PROMOGRAN™
MATRIX FAMILY

PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix

Monograph

3M + KCI™

Preface

The increasing prevalence of wounds that fail to heal with standard therapies has led to the development of advanced wound dressings designed to target wound environments that can delay healing. Both PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix help maintain a physiologically moist microenvironment that is conducive to granulation tissue formation, epithelialization, and rapid wound healing. This document will provide the following:

- Introduction to PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix
- Clinical literature review of PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix
- Description of PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix
- Science supporting PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix
- Case studies

Introduction

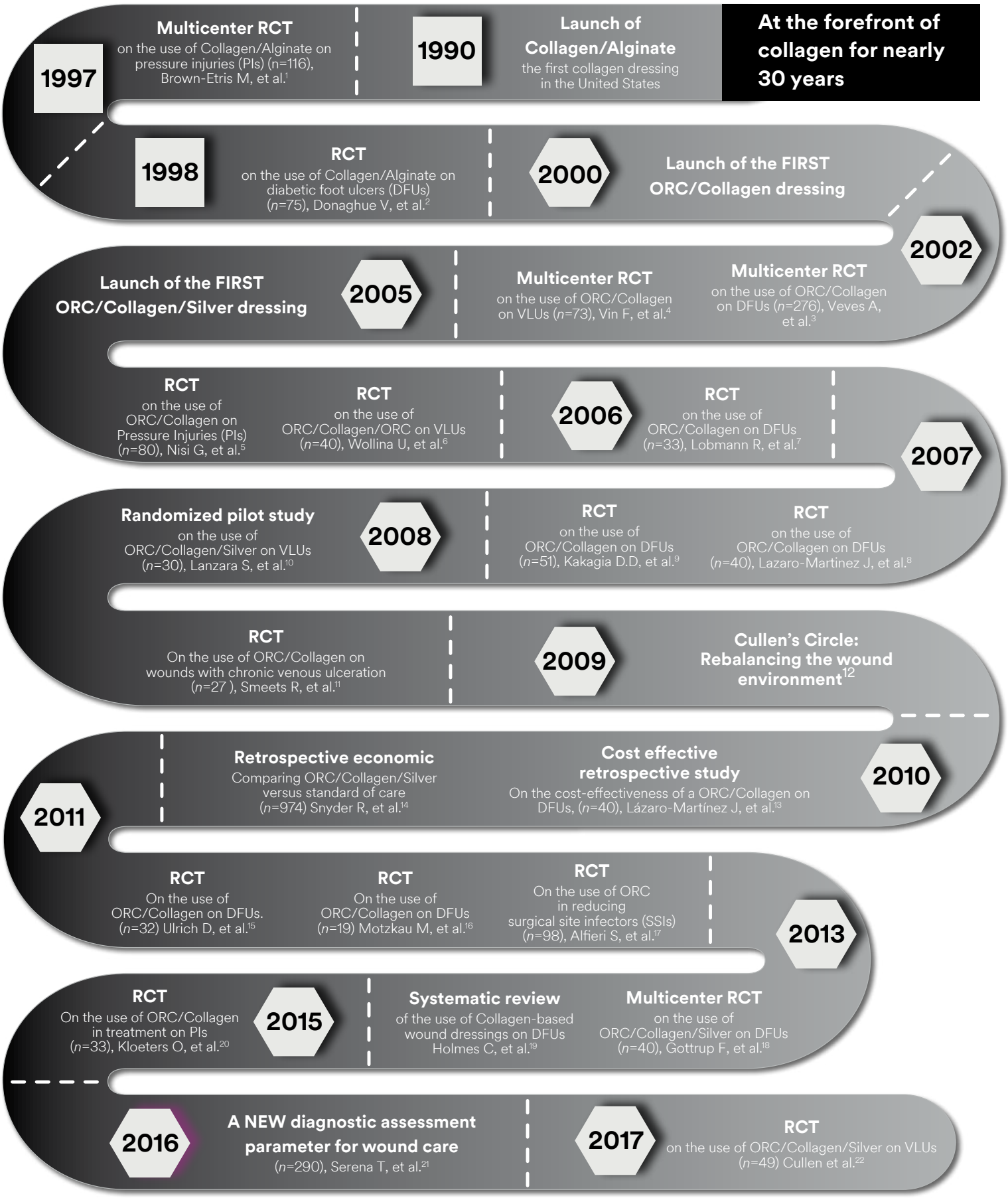
Healthcare systems in the United States and in other countries are being challenged to manage an increasing number of wounds that have failed to complete an orderly process of healing despite treatment with standard therapies. Factors contributing to these nonhealing (chronic) wounds include aging populations, increasing prevalence of comorbid conditions (eg, diabetes, obesity) that can impair a patient's healing capability, and imbalances within the wound microenvironment.

