Reduction of Multi-Drug Resistant Pathogens and Associated Virulence Factors in a Burn Wound Infection Model: Further Understanding of the Effectiveness of a Hydroconductive Dressing

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Introduction

Virulence factors produced by pathogens can impede wound healing by creating a more invasive infection and altering the host's immune response. Methicillin-resistant *Staphylococcus aureus* (MRSA) produces virulence factors that have been found to induce shock and sepsis, and enhance bacterial survival. A unique hydroconductive dressing has been designed to move large amounts of exudate, slough, necrotic tissue, bacteria, and other wound debris from the wound to the dressing. In pilot work, this experimental dressing was observed to reduce both bacteria and virulence factor levels in MRSA-infected burn wounds. The present experiments were designed to further evaluate the efficacy of Drawtex® (experimental dressing) as compared to a standard of care foam dressing (control dressing) in an in vivo model of burn wound infection.

Day 0: Burn Wound Creation
Paired 2 cm x 2 cm wounds
Aluminum billets, 100 ° C

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Day 1: Inoculation with 1 x 10^8 CFU MRSA

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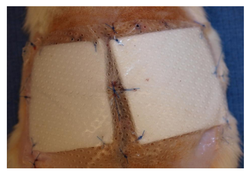
Day 2: Control or experimental dressing application



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Days 3, 6, 9, and 14: Wound and dressing biopsies and imaging

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Quantitative cultures, ELISAs, and gene expression analysis of biopsy samples

Methods

An infected burn wound model in Sprague-Dawley rats was used to characterize the in vivo impact of this dressing on infection and healing (see above). Both wounds on an individual animal received the same dressing type (n=6). MRSA and virulence factors (toxic shock syndrome toxin-1; TSST-1 and Panton-Valentine leukocidin; PVL) were quantified using quantitative cultures and ELISA respectively. Laser Doppler imaging (LDI) was used to examine wound perfusion. Local immune response was assessed by quantifying mRNA expression of genes involved in innate immunity using gene-specific primers in real time RT-PCR.

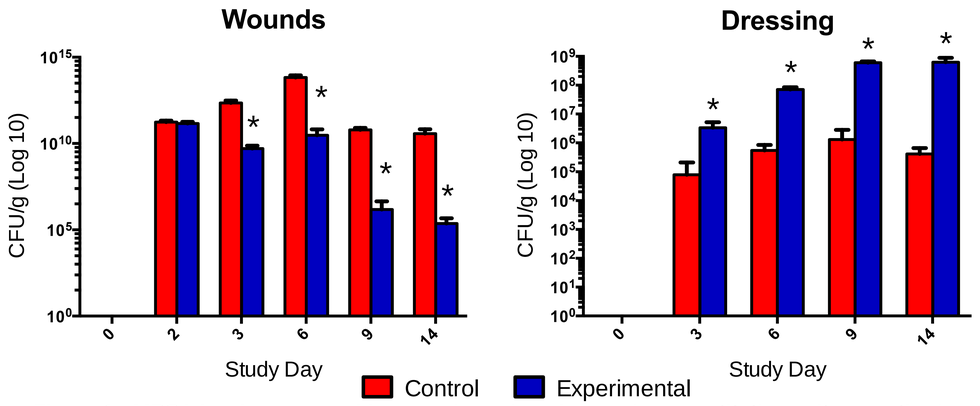

Figure 1: MRSA levels measured in wounds or dressings using quantitative culture methods
***significant differences vs. control (t-test, p<0.05)**

