Use of Biologic Agents in Extremity Reconstruction

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Abstract

Skin and soft tissue defects of the lower extremity present a unique challenge for the reconstructive surgeon. Successful repair of the lower extremity relies not only on strong anatomical knowledge and surgical expertise, but also on careful consideration of the numerous preoperative factors and indications that may alter the patient's response to operative management. While many of these injuries result from burns, avulsive trauma, diabetes, or vascular insufficiencies, a significant portion can be associated with resection of neoplastic pathologies. This review outlines the uses, indications, and considerations for biologic wound agents in reconstructing skin and soft tissue defects of the lower extremity following Mohs micrographic surgery.

Keywords

- Mohs micrographic surgery
- lower extremity
- Integra
- fasciocutaneous flap
- melanoma
- cutaneous malignancies

Cutaneous malignancies are the most common cancers overall with ultraviolet light being the most significant risk factor for their development.[1] The face, more specifically the H-zone, is an area with a high incidence of carcinogenesis.[2] In contrast, the lower extremities, which are typically less exposed to the sun in many regions, occur less frequently. Both non-melanoma and melanoma skin cancers can be locally destructive to tissue, with the latter having significant risk for metastasis.[2,3] Additionally, some types of melanomas skin cancers are notorious for developing in areas not directly exposed to the sun—commonly in the soles and subungually.[4–6] The current standard of care for nonmelanoma and melanoma skin cancers is Mohs micrographic surgery and wide local excision, respectively.[7–9] These resections result in defects that vary in complexity and size and are often a source of significant functional and psychosocial impairment for affected patients.

When compared with the thigh, defects of the legs and feet can be exceptionally difficult to reconstruct given the paucity of adjacent tissue available for reconstruction with local muscle and fasciocutaneous flaps. Furthermore, many defects, particularly those located at the distal one-third of the leg and the dorsal aspect of the foot, result in exposure of underlying tendon and bone. Free tissue transfer is often seen as the gold-standard reconstructive modality to correct these defects; however, biologic wound agents serve as an excellent alternative to free tissue transfer should microvascular reconstruction be contraindicated.[10] In this overview, we describe the use of biologic wound agents to reconstruct soft tissue defects of the lower extremity following Mohs micrographic surgery.

Biologic Wound Agents

Recent advances in wound care technology have resulted in many alternatives available to repair soft tissue defects of the lower extremity. Biologic wound healing agents are broadly categorized into cellular and acellular products. Cellular products are aptly named based on their composition of live keratinocytes and fibroblasts, which have been

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demonstrated to enhance the wound healing process.[11] Alternatively, acellular products, such as Integra (Integra LifeScience Corporation, Princeton, NJ), are often composed of collagen and basement membrane matrix creating a scaffold for the formation of a neodermis.[12]

Biologic wound agents facilitate cellular proliferation and structural repair by acting as a base for fibroblast migration and neovascularization.[13] Once applied to the wound bed, these products exert their action over four phases. The initial imbibition phase begins within minutes as the product adheres itself to the wound bed. Over the next 7 days, the matrix encourages collagen secretion by fibroblasts, laying the groundwork for the third phase, neovascularization. In the following weeks, new blood vessels form in the matrix until the host's native collagen begins to replace the dermal template, forming a final, matured wound bed capable of supporting a graft. Within 2 years, this transition will be completed, and the matrix will be completely replaced by host collagen.[14]

Reconstructive Approach

Thorough preoperative planning is critical to optimizing functional and aesthetic results following reconstruction of defects of the leg and feet. When evaluating a defect, the surgeon must note the defect's location, size, and depth along with the quality and laxity of surrounding soft tissue. In addition to examining the wound, the surgeon must collect a thorough medical and social history to identify any medical conditions or lifestyle practices that may negatively influence reconstructive outcomes. Most notably, patients who are smokers, have a history of radiation therapy, or who have peripheral artery disease are particularly susceptible to developing postoperative complications.[15,16]