Research into the pathophysiology of wound healing has provided insight into the distinctions between healing and nonhealing wound environments. In an acute wound that achieves healing, there is an orderly transition through the repair processes starting with removal of damaged tissue and ultimately leading to new tissue formation and reepithelialization. The microenvironment of a chronic nonhealing wound is characterized by a prolonged inflammatory phase, in which proteases (especially human neutrophil-derived elastase [HNE] and matrix metalloproteinases [MMPs]) degrade the growth factors and extracellular matrix required to transition to the proliferative phase of healing.

PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix are advanced wound dressings composed of collagen and oxidized regenerated cellulose (ORC). PROMOGRAN PRISMA™ Matrix **(Figure 1)** has the added benefit of silver, a well-known antimicrobial agent.

Figure 1. PROMOGRAN PRISMA™ Matrix

Collagen RCT history by numbers



Clinical Evidence Review

Thirteen randomized controlled trials (RCTs) have compared PROMOGRAN™ Matrix Wound Dressing and/or PROMOGRAN PRISMA™ Matrix to standard care and reported favorable outcomes with use of the 2 matrix dressings **(Table 1)**. A number of retrospective studies and case series have presented similar results.

Table 1: Key Clinical Evidence Supporting Use of PROMOGRAN™ Matrix/PROMOGRAN PRISMA™ Matrix

Year/ Author	Wound Type	Study Type and Patients	Results/Conclusions
2002 Veves A et al[3]	DFUs	• A 12-week multicenter RCT involving DFU • PROMOGRAN™ Matrix Wound Dressing (*n*=138) vs saline-moistened gauze (*n*=138)	• More wounds achieved complete healing with PROMOGRAN™ Matrix Wound Dressing, especially in wounds < 6 months duration (45% vs 33%, *p*=0.056)
2002 Vin et al[4]	VLUs	• A 12-week multicenter RCT involving VLU patients • PROMOGRAN™ Matrix Wound Dressing + compression (*n*=37) vs Control (nonadherent dressing + compression; *n*=36)	• 47.6% more wounds (62% vs 42%, *p*=0.0797) were characterized as healing or improved (≥ 50% wound area reduction at week 12) in the PROMOGRAN™ Matrix Wound Dressing + compression group than in the Control group • A significant reduction in wound areas was achieved in the PROMOGRAN™ Matrix Wound Dressing + compression group compared to Control (54.4% vs 36.5%, *p*<0.0001)
2005 Nisi et al[5]	PIs	• A 6-week RCT involving PI patients • PROMOGRAN™ Matrix Wound Dressing (*n*=40) vs Control (moist wound healing—vaseline gauze and hydropolymer patch; *n*=40)	• More patients with pressure injuries completely healed compared in the PROMOGRAN™ Matrix Wound Dressing group compared to the Control group (90% vs 70%, respectively) • The time to complete healing was shorter and more cost effective in the PROMOGRAN™ Matrix Wound Dressing group (360 days overall hospitalization vs 1164 days in the Control group)

Year/ Author	Wound Type	Study Type and Patients	Results/Conclusions
2005 Wollina U et al[6]	VLUs	• A 2-week RCT involving chronic VLU patients • PROMOGRAN™ Matrix Wound Dressing + good ulcer care (*n*=30) vs Control (good ulcer care only; *n*=10)	• A significantly greater mean wound area reduction was achieved in the PROMOGRAN™ Matrix Wound Dressing group compared to Control ($p<0.05$) • Wounds allocated to the PROMOGRAN™ Matrix Wound Dressing group reported a significant reduction in pain scores at week 2 (baseline mean pain score was 8.72 compared to 3.84 at week 2, $p<0.05$)
2006 Lobmann[7]	DFUs	• A single-blinded RCT measuring wound size reduction and biochemistry in DFU patients over an 8-day period • PROMOGRAN™ Matrix Wound Dressing (*n*=18) vs Control (standard good wound care; *n*=15)	• No differences detected between both groups and at the 3 time points for the mRNA levels of MMPs as well as of IL-1β and TNF-α • MMP levels in wound tissue (analyzed by ELISA) were not significantly different between both groups
2007 Lazaro-Martinez JL et al[8]	DFUs	• A 6-week single center RCT involving DFU patients • PROMOGRAN™ Matrix Wound Dressing (*n*=20) vs Control (moist wound healing—standard wound care protocol; *n*=20)	• Significantly more wounds achieved complete healing with PROMOGRAN™ Matrix Wound Dressing vs Control (63% vs 15%; $p<0.03$) • Mean time to achieve healing was 23.3 days in the PROMOGRAN™ Matrix Wound Dressing group compared with 40 days in the Control group ($p<0.01$)

