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ORIGINAL ARTICLE
Reconstructive

Dermal Regeneration Template in the Management and Reconstruction of Burn Injuries and Complex Wounds: A Review

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Background: Dermal scaffolds have created a paradigm shift for burn and wound management by providing improved healing and less scarring, while improving cosmesis and functionality. Dermal regeneration template (DRT) is a bilayer membrane for dermal regeneration developed by Yannas and Burke in the 1980s. The aim of this review is to summarize clinical evidence for dermal scaffolds focusing on DRT for the management and reconstruction of burn injuries and complex wounds.

Methods: A comprehensive search of PubMed was performed from the start of indexing through November 2022. Articles reporting on DRT use in patients with burns, limb salvage, and wound reconstruction were included with focus on high-level clinical evidence.

Results: DRT has become an established alternative option for the treatment of full-thickness and deep partial-thickness burns, with improved outcomes in areas where cosmesis and functionality are important. In the management of diabetic foot ulcers, use of DRT is associated with high rates of complete wound healing with a low risk of adverse outcomes. DRT has been successfully used in traumatic and surgical wounds, showing particular benefit in deep wounds and in the reconstruction of numerous anatomical sites.

Conclusions: Considerable clinical experience has accrued with the use of DRT beyond its original application for thermal injury. A growing body of evidence from clinical studies reports the successful use of DRT to improve clinical outcomes and quality of life across clinical indications at a number of anatomical sites.
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INTRODUCTION

Open skin wounds in mammals heal by scarring and wound contraction.[1] Scarring produces tissue that is stiff with an irregular contour and color. Contraction results in a ratcheting effect of the extracellular matrix within tissues that limits mobility around joints. For severe burn patients, advances in the 1960s and 1970s improved survival rates, but left patients with heavy scars and contractures. Allografts from other donors worked temporarily but would induce an intense rejection response within 2 weeks.[2] John F. Burke, a pioneer in early excision and grafting of burn injuries, realized that the scarring and contraction pathophysiology were related to the dermis. Dr. Burke collaborated with Yannas, at Massachusetts Institute of Technology, to develop a polymeric dermal regeneration template (DRT; Integra LifeSciences Corporation), designed to recreate a histologic and functional dermis following repopulation of the scaffold with cells,[3,4] which is subsequently degraded.[5]

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DRT is a bioengineered bilayer system consisting of two components: (1) a dermal analog of cross-linked bovine type I collagen and chondroitin-6-sulfate that permits the migration of fibroblasts, macrophages, and lymphocytes, and capillary ingrowth; and (2) an epidermal analog of a thin silicone elastomer.[4,5] After application of DRT, the neodermis typically matures and revascularizes in approximately 2–3 weeks, after which the silicone layer is removed, and an epidermal autograft, a split-thickness skin graft, is applied to close the wound.[3,4] DRT has been used in combination with negative-pressure wound therapy (NPWT).[6,7]

Originally developed for the postexcisional treatment of life-threatening (full-thickness or deep partial-thickness) thermal injuries in which autograft is limited,[8] DRT use has expanded over the years to reconstructive surgery.[9,10] The clinical outcomes and safety of DRT in acute and reconstructed burns was recently reviewed and the results demonstrated improved cosmesis and functional outcomes in the majority of patients across a wide range of anatomic sites (Table 1).[11] This review summarizes the clinical evidence of the most common uses of DRT.

METHODS

A literature search was conducted in PubMed to identify studies evaluating the use of DRT in burns, limb salvage, wound reconstruction, and trauma from the start of indexing through November 2022. Search terms of "dermal template" or "dermal regeneration template" or "dermal regeneration" or "bovine collagen matrix" or "bilayer wound matrix" were used. Identified articles were reviewed and selected based on quality of evidence. The focus was on high-level clinical evidence [ie, randomized controlled trials (RCTs)], although supporting data from lower-level studies, such as observational, retrospective, or real-world experience, are also included.

Table 1. Anatomic Sites of Use of DRT for Acute Burns and Burn Reconstruction (Frequency Based on a Review of 72 Studies and 561 Treated Sites)[11]

Anatomical Location	Acute Burn, %	Reconstruction, %
Abdomen	5.1	9.2
Axilla	0.5	13.6
Back	2.3	0.9
Breast	NR	5.8
Chest	11.6	9
Face/head	23.7	2
Groin	1.9	1.4
Hand/wrist	20.5	14.7
Iliac crest	0.5	NR
Lower extremities	20.5	13.9
Mouth/lip/oral	0.5	0.9
Neck	1.4	17.9
Upper extremities	11.6	10.7

NR, not reported.

Takeaways

Question: Have dermal scaffolds changed burn and wound management since their development 40 years ago?

Findings: Dermal regeneration templates have become an established alternative option for the management of full- and deep partial-thickness burns, diabetic foot ulcers, and traumatic and surgical wounds with improved outcomes in areas where cosmesis and functionality are important.

