



HydroClean[®] plus

**Hydro-Responsive Wound
Dressing (HRWD):
Clinical and Scientific
Monograph**

Mark G. Rippon , PhD.¹ and Karen Ousey, PhD.²

¹Visiting Clinical Research Fellow & ²Reader Advancing Clinical Practice, School of Human and Health Sciences, Institute of Skin Integrity and Infection Prevention, University of Huddersfield, Queensgate, Huddersfield

THE AUTHORS

The importance of moist wound healing as the basis for modern wound care has been well established since the seminal papers of George Winter in the early 1960s and an optimal hydration balance is seen as one of the key components of wound bed preparation.¹ A recent European Wound Management Association document on debridement and its role in wound care emphasises wound cleansing or debridement as a common component in the care of acute and chronic wounds, necessary to prepare the wound bed and to promote the progression of the healing response along the wound healing continuum.²

The cleansing (removal of “dirt” – loose cellular debris or foreign material) and debridement (the removal of tissues including (but not limited to) necrotic tissue, eschar, devitalised tissue and infected tissue) remove the foci for wound tissue irritation and bacterial colonisation and/or proliferation that are likely to elevate the inflammatory status of the wound and impair the progress to healing.²

Several techniques are available to the clinician to achieve wound cleansing and debridement including mechanical, enzymatic and autolytic debridement.^{2,3} Autolytic debridement is the term which describes the natural process by which a moist environment promotes the removal of necrotic, sloughy or devitalised tissue,² and it is a process which is supported and enhanced by moist wound healing. Via a dual mode of action, wound dressings which act via autolytic debridement donate fluid to the wound bed and absorb excessive tissue-damaging wound exudate components (e.g., proteinases such as Matrix Metallproteinases (MMPs)). Moderate levels of the patients’ endogenous enzymes then soften and break down necrotic and sloughy tissue which can be easily removed at subsequent dressing changes.

This document focuses on the cleansing and debridement of the wound bed of chronic wounds as part of a phase-adapted wound treatment, promoting the wound bed for new granulation tissue formation and progression of the healing response. It examines the evidence relating to Hydro-Responsive Wound Dressings (HRWD) containing superabsorbent polyacrylate particles ‘activated’ with Ringer’s solution.

TABLE OF CONTENTS

TABLE OF CONTENTS	3
FOREWORD	4
EXECUTIVE SUMMARY	5
1. ABSTRACT	6
2. INTRODUCTION	6
i. Moist wound environment	6
ii. Damaging nature of chronic wounds	7
iii. Wound environment optimisation	7
3. HYDRO-RESPONSIVE WOUND DRESSING (HRWD)	8
i. Overview	8
ii. Superabsorbent polyacrylate	9
iii. Intended uses	10
iv. Method of use	10
4. SCIENTIFIC AND CLINICAL EVIDENCE	10
i. Literature search methodology	10
ii. In vitro properties	10
a. Cleansing	10
b. Matrix metalloproteinases	12
iii. Clinical evaluations	12
a. Burns	12
b. Acute wounds	13
c. Chronic wounds	16
d. Skin grafting	25
e. Miscellaneous wounds	25
f. Cost-effectiveness of Hydro-Responsive Wound Dressings	26
5. CONCLUSION	27
6. REFERENCES	28
7. INDEX	30
8. APPENDIX	31

FOREWORD

The importance of moist wound healing as the basis for modern wound care has been well established since the seminal papers of George Winter in the early 1960s and an optimal hydration balance is seen as one of the key components of wound bed preparation.¹ A recent European Wound Management Association document on debridement and its role in wound care emphasises wound cleansing or debridement as a common component in the care of acute and chronic wounds, necessary to prepare the wound bed and to promote the progression of the healing response along the wound healing continuum.²

The cleansing (removal of “dirt” – loose cellular debris or foreign material) and debridement (the removal of tissues including (but not limited to) necrotic tissue, eschar, devitalised tissue and infected tissue) remove the foci for wound tissue irritation and bacterial colonisation and/or proliferation that are likely to elevate the inflammatory status of the wound and impair the progress to healing.²

Several techniques are available to the clinician to achieve wound cleansing and debridement including mechanical, enzymatic and autolytic debridement.^{2,3} Autolytic debridement is the term which describes the natural process by which a moist environment promotes the removal of necrotic, sloughy or devitalised tissue,² and it is a process which is supported and enhanced by moist wound healing. Via a dual mode of action, wound dressings which act via autolytic debridement donate fluid to the wound bed and absorb excessive tissue-damaging wound exudate components (e.g., proteinases such as Matrix Metallproteinases (MMPs)). Moderate levels of the patients’ endogenous enzymes then soften and break down necrotic and sloughy tissue which can be easily removed at subsequent dressing changes.

This document focuses on the cleansing and debridement of the wound bed of chronic wounds as part of a phase-adapted wound treatment, promoting the wound bed for new granulation tissue formation and progression of the healing response. It examines the evidence relating to Hydro-Responsive Wound Dressings (HRWD) containing superabsorbent polyacrylate particles ‘activated’ with Ringer’s solution.



Hans Smola, MD

Professor of Dermatology
University of Cologne, Germany

Director Medical Competence Center
PAUL HARTMANN AG, Germany

-
1. Wound Healing: Evidence-Based Management (4th edition), McCulloch JM, Kloth LC, eds., F. A. Davis Company, Philadelphia, USA.
 2. Strohal R, Apelqvist J, Dissemond J, O’Brien JJ, Piaggese A, Rimdeika R, Young T. EWMA document: debridement. *Journal of Wound Care* 2013; 22: (Suppl. 1), S1-S52.
 3. Hinchliffe RJ, Valk GD, Apelqvist J, Armstrong DG, Bakker K, Game FL, Hartemann-Heurtier A, Löndahl M, Price PE, van Houtum WH, Jeffcoate WJ. A systematic review of the effectiveness of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes/Metabolism Research and Reviews* 2008; 24: (Suppl. 1), S119-S144.

EXECUTIVE SUMMARY

- The primary objective of this document is to review the scientific and clinical evidence in support of the Hydro-Responsive Wound Dressing (HRWD)
- Scientific evidence: laboratory studies provide evidence for sequestration of proteins and bacteria from model and clinical fluids into dressings. Levels of damaging tissue-degrading proteins found in clinical samples reduced when incubated with HRWD
- Clinical evidence: HRWD promotes removal of devitalised tissue from a variety of chronic wounds (e.g., burns, venous leg ulcers, pressure ulcers, diabetic foot ulcers) via autolytic debridement and promotes new granulation tissue formation and wound progression towards healing
- Clinical evidence: cost-benefit analyses, where carried out, show the potential for significant cost savings associated with the use of HRWD
- Clinical evidence: HRWD is safe and well tolerated by patients. Patients and clinicians report being very satisfied when HRWD is used with reductions in wound pain and pain experienced at dressing changes being frequently reported
- The majority of clinical studies are non-comparative observational studies, with case reports and case series studies being the predominant study type. Additional and more rigorously designed comparative clinical studies, published in peer-reviewed journals would increase the products' evidence base

1. ABSTRACT

Wound healing progresses via a series of co-ordinated phases. Impaired healing arises when there is a disruption in the normal progression of any one of these phases. The healing response of chronic wounds such as ulcers is halted in the early inflammatory phase and treatment of the local wound environment to establish a moist healing environment, as well as treating the underlying disease processes, is required to maximise subsequent healing. The Hydro-Responsive Wound Dressing (HRWD) containing polyacrylate superabsorbent particles is an advanced wound dressing that promotes a moist wound environment, debrides and desloughs, cleanses the wound bed and absorbs excessive wound exudate (fluid and damaging biological components), thus conditioning the wound bed for subsequent granulation tissue formation and healing.

KEY WORDS: wound care; wound healing; pain; wound infection; clinical effectiveness; quality of life; health economics; superabsorbent; wound progression; debridement; hydro-responsive, desloughing PHMB, Ringers Solution

2. INTRODUCTION

2.1 MOIST WOUND ENVIRONMENT

The maintenance of an optimal hydration balance in the skin is necessary for the skin to function. Once breached, the disruption of the skin barrier and the formation of a wound to the open external environment introduces a number of challenges to these optimisation processes that maintain the ideal moisture levels.¹ When left exposed, wound tissue dries out and forms a dry crust over the wound surface. This process, together with the biochemical cascade of haemostasis, ensure that blood and additional fluid loss is halted and the open wound is sealed off from the exposure to potential contaminants (e.g., bacteria). However, the formation of an eschar/scab over the wound leads to delays in healing.

There is growing evidence that good tissue hydration may be the single most important external factor responsible for optimal wound healing.² George Winter's landmark pre-clinical studies³ and Hinman & Maibach's clinical work⁴ of the 1960s were the first to show that the level of tissue hydration had a significant impact in the healing response. Skin wounds occluded with a polyurethane film were prevented from drying out and a moist environment was promoted. Occluding the wounds led to an improvement in the speed and quality of healing. Re-epithelialisation rates were increased and scarring of the wound site was reduced. Subsequent pre-clinical and clinical studies have provided supportive evidence for the concept of moist wound healing^{5,6,7,8} despite concerns that promoting a moist healing environment would result in increased levels of bacterial numbers in wounds.⁹ However, misgivings about increased infection rates under occlusion appear unfounded as studies have shown reduced infection rates in wounds under occlusion despite the wounds being colonised by bacteria.¹⁰ There have been a myriad of dressings developed that supposedly promote the establishment of a moist healing environment.¹¹

Although it has been difficult to establish what the required level for an "optimal moist wound healing environment" should be,¹² it has been assumed that the presence of free fluid at the tissue-dressing interface is to be avoided. Tissue maceration due to the prolonged exposure of tissue – particularly peri-wound skin - to moisture has been a concern. In particular, the clinical observations of peri-wound damage and tissue maceration around more complex wounds where management of wound exudate has been lacking, have focused clinicians and wound dressing developers to minimise the levels of free fluid exposure of wound tissue and wound margin skin.^{13,14} However, a number of studies have suggested that wounds treated in a wet environment, i.e., wounds bathed in fluid, does not result in tissue maceration^{5,6,8,15} Rather, these wounds appear to benefit from the advantages of moist wound healing. When wounds are covered with chambers in order to bathe wounds in saline fluid to create a wet healing environment, pre-clinical and clinical studies have

shown wet wound healing to be a safe and supportive environment. Wounds under wet healing conditions appear to progress in a similar manner to moist wounds – wounds show less tissue necrosis, faster healing rates and a better quality of healing (reduced scarring) compared with dry wounds.^{8,16} Recent studies have suggested that a wet environment may promote wound healing via skin grafts.^{17,18}

It appears that it is the components within wound exudate rather than the aqueous component that may be responsible for the exudate-related tissue damage seen in chronic wounds treated with dressings with sub-optimal fluid management capabilities.

2.ii DAMAGING NATURE OF CHRONIC WOUNDS

Dermal wound healing progresses through a series of distinct but overlapping, inter-dependent steps (phases) to ensure that any disruption in skin integrity is repaired as quickly as possible. Any disruption of the normal progression of any phase of healing leads to delayed healing. Investigations suggest that the underlying disease processes that cause chronic wounds such as venous leg ulcers, pressure ulcers and diabetic foot ulcers disturb the normal progression of wound healing, halting the healing response in the inflammatory phase.¹⁹ The sustained and elevated levels of localised inflammation at the wound site results in a feedback of further irritation of the wound tissue. Consequently, ulcers are highly inflamed tissues where disruption in healing is due to the combined influences of the underlying disease processes and localised tissue irritation.^{19,20}

One of the key causes of delayed healing in ulceration is the increased levels of protein-degrading enzyme activity within the wound.²¹ Whereas an ordered and appropriate inflammatory response in normal wound healing means a controlled proteolytic activity responsible for the ordered degradation and removal of necrotic tissue and damaged dermal matrix,²² the uncontrolled and elevated level of inflammatory cells in chronic wound

tissues results in a correspondingly disruptive tissue degradation. Inflammatory cell-derived protein-degrading enzymes such as matrix metalloproteinases (MMPs)^{23,24} and neutrophil elastase (HNE)^{21,25,26} break down the tissue matrix proteins and growth factors necessary for healing to progress.^{25,27} Due to the chaotic nature of the biological and biochemical processes of the chronic wound, inefficient “useful” tissue breakdown is also seen, leading to the persistence of necrotic tissue and sloughy material on the wound surface and the favouring of bacterial colonisation (Figure 1). Areas of wound dressing research have focused on developing new dressings designed to target the excessive and damaging proteinases present in chronic wounds.^{28,29,30,31}

2.iii WOUND ENVIRONMENT OPTIMISATION

As a result of the pathophysiology of chronic wounds such as venous leg ulcers, local wound treatment is just as important as appropriate clinical treatment of the underlying disease causes. The promotion of an optimal wound healing environment to aid healing is central to the use of modern wound dressings in the management of chronic wounds.³⁰ The objective of a dressing that promotes a moist environment is to provide the wound surface with 100% humidity without there being any free water¹. The establishment of a moist healing environment promotes the cleansing of the wound (via autolytic debridement) and the conditioning of the wound bed, optimising the conditions for subsequent healing.^{22,32} Polyacrylate superabsorbent particles are a heterogeneous class of synthetic polymers with remarkable physico-chemical properties and are able to absorb large volumes of water compared with their own dry weight.^{33,34} The material's high density of ionic charges accounts for their protein-binding capacity^{29,35,36} as well as their interaction with water. These polymers were first used in nappies (diapers), feminine hygiene products and later developed for wound dressing applications (pre-swollen with Ringer's solution). Pre-swollen wound dressings containing polyacrylate



Figure 1 A-D: Necrotic tissue and slough in wounds of differing aetiologies: A) Venous leg ulcer with high levels of wound exudate and showing a sloughy wound bed; B) Grade 4 pressure ulcer with wound cavity filled with slough. Presence of sloughy material within the cavity prevents an accurate measurement of wound depth; C) Dehisced surgical wound with presence of necrotic and sloughy tissue in the wound bed; D) Diabetic foot ulcer with wound bed containing both slough and granulation tissue.

superabsorbent particles are able to provide moisture to a wound and promoting a moist wound environment whilst, at the same time, absorb significant amounts of wound exudate as well as the destructive components contained within the fluid (e.g., proteolytic enzymes).³⁷ These dressings are particularly effective at cleansing the wound during the early inflammatory phase and contribute to reducing the level of localised tissue irritation and damage, thus promoting wound progression.

3. Hydro-Responsive Wound Dressing (HRWD)

The HRWD product group comprises of the following:

- TenderWet
- TenderWet 24
- TenderWet 24 active (now known as HydroClean)
- TenderWet plus (now known as HydroClean plus)

The first generation of the HRWD product range received the CE mark in 1995. Over the years, the core technology of these dressings has remained essentially unchanged, though there have been slight modifications to improve some aspects of the dressing, e.g., ease of application. Early HRWD versions require a “pre-activation” step with a defined volume of Ringer’s solution prior to dressing application, in order to hydrate the superabsorbent core. In contrast, more recent HRWD products are pre-activated with Ringer’s solution and are presented in a ready-to-use form. Table 1 shows a summary of the evolution of the different product types. For the purposes of this discussion, the name HRWD is used as a general term for the product group.

3.i OVERVIEW

The HRWD is an advanced wound dressing that consists of a wound pad that incorporates superabsorbent particles pre activated with Ringer’s Solution. Ringer’s solution is a physiological solution composed of a number of salts (Sodium Chloride, Potassium Chloride, Calcium Chloride) dissolved in water. The advantages of Ringer’s solution

Product	TenderWet®	TenderWet® 24	HydroClean® (TenderWet® 24 active)	HydroClean® plus (TenderWet® plus)
Pre-moistened SAP			X	X
PHMB				X
Duration of use (h)	12	24	24	72
On the market	1995	1999	2004	2011
Notes	Now discontinued	Now discontinued	Unavailable in the UK	Currently available in the UK

Table 1: Summary of HRWD product range

over normal saline (Sodium Chloride) is that the former is an artificial extracellular fluid designed to substitute for body fluids such as blood plasma, haemolymph with respect to important variables such as ionic concentration, pH and osmotic pressure. HRWDs cleanse the wounds devitalised tissue (necrosis and slough) and absorb wound exudate. HRWDs contain the antimicrobial antiseptic Polyhexamethylene biguanide (PHMB) bound to the superabsorbent core which provides an antibacterial effect. The use of antiseptics as a means of preventing bacterial proliferation provides an alternate strategy to controlling bacterial numbers in the wound. Because of the ability of antiseptics to affect multiple targets, antiseptics such as PHMB are less likely to generate resistance in bacterial populations when used over extended periods of time.³⁸ For example, in over 60 years of use there has been no evidence of the development of bacterial resistance to PHMB. In addition, there has been little evidence of toxicity to PHMB. The wound dressing pad consists of:

- a hydrophobic wound contact layer;
- a superabsorbent polyacrylate hydrogel core pad (may also contain PHMB) pre-activated by Ringer's solution;
- a semi-occlusive backing

Silicone strips applied to the wound contact layer of HRWDs prevent the dressing from adhering to the wound.