Year/ Author	Wound Type	Study Type and Patients	Results/Conclusions
2007 Kakagia et al[9]	DFUs	• An 8-week RCT involving DFU patients • PROMOGRAN™ Matrix Wound Dressing (*n*=17) vs autologous growth factors (*n*=17) vs combination (PROMOGRAN™ Matrix Wound Dressing + autologous growth factors) (*n*=17)	• PROMOGRAN™ Matrix Wound Dressing was more effective at reducing ulcer size than autologous growth factors; however, the combination was significantly better than the other groups ($p<0.001$)
2008 Smeets et al[11]	VLUs	• A 12-week RCT involving VLU patients • PROMOGRAN™ Matrix Wound Dressing (*n*=17) vs Control (hydrocolloid dressing; *n*=10)	• Wound fluid biochemistry data indicated a more favorable environment in wounds to which PROMOGRAN™ Matrix Wound Dressing was allocated
2011 Ulrich[15]	DFUs	• A 12-week RCT measuring wound area reduction and biochemistry in DFU patients (Wagner Status 2-4) • PROMOGRAN™ Matrix Wound Dressing (*n*=22) vs Control (hydrocolloid dressing; *n*=10)	• There were significant differences ($p<0.05$) in wound area reduction on days 14 and 28 in the PROMOGRAN™ Matrix Wound Dressing group vs Control • Wound fluid biochemistry data also indicated a more favorable environment in wounds to which PROMOGRAN™ Matrix Wound Dressing was allocated
2011 Motzkau et al[16]	Diabetic foot lesions	• An RCT involving chronic diabetic foot lesion patients • PROMOGRAN™ Matrix Wound Dressing (*n*=13) vs Control (standard good wound care; *n*=6)	• No differences in the mRNA levels of MMPs, IL-1β and TNF-α were observed between both groups

Year/ Author	Wound Type	Study Type and Patients	Results/Conclusions
2013 Gottrup et al[18]	DFUs	• A 14-week multicenter RCT involving DFU patients • PROMOGRAN PRISMA™ Matrix (*n*=24) vs Control (best standard of care; *n*=15)	• Significantly more responders (≥50% reduction in wound area measured by the Margolis index) in the PROMOGRAN PRISMA™ Matrix group compared with the Control group (79% vs 43%, respectively; *p*=0.035) at week 4 • There were significantly fewer withdrawals due to infection in the PROMOGRAN PRISMA™ Matrix group compared with the Control group (0% vs 31%, respectively; *p*=0.012) • At week 14, the number of wounds completely healed was 52% vs 31%, respectively
2015 Kloeters et al[20]	PIs	• A 12-week RCT involving PI patients • PROMOGRAN™ Matrix Wound Dressing (*n*=23) vs Control (TIELLE™ Foam Dressing; *n*=10)	• Compared to the Control group, the PROMOGRAN™ Matrix Wound Dressing treated pressure injury patients showed a significantly (*p*<0.05) faster healing rate
2017 Cullen et al[22]	VLUs	• A 12-week RCT involving VLU patients • PROMOGRAN PRISMA™ Matrix in conjunction with standard of care (*n*=22) vs Control (standard of care alone; *n*=27)	• Intent-to-treat analysis showed a mean percentage wound area reduction at 12 weeks of 85.6% for the intervention group vs 72.5% for the control group. • A higher healing rate was reported in the intervention group compared with patients who received standard of care only at both week 4 (23% vs 11%) and week 12 (64% vs 59%)

PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix

Product Descriptions

PROMOGRAN™ Matrix Wound Dressing is composed of 45% ORC and 55% bovine collagen.

PROMOGRAN PRISMA™ Matrix consists of 44% ORC, 55% bovine collagen, and 1% silver/ORC of which 1/4 of the total weight of the silver-ORC is silver **(Figure 2)**. PROMOGRAN PRISMA™ Matrix also has an increased density (approximately twice as much collagen and ORC) of collagen and ORC compared to the PROMOGRAN™ Matrix Wound Dressing.

