# Using TLC-NOSF advanced wound dressing to improve outcomes for patients with leg and diabetic foot ulcers

Healthcare providers are under pressure to balance cost of care with the delivery of high-quality patient outcomes. Breaking the cycle of hard-to-heal wounds requires a proactive approach that includes recognising and understanding the extent of the problem, and early intervention using advanced wound technologies that improve healing rates, reduce clinical time, avoid hospital admission and improve patient satisfaction. There is evidence that some advanced wound dressings are effective in improving healing rates when used as part of a holistic approach to leg and diabetic foot ulcer management, contributing to improved patient outcomes and more effective use of resources. This article reviews the use of technology lipido-colloid nano-oligosaccharide factor (TLC-NOSF) and the evidence for its use.

KEY WORDS
- Clinical evidence
- Hard-to-heal wounds
- Improving outcomes
- Protease-inhibiting enzymes

Wounds are a significant source of cost to patients as well as to the health economy. Leg ulcers and diabetic foot ulcers (DFUs) are often hard to heal, resulting in a cycle of pain, anxiety and reduced quality of life for the individual patient. The cost of treating chronic wounds in the UK has been estimated at between £2.5 million and £3.1 million per 100,000 population per annum, accounting for 2–3% of the healthcare budget (Posnett et al, 2009). In a more recent study, the annual cost to the NHS of wound management and associated comorbidities was estimated at £5.3 billion (Guest et al, 2017).

Delayed wound healing and related complications add considerably to the cost of care and are associated with longer and more intensive treatment, extended hospital stays, readmission and specialist intervention. The demand for wound care is predicted to increase due to the rising elderly population with long-term conditions and more complex needs. Data on health service expenditure suggest that healthcare funding is unlikely to keep pace with demand and that fundamental changes need to be made in the way wound care is delivered if we are to reconcile supply with demand (Dowsett et al, 2014). To balance cost and care, in the future clinicians will need to be more proactive in their approach to wound care, adopting new and advanced technologies that increase healing, empower and involve patients in their care and create economic value. Poor quality care is more costly for the patient and the health economy (Dowsett and White, 2010). When we make our treatment choices for patients, we need to ensure they offer the best opportunity for healing.

## RECOGNISING WOUND HEALING ISSUES

Wound healing can be delayed by:

- Patient-related factors, such as underlying pathology and comorbidities
- Wound-related factors, such as ulcer size, duration and location
- Clinical competency factors, such as the knowledge and skill of the clinician
- The presence of devitalised tissue, infection, inflammation and excess exudate. Implementing a programme of wound-bed preparation is necessary to progress a wound to healing (Schultz et al, 2003).
- Resource- and treatment-related factors, such as dressing availability and selection, can also influence how long the wound will take to heal (Vowden, 2011).

Recognition of non-healing wounds demands careful assessment and re-assessment of the patient and the wound as well as reviews of systems of care,

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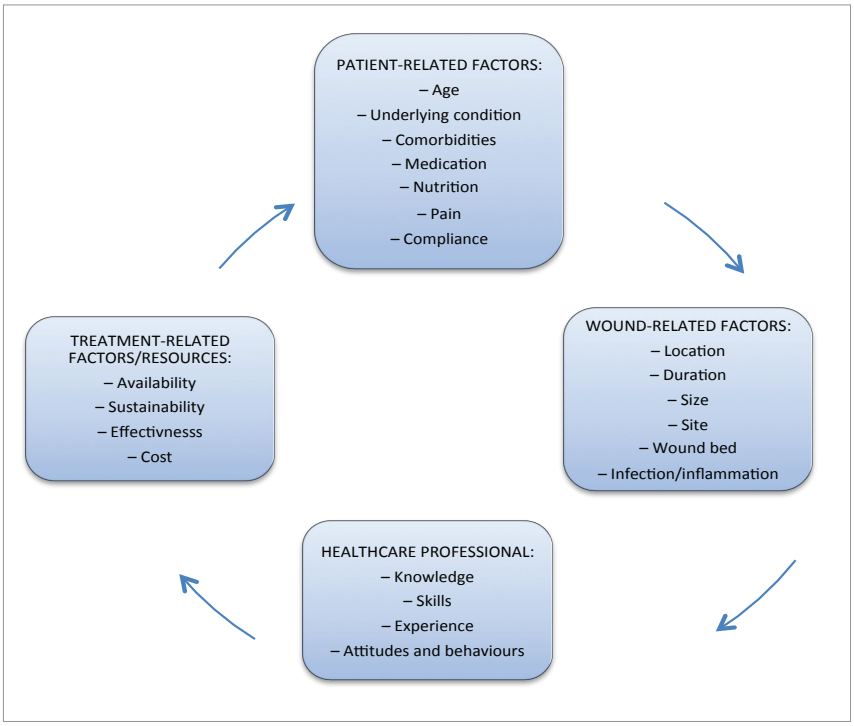


**Figure 1. Assessment of factors that have an impact on healing (Dowsett, 2015)**

so that intrinsic and extrinsic barriers to healing are identified and addressed, see *Figure 1*. Wounds in community care that are hard to heal are more likely to require hospital referral for specialist assessment, and in some cases hospital admission for treatment. Strategies that focus on early recognition of patients at risk of poor healing and wounds on a trajectory to delayed healing are essential to break the cycle of delayed discharge and re-admission as a result of wound complications.