3.ii SUPERABSORBENT POLYACRYLATE

Polyacrylate superabsorbent materials are a class of synthetic polymers with hydro-responsive properties. Composed of polymerised polyacrylic acid, these polymers are able to absorb several times their own dry weight in fluid due to their high density of ionic charges.³³ There are different varieties available which differ in their physico-chemical properties.³³ When pre-activated with Ringer's solution, salt solution is donated to the wound environment, whilst at the same time, bacteria and tissue debris-laden wound exudate are absorbed into and retained by the polyacrylate core. This exchange occurs due to the higher affinity of the polyacrylate polymer for the protein in wound exudate compared with the Ringer's solution salts. This effect produces a continuous rinsing effect for supporting effective wound bed preparation (Figure 2).

In vitro and in vivo studies have demonstrated that HRWD polyacrylate polymers are able to sequester protein-degrading enzymes such as MMPs. Studies have

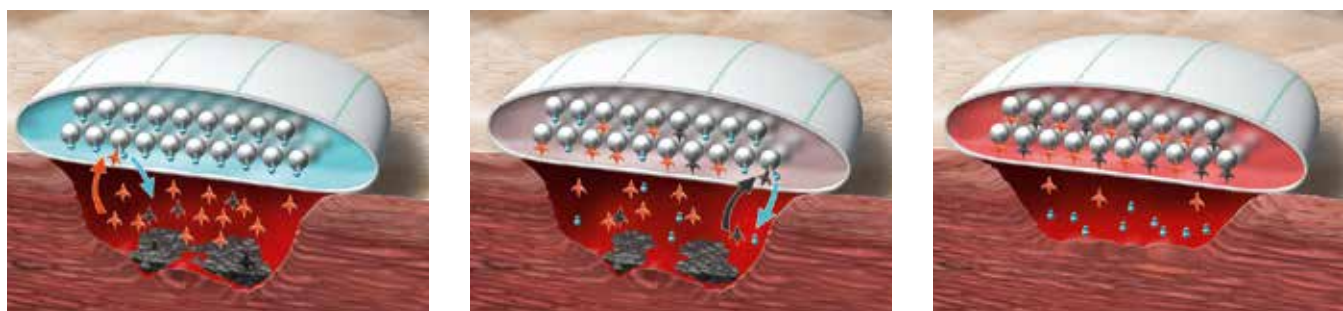


Figure 2: Method of action of hydro-responsive wound dressing (HRWD): Rinsing-Absorption Mechanism. Cleanses fibrin and necrotic tissue effectively by its rinsing-absorption action (left), absorbs exudate and binds bacteria and proteins that inhibit healing (centre), and stimulates the formation of granulation tissue.

also demonstrated bacteria uptake into the polyacrylate polymer core.^{35,39}

3.iii INTENDED USES

HRWDs can be used on a variety of acute and chronic wounds including: pressure ulcers, leg ulcers (venous, arterial, mixed aetiology), diabetic foot ulcers, acute wounds, surgical wounds, burns, donor sites, malignant wounds, traumatic wounds (e.g., skin tears), abrasions (e.g., road rash). HRWDs may also be used on infected and fungating wounds. HRWDs are not intended to replace anti-microbial therapy (including systemic antibiotics) and infected wounds should continue to be treated as per local clinical protocols. HRWDs can be used under compression bandaging.

HRWD are designed for the management of wounds needing good exudate management together with cleansing and conditioning of the wound bed in order to encourage an optimal wound environment and to support wound healing progression. Indicated wound types include complex wounds with high exudate levels, infected wounds or in various chronic wounds (e.g., leg ulcers, diabetic foot ulcers and pressure ulcers). HRWD can be used under compression bandaging.

3.iv METHOD OF USE

Local standard clinical practices should be adhered to prior to and following the dressing change:

1. The wound may be cleaned prior to application of the dressing.
2. The dressing's packaging should be opened and the white side of the HRWD dressing applied to the entire surface of the wound. The side of the dressing with green stripes should be uppermost and be facing away from the patient.
3. Pack deeper wounds with a cavity version of HRWD. This dressing does not have green stripes (indicating no water-repellent layer). This dressing may be covered with regular HRWD if managing high levels of wound

exudate.

4. HRWD can be secured with a bandage or other fixation, as required.

4. SCIENTIFIC AND CLINICAL EVIDENCE

4.i LITERATURE SEARCH METHODOLOGY

Searches of internet reference databases (e.g., MEDLINE) were undertaken to identify published articles describing scientific and clinical data relating to HRWD. The search covered the period January 1970 to June 2015. In addition, manual searches of peer-reviewed journals and conference proceedings of relevant to wound management were performed.

In several instances, reference is made to clinical data that

Figure 3A: Delivery of liquid content

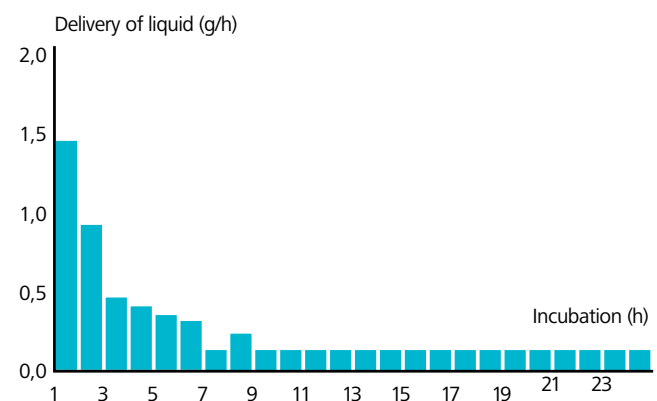


Figure 3B: Protein content

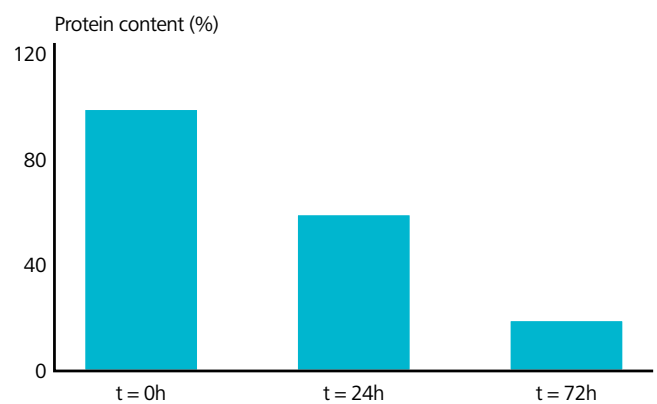


Figure 3: In vitro demonstration of rinsing and absorption effect.

A) HRWD delivers Ringer's solution to the surroundings over a period of 24 hours; B) The protein content in the 'in vitro' wound model decreases after HRWD application over a period of 72 hours. Approximately 80% of the protein is absorbed into the core of the HRWD, with 20% being firmly bound to the superabsorbent material.⁴¹

has the status of "Data on file".⁴⁰ In these cases, the data is available as part of published HARTMANN marketing documents.

4.ii IN VITRO PROPERTIES

4.ii.a CLEANSING

Standard laboratory investigations are used to show the effectiveness of dressing properties. The rinsing and absorbing and rinsing effect of bacteria-laden wound exudate by HRWD has been demonstrated in laboratory studies.

In laboratory investigations, Ringer's solution-activated HRWD continuously delivers Ringer's solution to its surroundings over a 72 hour period. Fluid delivery was particularly efficient in the first few hours, with maximal fluid delivery rates peaking at almost 1.5 g/h (Figure 3a).⁴¹ As well as donating fluid to the dressing's surroundings, the HRWD is capable of absorbing proteins from the wound model and binding them into the superabsorbent core. The protein content of the wound model fluid decreases steadily after dressing application over a period of 72 hours (protein content at this time is 20% of initial levels). In addition, of the 80% of the protein that is absorbed into the HRWD, 20% is firmly bound to the superabsorbent polyacrylate material (Figure 3b).⁴¹

Retention of micro-organisms

As well as absorbing protein from the wound model

"exudate", laboratory studies have shown that HRWD is capable of absorbing and retaining micro-organisms. HRWD significantly reduced (versus controls) the number of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa* and *Candida albicans* in suspension cultures after 24 hours incubation, when HRWD is placed in the inoculated solution (Figure 4).⁴² When the test micro-organisms were grown as a lawn culture on the surface of agar plates, the application of HRWD onto these cultures resulted in a 1 to log10 reduction in the number of viable organisms under the dressing compared with the number of organisms on the adjacent non-covered border area (Figure 5).^{41,42} These results were replicated using clinical cultures obtained from 2 patients with chronic wounds.⁴² After incubation with *Staphylococcus aureus* cultures, examination of the HRWD superabsorbent material using high magnification electron microscope, showed the bacteria adherent to the

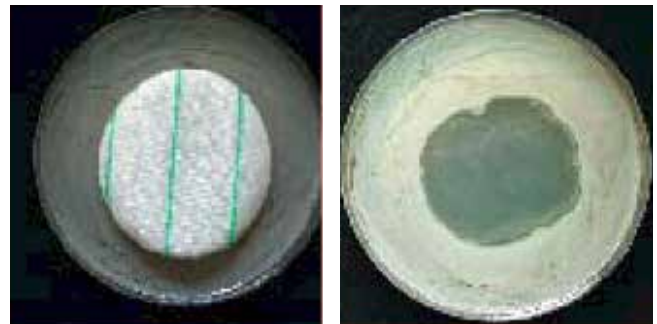


Figure 5: Agar plates inoculated with *Staphylococcus aureus* and HRWD applied and then removed. Bacteria have been absorbed and removed by the HRWD. The placement site is clearly visible as a hole in the bacterial lawn.^{41,42}

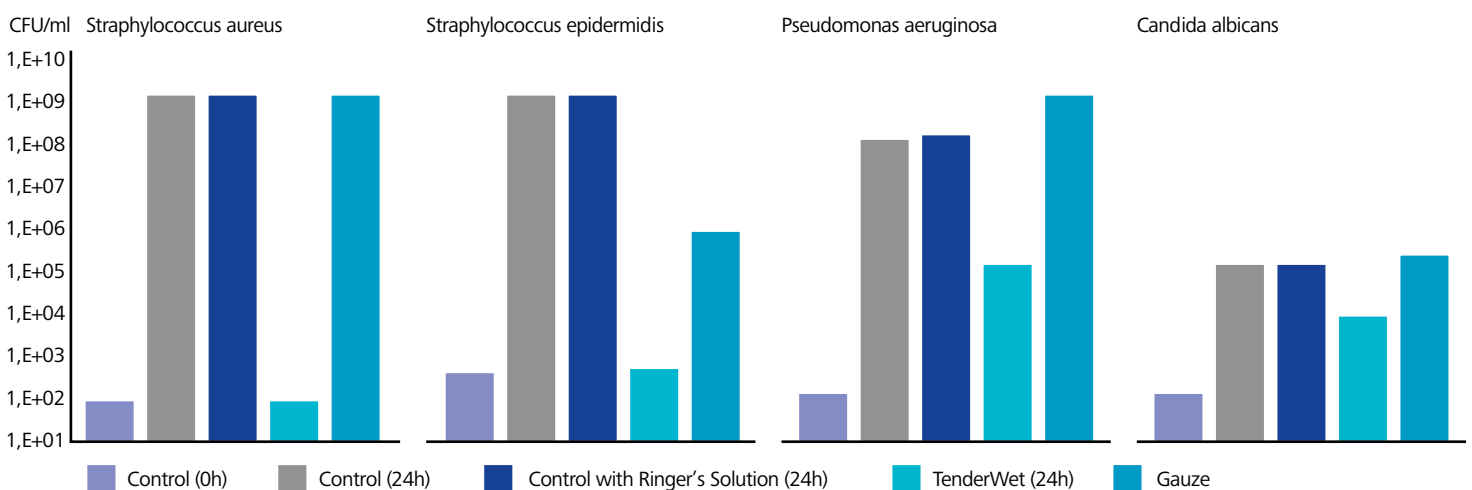


Figure 4: Bacterial count of suspension after 24-hour incubation. When HRWD is placed in the inoculated nutrient solution, the bacterial count falls significantly compared with the controls.⁴²

surface of the absorbent material (Figure 6).⁴² The addition of water did not wash out the bacteria. Courderot-Masuyer and co-workers developed a laboratory model to study the behaviour of normal dermal and ulcer-derived fibroblasts in contact with *Pseudomonas aeruginosa* and HRWD.⁴³ Normal dermal and venous ulcer-derived fibroblasts were embedded within collagen lattices cultures to mimic the ulcer wound bed. Cultures of *Pseudomonas aeruginosa* were placed on to the surface of the fibroblast-containing collagen gels. HRWD was also applied to the surface of the collagen matrix in order to study the behaviour of the cells in response to contact with the wound dressing and to measure the absorbing power of the HRWD for the bacterial culture. The results showed that HRWD had little effect on the normal behaviour of the fibroblasts embedded within the collagen matrix and that the dressing absorbed the bacteria.

4.II.b MATRIX METALLOPROTEINASES

Excessive protein-degrading enzymes have been seen in the wound exudate of chronic wounds. The presence of these enzymes is thought to play a key role in preventing the progression of wounds into the healing phase by interfering with the development of granulation tissue. It is thought that a reduction in the levels of these degrading enzymes,

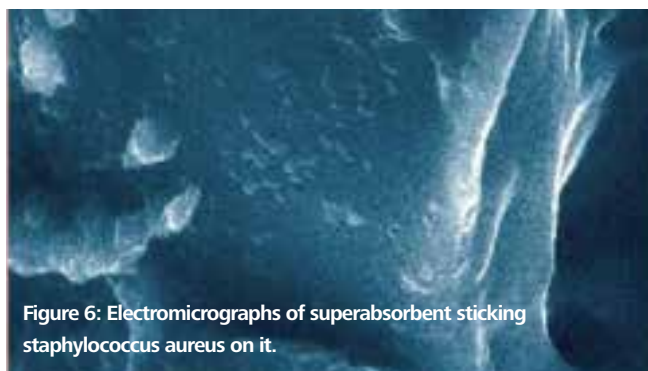


Figure 6: Electromicrographs of superabsorbent sticking staphylococcus aureus on it.

particularly the matrix metalloproteinases (MMPs), may aid the optimisation of the wound environment and encourage healing. A recent study by Eming et al. showed that superabsorbent polyacrylate particles inhibits MMP activity.³⁵ Laboratory studies showed that MMP activity was reduced by more than 87% (Figure 7). In addition, when treated with HRWD, MMPs from the wound exudate

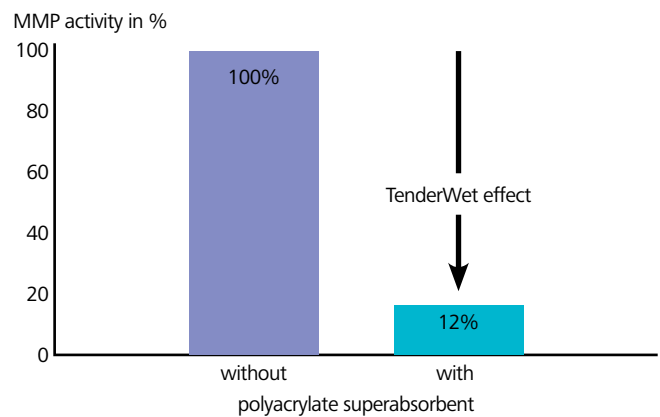


Figure 7: The superabsorbent polyacrylate of the dressing core removes up to 88% of the proteinase activity from wound exudate.³⁵

of 3 patients with chronic venous leg ulcers were strongly bound to the superabsorbent particles of these dressings reducing the excess levels of these degrading enzymes.³⁵ It was also shown that these particles were able to inhibit MMP activity by binding MMPs directly once they were absorbed by the polyacrylate particles via an indirect mechanism involving the binding of divalent cations necessary for enzyme activity (e.g., calcium and zinc.)⁴⁴ in the presence of superabsorbent material, divalent cation levels are reduced, leading to a corresponding reduction in MMP activity in vitro.³⁵

4.III CLINICAL EVALUATIONS

Wound dressings that promote the creation of a moist wound healing environment encourage wound healing and are indicated when the wound needs to be actively cleansed and the wound bed prepared for wound healing progression. Chronic wounds tend to be highly exuding and contain large amounts of tissue debris and a high bacterial load. These characteristics must be controlled in order for the healing environment to be optimised.

