The Use of Dermal Substitutes for Reconstruction of Extensive Foot and Ankle Wounds

Adi Maisel Lotan MD, Shirly Shohat MD, Gilad Spiegel MD, Elad Sela MD, Rami Binenboim MD, and Yoav Gronovich MD MBA

Department of Plastic and Reconstructive Surgery, Shaare Zedek Medical Center, affiliated with Hadassah–Hebrew University School of Medicine, Jerusalem, Israel

ABSTRACT **Background:** Soft-tissue defects of the lower limb pose a reconstructive challenge. Soft tissue loss with exposed bone, tendon, or cartilage often requires free flap reconstruction. Dermal substitutes are used for treatment of extensive burns to replace damaged skin and may be ideal for lower limb reconstruction in selected cases.

Objectives: To present our experience with reconstruction of lower limb wounds using Integra® Bilayer Wound Matrix (Integra LifeSciences Corp., Plainsboro, NJ, USA) and MatriDerm® (MedSkin Solutions Dr. Suwelack AG, Billerbeck, Germany).

Methods: This single center retrospective study comprised 10 patients who underwent reconstruction of extensive tissue defects of the distal lower limbs with dermal matrices and split-thickness skin grafts.

Results: All patients were successfully reconstructed and resumed normal ambulation. Six patients had complete and four partial graft takes that was treated conservatively until full wound healing. Older patients with medical co-morbidities or history of wound infection were more likely to have partial graft take. One postoperative infection was recorded in the study.

Conclusions: Dermal substitutes are easy to apply and safe, show minimal donor site morbidity, provide good functional and aesthetic outcomes, and should be used for reconstruction of complex lower limb wounds.

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KEY WORDS: dermal substitute, lower limb, reconstruction, trauma

The distal lower extremity is unique in function and form, critical for weight bearing, shoe fitting, and ambulation. Soft tissue defects of the foot and ankle caused by trauma, infection, tumors, or diabetes are relatively common and often present a reconstructive challenge for plastic surgeons due to the lack of locally available flaps for transposition, poor distal vascular circulation, and complex mechanical structures [1].

Several options have been described for the reconstruction of the distal lower limb including skin grafts, cross leg flaps, local fasciocutaneous flaps, and free flaps. Each option has its benefits and drawbacks, and no procedure is considered the gold standard [2].

Innovations in the field of tissue engineering have introduced viable alternatives for provisional skin coverage, particularly novel skin substitutes [2]. Integra® Bilayer Wound Matrix (Integra LifeSciences Corp., Plainsboro, NJ, USA) is a bilayer dermal regenerative template consisting of cross-linked bovine tendon collagen, glycosaminoglycan, and polysiloxane. It was first introduced in the 1970s and has since gained widespread use for the treatment of burns, wounds, and scar contractures [3-5]. MatriDerm® (MedSkin Solutions Dr. Suwelack AG, Billerbeck, Germany) is a three-dimensional elastic stable neo-dermis consisting of bovine collagen type I, III, and V, supplemented by elastin hydrolysate. The product is 1.0 mm thick, allowing for a single-stage procedure in combination with an autologous split thickness skin graft (STSG). Within several weeks of placement, the dermal matrix is replaced by endogenous collagen and the resulting skin is of better quality, thickness, and pliability compared to reconstructions with STSG alone [6,7]. Dermal substitutes are suitable for coverage of tendon, cartilage, and bone and are particularly suitable for lower limb reconstruction [8].

Janis and colleagues [7] used dermal substitutes for the treatment of wounds with exposed bone and tendon, while for wounds greater than 2 cm with exposed bone or tendon, they suggest negative pressure wound therapy (NPWT) followed by reconstruction with a dermal substitute and a STSG.

To date, the management of complex lower limb injuries remains controversial, and the final decision relies mostly on surgeon preferences and patient medical history [7]. While multiple studies have shown the advantages of dermal matrices for the treatment of wounds and burns [9,10],

our study investigates their role in the setting of lower limb traumatic wounds. In this study, we present a series of 10 patients with foot or ankle defects who were successfully reconstructed with dermal substitutes and STSG.