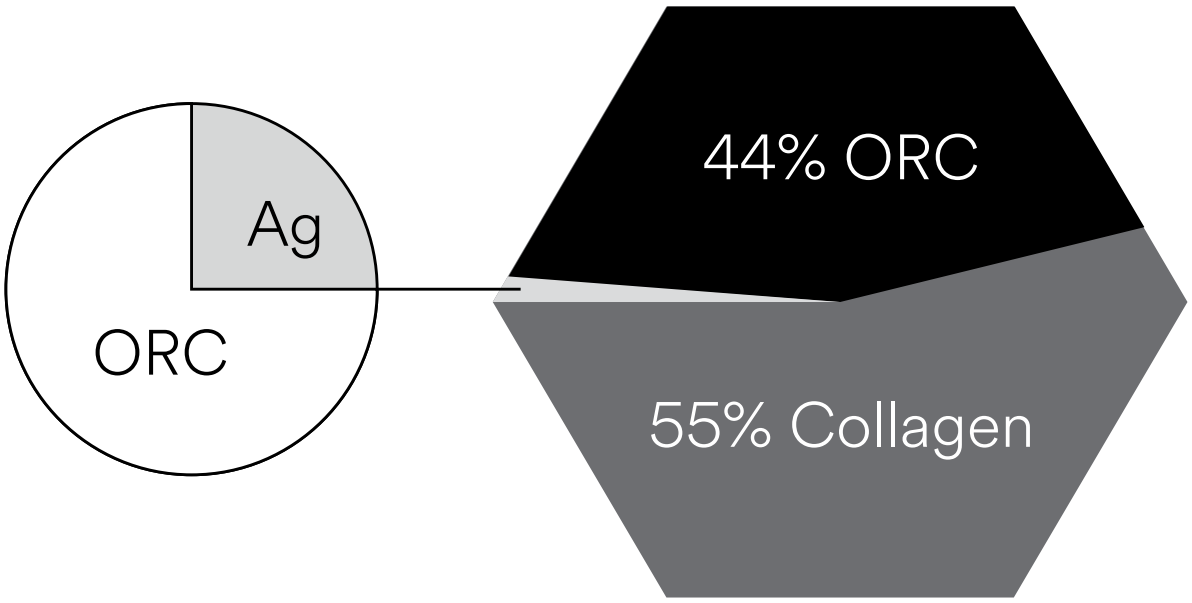
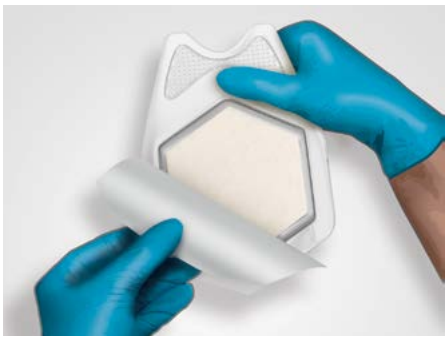


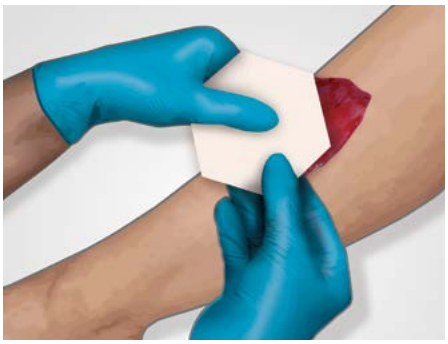
Figure 2. PROMOGRAN PRISMA™ Matrix

There are many similarities between the two matrix dressings. In the presence of fluid/exudate in the wound, both dressings transform into a soft, conformable, biodegradable gel that allows contact with all areas of the wound. Depending on wound exudate levels, the collagen and ORC in the PROMOGRAN PRISMA™ Matrix may take a longer time to biodegrade in the wound. In a wound with low or no exudate, the matrix dressing should be hydrated with saline solution to initiate the transformation of the dressing into a gel matrix. Both matrix dressings must be covered with a semiocclusive or nonocclusive moist wound healing secondary dressing and, if needed, fixed to the skin with nonirritating tape **(Figure 3)**.

With the supervision of a healthcare professional, both may be used under compression bandages. Also, both can be cut with sterile scissors to fit the wound shape or premoistened to form a gel that can be molded to fit the wound. Residual matrix from both dressings does not need to be removed during dressing changes.



A. Removal from package



B. Placement over wound

C. Application of secondary dressing

Figure 3. Dressing application: PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix

Indications for Use

The PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix are intended for the management of exudating wounds including:

- Diabetic ulcers
- Venous ulcers
- Pressure injuries
- Ulcers caused by mixed vascular etiologies
- Full-thickness and partial-thickness wounds
- Donor sites and other bleeding surface wounds
- Abrasions
- Traumatic wounds healing by secondary intention
- Dehisced surgical wounds

Contraindications

PROMOGRAN™ Matrix Wound Dressing is not indicated for wounds with active vasculitis, third-degree burns, or patients with known sensitivity to ORC or collagen. PROMOGRAN PRISMA™ Matrix is not indicated for third-degree burns or patients with known sensitivity to silver, ORC, or collagen.

