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Surgical Management May Be a Viable Option for Stage 3 and 4 Pressure Injuries Following Appropriate Selection Criteria

PROGRAM | WHITE PAPER

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Program Overview

+ Educational Need

Late-stage pressure injuries (PIs) are challenging to manage due to the involvement of deeper tissues. This can result in costly, resource intensive interventions to bring wound closure. Surgical reconstruction may be a viable option, however the numbers of patients undergoing this intervention are low and may be limited by the lack of clear guidelines or a consistent approach.

A multidisciplinary working group was convened to review the existing literature and propose an algorithm for surgical reconstruction of stage 3 and 4 PIs. The surgical algorithm provides a treatment pathway with an emphasis on patient selection criteria and which blends available tools including negative pressure wound therapy (NPWT) and bioscaffolds to help improve outcomes.

+ Learning Objectives

- To examine a newly proposed algorithm that helps identify and manage candidates that may benefit from surgical intervention
- To understand which candidates may be suitable
- To understand the different types of surgical approaches
- To help evaluate the post-operative environment in order to optimize recovery

+ Target Audience

This white paper was developed for physicians and non-physician clinicians who are involved in the management of PIs.

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The Burden of Pressure Injuries Is Significant

Pressure injuries (PIs), also known as pressure ulcers, are defined as areas of localized tissue damage caused by unrelieved pressure, friction, or shearing on any part of the body.[1] PIs are commonly located over a bony, weight-bearing prominence such as the tailbone, heels, ankles, hips, back, elbows, shoulder blades, and/or the back of the head.[1,2] Additionally, PIs can arise from pressure under a medical device, also known as a medical device-related pressure injury (MDRPI).[3,4]

PIs are among the most prevalent skin injuries and present a significant challenge in the hospital environment.[3] In the US, roughly 2.5 million PIs occur annually; however, the site of care greatly impacts PI prevalence. Rates are often lowest in medical-surgical inpatient care facilities and highest in intensive care units (ICUs).[5] ICU patients experience a greater risk for PIs because of several concomitant factors such as immobility, sedation, vasopressors, mechanical ventilation, hemodynamic instability, poor nutritional status, and comorbidities.[4,5] Proportionally, ICU patients also develop more severe PIs compared to step-down or medical-surgical inpatient units. Additionally, approximately 30% of PIs occur in long-term care facilities.[5] In 2019 alone, PIs cost the US health care system approximately $26.8 billion, with 59% of these costs attributed to stage 3 and 4 PIs.[5]

The Agency for Healthcare Research and Quality (AHRQ) National Scorecard Data on hospital-acquired conditions reports that over 1 million patients in the US develop a PI within the hospital, also known as a hospital-acquired pressure injury (HAPI). These patients are 2.8 times more likely to die during their hospital stay and 1.69 times more likely to die within 30 days of discharge.[6] Risk factors for HAPI development include older age, immobility, altered mental condition, urinary or fecal incontinence, reduced appetite, and nasogastric tube or intravenous nutrition.[7] HAPIs result in increased lengths of stay and healthcare costs.[4]

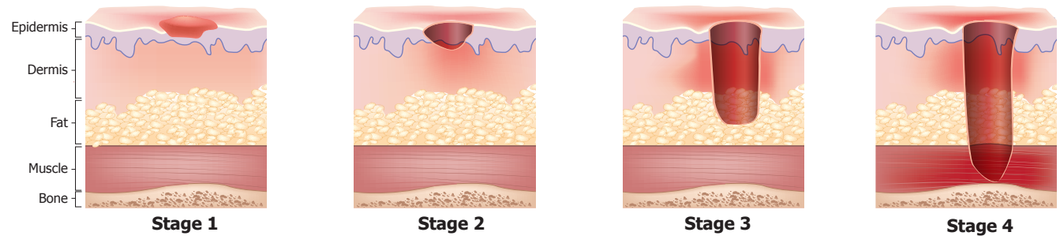
In addition to the financial burden, PIs take a significant toll on patients' mental health and health-related quality of life.[4] Pain, discomfort, wound drainage management, odor, and loss of mobility are all factors that reduce the quality of life for patients with PIs.[5,6] In addition, these psychosocial and physiological patient factors can negatively impact wound healing.[5,7] Research provides minimal data on the true mortality attributed to PIs.[5]

