

Modulating Inflammation in Chronic Wounds with Collagen/ORC/Silver



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ABSTRACT

Aim: To determine if a collagen/oxidised regenerated cellulose (ORC)/silver therapy can aid in inflammatory protease reduction and improve chronic wound healing.

Introduction: Approximately 1-2% of the population has a chronic wound. Chronic wounds therefore pose a significant problem to the health service. A distinct feature associated with these wounds is the abnormally high level of inflammatory protease activity, which can result in the degradation of the extracellular matrix and growth factors thereby impeding the wound healing process. A product which helps reduce protease activity could therefore be therapeutic.

Method: In this study a Collagen/ORC/Silver therapy was used to treat patients with chronic venous leg ulcers. In addition to recording the clinical outcomes, wound fluid samples were taken before and during treatment to evaluate the effect of Collagen/ORC/Silver on inflammatory protease activity. Inflammatory proteases were measured in wound fluid using standard methods. Wounds which achieved >50% reduction in wound area by Week 4 (Margolis index) were considered to have responded to treatment and on a healing trajectory.

Results: By Week 4 more patients had responded to Collagen/ORC/Silver than the control treatment; this was indicative of total healing by Week 12. A reduction in inflammatory protease activity was also recorded as wounds progressed towards healing, indicating that these wounds were no longer stagnating in the chronic inflammatory state.

Conclusion: the clinical evidence presented here supports previous data; Collagen/ORC/Silver helps reduce excessive inflammatory protease activity which can help promote healing.

OBJECTIVES

- To compare the effect of a Collagen/ORC/Silver product with standard therapy for the treatment of venous leg ulcers
- To measure the effect on healing
- To determine the effect of the Collagen/ORC/Silver on wound biochemistry

CLINICAL PROTOCOL

- Pilot RCT: 30 consecutive VLU patients (2 arms, 15 control & 15 Collagen/ORC/Silver)
- Treatment for 12 weeks with test dressing and compression
 - Control: Moist wound healing (TIELLE) + short stretch multi-layer compression
 - Collagen/ORC/Silver + Moist wound healing + short stretch multi-layer compression
- Dressings were changed weekly
- Wound bed preparation was followed (TIME principles)
- Wound fluid collected bi-weekly (Cullen et al. Wound Rep Reg 2002;10 16-25)

WEEKLY MEASUREMENTS

Wound size (Visitrak measurement system)
Wound aspect (photographic documentation)

CLINICAL ENDPOINTS

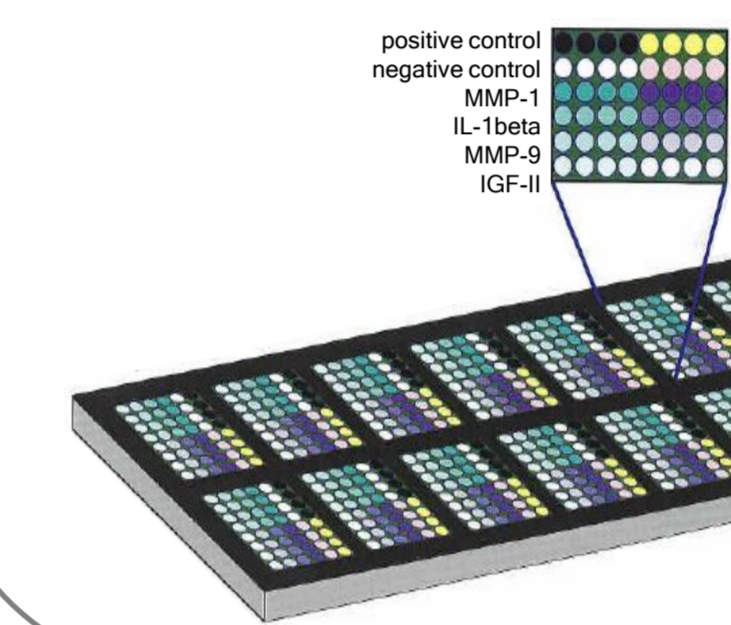
Healing rate at week 12
Wound area reduction throughout treatment
Wounds with reduction in wound size >50% at Week 4 (Margolis index)

METHODS

Wound fluid was collected from chronic venous leg ulcers initially upon presentation (wk 0) and bi-weekly thereafter. This fluid was recovered by elution from the wound dressings using a mild detergent (0.1M Tris/HCl, pH 7.4, 0.1% triton X-100; 500ul/cm²).