Precautions

PROMOGRAN PRISMA™ Matrix may be used when visible signs of infection are present in the wound area only when proper medical treatment addresses the underlying cause. PROMOGRAN PRISMA™ Matrix is not intended to be a substitute for appropriate treatment of infection. Clinicians and healthcare professionals should be aware that there are very limited data on prolonged and repeated use of silver containing dressings, particularly in children and neonates.

Science Supporting PROMOGRAN™ Matrix Wound Dressing and PROMOGRAN PRISMA™ Matrix

The following summaries are preclinical descriptions of benchtop *in vitro*, laboratory animal *in vivo* and *ex vivo* studies supporting ORC/collagen dressing technology.

An *in vitro* study evaluated the effect of an ORC/collagen dressing.125 on wound fluid taken from patients with diabetic foot ulcers (DFUs) with surface area >1cm² and duration >30 days.[22] Compared to Control samples (wound fluid only), samples exposed to ORC/collagen showed a marked decrease in collagenase-like activity during the first hour of testing, an effect that was maintained for the rest of the 28-hour test. MMP-2 and MMP-9 levels were also significantly reduced in wound fluid incubated with ORC/collagen. Other tests demonstrated that ORC/collagen was more effective at scavenging oxygen-free radicals than collagen/alginate or carboxymethyl-cellulose and that ORC was able to bind iron and zinc ions. Compared to ORC and collagen tested separately, the combination of ORC/collagen was able to bind and protect a significantly greater amount of growth factors in wound fluid. This *in vitro*, non-clinical study demonstrated that ORC/collagen was able to bind and inactivate proteases while also having no detrimental effect on growth factors in chronic wound fluid.[22]

Another preclinical study also demonstrated that ORC/collagen has a positive role in promoting cell proliferation.[23] This study investigated the effects of ORC/collagen on fibroblast migration and proliferation *in vitro* and its effects on accelerated wound repair in a diabetic mouse model. *In vitro* results showed that ORC/collagen was found to promote fibroblast proliferation and cell migration. *In vivo* studies demonstrated that ORC/collagen significantly ($p<0.01$) accelerated diabetic (mouse) wound closure and resulted in a measurable improvement in the histological appearance of wound tissues.[23]

An *in vivo* rat model was used to investigate the effects of ORC/collagen on dermal and epidermal healing and growth factor concentration in acute wounds.[24] Full-thickness excision wounds were created, and each wound received either an ORC/collagen plus a hydrocolloid dressing or a hydrocolloid dressing alone. Results showed that rat wounds treated with ORC/collagen displayed a significantly ($p>0.05$) greater area of reepithelialization than wounds treated with hydrocolloid alone (Control). Furthermore, ORC/collagen-treated wounds showed significantly higher levels of platelet-derived growth factor and increased dermal and epidermal insulin-like growth factor-I protein concentration compared to Control wounds. No significant differences were found in collagen morphology or deposition, neoangiogenesis, or vascular endothelial growth factor concentration between both groups. The authors concluded that in this model, ORC/collagen enhanced epidermal regeneration and increased specific growth factor concentrations, which had beneficial effects on acute wounds.[24]

Cited Case Studies

The following represent real-world product applications. As with any case study, the results and outcomes should not be interpreted as a guarantee or warranty of similar results. Individual results may vary, depending on patient circumstances and conditions.

Reference Clinical Case Studies

Case Study 1

Patient was a 70-year-old white male with a history of long-standing diabetes mellitus and diabetic peripheral neuropathy who presented with a chronic, nonhealing DFU on the right foot **(Figure 4A)**. Multiple treatments, debridements and antibiotic topical therapy were provided by other physicians but with no success. The DFU remained a noninfected full-thickness wound with hypergranulation on the first submetatarsal head with minimal exudate drainage. There was no gross deformity or bony involvement. A gastrocnemius equinus contracture was noted on patient's right lower extremity that increased the forefoot pressures. Upon vascular examination, patient had intact pedal pulses with adequate ankle brachial index and digital pressures, but there was loss of protective sensation. Management consisted of a full-thickness, sharp excisional debridement into and through the subcutaneous tissue, which removed any fibrotic tissue. Wound was debrided down to a healthy pink granular base, followed by application of PROMOGRAN PRISMA™ Matrix. An offloading boot was also provided to reduce the forefoot pressures. At 3 and 7 weeks post initiation of PROMOGRAN PRISMA™ Matrix **(Figures 4B and 4C)**, the DFU continued to heal. At 3 months, the DFU was fully closed **(Figure 4D)**.

