EVALUATION OF AN ULTRATHIN SYNTHETIC ANTIBIOFILM MATRIX IN THE HEALING OF FULL THICKNESS BURN WOUNDS IN A PORCINE MODEL

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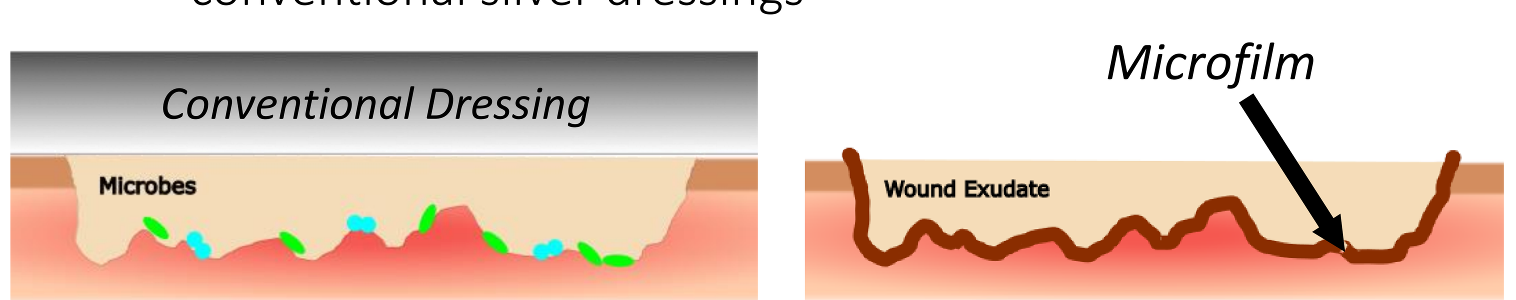
INTRODUCTION

Biofilms are present in an estimated 60% of burn wounds.[1] These bacterial communities contribute to chronic inflammation, delayed healing, and infection/sepsis. The associated healthcare costs for treating chronic and burn wounds in the United States range from $25 billion to $98 billion annually.[2] Here we report the evaluation of a synthetic matrix (microfilm), made of polyvinyl alcohol with a polymeric multilayer coating impregnated with silver and gallium that together kill biofilm bacteria, in healing of full thickness porcine burn wounds. The matrix has been shown to kill > 4 Log10 CFUs of clinically relevant planktonic and single-/multispecies biofilm bacteria (reported elsewhere).

Microfilm Matrix

- The thin-film form factor (~20 µm) allows the microfilm to conform to the wound bed, providing intimate contact with the tissue surface
- Well-controlled loading of therapeutic bioactives
- Maintains moist wound microenvironment
- Due to the conformity of the microfilm to the wound bed, lower doses of compounds are usually needed for effectiveness
    - Ex. Silver-loaded microfilms require 1000x less silver than conventional silver dressings



Microfilm-Ag/Ga

- Biofilms are bacteria encased in extracellular polymeric substance (EPS) and are 1000 times more resistant to antibiotics/ antimicrobials than planktonic bacteria[3,4]
- Both ionic silver and gallium have been shown to be both antimicrobial and biocompatible.[5]

