Retrospective Analysis of nearly 300 Wounds from Porcine Wound Healing Studies Performed over 6 Years

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ABSTRACT

Pigs are one of the most heavily utilized models for the development and testing of novel drugs and dressings in the field of wound healing. As a contract laboratory specializing in wound care, BRIDGE PTS, Inc. has a large body of historical data on wound healing rates in Yorkshire pigs within a specific range of age and size.

The purpose of this analysis was to compare the data from nearly 300 control wounds from multiple wound healing studies performed over a roughly 6-year period. Data from these studies was collated and overall trends were delineated. The analysis shows that, in this model, a clearly recognizable healing curve can be observed: with the inflammatory phase occurring from Days 0 to 4, the regenerative phase occurring from Days 4 to 14, and the remodeling phase occurring from Day 14 onward. Extrapolated rates of change for these different periods are also reported.

This data could be useful in future studies for the verification of normative wound behavior and as a baseline for comparison with novel wound healing agents or dressings designed to accelerate or decelerate wound healing.

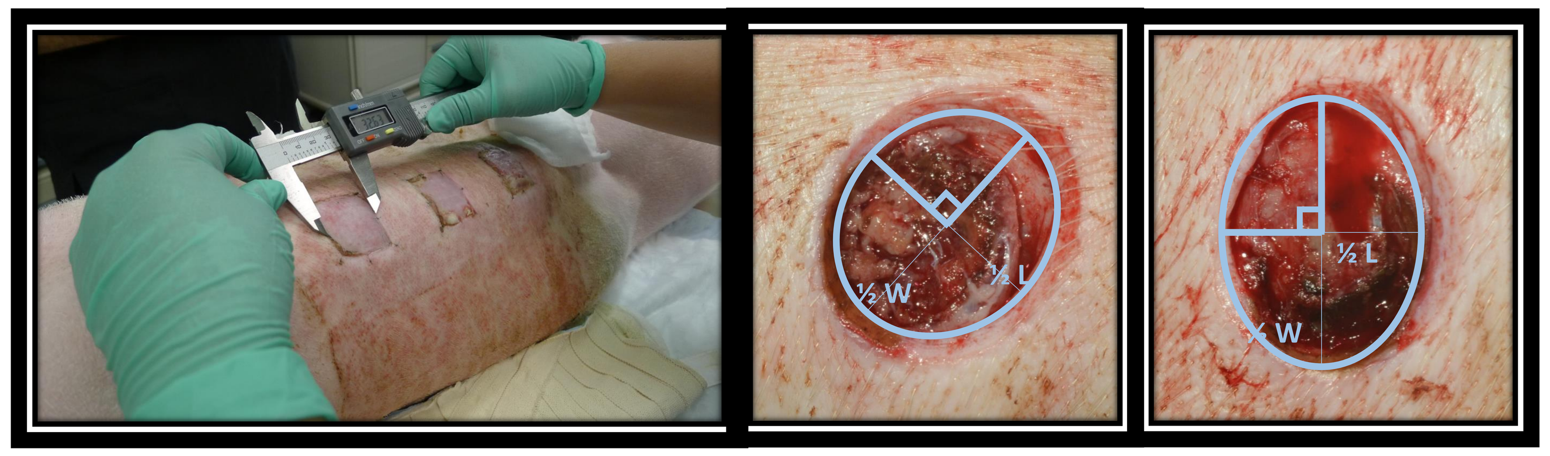
METHODS

This data analysis looked at nine studies, performed by BRIDGE PTS, occurring over a six year period. In total, data from thirty (30) Yorkshire-cross pigs was included in the investigation, for a total of 295 wounds. The pigs were selected from breeding stock to be within 30–40 kg at the start of their respective studies and were assigned randomly. The studies varied in length from 7 days to 29 days. The analysis was solely concerned with control wounds, receiving standard-of-care treatment only.

