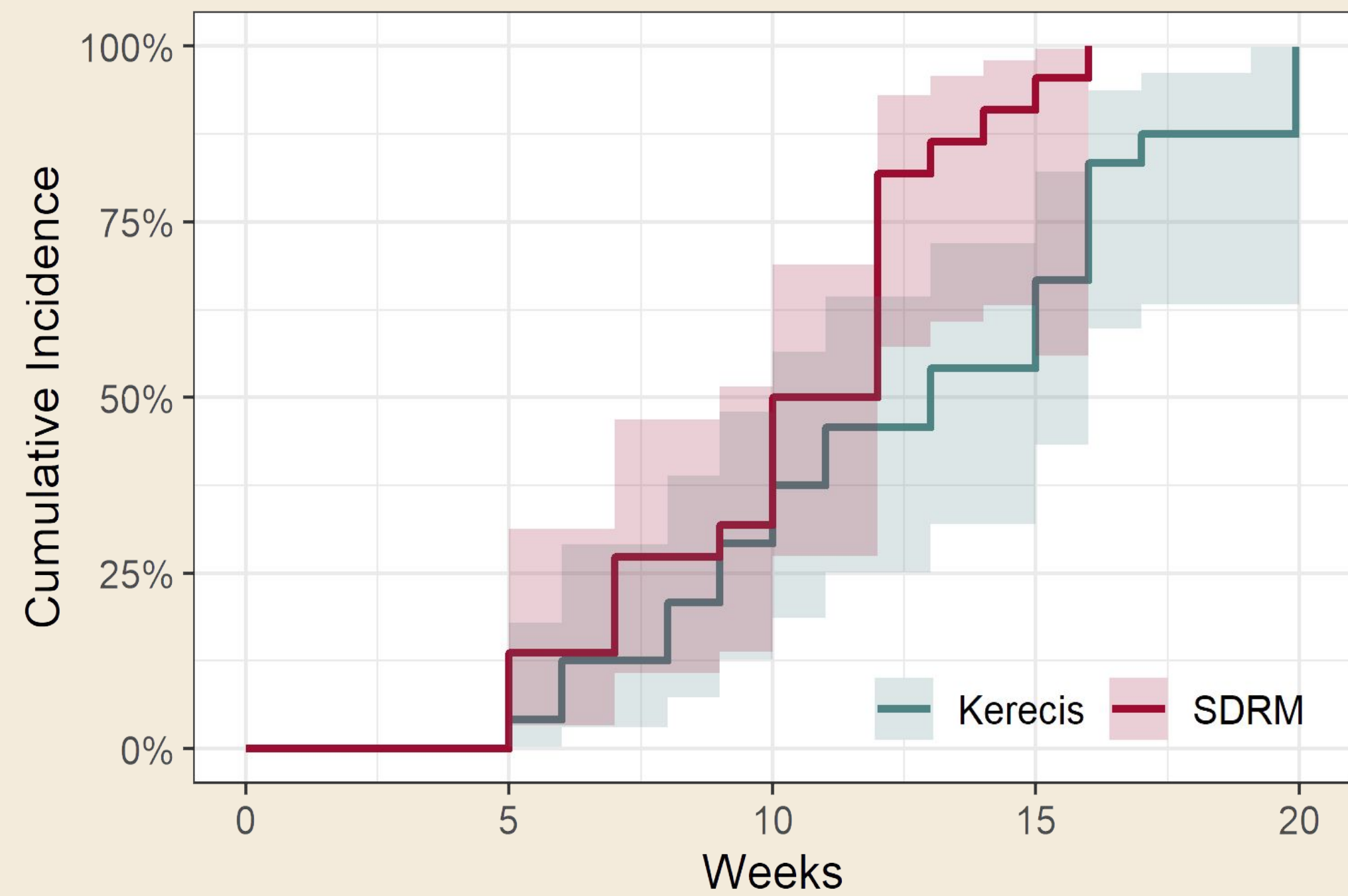


For the wounds that **healed by 12-weeks**, full healing of the wounds was achieved in 8.5 ± 2.1 vs. 9.4 ± 2.7 weeks ($p=0.29$) in the fish skin xenograft vs. PLA group.