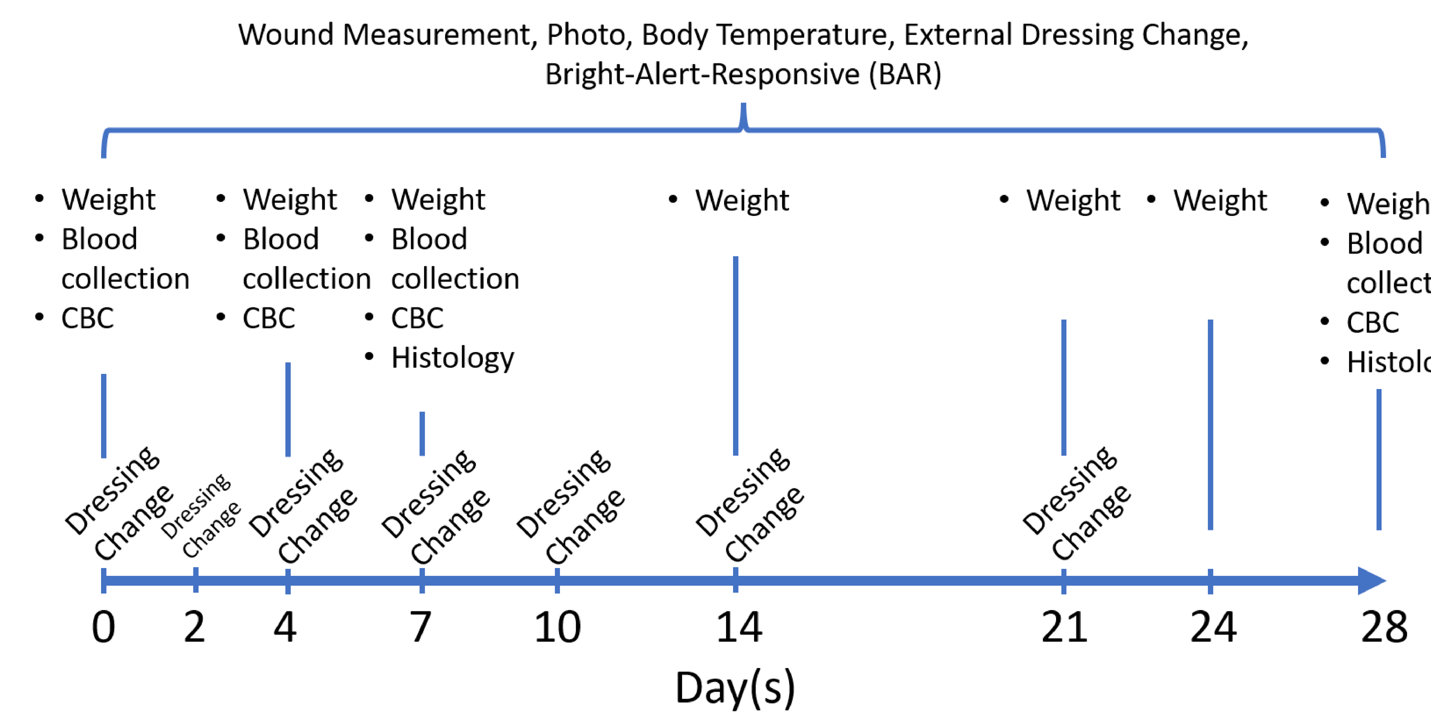
METHODS

20 full thickness burn wounds of 2 cm diameter were created on the back of 3 pigs using heated brass rod following a published method (Telgenhoff et al. 2007). Post burn, the wounds were excised and ten wounds on either side of the spine on each animal were treated with/without microfilm-Ag/Ga and wrapped with a protective Curad® pad and ELASTIKON® to secure the dressings. The dressings were reapplied on days 2, 4, 7, 10, 14 and 21. On days 0, 3, 7 and 28 blood samples were collected for complete blood count and -

METHODS *Continued*

quantification of silver and gallium in the blood plasma by inductively coupled plasma – mass spectrometry (ICP-MS). Samples for histology were collected on Days 7 and 28. After euthanasia, gross necropsy of all major organs were performed.

Timeline



RESULTS

Macroscopically and microscopically, wound healing followed the normal progression at all intervals and the wounds were healed completely by day 28. No major differences in the average scores for wound healing parameters -- including granulation tissue, erythema, edema and re-epithelialization -- at 7 and 28 days of treatment was observed (Figure 1, 2)

