Emerging Technologies

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KEYWORDS

• Emerging technologies • Skin substitutes • Grafting techniques

KEY POINTS

- Recent and ongoing technological developments have had a large impact on burn care and wound management.
- Integration of artificial intelligence with clinical decision support tools has allowed for more accurate burn depth measurement and administration of supportive care.
- When treating full-thickness burns, there are a growing number of synthetic, biological, and hybrid alternatives/adjuncts to autologous split-thickness.
- Scar contractures can significantly decrease a patient's range of motion and degrade their quality of life, though newer, minimally invasive techniques to release contractures are proving effective.

INTRODUCTION

Burn care as a surgical specialty evolved in the 1970s when Zora Janzekovic introduced surgical eschar removal and early skin grafting.[1,2] Before that point, burn care focused on wound care instead of surgery. The early removal of eschar, earlier wound closure, and intensive care support for the patient led to significant improvements in survival and outcomes.[2] Emerging technologies are constantly helping to improve burn care even further. Diagnostic, intensive care, surgical, reconstruction techniques, and technological advances are being continuously developed, many of which will be discussed here. While far from an all-inclusive list, the technologies discussed have been chosen by the author as clinically relevant today and are divided into 3 areas: advances in acute burn care, wound closure, and reconstruction.

ACUTE BURN CARE

Objective Injury Depth Evaluation

Two factors determine burn severity: (1) burn size, or the extent of the injured skin surface area, measured in total burn surface area (in clinical practice, more commonly estimated by charts, computer programs, and applications) and (2) burn depth. The depth of a burn injury cannot be as easily determined as the size. Ultimately, a biopsy determines the actual depth of injury, but since most burn wounds contain several regions with variable injury depth, this method is not clinically relevant. Recent technologies in this area include optical devices like the laser Doppler imager, the Spectral MD camera, forward looking infrared (FLIR), and the indocyanine green dye technique, which all measure blood perfusion and hemoglobin reflection/absorption by the tissue (**Figs. 1–4**). Most recently, image interpretation has been augmented by deep learning algorithms.[3,4] Optical imaging is beneficial for measuring multiple properties of soft tissue.[5] Because of the wide variety of ways different soft tissues absorb and scatter light, optical imaging can measure metabolic changes that are early markers of abnormal functioning of organs and tissues.[5]

Fluid Resuscitation

After burn injury, fluid resuscitation that is both adequate and precisely individualized is essential to ensure survival, prevent organ dysfunction (kidney failure, compartment syndrome, cardiac failure, and so forth), and provide optimal skin perfusion to prevent burn wound progression. An artificial intelligence–supported resuscitation support

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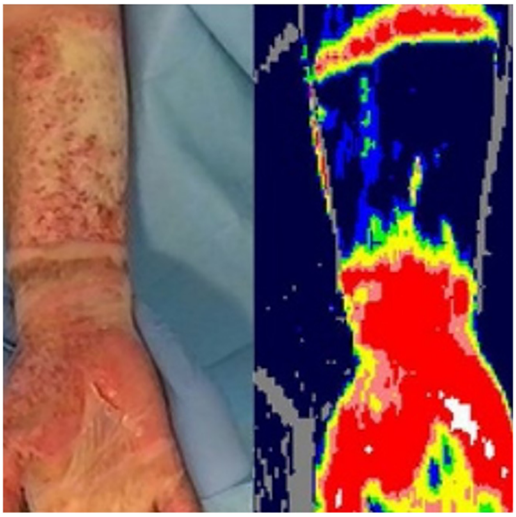

Fig. 1. Laser Doppler Imaging of a burn wound. Hop, M.J., Hiddingh, J., Stekelenburg, C.M. et al. Cost-effectiveness of laser Doppler imaging in burn care in the Netherlands. BMC Surg 13, 2 (2013). https://doi.org/10.1186/1471-2482-13-2.

system has been developed by ArcosTM. This system supports individualizing fluid administration through real-time feedback systems not dependent on human data entry and interpretation alone.[6]

Fig. 2. The Spectral MD wound imaging device uses artificial intelligence and multispectral imaging to assess wound severity. Used with permission from Spectral AI, Inc.

Fig. 3. Indocyanine green image of blood vessels (eye). This image was originally published in the Retina Image Bank® website. Gareth Lema MD, PhD. Photographer Sandra Boglione.Polypoidal Choroidal Vasculopathy - IVFA/ICGA. Retina Image Bank. 2018; 28352. © The American Society of Retina Specialists.