PATIENTS AND METHODS

STUDY DESIGN

We conducted a single center, retrospective study between January 2015 and August 2018. During this period, consecutive patients with foot or ankle injuries with exposed bone or tendons were reconstructed with dermal matrix and skin graft. Either Integra or MatriDerm were used for reconstruction.

SURGICAL TECHNIQUE

Reconstructions had two stages. First, wounds were thoroughly cleaned and debrided in the operating room and dressed with V.A.C.® Negative Pressure Wound Therapy (3M Science. Applied to Life. St. Paul, MN, USA) or antibacterial dressing. Second, we used a combination of MatriDerm and STSG in seven patients (n=7), or Integra in three patients (n=3). MatriDerm was covered with 1:1.5 meshed STSG harvested from the ipsilateral thigh and dressed with Xerform gauze or V.A.C. therapy. Integra matrix was dressed with V.A.C. therapy was continued for 3 weeks, at which time an ultra-thin STSG was placed over the matrix. The first dressing change was performed on postoperative day 5 for MatriDerm and postoperative day 7 for Integra.

ASSESSMENT

Follow-up occurred at 2 weeks, 1 month, 3 months, and 6 months (range 6–33 months) after surgery. We evaluated skin graft take, surgical revisions, ambulation, and shoe-fitting limitations.

RECONSTRUCTIVE SETTINGS

All wounds were initially debrided. Seven patients were treated with V.A.C. therapy before reconstruction. Seven patients had a single stage procedure with MatriDerm and STSG, and three underwent a two-stage procedure with Integra and STSG (mean 21 days, range 16–26 days) later.

PATIENTS

Ten patients underwent foot reconstruction with dermal matrix (seven males and three females). Mean patient age was 43.6 (range 3–72) [Table 1]. Five patients presented with traumatic injuries (open fractures with exposed bone and tendons), three showed surgical wound dehiscence, and one presented with skin necrosis due to an infected third-degree plantar burn. Six wounds (60%) were infected before surgery and treated with antibiotics. Two cases are highlighted.

Patient 2 in detail

A 9-year-old healthy male sustained a motor vehicle accident as a pedestrian. He presented with an open fracture of the distal tibia, exposed talus and first metatarsus, rupture of extensor hallucis longus and tibialis anterior tendons, and extensive soft tissue deficit of the dorsal forefoot. Internal fixation of the tibia fracture, marking of the ruptured tendons, and debridement of necrotic tissue was performed in the operating room [Figure 1A]. V.A.C. therapy. was applied for one month in an ambulatory setting. The wound was reconstructed with MatriDerm and STSG in a single stage procedure [Figure 1B] and treat-

Table 1. Patient demographics

Patient	1	2	3	4	5	6	7	8	9	10
Age, in years	3	9	16	34	62	65	67	72	52	53
Sex	Female	Male	Female	Female	Male	Male	Male	Male	Male	Male
Co-morbidities	–	–	–	–	T2DM, HTN, PVD, Neuropathy, IHD	T2DM, HTN, PVD, IHD, Smoker	NIDDM, ESKD, HTN, IHD, PVD	T2DM, AF, HTN, Hyperlipidemia, Gilbert's syndrome	Drug induced neutropenia	–
Smoking	–	–	–	–	–	Yes	–	Yes	–	–
Body mass index, kg/m²	–	–	23	22	30	35	37	26	18	25

AF = atrial fibrillation, ESKD = end-stage kidney disease, HTN = hypertension, IHD = ischemic heart disease, NIDDM = non–insulin dependent diabetes mellitus, PVD = peripheral vascular disease, T2DM = type 2 diabetes mellitus

ed with V.A.C. therapy for 6 days. The graft take was good with no postoperative complications at 5 months follow-up [Figure 1C].

