

INTRODUCTION

Current solutions for chronic lower extremity wound management using advanced skin substitutes while readily available in many configurations have several disadvantages, including risks of rejection, disease transmission from mammalian sourced materials, and cultural issues prohibiting the use of some products. Further complications for this patient population are co-morbidities extending the time for or preventing wound closure leading to the risk of amputation.

Here, we describe use of the first xenograft tissue derived from the dermis of a regenerative species, neotenic¹ salamanders (*Ambystoma mexicanum* - the axolotl) for clinical wound management in 3 diabetic patients with long-term recalcitrant foot wounds.

¹ - Neotenic – organism retaining juvenile traits into adulthood

METHODS

The medical records of three diabetic, hypertensive patients with non-healing wounds for over 6 months who then received axolotl dermis patches were retrospectively reviewed. These patients (mean age 73.6 years) all failed to progress or close with other advanced dressings before receiving axolotl dermis.

Standard treatment involved:

- Surgical debridement & irrigation
- Application of the FDA-cleared axolotl collagen wound matrix
- Non-adherent primary and appropriate secondary dressings to manage moisture
- Off-loading



Sterile - Elliptical Shape
Axolotl ECM

The wounds were treated with the axolotl dermal collagen wound matrix once a week.

RESULTS

All three patients achieved complete wound closure. Relevant comorbidities related to delayed wound closure include: T2D=3 (100%), HTN=3 (100%); A-fib, hypothyroidism, and hypolipidemia were also documented. All were non-smokers. 100% of the foot wounds treated with axolotl patches epithelialized without reopening during the follow-up period of 3 months or more.

DISCUSSION

All 3 diabetic patients observed as part of this study, with recalcitrant foot ulcers for longer than 1 year, previously unsuccessfully treated with other wound matrices, exhibited 100% wound closure and epithelialization which persisted over a follow-up period of 3 months and up to 5 months as observed during follow up visits.

Use of pro-regenerative axolotl dermis patches for wound management has favorable potential in improving wound closure, preventing poor overall outcomes, and warrants further investigation, and continuing data collection in clinical setting.

Patient 1

Patient 1 : A 68-year-old female with T2D developed a plantar surface heel wound. She was treated with standard of care and bone spur removal after 1 year and developed osteomyelitis. Patient was treated with antibiotics for 6 weeks. The wound remained recalcitrant to standard of care, other advanced dressings and non-weight bearing for 2.5 years. The wound did close 1 time but reopened 1 week later. Axolotl dermis collagen matrix wound patches were applied once a week following debridement. Wound closure was achieved with three applications (% closure: W1=73%, W2=98%, W3=100%). Stable wound closure persisted >5 months as of last follow up visit.

Initial Treatment



Wound: 15mm x 6mm x 2mm
Axolotl WM: 1 patch 1cm x 2cm

Visit 2 – 1 Week



Wound: 15mm x 6mm x 1mm
(3 smaller wounds; measured entire wound)
Axolotl WM: 1 x 15 mm disc

