Anatomical Effects in the Development of a Delayed Wound Healing Model

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Statement of Purpose: ACell currently markets multiple configurations of its Urinary Bladder Matrix (UBM) MatriStem® biomaterials. A delayed healing model of ischemic wound sites with intrinsic controls [1] was developed to investigate the vulnerary properties of a novel gel form of the extracellular matrix (ECM)-derived MatriStem wound dressing. A second study was initiated to 1) evaluate the validity of the use of the lateral control wounds on the ischemic model and 2) determine if there were systemic effects of the bipedical flap on the healing of the lateral control wounds in the first study.

Methods:
Study 1: Four 8.0mm wounds were created in 16 Sprague-Dawley rats, down to but not through the anterior fascia of the panniculus carnosus muscle layer of the skin, 2.0cm down from the cranial edge of the dorsal midline of each rat. The location and size of the wounds were optimized in 3 preceding studies. A bipedical skin flap was created using two linear incisions in the cranio-caudal direction, measuring 8.0cm long and 3.0cm wide. The bipedical flap was then lifted from the underlying tissue and a 6.0cm x 4.0cm pre-cut sterile silicone sheet was placed underneath the flap. The silicone was cut shorter than the bipedical flap to avoid fluid buildup of the wound and buckling of the silicone sheet. Silicone sheets were sutured to the flap and native tissue. Ischemic wounds (within the flap) were treated with the appropriate saline volume (20µl) on Day 0. Wounds outside the flap were considered internal controls for all animals (n=16). All wounds were covered with a sterile non-adherent silicone dressing (Mepitel, Molnycke) followed by a sterile occlusive dressing (Renasys, Smith & Nephew). Digital photography, wound measurements, and dressing changes occurred on Days 0, 3, 7, 10, and 14, and Days 17 and 21 as needed.

Study 2: Four 8.0mm wounds were created in 10 Sprague-Dawley rats, down to but not through the anterior fascia of the panniculus carnosus muscle layer of the skin, 2.0cm down from the cranial edge of the dorsal midline of each rat. The pattern and location of the four wounds were identical to those in Study 1 with the exception that no bipedical skin flap was created. Wounds in the center where the flap would be were treated with saline as previously performed. Outside wounds were left untreated. These control treatments replicated those in Study 1.

Results:
Study 1: On average, ischemic wounds showed delayed healing when compared to control wounds at Days 3, 7, 10, 14, and 17 days (Figure 1). The data suggested that the model could be used for ischemic wounds with two internal controls for each rat.

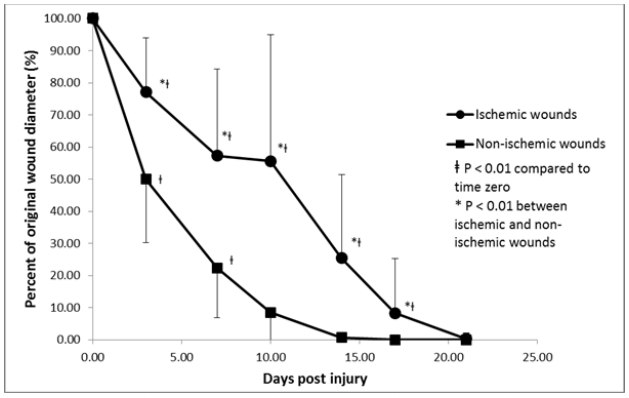

Figure 1: Ischemic wounds compared to non-ischemic control wounds.

Study 2: The rate of healing of the 2 lateral wounds were compared to the 2 medial wounds to determine whether the outside wounds could serve as controls for the ischemic wound model. Results showed that the outside wounds healed much faster than the inside wounds, even with adequate vascularization (Figure 2). These data suggest that there are positional effects that vary with the anatomy of the rat, which means that the lateral wounds are inadequate controls for the medial ischemic wounds.

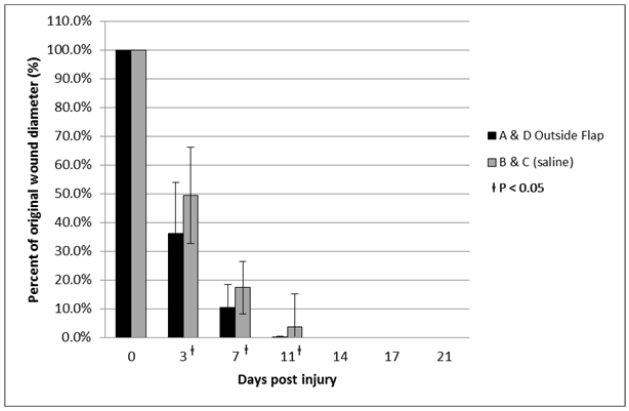

Figure 2: Positional effects of control wounds on a rat model.

Conclusions: Positional effects of wounds are an important parameter to evaluate before finalizing any wound model. It is important to consider where the model may have deficiencies in order to save time and resources on future studies.

References:
1 Kentner et al. 2013. Wound Healing Society 2013 Annual Meeting. Denver CO, May 2013 [accepted].

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