

# Pilot investigations into the impact of microcurrent Electrical Stimulation Therapy (EST) and Negative Pressure Wound Therapy (NPWT) - alone and in combination - in a porcine full-thickness excision wound model

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## Introduction:

Microcurrent electrical stimulation therapy (EST) has been shown to both relieve pain and expedite the healing of a range of acute and chronic wounds.<sup>1</sup> This pilot *in vivo* study was undertaken to compare the impact of EST on wound healing with that of single-use negative pressure wound therapy (sNPWT) and to investigate the possibility of synergistic effects when both therapies are combined.

## Methods:

- This study employed a previously described porcine model.<sup>2</sup>
- Briefly, under anaesthesia, two full-thickness circular excisional wounds (3.0 cm diameter) were created on both dorsal flanks of 6 large white domestic pigs (4 wounds per animal).
- All wounds on a given animal received the same treatment: wounds on 2 animals (n=8 wounds) received:
  - EST (Accel-Heal Solo)\* with Allevyn Gentle Border (Smith & Nephew, Hull, UK) as a secondary dressing. The EST electrodes were positioned 10 cm apart either side of the wound.
  - NPWT (PICO, Smith & Nephew, Hull, UK; no secondary dressing needed)
  - EST + NPWT at the same time (no secondary dressing needed).
- Dressings/treatment devices were applied on Day 0, immediately after injury, and subsequently removed and replaced under anaesthesia on post-wounding days 3, 6 and 9.
- Wounds and devices were protected from damage during the study using padding and custom-made jackets.
- Wound healing was assessed through overall wound area reduction and its component contraction and re-epithelialisation by image analysis at day 3, 6, 9 and 12.
- Animals were euthanised on day 12 and tissues were taken for histology.
- Histological parameters, including granulation tissue deposition, re-epithelialisation, collagen deposition, cellular proliferation, angiogenesis and  $\alpha$ -smooth muscle actin expression were assessed at day 12.
- Statistical comparison was carried out using the two sample Mann-Whitney test.

## Results:

- EST and NPWT therapies operated normally, alone or in combination, with no electrical interference detectable between the 2 devices.
- Similar rates of wound closure were observed between groups with a mean of 86.5% or more of the original wound area closed by day 12: (EST 89.1%  $\pm$  9.8; NPWT 85.25%  $\pm$  9.0; EST + NPWT 85.17%  $\pm$  9.1 (mean  $\pm$  standard error, n=8, **Figure 1**).