Protein levels were measured using Bradford protein Assay (Biorad Cat no. 500-0207).

Biomarker analysis was carried out using cytokine microarray technology (Whatman International Ltd.) . The configuration of the antibody array on the FAST® slide is illustrated in the figure.

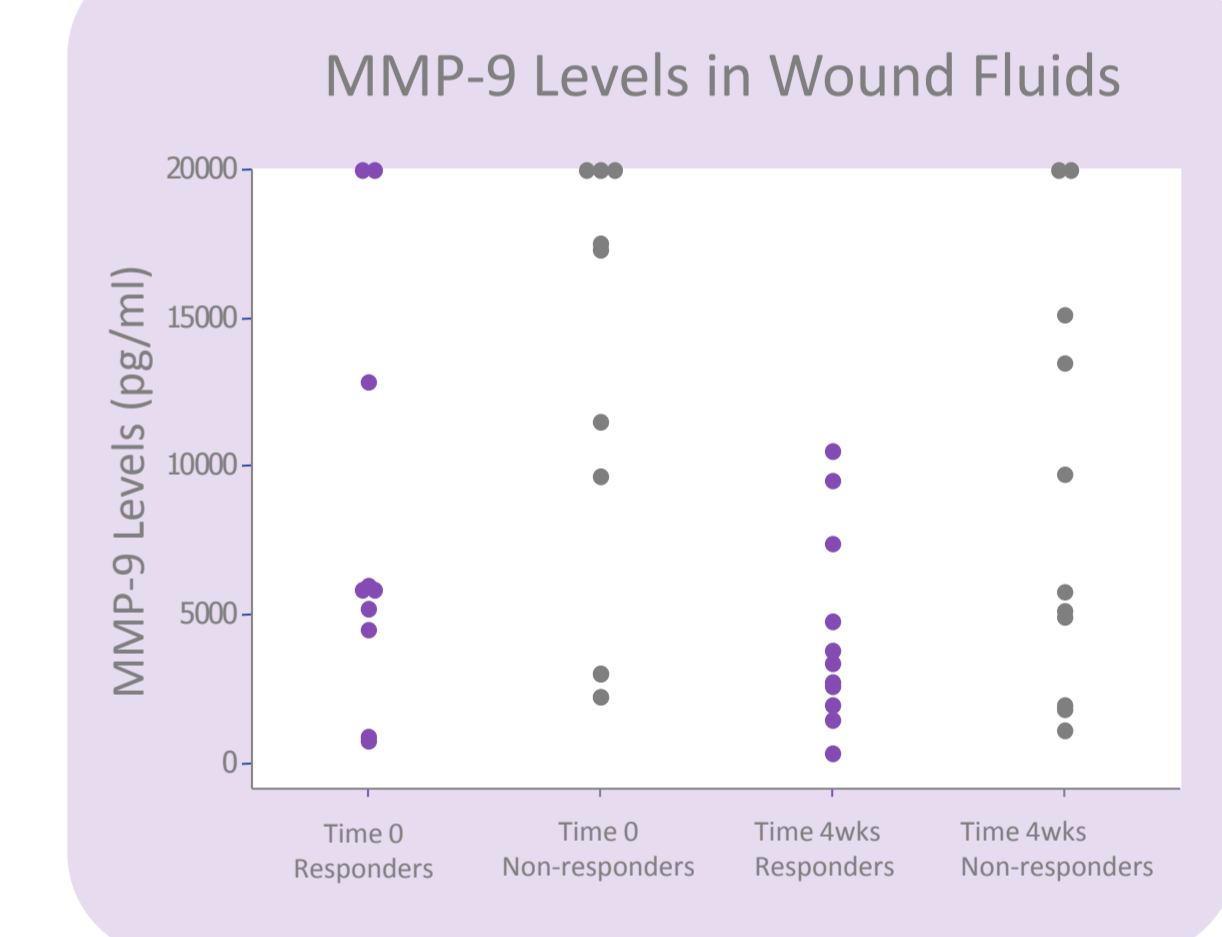
