Porcine Integumentary System Models: Part 2-Wound Healing

M. Michael Swindle, DVM, Professor and Chairman, Department of Comparative Medicine, Medical University of SC, Charleston, SC 29425

Introduction
Swine have been a standard model for wound healing for many decades. This manuscript provides an overview of the models that may be utilized for studying wound healing, closure techniques, wound treatments and bandaging. This manuscript is complementary to Porcine Integumentary System Models: Part 1-Dermal Toxicology which is located on this website and contains information on the anatomy and physiology of pig skin. An overview of the techniques of producing these wound models surgically and the perioperative care issues involved in their maintenance has been published.1

Comparison to Other Animal Models
Rodents, rabbits and pigs have been most commonly used as models of epidermal regeneration and dermal repair. Aspects of epidermal regeneration that have been studied in swine include migration, proliferation and differentiation. Wound closure, tensile strength and bioassays of specific components, such as collagen, have been performed in pigs and compare favorably to humans. Surgical wounds heal by a combination of epithelization and dermal repair. Within hours epithelial cells at the margin of a wound begin to migrate and proliferation starts occurring within 24 hours. Differentiation follows as cells migrate from the basal epithelial layer. The dermal layer heals by the formation of clots and inflammation by leukocytes and macrophages which signal fibroblasts to synthesize collagen. Full thickness excisional wounds undergo wound contraction which can be grossly quantified as a phase of wound repair.1-8 Because of their size multiple wounds can be placed on the same animal, thus allowing the animal to serve as its own control. Most studies place the wounds bilaterally on the flanks.

Rabbit and rodent models are used in wound healing mainly because they are inexpensive and can be used for screening tests, however, they have significant differences from humans because they have dense pelage, a thin epidermis and dermis and they heal predominately through wound contraction.7 Because pigs have fixed skin their gross healing characteristics quantify as being similar to humans including having similar elastic properties. Swine and humans have a comparable dermal:epidermal ratio of 10-13:1 and actual skin thickness varies between regions of the body.7 Reepithelization is an important component of wound healing in swine as in humans. Farm pigs may have exaggerated wound healing because of their rapid growth characteristics. Miniature pigs have been used for chronic wound healing models because they more accurately simulate adult human healing rates.3

Swine have been used extensively as a model for partial thickness and full thickness excisional...
wounds, as well as for skin substitutes, burn treatment and plastic surgical techniques.\textsuperscript{1-10} In comparison to humans 25 porcine wound therapies were compared to studies in humans, small mammals and in vitro techniques. The porcine models were in agreement with human studies 78\% of the time as compared to <60\% of the time with the other types of studies.\textsuperscript{7}

**Excisional and Incisional Wound Models**

Partial thickness cutaneous wounds in swine have significant reepithelization as a primary component of the healing process. Full thickness excisional wounds require wound contraction and granulation as the initial process for healing. These are different from incisional wounds made by a scalpel.

Partial thickness wounds are created with a dermatome. The size of the lesions varies between studies but generally they are square lesions which fall in the range of 2.2 – 3.0 cm on each side (ie 2.5 X 2.5 cm).\textsuperscript{1-10} Dermatomes are set at varying depths. Split thickness skin grafts are an average of 300 µm in depth and that is a starting point for some studies.\textsuperscript{9} Most studies range from 270 µm to 400 µm in depth for superficial wounds. Deep wounds may be made >800 µm in depth. In general the wounds do not exceed a total of 24 on the flanks of the pigs (12 on each side). There is a significant difference in the healing rate of these wounds between farm breeds and Yucatans. Farm pigs have a 50\% reepithelization rate in 54 hours versus 96 hours for sexually mature Yucatan minipigs.\textsuperscript{3} This difference is due to a difference in maturity at the same weight. Likewise deep wounds heal faster in farm pigs. Miniature pigs would probably more closely resemble the human situation than farm pigs.

Full thickness wounds are created using either scalpel incisions or biopsy punches to create a lesion to the depth of the fascia (Figure 1). These deep wounds have wound contraction and granulation as the predominate form of healing initially. Excision wounds at this depth are generally made in a size of 3-5 cm on a side. Circular lesions may be created with biopsy punches in a size of 1-2 cm. These wounds tend to heal by development of scar tissue. The depth of the wounds varies from 0.8-1.5 cm depending upon the location of the wound. The most common area is bilaterally on the flank. Wounds of this size usually have a volume of 10-15 ml. Full thickness wounds are generally limited to 8 per animal. Wounds of this size would be expected to achieve 40\% reduction with granulation in 7-8 days.\textsuperscript{1, 3, 10}

Incisional wounds are made with a scalpel or test devices such as electrocautery units or lasers (Figure 1). Incisional wounds are also studied for testing new closure devices or suture materials (Figure 2). The depth and location may vary depending upon the goals of the study. Wound healing is quicker than for the other types of
wounds and each animal should be used for its own control.