4.III.a BURNS

Burn wounds are particularly complex wounds and, although they are generally considered to be acute wounds, their complexity in terms of the spectrum of burn types they can present as clinically (e.g., acute, chronic, traumatic and surgical) means that they can be considered

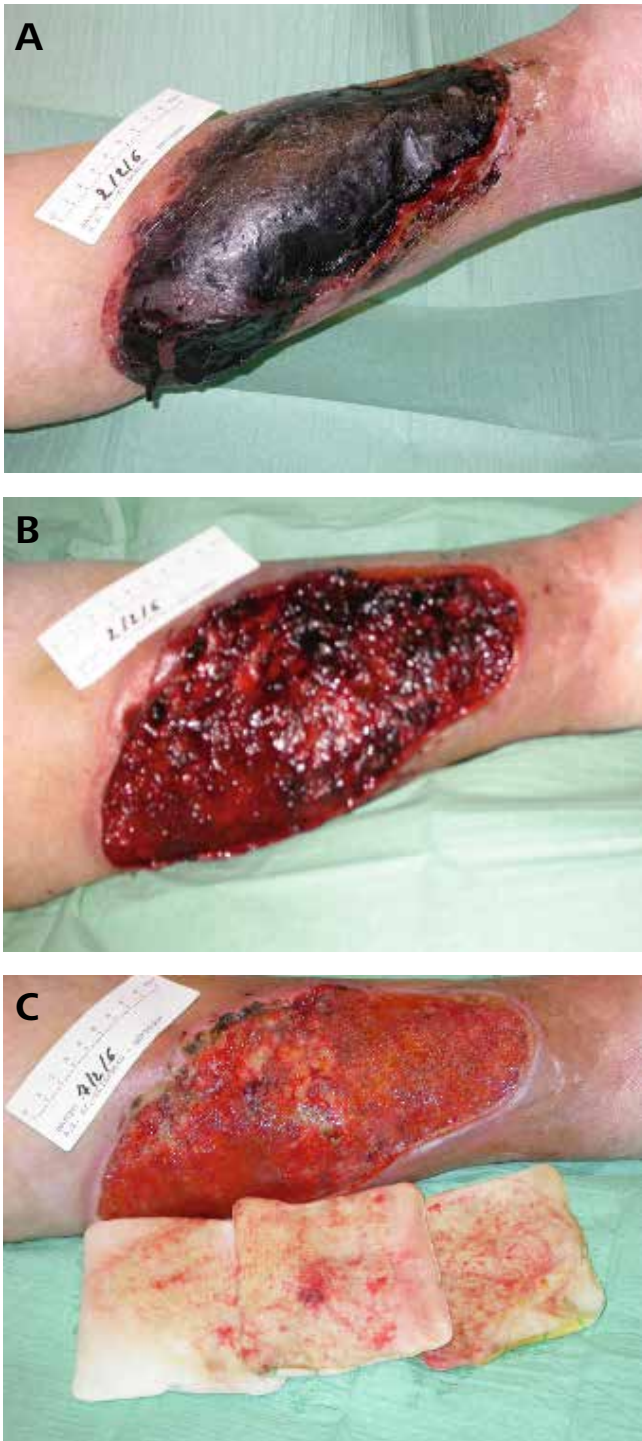


Figure 8: Haematoma formed after a fall which later ruptured and released the clot treated with HRWD. A) First assessment; B) Mechanical debridement of haematoma with thorough flushing of wound and HRWD applied; C) Wound fully debrided 5 days after start of treatment. Photographs courtesy of F. Meuleneire, Zottegem, Belgium.

as a separate wound type.⁴⁵ The management of burn wounds is based on the amount, depth and severity of burns and by the designations as superficial, partial- and full-thickness injuries.⁴⁶

A number of clinical evaluations (Table 2) have demonstrated positive outcomes of using HRWD on burns. Positive results have been reported in the use of HRWD for treating burns over the last few years, particularly in the treatment of small partial-thickness burn wounds and for residual areas of grafted burn wounds which arise when autografts are partially unhealed. Positive clinical results have also been reported in the first few days of treatment in deep dermal wounds.

Case reports on patients with deep dermal burns

In a case report, HRWD was used in the treatment of a 22-year old patient who was suffering from full-thickness burn wounds.⁴¹ Despite healing of the burn wound within one month, the new epithelium broke down as a result of a mixed infection (*Staphylococcus aureus*, *Escherichia coli* and *Enterococcus*) and treatment with HRWD was begun. Within 4 days, the wound was healed after the promotion of new epithelial tissue at the wound site. HRWD was used to help cleanse the wound and condition the wound bed in order to optimise the chances of an allograft “take”. In a 51-year old patient with deep dermal burns, the use of HRWD cleaned the wound of slough and necrotic tissue and reduced significant wound exudation. After 3 days of HRWD application the wound was covered by a cultured epidermal autograft. HRWD was used to help protect the applied graft and within 5 days the wound healed completely.⁴¹

Clinical evaluation in second and third degree burns

A small (n=5), prospective evaluation by Azevedo et al. investigated the response of 2nd and 3rd degree burn wounds treated with HRWD, assessing wound bed preparation/conditioning, wound debridement and the effect of the application of HRWD on patients’ wound pain perception.⁴⁷ The majority of patients reported significant clinical improvement in wound bed appearance within 1-9 days after dressing application and there was a significant reduction in wound pain reported by 3 of the 4 patients surveyed.

4.iii.b ACUTE WOUNDS

Acute wounds, such as surgical wounds, are wounds that progress through the wound healing response in a timely manner and do not need medical intervention. This occurs if the patient is in good health and suffers from no co-morbidities. However, a proportion of these wounds will not progress as expected, leading to a number of problems such as wound site haematoma or wound dehiscence.

Clinical evaluation in surgical wounds treated in community setting

A recent clinical evaluation, 20 patients with a variety of wound types – including surgical wounds (n=6) – were treated in the community with HRWD over a maximum treatment evaluation period of 4 weeks. Overall dressing performance and the ability of the hydro-responsive wound dressing to facilitate wound bed preparation and wound progression were primary outcome measures.⁴⁸ HRWD rapidly reduced devitalised tissue in the wound bed and the progression of wounds towards healing was observed.

Case reports: haematoma wound

A number of case studies have been reported evaluating the use of HRWD in acute wounds where clinical intervention is required to aid healing (Table 3). In one case, HRWD was used in order to prepare the wound for subsequent wound care therapy. The 76-year old patient had developed a haematoma at the incision site following intestinal surgery. The haematoma was cleared and the wound was rinsed out and the HRWD was applied. Over the subsequent days, the wound cavity shrunk significantly and by day 13 post-treatment a combination of wound contraction and new granulation tissue raised the wound base to the height of the surrounding epidermis. Subsequent treatment with a hydrocellular gel dressing resulted in wound healing after 39 days.⁴¹ The development of a haematoma with necrotic tissue and subsequent blister in an 82-year old patient after she bumped against her wheelchair was treated by the surgical removal of the blister followed by

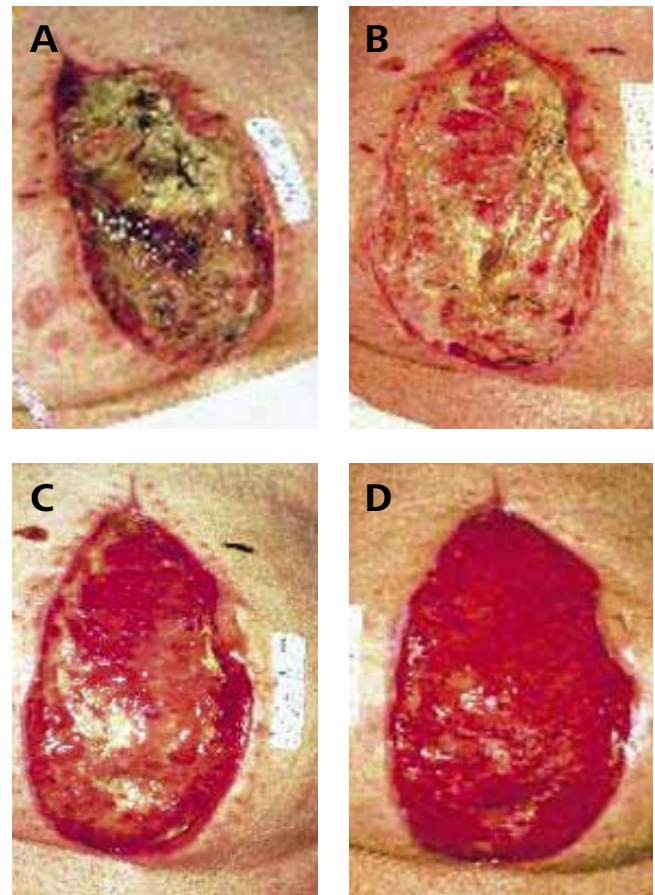


Figure 9: Dehiscent medial abdominal wound treated with HRWD. A) First assessment; B) Reduction in necrosis and slough 2 days after start of treatment; C) Wound almost completely clean and granulation tissue formation progressing; D) Wound filled with healthy granulation tissue and epithelialisation has begun from the wound margins 3 weeks after start of treatment.⁴¹

application of HRWD. Over the course of the following 8 weeks there was significant improvement of the wound bed as healing progressed.⁴⁹

Case report: traumatic wound of tibia

Meuleneire described how the atraumatic nature of HRWD resulted in the minimising of stress in a patient receiving treatment for a traumatic necrotic wound on the tibia.⁴⁹ Having developed a necrotic wound due to blunt trauma on the lower limb, a 69-year old female received debridement to cleanse her wound of necrosis, followed by application of HRWD to progress the conditioning of the wound bed for subsequent healing. The atraumatic dressing changes causing little or no pain and minimising the number of changes needed during treatment.



Figure 10: Traumatic wound resulting in soft tissue amputation of tip of big toe treated with HRWD. A) First assessment, 90% of wound covered with fibrin slough; B) Debridement of wound 4 days after start of treatment; C) Epidermis formed at wound margin by 18 days; D) Wound is 90% epithelialised one month after start of treatment. Regrowth of nail also noted. Photographs courtesy of F. Sterpione, Echirolles, France.

Case reports: dehisced abdominal surgical wound

In another case report, an 83-year old patient showed clinical signs of localised infection after a laparotomy. The wound dehisced and presented with large amounts of malodorous exudate and the wound base was covered by a thick necrotic layer. HRWD was applied in order to cleanse the wound and prepare the wound bed for a skin graft. Within 2 days of commencing HRWD treatment the wound eschar had reduced by 50% and after 18 days there was no necrotic tissue present in the wound and healthy granulation tissue was present. HRWD treatment had conditioned the wound for the next stage of the patient's care: further treatment with a hydrocellular gel dressings led to the successful coverage of the wound with a skin graft.⁴¹ A recent case report on the effectiveness of HRWD on the treatment of a patient with a dehisced abdominal surgical wound highlighted the dressing's ability to cleanse wound bed tissue.⁵⁰ Following the breakdown

of an abdominal wound following a laparotomy for small bowel obstruction, HRWD was applied to the wound after treatment with negative pressure wound therapy. Upon application with HRWD there was a rapid development of the wound bed granulation tissue and it was noted that the peri-wound skin remained healthy looking and appeared well hydrated. Wound closure was achieved within 7 weeks of first applying the hydro-responsive dressing.

Case report: lower limb amputation wound

HRWD was applied to a 57-year old patient to remove wound exudate, cleanse the wound of slough and tissue debris and to initiate the formation of healthy granulation tissue. The patient underwent a lower limb amputation due to an ischaemic event above the knee. Following the operation, the wound became infected, producing a malodorous exudate and as the wound steadily worsened levels of necrotic tissue in the wound bed built. HRWD application led to the removal of the necrotic tissue within 2 weeks and the slough was significantly reduced. Healthy-looking granulation tissue formed and within 2 months of the commencement of treatment with HRWD the wound had progressed significantly and healing was completed with the application of a calcium alginate dressing after 4 weeks.⁴¹

Case reports: traumatic wounds

A number of case studies have been reported, which document the use of HRWD in a diverse number of traumatic wounds where these wounds require cleansing to allow healing processes to commence.⁵¹ An 85-year old female presented with a haematoma which had formed subsequent to the patient injuring her lower leg above the ankle. After surgical debridement of the haematoma, the remaining wound surface appeared fibrinous and the peri-wound skin appeared inflamed and fragile. After 10 days treatment with HRWD, the wound was 100% covered with healthy-looking granulation tissue. And after a further 14 days treatment with HRWD to control heavy wound exudate production, the status of the wound had improved enough to allow subsequent treatment and

healing to occur. A 78-year old female with a number of underlying medical conditions (including diabetes mellitus and chronic venous insufficiency) suffered a traumatic wound to the ankle region that showed little sign of healing. Also very painful, an early clinical goal was to promote wound healing by cleansing the wound and optimising the wound environment. Within 14 days of initiation of HRWD treatment, the wound bed took on a healthy and cleansed appearance and the healing response began. HRWD use was stopped and subsequent treatment lead to almost complete healing within 3 months of start of treatment. A traumatic wound to the lower leg of a 54-year old female was admitted to hospital for the debridement of a formed haematoma and necrotic tissue. Negative pressure therapy was initiated in order to promote infilling of the resultant wound cavity with granulation tissue. Local wound treatment using HRWD was then initiated and a well-vascularised wound bed resulted within 14 days and the wound progressed to healing soon after.

Case report: wound healing after failed skin graft

HRWD has been used in healing wounds where there has been a previous failure of a skin graft. Sixteen days after receiving a skin graft on her lower leg to cover a wound with an impaired healing response, the graft failed leaving only 10% of the original graft in place. Appearing to contain significant levels of fibrinous slough, treatment with HRWD was started in order to cleanse the wound. A significant cleansing of the wound was seen within 2 days of initiating dressing treatment and epithelialisation of the wound from the islands of grafted skin was observed after a further 3 days. HRWD cleansed and conditioned the wound bed for healing and the wound went on to heal without further problems.⁵¹

Acute wounds such as haematoma, dehisced abdominal wounds and traumatic wounds that were successfully treated with HRWD are presented in Figures 8-10.

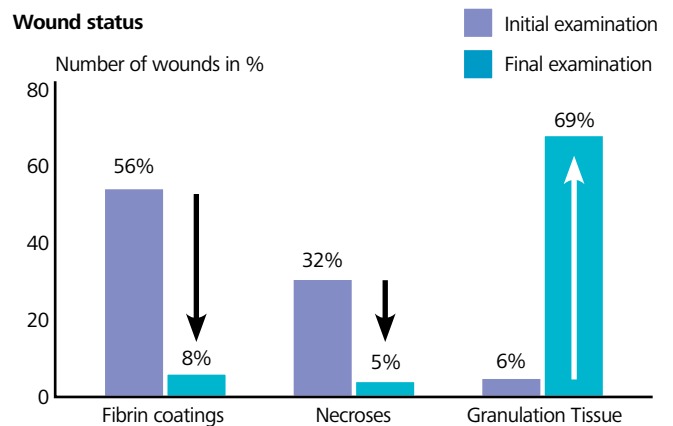


Figure 11: The proportion of wounds with >50% necrosis/slough coverage reduced by the end of HRWD treatment. The proportion of wounds with >50% granulation tissue coverage increases.⁵²

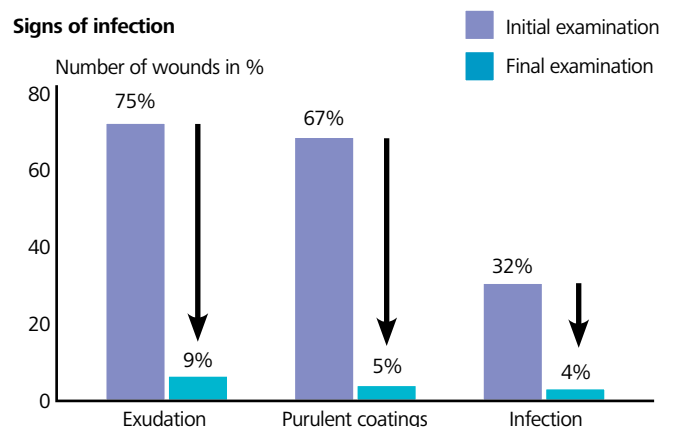


Figure 12: During the course of treatment with HRWD signs of infection decreases.⁵²

4.iii.c CHRONIC WOUNDS

A number of clinical studies have been undertaken to evaluate the use of HRWDs in the treatment of chronic wounds (Tables 4 and 5).

Clinical evaluation in 403 patients with complex wounds (e.g., venous leg and pressure ulcers)

The effectiveness, tolerability and handling of HRWDs was investigated in a clinical, prospective, non-comparative, multi-centre observational study involving patients with a number of wound aetiologies (>75% patients with chronic wounds such as venous leg, pressure, diabetic foot and mixed aetiology ulcers). One hundred and twenty seven physicians (55 general practitioners, 34 dermatologists, 20 surgeons, 9 internal medicine specialists and 9 orthopaedic specialists) documented the course of

Wound site	Initial examination	Final examination
Without pathological symptoms	10	52
Oedema	34	9
Maceration	25	6
Overheating	26	2
Eczema	21	6
Hyperkeratosis	10	5
Reddening	70	26

Table 6: Improvement of wound site⁵²

treatment with HRWDs for an average period of one month. Data collection took place at the beginning of the trial period and the course of the healing was evaluated using a points scale system based on various wound condition parameters (e.g., wound coatings, granulation tissue formation, wound infection and pain). At the end of the study period, the physicians evaluated the wound dressing for effectiveness, handling, product properties and to what extent the product met their expectations. Patients were asked to rate their experiences in terms of tolerability, comfort and pain during treatment.⁵²

Four hundred and three patients were recruited into the study. During the course of treatment with HRWDs, the proportion of wounds with >50% fibrin slough on the wound surface reduced from 56% to 8% over the course of the study period. Levels of necrotic tissue also showed a significant reduction (32% vs. 5%). Clinicians also noted a

corresponding increase in the levels of granulation tissue. At the start of HRWD treatment only 6% of wounds had >50% healthy granulation tissue. This proportion increased ten-fold to 69% by the final examination (Figure 11). Seventy-five percent of wounds showed moderate to high levels of exudation at the start of the study, reducing to only 9% at the final examination. Correspondingly, there were also clear signs of improvement in infection levels. At the initial examination, 32% of the wounds showed clinical signs of moderate to severe infection with only 4% of the wounds showing similar infection levels after treatment with HRWD. Sixty-seven percent of patients presented with moderate or complete coverage of the wounds with purulent material which reduced to 5% at the final examination (Figure 12). Over the course of the treatment fewer patients complained of wound pain. At the final examination, only 13% of patients reported moderate to severe wound pain (compared with 65% at the start of the study) (Figure 13). The effective fluid handling properties of the absorptive HRWD protected the peri-wound skin and led to an improvement in the tissue quality of the skin surrounding the treated wounds. Upon initial examination of the wound sites, only 10% of patients showed no evidence of pathological conditions such as maceration and skin reddening. At final clinical examination and after HRWD treatment, that figure had improved to over 50% of patients showing no skin irritation. For example, maceration of the peri-wound

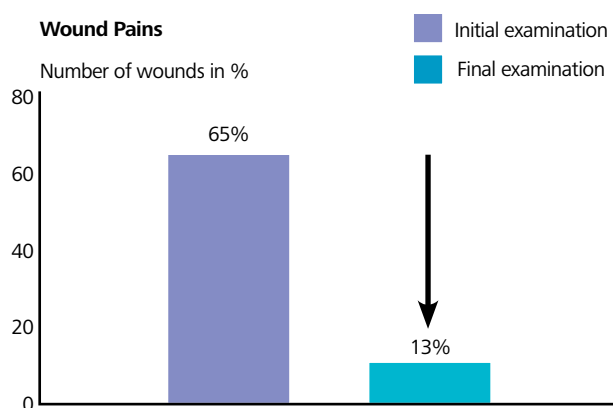


Figure 13: Wound pain. During the course of treatment with HRWD patients experiencing moderate to very severe pain reduces from 65% to 13%.⁵²

skin reduced from 25% to 6% (pre- and post-treatment, respectively) and skin reddening cases reduced from 70% to 26% (Table 6).