On Day 0, full-thickness, circular, 2cm diameter wounds were created on the dorsal sides of the pigs, parallel to the spine. The number of control wounds on each animal varied from study to study, but was on average ten (10) wounds. Dressing changes took place every three to four days, with special care taken to promote moist wound healing. Wound size was measured using digital calipers and the area calculated using the equation for an ellipse. The percentage change of wound size was calculated by dividing the area of each wound on its measurement day by the initial wound size, measured on Day 0.

In addition, a pair of studies taking place roughly five years apart was analyzed to determined whether or not a statistical difference could be observed in the wound healing rates over that five year period of the organization's operation.

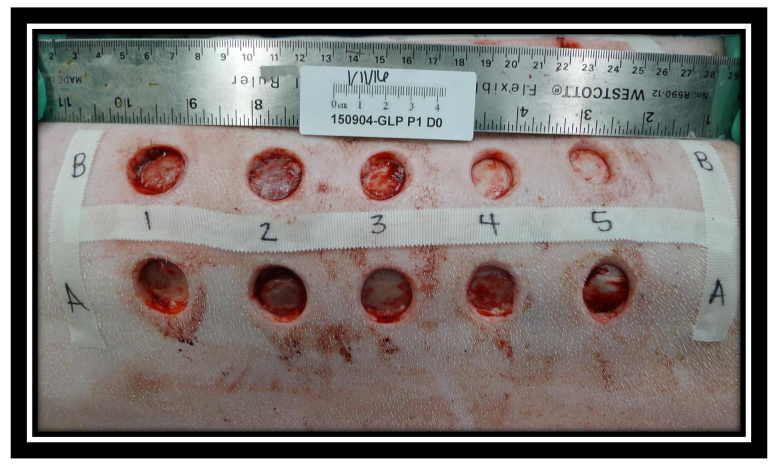
WOUND MEASUREMENT METHODOLOGY



The wounds were measured at least once every seven days (with periodic measurements scheduled between, dependent on the specific study's design). Digital calipers were used to measure the distance across the widest part of the wound as well as the narrowest part of the wound. The estimated wound area was approximated using the equation for an ellipse.

RESULTS

Full-Thickness Wounds Captured on Day 0, Day 14, and Day 28



A representative image of Day 0 wounds, immediately following wounding and hemostasis.

A representative image of Day 14 wounds, immediately following bandage opening. Typical of this timepoint, fresh granulation tissue has completely refilled the wound space.

A representative image of Day 28 wounds, immediately following bandage opening. Typical of this timepoint, reepithelialization and remodeling have resulted in near-total wound closure.