Superficial defects that spare the underlying musculature, tendons, and bone can often be reconstructed using split-thickness skin grafting (STSG) with acceptable results.[15] Larger superficial defects, however, frequently benefit from the addition of biologic wound agents prior to graft placement.[17] Similar to results seen in the management of patients with third-degree burns, biologics followed by STSG has been shown to greatly decrease scar contracture over time.[18]

Defects with exposure of the underlying tendon or bone, on the other hand, require more complex management. The tendons inherently suffer from poor vascularity and rely heavily on synovial fluid and overlying soft tissue for nutrition, lubrication, and protection from the external environment.[19] Exposure leaves tendons susceptible to dehydration, resulting in decreased compliance and a limited capacity for fluid movement with each muscle contraction and relaxation.[19] Bony tissues, on the other hand, are well vascularized but are prone to infection, when lacking soft tissue coverage.[20] Coverage of deeper defects exposing paratenon or periosteum requires a more intricate surgical plan as typical autologous skin grafts are unsuitable for use in these instances.

Various locoregional flaps have been successfully used on defects up the upper, middle, and lower third of the leg. For example, the gastrocnemius flap has been used in the proximal third of the leg, while the soleus flap is more suitable for defects of the middle third of the leg.[21,22] The reverse sural artery fasciocutaneous flap has been utilized for small defects at the distal one-third; however, large defects, particularly at the distal one-third of the leg, frequently require free tissue transfer or biologic wound agents to repair the defect.[10,23,24]

Biologic wound agents offer a multitude of advantages for both the patient and surgeon. First, use of biologic wound agents is one manner in which soft tissue coverage can be

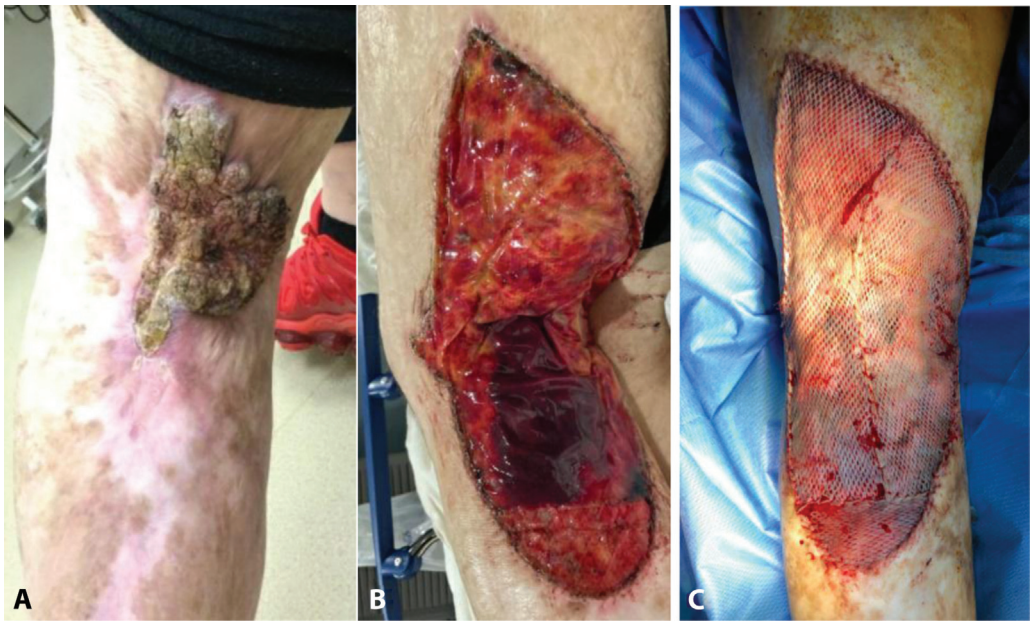

Fig. 1 Use of Integra to reconstruct a post-ablative defect of the posterior leg and thigh following resection of a large squamous cell carcinoma in a 35-year-old male. Preoperative photography (**A**), 90 days postoperatively demonstrating complete take of Integra (**B**), definitive reconstruction of the leg defect with STSG at 90 days postoperatively (**C**).