Visit 3 – 2 Weeks

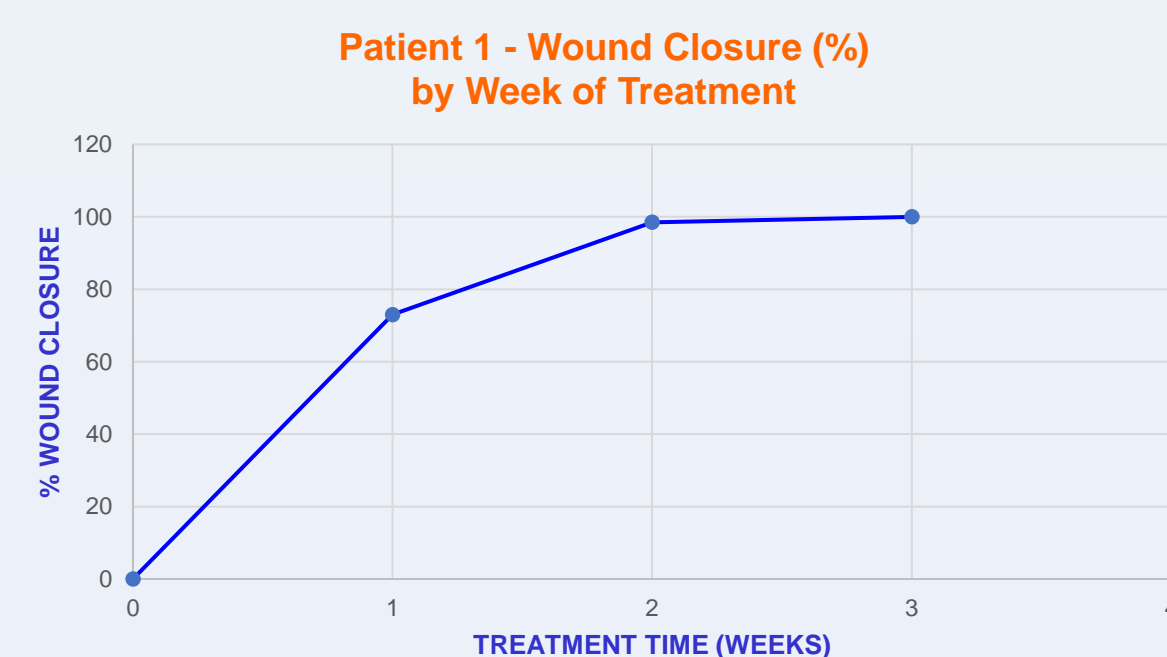


Wound: 4 mm x 4 mm x 0.5 mm
Axolotl WM: 1 x 8 mm disc

Visit 4 (Final) – 3 Weeks - Closed



Remained closed during > 5 months follow-up



Patient 2

Patient 2: A 69-year-old male with controlled T2D developed osteomyelitis following surgical repair of a calcaneal fracture. He was treated with IV antibiotics and developed post-surgical dehiscence along the distal medial malleolus extending to the posterior calcaneus with a total 3.6 cm² wound. Foot pulses were palpable. The wound was managed with standard of care, advanced collagen dressings and off-loading for 18 months but remained open with the presence of necrotic tissue. Axolotl dermis collagen wound matrix patches were applied once a week demonstrating closure of the incision site after 1 week and closure rate of the calcaneal wound W1=17%, W6=94%, W10=100%. Full closure was maintained during a 3-month follow-up period.

Initial Treatment



Wound: 45mm x 8 mm x 4 mm
Axolotl WM: 2 – 2 cm x 3 cm
1 – 1 cm x 2 cm

Visit 2 – 1 Week



Reduced erythema, Incision site Closed

Visit 3 – 2 Weeks



Pain reduced
IV Antibiotics discontinued by Visit 4 and started oral antibiotics

Visit 5 – 4 Weeks



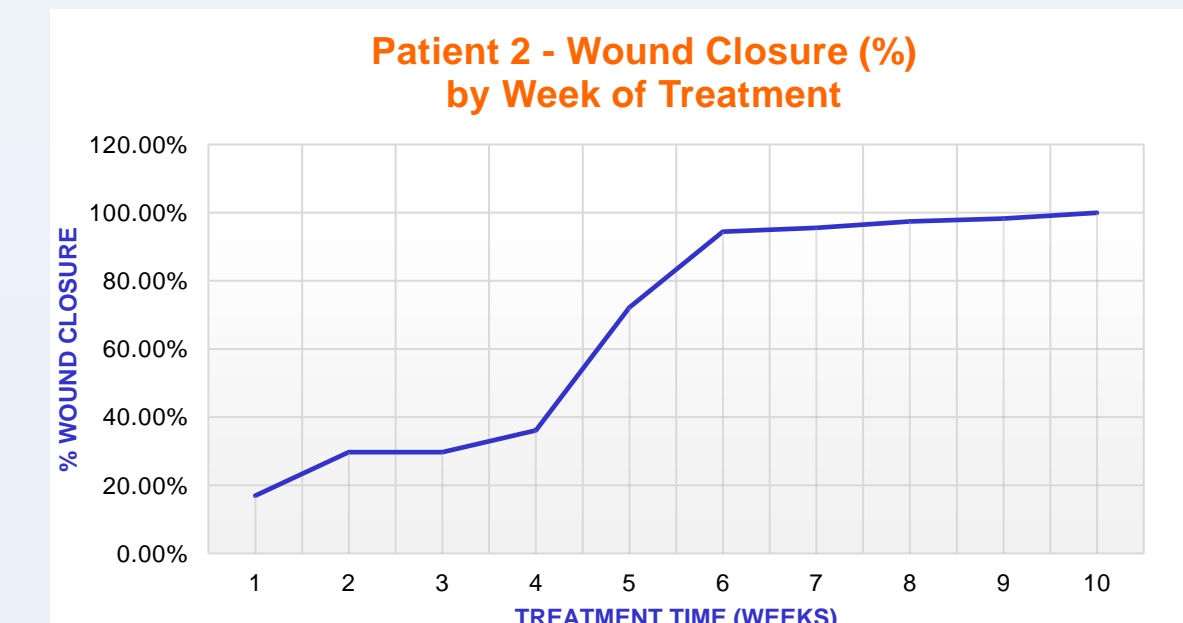
No Pain. Appears closed with pinpoint opening after crust removal