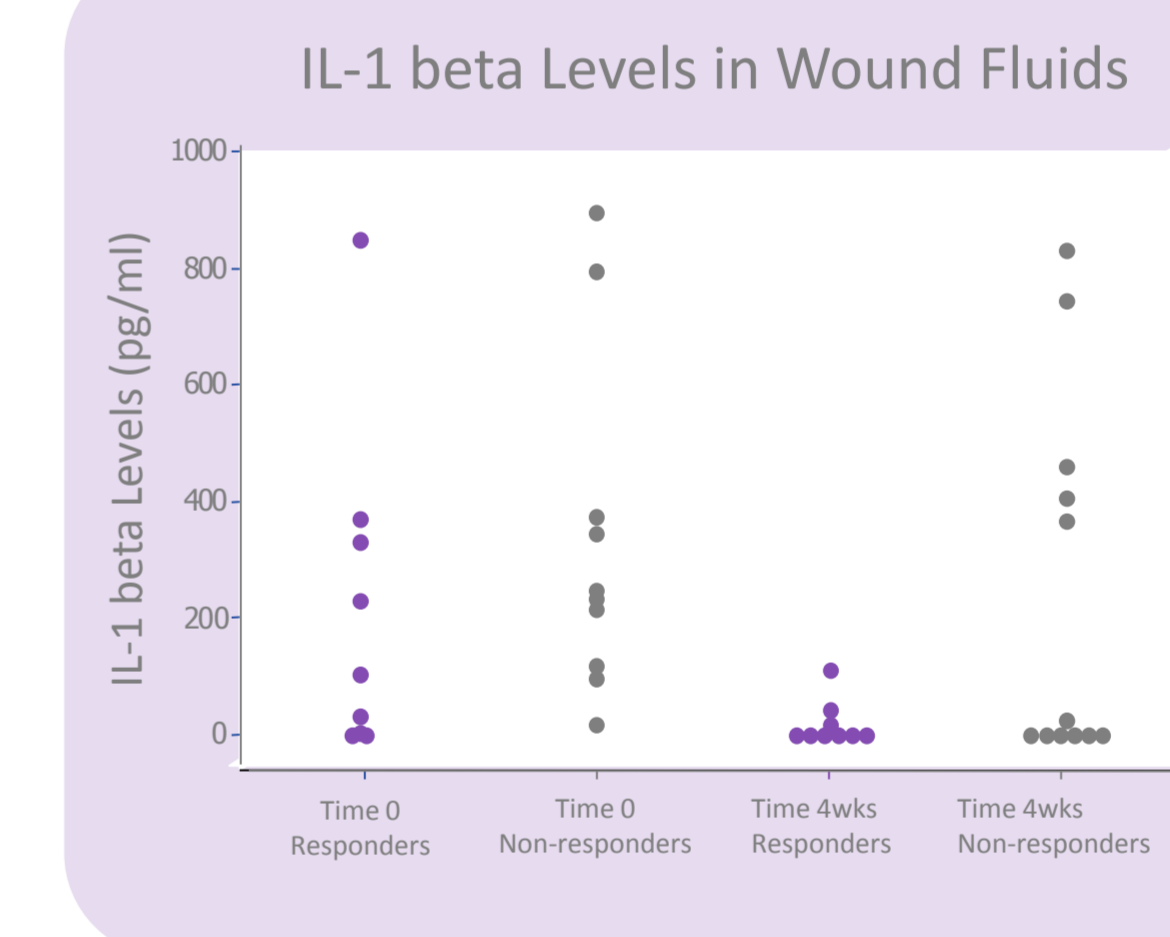


Within the array each antibody is present on the slide in triplicate. There are 12 landing light controls (CTRL) per array. Upon development of an antibody micro-array, fluorescence is detected and the intensity of the fluorescence is measured.

