

Advancing Standard of Care in Difficult-to-Heal Wounds: Rationale for OASIS[®] Wound Matrix as the Next Step in Therapy

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OASIS[®] Wound Matrix is a natural extracellular matrix that has an intact three-dimensional structure that replaces the body's missing or failing extracellular matrix.¹¹

Wounds that fail to heal in a timely fashion can be both a frustrating and costly experience. These wounds, most frequently venous, diabetic, or pressure ulcers, are time consuming for patients and clinicians and oftentimes interfere with patient quality of life.¹

The direct financial costs of these wounds are staggering, totaling many billions of dollars annually in the United States. For instance, the cost of treating uninfected diabetic foot ulcers alone has been estimated at more than \$6 billion annually.² Wound complications such as infection and subsequent hospitalization are the largest contributors to costs.³

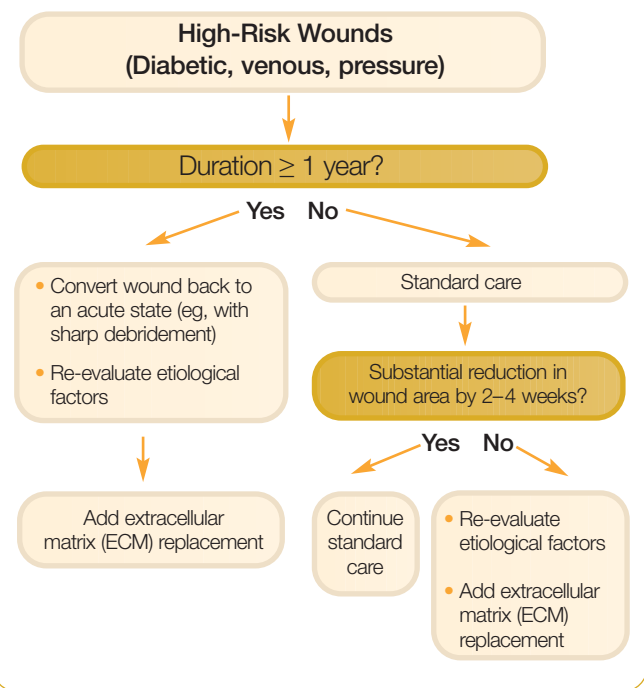
In order to reduce patient suffering and avoid costly and potentially life-altering complications, expeditious wound healing is an important goal. However, even with the diligent application of standard of care, many difficult-to-heal wounds fail to close within 3 or 4 months.⁴ This observation has led to attempts at defining strategies for predicting which wounds will and which will not close with several months of standard of care.⁵ Wounds that are less likely to heal with routine standard of care can then be targeted appropriately for early additional intervention.⁵

Important variables in evaluating whether wounds are more likely to heal with standard of care are wound duration and size. Venous leg ulcers that are ≥ 1 year in duration and larger than 10 cm² have been shown to be less likely to heal even after 6 months of standard of care.⁶ Such wounds may require conversion back into an acute state with sharp debridement before additional active interventional strategies can be expected to be effective. A re-evaluation of etiological factors is also in order.

For other wounds, treatment may begin with standard of care. The results of several studies indicate that progress toward healing within the first 2 to 4 weeks of standard of care is a predictor of complete healing at 3 or 4 months.^{5,7} More specifically, the study showed that wounds that fail to progress toward healing following 2 to 4 weeks of standard of care are unlikely to heal within 3 or 4 months. For instance, a study of 203 patients with diabetic foot ulcers found that 58% of wounds that showed progress at week 4 — defined in this report as $\geq 53\%$ reduction in wound area — healed within 3 months, compared with only 9% of wounds that showed slower

2–4 weeks: a critical time in wound management^{5,7,15}

- In diabetic foot ulcers, among wounds that showed <53% area reduction at week 4, only 9% were successfully closed at week 12⁵



progress at week 4.⁵ Another study of full-thickness venous leg ulcers found that a $\leq 30\%$ wound area reduction at 2 weeks correlated with wounds that healed significantly more slowly than those with a $>30\%$ reduction in area.⁷ These findings suggest that if wounds have not progressed sufficiently toward healing after 2 to 4 weeks of standard of care, they may need additional intervention to promote timely healing.⁵ It should be noted that, while the aforementioned studies provide useful insights, there are currently no definitive guidelines in the literature as to specific predictive measures across all wound types. Accordingly, until such data are available, determining the appropriate reduction in the wound area at 2 to 4 weeks may simply be a matter of good clinical judgment.

The Next Step in Therapy

If wounds that are unlikely to respond to standard of care alone can be identified after 2 to 4 weeks, what should be the next step in therapy? In attempting to answer this question, it may be useful to consider the deficits in difficult-to-heal wounds that may interfere with healing ability.

A frequently overlooked and important entity in wound healing is the extracellular matrix. Extracellular matrix refers to the collection of structural and functional molecules that coordinate the healing process and provide a scaffold to support cellular proliferation.⁸ The extracellular matrix is critical to wound healing, stimulating the attachment, migration, differentiation, and proliferation of cells, as well as regulating growth factor function.^{8,9} If the extracellular

matrix is absent or dysfunctional, healing does not progress normally. Indeed, the extracellular matrix of chronic wounds reveals many abnormalities.¹⁰ It is possible that these biochemical abnormalities are developing in difficult-to-heal wounds. The multifaceted role of the extracellular matrix in wound healing suggests that strategies designed to address extracellular matrix deficits in difficult-to-heal wounds may be beneficial.

