Porcine Model of Delayed Wound Healing: Effect of Surgical Debridement
Angana Kharge1, Ankur Gandhi1, Paul Attar2, Sarah Korn2, Kan Lam2, Sunil Saini1
1Integra LifeSciences, Plainsboro, NJ
2BRIDGE PTS, Inc., San Antonio, TX

**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. Previously1, 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 hyperglycemia2. 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:**