RESULTS – INFLAMMATORY MEDIATORS & PROTEASE ANALYSIS

CLINICAL RESULTS

- Patients were 4 times more likely to heal in the Collagen/ORC/Silver group
- Significant difference in healing rate at Week 12 (p=0.04)
 - Collagen/ORC/Silver group 73% (11/15 patients)
 - Control group 47% (7/15 patients)
- Significant reduction in wound size in Collagen/ORC/Silver versus control group (p=0.00005)
- Margolis index was used to determine responders to treatment: Reduction in wound size >50% by wk4.
 - Collagen/ORC/Silver group 67% (10/15 patients)
 - Control group 47% (7/15 patients) at wk4



PATIENT SELECTION CRITERIA

Inclusion Criteria

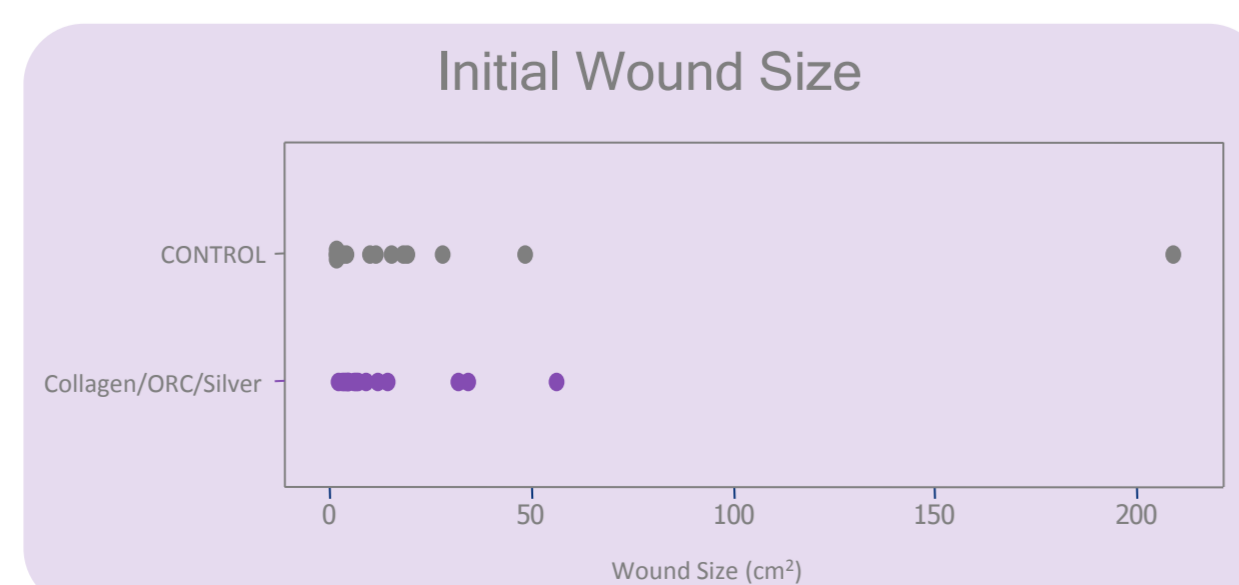
- Males/Females ages 35-90 years
- VLU aetiology confirmed by recent Doppler ultrasound examination & ABI >0.8
- VLU duration at least 30 days
- Ulcer of any size
- Patients compliant to weekly assessments
- Signed informed patient consent

