

# A Pilot Randomized Clinical Trial on The Use of a Novel Polylactic Acid Dermal Matrix for Diabetic Foot Ulcer Closure

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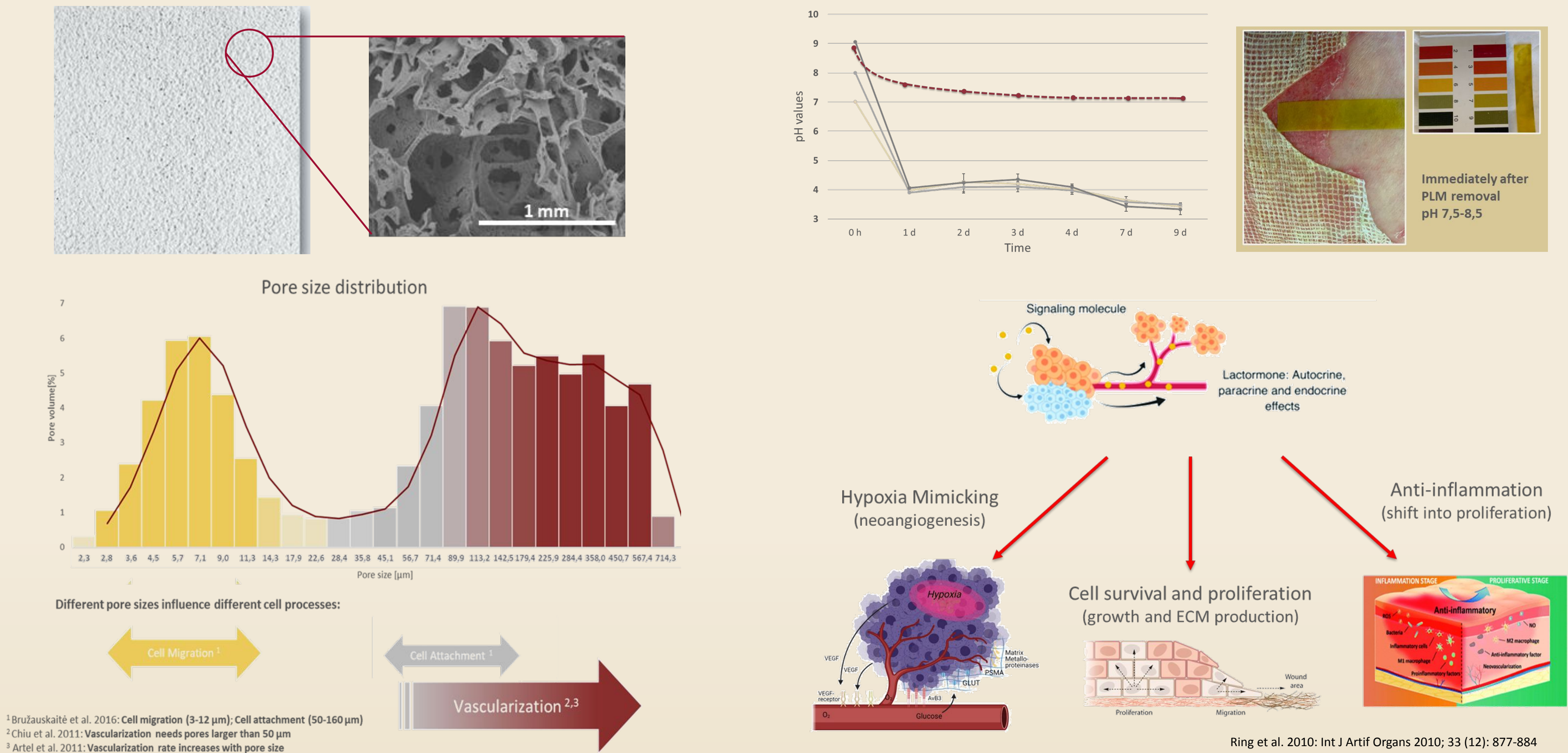
## Background

### Objective:

- To compare the performance of a **poly-lactic acid (PLA)** guided closure matrix vs. a collagen dressing to achieve 100% closure of diabetic foot ulcers.