Staging of Late-Stage PIs

Health care providers (HCPs) assess PIs using a four-part staging system based on the degree of tissue damage **(Figure 1)**. Such staging allows HCPs to determine the best treatment course. Early-stage PIs (stages 1 and 2) represent mild to moderate tissue damage, and when treated early, these less severe PIs can heal in a few days to a few weeks.[2]

On the other hand, late-stage PIs (stages 3 and 4) represent more severe tissue damage, and these PIs are frequently more costly, time-consuming, and challenging to treat.[2,5] Stage 3 PIs have broken completely through the top two layers of skin and into the fatty (adipose) tissue below, and these injuries often take 1 to 4 months to heal fully.[2] Stage 4 PIs have the most extensive tissue damage, extending below the subcutaneous fat into the deep tissues, including muscle, tendons, and ligaments. In extreme cases, the wound can extend to cartilage or bone.[2] Stage 4 wounds carry a high risk of infection, especially a serious infection of the bone known as osteomyelitis. Infections in these PIs can also lead to sepsis, a potentially life-threatening blood infection.[8] These wounds can take anywhere from 3 months to 2 years to fully heal.[2]

FIGURE 1. STAGING OF PRESSURE INJURIES



Late-Stage PIs Are Challenging to Heal

Late-stage PIs bring a significant cost burden and are associated with cellulitis, osteomyelitis, sepsis, and higher rates of morbidity and mortality.[9] However, healing of late-stage PIs via traditional wound care can be a slow process. It may not be realistic in some cases due to the involvement of deeper tissues and exposed structures.

Patients often have co-morbidities that can complicate healing and limit treatment options. One randomized controlled study reported that only 13.7% of patients with stage 3 or 4 PIs were completely healed within 1 year, and the average healing time of stage 3 and 4 PIs was 118.9 days.[5,9] For stage 3 or 4 PIs that do not respond to traditional wound care, providers may consider surgical intervention to remove necrotic tissue and cover the wound with healthy, vascularized tissue.[5]

Surgical Management of Stage 3 and 4 PIs

Surgical intervention, or surgical reconstruction, is defined as any surgical procedure that leads to primary epithelial closure of the wound. Debridement of unhealthy and necrotic tissue, underlying bursae, and bone remains the cornerstone of surgical wound management. Thorough debridement involves the excision of fibrotic tissue around the chronic wound down to healthy bleeding tissue. Once debridement is complete, surgical reconstruction may be performed as a one-stage or multi-stage procedure.[10] Reconstructive surgical methods vary in their complexity; these include, from least to most invasive, primary closure, skin grafts, tissue expansion, local/regional flaps, and free flaps.[11]

Techniques for Closure Following Reconstruction

+ Primary Wound Closure

Primary wound closure involves direct advancement of the wound edges, directly or in layers, to close the wound.[10] Simple wounds can be closed by primary suturing, sometimes in a primary care setting. Primary closure is not ideal in heavily contaminated wounds. Instead, a delayed closure approach may be applied later. Alternatively, wounds with an increased risk of infection may be healed by secondary intention, in which the wound is left open and allowed to reepithelialize. It should be noted that healing by secondary intention is slow and can lead to contractures, scarring, and restriction of movement.[12]

+ Skin Grafts

Skin grafts may be used where skin defects are too large with significantly diminished skin apposition, eliminating the utility of primary wound closure or secondary intention.[12] Grafts require the harvesting of a thin piece of skin that is surgically removed from another area of the body (donor area) to replace skin in the defective area. Skin grafts are used when all contributing factors to PI formation have been removed, and they can facilitate rapid wound cover and healing.[10] Skin grafts are a mainstay of treatment for large wounds like burns.[12]

+ Tissue Expansion

Tissue expansion is used to increase the amount of locally available skin.[12] This involves a gradual stretching of the tissue surrounding a PI. The skin is expanded with a tissue expander inserted into a subcutaneous pocket near the PI. It is then slowly expanded at a defined rate with saline. When the skin and soft tissues are sufficiently expanded to a volume capable of covering the area, the expander is removed, and the expanded tissue is advanced to cover the wound. Alternatively, slow skin traction can be applied over the wound with an incremental traction dressing. This promotes tissue creep, and the extra skin will eventually be recruited to close the wound.[10]