Figure 1. Wound Size as a Percentage of Day 0

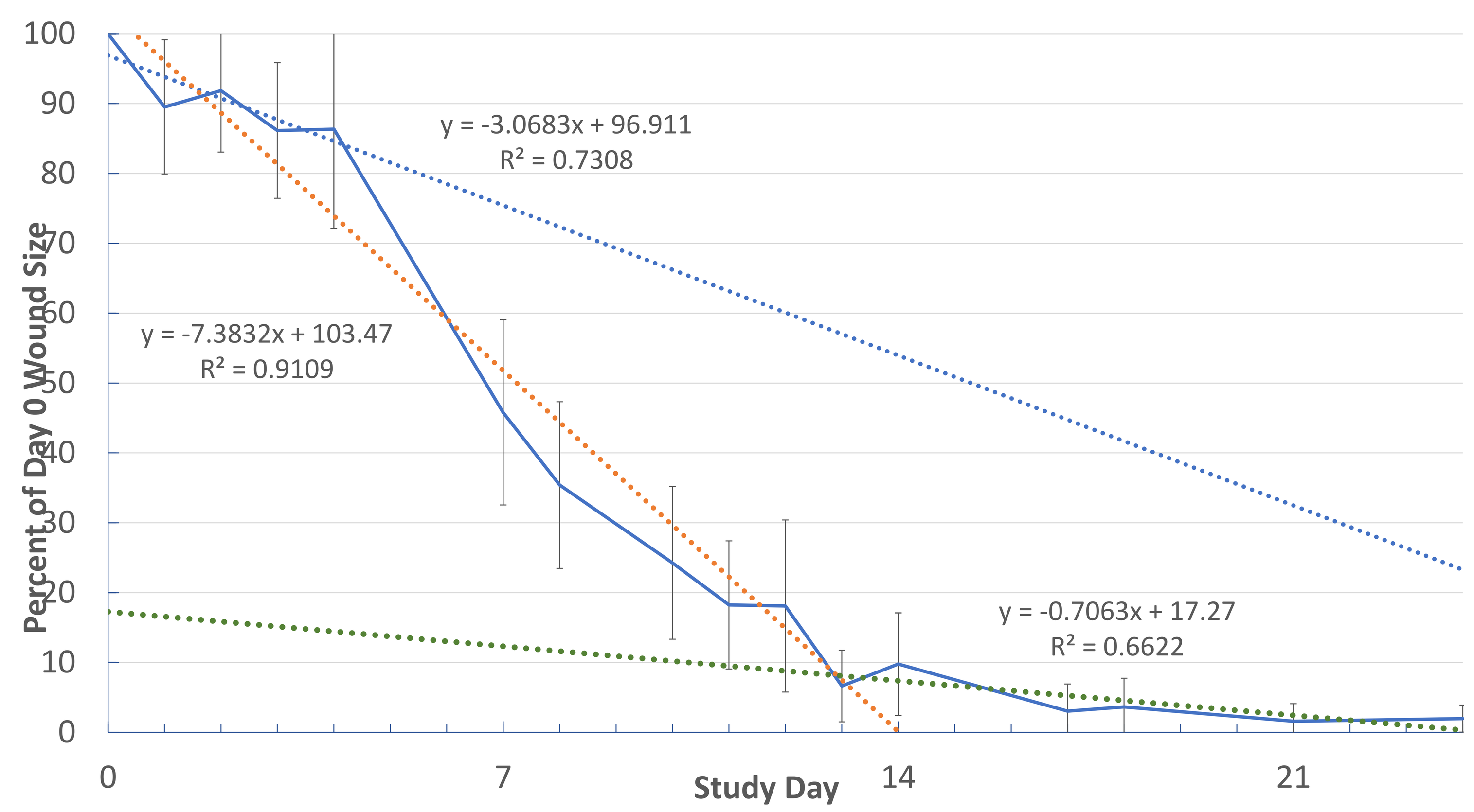


Figure 1 demonstrates the rate of healing of the wounds across all nine studies over six years. The data very closely approximates a typical healing curve with the slow "Inflammatory" phase followed by the rapid "Regenerative" phase and the "Remodeling" tail-end clearly discernable. Three linear regression lines have been included – one representing the period from Day 0 to Day 4, demonstrating the Inflammatory phase, one representing the period from Day 4 to Day 14, demonstrating the Regenerative phase, and the third representing the period from Day 14 to Day 24, demonstrating the Remodeling phase of healing.

RESULTS (CONTINTUED)

Figure 2. Wound Size as a Percentage of Day 0

	Study Day																
	0	1	2	3	4	7	8	10	11	12	13	14	17	18	21	25	29
Average (%)	100	89.52	91.85	86.15	86.35	45.79	35.39	24.26	18.24	18.09	6.62	9.76	3.03	3.63	1.57	1.96	1.49
Standard Deviation (%)	0.0	9.60	8.80	9.71	14.18	13.25	11.92	10.93	9.18	12.32	5.12	7.34	3.89	4.12	2.52	1.93	1.92
Median (%)	100	89.90	91.15	83.10	86.70	44.00	33.55	22.95	17.10	14.45	5.35	8.10	1.45	2.70	0.40	1.40	1.00

The table above is a numeric representation of the average wound sizes and standard deviations plotted in the graph to the left. Also included in this table are the median percentage wound size for each timepoint. Averages and medians are reported as percentage of Day 0 wound size.