Pain Control

Adequate pain control is prominent in acute burn care, wound debridement, dressing changes, and daily personal hygiene. A nursing-driven nitrous oxide pain protocol, administered via the Pro-Nox device, has been developed and is supported by the American Association of Anesthesiologists and others.[7] Nitrous oxide provides pain relief by acting as a partial opioid receptor agonist. It does not get metabolized and is excreted by exhalation (**Fig. 5**). Using this technique for moderate sedation enables the providers and caretakers of a burn patient to provide adequate wound care without the excessive use of opioids, thereby decreasing the contribution to opioid dependency and abuse.[7]

Removal of Burn Eschar

Early and complete removal of burn eschar, which means necrotic tissue, contributes most significantly to survival and outcome. Throughout the years, since the introduction of surgical excision, the technique evolved from the excision down to fascia level to the modern tangential excision of only perceived necrotic tissue. Preservation of dermal elements and fat tissue, if possible, has shown to yield better long-term outcomes including function and esthetic appearance. Since the technology for real-time exact determination of burn depth remains to be developed, the decision of depth of excision presently depends on the

Fig. 4. Nitrous Oxide setup by Porter. Nitronox Plus, Porter Instrument, Hatfield, PA.

surgeon's experience. Because of the many contour variations and skin thickness differences in different parts of the human body, over-excision and under-excision are common. Clinical indicators like punctate bleeding and the color of the underlying tissue are notoriously imprecise. Recently, an enzyme has been introduced, based on bromelain, which appears to be powerful enough to enzymatically degrade necrotic tissue while preserving healthy tissue within a reasonable time frame.[8] After application and incubation of the enzyme, the necrotic tissue disintegrates enough to be removed by scraping (**Fig. 6**). The process is painful and requires significant pain control, and although significantly reduced when compared to surgical excision, a risk of bleeding remains.[8]

Other more precise technologies for eschar removal include the Versajet device, which works on the basis of hydro-dissection by the Venturi effect, cutting (indiscriminately) with a high-velocity stream of water, which creates "suction" at the same time. The Versajet device is most useful for softer tissue like granulation tissue. Removing hard burn eschar can be time consuming. The Misonix ultrasound device—which works on the principle of ultrasonic destruction of cell walls, combined with suction—is beneficial in contaminated wounds because it destroys bacterial cell walls some distance into tissue. (The Sonicare toothbrush works similarly, destroying bacterial cell walls in gum recesses, without destroying the mucosa). The Amalgatome is a device originally developed for meat processing. A rotating disk knife, set to a certain thickness, is used to "slice" through tissue. It can be used for burn eschar excision and is particularly helpful in concave body areas, fat tissue, and large surface areas like the back or chest. It leaves a smoother wound bed and cleaner edges than the Weck or Watson knife. In addition, it is now widely used for skin harvesting.[9]

WOUND CLOSURE

Deep burn wounds have little or no intrinsic healing potential because the epidermal stem cell layer was destroyed. Wound closure ultimately depends on autologous epidermal and dermal cells being introduced into the wound bed to achieve closure. Skin grafting, whether full-thickness or split-thickness, has been the standard of care. The creation of a significant donor site, with its sequelae and complications, is one major drawback of this technique, as well as significant scarring. Cultured cells were introduced in 1975 by Rheinwald and Green and have been used in extensive burn wounds since 1981.[10] A significant time delay of approximately 3 weeks is necessary to grow the cell grafts in a commercial laboratory, and the purely epidermal cell sheets need a dermal component to engraft. A more recent solution for point-of-care epidermal coverage was developed by Dr. Fiona Woods, using a small split-thickness skin donor to process cell suspension, which can be sprayed onto the prepared wound bed in a maximum 1:80 expansion ratio.[11] The preparation kit is commercially available in the United States as Recell by Avita Medical. Other applications of the autologous cell suspension include repigmentation in vitiligo, augmented donor site healing, and healing of traumatic wounds.

A self-assembled skin substitute consisting of fibroblasts and keratinocytes is currently under

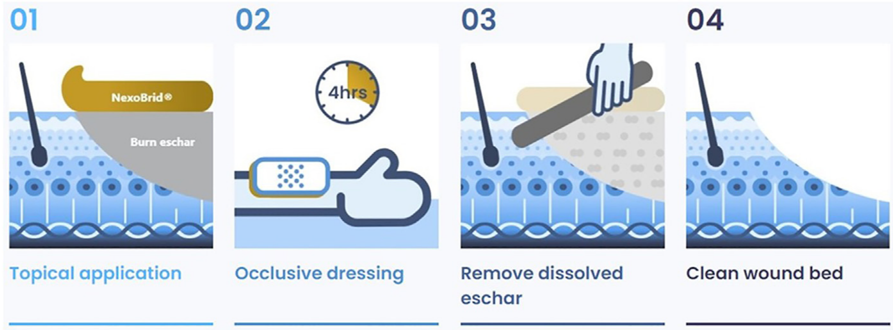

Fig. 5. Enzymatic debridement process. Used with permission from MediWound.

investigation.[12] Many other tissue engineering projects are currently under investigation in animal and human trials, all based on a scaffold, whether synthetic or biological, which populates with fibroblasts and keratinocytes. In addition, researchers are investigating cell modulation and bioprinting.