Patient 5 in detail

A 62-year-old male with a history of essential hypertension, type two diabetes mellitus, ischemic heart disease, peripheral neuropathy, after cerebral vascular accident and peripheral vascular disease was admitted with a 10 cm × 15 cm third degree infected contact burn of the medial and central aspect of the plantar foot. He was hospitalized for burn care, which included intravenous (IV) antibiotics and surgery. Treatment with IV cefazolin 2 grams three times daily, and local wound care with mafenide acetate 5% dressing twice daily were initiated until the infection subsided. He underwent debridement and first stage reconstruction with bi-layered Integra.

After 26 days the second stage of treatment was initiated. Integra was covered with a STSG. The graft took partially with delayed wound healing. Five months after injury the wound healed with application of antibacterial ointment [Figure 2C].

Figure 1. Open fracture of the distal tibia, exposed talus and first metatarsus, rupture of extensor hallucis longus and tibialis anterior tendons, and extensive soft tissue deficit of the dorsal forefoot
VAC = V.A.C.® . Therapy (3M Science. Applied to Life.TM, St. Paul, MN, USA)

[A] VAC therapy was applied for 1 month in an ambulatory setting

[B] The wound was reconstructed with MatriDerm® and STSG in a single stage procedure dressed with VAC

[C] Graft take was good with no postoperative complications at 5-month follow-up

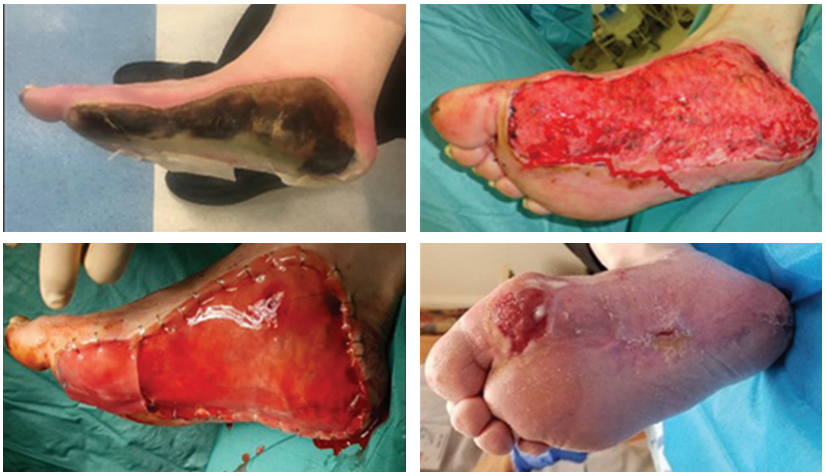
Figure 2. A 62-year-old male with 10 cm × 15 cm third degree infected contact burn of the medial and central aspect of the plantar foot from a hot bottle
VAC = V.A.C. Therapy (3M Science. Applied to Life.TM, St. Paul, MN, USA)

[A] Treatment with IV Cefazolin 2 grams three times daily and local wound care with mafenide acetate 5% dressing twice daily were initiated until infection subsided

[B] First stage: wound debridement before application of Integra dual-layer

[C] Second stage after 26 days of VAC therapy. Vascularized Integra® was covered with a split thickness skin graft

[D] Partial graft take with delayed wound healing 5 months after surgery



RESULTS

We used MatriDerm for vascularized wounds (wounds that had paratenon or periosteum) to improve skin quality. MatriDerm is only 1 mm thick and facilitates STSG application in a single stage procedure. Improving skin quality, elasticity, and playability in this particular anatomic location reduced postoperative scar complications and resulted in a better outcome.

For wounds that were inadequate for skin graft take due to lack of a vascularized wound bed (lacking paratenon or periosteum), we used Integra dual layer. After 3 weeks of V.A.C. therapy, the Integra matrix was vascularized, and we were able to cover it with STSG and complete the reconstruction.

Six patients (60%) had full and four (40%) partial graft take managed with dressing changes. There was one case of post-surgical infection, which was managed with antibiotics. One patient had hallux contracture release using the Z-plasty technique. Mean follow-up was 20.7 months (range 2–60 months) [Table 2].