### Background:

- Foot ulcers affect up to 35% of people with diabetes and represent a challenge for closure.
- Guided closure matrices are often required to accelerate the healing process.
- We recently developed a novel closure matrix made of PLA.
- 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**
- In addition, the lactate causes acidification of the wound bed and a **pH shift** to neutral values.



## Methods

- Patients with diabetes mellitus and a single foot ulcer of at least 3 months of evolution were **included** in the trial.
- Exclusion criteria** were presence of active infection, uncontrolled diabetes mellitus or any other uncontrolled comorbidity, and use of drugs or medications that would affect wound healing.
- Patients were **randomized** to receive either the weekly applications of a PLA matrix or collagen dressings as adjuncts to the standard of care.
- All patients were enrolled in a **single high-volume center** and were treated by the same surgeon.
- The **primary objectives** of the trial was the number of weeks required to attain full closure of the wound.
- The **secondary objectives** included the odds of attaining closure by 12-weeks and 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:

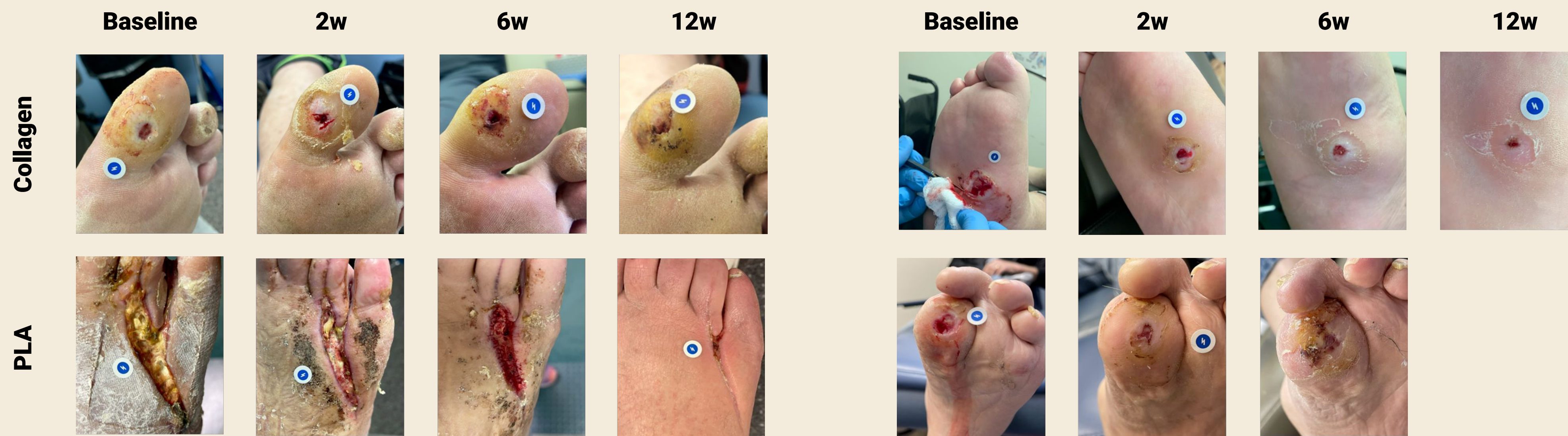
	Collagen (N=10)	PLA (N=10)	Total (N=20)	p-value
Age (years)				0.972 <sup>1</sup>
Mean (SD)	63.800 (14.513)	64.000 (10.488)	63.900 (12.324)	
Range	41.000 - 88.000	49.000 - 78.000	41.000 - 88.000	
Gender				0.653 <sup>2</sup>
Female	5 (50.0%)	4 (40.0%)	9 (45.0%)	
Male	5 (50.0%)	6 (60.0%)	11 (55.0%)	
BMI				0.675 <sup>1</sup>
Mean (SD)	31.800 (8.904)	30.500 (3.719)	31.150 (6.675)	
Range	23.000 - 55.000	27.000 - 36.000	23.000 - 55.000	
Use of tobacco				0.639 <sup>2</sup>
No	7 (70.0%)	6 (60.0%)	13 (65.0%)	
Yes	3 (30.0%)	4 (40.0%)	7 (35.0%)	
HbA1c (%)				0.200 <sup>1</sup>
Mean (SD)	7.570 (0.886)	8.190 (1.179)	7.880 (1.064)	
Range	6.400 - 9.100	6.600 - 10.000	6.400 - 10.000	
Creatinine (mg/dL)				0.271 <sup>1</sup>
Mean (SD)	1.201 (0.589)	1.312 (0.486)	1.265 (0.579)	
Range	0.900 - 2.170	0.814 - 2.310	0.814 - 2.310	
ABI				0.417 <sup>1</sup>
Mean (SD)	1.049 (0.116)	0.994 (0.174)	1.022 (0.147)	
Range	0.840 - 1.210	0.740 - 1.290	0.740 - 1.290	