The Meek technique is widely accepted globally to cover extensive burn wounds with split-thickness grafts.[13] Any small piece of split-thickness skin graft (STSG) is placed on a carrier after being cut into 0.4 × 0.4 cm squares. The carrier is folded in a plisse-type fashion, and the little squares of skin are separated by opening the plisse folds. The entire carrier with STSG is then placed on the wound, allowing from 1:2 to 1:8 expansion.[13]

Whether biological or synthetic, skin substitutes are an ever-expanding field of emerging technology; some are designed as epithelial cover substitutes, some as dermal, and some as both. Relevant in current burn care are several dermal substrates with a synthetic epidermal placeholder, some dermal scaffolds without cover, and epidermal substrates.[14] Integra, BTM, Biobrane (not available in the United States and mostly established for partial thickness wounds), Matriderm, Hyalomatrix, and Pelnac all function as (partially) biologic scaffolds for dermal regeneration with a temporary synthetic cover to mimic epidermal coverage until autologous epidermis can be transplanted (**Figs. 7** and **8**).[15] On the other hand, Primatrix, Supra SDRM, Matriderm, Acell, Alloderm, and fish skin function as dermal scaffolds, promoting the ingrowth of fibroblasts and the formation of granulation tissue for wound bed conditioning without a cover membrane.[15] These substances can sometimes bridge small areas of avascular structures like exposed tendons and bone and avoid chronic open wound formation in those areas. In addition, the scar contracture after dermal scaffold use is often decreased, thereby preventing some degree of joint contractures in the long term. Epidermal skin substitutes currently in use are cryopreserved or glycerol-preserved cadaver allodermis and xenografts like fish or porcine grafts, including all their processed/acellular derivatives (amniotic substrates, mucosal substrates, and so forth) which are biologic, as well as Suprathel and Biobrane, which are synthetic (**Fig. 9**).[15] These protect the wound's natural/intrinsic healing potential, preventing infection and augmenting cell proliferation. While Suprathel is biodegradable and does not integrate into the wound, Biobrane (including the cell-seeded derivatives Dermagraft, Apligraf, and so forth) needs to be removed and does integrate into the wound bed if the dermal injury extends beyond the papillary dermis.[14]

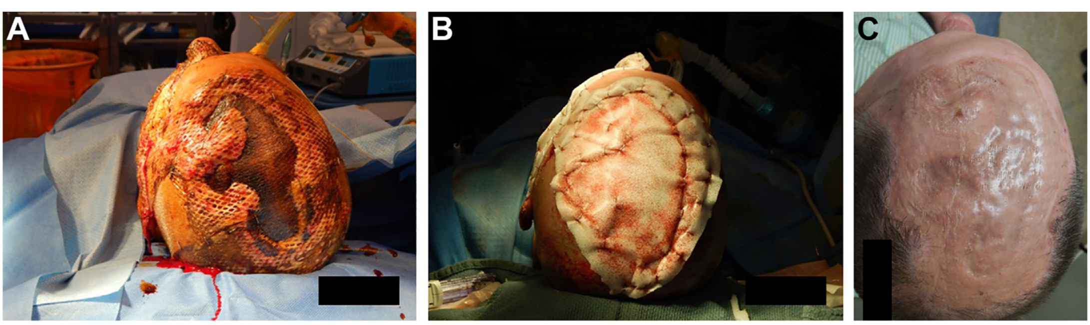

Fig. 6. BTM on exposed bone (skull): Injury, BTM in place, Skin graft healed on top of BTM after 12 weeks.

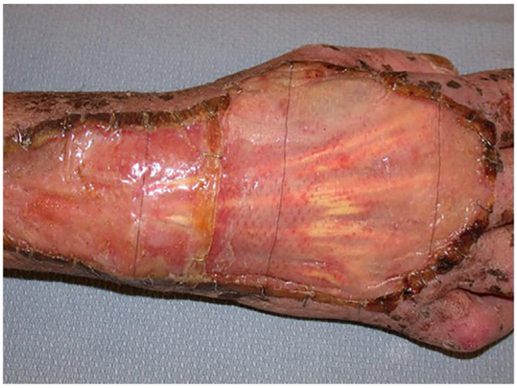

Fig. 7. Integra on exposed tendon, ready for skin grafting.