+ Local and Regional Flaps

Many wounds with exposed bone or tendon, are not suitable for grafting and require more complex treatments on the reconstructive ladder, like flap reconstruction. A flap is a unit of tissue that survives on its own blood supply when relocated to another location.[12] Local random pattern flaps involve surgically moving the local tissue surrounding the wound into the wound defect based on a random pattern of blood supply.[10]

Regional flaps are not directly adjacent to the wound defect. Rather, they are taken from an adjacent region on the body.[10,12] These can include muscle or musculocutaneous flaps, fascial or fasciocutaneous flaps, or perforator flaps. Muscle flaps involve moving the whole or part of a given muscle, depending on a defined blood supply. This can occur with or without a skin island to provide wound cover. Fascial flaps involve moving a surgically defined fascial-based tissue island with an intact blood supply. Again, this approach can occur with or without skin to cover the wound. The perforator flap approach refines the previous approaches so that the specific perforating blood vessels are identified in the flap and dissected to allow either greater movement or less muscle sacrifice.[10] A flap with an intact vascular pedicle can provide increased length for greater mobility and versatility.[12]

+ Free Flaps

When no options are available for local or regional wound flaps, tissue may need to be harvested from elsewhere on the body using microvascular techniques in a tissue transfer called a free flap.[12] With a free flap procedure, a defined island of tissue with an artery and vein is raised, surgically detached, and moved to the wound site with other local arteries or veins of similar size. The vessels are then surgically connected to reestablish blood flow to the island of tissue.[10] Free flap reconstruction marks the top of the reconstructive ladder. Any tissue–including muscle, skin, fascia, fat, nerve, or bone–that can be isolated on a suitable vascular pedicle can be a candidate for a free flap.[12]

Advanced Modalities to Augment Surgical Reconstruction of Stage 3 and 4 PIs

+ Adjunctive Negative Pressure Wound Therapy (NPWT)

Adjunctive NPWT can augment the surgical reconstruction of PIs. Studies report that NPWT reduced PI healing time and decreased both dressing change frequency and hospitalization costs.[13] NPWT, with periodic installation of fluid (NPWTi-d), uses wound cleansers such as hypochlorous acid to enhance moisture, which helps to remove bacterial contamination, sloughing, and necrotic tissues. Closed incision NPWT (iNPWT) is a valuable option for high-risk closed surgical incisions to help prevent surgical site infections and complications. Overall, the type of NPWT applied depends on the patient's case and the available resources.[5]

+ Bioscaffolds

If traditional surgical interventions prove insufficient for effective wound closure, a bioscaffold can be applied to the wound bed, often with adjunctive NPWT to augment healing.[5] Bioscaffolds, also referred to as skin substitutes or dermal matrices, are devices that support a patient's own cells to aid in tissue regeneration. The ultimate goal is to build well-vascularized tissue to fill the defect.[5] Bioscaffolds negate the risk as they don't require a donor site and can reduce surgical complexity compared to flap procedures.[14] Available bioscaffolds include placental-derived products, synthetic polymer devices, and tissue-derived structures.[14] Tissue-derived matrices are typically sourced from mammalian tissue where the extracellular matrix (ECM) has been decellularized.[14] The decellularized material retains many of the biological components of the source ECM that promote tissue regeneration by providing a framework for cell infiltration, proliferation, and neovascularization.[14] The formation of a neodermis then allows for sufficient wound closure.[14,15]

While research is limited, some published findings suggest that bioscaffold material helps reduce dead space, augments standard wound management, and improves healing outcomes, especially compared to NPWT alone.[5] Several bioscaffolds are available for treating stage 3 and 4 PIs. These can vary widely in the source tissue (eg, human, porcine, bovine, ovine, equine) and the processing technique used to decellularize the tissue.[14] In choosing an appropriate bioscaffold, providers should consider several factors (Table 1).