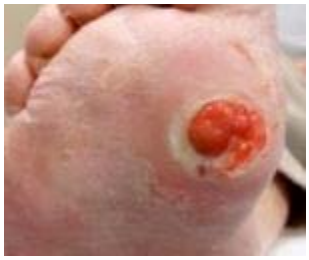


Figure 4A. DFU at presentation

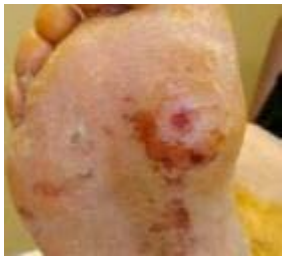


Figure 4B. 3 weeks post sharp excisional debridement and initiation of PROMOGRAN PRISMA™ Matrix, wound size was notably decreased

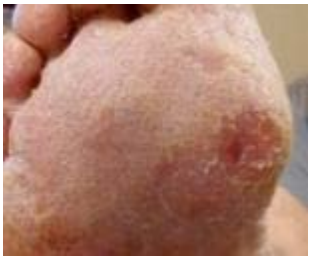


Figure 4C. At 7 weeks, DFU was nearly reepithelialized

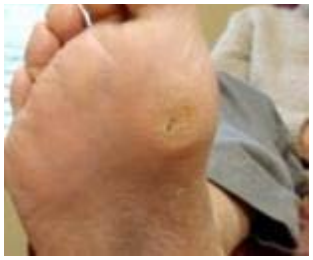


Figure 4D. After 3 months of PROMOGRAN PRISMA™ Matrix and offloading, DFU was closed

Case Study 2

Patient was an 81-year-old male with Type 2 diabetes and a recurrent venous leg ulcer of 11-months duration with failure to progress for approximately 6 months. This patient did have a remote history of a previous ulcer, which was able to achieve complete healing.

The patient presented with an inactive ulcer to his right lateral malleolus **(Figure 5A)**. The ulcer measured 3.5cm^2 with an approximate depth of 0.3cm and no apparent undermining. The surrounding skin was macerated, erythematous, and excoriated with eczema and atrophie blanche. Exudate levels were moderate, and there was a slight odor present. He had previously been treated with a sodium carboxymethylcellulose primary wound dressing (Aquacel® EXTRA™, ConvaTec, Greensboro, NC) and had also treated the wound himself with Manuka honey. He was complaining of mild, intermittent pain.

The wound was dressed with a PROMOGRAN PRISMA™ Matrix. As a result of presenting symptoms, it was felt the use of silver in the dressing may prevent the development of any local infection. The dressing was prescribed for use twice weekly, in conjunction with modified compression therapy. The patient had been unable to tolerate high compression bandaging in the past. A thin knitted viscose secondary dressing (N-A™ Ultra Silicone Coated Knitted Viscose Dressing, Systagenix, an ACELITY Company, Gargrave, UK) was used with gauze padding. A steroid cream (Eumovate) and white soft paraffin were applied to protect the surrounding skin. Tracings and photographs were taken every 1 to 2 weeks.

Two weeks after commencing treatment, the wound bed appeared healthier, with granulation tissue visible at the base. The wound measured 2.5cm^2 in area, and depth had decreased to 0.2cm. Two weeks later, the wound appeared to be 100% granulating with no depth and an area of 1cm^2.

On the last recorded assessment, the wound was unchanged in area but had a slight depth again of 0.2cm **(Figure 5B)**. The wound remained healthy in appearance. He had also reduced the amount of compression during this time, which may have affected gauze padding. A steroid cream (Eumovate) and white soft paraffin were applied to protect the surrounding skin healing. Over the course of 6 weeks, the patient has made good progress toward healing with the use of a PROMOGRAN PRISMA™ Matrix in conjunction with compression therapy plus gauze padding, a steroid cream (Eumovate), and white soft paraffin applied to protect the surrounding skin.