BURN RECONSTRUCTION

The prevalence of developing a hypertrophic scar following a burn-related injury has been reported to be as high as 70%. These scars can be cosmetically unappealing, with associated symptoms of pruritus, pain, and restricted range of motion, which can impair a person's quality of life. Such scars are thought to develop from patterns of dysregulation of normal wound healing after trauma to the skin. Surgical scar removal and contracture release remain important corrective therapies; however, these techniques have high risks of scar recurrence.[16] Nonsurgical interventions are often attempted prior to surgical interventions to inhibit or slow scar progression. Nonsurgical interventions include pressure garments, silicone gel sheeting, intralesional injections, cryotherapy, radiation therapy, and laser and light therapy. Laser and light therapies have now emerged as minimally invasive, low-risk therapies with a short postoperative recovery period.[17]

Prevention and release of contractures using skin substitutes/dermal templates play a significant role in modern burn reconstruction. All of the previously mentioned modalities have been used. The most recently developed substrates are BTM and Zurich skin. Most substrates require the release of contractures and application of dermal substrate, followed by a period of ingrowth of fibroblasts and the formation of a dermislike layer that will then be skin grafted.[18] (See earlier description in acute burn treatment)

Fig. 8. Recell epidermal autograft suspension sprayed onto dermal wound bed.

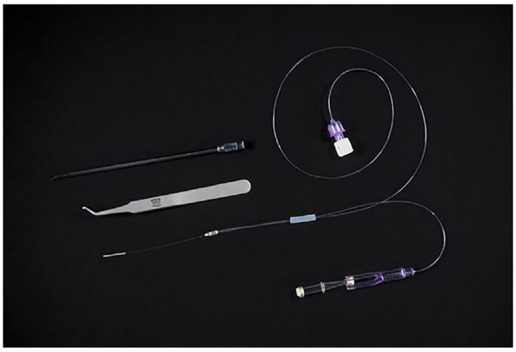

Fig. 9. Microdialysis catheter.

Flap reconstruction is a common technique in burn reconstruction. Newer preoperative mapping techniques for supplying vessels and postoperative monitoring devices have been developed.[19] Thermography (FLIR) is based on heat detection and is used to map vessels preoperatively. Similarly, indocyanine green fluoroscopy can be used to map blood vessels preoperatively and postoperatively. Laser Doppler flowmetry is based on the reflection of laser light by erythrocytes. Microlight-guided spectrophotometry uses optical techniques to distinguish well perfused and not well-perfused tissues. The amount of light absorption by hemoglobin depends on its oxygenation level and the wavelength of the light. By analyzing the spectrum of the reflected light, the device can calculate the tissue's oxygen saturation and blood flow. Tissue pH monitoring and microdialysis are 2 other invasive monitoring techniques based on the chemical composition of interstitial fluid in the tissues (**Fig. 10**). Technetium-99 m sestamibi scintigraphy and perfusion-weighted MRI are 2 of the less studied and more expensive modalities.[19,20]

Fat grafting has been used in burn reconstruction, mainly to improve contour irregularities and to treat skin-to-muscle or tendon adhesions (**Fig. 11**). Modern harvesting techniques (laser or ultrasound-assisted) can be used; however, manual harvesting usually yields sufficient material (**Fig. 12**).[21]

Botulinum toxin is used in burn reconstruction to augment contracture release procedures by relaxing the contracted underlying musculature. It is also believed that the relaxation of myofibroblasts is an adjunct in keloid and hypertrophic scar treatment.[22] There is emerging evidence that it can influence fibroblast activity and minimize tension around the scar by muscular chemo-immobilization.[23]