TABLE 1. IMPORTANT CONSIDERATIONS IN CHOOSING A BIOSCAFFOLD

- Wound protease modulation
- Tolerates a contaminated defect
- Affordability
- Biological components important in healing

First, the elevated concentrations of wound proteases and the inflammatory state of PIs suggest the importance of wound protease modulation. Second, the common bacterial contamination found in PIs indicates that bioscaffolds should ideally tolerate bacterial infiltration, whereas synthetic bioscaffolds can be prone to infection.[5] Affordability is another concern when choosing a bioscaffold product due to the high risk of complications and potential for reoperation. Bioscaffolds should also provide sufficient volume to fill the necessary dead space. Morselized, or powdered, scaffolds help to provide tissue infill of tunneled, undermined, and irregular wound surfaces. Products indicated for implantation offer additional utility for use with skin flap applications beyond those designed only for topical use in skin flap applications. Additionally, bioscaffolds that necessitate repeated applications increase patient burden, risk for complications, and cost.[5]

Unmet Needs in the Surgical Management of Stage 3 and 4 PIs

Late-stage PIs are difficult to manage due to three main factors: bacterial/biofilm contamination, dead space (a subcutaneous pocket created during wound closure), and local tissue inflammation. Surgical intervention can assist with these challenges but can still bring relatively high rates of postoperative complications.

Some reports indicate that stage 3 and stage 4 PIs heal faster and with less scar tissue after surgical intervention.[5] However, the published evidence on the use of surgical intervention for treating stage 3 and 4 PIs is limited. One review of over 676 000 patients with PIs reported that approximately 50% of patients underwent surgical or excisional debridement, and less than 1% (n=5462) received multiple excisional debridements.[5] Since surgical intervention is relatively low in proportion to the overall occurrence of PIs, this suggests that surgery is reserved for more complex PIs.[10] As a result, no clear, recommended standards have been established for the surgical management of stage 3 and 4 PIs.[5]

Given the lack of a consistent approach to surgical management of complex PIs, a multidisciplinary working group was convened to review the existing literature and propose an algorithm for surgical reconstruction of stage 3 and 4 PIs.[5] See **Figure 2**. The working group proposed several factors that should be evaluated when considering surgical intervention for the treatment of complex, stage 3 and 4 PIs.[5] Based on the considerations outlined in Table 1, the working group selected Myriad Matrix(TM), an ovine forestomach matrix (OFM), as the bioscaffold of choice for the proposed algorithm.

+ Considerations for Surgical Management of Complex PIs

Interprofessional Team and Hospital System Support

The surgical management of complex PIs requires an interprofessional approach with support from the hospital system, patients, families, and multiple provider specialties. However, the difficulty in assembling this team and gaining hospital support may limit the number of clinical teams willing to take on this commitment. In addition to the difficulties in assembling the required team, the high rate of complications following PI surgical reconstruction can deter both clinicians and hospitals from taking on these patients.[5]