DISCUSSION

Reconstruction of lower extremity injuries remains a surgical challenge. With advances in reconstructive techniques and increasing proficiency in microsurgery, the traditional reconstructive ladder is often succeeded by the reconstructive elevator, with free flap reconstruction as the first line of treatment [1]. In planning reconstruction, many factors must be considered, including the type of defect, concomitant injuries, medical co-morbidities, patient preferences, and surgeon skills [11].

Dermal substitutes have been widely used for coverage of full-thickness skin defects in simple surgical procedures on well-vascularized wound beds. The dermal matrix has many advantages compared to skin-graft-only procedures including better skin graft survival, smoother contour of the healed skin, less scar contraction, improved scar elasticity, and higher patient satisfaction [12]. MatriDerm reduces wound contracture and promotes dermal restoration by preventing myofibroblasts in the dermis from differentiating into contractile myofibroblasts in the early stage of wound treatment. Elastin within the MatriDerm regulates collagen contraction, interrupts the differentiation of myofibroblasts, and reduces the formation of scars [13].

When compared with microsurgical reconstructions, dermal matrices necessitate shorter operating and hospitalization times, are technically easy to perform, lack donor site morbidity, and often produce better cosmetic and

Table 2. Injury type, treatment, reconstruction, and outcome

Patient	1	2	3	4	5	6	7	8	9	10
Cause	Trauma	Trauma	Trauma	Trauma	Burn	Dehiscence	Dehiscence	Trauma	Infection	Dehiscence
Fracture	Yes	Yes	Yes	Yes	–	Yes	–	Yes	–	–
Exposed tendon	Yes	Yes	Yes	Yes	–	–	Yes	Yes	Yes	Yes
Exposed bone	Yes	Yes	Yes	Yes	–	–	Yes	Yes	Yes	–
Infection	–	–	–	–	Yes	Yes	Yes	Yes	Yes	Yes
Wound size (cm)	7 × 5	15 × 7	25 × 15	–	30 × 15 × 5	–	2 × 7 × 5	7 × 5	18 × 10	2 × 5
Dermal matrix	Integra®	Matriderm®	Matriderm®	Matriderm®	Integra®	Matriderm®	Matriderm®	Matriderm®	Integra®	Matriderm®
Post-surgical dressing	VAC	VAC	Xeroform	VAC	VAC	Xeroform	VAC	VAC	VAC	Xeroform
VAC (days)	16	6	–	5	26	–	5	5	21	–
2nd stage (days)	16	–	–	–	26	–	–	–	21	–
Graft take	Full	Full	Full	Full	Partial	Partial	Partial	Full	Full	Partial
Post-surgical complications	–	–	–	–	–	–	Infection	–	–	–
Revision surgery	Contracture release	–	–	–	–	–	–	–	–	–
Follow-up (months)	60	41	51	2	5	2	3	3	5	3

VAC = V.A.C.® Therapy (3M Science. Applied to Life.™, St. Paul, MN, USA)

functional outcomes. The use of a dermal matrix further improves donor site morbidity by necessitating harvest of a thinner graft (0.005–0.006-inch depth rather than 0.010–0.015 inch) [14].

Our results are promising and confirm previous findings described by other groups [8,15]. We used MatriDerm for reconstruction of defects that had an adequate vascular wound bed for graft take, but due to their anatomic structure and function needed better skin quality and texture to avoid functional problems (i.e., ambulation, deformity, resistance to sheer). Integra was used for reconstruction of wounds with exposed bones or tendons and a poor vascular wound bed that would not facilitate skin graft take in a single operation. In one case, Integra was used for plantar sole reconstruction to sustain sheer forces during ambulation.

Our data showed that dermal substitutes are a viable option for reconstruction of foot and ankle soft tissue defects with exposed tendon or bone and open fractures. Age progression, medical co-morbidities, and infected wounds are less favorable conditions for dermal grafts; however, such patients are not good candidates for free flaps. We recorded one postoperative infection that was treated conservatively. Four patients with partial graft take were treated with local antimicrobial dressings until the wounds healed. Other studies have also shown promising clinical results with reduced wound contracture, reduced scaring, low rate of complication, and high patient satisfaction [16,17].