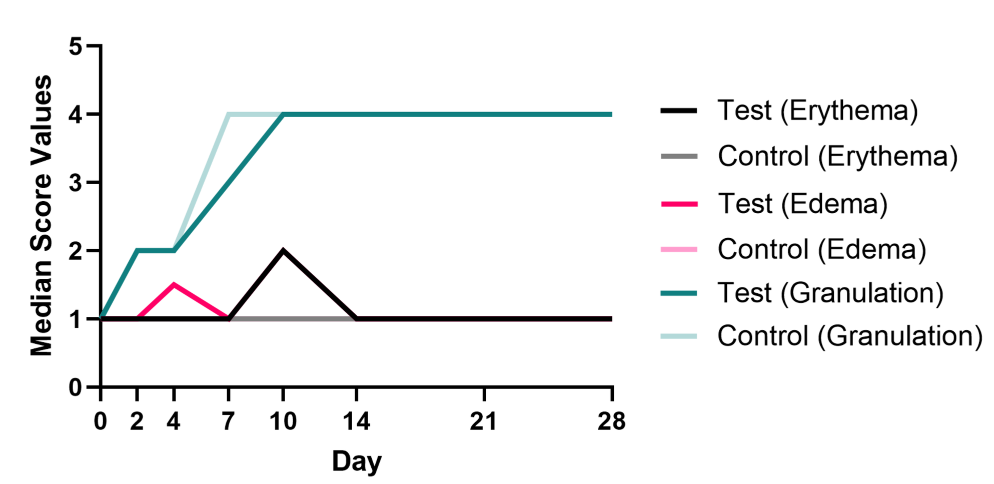


Figure 1: Clinical Visual Wound Assessment Results – Scores graded from 1 = Normal, to 4 = Severe