## THE CHRONIC WOUND ENVIRONMENT

Recent advances in wound care have led to a greater understanding of how wound physiology and microclimate impact on healing. Regardless of the underlying cause, wounds with delayed healing generally share similar biochemical characteristics, including elevated inflammatory markers, high levels of proteases (including matrix metalloproteinases; MMPs) and diminished growth factor activity in cells within the wound (Dissemond et al, 2013). These characteristics result in a hostile environment in which new tissue and growth factors are degraded and the wound is perpetuated. Wounds in this situation are often referred to as being 'stuck' in the inflammatory phase of healing, where they can remain for months or even years (Wounds International, 2011).

## THE ROLE OF MMPS AND THEIR INHIBITORS IN WOUND HEALING

MMPs are enzymes that play an essential and beneficial role in wound healing. During the inflammatory stage, MMPs break down the damaged extracellular matrix (ECM), enabling new ECM components (e.g. collagen, fibronectin and proteoglycans) synthesised by wound cells to integrate correctly with intact ECM components at the wound's edges. In the proliferative stage, MMPs promote angiogenesis by degrading the basement membrane surrounding capillaries, allowing vascular endothelial cells to migrate from capillaries near the wound to establish new blood vessels into the wound bed. MMPs also have a role in the contraction and remodelling of scar tissue. The low levels of MMPs that are produced during this phase of wound healing increase the strength of the wound (Argen et al, 2001).

Substantial evidence suggests that MMPs are highly elevated in wounds with delayed healing compared to acute healing wounds. Several groups have shown that the amount of active MMP-9 is inversely correlated with wound closure rate (Ladwig et al, 2002; Rayment et al, 2008; Liu et al, 2009). Although MMPs have the important role of breaking down proteins so new tissue forms, when MMPs levels in a wound bed are too high for too long a time and in the wrong place, they begin to degrade proteins such as growth factors, receptors and ECM proteins that are essential for wound repair and healing (Gibson et al, 2009).

In contrast to MMPs, levels of tissue inhibitors of metalloproteinases (TIMPs) – which regulate MMPs – are lower in chronic than acute wounds (Trengrove et al, 1999). TIMPs work by inhibiting activated MMP enzymes and preventing the activation of inactive MMPs (pro-MMPs). The low TIMP levels in leg ulcer and DFUs therefore compound the effects of high MMP levels.

## WOUND DRESSINGS AND TREATMENTS

When treating a patient with a wound, it is essential to treat the underlying cause and address underlining comorbidities. To optimise treatment, it is necessary to understand when a wound is likely to be hard-to-heal or there is delayed healing. This

requires careful assessment and reassessment at each dressing change. Wounds that are not healing despite correction of the underlying condition and optimisation of the wound bed may be stuck in a persistent inflammatory state and benefit from dressings that regulate protease activity (Wounds International, 2011).

Dressings remain the mainstay of treatment for patients with wounds. A wide variety are available for use. Selection will be based on a number of factors including:

- A detailed patient and wound assessment
- Identification of the underlying cause
- The objective of treatment
- Cost-effectiveness
- The availability of the dressing
- Patient preference.

Advanced wound therapies have become available that can improve outcomes and reduce cost by facilitating early discharge from hospital, reducing dressing frequency and promoting faster healing. Although new technologies are more expensive than traditional dressings, they can be cost-effective if wounds heal faster and fewer treatments are required.

## MMP INHIBITORS

New treatment options offer clinicians an opportunity to change the wound environment and improve healing. There is evidence that dressings directed at inhibiting MMPs can reduce healing time in a variety of wounds, and therefore improve patient outcomes. A number of studies have demonstrated their efficacy in improving healing rates in leg ulcers, DFUs and pressure ulcers (Schmutz et al, 2008; Meaume et al, 2012; Tsantilas et al, 2013).