**Figure 1.** Full thickness wounds made with a biopsy punch (left) and incisional wounds made with a scalpel (right).

The effects of radiation, steroids, infections and chemicals can be studied as they affect wound healing in any of these models. The wounding is followed sequentially by photography, measurement and testing of biopsies.

**Skin Flaps and Grafts**
Swine have long been utilized as models to study the effects of treatments on skin flaps and grafts due to the physiologic similarities to humans as discussed above. Kerrigan et al. published a detailed summary of the various types of flaps and grafts studied in plastic surgery. Her outline will be used to discuss the procedures in this manuscript. Generally the lengths of the skin flaps are longer than the length described in order to ensure a zone of necrosis.

Random skin flaps are made on the dorsal flank, the buttocks or the limbs. They are generally made as full thickness flaps. The survival sizes for the various flaps are as follows: dorsal flaps = 4 cm wide X 6.75 cm long, buttocks flaps = 10 cm wide X 4.6 cm long, forelimb = 7.2 cm long, hindlimb = 6.7 cm long. Illustrations of these procedures have been published.

Arterial skin flaps include an arterial pedicle. These are formed on the ventral abdomen with the intercostal artery, on the buttocks with the superficial circumflex iliac artery and on the hindlimb with the saphenous artery. Survival lengths are: ventral = 4 cm wide X 8.6 cm long, buttocks = 10 cm wide X 13.3 cm long. The saphenous arterial flap is easily damaged by the pig because of its location on the inner thigh and has a poorly defined survival length.

Myocutaneous flaps include the underlying muscle and a vascular supply and fasciocutaneous flaps include the skin and deep fascia. Many types of myocutaneous flaps have been utilized including: latissimus dorsi, gracilis, rectus abdominus, trapezius, pectoralis profundus and biceps femoris. The most commonly used and best defined flap is the latissimus dorsi muscle with the thoracodorsal artery. A flap of 10 cm width X 16 cm length is the survival size. The gracilis flap uses the femoral artery and has the
disadvantage of being on the medial aspect of the thigh. The rectus abdominis flap includes the cranial epigastric artery. Both of these are easily damaged by the pig because of their location. The other flaps are rarely used and only for a specific reason, such as the muscle type. The latissimus dorsi is a Type V, the gracilis a Type II and the rectus is a Type III. The fasciocutaneous flaps are on the fore and hindlimbs. The forelimb has a survival length of 8.2 cm and the hindlimb 7.9 cm.

Grafts have been frequently studied as treatments for conditions such as burn injuries or radiation damage. Artificial skin grafts and various bandage materials have been used.

Burns can be induced by using brass blocks heated to 170° for 10 sec for superficial wounds or 20 sec for deep wounds. Untreated wounds of 50 cm² can be expected to heal in 2-3 wk. Scalds are made by 800 water poured into a PVC cylinder for 10-40 sec. They may also be induced by heat pads or laser injuries as well as radiation exposure.

Postoperative Care
All of these models require anesthesia during induction of the lesions and complete aseptic technique. Use of some analgesics, such as anti-inflammatory NSAIDs, can be contraindicated because of their effects on inflammation and healing. However, if they are not contraindicated they should be used. The use of morphine

Figure 2. Wound closure with an experimental subcutaneous stapling device.

Figure 3. Thermal injury caused by a dispersive electrode grounding pad used in radiofrequency ablation.
epidural injections has been demonstrated to be effective for wounds caudal to the thorax. Use of bandaging materials, such as orthopedic stockinette around the whole body, should be used to protect the wound. Animals should be monitored closely for discomfort and infection. Use of deep bedding or padded floors may be useful. ¹

Animals may be lightly sedated with diazepam (0.5mg/kg po) for daily examinations and photography. Midazolam (100-500 µg/kg) can be utilized for complete restraint of a short duration. Techniques are described completely in the references and also on the anesthesia and perioperative care modules on this website. ¹

References
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