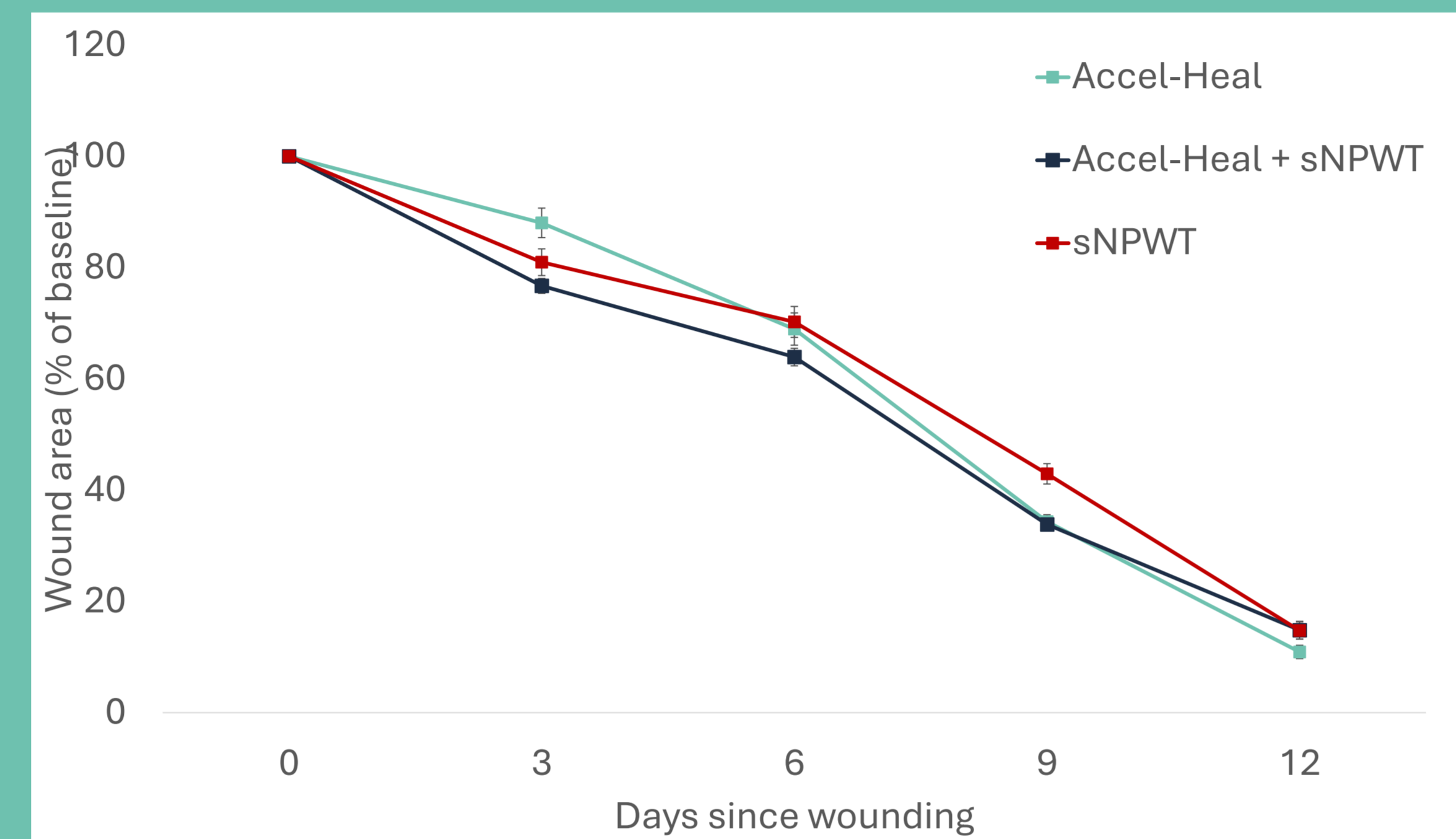


Figure 1. Wound Closure over time (% Wound Area Remaining,  $\pm$  SEM, n=8).

- The ratio of wound closure by contraction or re-epithelialisation was 80:20 for wounds treated with Accel-Heal vs 65:35 for those treated with sNPWT and an intermediate value (74:26) for those treated with both treatment types (**Figure 2**) whereas NPWT favoured wound closure with re-epithelialisation: 65% contraction 35% re-ep (**Figure 2**).
- By day 9 and 12 post-wounding, the rate of wound closure by contraction was significantly greater in wounds treated by Accel-Heal than sNPWT ( $p < 0.01$ )