UrgoStart® is a protease inhibitor dressing combining a soft-adherent technology lipido-colloid nano-oligosaccharide factor or TLC-NOSF layer with an absorbent foam pad and semi-permeable backing. Urgo start is available in 3 products – wound contact layer, foam, and bordered foam. The polysaccharide structure of the NOSF healing accelerator partially dissolves to form a colloidal substance that is capable of binding onto the wound surface. NOSF also interacts with the MMPs present in the wound exudate, reducing their numbers and thus inhibiting their detrimental activity. Through this mechanism, NOSF restores the wound balance.

### Evidence for use

Two randomised controlled trials (RCTs) have shown that wounds heal significantly faster with UrgoStart®. Schmutz et al (2008) evaluated UrgoStart versus Promogran™ in 117 patients with venous leg ulcers (VLUs) with an average duration of 11.2 months and an average size of 10.9 cm. The relative median wound area reduction was 54.4% with UrgoStart and 12.9% with Promogran at 12 weeks ($P$=0.0286). The mean healing rate was significantly higher in the UrgoStart group ($P$=0.029). In a double-blind RCT comparing UrgoStart with neutral foam dressing in a cohort of 187 patients, significantly more VLUs in the UrgoStart group had surface areas that were reduced by 40% (65.6% versus 39.4%; $P$=0.0003). The healing rate in this study was twice as fast with UrgoStart, resulting in a 10.83 $mm^2$/day reduction in size compared to 5.15 $mm^2$/day with Promogran ($P$=0.0056) (Meaume et al, 2012).

In a multicentre observational study of 1,248 patients with chronic wounds (Tsantilas et al, 2013), 45% of the wounds treated with UrgoStart had healed by week 8. A further 49% of wounds treated with this technology improved during this time (36% significantly and 13% slightly). The highest healing rate was noted in DFUs, of which 61% (116) healed.

Münter et al (2017), in an attempt to determine whether the clinical trial results for UrgoStart translated into routine management of wounds, pooled the data from real-life observational studies including 10,220 patients. The authors concluded that using UrgoStart in routine management can reduce the healing time of leg ulcers, DFUs and pressure ulcers by 100 days on average. The study results also suggest that the earlier the decision is made to use the dressing, the shorter the time to closure, whatever the severity and nature of the wound. A recent Cochrane review, however, suggested uncertainty in the evidence for the use of protease-modulating matrix treatments for healing VLUs (Westby et al, 2016).

### Application in clinical practice

The reality in clinical practice is that clinicians are faced with making difficult treatment choices from a vast array of products and want to achieve the best outcomes for their patients. It is necessary to balance the recommendations from systematic reviews, RCTs and observational studies with clinician and patient

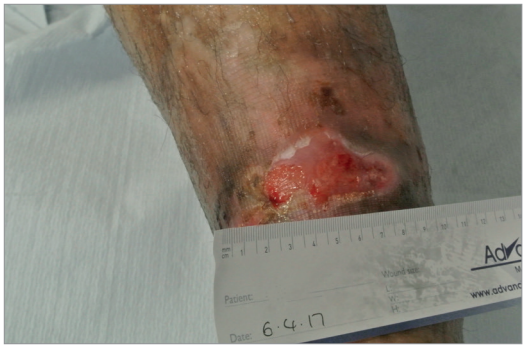


**Figure 2. At presentation, the patient's leg ulcer had been present for 18 months**

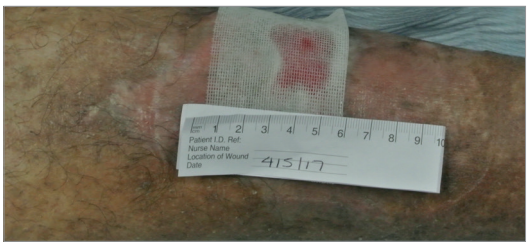


**Figure 3. UrgoStart was first applied on 6 April**

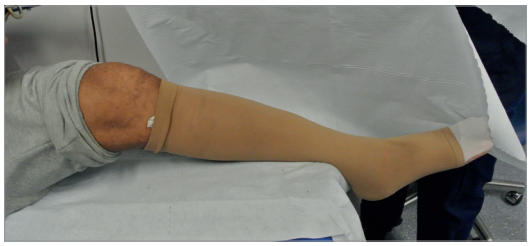

**Figure 4. The patient in the UrgoStart hoisery kit**

feedback to support a best practice decision.

When we make treatment decisions for patients, we need to address the underlying cause of the wound, treat underlying comorbidities and optimise the wound bed through debridement, exudate management, and infection prevention and control. Assessment through consultation and clinical examination should provide a clear diagnosis, as without this the process will fail and the wound will not heal effectively. Assessment should identify factors that suggest the wound may be hard to heal, e.g. large wound size, long duration and diabetes. When present, the use of an advanced wound dressing should be considered as the first-line intervention to give the wound the best chance of healing in the shortest time. Based on the evidence, time to wound closure appears to be substantially shorter when UrgoStart is used as first-line treatment rather than second-line treatment after another primary dressing.