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

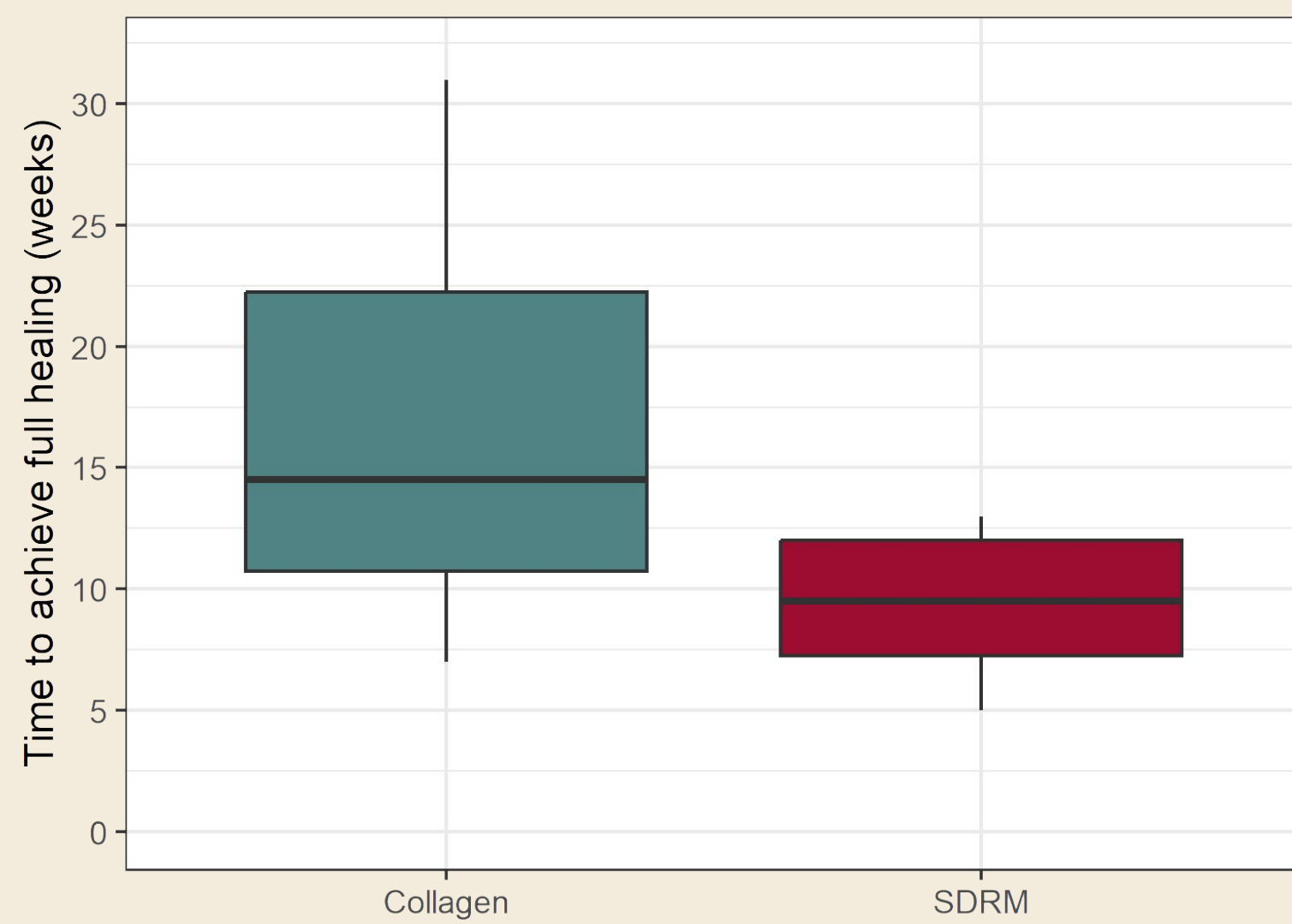
- No significant differences between wound characteristics were found at baseline:

	Collagen (N=10)	PLA (N=10)	Total (N=20)	p-value
Ulcer age (weeks)				0.636 <sup>1</sup>
Mean (SD)	15.400 (3.748)	16.800 (8.390)	16.100 (6.365)	
Range	12.000 - 24.000	10.000 - 38.000	10.000 - 38.000	
Ulcer site				0.287 <sup>2</sup>
Dorsum	4 (40.0%)	4 (40.0%)	8 (40.0%)	
Heel	1 (10.0%)	0 (0.0%)	1 (5.0%)	
Metatarsal	2 (20.0%)	2 (20.0%)	4 (20.0%)	
Plantar	3 (30.0%)	4 (40.0%)	7 (35.0%)	
Granulation tissue area (%)				0.108 <sup>1</sup>
Mean (SD)	44.000 (25.906)	62.000 (21.499)	53.000 (24.942)	
Range	10.000 - 80.000	10.000 - 80.000	10.000 - 80.000	
Non-viable tissue area (%)				0.108 <sup>1</sup>
Mean (SD)	56.000 (25.906)	38.000 (21.499)	47.000 (24.942)	
Range	20.000 - 90.000	20.000 - 90.000	20.000 - 90.000	
Depth (cm)				0.344 <sup>1</sup>
Mean (SD)	0.338 (0.239)	0.473 (0.369)	0.406 (0.310)	
Range	0.100 - 0.800	0.100 - 1.200	0.100 - 1.200	
Area (cm <sup>2</sup> )				0.120 <sup>1</sup>
Mean (SD)	4.066 (2.186)	6.414 (3.984)	5.240 (3.352)	
Range	1.700 - 7.390	2.090 - 12.300	1.700 - 12.300	