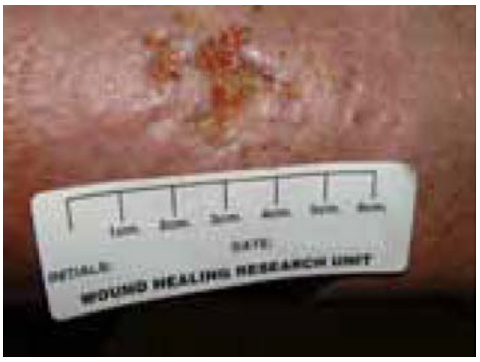


Figure 5A. Nonhealing ulcer on right malleolus prior to treatment with the PROMOGRAN PRISMA™ Matrix

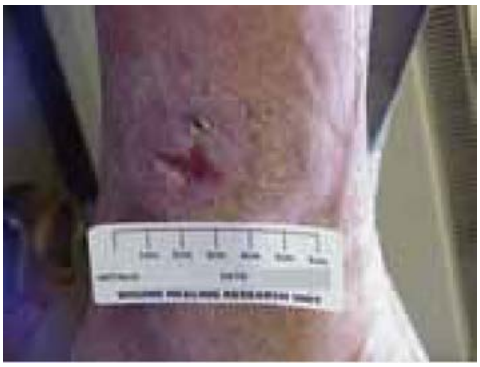


Figure 5B. Appearance after 3 weeks of treatment with the PROMOGRAN PRISMA™ Matrix

Case Study 3

The patient was a 59-year-old female hospitalized on January 23, 2010, with the diagnosis of nonhealing left transmetatarsal amputation site. Past medical history was significant for chronic obstructive pulmonary disease, hypertenstion, hypothyroidism, renal failure requiring hemodialysis 3 times per week, and peripheral vascular disease. Past surgical history was significant for: right below the knee amputation, left femoral-popliteal bypass in December 2009, and a left transmetatarsal amputation in December 2009, due to nonhealing toe wounds.

Upon admission, the left transmetatarsal amputation was debrided via pulse lavage and negative pressure wound therapy (NPWT, V.A.C.® Therapy, KCI, an ACELITY Company, San Antonio, TX) to prepare the wound for a split-thickness skin graft (STSG). On February 1, 2010, the patient underwent surgical debridement of the left transmetatarsal amputation and fourth metatarsal resection with placement of a STSG over the defect **(Figure 6A)**.

The donor site on the left lateral thigh measured 10cm x 7cm and was covered initially with a thin film dressing left in place until postoperative day 5, and was changed and ordered to be changed weekly. On postoperative day 11, the donor site had become more exudative, requiring an increased frequency of dressing changes by the staff daily. The donor site was reevaluated and found to have a gelatinous slough covering the base. The measurements remained the same from the initial harvest. The skin surrounding the donor site developed dermatitis **(Figure 6B)**.

The donor site was cleansed with antibacterial soap and normal saline, rinsed, and then patted dry with the application of skin prep to protect the surrounding skin. A PROMOGRAN PRISMA™ Matrix was applied over the donor site and covered with an adhesive hydropolymer foam dressing (TIELLE™ Hydropolymer Adhesive Dressing with LIQUALOCK™ Technology, Systagenix, an ACELITY Company, Gargrave, UK) **(Figure 6C)**. On postoperative day 14, the dressing was changed. There was an increase in healthy granulation tissue, and new areas of reepithelialization were noted. The surrounding dermatitis had also improved **(Figure 6D)**.

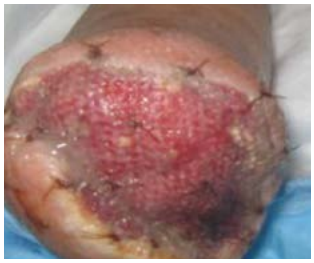


Figure 6A. STSG over wound

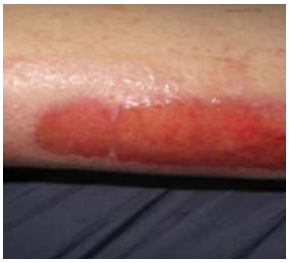


Figure 6B. Left lateral thigh donor site with dermatitis

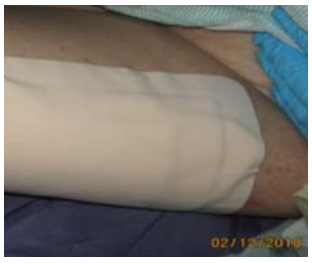


Figure 6C. Hydropolymer foam dressing applied over PROMOGRAN PRISMA™ Matrix, which covered the donor site

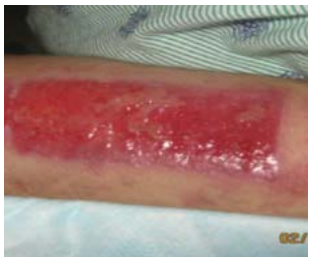


Figure 6D. Donor site post-operative day 14 after removing the PROMOGRAN PRISMA™ Matrix and hydropolymer foam dressings

Case Study 3 (CONT.)