Patient Optimization

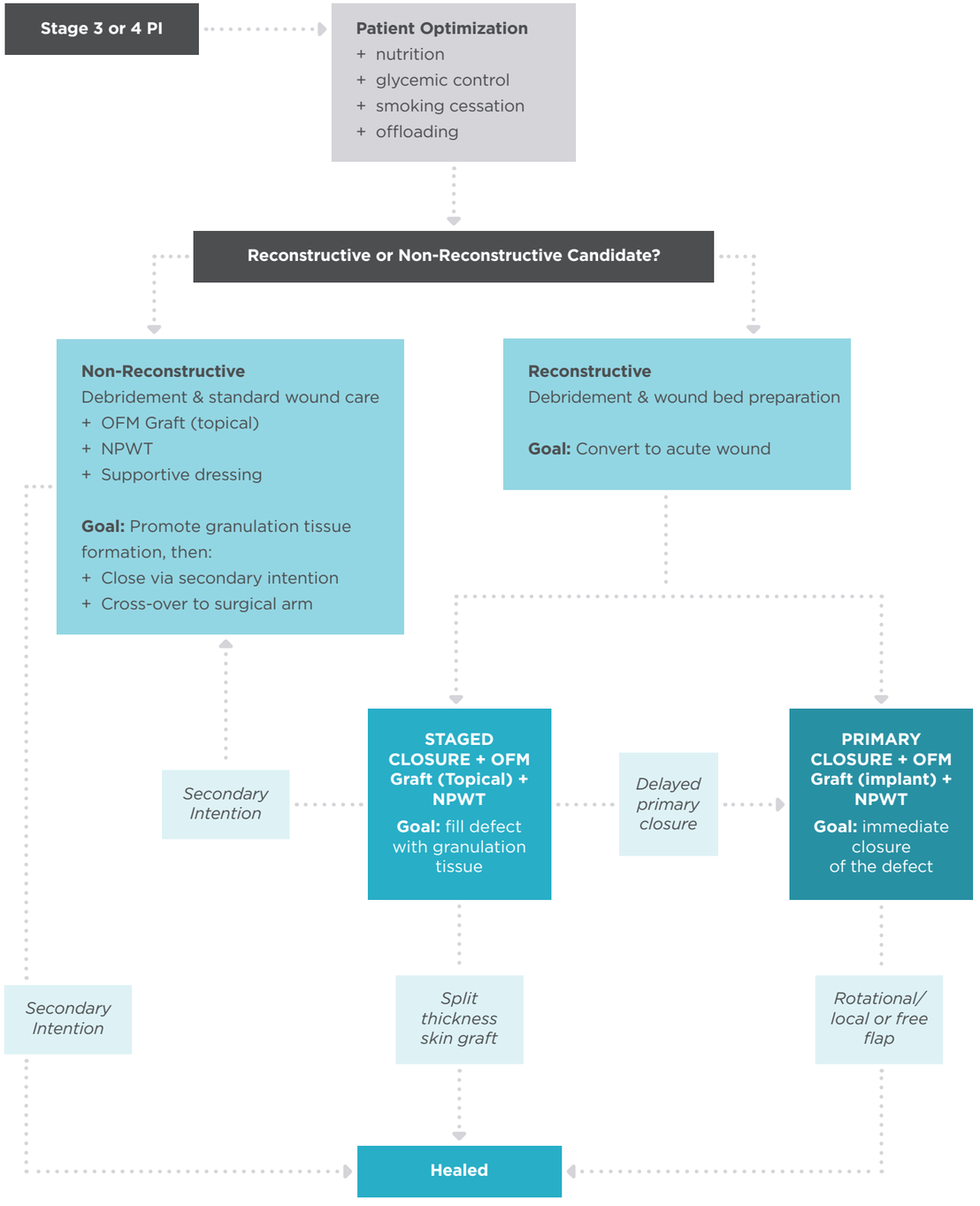
Pre-operative patient optimization is key for improved healing outcomes. As such, the working group strongly recommended the following:[5]

- Optimize patient nutrition, including high-calorie, high-protein nutrition supplements containing arginine, zinc, and antioxidants, especially when deficiencies occur.
- Provide nicotine cessation counseling, as smoking has been linked to poor healing outcomes.
- Control hemoglobin A1c levels to help lower the risk of postoperative complications.
- Conduct an osteomyelitis workup, including multiple bone biopsies.
- Improve patient pressure redistribution through proper cushion selection and needed accessories.
- Provide appropriate local wound bed preparation.
- Assess patients' social support systems and provide suggestions for improvement, if necessary.

Patient Selection

The working group proposed several criteria for assessing the surgical suitability of patients with PIs (**Table 2**).[5] Clinical judgment may supersede these criteria.

FIGURE 2. SURGICAL ALGORITHM



Proposed Surgical Algorithm

For patients that meet the criteria for surgical intervention, the working group made the following recommendations:[5]

- Where appropriate, patients with pelvic PIs should undergo fecal diversion to reduce the risk of surgical site contamination.
- Multiple bone biopsies should be tested for osteomyelitis and bacterial pathogens for targeted antibiotic therapy.
- Given the wide variety of available tissue-transfer procedures and patient factors, the attending surgical team is best positioned to decide on the appropriate reconstructive approach.
- If the wound can be surgically closed after debridement using a muscle flap, musculocutaneous flap, or fasciocutaneous flap closure, a bioscaffold may be considered for implantation at the base of the surgical site prior to closure to reduce local inflammation and obliterate dead space.
- NPWT may aid long-term outcomes by reinforcing and protecting the surgical closure during the initial healing period.
- Inclusion of surgical drains is necessary to help remove fluid and reduce the risk of seroma.
- If the patient cannot undergo surgical closure after debridement, a bioscaffold may be applied to the wound bed, ideally with NPWT, to fill the tissue defect and cover exposed structures rapidly. Once this immediate goal is achieved, then several options become available:
  - Definitive closure via placement of split-thickness skin graft (STSG), depending on the location of the PI.
  - Closure via secondary intention using standard wound care; a bioscaffold and/or NPWT may be included to accelerate reepithelialization
  - Reconstructive procedures such as muscle, musculocutaneous, or fasciocutaneous flap closure