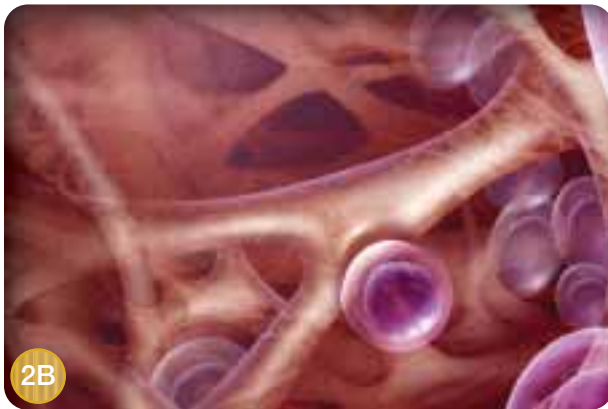
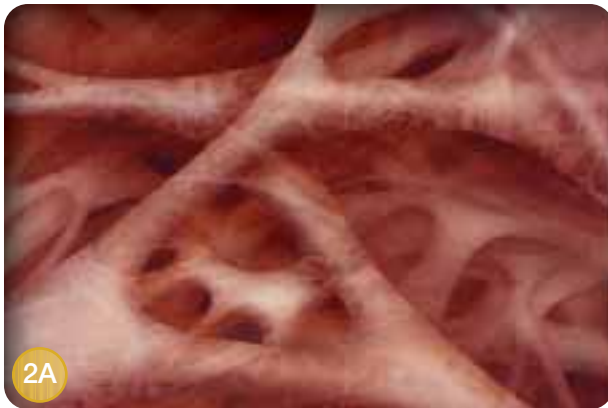
OASIS® Wound Matrix is a natural extracellular matrix that has an intact three-dimensional structure that replaces the body's missing or failing extracellular matrix.¹¹ OASIS contains key components of the dermal extracellular matrix such as collagen, elastin, glycosaminoglycans, glycoproteins, and proteoglycans.¹¹ It is derived from porcine small intestinal submucosa and retains the biological structure of extracellular molecules to provide the scaffolding to support cell proliferation and adherence¹¹ (see Figures 2A – 2D).

OASIS should be considered a logical choice as the next step addition to standard of care. It has been shown to significantly improve wound management¹² and possesses several practical features that may make it conducive to clinical use. For instance, OASIS is stored at room temperature and has a shelf life of up to 2 years.¹³ It can be applied weekly and is resorbed by the body, so that the previously placed OASIS does not need to be removed. Additionally, the cost of OASIS is reasonable: in recent clinical studies, the average cost of 12 weeks of OASIS (ie, product only) in venous leg ulcers was \$320 and in diabetic foot ulcers was \$250.^{12,14}

The efficacy and safety of OASIS were examined in a randomized clinical trial for the treatment of full-thickness venous leg ulcers.¹² Patients were randomly assigned to weekly topical administration of OASIS plus standardized compression therapy or non-adherent dressing and compression therapy.¹² After 12 weeks, 55% of patients in the OASIS group had been successfully managed as compared with 34% of patients in the group that received standard of care only ($P = 0.0196$).¹² OASIS was well tolerated and no significant between-group differences in treatment-related adverse events were reported. Based on these data, the authors concluded that OASIS, when used as an adjunctive therapy, significantly improves wound management of chronic leg ulcers over standard therapy alone.¹²

Conclusion

Given the enormous impact of difficult-to-heal wounds and their complications on patients, their families, and society, it is imperative that these wounds be closed as quickly as possible. Although some wounds heal expeditiously with standard of care, others require more aggressive interventional strategies to establish an environment for healing. If difficult-to-heal wounds fail to make healthy progress toward healing after 2 to 4 weeks of standard care, more aggressive intervention may be in order.



FIGURES 2A—2D: OASIS replaces the missing or falling ECM (2A), scaffolding supports cell adherence (2B), promotes rapid cellular proliferation and capillary ingrowth (2C), is eventually absorbed and replaced by host tissue (2D).

The next step in treatment for these wounds may be most useful if it addresses deficits in the wound healing environment and is practical for routine clinical use. The body's natural extracellular matrix — a collection of structural and functional molecules that coordinate the healing process and provide scaffolding support for cellular migration and proliferation — is critical to wound healing. Extracellular matrix deficits are characteristic of many chronic wounds.

OASIS is a natural extracellular matrix that can replace the missing or failing extracellular matrix in difficult-to-heal or chronic wounds with such deficits. Its practical features, such as up to 2-year storage at room temperature, weekly application, and resorption by the body, make it practical for clinical use. Furthermore, the cost of OASIS was shown to be \$320 per week in a recent 12-week venous ulcer trial.¹² In this trial, OASIS significantly increased the percentage of venous ulcers successfully managed at week 12 compared with standard care alone.¹² Based on these properties, OASIS combined with standard of care may be a logical choice for the next step in therapy for difficult-to-heal wounds.

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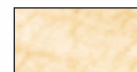
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