For the wounds that **healed in more than 12-weeks**, full healing of the wounds was achieved in 16.2 ± 2.3 vs. 14.5 ± 1.3 weeks ($p=0.09$) in the fish skin xenograft vs. PLA group.

The **overall healing time** was 12.7 ± 5.1 vs. 10.3 ± 3.4 weeks ($p=0.048$) in the fish skin xenograft vs. PLA group.

Cumulative Incidence of Healing



The cumulative incidence for achieving full closure by 12 weeks with **PLA matrices was 82% (95%CI 57 to 93)**, compared to 46% (95%CI 25 to 64) in the fish xenograft group ($p = 0.009$).

The **odds ratio** of achieving full closure by 12-weeks was **1.64 (95%CI 1.17 to 2.28, $p = 0.015$)** in the PLA group, compared to the fish skin xenograft group.

- No complications or adverse events were recorded on this group of patients.

Discussion

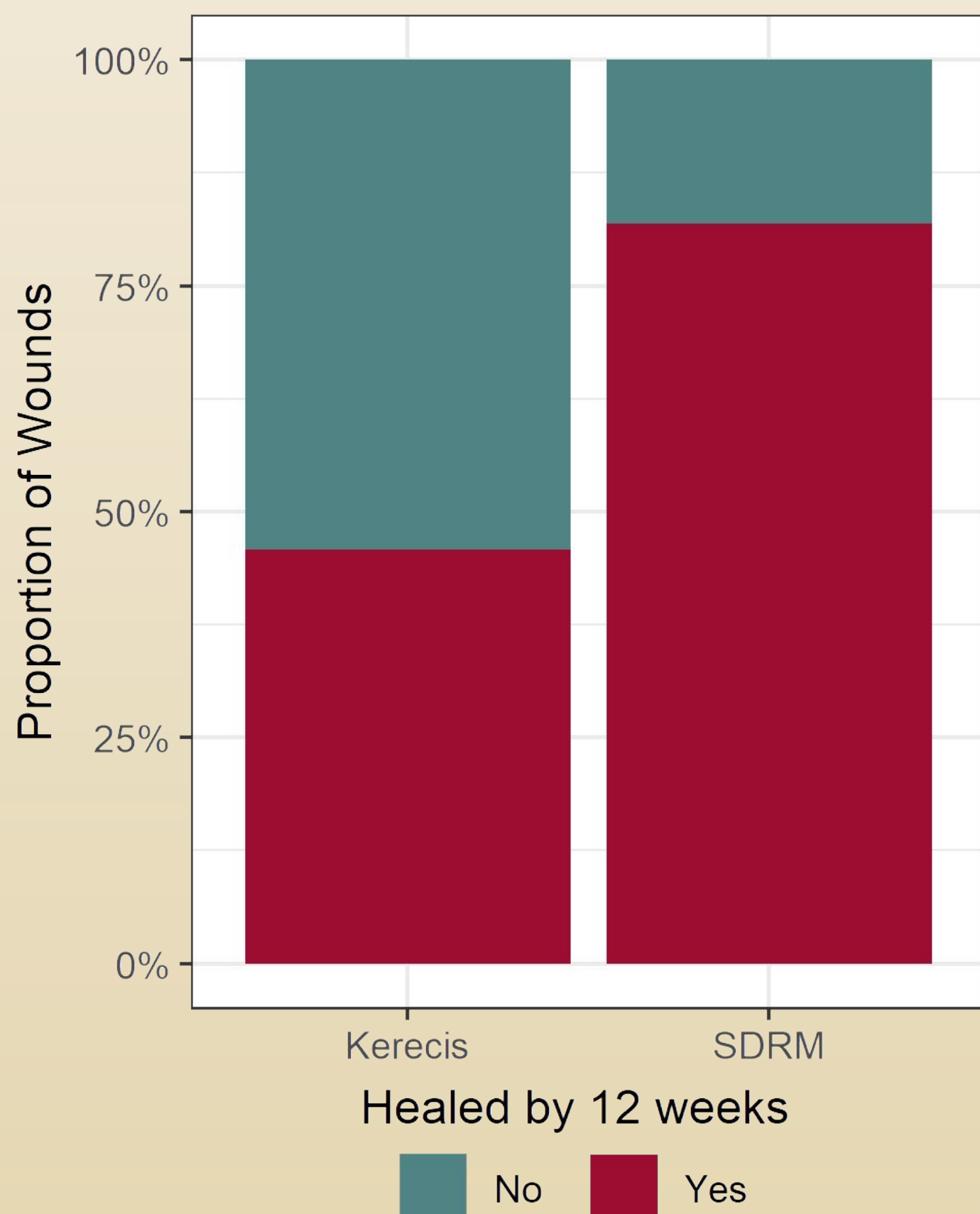
- The ideal dermal closure matrix for DFU treatment should be a material that **promotes rapid healing, is easily integrated** into native tissue, **does not elicit an aggressive immune or anaphylactic response**, and is easily **degraded** into non-toxic metabolites.
- Synthetic materials such as PLA fulfill these criteria**, as they increase the time to achieve healing, promote a robust formation of granulation tissue, possess anti-inflammatory effects, and degrade into H₂O and CO₂.
- Furthermore, PLA matrices are **well-positioned for reimbursability** in their use.