Clinicians rated HRWD highly in terms of the properties and ease of use. Over 90% of treating physicians rated absorption capacity, ease of dressing removal and handling of the dressing as "good" or "very good", with 92% of respondents having a "good" or "very good" overall impression of the course of treatment. Fluid handling by HRWD was effective even when used in conjunction with compression therapy. Fifty-six percent of patients received compression treatment alongside HRWD. Because of the firm binding of fluid within the polyacrylate core of HRWD, 90% of clinicians rated the dressings as "very well" or "well" suited for wearing under compression bandages or stockings. A significant proportion of the physicians responded that HRWD fulfilled or exceeded their expectations (52% and 24% of cases, respectively) and in fewer than 5% of treatments, physicians' expectations were "not really fulfilled" or "not fulfilled" (5% and 1%, respectively). In more than 90% of the patients, HRWD was rated as "good" or "very good" in >90% patients when it came to comfort and tolerability. Clinical experience found that the dressing did not adhere to the wound surface and therefore few cases of excessive pain was reported during dressing changes. Eighty-nine percent of patients rated the dressing as "very good" or "good" with regard to pain experienced during dressing change. Ninety-four percent of patients rated their overall impression as "very good" or "good".⁵²

Clinical evaluation in 170 patients with complex wounds (e.g., venous leg, pressure and diabetic foot ulcers)

In another multi-centre, observational study, different types of chronic and acute wounds (predominantly leg ulcer and pressure ulcers but also diabetic foot ulcers and acute wounds such as traumatic and post-surgical wounds) were treated with HRWD and investigators monitored the treatment regimen for an average of eight days or over three dressing changes.⁵³ The condition

of the wound (in terms of levels of tissue necrosis and wound surface fibrin slough, using a point scale), levels of granulation tissue, clinical signs of infection, status of peri-wound skin, ongoing/persistent pain in the wound and pain at dressing change and levels of dressing adherence to the wound were measured at the initial and final examination/dressing change. In total, 170 patients were included in the study. The average age of the patients was 75 years and investigators assessed the patients' general conditions as "good" or "very good" in 68% of cases. In 32%, the general condition was rated as "reduced". The patients had had their wounds for an average of 5 months (with some patients having had their wounds for 20 years or more). In 29% of patients, accompanying compression therapy was applied and in 51% of the patients, additional pressure-relieving measures were taken. In some cases, HRWD had been covered with a secondary dressing. The results of the study demonstrated that, by the end of the observation period, there was a reduction in the number of patients with wounds covered with necroses and fibrin coatings/slough (17% reduced to 10% and 41% down to 33% respectively). The proportion of patients exhibiting wound granulation tissue formation increased from 35% to 46% and the proportion of epithelial tissue increased from 6% to 11%. In addition, 71% of wounds exhibited damaged wound margins at the start of treatment and had reduced to 62% at the final observation.

The results also demonstrated that, by the end of the study period, the proportion of wounds with clinical signs of infection reduced from 24% to 17%. Also, pain severity in the wound and that associated with dressing change were reduced. At the start of treatment, 35% of patients experienced moderate to severe wound pain but this was reduced to only 19% at the end of the study. The proportion of patients experiencing moderate to severe wound pain decreased during dressing change from 28% at the start of the study to 11% at the final examination. HRWD was rated as "good" or "very good" in 96% and 86% of the investigators evaluations for removability and skin compatibility, respectively. The dressing was

rated as “good” to “very good” in 92% of cases by the investigators. HRWD was rated as fulfilling (52%) or even exceeding (24%) expectations with investigators and, when asked if they would use the product in comparable wounds again, 64% answered “very definitely” and 32% answered “possibly”. In only 4% of cases were investigators certain that they would not use the product again. When asked, patients’ acceptance of treatment with HRWD, it was very high. Eighty-seven percent and 63% of patients, respectively, found that the product was “good” or “very good” on wearing and compatibility. In addition, 62% of patients found their expectations “fulfilled” and 15% “exceeded”.⁵³

Clinical evaluation of 221 patients with complex wounds

An open, prospective observational study evaluated HRWD on wound cleansing and induction of granulation tissue in 221 patients with chronic wounds.⁵⁴ Over a period of 1 month, patients with a variety of chronic wounds received treatment with HRWD and the status of the wound was

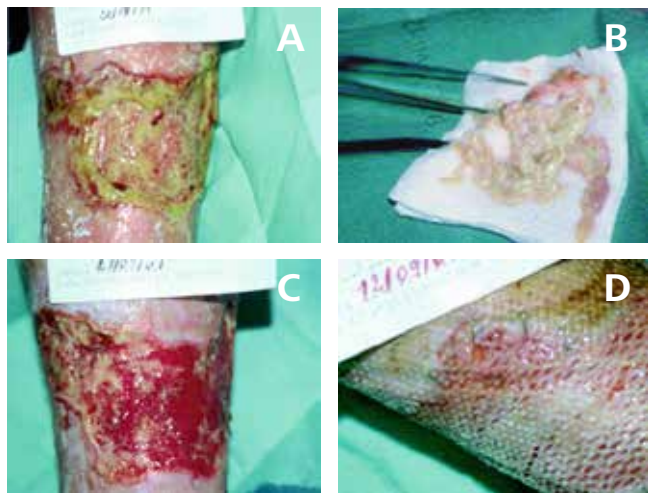


Figure 14: Infected venous leg ulcer treated with HRWD. A) First assessment. Wound is infected, treated with HRWD containing PHMB in conjunction with mechanical debridement and antibiotic therapy; B) Removal of slough from wound during first assessment; C) Wound debridement progressing well 8 days after start of treatment; D) Mesh graft applied to wound 3.5 months after start of treatment. Photographs courtesy of F. Meuleneire, Zottegem, Belgium.

assessed using a standardised questionnaire. The number of wounds completely or partially covered with fibrinous slough (i.e., >50% of wound bed surface area) decreased from 54% to 9% and the number of wounds exhibiting

granulation tissue (>50% surface area) increased from 5% to 74%. The number of wounds showing clinical signs of infection decreased from 53% to 9%, whereas 74% of wounds exhibited high exudate levels which reduced to 10% after the treatment period. When questioned about their experience of pain during the study, the number of patients reporting “intermediate” and “high” levels of wound pain decreased from 64% to 19%. The clinicians concluded that HRWD provided potent debridement activity in the clinic and promoted granulation tissue formation.

Randomised controlled trial (n=75) evaluating wound bed preparation ability vs. amorphous gel

Humbert et al. reported on the results of an open, prospective, randomised, controlled trial that was designed to evaluate the wound bed preparation ability of HRWD (versus an amorphous gel) in patients with venous leg ulcers.³⁹ The study was designed as a multi-centre, two-arm parallel-group study. Seventy-five patients were recruited into the study (HRWD, n=34; amorphous gel, n=41) and the main inclusion criteria included patients with a venous leg ulcer for a minimum of 4 weeks and the wound coverage was >70% fibrin and/or necrotic tissue. Dressings were applied according to the manufacturers’ recommendations and according to wound status and wound beds were evaluated by 3 blinded experts using photographs taken on days 0, 7 and 14. Both groups reduced the proportion of slough and necrosis and an increase in granulation tissue within 14 days. The proportion of ulcer area covered by slough and necrosis decreased by $37.6\% \pm 29.9\%$ in the HRWD group and by $16.8\% \pm 23.0\%$ in the hydrogel group compared to the baseline ($P=0.004$). These changes corresponded to a relative decrease of $43\% \pm 36.7\%$ in the HRWD group and of $21.9\% \pm 39.4\%$ in the amorphous gel group ($P=0.018$). HRWD -treated wounds showed a larger reduction in fibrin slough and necrotic tissue compared to amorphous gel-treated wounds. The proportion of the ulcer covered by granulation tissue increased by $36.0\% \pm 27.4\%$ in the



Figure 15: Stagnating venous leg ulcer treated with HRWD. A) First assessment. Significant fibrin slough present in wound bed. HRWD treatment started in combination with compression; B) Debridement of wound bed 9 days after start of treatment; C) Debridement progresses 22 days after start of treatment. Photographs courtesy of F. Meuleneire, Zottegem, Belgium.

HRWD group and by $14.5\% \pm 22.0\%$ in the amorphous hydrogel group compared to the baseline ($P=0.005$). The probability of having $>50\%$ covered with granulation tissue on day 14 was 16-times higher for wounds treated with HRWD compared with the amorphous hydrogel. In

addition, a comparison of the response rates of ulcers of more than 6 months duration led the study's authors to suggest that these wounds in particular benefited most from treatment with HRWD.³⁹

Clinical evaluation of 20 patients with complex wounds treated in community setting

A recent, multi-centre, community-based clinical evaluation of 20 patients (chronic wounds, $n=13$) found that 1 month treatment with HRWD was effective in debriding devitalised tissue from and facilitating wound progression in wounds of a number of aetiologies.⁴⁸ Overall, at the beginning of the observation period, the mean percentage of devitalised tissue present in the wound bed was 58% and this reduced to 22% after 4 weeks (representing a reduction of 62%). Furthermore, HRWD facilitated an overall reduction in wound size. There was a mean reduction in wound area and wound depth of 21.5% and 45.7%, respectively. Effective wound exudate management resulted in an improvement in peri-wound skin condition, with an increase in the percentage of patients with healthy wound margin skin from 25% to 55%. The reduction of both wound pain experienced by patients and wound malodour, and the positive experiences of patients and clinicians in terms of dressing application and removal plus dressing wear meant that patient and clinical satisfaction was scored as being "highly satisfied."

Clinical observation study in 37 patients with venous leg ulcers

Scholz et al. conducted a 37-patient single-centre observational study where HRWD was used in the treatment of venous leg ulceration.⁵⁵ The study reports on the positive clinical experience when using the hydro-responsive dressing. The patients (some of which also received compression therapy) were treated with HRWD for an average of 19 days. When assessed at the end of the treatment period, HRWD greatly reduced the fibrinous and necrotic slough covering the wound bed and promoted the formation of granulation tissue. The effect of HRWD to



Figure 16: Arterial ulcer treated with HRWD. A) First assessment; B) and C) Debridement of adherent fibrin slough and exudate management; D) Wound is granulating and epidermis has formed at wound margins 3 weeks after start of treatment. Photographs courtesy of A.-A. Allain, Rennes, France.

condition the wound bed and move the healing response on towards healing was noted by the observation that the severity of exudate production was reduced markedly over the study period. At the start of the observation period, 24% of patients showed only slight exudation, 57% of patients exhibited moderate exudation and 19% of patients showed severe wound exudation. After HRWD treatment, 78% of patients had slight exudate levels and 22% of patients showed moderate exudation. No HRWD treated patient showed severe exudation. The findings of this small observational study indicate that HRWD has its greatest impact during the cleansing and granulation stage.

In addition to the wound cleansing properties of HRWD, Scholz and colleagues also reported that, when the patients were asked questions related to their experience of pain during dressing changes, 89% of patients (n=33) reported that they experienced no or "slight" pain during dressing changes and only 4 patients said they experienced "severe" pain during dressing changes.⁵⁵

Clinical observation study of 14 patients with leg ulcers

An observational study on the healing response of 14 patients with leg ulcers (venous and mixed aetiology) when treated with HRWD for 10 days showed that fibrin slough and necrotic tissue levels were significantly reduced in the wound bed during the course of the study.⁴¹ Levels

of granulation tissue increased during the corresponding time period. Existing erythema was noted as improving in 5 patients and a reduction in desquamation was seen in 3 patients perhaps indicating an improvement in exudation levels. The authors of this observational study commented that HRWD effectively conditioned both the ulcer and the surrounding skin.

Randomised clinical trial (n=42) evaluating cleansing efficacy of leg ulcers vs. enzymatic preparation

The effectiveness of HRWD at cleaning and debriding wounds is of benefit for patients requiring skin grafts as part of their wound care. The cleansing effect efficacy of HRWD and enzymatic wound cleansing (using *Chlostridium* peptidase) were compared in a prospective, randomised trial involving 42 patients with leg ulcers.⁵⁶ Data collection took place over 3 weeks after first application of either HRWD or the enzyme preparation. Although slough was reduced by 19% for HRWD compared with 9% for the enzymatic preparation and granulation tissue showed an increase of 26% and 10% respectively, statistical significance could not be achieved between treatments and both wound cleansing methods were noted to be equally effective. The use of HRWD was concluded to be advantageous over enzymatic debridement for a number of reasons. Firstly, the ability of the hydro-responsive dressing to maintain a moist wound environment and to control the levels of wound exudate, thus maintaining an optimal healing environment, was beneficial for promoting subsequent healing, and secondly, the better incorporation and removal of debrided material by HRWD compared with that removed by the dry gauze dressing used as a secondary dressing, aids wound cleansing by the hydro-responsive dressing.

Clinical case series (n=10) evaluating wound bed preparation

Mwipatayi et al. conducted a 10-patient case series, involving patients with a variety of chronic wounds, examining the effectiveness of HRWD in preparing the

wound bed.⁵⁷ Patients were assessed as being suitable for autolytic debridement at being an appropriate method for wound bed preparation. The amount of tissue requiring debridement was assessed and the degree of debridement during HRWD application was followed. A rate of wound debridement was estimated as an average of 6% per day. It was concluded that larger studies were needed to establish statistical significance for the clinical benefits noted from this study.