Meaning: A growing body of evidence from clinical studies demonstrates the successful use of dermal regeneration templates to improve clinical outcomes and quality of life across indications at a number of anatomical sites.

RESULTS

Burn Injuries

DRT has become a well-established adjunct to autologous split-thickness skin graft for the treatment of full- and deep partial-thickness burn injuries based on the results of RCTs and large nonrandomized studies. An early multicenter RCT compared DRT to conventional procedures (ie meshed autograft, allograft, xenograft, synthetic dressing) in 106 adults and children hospitalized with extensive flame or scald burns considered to be life-threatening.[12] The median take rate of the matrix was significantly lower in the DRT group versus all controls (80% versus 95%); however, the DRT take rate was similar to that seen for all nonautograft controls. Donor thickness was significantly lower (0.006 versus 0.013 inch) and donor sites healed significantly faster (10 versus 14 days;) in the DRT group versus controls.[12] Further, on long-term evaluation, patients and physicians preferred DRT over control graft.[12] Nonrandomized trials have shown DRT to be associated with a high take rate and with restoration of normal function in acute burns.[11,13,14]

There are limited data comparing DRT with other dermal matrices, and many of the studies are underpowered. A retrospective study at a regional burn center comparing DRT with a single-layer collagen-elastin dermal matrix (CEDM; MedSkin Solutions Dr. Suwelack) found a similar take rate for both devices.[15] Patients treated with DRT had significantly larger burn wounds compared with those who received CEDM. CEDM was associated with shorter healing times and length of stay, but this may be related to the larger burn size of the DRT group. The authors concluded that DRT is useful in large burns with limited donor sites.

An RCT in 24 patients with restricted mobility due to deep partial- or full-thickness burns compared DRT with CEDM.[16] Patients treated with DRT had significantly greater improvement in mobility, retraction rate (ie, secondary contraction), and skin quality. The degree of mobility improved more significantly in the DRT group as measured by movement improvement rates.[16] Retraction was significantly smaller in the DRT group from 3 months postsurgery through 12 months. Finally, DRT showed significant improvements from baseline in skin quality, as

measured by the Vancouver Scar Scale, from presurgery to 1-, 3-, 6-, and 12-months postsurgery, with a significant between-group difference at 12 months.[16]

Retrospective and observational studies have shown improved outcomes with the use of DRT in areas where cosmesis and functionality are important. An analysis of 13 severely burned patients undergoing reconstructive surgery of their upper extremities found that use of DRT was associated with increased range of motion (ROM) and improved skin quality compared with preoperative assessments.[17] ROM improvements were seen in elbow (10–50 degrees), wrist (20–45 degrees), axilla (40–90 degrees), and forearm (30 degrees) extension. A significant improvement in postoperative Vancouver Scar Scale from presurgery was also observed. In a series of 20 burn patients undergoing reconstructive surgery, DRT was associated with a 72% improvement from baseline in ROM,[18] and a retrospective analysis of 89 consecutive contracture release procedures found DRT was associated with significant improvement or maximal range ROM, by physicians, at 76% of release sites.[19] Similarly, among 11 patients with deep hand burns, treatment with DRT resulted in improvements in cosmetic appearance and functionality, with statistically significant improvements from baseline observed in thumb opposition score, fingertip-to-palm distance, and prehensile score from pretreatment.[13]

An RCT, conducted in pediatric patients, compared DRT with standard autograft/allograft technique in 20 children with severe burns of 50% or more TBSA or full-thickness burns of 40% or more TBSA.[20] DRT was associated with significantly better short-term (eg, decreased resting energy expenditure and increased levels of serum constitutive proteins) and long-term outcomes (eg, increased bone mineral density, and improved scarring). A retrospective cross-sectional study of 44 pediatric burn patients found that the use of DRT in combination with NPWT improved take rate (>99% versus 85%) versus DRT alone.[21]

DRT seems to be associated with a low rate of clinically meaningful complications. Vana et al in an RCT reported no intra- or postoperative complications (eg, infection, hematomas, blisters, seromas).[16] In a systematic review of DRT-based reconstruction, the incidence of infectious complications in burn reconstructions was 18.1%, with the vast majority being superficial.[22] Having a clean wound before applying DRT and adherence to strict infection control measures are required to avoid wound contamination during and after surgery.[22]

The data show that DRT provides a valuable treatment option with a low rate of infectious complications in adult and pediatric patients with extensive burns who have inadequate donor skin available for immediate autografting. Compared with other dermal matrices, DRT is associated with improved cosmesis and functionality, less retraction, and increased ROM. It is particularly well-suited for reconstruction in large burn sites.