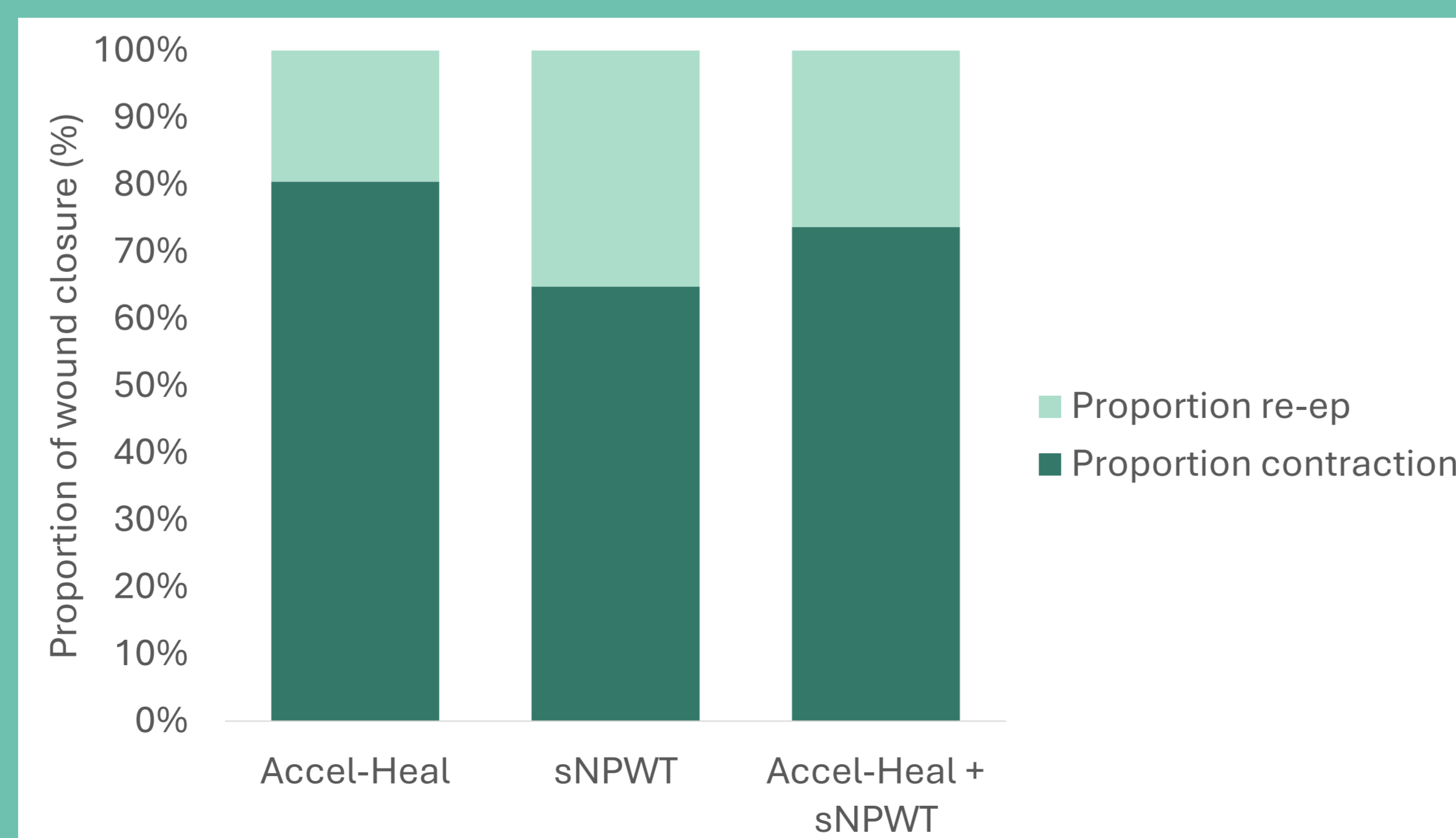


Figure 2. Proportion of wound closure due to contraction or re-epithelialisation. Represents the closed wound areas after 12 days, n=8. wounds.

- H&E histology at day 12, identified similar width of re-epithelialisation with Accel-Heal treatment compared to the other two treatment groups (not significant, **Figure 3**).