Case reports of patients with pressure ulcers

A number of case study reports in patients with pressure ulcers treated with hydro-responsive wound dressings, particularly HRWD, significantly improve treatment success with these wounds that can persist for many months. Following a femur fracture in a 75-year old patient, a large sacral pressure ulcer formed. Over a 5 month period the ulcer was treated with HRWD and, during this time, the wound was rapidly cleaned of necrotic tissue and sloughy material covering the surface of the wound. Once cleaned, healthy granulation tissue formed and the size of the ulcer reduced significantly over the time the ulcer was treated with HRWD. In a similar case, a 72-year old patient, also with a sacral region pressure ulcer showed significant improvement after 6 weeks of treatment with a calcium alginate dressing used in combination with HRWD. The wound was clean and showed healthy granulation tissue formation with epithelialisation of the wound beginning after a further 3 months treatment. Ulcer healing was

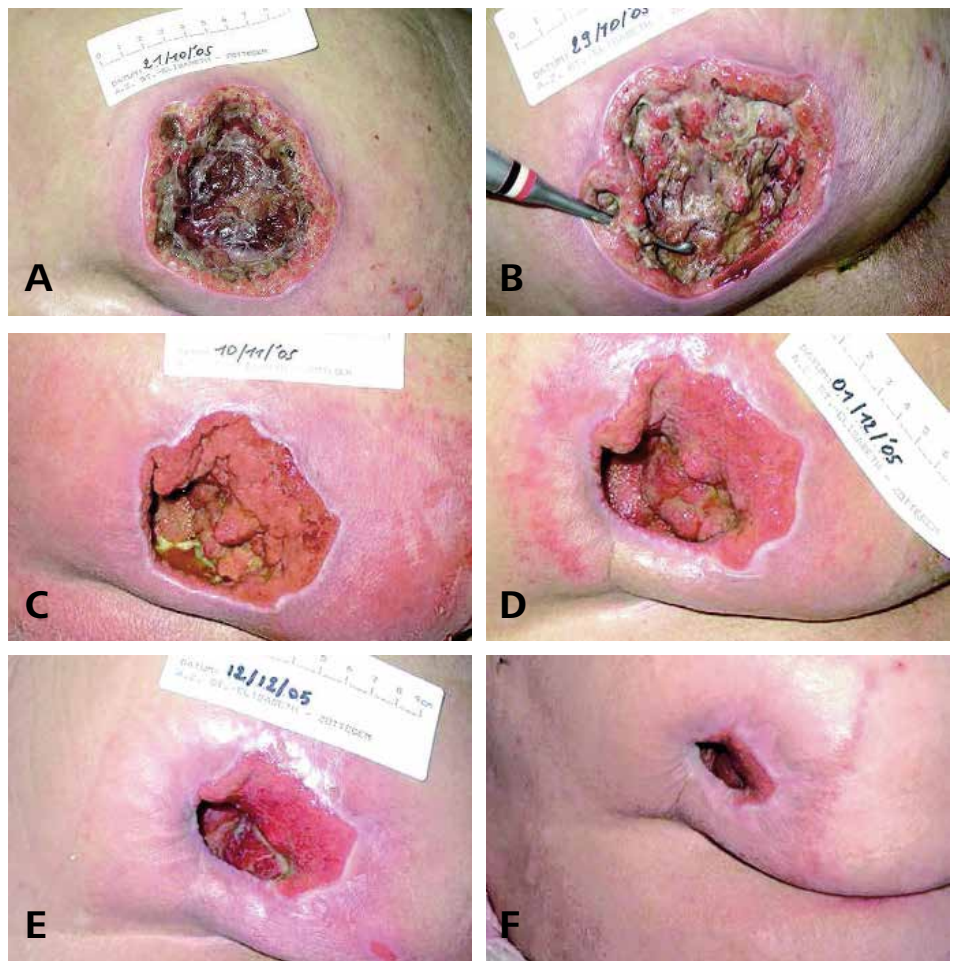


Figure 17: Pressure ulcer treated with HRWD. A) First assessment; B) Removal of necrotic tissue 8 days after start of treatment; C) Wound debridement and cavity treatment continues 22 days after start of treatment; D) Wound progression 43 days after start of treatment; E) Granulation tissue formation in wound bed 55 days after start of treatment; F) Significant wound closure 2.5 months after start of treatment Photographs courtesy of F. Meuleneire, Zottegem, Belgium.

complete one month later. As well as having a sacral ulcer this patient also had necrosis of the left heel and a pressure ulcer on the left hip. Both wounds showed significant improvements over the coming months of treatment with HRWD with complete healing being the positive outcome.⁴¹

Case report: infected diabetic foot ulcer

The use of HRWD to cleanse and condition the wound bed for subsequent healing and help prevent the need for amputation has been reported in patients with diabetic foot ulcers. One case report documented the experience of a 50-year old patient suffering from diabetes mellitus and who was hospitalised due to an infected diabetic foot ulcer on the right big toe. The toe exhibited both soft tissue infection and osteolytic changes. Upon refusing

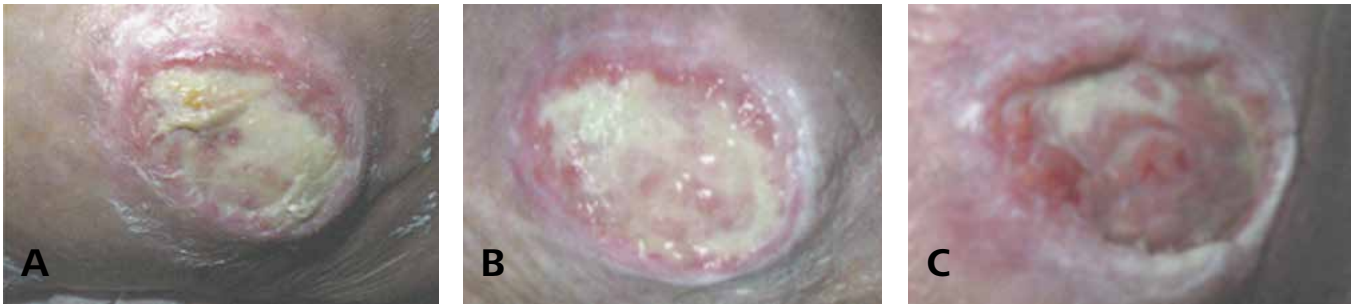


Figure 18: Pressure ulcer on the outer right malleolus treated with HRWD. A) First assessment. Wound covered 90% with fibrinous slough. HRWD started in conjunction with mechanical debridement; B) Improvement in wound bed 4 days after start of treatment; C) Significant reduction in levels of slough and increase in healthy granulation tissue 10 days after start of treatment. Photographs courtesy of C. van Wijk and M. Wiser, Melun, France.

the recommended course of care, i.e., amputation, the ulcer was opened and surgically debrided and HRWD was applied. Significant wound cleansing was observed and healthy granulation tissue formed. Because of good wound healing progression the patient was discharged 7 weeks after the surgical procedure and daily application of HRWD was continued at home. After a total of 4 months the wound was completely healed and the patient was able to put full loading on it without difficulty.⁴¹

Case reports: promotion of wound progression in patients with complex wounds

Numerous case reports have described the positive clinical outcome of patients with leg ulcers of various aetiologies whose ulcers have been shown promoted wound healing when treated with HRWD. In one example, a 66-year old patient with a venous leg ulcer presented after having previously been treated with a variety of treatments for 10 months without success. Following a change-over in treatment to HRWD, wound exudate levels reduced quickly and wound was visibly cleaner. Healthy granulation tissue slowly formed in the wound bed. Over the course of the next 3 months the ulcer size reduced until complete healing was achieved.⁴¹ In another care report, the gaiter region venous leg ulcer of an 87-year old woman that had been present for 35 years was healed over the course of the year after treatment with HRWD. What was particularly remarkable with this case was that, due to the patient's poor general health, the underlying chronic venous insufficiency that was probably responsible for the leg ulcer could not be treated but

treatment with HRWD alone led to complete ulcer healing.⁴¹ A 40-year old patient, with a history of recurrent venous leg ulcers over a 4-year period, showed significant improvement in their wounds within 3-weeks of commencement of HRWD application.⁵⁸ Wound coatings, levels of wound exudate and wound pain were significantly reduced and there was an increase in granulation tissue and the formation of new epithelial tissue was seen. The size of the wounds had reduced by approximately one-third within a month of HRWD treatment. As well as an improvement in the wound bed and the commencement of healing, the peri-wound region showed significant improvement also, with reductions in the levels of wound margin oedema, maceration, eczema, hyperkeratosis and reddening being seen.

A case series of 3 patients with a number of different chronic wounds evaluated the ability of HRWD to promote wound bed cleansing.⁵⁹ All three chronic wounds saw a significant reduction in the level of wound bed coverage by fibrinous slough when the hydro-responsive dressing was applied (see Table 5 for details). A similar outcome is reported in a 3-patient case series of a variety of chronic wounds when HRWD was applied: the ulcer wound beds were cleansed via effective debridement of fibrinous slough.⁶⁰ Additionally, 2 out of 3 patients observed significant effect on pain perception during treatment. In a patient with a post-traumatic venous leg ulcer, pain-free dressing changes were reported and in a second case (pressure ulcer in the sacral region), a significant reduction in wound pain was observed in tandem with marked decrease in exudate levels and inflammation. Separately, Meuleneire also reported



Figure 19: Mixed aetiology ulcer treated with HRWD. A) First assessment. Wound is necrotic and fibrinous in appearance; B) Wound is fully debrided 24 days after start of treatment; C) Wound progression seen 47 days after start of treatment; and D) Wound is healed 71 days after start of treatment. Photographs courtesy of L. Balta, Spain.

good debridement of a pressure ulcer covered with necrotic tissue and slough.⁶¹ The initiation of pressure relief, an initial phase of mechanical debridement followed by the application of HRWD resulted in the removal of remaining necrotic tissue within 3 weeks of hydro-responsive dressing application.

Finally, two recent evaluations of HRWD brought together a number of case reports highlighting the wound cleansing and granulation tissue promoting properties of the hydro-responsive wound dressing in patients with a number of wound aetiologies.^{62,63} In a number of cases of patients with venous leg ulcers, all showed a decrease in the level of devitalised tissue in the wound bed with application of HRWD. In one case, the ulcer of an 86-year old patient showed significant improvement with HRWD application: fibrinous slough decreased and wound area decreased with a corresponding presence of new epithelium (indicating improved granulation tissue). In a further two patients who presented with ulcers of significant duration (3 months and 16 years), rapid improvements in the wound condition were seen, with decreased wound slough and increased granulation tissue levels being reported. In a 74-year old patient with ulceration, treatment was complicated by pyoderma gangrenosum which precluded mechanical debridement. Application of HRWD softened the fibrinous slough via autolytic debridement for easy removal. Additionally, the patient reported decreased levels of wound pain and pain experienced at dressing change. In 4 cases of patients presenting with pressure ulceration on the heel, reductions in fibrinous slough material and increased granulation tissue subsequent to the start of HRWD treatment were common findings. A 75-year old patient with a heel pressure ulcer that had responded poorly to treatment for the previous 6 months, quickly responded to HRWD application and reduced slough, increased granulation tissue and new epithelium were seen. A 73-year old patient with an ulcer of arterial origin also had decreased fibrinous slough, increased wound bed granulation and the formation of new epithelial tissue once HRWD treatment was started. A small number of patients

with more complex wounds also showed improvement with the commencement of HRWD treatment. The case of a 72-year old patient with a chronic wound over the tibia region of the lower limb is of particular interest. This wound had stagnated for the previous 4 years but, as reported with many other wounds, HRWD application led to significant wound cleansing, new granulation tissue formation and new epithelium. This case was complicated by an underlying skin sensitivity and peri-wound irritation. The atraumatic nature of the wound dressing meant that the wound progressed despite the sensitivity. These and other clinical evaluations documented in these publications are summarised in Table 5.

Chronic wounds such as venous leg, pressure, arterial and mixed aetiology ulcers that were successfully treated with HRWD are presented in Figures 14-19.

4.iii.d SKIN GRAFTING

The probability of success for graft take is increased if the recipient wound bed is cleaned of slough, necrotic tissue and other debris. The cleansing and conditioning effects of HRWD suggests that the wound dressing pad would be an effective dressing for wound bed preparation prior to skin grafting. A prospective, randomised study in 42 patients with leg ulcers compared the cleansing effect of HRWD with the effects of enzymatic wound cleansing (Table 7). Patients were treated with either the wound dressing pad or the enzymatic preparation for up to 8 weeks and the wound beds were assessed for level of tissue conditioning of the wound base for autologous skin grafting. The two cleansing methods proved equally effective at reducing necrotic wound tissue and the presence of sloughy material and at promoting granulation tissue quality. However, the use of HRWD was assessed as being superior because of the dressing's ability to maintain optimal healing conditions in the wound base and thus maximising the chances of skin graft take.⁴¹

There are a number of case reports describing that HRWD conditions the wound base before a skin graft. In one

particular case was the use of HRWD as part of a treatment regimen for a 20-year old woman who had suffered severe pelvic fractures and significant abrasions of the skin over a large area as a result of having been run over by a lorry. Due to the significant trauma received, the patient underwent numerous operations and the large wound site required repeated debridement and infection control. Despite best efforts, the wound became infected with multiple micro-organism species and clinicians decided rapid wound closure via mesh grafting was necessary. Multiple pieces of HRWD were applied to the wound surface in order to clean the wound of general wound detritus and micro-organism contamination and to promote the wound into the granulating phase of healing. After 1 week of HRWD treatment (with daily dressing changes) the wound base was prepared ready for mesh grafts to be applied successfully.⁴¹

In the case of a 62-year old patient suffering from necrotising fasciitis, extensive surgical debridement and antibiotic medication followed by the large resultant tissue defects being covered with HRWD, led to the conditioning of the wound base for mesh grafting and subsequent secondary coverage with grafts.⁴¹

4.iii.e MISCELLANEOUS WOUNDS

A small number of case reports are available documenting the application of HRWD to wounds of varying aetiologies where wound cleansing is required (Table 8).

An extensive skin tearing injury on the back of the hand in an 82-year old patient was dressed with HRWD for 4 days.⁶³ After only 2 days the wound was cleansed of wound debris and slough and there was a significant decrease in the level of wound pain experienced. Within 4 days the wound bed was cleansed enough for treatment to progress to the application of a hydro-responsive foam dressing. Wound healing was achieved after 4 weeks.

After the surgical removal of necrotic tissue from a chronic wound that had developed in a 45-year old patient after an insect bite, HRWD was applied to promote debridement and wound bed conditioning.⁵⁸ All the remaining necrotic

tissue present in the wound had been removed within 5 days of first HRWD application (the wound had remained unchanged for 45 days prior to treatment). Epithelialisation of the wound granulation tissue had reached 60% wound coverage within 2 weeks. Due to the atraumatic nature of the wound dressing, the patient assessed the dressing positively in terms of tolerance and wearing comfort.

In one documented case study found that the use of HRWD resulted in the removal of tissue necrosis from a wound following an intramuscular injection.⁵¹ A 55-year old patient developed a black skin necrosis within 10 days following an intramuscular anti-inflammatory injection. The remnants of the tissue necrosis detached within 3 days of initiating HRWD treatment and the appearance of the wound improved for the remainder of dressing application (a further 6 days). A stage-oriented treatment regime meant that, once the wound bed showed good granulation tissue following HRWD application, the dressing was changed to a hydro-responsive foam dressing and the wound progressed to complete healing.

4.iii.f COST-EFFECTIVENESS OF HYDRO-RESPONSIVE WOUND DRESSINGS

Kaspar et al.⁶⁴ performed a cost-effectiveness analysis as part of a study to evaluate the clinical efficacy of HRWD versus an amorphous hydrogel in patients with leg ulcers of >4 weeks duration and a wound coverage of $\geq 70\%$ fibrin and/or necrotic tissue.³⁹ Within this study, the costs were estimated from the German payer's perspective with medical costs including study treatment, wound treatment supply and labour time.⁶⁴ The increase in healthy granulation tissue is considered to be a valuable end point and a wound bed with >50% granulation tissue was defined as a suitable clinical end point. The clinical data indicated that wounds treated with HRWD dressing were in the state of having >50% granulation tissue for an additional 2.5 days compared with the amorphous hydrogel. Cost effectiveness analysis indicated that there was no additional medical costs required to achieve the 2.5 days with >50% granulation tissue within the 14 days

of venous leg ulcer care. The estimated total direct costs per patient and per 14 days of therapy were €306 for both HRWD and amorphous gel treatments. Although the total treatment costs for 14 days of leg ulcer care was the same for both HRWD and the amorphous hydrogel treatments, an estimate of the additional cost necessary to achieve an additional day with >50% granulation tissue (as defined by the incremental cost-effectiveness ratio [ICER]) for treatment with HRWD was €0. Therefore, the cost benefit analysis favoured HRWD because it was better able to produce an improvement in wound bed condition with no additional cost.⁶⁴

Spruce reported on a recent evaluation of HRWD in 20 patients receiving standard wound care in the community setting.⁴⁸ After 1 month of treatment, the hydro-responsive dressing was effective in debriding devitalised tissue from wounds of varying aetiologies, reducing the level of wound bed devitalised tissue by 62% over the 4-week observation period. Treatment of the wounds also resulted in a reduction in both wound area and wound depth. In a cost of care analysis of the clinical data, data from both the cost of the dressings and the clinical time (including clinical time of 15 minutes for dressing changes) based upon assumptions used by the National Institute for Health and Care Excellence were used to estimate potential cost savings where clinical endpoints were achieved.⁶⁵ When compared to NICE's published cost analysis of wound debridement using a monofilament pad,⁶⁵ the costs associated with using HRWD were found to be competitive. For example, in patients whose wounds had progressed to complete healing and required no further treatment (10%), total cost savings compared with standard treatment was £94.71, and in patients with a high percentage (80-99%) of devitalised tissue removal (35%), savings of £289.52 were achieved. It was concluded that there was a potential cost saving associated with using this dressing and that the dressing would be beneficial for use in the community setting.

5. CONCLUSION

HRWDs address the challenges that prevent some nurses debriding wounds allowing optimal wound bed preparation. HRWDs are designed to provide a cleanse–debride– absorb function and have been shown to achieve wound progression and to promote granulation tissue formation in a range of acute and chronic wounds.

Furthermore, HRWD have excellent fluid-handling properties, are easy to use, and are comfortable for the patient. HRWDs have been shown to reduce levels of wound pain and pain experienced at dressing changes.

This document shows that Hydro-Responsive Wound Dressings provide an optimal healing environment for wound progression by promoting the autolytic debridement and removal of wound bed devitalised tissue.

