Porcine Model of Delayed Wound Healing: Effect of Surgical Debridement

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Background: Rodent or porcine diabetic models are frequently used to model chronic wounds but these models are unable to fully replicate the clinical complications, especially chronicity of the wound. Previously[1], we demonstrated a model to simulate healing impairment in chronic wounds, such as diabetic ulcers, caused by glycosylation of collagen resulting from extended exposure to hyperglycemia[2]. We showed *in vivo* that glutaraldehyde crosslinking of dermal tissue can significantly delay wound closure. In this follow-up study, to simulate clinical intervention, we surgically debrided the crosslinked wounds and treated with a collagen based scaffold to evaluate the impact on healing time and tissue quality.

Methods: Circular full-thickness wounds (2 cm diameter) were created on the dorsum of Yorkshire pigs. To rapidly simulate glycosylation of collagen, wounds were immediately treated with 5% (v/v) glutaraldehyde for 5 minutes to crosslink collagen and other connective tissue followed by a flush of isotonic saline to remove any residual treatment. Crosslinking treatment was repeated on Day 0 and 1. Wounds were surgically debrided on Day 3. A collagen based dermal matrix was applied either immediately post debridement or 4 days after. Animals were sacrificed at Day 21 and wounds were harvested for histology.

Results: The control (non-crosslinked, non-debrided) wounds healed more rapidly than glutaraldehyde-treated wounds. The control, debrided wounds were smaller than the glutaraldehyde-treated wounds (whether debrided or not) on days 17 and 21. Further, in crosslinked tissues, no effect of collagen treatment 4 days post debridement could be detected. The use of a collagen matrix did not accelerate or delay healing of test or control wounds in this model over a 21-day time-course. Histology revealed that inflammation associated with crosslinking often masked subtle changes of debridement and/or collagen scaffold treatment.

Conclusion: Glutaraldehyde-treatment of dermal tissue can significantly delay wound healing *in vivo*. However, 5% glutaraldehyde exposure causes inflammation and tissue destruction that diminishes the ability of the model to detect post-debridement related changes. It remains to be studied if the degree of wound closure and/or intensity of tissue damage can be modulated by varying the concentration of the crosslinking agent.

References:

1. Kharge A et. al. Development of a Porcine Model of Delayed Wound Healing, podium presentation, Session 3B, the 2016 Symposium on Biomaterials Science, Oct 2016.
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