Limb Salvage

Patients with exposed bone, joints, and tendons are at risk for amputation. Treatment options for such patients include partial/full-thickness skin grafts, local rotation flaps, pedicle advancement flaps, tissue expansion, and free vascular pedicle flaps.[23] Data show that DRT has the potential to decrease amputations through a reduced risk of infection due to early dermal coverage of exposed bone, tendons, and joints.[23] The majority of studies evaluating limb salvage with DRT are in patients with diabetic foot ulcers. In a multicenter RCT, DRT was compared with standard of care in 307 adults with full-thickness diabetic foot ulcers. (**See table, Supplemental Digital Content 1**, which displays the summary of RCTs evaluating DRT. **http://links.lww.com/PRSGO/D107**).[24] DRT was associated with increased rate of complete ulcer closure (51% versus 32%), reduced time to complete closure (43 days versus 78 days), increased rate of reduction in wound size (7.2% versus 4.8% per week), and improved quality of life versus standard of care.[24] In addition, DRT was associated with fewer moderate (31.8% versus 42.5%) and severe (15.6% versus 26.8%) adverse events compared with the control group.[24] A prospective, single-center database study in 85 patients with DFU, most of whom were at high risk of amputation (25%–50% predicted risk), reported that DRT was associated with good wound healing and limb salvage outcomes.[25] The rate of successful wound granulation was 66.7%, the mean time to complete wound healing was 198 days, and major amputation was required in 11.2% of wounds.[25] Another prospective study of 11 patients with DFU reported complete closure seen as early as 4 weeks (mean time 7.4 weeks).[26] In a retrospective study of 30 patients with DFU who underwent surgical debridement and used DRT to cover exposed tendon and bone, complete wound healing occurred in 26 patients (87%) with an average healing time of 74 days.[27] Four patients required a more proximal amputation, but no patient underwent major amputation. Similarly, among 26 diabetic patients who achieved complete wound healing of no-option critical limb ischemia, DRT (n = 13) was associated with faster healing time (84 versus 140 days) and a lack of major amputations (0 versus 15%) compared with a control group (n = 13) not receiving a dermal matrix.[28]

For patients with DFU, DRT is associated with improved wound closure, a low rate of amputation, and improved quality of life. There are limited data on limb salvage in other patient groups. In a prospective registry of 44 patients with wounds involving complex soft tissue loss who received multiple layers of DRT, DRT was associated with a statistically significant lower rate of amputation (5.7% versus 31.5%) compared with matched controls.[23]

Reconstruction after Trauma or Oncologic Excision

Options for reconstruction surgery include skin grafting, locoregional flaps, staged tissue expansion, and vascularized tissue transfer.[29,30] DRT has been used in a variety of reconstruction applications (eg, oncology, trauma) and anatomical sites (eg, extremities, scalp, facial). In a retrospective study of 302 patients who underwent reconstruction following skin cancer excision at any site, 88.9% of patients had successful DRT take (defined as attachment within 21 days after surgery without infection, hematoma, or dermal matrix dehydration) with success observed at

all tumor sites (ie, upper limbs, trunk, face, scalp, lower limbs).[31] Complication rates were generally low, with infection being the most common (9.9%).

Extremities

In an early RCT, fibrin glue-anchored DRT plus postoperative NPWT was compared with conventional DRT therapy for reconstruction of acute and chronic wounds of the extremities in 12 patients, six of which were traumatic.[32] DRT in combination with fibrin glue and NPWT was associated with a higher take rate (98% versus 78%) and shorter time between coverage and skin transplantation (10 versus 24 days) compared with conventional DRT. There are limited data comparing DRT with other dermal matrices in trauma surgery, and these studies are small and underpowered. An RCT compared long-term outcomes with DRT versus another bilayer matrix composed of bovine collagen type I, bovine bilayer matrix (bBLM, Symatese), in 30 patients with posttraumatic limb wounds without tendon or bone exposure.[33] There were no statistically significant differences in healing time, pain-related visual analog scale scores, self-estimation at complete healing, short-term scar scores, and re-epithelialization between groups. The bBLM was associated with better scar scores at 3-year follow-up. In a prospective observational study over 1 year, DRT was compared with a bilayer matrix derived from porcine tendon, porcine bilayer matrix (pBLM, TheraGenesis), in 71 patients with partial- and full-thickness posttraumatic wounds and postiatrogenic cutaneous defects, primarily of the extremities.[34] Both scaffolds were associated with renewed collagen and revascularization. The pBLM was associated with improved Vancouver Scar Scale score and an increase in contraction, whereas DRT was associated with a greater reduction in wound surface area and shorter healing time for wounds more than 1.5 cm deep. The authors concluded that both dermal matrices were effective, but preferred pBLM for superficial wounds and DRT for deep wounds.