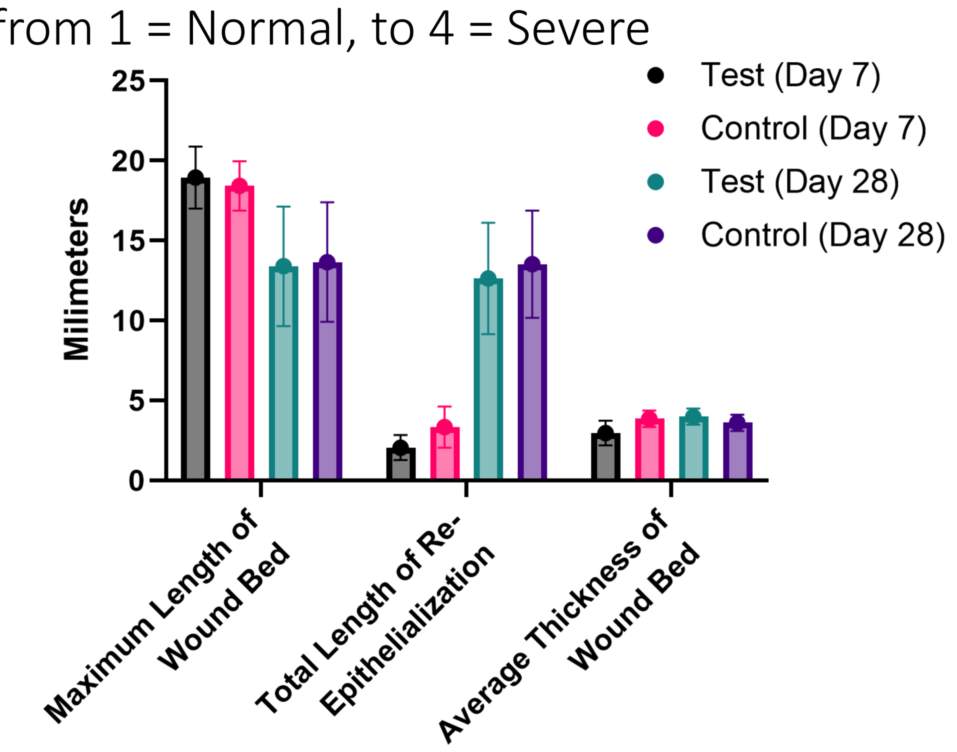


Figure 2: Microscopic Wound Measurements at 7 and 28 Days

RESULTS *Continued*

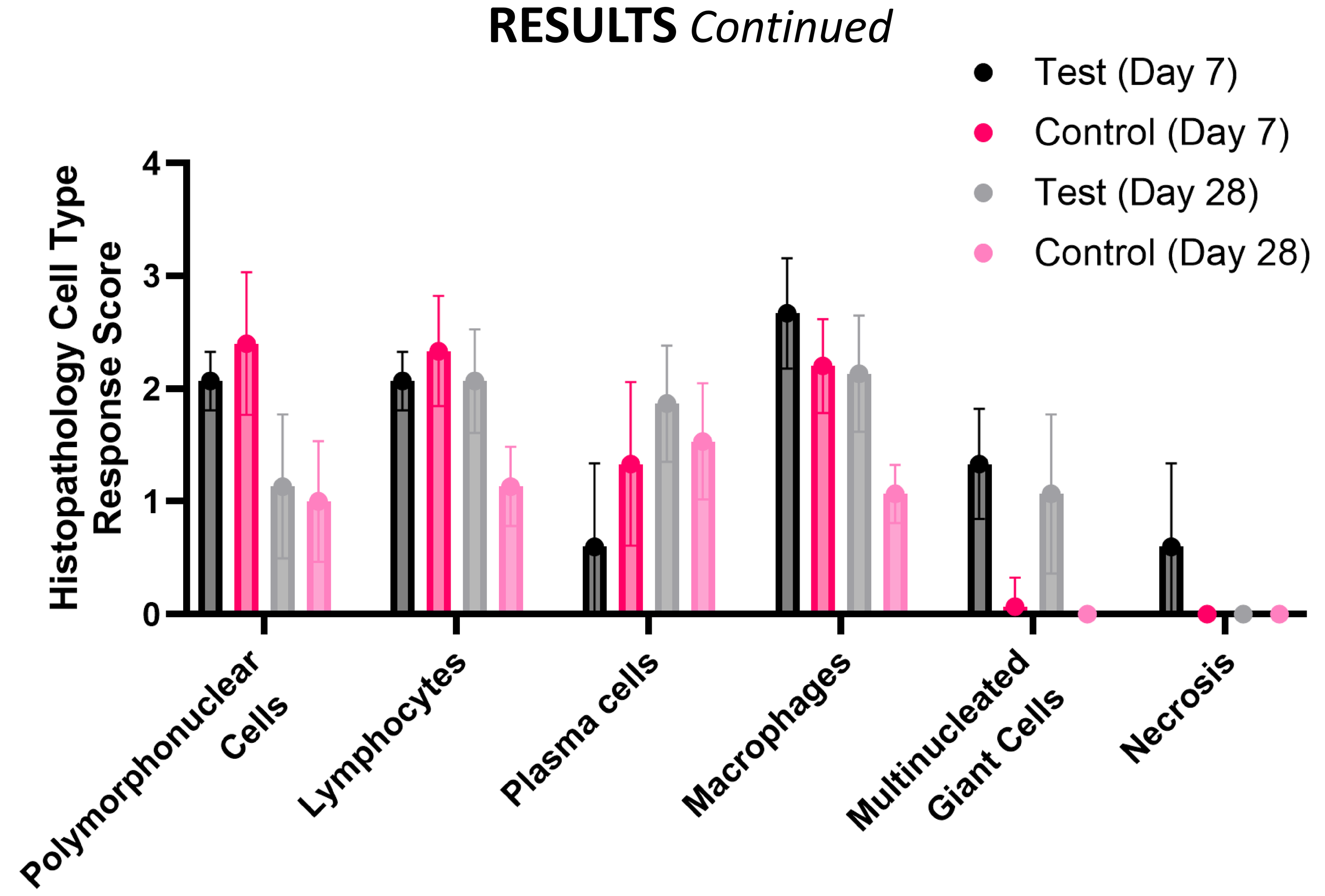


Figure 3: Histopathological Wound Site Scoring of Cellular Response - 0 = None, 1 = Minimal, 2 = Mild, 3 = Moderate, 4 = Marked

Histology analysis showed similar to near identical healing response scores at days 7 and 28. The microfilm-Ag/Ga was classified as slight irritant when compared to Curad® pads (control) at day 28, however this did not appear to affect wound healing, thus showing that the microfilm is safe for use in full thickness burn wounds (Figure 3). Furthermore, the levels of silver and gallium in blood plasma assessed by ICP-MS were found to be below the limit of detection (0.5 ppb), thus confirming that there was no systemic absorption of silver or gallium during the 28-day healing period from the repeated topical applications of the microfilm.

CONCLUSION

The antibiofilm silver/gallium microfilm did not impair the healing of full thickness thermal burn wounds in a preclinical porcine model, exhibiting a high potential for clinical use.

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