TABLE 2. CRITERIA FOR ASSESSING PATIENT SUITABILITY FOR PI RECONSTRUCTIVE SURGERY

Inclusion criteria	Exclusion criteria
• Adequate Nutrition • Stage 3 or 4 PI • Ability to Comply With Postsurgical Recommendations	• Under Palliative Care • No Social Support/ Resources • Unresectable Pelvic Osteomyelitis • No Anesthesia Clearance • Poor Mental Status • Unwillingness to Stop Nicotine Use • Severe Malnutrition

+ What is Myriad?

Myriad is an advanced ECM derived from AROA ECM™ technology, for the surgical management of soft tissue repair. It is available as both Myriad Matrix sheets and Myriad Morcells, a morsellized version. Myriad Matrix comes in either 2-, 3- or 5-Layers of high-volume, porous ECM. The Myriad Matrix 5-Layer device is recommended for local or regional flaps, especially for large volumetric soft tissue defects. For staged surgical closure, the Myriad Morcells™ morselized version is recommended for undermining or wound bed irregularity, or the 5-layer sheet version may be used. For closure by secondary intention, an initial application of Myriad Morcells is recommended to help address undermining or wound bed irregularity or the Myriad Matrix 3- or 5-layer sheets, depending on the surgeon's goal and the defect size. This may then be followed through to closure by applications of the single-layer version of AROA ECM marketed as Endoform™.

+ Why Use Myriad as the Bioscaffold of Choice?

One challenge of managing stage 3 and 4 PIs is their significant depth, often compounded by extensive debridement and the subsequent required tissue infill. Wound bed irregularity and tunneling/undermining can also further complicate wound management. Application of a bioscaffold, such as Myriad Matrix™, can help fill surgical dead space and reduce the risk of seroma or hematoma formation.[14-17] This is supported by research in an in vivo porcine mastectomy model, which demonstrated a link between the amount of applied ECM and reductions in seroma formation.[18]

As shown in Table 1, a comparison among available bioscaffolds demonstrated that Myriad possesses several key properties that make it an effective bioscaffold material. Myriad modulates wound proteases to counter the elevated concentration of proteases observed in most

PIs.[19] It also tolerates bacterial infiltration, which promotes optimal healing. Furthermore, Myriad is one of the most affordable options among available bioscaffolds. A morselized format that provides beneficial tissue infill of tunneled or irregular wound surfaces is also available. Moreover, Myriad Matrix can be applied in multiple layers to achieve a thick depth of volumetric infill. Notably, Myriad Matrix is the only bioscaffold indicated for implantation, which offers utility beyond topical use in skin flap applications. Lastly, Myriad can be used as a single application, greatly reducing patient burden, risk of complications, and overall cost.[5]

A retrospective multicenter case series evaluated the efficacy of Myriad Matrix and Myriad Morcells in complex lower-extremity reconstructions at risk of complications, such as infection or limb amputation, due to significant comorbidities.[14] This study collected data from patients who had undergone inpatient lower-extremity reconstruction using Myriad Matrix products in a 3-year span across seven locations. The bioscaffolds were used to regenerate a neodermis before skin graft placement. The primary endpoint was the median time to 100% granulation of the neodermis. Results showed that Myriad Matrix produced a 100% granular neodermis with a median time of 26 days, which is comparable to other available bioscaffolds.[14] One significant finding of this study was the median number of applications needed to achieve 100% granulation over exposed vital structures. Myriad Matrix facilitated 100% granulation within a single application, compared to other bioscaffolds that often require repeated applications due to graft loss or failure to integrate.[14]