A retrospective analysis was conducted in 501 patients with complex lower extremity reconstruction receiving DRT, local tissue rearrangement, or free flap reconstruction.[35] The 180-day graft success rate was 69.2%, 91.3%, and 93.3% in the three groups, respectively. A case control study from multiple hospitals evaluated reconstruction of lower extremity in 147 patients with 191 wounds managed using DRT.[36] Overall, 70% of wounds healed successfully with failure rates for DRT at 60, 120, and 180 days of 19%, 25%, and 30%, respectively. Comparison of successful versus unsuccessful procedures found that successful reconstruction was associated with improved outcomes (decreased complications, amputations) and decreased costs. The use of DRT for tendon coverage was prospectively assessed in 42 patients with exposed tendons due to trauma, cancer excision, or chronic wounds.[37] DRT was associated with a take rate of 93%, and the average ROM was 91% that of the contralateral side. In a retrospective review of 10 patients (nine of whose wounds extended to the bone and/or tendon) with reconstruction of degloving injury, DRT followed by split-thickness autografts was associated with complete take of the matrix in nine patients with excellent cosmesis and functional outcomes.[38] Other small studies have reported the successful use of DRT and recovery of function after reconstruction of traumatic hand/digit injury[39–41] and foot/ankle injury.[42]

Scalp

Numerous retrospective studies have evaluated the use of DRT for scalp wound reconstruction, primarily after tumor excision.[43–49] Among 58 patients with 68 full-thickness scalp defects and exposed bone, no local recurrences of the primary tumor occurred after long-term follow-up. In addition, the postsurgical complication rate was low (13%), primarily consisting of template necrosis and infection with no reports of bleeding, hematoma, scar strands, or keloids.[43] In another study of 102 patients who underwent scalp tumor resection, the average skin graft take rate was 94.5% in full-thickness wounds and 99.5% in partial-thickness wounds.[47] Among those who received NPWT as supportive therapy (40.2% of cases), healing rates were higher after adjustment for the use of preoperative radiotherapy and other clinical factors. In a comparison of DRT versus flap surgery in 35 patients who had scalp defects with bone exposure, both treatments led to good healing.[49] A cost analysis reported that DRT was associated with lower costs for lesions more than 100 cm^2 compared with flap surgery.

A few small studies have described the use of DRT in reconstruction of the orbital socket.[50–52] Overall, DRT was associated with rapid epithelialization and a low incidence of complications. In a report involving 10 patients, the mean granulation time of the cavity was 3.3 weeks.[50]

Radial Forearm Donor Sites

Several case series have described the successful use of DRT in radial forearm donor sites with rapid healing (4–6 weeks), excellent cosmetic outcomes, minimal scar contracture, and few complications.[53–55] Additional, larger-scale studies will be needed to evaluate the utility of DRT in this procedure.

Overall Conclusions for Reconstruction

These studies show that DRT has been associated with successful reconstruction outcomes at multiple anatomical sites after trauma, in patients with skin cancer, and in patients needing scalp wound reconstruction after tumor excision. A consensus report from a multidisciplinary advisory board of dermatologists and plastic surgeons noted that DRT is particularly useful for older patients with comorbidities and in the reconstruction of large and complex scalp wounds.[30]

DISCUSSION

Over the years, dermal scaffolds have been sourced from decellularized tissues, processed biological materials (semisynthetic), and totally synthetic materials. Decellularized scaffolds have the advantage of having many natural bio-molecules but have the disadvantages of needing to be tested for communicable diseases and with a higher probability of product variation. Semi-synthetic scaffolds can be manufactured preserving many biological

functions with intermediate production costs. Synthetic scaffolds can be produced with high reproducibility but may not have the activity of biologically-derived materials. Among those, a decellularized dermal component from fresh human allograft, without epidermis and dermal cells with no or little antigenicity (LifeCell Corp.), has been successfully used in burns in small cases series.[56–58] A synthetic polyurethane dermal matrix composed of wound-facing biodegradable foam bonded to a non-biodegradable transparent sealing membrane (PolyNovo, Inc.) has been successfully used to reconstruct complex wounds with a range of etiologies, including deep dermal and full-thickness burns, necrotizing fasciitis and free flap donor site.[59–62] Current literature reviews highlighted the fact that the clinical utility of dermal matrices is evolving across a broad range of applications, and more research is needed to determine which matrix has the best outcome for each clinical scenario.[63,64]

DRT has led to considerable improvements in the ability to achieve successful and durable wound closure and reconstruction after severe burn injuries and complex wounds (**See table, Supplemental Digital Content 2,** which displays summary of findings associated with DRT by surgery type. **http://links.lww.com/PRSGO/D108**).[65] Some of the advantages of DRT in reconstruction include (1) readily available "off-the-shelf" dermal regeneration method; (2) absence of native tissue loss if an initial application fails or needs to be revised; (3) simplicity and reliability of the technique; (4) ability to contour restoration; and (5) avoidance of donor site morbidity and scars.[5,42]