Wound: 23mm x 1 mm x 2 mm
Axolotl WM: 1 15 mm & 1 10 mm disc

7-9 Weeks Pinpoint Opening 8mm disc applied each week

Visit 11 – 10 Weeks Closed

Patient has remained closed for 11 months and returned to work on his cattle ranch.



Patient 3

Patient 3: This 76-year-old female presented with a full thickness persistent plantar heel pressure wound present for 5 months, no foot pulse, patient undergoing chemotherapy and irradiation for Stage IV Lung Cancer. Axolotl dermis patches were applied once a week demonstrating closure rate of W1=35%, W9=96%, W10=100% resulting in durable wound closure sustained for 3 months.

Visit 1 – Initial Treatment



Wound: 20mm x 13 mm x 1mm
Axolotl WM: 1 – 1cm x 2cm

Visit 2 – 1 Week



Wound: 17mm x 10 mm x 1mm;
Axolotl WM: 1 – 1cm x 2cm

Visit 3 – 2 Weeks (no picture) Wound: 15mm x 9mm x 1mm

Axolotl WM: 1 – 10 mm disc

Visit 5 - 4 Weeks

Wound: 13mm x 9mm x 1mm
Axolotl WM: 1 15 mm disc

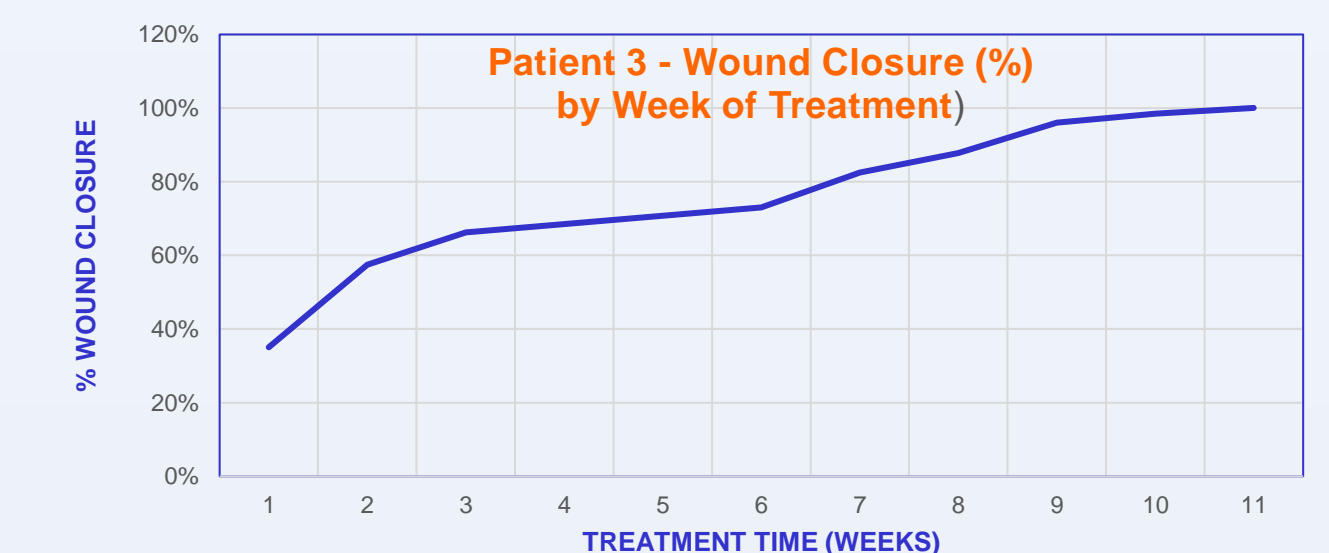


4-7 Weeks (no picture) Plateau

8 Weeks (no picture) significant reduction in size to 4mm x 4mm

9 Weeks (no picture) significant reduction in size to 2mm x 3mm

10 Weeks – 100% closure



REFERENCES

- (1) Mu et al, FASEB J. 2014 Sep 28(9): 3919–3929.
- (2) Seifert et al, PloS One 2012 7(4): e32875.
- (3) McCusker et al, Gerontol 2011 57: 565–571.

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