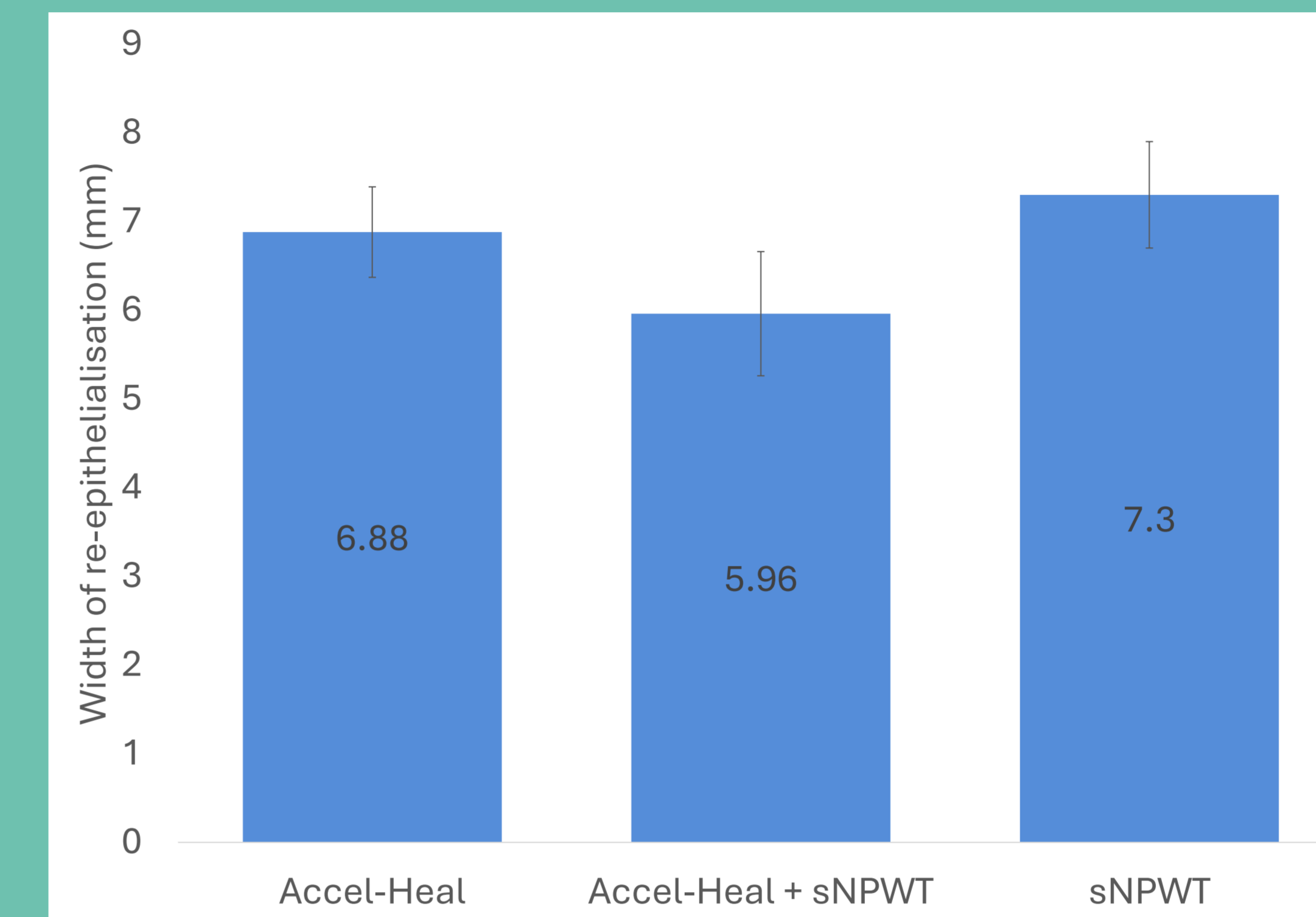


Figure 3. Width of re-epithelialisation measured by histology. n=8. wounds.

- Immunohistochemical assessment of % granulation tissue area expressing  $\alpha$ -smooth muscle actin revealed an increase in SMA expression in wounds treated with both devices ( $p < 0.001$ ) vs sNPWT only or Accel-Heal only (**Figure 4**).