Exclusion Criteria

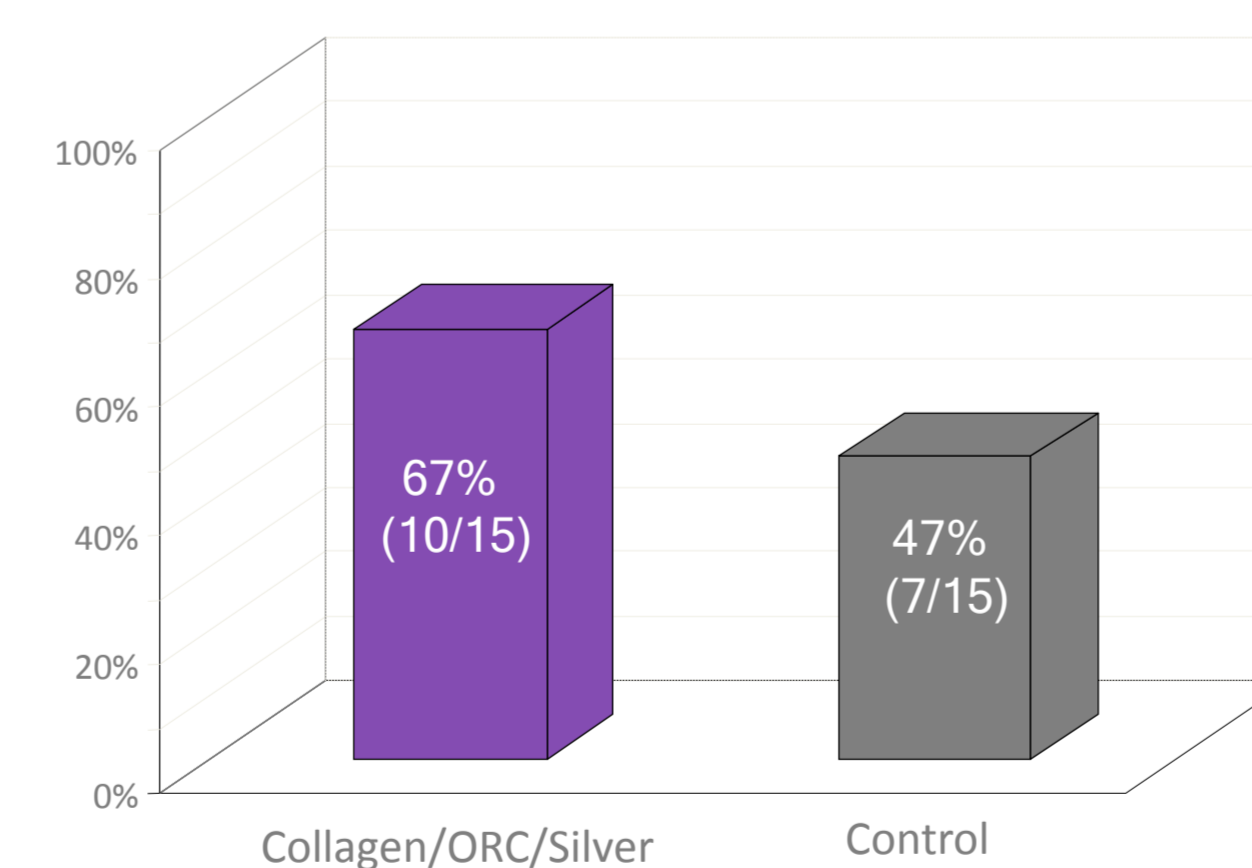
- Known allergic reaction to Collagen/ORC/Silver
- Clinical sign of wound infection
- Peripheral arterial disease
- Pregnancy or lactation
- Misuse of drugs or excessive alcohol
- Malignant wounds
- Diabetes
- Severe cardiac, hepatic, renal or pulmonary insufficiency, anemia or malnutrition
- Therapies with antibiotics, chemotherapeutics, immunosuppressants or radiation