6. REFERENCES

1. Kruse CR, Nuutla K, Lee CCY, Kiwanuka E, Singh M, Caterson EJ, Eriksson E, Sørensen JA. The external microenvironment of healing skin wounds. *Wound Repair and Regeneration* 2015; 23: 4, 456-464.
2. Atiyeh BS, Hayek SN. Intérêt d'un onguent chinois (MEBO) dans le maintien local de l'humidité." *Journal des Plaies et Cicatrisation* 2005; 9: 7-11.
3. Winter GD. Formation of the scab and the rate of epithelialization of superficial wounds in the skin of the young domestic pig. *Nature (London)* 1962; 193: 293-294.
4. Hinman CD, Maibach H. Effect of air exposure and occlusion on experimental human skin wounds. *Nature (London)* 1963; 200: 377-378.
5. Breuing K, Eriksson E, Liu P, Miller DR. Healing of partial thickness porcine skin wounds in a liquid environment. *Journal of Surgical Research* 1992; 52: 1, 50-58.
6. Svensjö T, Pomahac B, Yao F, Slama J, Eriksson E. Accelerated healing of full-thickness skin wounds in a wet environment. *Plastic and Reconstructive Surgery* 2000; 106: 3, 602-612.
7. Dyson M, Young S, Pendle CL, Webster DF, Lang SM. Comparison of the effects of moist and dry conditions on dermal repair. *Journal of Investigative Dermatology* 1988; 91: 5, 434-439.
8. Vogt PM, Andree C, Breuing K, Liu PY, Slama J, Helo G, Eriksson E. Dry, moist, and wet skin wound repair. *Annals of Plastic Surgery* 1995; 34: 5, 493-499.
9. Nelson EA. Moist wound healing: critique II. *Journal of Wound Care* 1995; 4: 8, 370-371.
10. Hutchinson JJ, Lawrence JC. Wound infection under occlusive dressings. *Journal of Hospital Infection* 1991; 17: 2, 83-94.
11. Sibbald RG, Elliott JA, Ayello EA, Somayaji R. Optimizing the moisture management tightrope with Wound Bed Preparation 2015©. *Advances In Skin and Wound Care* 2015; 28: 10, 466-476.
12. Bishop SM, Walker M, Rogers AA, Chen WYJ. Importance of moisture balance at the wound-dressing interface. *Journal of Wound Care* 2003; 12: 4, 125-128.
13. Cutting KF. The causes and prevention of maceration of the skin. *Journal of Wound Care* 1999; 8: 4, 200-201.
14. Cutting KF, White RJ. Maceration of the skin and wound bed 1: Its nature and causes. *Journal of Wound Care* 2002; 11: 7, 275-278.
15. Vranckx JJ, Slama J, Preuss S, Perez N, Svensjö T, Visovatti S, Breuing K, Bartlett R, Pribaz J, Weiss D, Eriksson E. Wet wound healing. *Plastic and Reconstructive Surgery* 2002; 110: 7, 1680-1687.
16. Junker JP, Kamel RA, Caterson EJ, Eriksson E. Clinical impact upon wound healing and inflammation in moist, wet, and dry environments. *Advances In Wound Care* 2013; 2: 7, 348-356.
17. Zuhaili B, Aflaki P, Koyama T, Fossum M, Reish R, Schmidt B, Pomahac B, Eriksson E. Meshed skin grafts placed upside down can take if desiccation is prevented. *Plastic and Reconstructive Surgery* 2010; 125: 3, 855-865.
18. Hackl F, Bergmann J, Granter SR, Koyama T, Kiwanuka E, Zuhaili B, Pomahac B, Caterson EJ, Junker JP, Eriksson E. Epidermal regeneration by micrograft transplantation with immediate 100-fold expansion. *Plastic and Reconstructive Surgery* 2012; 129: 3, 443e-452e.
19. Chen WYJ, Rogers AA. Recent insights into the causes of chronic leg ulceration in venous diseases and implications on other types of chronic wounds. *Wound Repair and Regeneration* 2007; 15: 4, 434-449.
20. Attinger CE, Janis JE, Steinberg J, Schwartz J, Al-Attar A, Couch K. Clinical approach to wounds: debridement and wound bed preparation including the use of dressings and wound healing adjuvants. *Plastic and Reconstructive Surgery* 2006; 117: 7 Suppl, 72S-109S.
21. McCarty SM, Percival SL. Proteases and delayed wound healing. *Advances In Wound Care* 2013; 2: 8, 438-447.
22. Schultz GS, Sibbald RG, Falanga V, Ayello EA, Dowsett C, Harding K, Romanelli M, Stacey MC, Teot L, Vanscheidt W. Wound bed preparation: a systematic approach to wound management. *Wound Repair and Regeneration* 2003; 11: Suppl 1, S1-S28.
23. Caley MP, Martins VLC, O'Toole EA. Metalloproteinases and wound healing. *Advances In Wound Care* 2015; 4: 4, 225-234.
24. Gibson DJ, Schultz GS. Molecular wound assessments: matrix metalloproteinases. *Advances In Wound Care* 2013; 2: 1, 18-23.
25. McDaniel JC, Roy S, Wilgus TA. Neutrophil activity in chronic venous leg ulcers – a target for therapy? *Wound Repair and Regeneration* 2013; 21: 3, 339-351.
26. Wilgus TA, Roy S, McDaniel JC. Neutrophils and wound repair: positive actions and negative reactions. *Advances In Wound Care* 2013; 2: 7, 379-388.
27. Chen SM, Ward SI, Olutoye OO, Diegelmann RF, Cohen IK. Ability of chronic wound fluids to degrade peptide growth factors is associated with increased levels of elastase activity and diminished levels of proteinase inhibitors. *Wound Repair and Regeneration* 1997; 5: 1, 23-32.
28. Vasconcelos A, Cavaco-Paulo A. Wound dressings for a proteolytic-rich environment. *Applied Microbiology and Biotechnology* 2011; 90: 2, 445-460.
29. Wiegand C, Abel M, Ruth P, Hipler UC. Superabsorbent polymer-containing wound dressings have a beneficial effect on wound healing by reducing PMN elastase concentration and inhibiting microbial growth. *Journal of Materials Science. Materials in Medicine* 2011; 22: 11, 2583-2590.
30. Wiegand C, Hipler UC. A superabsorbent polymer-containing wound dressing efficiently sequesters MMPs and inhibits collagenase activity in vitro. *Journal of Materials Science. Materials in Medicine* 2013; 24: 10, 2473-2478.
31. Edwards JV, Caston-Pierre S. Citrate-linked keto- and aldo-hexose monosaccharide cellulose conjugates demonstrate selective human neutrophil elastase-lowering activity in cotton dressings. *Journal of Functional Biomaterials* 2013; 4: 2, 59-73.
32. Gottrup F, Apelqvist J, Price P, European Wound Management Association Patient Outcome Group. Outcomes in controlled and comparative studies on chronic wounds: recommendations to improve the quality of evidence in wound management. *Journal of Wound Care*. 2010; 19: 6, 237-268.
33. Buchholz F, Graham A. Modern superabsorbent polymer technology. John Wiley & Sons, New York, USA, 1998.
34. Dutkiewicz JK. Superabsorbent materials from shellfish waste—a review. *Journal of Biomedical Materials Research* 2002; 63: 3, 373-381.
35. Eming S, Smola H, Hartmann B, Malchau G, Wegner R, Krieg T, Smola-Hess S. The inhibition of matrix metalloproteinase activity in chronic wounds by a polyacrylate superabsorber. *Biomaterials*. 2008; 29: 19, 2932-2940.

36. Paustian C, Stegman MR. Preparing the wound for healing: the effect of activated polyacrylate dressing on debridement. *Ostomy Wound Management* 2003; 49: 9, 34-42.
37. Mahr R. The mode of action of a superabsorbent polymer wound dressing (TenderWet). *Ostomy Wound Management* 2003; Suppl: 8-9.
38. Moore K, Gray D. Using PHMB antimicrobial to prevent wound infection. *Wounds UK* 2007; 3: 2, 96-102.
39. Humbert P, Faivre B, Véran Y, Debure C, Truchetet F, Bécherel PA, Plantin P, Kerihuel JC, Eming SA, Dissemond J, Weyandt G, Kaspar D, Smola H, Zöllner P, on behalf of the CLEANSITE study group. Protease-modulating polyacrylate-based hydrogel stimulates wound bed preparation in venous leg ulcers - a randomized controlled trial. *Journal of the European Academy of Dermatology and Venereology* 2014; 28: 12, 1742-50.
40. White R, Cutting K, Eyre M. Is "data on file" a valid reference? *Wounds UK* 2005; 1: 3, 128-129.
41. Knestele M. The treatment of problematic wounds with TenderWet – 10 years of clinical practice. *HARTMANN WundForum, Special Issue*, 2004, [Data on file].
42. Bruggisser R. Bacterial and fungal absorption properties of a hydrogel dressing with a superabsorbent polymer core. *Journal of Wound Care* 2005; 14: 9, 438-442.
43. Courderot-Masuyer C, Robin S, Bertrand X, Plesiat P, Tholon N, Humbert P. Étude du comportement des fibroblastes sains et d'ulcère veineux après infection par *Pseudomonas aeruginosa* et en présence du pansement HydroClean active. *Journal des Plaies et Cicatrisations* 2005; 9: 51, 3-7.
44. Gill SE, Parks WC. Metalloproteinases and their inhibitors: regulators of wound healing. *International Journal of Biochemistry and Cell Biology* 2007; 40: 6-7, 1334-1347.
45. Burd A. Evaluating the use of hydrogel sheet dressings in comprehensive burn wound care. *Ostomy Wound Management* 2007; 53: 3, 52-62.
46. Wilson R. Massive tissue loss: burns. In: *Acute and Chronic Wounds Nursing Management*, 2nd Edition. Bryant RA, eds. Mosby, St. Louis 2000: 197-220.
47. Azevedo M, Simoes L, Sousa R, Sampaio R. Estudio Prospectivo. Quemaduras en fase inicial - TenderWet active en quemaduras de 2º y 3º grado. *HARTMANN document*, 2004, [Data on file].
48. Spruce, P. Report on HydroClean Plus dressing: a 20 patient evaluation within the community setting, 2015, [Data on file].
49. Meuleneire F. TenderWet plus in the treatment of patients with problem wounds. *HARTMANN document*, 2013, [Data on file].
50. Parker B. Rapid healing in a dehisced abdominal surgical wound using hydro-active dressings. *Australian Wound Management Association. Connective Issue* 2014; 16: 4, 11-14.
51. Meuleneire F. Stage-adapted wound treatment using TenderWet, Perma-Foam and HydroTac. *HARTMANN Document*, 2011.
52. Effective wound cleansing with TenderWet Active – observational study with 403 patients. *HARTMANN Document*, 2010, [Data on file].
53. Kaspar D. TenderWet plus. Therapeutic effectiveness, compatibility and handling in the daily routine of hospitals or physician's practices. *HARTMANN Document*, 2011, [Data on file].
54. Kaspar D, Dehiri H, Tholon N, Smola H, Zöllner P. Efficacité clinique du pansement irrigo-absorbent HydroClean active contenant du polyacrylate superabsorbent dans le traitement des plaies chroniques – étude observationnelle conduite sur 221 patients. *Journal des Plaies et Cicatrisations* 2008; 13: 63, 21-24.
55. Scholz S, Rompel R, Petres J. A new approach to wet therapy of chronic leg ulcers. *Arzt Praxis* 1999; 53: 816, 517-522.
56. König M, Vanscheidt W, Augustin M, Kapp H. Enzymatic versus autolytic debridement of chronic leg ulcers: a prospective randomised trial. *Journal of Wound Care* 2005; 14: 7, 320-323.
57. Mwipatayi BP, Angel D, Dixon P, Higgins S, Gregory G, Sieunarine K. Clinical experiences with activated polyacrylate dressings (TenderWet 24). *Primary Intention* 2005; 13: 2, 69-74.
58. Kapp H. Effective cleansing, better handling - clinical observations using new TenderWet active. *HARTMANN Document*, 2004, [Data on file].
59. Malone M, Dickson H. A hydroactive dressing with PHMB. Analysis of clinical effectiveness using 3D wound imaging. Poster presented at the Australian Wound Management Association meeting, Gold Coast, Queensland, Australia, 2014.
60. Meuleneire F. Clinical evaluation of TenderWet plus. *HARTMANN document*, 2011, [Data on file].
61. Meuleneire F. Prise en charge efficace de escarres de decubitus profonds: résultats de la synergie du soulagement de la pression, du débridement mécanique et du choix d'un pansement adéquate. Poster presented at Conférence Nationale des Plaies et Cicatrisations, Paris, France, 2007.
62. Zollinger C, Schwab R, Locherer E, Fischlmayer A, Wegmann C, Lörger H, Deseö-Schütz K, Kaiser M, Lindo C, Semon A, Weiss K, von Siebenthal D, Smola H. HydroTherapy. Application study. *HARTMANN document*, 2014, [Data on file].
63. Scherer R, Kägi M, Geiges R, Huber D, Berli A, Kolb C, Sutter M, Herrmann K, Michel-Nufer T, Barmettler B, Gutierrez V, von Siebenthal D, Smola H. HydroTherapy. Application study. *HARTMANN document*, 2015, [Data on file].
64. Kaspar D, Linder J, Zöllner P, Simon U, Smola H. Economic benefit of a polyacrylate-based hydrogel compared to an amorphous hydrogel in wound bed preparation of venous leg ulcers. *Chronic Wound Management and Research* 2015; 2: 63-70.
65. National Institute for Health and Care Excellence. NICE medical technology guidance 17. The DermaSoft monofilament debridement pad for use in acute or chronic wounds, March 2014.
66. Cooper P. TenderWet: an innovation in moist wound healing. *British Journal of Surgery* 1998; 7: 20, 1232-1235.

7. INDEX

- Abdominal wound, 14, 15, 16, 32
- Acute wounds, 13, 14, 16, 18, 32, 34
- Amputation wounds, 15, 32, 36, 37
- Arterial leg ulcer, 21, 24, 33, 34, 37
- Atraumatic, 14, 24, 25
- Autolytic debridement, 4, 5, 7, 21, 24, 32, 35, 36, 37
- Bacteria, 4, 5, 6, 7, 9, 10, 11, 12
- Bacterial uptake, 10
- Blisters, 14, 32
- Burns, 5, 12, 13, 31, 33
- Candida albicans, 11
- Cations, 12
- Chronic wounds, 4, 5, 6, 7, 10, 11, 12, 15, 16, 18, 19, 20, 21, 23, 24, 25, 32, 33, 34, 35, 36, 37, 38
- Collagen matrix, 11, 12
- Compression bandaging, 10, 17, 18, 20, 36, 37
- Cost-effectiveness, 5, 26, 34
- Debridement, 4, 5, 6, 7, 13, 14, 15, 16, 19, 20, 21, 22, 23, 24, 25, 26, 27, 31, 32, 34, 35, 36, 37, 38
- Dehiscence, 8, 13, 14, 15, 16, 32
- Desquamation, 21, 33
- Devitalised tissue, 4, 5, 9, 14, 20, 23, 26, 27, 34, 35, 37
- Diabetic foot ulcer, 5, 7, 8, 10, 16, 18, 22, 33, 34, 35
- Dressing adherence, 18
- Dressing change-associated pain, 5, 13, 14, 16, 18, 20, 21, 24, 27, 31, 32, 33, 34, 36
- Dry wounds, 6, 7
- Elastase (neutrophil), 7
- Enterococcus sp., 13, 31
- Enzymatic debridement, 4, 21, 25, 33, 38
- Erythema, 21, 33
- Escherichia coli, 13, 31
- Exudate, 4, 6, 7, 8, 9, 10, 11, 12, 14, 15, 19, 20, 21, 23, 32, 33, 35, 36, 38
- Fibroblasts, 11, 12
- Fluid delivery properties, 10, 11
- Granulation tissue, 4, 5, 6, 8, 9, 12, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 32, 33, 34, 35, 36, 37, 38
- Haematoma, 13, 14, 15, 16, 32
- Hand injury, 25, 38
- Hydration, 4, 6
- Hydro-Responsive Wound Dressing (HRWD), 5, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 31, 32, 33, 34, 35, 36, 37, 38
- In vitro studies, 9, 10, 12
- Insect bite, 25, 38
- Infection, 6, 13, 14, 16, 17, 18, 19, 22, 25, 31, 32, 33, 35, 38
- Maceration, 6, 17, 23, 36, 38
- Matrix metalloproteinases (MMPs), 4, 7, 9, 10, 12
- Mixed aetiology ulcer, 16, 24, 25, 33, 35
- Moist wound healing, 4, 6, 7, 8, 12, 21
- Necrotic tissue, 4, 7, 8, 9, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 31, 32, 33, 34, 35, 36, 37, 38
- Necrotising fasciitis, 25, 38
- NPWT (negative pressure wound therapy), 15, 16, 32
- Optimal wound environment, 4, 6, 7, 10, 21, 25, 27, 38
- Pain, 5, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 31, 32, 33, 34, 36, 38
- Peri-wound tissue, 6, 14, 15, 17, 18, 20, 21, 23, 24, 32, 33, 34, 36, 37
- PHMB (polyhexamethylene biguanide), 9, 19
- Polyacrylate superabsorbent, 4, 6, 7, 8, 9, 10, 11, 12, 18
- Pressure ulcer, 5, 7, 8, 10, 16, 18, 21, 22, 23, 24, 33, 35, 36, 37
- Protein-degrading enzymes (proteinases), 4, 5, 7, 8, 9, 12
- Pseudomonas aeruginosa, 11
- Pyoderma gangrenosum, 24, 36
- Ringer's solution, 4, 7, 8, 9, 10, 11
- Satisfaction, clinical, 20
- Satisfaction, patient, 20
- Scarring, 6, 7
- Skin graft, 7, 13, 14, 15, 16, 19, 21, 25, 31, 32, 33, 38
- Skin tears, 25, 38
- Slough, 4, 7, 8, 9, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 31, 32, 33, 34, 35, 36, 37, 38
- Staphylococcus aureus, 11, 12, 13, 31
- Staphylococcus epidermidis, 11
- Stress, 14, 32
- Surgical wounds, 8, 12, 13, 14, 15, 18, 32, 37
- Traumatic wounds, 12, 14, 15, 16, 18, 25, 32, 33, 36, 38
- Ulcers, 5, 6, 7, 8, 10, 12, 16, 18, 19, 20, 21, 22, 23, 24, 25, 26, 33, 34, 35, 36, 37, 38
- Venous leg ulcer, 5, 7, 8, 12, 16, 18, 19, 20, 21, 23, 24, 26, 33, 34, 35, 36, 37, 38
- Wet wound healing, 6, 7
- Wound bed preparation, 4, 9, 12, 13, 14, 19, 21, 25, 31
- Wound cleansing, 4, 6, 7, 8, 9, 10, 12, 13, 14, 15, 16, 19, 20, 21, 22, 23, 24, 25, 27, 31, 32, 33, 35, 36, 37, 38
- Wound conditioning, 6, 7, 10, 13, 14, 16, 21, 22, 25, 31, 35, 36, 38
- Wound epithelialisation, 6, 13, 14, 15, 16, 18, 22, 23, 24, 25, 31, 32, 33, 35, 36, 37, 38
- Wound eschar, 4, 6, 14, 32, 33
- Wound odour, 20
- Wound progression, 4, 5, 6, 7, 8, 10, 12, 13, 14, 19, 20, 22, 24, 27, 32, 34, 35, 36, 37, 38
- Wound-related pain, 5, 13, 16, 17, 18, 19, 20, 23, 24, 25, 27, 31, 32, 33, 34, 36, 38