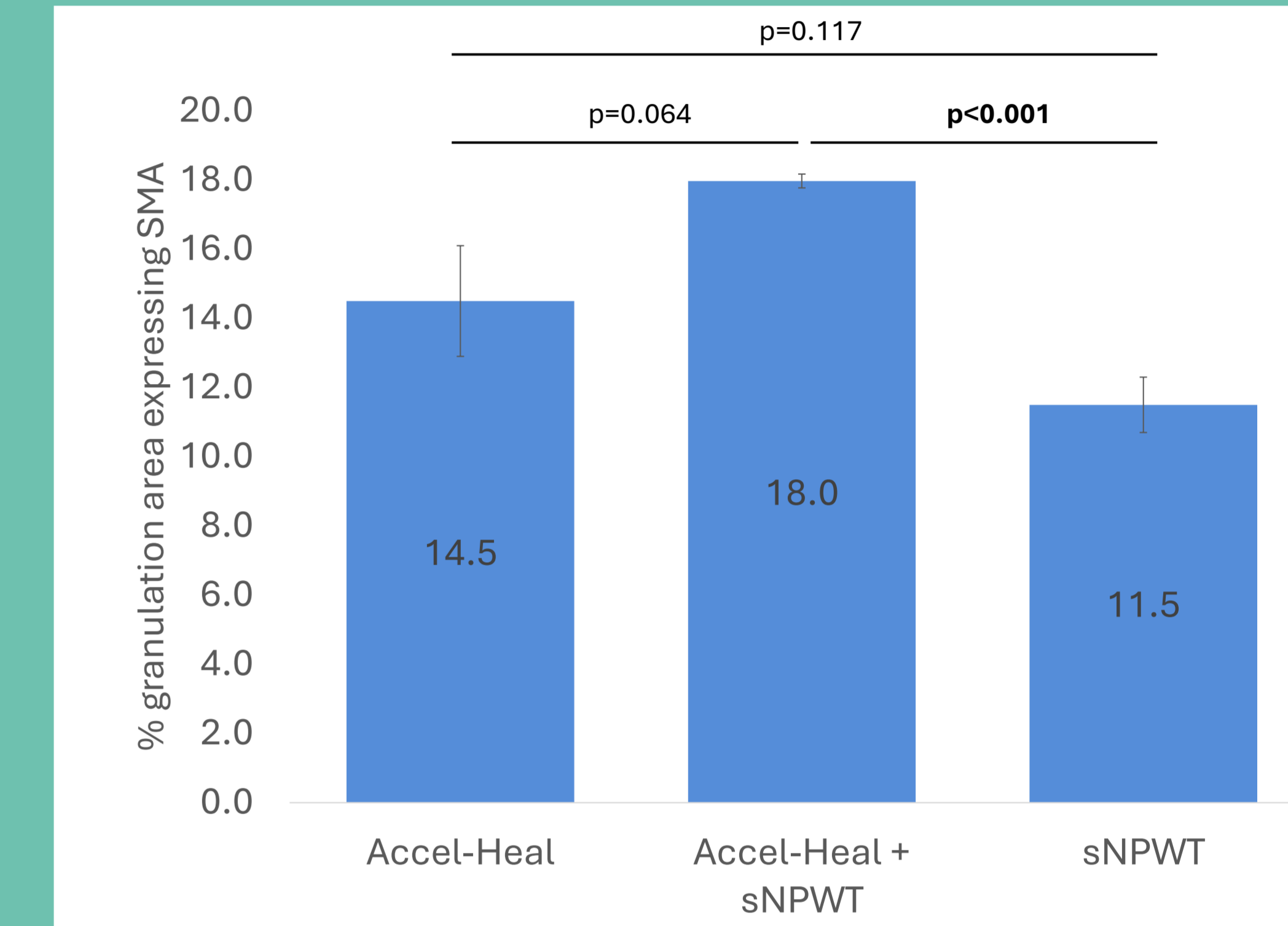


Figure 4. Area of granulation tissue composed on SMA. n=8. wounds. SMA, alpha-smooth muscle actin.

## Discussion:

- This pilot scale study of wound closure in an acute porcine model suggests some differences in the wound response to advanced wound management devices alone or in combination.
- Although similar overall rates of wound closure were seen between groups, there was a suggestion that the mechanism of closure may differ slightly. The proportion of the wound closed by either contraction or re-epithelialisation at day 12, suggested that EST favoured closure through tissue contraction (compared with wounds treated with sNPWT), a finding further supported by the increased  $\alpha$ -smooth muscle actin in wounds treated with Accel-Heal and validated previously in similar models.<sup>3</sup>
- This preclinical data suggests that combined treatment with EST and NPWT, with promotion of contraction by EST together with the promotion of re-epithelialisation by NPWT, may be an effective clinical protocol by which to promote the healing of chronic wounds.
- The findings are supportive of clinical observations using EST where a faster rate of healing has been reported compared to standard of care in venous leg ulcers,<sup>4</sup> and activation of healing and reduction in pain demonstrated across various chronic wounds.<sup>1</sup>

## Conclusion:

Microcurrent EST and NPWT have been used together successfully in an acute excisional wound model with data suggesting a stimulation of wound closure by tissue contraction adding further support to the mode of action of EST and its impact on wound healing. Further studies are recommended to confirm these findings and explore combination EST/NPWT therapy in patients with hard to heal wounds.

Poster presented at Wounds UK, Harrogate, UK, Nov 2024.

\*Accel-Heal Solo, Accel-Heal Technologies Limited, Hever, Kent, UK. This study was funded by Accel-Heal Technologies Limited, Kent, UK and medical writing support provided by JMS medical writing services Ltd.

References 1. Kurz, P., et al. Int. Wound J. 20, 2053–2061 (2023). 2. Brownhill, V. R. et al. Adv. Wound Care 10, 345–356 (2021). 3. Yang, J. et al. Bioelectrochemistry 148, 108247 (2022). 4. Guest J. et al. J Wound Care. 2018;27(4):230-243,



Figure 1. Microcurrent EST device, Accel-Heal Solo\*