Figure 3. Comparison of Wound Size at Days 7, 14, and 21 between a 2010 and a 2015 Study

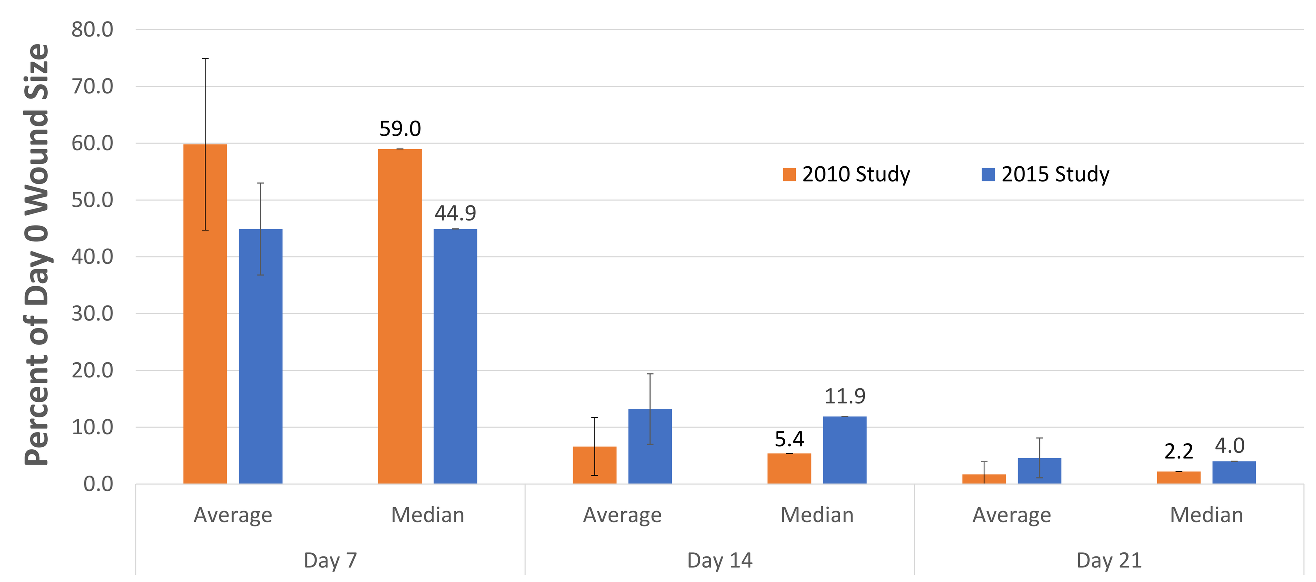


Figure 3, above, demonstrates the variability in the model across time. Two individual studies, taking place approximately five years apart, were selected as representative of the performance of the model at their respective times of completion. As the graph demonstrates, the difference between the rates of healing was greatest at Day 7 and then decreased as the respective studies progressed. By Day 21, the difference appeared quite small, but an unpaired t-test revealed that the results at each timepoint were extremely statistically significant, with *p*-values of less than 0.0001.

CONCLUSIONS

This retrospective analysis demonstrated why swine remain a standard test system for wound healing studies. For pigs within a specific range of age and size, a wound-healing curve was extrapolated that very closely approximates a classical healing curve, with all three phases clearly delineable.

Surprisingly, however, the comparison between studies performed five years apart demonstrated the high variability inherent in the model. Potential causes could include generational changes in the animals' anatomies and/or changes in staff at Bridge PTS over the five-year period. In future studies, a larger sample size may be needed to overcome this variability between individuals.

Currently, this data is relevant only to Yorkshire-cross pigs within a narrow range of size and age. Further analysis of control wounds created on pigs of varying strain, size, and/or age would be needed to produce healing curves that would be applicable to these groups.

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