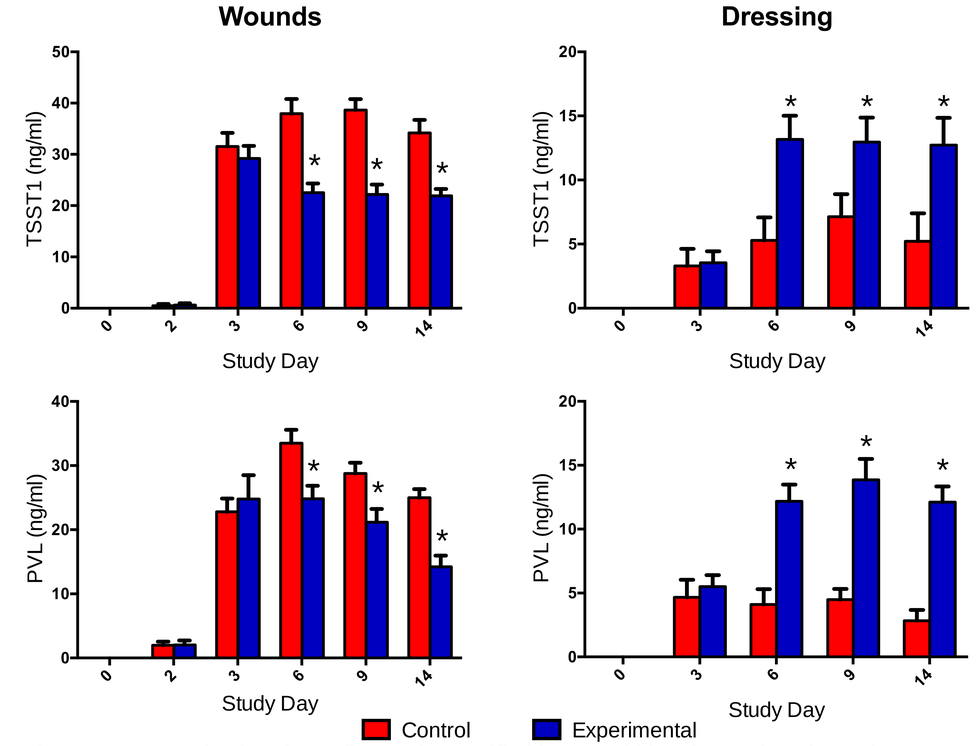

Figure 2: TSST-1 (top) and PVL (bottom) quantified in wound biopsies or dressing using ELISA
***significant differences vs. control (t-test, p<0.05)**

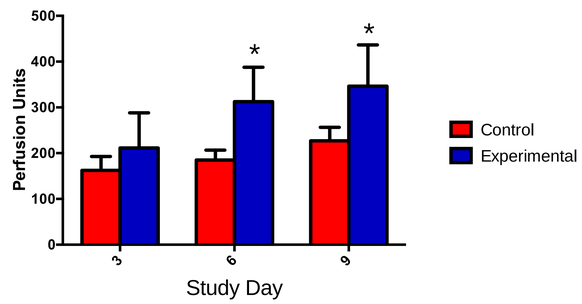

Figure 4: LDI assessment of wound perfusion, calculated as mean perfusion units in regions of interest

***significant differences vs. control (t-test, p<0.05)**

Results

By day 3, less (n=6, p<0.05) MRSA was measured in wounds treated with experimental dressing (5 x 10^9 CFU/g) compared to control dressing wounds (2.3 x 10^{12} CFU/g). Quantities remained lower in the experimental group on day 6 (p<0.001) and were further reduced on days 9 (1.5 x 10^6 CFU/g, p<0.001) and 14 (Fig. 1). More MRSA was quantified in the experimental dressing than in control dressing at all time points (p<0.05), increasing through day 9. Experimental dressing-treated wounds contained less TSST-1 and PVL than controls (p<0.01) on days 6, 9, and 14, while conversely, the experimental dressing itself contained more TSST-1 and PVL by day 6 than the control dressing (p<0.001; Fig. 2). Induction of TLR2, NLRP3, and IL6 was significantly lower in experimental-dressing treated wounds than in controls on days 6 and 9 (p<0.05; Fig.3). An increase in perfusion was seen in the experimental wounds after day 3 (Fig. 4).

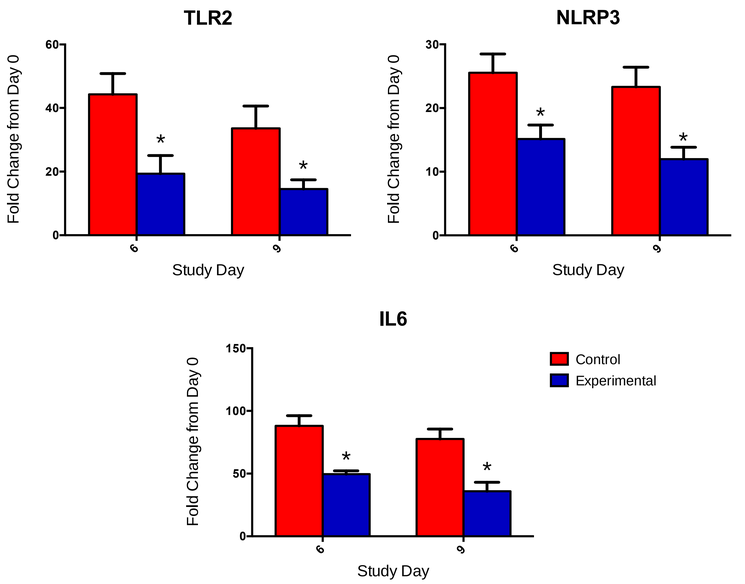

Figure 3: Transcript-level expression of genes involved in innate immune response shown as fold change from baseline/Day 0
***significant differences vs. control (t-test, p<0.05)**

Conclusion

In summary, the hydroconductive dressing provided a significant reduction in pathogen and virulence factors—exceeding that of a control dressing. Further, as a result of clearance of virulence factors from the wound bed, a requisite reduction in host innate immune response was observed.

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