8. APPENDIX

Table 2: Clinical evaluations of HRWD on burn wounds

Reference	Methodology	Main results
Knestele ⁴¹	<p>Case series</p> <p>Full-thickness burns on upper limb:</p> <ul style="list-style-type: none"> - Treated with TenderWet after wound breakdown due to mixed infection (Staphylococcus aureus, Escherichia coli & Enterococcus) - Treatment duration: 4 days <p>Deep dermal burns on upper torso:</p> <ul style="list-style-type: none"> - Two days post-burn wounds covered with slough and necrotic tissue and heavily exuding - Treated with TenderWet to cleanse and condition wound bed prior to allograft application - Treatment duration: 3 days 	<p>Full-thickness burns on upper limb:</p> <ul style="list-style-type: none"> - No signs of infection observed after treatment with TenderWet - New epithelium formed - Wound healed <p>Deep dermal burns on upper torso:</p> <ul style="list-style-type: none"> - Wound cleansed and covered with cultured epidermal allografts - TenderWet used to protect graft - Wounds covered with grafts healed completely within 5 days
Azevedo et al ⁴⁷	<p>Case series</p> <ul style="list-style-type: none"> - Prospective study in patients (n=5) with 2nd or 3rd degree burn wounds - Assessed wound bed preparation using TenderWet active, wound debridement, and effect on wound pain - Treatment duration: unknown 	<ul style="list-style-type: none"> - Clinical improvement in wound bed appearance within 1-9 days - Significant reduction in wound pain reported by 3 of 4 patients surveyed

Table 3: Clinical evaluations of HRWD on acute wounds

Reference	Methodology	Main results
Knestele ⁴¹	<p>Case series</p> <p>Haematoma at incision site post-intestinal surgery:</p> <ul style="list-style-type: none"> - Surgical removal of haematoma and cleaning of wound with saline - TenderWet applied to clean wound - Treatment duration: 13 days <p>Dehiscent medial abdominal wound:</p> <ul style="list-style-type: none"> - Clinical signs of infection after laparotomy, large amounts of malodorous wound exudate and wound base covered by necrotic tissue - Treatment duration: 18 days <p>Amputation wound with post-operative dehiscence:</p> <ul style="list-style-type: none"> - Clinical signs of infection, large amounts of malodorous wound exudate and wound base covered by necrotic tissue - Treatment duration: up to 60 days 	<p>Haematoma at incision site post-intestinal surgery:</p> <ul style="list-style-type: none"> - New granulation tissue formation within 3 days of start of TenderWet application - Granulation tissue reached height of surrounding skin within 13 days - Wound prepared for subsequent treatment and healing <p>Dehiscent medial abdominal wound:</p> <ul style="list-style-type: none"> - Wound eschar reduced by 50% within 2 days of TenderWet application - Complete necrosis tissue removed by 18 days with associated granulation tissue formation - Wound prepared for subsequent grafting <p>Amputation wound with post-operative dehiscence:</p> <ul style="list-style-type: none"> - Removal of necrotic tissue within 2 weeks of TenderWet application - Formation of healthy granulation tissue - Wound progressed to healing with stage-oriented treatment
Parke ⁵⁰	<ul style="list-style-type: none"> - Case study - Dehiscent abdominal wound following laparotomy for small bowel obstruction - Wound originally managed by negative pressure wound therapy, replaced by TenderWet plus upon patient discharge - Treatment duration: 7 weeks 	<ul style="list-style-type: none"> - Rapid development of wound bed granulation tissue - Peri-wound skin remained healthy and well hydrated - Wound closure was achieved within 7 weeks of TenderWet plus application
Meuleneire ⁵¹	<p>Case series</p> <p>Haematoma developed after injury of lower leg:</p> <ul style="list-style-type: none"> - Wound was very painful. Post-debridement, wound was inflamed, fibrinous and fragile in appearance - Treatment duration: up to 120 days <p>Wound developed after injury of lower leg:</p> <ul style="list-style-type: none"> - Wound stagnation probably due to underlying diseases (including diabetes mellitus, cardiomyopathy and chronic venous insufficiency) - Goal to overcome stagnation and aid wound healing - Treatment duration: 14 days <p>Haematoma developed after injury of ankle:</p> <ul style="list-style-type: none"> - Patient hospitalised for haematoma and necrotic tissue debridement - Negative pressure therapy started to allow wound bed infilling - Treatment duration: up to 30 days <p>Wound caused by failure of skin graft on lower leg:</p> <ul style="list-style-type: none"> - Skin graft failed on wound of indeterminate origin - 10% of original graft remained in situ (cell islands) - Wound contained significant levels of sloughy material - Treatment duration: 19 days 	<p>Haematoma developed after injury of lower leg:</p> <ul style="list-style-type: none"> - Wound covered to 100% with fresh granulation tissue within 10 days after treating with TenderWet 24 active - Treatment with TenderWet 24 active continued for further 10 days due to severe wound exudate - Wound progressed to healing using PermaFoam and HydroTac <p>Wound developed after injury of lower leg:</p> <ul style="list-style-type: none"> - Treatment with TenderWet 24 resulted in wound cleansing and more healthy-looking wound bed - Treatment switched to HydroTac to maintain balanced moist wound environment - Promotion of re-epithelialisation <p>Haematoma developed after injury of ankle:</p> <ul style="list-style-type: none"> - Well-vascularised wound bed after 12 days treatment with TenderWet 24 active - Wound progressed to healing using PermaFoam and HydroTac <p>Wound caused by failure of skin graft on lower leg:</p> <ul style="list-style-type: none"> - Significant wound cleansing seen within 2 days of TenderWet 24 active application - Granulation tissue infilling of wound and new epithelialisation from epithelial islands observed after a further 3 days - Epithelialisation established by 9 days later with re-epithelialisation from the margins - Wound healing achieved approx. 40 days after commencement of TenderWet 24 active treatment
Meuleneire ⁴⁹	<p>Case series</p> <p>Haematoma on the Achilles tendon:</p> <ul style="list-style-type: none"> - Developed haematoma with necrotic tissue after trauma to lower leg - Blister surgically removed and wound treated with TenderWet 24 - Treatment duration: 8 weeks <p>Lower limb trauma with necrotic wound on tibia:</p> <ul style="list-style-type: none"> - Wound developed due to trauma with development of necrotic tissue - Wound treated with TenderWet 24 after surgical debridement - Treatment duration: approximately 8 weeks 	<p>Haematoma on the Achilles tendon:</p> <ul style="list-style-type: none"> - Promotion in the autolytic debridement of wound bed - Improvement in wound bed granulation tissue <p>Lower limb trauma with necrotic wound on tibia:</p> <ul style="list-style-type: none"> - Promotion of wound bed granulation tissue - Stress to patient minimised due to reduced number of dressing changes and atraumatic dressing changes with little or no pain

Table 4: Clinical studies of HRWD on chronic wounds^o

Reference	Design & methodology	Main outcome measures	Main results
Data on file ⁵²	<ul style="list-style-type: none"> - Prospective, non-comparative, multi-centre observational study - Chronic wounds (wound duration: 2 months) (n=403) including venous leg ulcers, arterial ulcers, decubitus ulcers, diabetic foot ulcers, mixed venous/arterial ulcers and burns - Documented treatment for average period of 1 month - Treatment: TenderWet active 	<ul style="list-style-type: none"> - Level of wound bed fibrinous coatings - Wound granulation - Clinical signs of infection - Wound pain - Physician evaluation of effectiveness and handling - Patient evaluation of tolerability, wearing comfort and pain during treatment 	<ul style="list-style-type: none"> - Number of wounds with >50% fibrinous coating decreased from 56% to 8% - Levels of necrotic tissue reduced from 32% to 5% of wounds - Number of wounds with florid granulation tissue increased from 6% to 69% - Significant reduction in wound pain - Infections decreased - Wound edge damage showed significant improvement - >90% of physicians evaluated TenderWet active "very good" or "good" - >94% of patients evaluated TenderWet active "very good" or "good"
Kaspar ⁵³	<ul style="list-style-type: none"> - Multi-centre observational study - Chronic wounds (wound duration: 5 months) (n=170) including venous leg ulcers, decubitus ulcers, arterial leg ulcers, diabetic foot ulcers and traumatic wounds - Documented treatment for 8 days or 3 dressing changes - Treatment: TenderWet plus 	<ul style="list-style-type: none"> - Level of wound bed fibrinous coatings - Level of wound bed necrosis - Wound granulation - Clinical signs of infection - Wound pain - Physician evaluation of effectiveness - Patient evaluation of tolerability, wearing comfort and pain during treatment 	<ul style="list-style-type: none"> - Number of wounds with necrosis decreased from 17% to 10% - Number of wounds with fibrinous coatings decreased from 41% to 33% - Proportion of granulation tissue increased from 35% to 46% - Proportion of epithelial tissue increased from 6% to 11% - Wound edge damage reduced from 71% to 62% - Wounds with clinical signs of infection reduced from 24% to 17% - Patients experiencing moderate to severe wound pain reduced from 35% to 19% - Levels of moderate to severe wound pain at dressing change decreased from 26% to 11% - Over 85% physicians evaluated dressing removability as "good" or "very good" - >90% physicians evaluated TenderWet plus "very good" or "good" - >80% patients evaluated TenderWet plus "very good" or "good"
König ⁵⁶	<ul style="list-style-type: none"> - Prospective, randomised study - Venous leg ulcers (n=42) - Treatment randomisation: TenderWet 24 vs. enzymatic wound cleansing agent - Treatment duration: 3 weeks 	<ul style="list-style-type: none"> - Levels of eschar, slough and necrotic tissue - Levels of granulation tissue formation 	<ul style="list-style-type: none"> - Slough within the groups reduced by almost 19% (TenderWet 24) compared with 9% (enzyme) - Granulation tissue area increased by 26% (TenderWet 24) compared with 10% (enzyme) - Dressing and enzymatic agent equally effective at reducing levels of necrotic tissue and wound coatings - TenderWet 24 promoted moist wound environment - TenderWet 24 managed excessive exudate and tissue debris
Knestele ⁴¹	<p>Single centre observational study in chronic wounds:</p> <ul style="list-style-type: none"> - Chronic wounds (wound duration: 9 months) (n=14) including venous leg ulcers and mixed (venous/arterial) aetiology ulcers - Treatment duration: average of 10 days 	<ul style="list-style-type: none"> - Level of fibrinous coating - Level of necrotic tissue - Granulation tissue formation - Patient tolerability of dressing - Peri-wound skin condition 	<ul style="list-style-type: none"> - Significant reduction in fibrinous and necrotic tissue - Promotion of granulation tissue formation - Improvement in peri-wound skin condition; reduction in erythema (n=5) and reduction in desquamation (n=3) - Wounds sufficiently cleansed for split-skin grafting within 7-10 days
Scholz ⁵⁵	<ul style="list-style-type: none"> - Single centre observational study - Venous leg ulcers (n=37) - Treatment duration: average of 19 days 	<ul style="list-style-type: none"> - Level of fibrinous coatings - Level of necrotic tissue - Granulation tissue formation - Exudate levels - Wound pain 	<ul style="list-style-type: none"> - Significant reduction in fibrinous and necrotic tissue - Promotion of granulation tissue formation - Wounds showing "moderate/severe" exudate decreased from 28 to 8 - 33 patients reported no or "slight" pain at dressing change
Kaspar ⁵⁴	<ul style="list-style-type: none"> - Open, prospective observational study - Chronic wounds (n=221) including venous leg ulcers, arterial ulcers, mixed aetiology ulcers, diabetic foot ulcers and burns - Treatment duration: 1 month 	<ul style="list-style-type: none"> - Level of fibrinous slough - Number of wounds showing granulation tissue formation - Clinical signs of infection - Wounds with high exudate levels - Wound pain 	<ul style="list-style-type: none"> - Number of wounds completely or partially (>50% surface area) covered in fibrinous slough decreased from 54% to 9% - Number of wounds showing granulation tissue (>50% surface area) increased from 5% to 74% - Number of wounds showing clinical signs of infection reduced from 53% to 9% - Number of wounds with high exudate levels reduced from 74% to 10% - Number of patients reporting "intermediate" to "high" levels of wound pain perception decreased from 64% to 19%

Table 4 continued

Reference	Design & methodology	Main outcome measures	Main results
Humbert et al ³⁹	<ul style="list-style-type: none"> - Open, multi-centre, prospective, randomised, controlled study - Venous leg ulcers (n=75) - Treatment randomisation: HydroClean (n=34) vs. amorphous gel (n=41) - Treatment duration: 14 days 	<ul style="list-style-type: none"> - Levels of slough and necrotic tissue - Granulation tissue formation - Cost-benefit analysis (Kaspar et al., 2015) 	<ul style="list-style-type: none"> - Greater reduction in HydroClean group of proportion of ulcer area covered by slough and necrotic tissue - Greater proportion in HydroClean group of proportion of ulcer covered by granulation tissue - Response rates of hard-to-heal ulcers of >6 months duration higher in HydroClean group - Cost-benefit analysis favoured HydroClean group (Kaspar et al., 2015)
Mwipatayi ⁵⁷	<ul style="list-style-type: none"> - Prospective non-controlled case series study - Chronic wounds (n=10) including venous leg ulcer, diabetic foot ulcer and arterial ulcers - Treated with TenderWet 24 - Treatment duration: average 6.5 days 	<ul style="list-style-type: none"> - Assessment of wound bed - Monitor reduction in wound area 	<ul style="list-style-type: none"> - Rate of wound debridement estimated as an average of 6% per day - Wound area reduction measured during TenderWet 24 application - Two patients exhibited no wound bed debridement - Three patients noted pain during dressing change. No follow-up was noted
Spruce ⁴⁸	<ul style="list-style-type: none"> - Multi-centre, non-comparative, clinical evaluation - Acute and chronic wounds (n=20) - Treatment: HydroClean plus - Treatment duration: 4 weeks 	<ul style="list-style-type: none"> - Assessment of wound bed preparation - Assessment of wound progression (wound area & wound depth) - Performance of dressing (ease of application, removal) - Cost-benefit analysis 	<ul style="list-style-type: none"> - Mean reduction in devitalised tissue between baseline and end of evaluation: 62% - 21.5% reduction in total wound area between baseline and final evaluation - 45.7% reduction in total wound depth between baseline and final evaluation - Increase in percentage of patients with healthy peri-wound skin from 25% to 55% between baseline and final evaluation - 58% reduction in patients experiencing wound associated pain between baseline and final assessment - No patients experienced pain on dressing change - Potential cost savings associated with using HydroClean plus