The use of a protease-inhibiting/modulating dressing should be a timed intervention, i.e. the proposed duration of treatment should be clearly documented and a review date set. It is essential that regular assessments of healing progress, e.g. wound margin, base and wound area, are conducted during treatment. For VLUs, a 20–40% reduction in wound area at 4 weeks indicates that healing is likely (Flanagan, 2003).

A recent evaluation of UrgoStart in the management of eight patients with leg ulcers, DFUs and pressure ulcers showed the impact of the dressing in 'kick starting' the wounds onto a healing trajectory. These case studies were carried out by myself and my team at the East London NHS Foundation Trust. The following two case studies from this evaluation are examples of the use of the dressing in clinical practice.

## Case study 1

A 40-year-old man presented with a static leg ulcer of 18 months' duration. The ulcer measured 5 cm × 2 cm, covering an area 7.9 $cm^2$, and consisted of 90% granulation tissue, see *Figure 2*. The patient had a history of varicose veins that were being managed with full compression. His care was shared with vascular services.

On 6 April 2017, UrgoStart Contact, a contact layer containing TLC-NOSF technology, was applied to the ulcer, see *Figure 3*. Four weeks later, the wound had reduced in size by 31%, see *Figure 4*. At this time, it measured 3.5 cm × 2 cm and covered an area of 5.3 $cm^2$. The patient was pleased with the progress made and requested training so that he could self-mange his wound and reduce the amount of time he had to take off work. His dressing was changed to UrgoStart Border and he was given an ulcer kit. The ulcer kit included linear and compression stockings, instead of compression bandages. The patient attended the clinic weekly, until the ulcer had healed and then went onto our healed pathway for follow up.

## Case study 2

An 82-year-old woman with a non-healing VLU of 48 months' duration presented for treatment. Her ulcer was 3.5 cm × 5.0 cm on 16 May 2017, see *Figure 5*. The ulcer was covered with 100% granulation tissue and was producing moderate levels of exudate. The patient had a history of asthma, hypertension and arthritis.

The woman's VLU was treated with UrgoStart® wound contact layer with multi-layer compression bandage. She was treated weekly by myself at the leg ulcer clinic. After 2 weeks the patient returned for assessment. Her ulcer had reduced in size by 0.5 cm, measuring 3.0 cm × 4.5 cm, see *Figure 6,* and progressed to healing.

## CONCLUSION

A non-healing wounds is a complex clinical problem that can take weeks or months to resolve. It is costly for both the patient and the health economy. The cycle of non-healing can be perpetuated by clinicians who fail to accurately diagnose the underling cause of the wound, make poor treatment choices, fail to recognise complications or seek timely advice.

Improving patient outcomes requires a proactive approach to care that includes treatment of the underlying cause of the wound and the patient's comorbidities, recognition of when wounds are hard to heal and early intervention using advanced wound dressings and technologies. Dressings directed at inhibiting/modulating MMPs can reduce healing times in a variety of chronic wounds and therefore improve patient outcomes. The patient and the impact of the treatment should be re-assessed and evaluated at each dressing change. If the wound is not progressing to healing, then a referral should be made to the most appropriate specialist. WUK

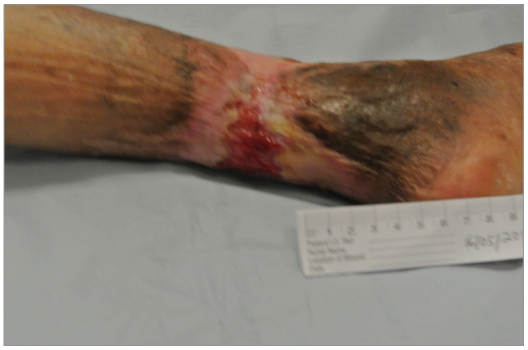

**Figure 5. At presentation, the venous leg ulcer was 3.5 cm × 5.0 cm with moderate exudate**

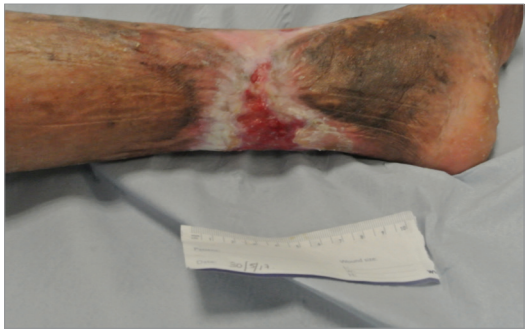

**Figure 6. After 2 weeks, the ulcer had reduced in diameter by 0.5 cm**

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