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

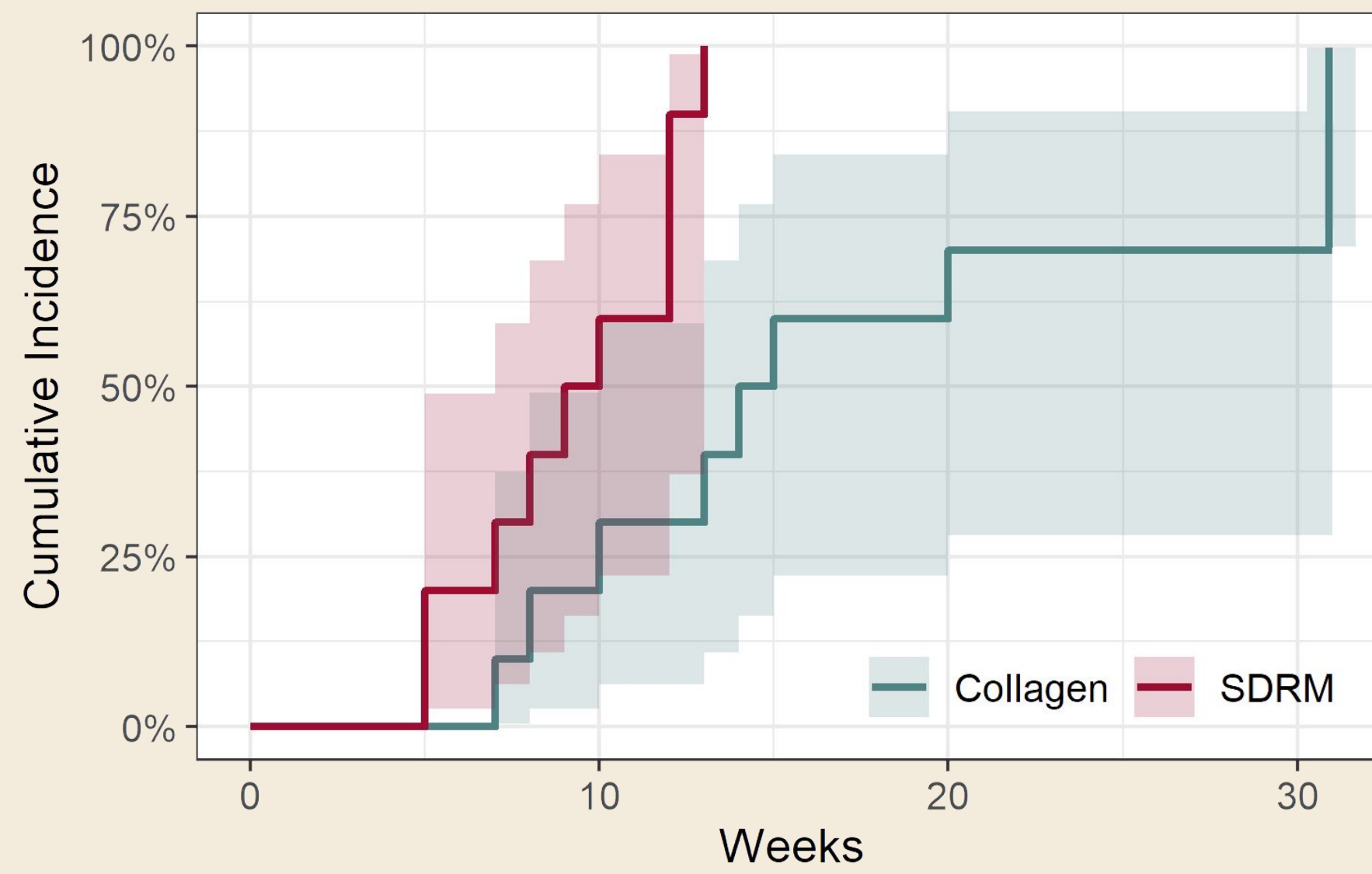


### Time to Heal



Full healing of the wounds was achieved in  $16.8 \pm 8.1$  vs.  $9.3 \pm 2.9$  weeks ( $p=0.021$ ) in the collagen vs. PLA group. This represents a **reduction of 44% of the time** needed to achieve full wound closure, compared to the standard of care.

### Cumulative Incidence of Healing



The cumulative incidence for achieving full closure by 12 weeks with PLA matrices was **90%**. Compared to collagen, the **OR of achieving full closure by 12 weeks was 2.23** (95%CI 1.37 to 4.54,  $p = 0.004$ ).

- No complications or adverse events were recorded during the trial.

## Discussion

- PLA matrices are more effective** than active collagen dressings in promoting diabetic wound closure.
- Its use **reduces the time required to achieve full closure** and **increases the odds of achieving closure by 12-weeks**.
- Proposed **reasons** for this include controlled pore sizes that promote cell attachment, migration, and vascularization of the scaffolds; changes toward a neutral wound pH that may inhibit bacterial growth and promote cellular recruitment; and improved cellular signalling to promote neo-vascularization of the wound.

**In summary, compared to standard of care, the use of a PLA guided closure matrix was more effective to promote closure of diabetic foot ulcers. Specifically, its use led to significant increases in granulation tissue and a reduction of 45% in the time required to achieve full closure of the wound.**

### References

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