Table 5: Clinical evaluations of HRWD on chronic wounds

Reference	Methodology	Main results
Knestele ⁴¹	<p>Case series</p> <p>Decubitus ulcer in the sacral region:</p> <ul style="list-style-type: none"> - Pressure ulcer formed following femur fracture - Patient with multiple morbidities - Treatment duration: 5 months <p>Decubitus ulcers in the sacral region, on the heel and hip region:</p> <ul style="list-style-type: none"> - Sacral ulcer treated locally with alginate dressings packed into wound and covered with TenderWet - Heel ulcer treated with TenderWet and surgical debridement followed by alginate/TenderWet combination - Hip region ulcer treated with TenderWet followed by alginate/TenderWet combination - All wounds received pressure relief - Treatment duration: 10 months <p>Diabetic foot ulcer on big toe:</p> <ul style="list-style-type: none"> - Diabetic foot ulcer with soft tissue infection and osteolytic changes on distal phalanx of toe - Wound opened to allow drainage of wound exudate, surgical debridement prior to TenderWet treatment - Treatment duration: 4 months <p>Venous leg ulcer:</p> <ul style="list-style-type: none"> - Unsuccessful treatment over a period of 10 months prior to TenderWet application - Treatment duration: 3 months <p>Venous leg ulcer in the gaiter area:</p> <ul style="list-style-type: none"> - Multimorbid patient with chronic venous insufficiency (CVI), poor health prevented treatment of CVI - Ulcer persisted for over 35 years - Treatment duration: 12 months 	<p>Decubitus ulcer in the sacral region:</p> <ul style="list-style-type: none"> - Rapid cleansing of necrotic tissue and fibrinous coatings - Granulation tissue formation - Wound prepared for subsequent therapy <p>Decubitus ulcers in the sacral region, on the heel and hip region:</p> <ul style="list-style-type: none"> - Sacral ulcer healing progressed well without setbacks, with good granulation tissue formation and epithelialisation and healing occurring within 4 months of wound treatment - TenderWet/surgical debridement revealed deep cavity wound which progressed to healing within 5 months with a combination of alginate/TenderWet and TenderWet only treatment - Initial TenderWet application led to necrosis detachment but wound persisted new necrosis formed as a result of ineffective pressure relief. A combination of alginate and TenderWet application resulted in ulcer healing within 10 months <p>Diabetic foot ulcer on big toe:</p> <ul style="list-style-type: none"> - After initial debridement by surgery, TenderWet application leads to wound cleansing and rapid formation of granulation tissue - Ulcer filling with granulation tissue with associated re-epithelialisation - Wound prepared for subsequent treatment with hydrogel and healing <p>Venous leg ulcer:</p> <ul style="list-style-type: none"> - Reduction in exudate levels within a few days of TenderWet application - Cleansing of the wound bed observed with the formation of healthy-looking granulation tissue - Ulcer healed after 3 months <p>Venous leg ulcer in the gaiter area:</p> <ul style="list-style-type: none"> - TenderWet application resulted in a marked improvement in ulcer condition despite not being able to treat CVI - Wound cleansing and epithelialisation progressed - Ulcer subsequently healed
Malone & Dickson ⁵⁹	<p>Case series</p> <p>Mixed aetiology ulcer of the heel:</p> <ul style="list-style-type: none"> - Chronic neuroischaemic ulcer stalled after vascular surgery - Application of TenderWet plus - Treatment duration: 16 days <p>Chronic wound in Achilles region:</p> <ul style="list-style-type: none"> - Ulcer stagnated after surgical debridement, angioplasty and VAC therapy - Wound heavily exuding and significant wound bed coverage by fibrin slough - Application of TenderWet plus - Treatment duration: 12 days <p>Decubitus ulcer to retro calcaneum following hip surgery:</p> <ul style="list-style-type: none"> - Ulcer required surgical debridement following infection - Soft tissue necrotic and devitalised with significant fibrin slough coverage of wound bed - No significant healing after 4 months - Application of TenderWet plus - Treatment duration: 7 days 	<p>Mixed aetiology ulcer of the heel:</p> <ul style="list-style-type: none"> - Reduction in wound bed coverage by fibrinous slough from 51% to 10% by Day 16 - Increase in wound bed granulation tissue coverage from 48% to 90% <p>Chronic wound in Achilles region:</p> <ul style="list-style-type: none"> - Reduction in wound bed coverage by fibrinous slough from 20% to 3% by Day 12 - Increase in wound bed granulation tissue coverage from 80% to 97% <p>Decubitus ulcer to retro calcaneum following hip surgery:</p> <ul style="list-style-type: none"> - Reduction in wound bed coverage by fibrinous slough from 43% to 8% by Day 7 - Increase in wound bed granulation tissue coverage from 57% to 93%
Meuleneire ⁶¹	<ul style="list-style-type: none"> - Case study - Decubitus ulcer with coverage of fibrinous slough and necrotic tissue - Combined therapy of mechanical debridement and autolytic debridement with application of HydroClean active - Treatment duration: 7 weeks 	<ul style="list-style-type: none"> - Pressure relief, mechanical debridement and HydroClean active treatment resulted in necrotic tissue removal within 3 weeks of commencement of treatment - Continued application of HydroClean active promoted wound cleansing and conditioning for further wound healing - Wound size significantly reduced within 7 weeks

Table 5 continued

Reference	Methodology	Main results
Meuleneire ⁶⁰	<p>Case series</p> <p>Post-traumatic venous leg ulcer:</p> <ul style="list-style-type: none"> - Ulcer located on the ankle - Did not respond to antimicrobial hydrogel therapy - Application of TenderWet plus and short stretch compression bandaging - Treatment duration: approximately 12 weeks <p>Decubitus ulcer in the sacral region:</p> <ul style="list-style-type: none"> - Sacral decubitus ulcer developed as a result of complete patient immobility - Ulcer wound bed partially covered by black/yellow necrotic tissue and wound was very painful - Application of TenderWet plus and use of pressure-relieving mattress - Treatment duration: approximately 16 weeks <p>Trauma-induced leg ulcer:</p> <ul style="list-style-type: none"> - Ulcer present for 2 months prior to commencement with TenderWet plus treatment - Wound bed coated with yellow fibrinous slough - Peri-wound skin reddened - Wound pain at dressing changes - Wound cleansed by irrigation and hydrogel therapy prior to commencement with TenderWet plus - Treatment duration: 5 weeks 	<p>Post-traumatic venous leg ulcer:</p> <ul style="list-style-type: none"> - Wound bed cleansed within 5 days of TenderWet plus application - No maceration of peri-wound region although slight reddening of wound margins - Pain-free dressing changes reported - Re-epithelialisation complete within 12 weeks of TenderWet plus application <p>Decubitus ulcer in the sacral region:</p> <ul style="list-style-type: none"> - Significant autolytic debridement of wound seen over the course of the first week of treatment despite large volumes of exudate production, peri-wound reddening and wound pain - Wound cleansing, reduced levels of exudate and significantly reduced inflammation and wound pain within 2 weeks of dressing application - Increased formation of granulation tissue over course of treatment - Once wound conditioning has taken place, wound progresses to complete healing with HydroTac <p>Trauma-induced leg ulcer:</p> <ul style="list-style-type: none"> - Reduction in peri-wound reddening and maceration within 3 days of TenderWet plus application, but wound pain remained significant - Autolytic debridement of fibrinous slough progressed slowly over subsequent days - Complete ulcer healing achieved after wound conditioned using TenderWet plus
Cooper ⁶⁶	<ul style="list-style-type: none"> - Case study - Patient presented with long-standing leg ulcer - Wound bed covered in yellow slough requiring debridement - TenderWet applied to promote debridement - Treatment duration: unknown 	<ul style="list-style-type: none"> - Effective and rapid debridement of yellow slough from ulcer wound bed - Healthy granulation tissue present - TenderWet treatment continued
Kapp ⁵⁸	<ul style="list-style-type: none"> - Case study - Recurrent history of venous leg ulcer over previous 4 years - Treatment duration: unknown 	<ul style="list-style-type: none"> - Significant improvement within 3 weeks of initiation of TenderWet 24 active treatment - Wound size reduced by approximately one-third within 1 month - Fibrinous coatings reduced - Reduced exudate levels - Reduced wound pain - Increased granulation tissue formation - New epithelium - Improved peri-wound skin condition (including reduced oedema, maceration, eczema and hyperkeratosis)
Zollinger ⁶²	<p>Case series</p> <p>Chronic wound over tibia:</p> <ul style="list-style-type: none"> - Stagnant wound for over 4 years - Underlying skin sensitivity with peri-wound irritation - HydroClean plus treatment to improve wound condition - Treatment duration: approximately 20 weeks <p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Post-lower limb amputation, patient re-admitted to hospital due to development of heel ulcer(s) - HydroClean and HydroClean plus application to remove fibrinous slough and promote healing - Autolytic and surgical debridement - Treatment duration: 6-7 months <p>Venous leg ulcer complicated by pyoderma gangrenosum (PG):</p> <ul style="list-style-type: none"> - Presence of PG prevented mechanical debridement - Leg ulcer coated with fibrinous slough - HydroClean plus application to promote autolytic debridement - Treatment duration: 2 weeks 	<p>Chronic wound over tibia:</p> <ul style="list-style-type: none"> - Wound condition improves slowly - Autolytic debridement with accompanying new granulation tissue formation noted - New epithelium - Wound healing progressing despite skin sensitivity factors <p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - HydroClean/HydroClean plus application reduced fibrinous slough - New epithelium formed - Significant reduction in wound area <p>Venous leg ulcer complicated by pyoderma gangrenosum (PG):</p> <ul style="list-style-type: none"> - Fibrinous slough softened within 2 days of HydroClean plus application and removed using compress - Wound pain and pain at dressing change reduced - Necrotic tissue peels off at 2 weeks - HydroClean plus promotes wound conditioning for subsequent wound care regimen

Table 5 continued

Reference	Methodology	Main results
Zollinger ⁶²	<p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Pressure ulcer on heel developed due to immobility after patient suffered fracture femur - HydroClean plus application to promote wound cleansing for subsequent wound care programme - Treatment duration: 3 weeks <p>Venous leg ulcer over ankle region:</p> <ul style="list-style-type: none"> - Wound bed almost completely covered with fibrinous slough - HydroClean plus application to promote autolytic debridement - Treatment duration: 3 weeks <p>Wound at forefoot amputation site:</p> <ul style="list-style-type: none"> - Shortly after surgical amputation wound site covered in fibrinous and necrotic tissue - Application of HydroClean plus to promote autolytic debridement of tissue - Treatment duration: approximately 10 weeks <p>Venous leg ulcer at ankle region:</p> <ul style="list-style-type: none"> - Ulcer duration: 16 years - Wound bed completely covered in fibrinous slough - HydroClean plus application to remove fibrin coating - Treatment duration: 4 weeks 	<p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Fibrinous slough softening 5 days after HydroClean plus application - Increased granulation tissue - Fibrin slough removed by HydroClean plus allowing subsequent wound treatments <p>Venous leg ulcer over ankle region:</p> <ul style="list-style-type: none"> - Fibrinous coating removed - New epithelium - Reduced wound area - Ulcer progressed to complete healing <p>Wound at forefoot amputation site:</p> <ul style="list-style-type: none"> - Removal of devitalised tissue achieved with HydroClean plus application - Patient reported good quality of life during dressing application <p>Venous leg ulcer at ankle region:</p> <ul style="list-style-type: none"> - Fibrinous coating removed - Granulation tissue increased - Wound conditioned ready for next treatment phase to promote healing
Scherer ⁶³	<p>Case series</p> <p>Stage 3 decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Poor healing response to treatment for 6 months prior to application of HydroClean plus - Ulcer surface covered by significant levels of yellow fibrinous slough - HydroClean plus application to remove fibrin and promote healing response - Treatment duration: 5 weeks <p>Chronic wound on knee/tibia region:</p> <ul style="list-style-type: none"> - Cleansing of wound bed required to remove areas of necrosis and fibrinous slough - HydroClean plus application - Treatment duration: 5 days <p>Arterial leg ulcer on lateral malleolus:</p> <ul style="list-style-type: none"> - Leg ulcer duration prior to HydroClean plus application: 9 months - Wound appearance devitalised with tendon exposed - HydroClean plus application to initiate healing - Treatment duration: 6 months <p>Venous leg ulcers on left and right lateral lower limb:</p> <ul style="list-style-type: none"> - Ulcers present for at least 3 months prior to treatment - Base of both wounds covered dry fibrinous slough - HydroClean plus applied - Compression therapy applied - Treatment duration: 10 days <p>Chronic leg ulcers on left and right malleolus:</p> <ul style="list-style-type: none"> - Duration of ulcers: 2 months - Wound beds partially covered with fibrinous slough - HydroClean plus application - Existing lymphoedema treated with compression therapy - Treatment duration: 20-40 days <p>Venous leg ulcers on the lateral lower leg:</p> <ul style="list-style-type: none"> - Two sites of ulceration in close proximity to one another - Peri-wound region reddened and inflamed appearance - Wound beds covered by fibrinous coating - Application of HydroClean plus - Treatment duration: 4 days <p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Duration prior to treatment: 2 weeks - Wound bed covered with necrotic tissue - HydroClean plus application - Treatment duration: 10 days 	<p>Stage 3 decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Autolytic debridement of wound bed observed 3 days after HydroClean plus application at first dressing change - Reduced fibrin coating - Increased granulation tissue - New epithelium - Reduction in wound area <p>Chronic wound on knee/tibia region:</p> <ul style="list-style-type: none"> - HydroClean plus application for 5 days cleans and conditions wound bed - Wound bed prepared for subsequent application of foam/hydrogel pad - Wound healing achieved <p>Arterial leg ulcer on lateral malleolus:</p> <ul style="list-style-type: none"> - HydroClean plus application quickly leads to autolytic debridement, necrosis and slough softened and removed - Wound bed takes on healthy appearance - Wound size reduced - Despite periods of stagnation, continued HydroClean plus application promotes epithelialisation - Wound area significantly reduced after 5 months and complete wound closure almost achieved after a further month <p>Venous leg ulcers on left and right lateral lower limb:</p> <ul style="list-style-type: none"> - Within 2 days of HydroClean plus application wound cleansing occurred with corresponding increase in granulation tissue formation - New epithelium - Wound area of both wounds reduced - Once wound cleansed, treatment continued with application of hydro-active foam dressing <p>Chronic leg ulcers on left and right malleolus:</p> <ul style="list-style-type: none"> - Removed fibrinous slough - Improvement in wound bed appearance - Increased granulation tissue <p>Venous leg ulcers on the lateral lower leg:</p> <ul style="list-style-type: none"> - Removal of fibrin slough coatings by 4 days - Wound bed conditioned ready for subsequent application of hydro-active foam dressings - Wounds progressed to complete healing within 6-7 weeks <p>Decubitus ulcer on heel:</p> <ul style="list-style-type: none"> - Rapid removal of necrotic tissue from wound bed - Absence of necrosis within 4 days of dressing application - Increased granulation tissue - Healthy, granulating wound allow for hydro-active foam dressing to be used for further wound care treatments

Table 7: Clinical evaluations of HRWD on tissue preparation for skin grafting

Reference	Design & methodology	Main outcome measures	Main results
Knestele ⁴¹	<ul style="list-style-type: none"> - Prospective, randomised study - Venous leg ulcers (n=42) - Treatment randomisation: TenderWet 24 vs. enzymatic wound cleansing agent - Treatment duration: maximum of 8 weeks 	<ul style="list-style-type: none"> - Level of fibrinous coating - Level of necrotic tissue - Granulation tissue formation - Assessment for level of tissue conditioning of wound base for autologous skin grafting 	<ul style="list-style-type: none"> - Dressing and enzymatic agent equally effective at reducing levels of necrotic tissue and wound coatings - Promotion of granulation tissue formation - TenderWet 24 promoted moist wound environment - TenderWet 24 managed excessive exudate and tissue debris - TenderWet 24 assessed to be superior due to dressing's ability to maintain optimal healing conditions in wound base, maximising chances of skin graft take
	<p>Case series</p> <p>Large area skin abrasions following road traffic accident:</p> <ul style="list-style-type: none"> - Severe pelvic fractures and large area of tissue trauma, including skin abrasions - Very large wound resultant after numerous surgical procedures - Clinical requirement for wound preparation for grafting - Treatment duration: 1 week <p>Necrotising fasciitis:</p> <ul style="list-style-type: none"> - Extensive tissue debridement and antibiotic medication prior to dressing application - Treatment duration: unknown 	<p>Large area skin abrasions following road traffic accident:</p> <ul style="list-style-type: none"> - Due to size, type and location of wound, infection was present - Wound bed prepared with TenderWet 24 application - TenderWet pads fixed together to form a large area dressing - After 1 week treatment with TenderWet wound base cleansed and conditioned for mesh grafting <p>Necrotising fasciitis:</p> <ul style="list-style-type: none"> - Conditioning of wound bed required prior to application of a mesh graft - Following surgical debridement of wound TenderWet applied - Wound bed prepared for successful mesh grafting 	

Table 8: Clinical evaluations of HRWD on miscellaneous wounds

Reference	Methodology	Main results
Meuleneire ⁵¹	<ul style="list-style-type: none"> - Case study - Black skin necrosis following intramuscular injection - Necrosis removed by surgery - Wound cleansing first step in healing process - Treatment duration: 9 days 	<ul style="list-style-type: none"> - Remnants of tissue necrosis had detached within 3 days of starting treatment with TenderWet 24 - Wound cleansing progressed for remainder of the treatment with TenderWet 24 - Treatment switched to PermaFoam and HydroTac as part of a stage-oriented approach to healing wound
Kapp ⁵⁸	<ul style="list-style-type: none"> - Case study - Development of a chronic wound after insect bite - Wound showed no sign of healing after 45 days - Very painful and wound bed showed signs of tissue necrosis - Treatment duration: 14 days 	<ul style="list-style-type: none"> - All necrotic tissue debrided and complete coverage with granulation tissue visible within 5 days of starting treatment with TenderWet active - Epithelialisation of 60% of wound base within two weeks of dressing application - TenderWet active did not stick to wound during dressing change - Patient assessed the dressing positively in terms of tolerance to dressing and wearing comfort
Scherer ⁶³	<ul style="list-style-type: none"> - Case study - Extensive skin tearing on back of hand - HydroClean plus application - Treatment duration: 4 days 	<ul style="list-style-type: none"> - All wound debris and slough removed from wound after 2 days HydroClean plus application - Patient observed pain relief with HydroClean plus application - Wound bed cleansed for application of hydro-active foam dressing - Wound healing achieved after 4 weeks



Dr. Karen Ousey

Reader Advancing Clinical Practice. Clinical Associate Professor, Australian Catholic University. Director of Institute of Skin Integrity and Infection Prevention, University of Huddersfield.



Dr. Mark Rippon

Clinical Research Fellow,
University of Huddersfield.



Going further
for health