In summary, here, we show that compared to fish xenografts, PLA matrices show a slightly shorter time-to-heal response of DFUs while increasing by 1.64 the odds of attaining full closure by 12 weeks.

References

- Edmonds M, Manu C, Vas P. The current burden of diabetic foot disease. Journal of Clinical Orthopaedics and Trauma. 2021 Jun 1;17:88–93.
- Mirhaj M, Labbaf S, Tavakoli M, Seifalian AM. Emerging treatment strategies in wound care. Int Wound J. 2022 Nov;19(7):1934–54.
- Hundeshagen G, Collins VN, Wurzer P, Sherman W, Voigt CD, Cambiaso-Daniel J, et al. A Prospective, Randomized, Controlled Trial Comparing the Outpatient Treatment of Pediatric and Adult Partial-Thickness Burns with Suprathel or Mepilex Ag. J Burn Care Res. 2018 Feb 20;39(2):261–7.
- Stone R, Saathoff EC, Larson DA, Wall JT, Wienandt NA, Magnusson S, et al. Accelerated Wound Closure of Deep Partial Thickness Burns with Acellular Fish Skin Graft. Int J Mol Sci. 2021 Feb 4;22(4):1590.
- Ring A, Goertz O, Al-Benna S, Ottomann C, Langer S, Steinstraesser L, et al. Accelerated angiogenic induction and vascular integration in a novel synthetic scaffolding matrix for tissue replacement. Int J Artif Organs. 2010 Dec;33(12):877–84.

Healing by 12 Weeks



	Kerecis (N=24)	SDRM (N=22)	Total (N=46)	p-value
Healed by 12-weeks				0.011
No	13 (54.2%)	4 (18.2%)	17 (37.0%)	
Yes	11 (45.8%)	18 (81.8%)	29 (63.0%)	

Fisher's exact test

Eighteen (82%) of patients in the PLA group achieved healing by 12-weeks. In contrast, 11 (46%) achieved full healing in the fish xenograft group.

Only 4 patients (18%) in the PLA group did not fully healed by 12-weeks, compared to 13 (54%) in the fish skin xenograft group ($p = 0.011$).