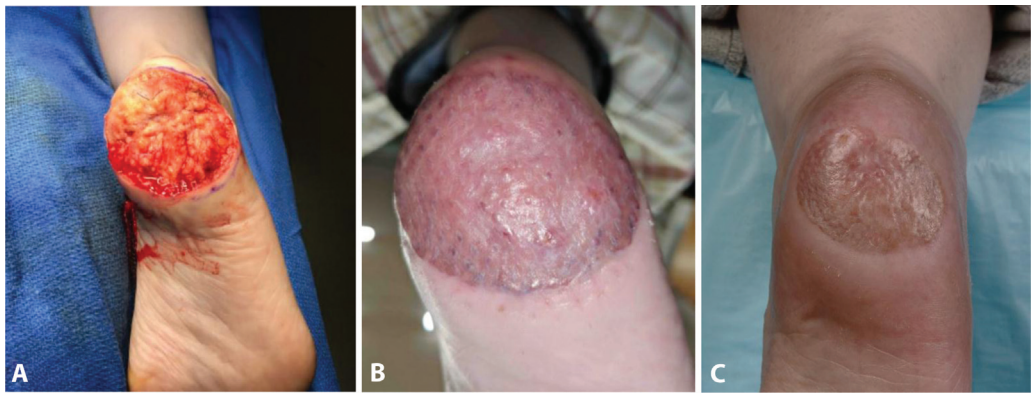

Fig. 2 Use of Integra to reconstruct a post-ablative defect of the heel following resection of a melanoma in a 66-year-old female. Photograph of post-ablative defect (**A**), 8 weeks following placement of Integra (**B**), 5 months following placement of Integra (**C**).

provided in an outpatient setting for patients who are medically unfit to undergo lengthy microsurgical reconstruction.[13,15] Given the fact that the majority of patients undergoing oncoplastic reconstruction of cutaneous malignancies are middle-aged or elderly, the incidence of medical comorbidities that can result in adverse surgical events is significantly higher than the general population.[25] Second, biologic wound agents may be employed should the size of the soft tissue defect reach a threshold where the size of the free flap needed for reconstruction causes unacceptable levels of donor site morbidity. Small defects in areas where locoregional tissue transfer is difficult, such as the dorsum of the great toe, may be easily reconstructed using biologic wound agents before definitive reconstruction with a STSG. Lastly, in the instance where the results of the surgical pathology evaluation are not completed, acellular dermal matrix products can be employed as a temporizing measure until the person is cleared for definitive reconstruction.