LIMITATIONS

Our study has several limitations. The literature on DRT has few RCTs and large case series. We conducted a retrospective search with a set of keywords, and included high-level clinical evidence, (ie, RCTs) and supporting data from lower-level studies rather than perform a formal systematic review, with a PRISMA flow chart and defined inclusion and exclusion criteria, with the caveat of selecting qualitative studies. As a result, the article is inherently biased for reports of positive outcomes for DRT with a relatively brief description of complications and other side effects associated with the technology. The retrospective nature of our search may have led us to omit relevant clinical data. The use of DRT is not without limitations. Among those are (1) the necessity of two operations for large areas, (2) the time to closure, (3) the cost of the product, and (4) the risks of infection under the silicone layer. This latter highlights the importance of meticulous preparation and of having a clean wound before applying DRT, as DRT is more susceptible to breakdown than an autologous skin graft if there is contamination or infection.[66] Post-debridement cultures can be very useful in reducing this risk.

FUTURE DIRECTIONS

Stem cell therapy offers new opportunities for the treatment of burns and complex wounds.[67,68] Initial investigations over 40 years ago showed a partial regeneration of skin when cells were added.[4] In full-thickness wounds, it is necessary to have an appropriate dermal replacement to avoid scarring and contraction of wounds. Dermal matrices and skin substitutes can either induce scar or a regenerative response depending on how they are applied.[5,68] Studies have reported loss of sensitivity, impaired pigmentation, and absence of adnexal structures in patients treated with DRT and dermal matrices.[18,68–71] Hence, combining the use of a dermal matrix with stem cells for the treatment of burns and wounds may lead to improved healing and tissue regeneration, and the restoration of skin appendages and nerves.[67,72] Pre-clinical studies, clinical studies, and clinical trials have reported and validated the use of various types of stem cells incorporated into DRT for wound healing.[73,74] Additional studies will aim particularly at determining the source, dose, timing and method of stem cells to be used, and the efficacy and safety of such procedures.

CONCLUSIONS

Clinical experience and evidence for the use of DRT in a variety of indications has accumulated since its original application for thermal injuries. Long-term results of a range of clinical studies and data from real-world use have shown that DRT is associated with improved functional, quality of life, and cosmetic outcomes without high complication rates across indications, such as burn, limb salvage, wound reconstruction after trauma or oncologic excision. The field of dermal matrices is evolving, and more research is needed to determine which matrix has the best outcome for each clinical scenario. Future studies will aim at generating clinical studies with high levels of evidence. Future directions will involve stem cell-based therapies in combination with dermal matrices.

Addendum

The purpose of this article is to review the published literature on DRT. Clinicians should consider the product labeling in their respective jurisdictions before using DRT products. For example, only some DRT products are indicated for use with NPWT, layering of DRT is not in accordance with the manufacturer's indications for use, and anchoring fibrin glue to DRT products is not in accordance with the manufacturer's indications for use.

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DISCLOSURES

SG is former consultant for Integra LifeSciences Corporation. NM is former consultant for Integra LifeSciences Corporation (≥5 years ago). JPF received research funding from the National Institutes of Health, and is consultant for 3M, AbbVie, Becton Dickinson, Baxter, Integra LifeSciences Corporation, and Gore. CEA is former consultant for Integra LifeSciences Corporation (≥5 years ago). MGJ received research funding and consulting

fees from Integra LifeSciences Corporation. PT is an employee of Integra LifeSciences Corporation and owns common stock of Integra LifeSciences Holdings Corporation, its parent corporation. DPO received research funding and consulting fees from Integra LifeSciences Corporation.