Another retrospective case series assessed the efficacy of Myriad Matrix and Myriad Morcells in the surgical management of contaminated volumetric soft tissue defects.[15] In this study, patients showed significant soft tissue loss, most with exposed vital structures. Here, the mean time to reach 100% granulation was 23.4 days, and the median number of product applications was one single use.[15] In addition, Myriad Matrix was shown to modulate wound proteases and tolerate bacterial contamination, in contrast to synthetic bioscaffolds.[14,15] Research attributes the antibacterial properties of Myriad Matrix to the beneficial biological components of OFM that quench matrix metalloproteinases and inflammation.[14]

Finally, a single-center retrospective case series evaluated the combined use of Myriad Matrix with local flap surgery in nine patients with complex PIs or surgical dehiscence.[16] Successful, uncomplicated healing was achieved in seven participants, and patients remained healed up to 6 months of follow-up.[16] Post-operative dehiscence occurred in two participants; however, both defects progressed to heal via secondary intention without additional surgical intervention.[16] Assessment of healed wounds demonstrated good cosmesis and excellent functionality.[16] The results of this study suggest that Myriad Matrix augmented flap closure may improve outcomes and minimize typical complications observed during standard flap closure surgery.[16] Please see the Appendix for supplementary case studies.

Overall, a growing body of evidence demonstrates that OFM-derived Myriad Matrix can facilitate the formation of functional soft tissue in large, volumetric defects.[14-17] Notably, it provides a valuable solution in regenerating soft tissues for patients experiencing compromised healing or bacterial contamination, local chronic tissue inflammation, or comorbidities.[14] Furthermore, 2-,3-, or 5-Layer grafts of this matrix offer superior thickness compared to most alternatives,[5] and *in vivo* studies demonstrate the rapid cell infiltration and neovascularization of these layered grafts.[14]

+ Myriad Key Benefits

- Can help fill surgical dead space and reduce the risk of seroma or hematoma formation
- Modulates wound proteases to counter inflammation
- Tolerates bacterial contamination
- Can be used as a single application to assist with cost savings

Conclusion

While there are no clear guidelines for the surgical intervention of stage 3 and 4 PIs, a new surgical algorithm has been proposed that blends available tools to help improve outcomes in the surgical management of these advanced wounds. Bioscaffolds offer a valuable augmentation to traditional approaches such as flap procedures. Furthermore, they allow for tissue infill and contour restoration in large, deep, and often irregular wounds. The adjunctive use of bioscaffolds with NPWT can collaboratively improve wound healing processes and improve patient experiences.

Many important considerations should be weighed when selecting a particular bioscaffold product, including protease modulation, tolerance for bacterial contamination, affordability, and the average number of applications. Fortunately, OFM-derived Myriad offers impressive and encouraging results in treating complex soft-tissue defects, such as stage 3 and 4 PIs, demonstrating favorable outcomes in common areas of concern. The future stands to benefit greatly from the continued development of innovative biomaterials and research to establish efficient treatment protocols.

Appendix

+ Case 1

A 51-year-old paraplegic male presented with a recurrence of a left ischial and trochanteric PI **(Figure A1)**. The patient previously had a gluteal flap procedure for the sacral ulcer and a V-Y hamstring flap for the left ischial ulcer **(Figures A2 and A3)**. The patient lost power during a hurricane, and the electric offloading bed and wheelchair failed. This resulted in stage 4 ischial and trochanteric PI with underlying osteomyelitis.

Figure A1. Image of Initial Left Ischial and Trochanteric PI

Figure A2. Images of the Gluteal Flap Procedure

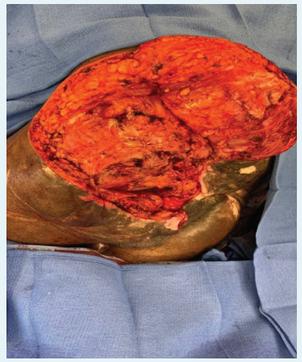
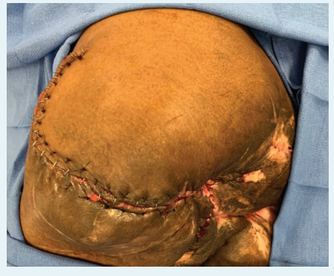
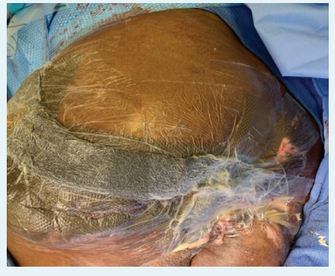
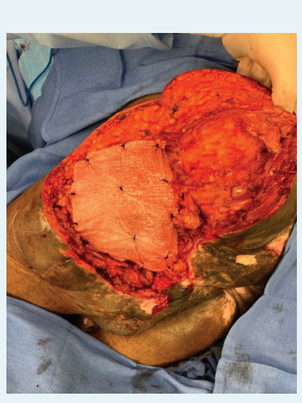