On postoperative day 15, the surgeon evaluated the donor site, so the dressing was changed. The wound continued to improve with more epithelial islets noted **(Figure 6E)**. The PROMOGRAN PRISMA™ Matrix and the hydropolymer foam dressings were left in place and changed on postoperative day 17, prior to the patient's discharge to an extended care facility **(Figure 6F)**.

The patient's donor site reepithelialized completely by the next dressing change on postoperative day 20. The dressing maintained a moist wound environment without maceration of the peri-donor skin, and the improved exudate management with the combination of the PROMOGRAN PRISMA™ Matrix and the hydropolymer foam dressings helped the dermatitis resolve.

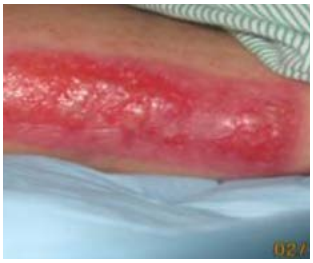


Figure 6E. Donor site postoperative day 15 after removal of PROMOGRAN PRISMA™ Matrix and hydropolymer foam dressings

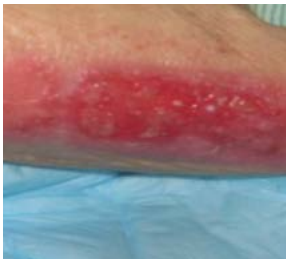


Figure 6F. Donor site postoperative day 17 at time of hospital discharge

Case Study 4

A 74-year-old male presented with a 2.5cm, 27-month-old diabetic foot ulcer (DFU) on the bottom of the right foot **(Figure 7A)**. The patient had a history of diabetes mellitus and had previously undergone a transmetatarsal amputation.

Wound fluid and measurements were taken at wound presentation and every 2 weeks up to 14 weeks. A PROMOGRAN PRISMA™ Matrix was applied over the wound. Wound fluid was tested for elastase and MMP-9 activity using either a fluorogenic substrate or immunocapture activity assay.

At presentation, MMP-9 activity was measured at 227.2 relative fluorescence units (RFU)/minute/mL and elastase measured at 568.6 RFU/minute/mL. At week 4, the wound showed a healthy pink granulation bed and slight enlargement of the wound **(Figure 7B)**. At week 12, MMP-9 and elastase activity measured 5.4 RFU/minute/mL and 277.1 RFU/minute/mL, respectively. This decrease in activity was calculated to a 97.6% reduction of MMP-9 activity and 51.3% reduction in elastase activity. By week 14, the wound was fully reepithelialized **(Figure 7C)**.

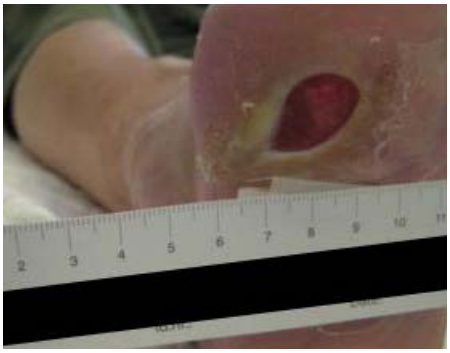


Figure 7A. Diabetic foot ulcer on bottom of right foot at presentation

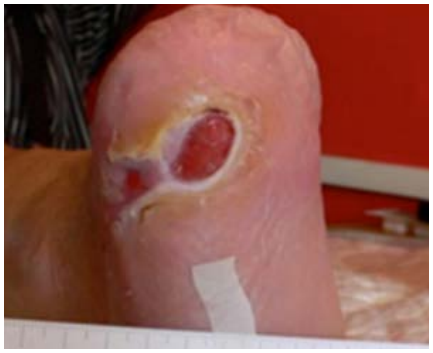


Figure 7B. Wound at week 4

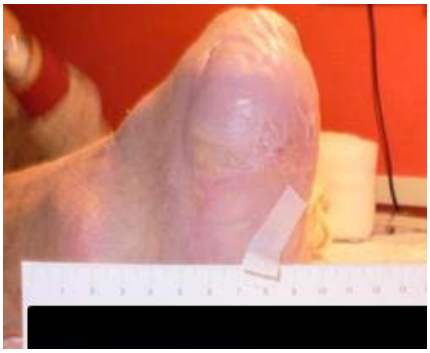


Figure 7C. Wound fully reepithelialized at week 14

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