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REFERENCES

1. Yannas IV, Tzeranis DS. Mammals fail to regenerate organs when wound contraction drives scar formation. *NPJ Regen Med.* 2021;6:39.
2. Alrubaiy L, Al-Rubaiy KK. Skin substitutes: a brief review of types and clinical applications. *Oman Med J.* 2009;24:4–6.
3. Burke JF, Yannas IV, Quinby WC, Jr, et al. Successful use of a physiologically acceptable artificial skin in the treatment of extensive burn injury. *Ann Surg.* 1981;194:413–428.
4. Yannas IV, Burke JF, Orgill DP, et al. Wound tissue can utilize a polymeric template to synthesize a functional extension of skin. *Science.* 1982;215:174–176.
5. Taupin P, Gandhi A, Saini S. Integra dermal regeneration template: from design to clinical use. *Cureus.* 2023;15:e38608.
6. Gonzalez GA, Castagno C, Carter J, et al. Negative pressure wound therapy on complex extremity wounds requiring coverage with a meshed bilayer wound matrix: a retrospective analysis. *J Wound Care.* 2022;31(Suppl 9):S8–S15.
7. Zhang L, Weng T, Wu P, et al. The combined use of negative-pressure wound therapy and dermal substitutes for tissue repair and regeneration. *Biomed Res Int.* 2020;2020:8824737.
8. Integra dermal regeneration template [instructions for use]. Princeton, N.J.: Integra LifeSciences Corporation; 2020.
9. Henning JA, Liette MD, Laklouk M, et al. The role of dermal regenerative templates in complex lower extremity wounds. *Clin Podiatr Med Surg.* 2020;37:803–820.
10. Prezzavento GE, Calvi RNJ, Rodriguez JA, et al. Integra Dermal Regeneration Template in reconstructive surgery for cutaneous tumours: a two-year retrospective review. *J Wound Care.* 2022;31:612–619.
11. Hicks KE, Huynh MN, Jeschke M, et al. Dermal regenerative matrix use in burn patients: a systematic review. *J Plast Reconstr Aesthet Surg.* 2019;72:1741–1751.
12. Heimbach D, Luterman A, Burke J, et al. Artificial dermis for major burns. A multi-center randomized clinical trial. *Ann Surg.* 1988;208:313–320.
13. Dantzer E, Queruel P, Salinier L, et al. Dermal regeneration template for deep hand burns: clinical utility for both early grafting and reconstructive surgery. *Br J Plast Surg.* 2003;56:764–774.
14. Lohana P, Hassan S, Watson SB. Integra in burns reconstruction: our experience and report of an unusual immunological reaction. *Ann Burns Fire Disasters.* 2014;27:17–21.
15. Phillips GSA, Nizamoglu M, Wakure A, et al. The use of dermal regeneration templates for primary burns surgery in a UK regional burns centre. *Ann Burns Fire Disasters.* 2020;33:245–252.
16. Vana LPM, Battlehner CN, Ferreira MA, et al. Comparative long-term study between two dermal regeneration templates for the reconstruction of burn scar contractures in humans: clinical and histological results. *Burns.* 2020;46:596–608.
17. Chou TD, Chen SL, Lee TW, et al. Reconstruction of burn scar of the upper extremities with artificial skin. *Plast Reconstr Surg.* 2001;108:378–84: discussion 385.
18. Moiemen NS, Staiano JJ, Ojeh NO, et al. Reconstructive surgery with a dermal regeneration template: clinical and histologic study. *Plast Reconstr Surg.* 2001;108:93–103.
19. Frame JD, Still J, Lakhel-LeCoadou A, et al. Use of dermal regeneration template in contracture release procedures: a multicenter evaluation. *Plast Reconstr Surg.* 2004;113:1330–1338.
20. Branski LK, Herndon DN, Pereira C, et al. Longitudinal assessment of Integra in primary burn management: a randomized pediatric clinical trial. *Crit Care Med.* 2007;35:2615–2623.
21. Pereima MJL, Feijo R, Oenning da Gama F, et al. Treatment of burned children using dermal regeneration template with or without negative pressure. *Burns.* 2019;45:1075–1080.
22. Gonzalez SR, Wolter KG, Yuen JC. Infectious complications associated with the use of Integra: a systematic review of the literature. *Plast Reconstr Surg Glob Open.* 2020;8:e2869.
23. Jeng JC, Fidler PE, Sokolich JC, et al. Seven years' experience with Integra as a reconstructive tool. *J Burn Care Res.* 2007;28:120–126.
24. Driver VR, Lavery LA, Reyzelman AM, et al. A clinical trial of Integra template for diabetic foot ulcer treatment. *Wound Repair Regen.* 2015;23:891–900.
25. Hicks CW, Zhang GQ, Canner JK, et al. Outcomes and predictors of wound healing among patients with complex diabetic foot wounds treated with a dermal regeneration template (Integra). *Plast Reconstr Surg.* 2020;146:893–902.
26. Yao M, Attalla K, Ren Y, et al. Ease of use, safety, and efficacy of integra bilayer wound matrix in the treatment of diabetic foot ulcers in an outpatient clinical setting: a prospective pilot study. *J Am Podiatr Med Assoc.* 2013;103:274–280.
27. Clerici G, Caminiti M, Curci V, et al. The use of a dermal substitute to preserve maximal foot length in diabetic foot wounds with tendon and bone exposure following urgent surgical debridement for acute infection. *Int Wound J.* 2010;7:176–183.
28. Dalla Paola L, Cimaglia P, Carone A, et al. Use of integra dermal regeneration template for limb salvage in diabetic patients with no-option critical limb ischemia. *Int J Low Extrem Wounds.* 2021;20:128–134.
29. Johnson MB, Wong AK. Integra-based reconstruction of large scalp wounds: a case report and systematic review of the literature. *Plast Reconstr Surg Glob Open.* 2016;4:e1074.
30. Magnoni C, De Santis G, Fraccalvieri M, et al. Integra in scalp reconstruction after tumor excision: recommendations from a multidisciplinary advisory board. *J Craniofac Surg.* 2019;30:2416–2420.
31. Ferrari B, Reggiani C, Francomano M, et al. Clinical factors influencing the outcomes of an acellular dermal matrix for skin cancer treatment: a retrospective study. *Adv Skin Wound Care.* 2020;33:367–374.
32. Jeschke MG, Rose C, Angele P, et al. Development of new reconstructive techniques: use of Integra in combination with fibrin glue and negative-pressure therapy for reconstruction of acute and chronic wounds. *Plast Reconstr Surg.* 2004;113:525–530.
33. De Angelis B, Orlandi F, Fernandes Lopes Morais D'Autilio M, et al. Long-term follow-up comparison of two different bi-layer dermal substitutes in tissue regeneration: clinical outcomes and histological findings. *Int Wound J.* 2018;15:695–706.
34. De Francesco F, Busato A, Mannucci S, et al. Artificial dermal substitutes for tissue regeneration: comparison of the clinical outcomes and histological findings of two templates. *J Int Med Res.* 2020;48:300060520945508.
35. Kozak GM, Hsu JY, Broach RB, et al. Comparative effectiveness analysis of complex lower extremity reconstruction: outcomes and costs for biologically based, local tissue rearrangement, and free flap reconstruction. *Plast Reconstr Surg.* 2020;145:608e–616e.
36. Shakir S, Messa CA, Broach RB, et al. Indications and limitations of bilayer wound matrix-based lower extremity reconstruction: a