PATIENT DEMOGRAPHICS

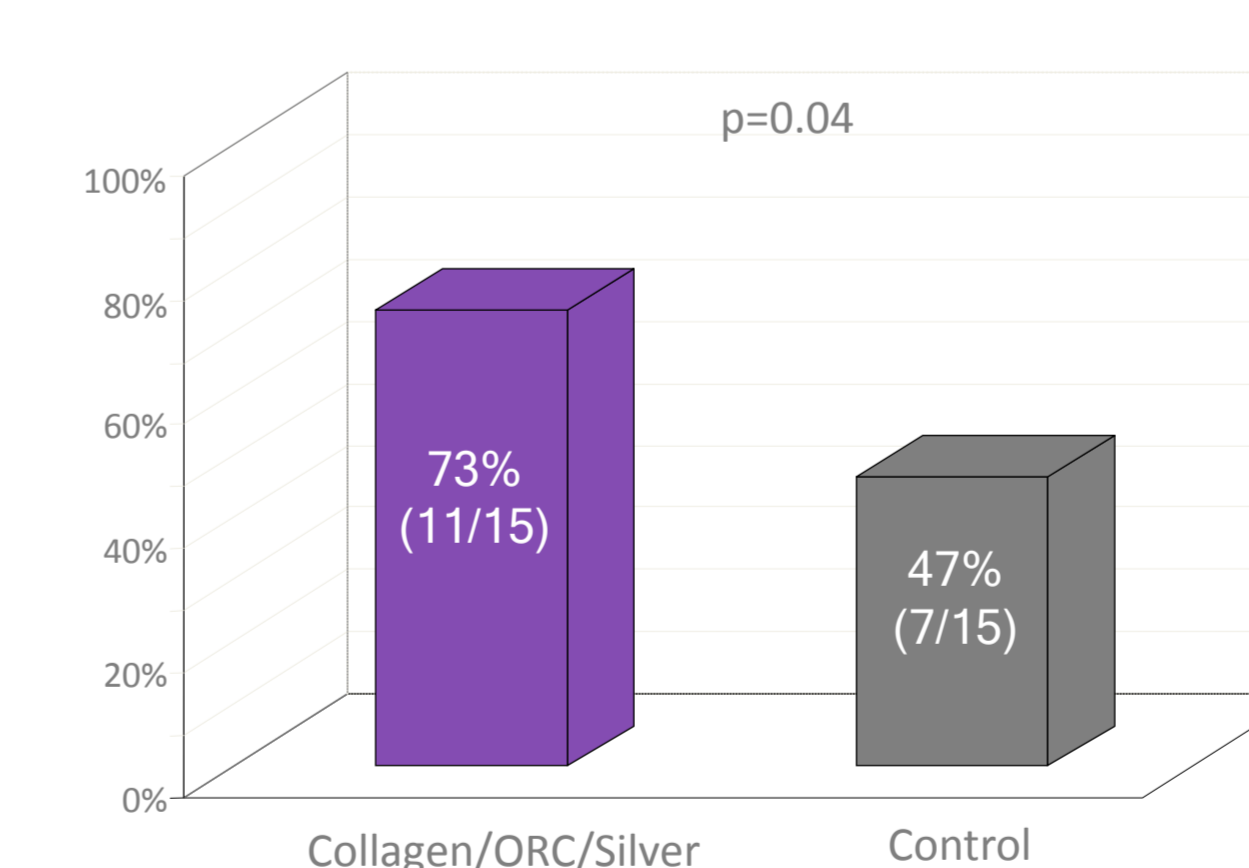
	CONTROL GROUP	Collagen/ORC/Silver GROUP
No. Males	8/15 (54%)	6/15 (40%)
No. Females	7/15 (46%)	9/15 (60%)
Patient Age	Range 53-93yrs 69.3 +/- 10.1yrs	Range 50-82yrs 76.6 +/- 10.8yrs



WOUND RESPONDERS >50% reduction Wound Area



HEALED AT WEEK 12 Significantly more healed with C/ORC/Silver



COLLAGEN/ORC/SILVER TREATED WOUNDS



CONCLUSION

- This pilot RCT demonstrates the clinical effectiveness of Collagen/ORC/Silver in the treatment of hard to heal venous leg ulcers
- Wounds which showed a >50% in wound area by week 4 (responders) correlated well with healing outcome at week 12 and could be used as a predictive marker of healing
- Biochemical analysis of wound fluid from the wounds pre and post treatment identified a number of markers which could be used as predictive indicators of clinical outcomes
- Inflammatory markers, IL-1 beta and MMP-9 levels were similar between both patient populations at time 0, however as the wound progressed to healing those levels reduced, providing an ability to monitor progress
- These markers confirm non-healing wounds are stuck in inflammation. Once this inflammatory cycle is broken and healing is initiated, these inflammatory markers decrease. This illustrates the benefits of combining biochemical analysis of wound fluid in addition to reporting clinical outcomes.