A potential drawback of collagen matrices is their high cost. Inhoff et al. [18] compared the overall cost of reconstruction of complex scalp wounds using allogenic fascia lata, artificial skin substitutes, or NPWT. The authors concluded that due to their short treatment period, fewer dressing changes and better patient comfort, dermal regeneration templates are financially feasible despite their high cost. Schiavon and colleagues [19] compared treatment of scalp wounds with Integra vs. free flaps and found no significant difference between the two groups in hospitalization length and overall costs. However, for patients with defects larger than 100 cm^2 for whom major surgery is needed, the treatment with Integra seemed to be less expensive than treatment with free or pedicled flaps [19].

Some limitations of our study include its retrospective nature and small patient cohort. In addition, patient satisfaction was not recorded using validated modules. A prospective, multicenter, randomized trial with a larger patient cohort is necessary.

CONCLUSIONS

Dermal substitutes should be considered for the reconstruction of complex lower limb defects as they are easy to apply, safe, minimize donor site morbidity, provide good functional and aesthetic outcomes, and may reduce surgical costs.

Correspondence

Dr. A. Maisel Lotan
Dept. of Plastic and Reconstructive Surgery, Shaare Zedek Medical Center, Jerusalem 9103102, Israel
Phone: (972-2) 666-6375
Email: lotanadi@szmc.org.il

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Capsule

Two mRNA vaccine trials tackle HIV

Intense research efforts are focused on the development of an effective HIV vaccine for humans. **Willis** and colleagues tested a messenger RNA (mRNA) vaccine strategy to help the immune system create rare antibodies capable of blocking many human immunodeficiency virus (HIV) strains. In two clinical trials, one in the US and one in Rwanda and South Africa, an initial vaccine activated the appropriate precursor immune cells in nearly all participants. In the US trial, a second, slightly different booster shot guided early immune cell maturation, a step toward antibodies with the potential to protect against HIV. Some participants experienced skin reactions, underscoring the need for further study and mitigation efforts. Overall, these findings provide clinical proof of concept for using mRNA technology to initiate an early immune response.

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Eitan Israeli

Capsule

A modular mRNA vaccine platform encoding antigen-presenting capsid virus-like particles enhances the immunogenicity of the malaria antigen Pfs25

Fougeroux et al. introduced a modular nucleotide vaccine platform combining the advantages of genetic and capsid virus-like-particle-based vaccines. This platform allows for the display of various antigens on different capsid virus-like particles, improving the magnitude, quality and longevity of the vaccine-induced immune responses. The authors applied this technology to enhance the immunogenicity of the Pfs25 antigen. Immunization with lipid-nanoparticle-formulated mRNA encoding Pfs25 capsid virus-like particles resulted in higher and potentially more durable anti-Pfs25 antibody responses, with enhanced functional activity, compared with an mRNA vaccine encoding soluble Pfs25. By improving both humoral and cellular immune responses, this approach may reduce the dose and number of administrations required for effective protection. As a result, it can improve the feasibility of both DNA- and mRNA-based vaccines targeting pandemic and endemic infectious diseases.

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Eitan Israeli

Capsule

Devilish jingchuviruses

Tasmanian devils are fierce, smelly, noisy, and highly endangered carnivorous marsupials from the eponymous island. One of their main threats is an infectious facial tumor disease, which interferes with feeding and can lead to starvation. It is considered the only known kind of infectious cancer, due to common genetics of this animal. **Mélade** et al. reported the isolation of a previously identified chu-like virus in a Tasmanian devil tumor cell line. Phylogenetic analysis indicates that this virus is a member of a hitherto unknown and divergent virus family. More intriguingly, the virus replicated in the two lineages of Tasmanian devil tumor cells but not in normal tissues or mosquito cells (a possible vector). Because canine distemper virus also replicates in these tumor cells, this new virus is not necessarily to blame for the Tasmanian devil's current plight.

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