multidisciplinary case-control study of 191 wounds. *Plast Reconstr Surg.* 2020;145:813–822.
37. Shores JT, Hiersche M, Gabriel A, et al. Tendon coverage using an artificial skin substitute. *J Plast Reconstr Aesthet Surg.* 2012;65:1544–1550.
38. Graham GP, Helmer SD, Haan JM, et al. The use of Integra Dermal Regeneration Template in the reconstruction of traumatic degloving injuries. *J Burn Care Res.* 2013;34:261–266.
39. Adani R, Rossati L, Tarallo L, et al. Use of Integra artificial dermis to reduce donor site morbidity after pedicle flaps in hand surgery. *J Hand Surg Am.* 2014;39:2228–2234.
40. Choughri H, Weigert R, Heron A, et al. Indications and functional outcome of the use of Integra® dermal regeneration template for the management of traumatic soft tissue defects on dorsal hand, fingers and thumb. *Arch Orthop Trauma Surg.* 2020;140:2115–2127.
41. Weigert R, Choughri H, Casoli V. Management of severe hand wounds with Integra dermal regeneration template. *J Hand Surg Eur Vol.* 2011;36:185–193.
42. Weigert R, Leclere FM, Delia G, et al. Long-term patient-reported functional and cosmetic outcomes following severe traumatic foot and ankle wound reconstruction with acellular dermal matrix. *J Cosmet Laser Ther.* 2015;17:321–329.
43. Benecke J, Koenen W, Mager L, et al. Reconstruction of full thickness defects on the scalp with artificial dermal regeneration template: analysis of long-term results in 68 cases. *Dermatol Surg.* 2021;47:e1–e4.
44. Bernstein JL, Premaratne ID, Levy AS, et al. Reconstruction of full thickness scalp defects in extremely elderly patients using dermal regeneration templates. *J Craniofac Surg.* 2020;31:e511–e514.
45. Faulhaber J, Felcht M, Teerling G, et al. Long-term results after reconstruction of full thickness scalp defects with a dermal regeneration template. *J Eur Acad Dermatol Venereol.* 2010;24:572–577.
46. Felcht M, Koenen W, Sassmann G, et al. Two-stage reconstruction of head and neck defects after tumor resection with a dermal regeneration template. *J Cutan Med Surg.* 2011;15:259–265.
47. Maus JC, Hemal K, Khan M, et al. Dermal regeneration template and staged skin grafting for extirpative scalp wound reconstruction: a 14-year experience. *Otolaryngol Head Neck Surg.* 2021;165:275–281.
48. Romano G, Bouaoud J, Moya-Plana A, et al. Integra dermal regeneration template for full thickness carcinologic scalp defects: our 6 years' experience retrospective cohort and literature review. *J Stomatol Oral Maxillofac Surg.* 2021;122:256–262.
49. Schiavon M, Francescon M, Drigo D, et al. The use of Integra® dermal regeneration template versus flaps for reconstruction of full-thickness scalp defects involving the calvaria: a cost-benefit analysis. *Aesthetic Plast Surg.* 2016;40:901–907.
50. Monjanel B, Baillif S, Lagier J, et al. Efficacy and safety of an artificial dermal graft for the reconstruction of exenterated sockets: a preliminary report. *Graefes Arch Clin Exp Ophthalmol.* 2021;259:2827–2835.
51. Ozgonul C, Diniz Grisolia AB, Demirci H. The use of Integra dermal regeneration template for the orbital exenteration socket: a novel technique. *Ophthalmic Plast Reconstr Surg.* 2018;34:64–67.
52. Rafailov L, Turbin RE, Langer PD. Use of bilayer matrix wound dressing in the exenterated socket. *Orbit.* 2017;36:397–400.
53. Murray RC, Gordin EA, Saigal K, et al. Reconstruction of the radial forearm free flap donor site using integra artificial dermis. *Microsurgery.* 2011;31:104–108.
54. Garland CB, Hansen SL, Hoffman WY, et al. Treatment of the radial forearm flap donor site with single-stage Integra™ artificial dermal matrix and autograft. *Plast Reconstr Surg.* 2014;134:28–29.