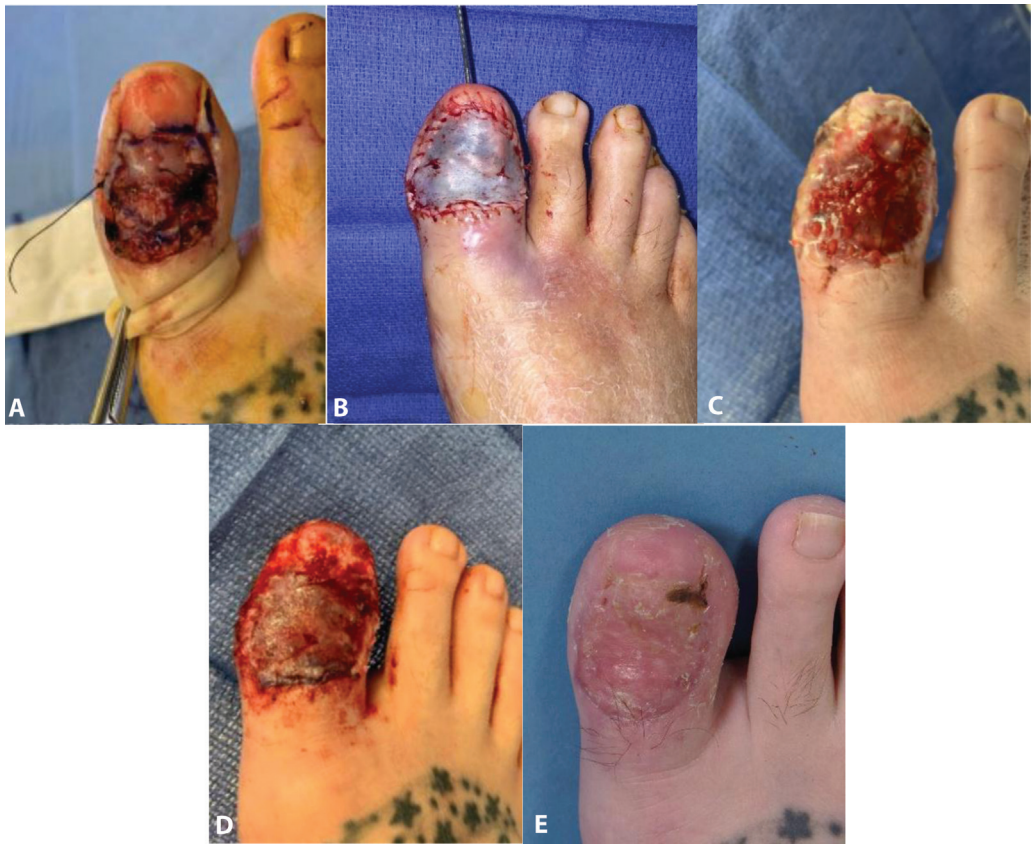

Fig. 3 Use of Integra to reconstruct a post-ablative defect of the great toe following resection of an ungual melanoma in a 72-year-old male. Photograph of post-ablative defect (**A**), percutaneous pin fixation with Kirshner wire used to stabilize the joint laxity that occurred secondarily to tumor excision (**B**), 25 days following placement of Integra (**C**), placement of STSG 25 days after initial excision and placement of Integra (**D**,**E**).

Case 1

A 35-year-old male patient presented to our clinic with a large fungating encrusted lesion on the posterior aspect of the leg. The patient successfully underwent Mohs micrographic surgery and achieved clear margins. A large sheet of Integra was placed in the popliteal fossa. Care was taken to ensure that the left leg was straight during the application to obtain an accurate template size. After 90 days a large STSG was applied over the Integra template for enhanced. wound healing and cosmesis (►**Fig. 1**).

Case 2

A 66-year-old female patient presented following melanoma excision of the right heel. Given the lack of subcutaneous tissue secondary to resection of the melanoma, a medial plantar artery flap was initially proposed; however, it was forgone due to the need for autologous skin graft harvest from the patients back. The decision was ultimately made to reconstruct the soft tissue defect using Integra without negative pressure wound therapy. The patient's wound successfully resolved after 5 months, and she was able to return to weight-bearing activities (►**Fig. 2**).

Case 3

A 72-year-old male patient presented with a full thickness defect of the great toe secondary to extirpation of an ungual melanoma. The patient showed signs of joint laxity of the toe due to the extent of the dissection and proximity to the extensor tendon. A single 0.62 Kirshner wire was employed to stabilize the joint, and Integra was applied to provide soft tissue coverage. On postoperative day 25, a STSG was applied over the Integra. Thirty-five days after the addition of the STSG the patient's wound resolved (►**Fig. 3**).

Conclusion

The limited tissue envelope and functional demands of the lower extremities often pose a significant challenge for the reconstructive surgeon. Biologic wound agents have proven to be both viable treatment additions and alternatives to current modalities in simple and complex reconstructive scenarios. Though biologic wound agents do have limitations, the author has demonstrated successful uses, techniques, and indications for these agents following Mohs reconstruction in the lower extremity. Ultimately, wound coverage options should be evaluated case-by-case, using the reconstructive modality that maximizes functional and aesthetic outcomes.

Conflict of Interest
None declared.

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