Figure A3. Images of the Gluteal Flap Closure and NPWT Application







Follow-up

Incisional NPWT was discontinued on postoperative day 8. On day 14, the incision was intact. No infection or complication was reported. An offloading bed was used for an additional 2-3 weeks.

+ Case 2

A 58-year-old female paraplegic with pre-diabetes and chronic kidney disease presented with a 6-month-old PI. The approximate wound size was 40 cm x 20 cm with a depth of 3-7 cm (**Figure A4**) and areas of undermining. The defect had undergone a previous flap reconstruction and failed with a subsequent exposed femur.

Figure A4. Preoperative Wound Image

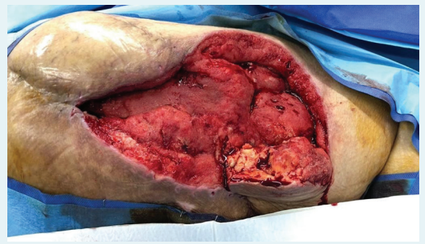


Figure A5. Intraoperative Image of Myriad Placement

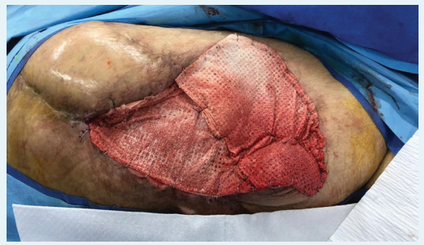


Figure A6. Image of Wound Healing Process

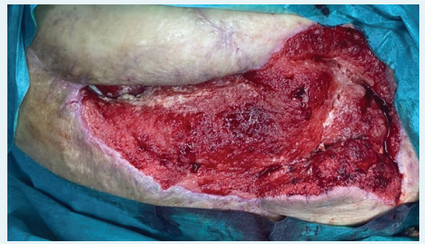


Figure A7. Wound Healing After 3 Weeks

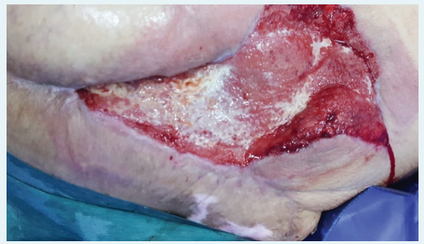


Figure A8. Wound Healing After 4 Weeks

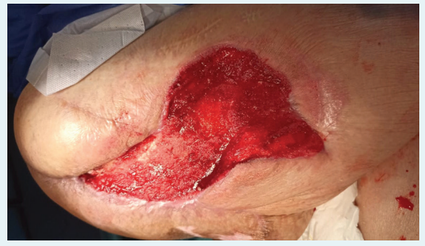


Figure A9. Image of Wound Healing After 6.5 Weeks and 1 Week After STSG

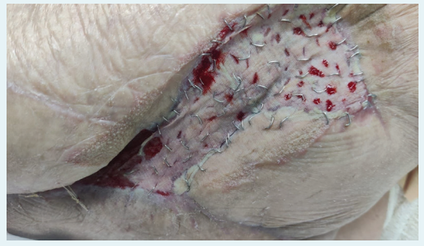
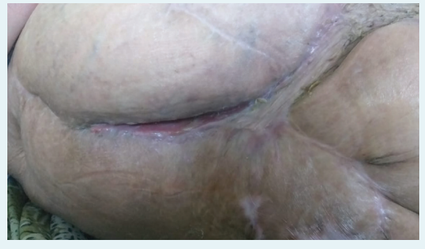


Figure A10. Image of Wound Healing After 9 Weeks and 2.5 Weeks After STSG



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