55. Gravvanis AI, Tsoutsos DA, Iconomou T, et al. The use of integra artificial dermis to minimize donor-site morbidity after suprafascial dissection of the radial forearm flap. *Microsurgery.* 2007;27:583–587.
56. Wainwright D, Madden M, Luterman A, et al. Clinical evaluation of an acellular allograft dermal matrix in full-thickness burns. *J Burn Care Rehabil.* 1996;17:124–136.
57. Lattari V, Jones LM, Varcelotti JR, et al. The use of a permanent dermal allograft in full-thickness burns of the hand and foot: a report of three cases. *J Burn Care Rehabil.* 1997;18:147–155.
58. Callcut RA, Schurr MJ, Sloan M, et al. Clinical experience with Alloderm: a one-staged composite dermal/epidermal replacement utilizing processed cadaver dermis and thin autografts. *Burns.* 2006;32:583–588.
59. Greenwood JE, Wagstaff MJ, Rooke M, et al. Reconstruction of extensive calvarial exposure after major burn injury in 2 stages using a biodegradable polyurethane matrix. *Eplasty.* 2016;16:e17.
60. Wagstaff MJ, Salna IM, Caplash Y, et al. Biodegradable Temporising Matrix (BTM) for the reconstruction of defects following serial debridement for necrotising fasciitis: a case series. *Burns Open.* 2019;3:12–30.
61. Sreedharan S, Morrison E, Cleland H, et al. Biodegradable temporising matrix for necrotising soft tissue infections: a case report. *Australasian J Plast Surg.* 2019;2:106–109.
62. Li H, Lim P, Stanley E, et al. Experience with NovoSorb® Biodegradable Temporising Matrix in reconstruction of complex wounds. *ANZ J Surg.* 2021;91:1744–1750.
63. Palackic A, Duggan RP, Campbell MS, et al. The Role of skin substitutes in acute burn and reconstructive burn surgery: an updated comprehensive review. *Semin Plast Surg.* 2022;36:33–42.
64. Petrie K, Cox CT, Becker BC, et al. Clinical applications of acellular dermal matrices: a review. *Scars Burn Heal.* 2022;8:20595131211038313.
65. Lagus H, Sarlomo-Rikala M, Bohling T, et al. Prospective study on burns treated with Integra(R), a cellulose sponge and split thickness skin graft: comparative clinical and histological study--randomized controlled trial. *Burns.* 2013;39:1577–1587.
66. Chang DK, Louis MR, Gimenez A, et al. The basics of integra dermal regeneration template and its expanding clinical applications. *Semin Plast Surg.* 2019;33:185–189.
67. Arno A, Smith AH, Blit PH, et al. stem cell therapy: a new treatment for burns? *Pharmaceuticals (Basel).* 2011;4:1355–1380.
68. Urciuolo F, Casale C, Imparato G, et al. Bioengineered skin substitutes: the role of extracellular matrix and vascularization in the healing of deep wounds. *J Clin Med.* 2019;8:2083.
69. Anderson JR, Fear MW, Phillips JK, et al. A preliminary investigation of the reinnervation and return of sensory function in burn patients treated with INTEGRA. *Burns.* 2011;37:1101–1108.
70. Zajíček R, Grossová I, Šuca H, et al. Experience with Integra at the prague burns centre 2002-2016. *Acta Chir Plast.* 2017;59:18–26.
71. Chang DK, Louis MR, Gimenez A, et al. The basics of Integra dermal regeneration template and its expanding clinical applications. *Semin Plast Surg.* 2019;33:185–189.
72. Amini-Nik S, Dolp R, Eylert G, et al. Stem cells derived from burned skin - the future of burn care. *EBioMedicine.* 2018;37:509–520.
73. Piejko M, Radziun K, Bobis-Wozowicz S, et al. Adipose-derived stromal cells seeded on integra dermal regeneration template improve post-burn wound reconstruction. *Bioengineering (Basel).* 2020;7:67.
74. Eylert G, Dolp R, Parousis A, et al. Skin regeneration is accelerated by a lower dose of multipotent mesenchymal stromal/stem cells—a paradigm change. *Stem Cell Res Ther.* 2021;12:82.