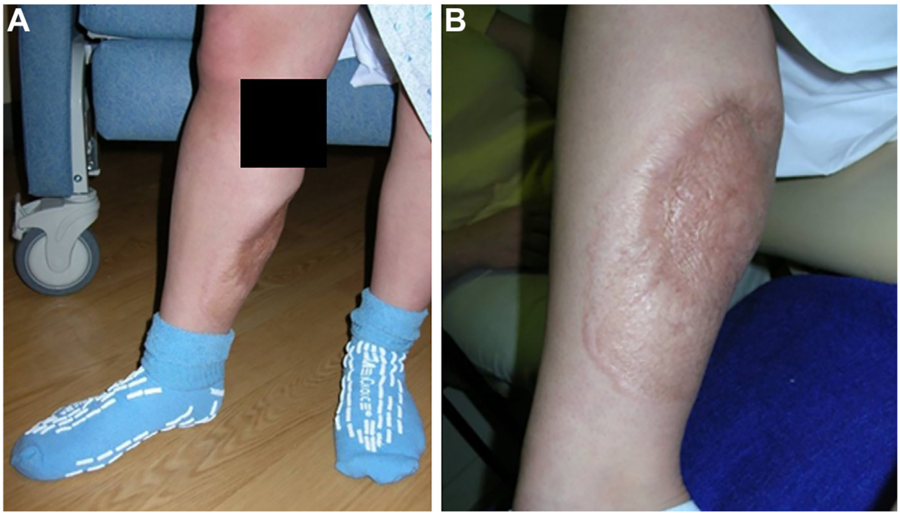

Fig. 10. Adherent scar before and after fat grafting.

Using self-inflating hydrophilic expanders has dramatically simplified tissue expansion for burn reconstruction, especially in children (**Fig. 13**).[24,25] Unfortunately, these devices are only approved in mini-formats for ear, nose, and throat doctors and dentistry in the United States.

Transplantation science and practice advances have made hand/face and abdominal wall transplantation possible.[26] According to a recent publication on face transplant outcomes, there have been 48 face transplantations worldwide in 46 patients since the first report of this procedure in 2005. Eleven of those recipients were burn survivors. Nine of 46 patients have since died and 2 transplants have been reported as rejected. The long-term recovery of facial expression was measured in the aforementioned study as restoration of facial motor function and smile at roughly 40%. A better outcome (42.7%) was found when nerve coaptation was performed at the distal branch level.[27–29] The long-term need for immunosuppression and psychological issues in the transplantation of non-vital organs limit its implementation in burn reconstruction in most burn survivors. Immunologic risk factors also need to be taken into account when undertaking face transplantation because patients with a past medical history of burns and transfusions may have developed immunosensitization.[28]

Fig. 11. Manually harvested and processed autologous fat used for scar fat grafting.

Minimally invasive techniques are understandably popular in the burn survivor community. Subcutaneous contracture band release, microneedling, and laser/light-based therapies have gained wide acceptance recently.

Fractional laser therapies have made scar treatment with ablation carbon dioxide (CO_2) lasers feasible. Burn scars resulting from deep dermal or full-thickness injuries have a relatively normal epidermis on a very abnormal dermis, which usually does not contain dermal adnexa and, therefore, no stem cell nests of epidermal cells. Treating a burn scar with ablation, be it by thin excision, dermabrasion, or ablation laser, would cause an open wound that resembles a new full-thickness burn, requiring epidermal coverage for healing. Fractional and non-ablative lasers can selectively injure the abnormal scar and stimulate remodeling without significant epidermal injury.[17] Fractional lasers, such as fractional CO_2 and fractional erbium: YAG lasers, create controlled micro-injuries within the scar tissue.[30] This stimulates collagen remodeling and tissue regeneration, leading to a smoother, more flexible scar. Laser therapy can also reduce scar redness and improve skin texture, helping patients regain confidence and function.[30,31]

Fig. 12. Self-inflated expanders in situ and removed.

Subcutaneous contracture band release can be performed under local anesthesia. Subcutaneous bands of scar tissue, often restricting the range of motion and leaving the burn survivor with the feeling of tightness, can be released by passing a braided suture subcutaneously under and over the band, thereby looping the scar band. The sawing motion then releases the band without cutting the epidermis. Joseph Haik[32] introduced the technique, first used for releasing platysma bands, and extrapolated it to neck burn contracture release. The author expanded the use to all other body areas and conducted a retrospective study on 97 such releases (currently under review for publication). The overall satisfaction with the procedure was very good and the measurable increase in range of motion was significant (measured by independent occupational therapists). The contracture bands do not re-form, rather, the patients notice other, previously not noticed, "bands" that can be released subsequently. It can be safely applied in any body area that demonstrates appropriate subcutaneous scar bands to relieve the feeling of tightness and ideally increase of range of motion. Underlying major vascular or nerve structures need to be mapped and avoided prior to this intervention.

Fig. 13. Minimally invasive contracture band release on a knee contracture.

Lymphedema is an unresolved problem for burn survivors. Be it through constricting scars or fascial excision. There often is a profound derangement of the lymphatic system. Compression therapy has been the mainstay of therapy. With newer treatment options for lymphedema in other conditions like cancer treatment–related disturbance of lymphatic flow, there is hope that these techniques can be applied to burn reconstruction.[33] These include lymph node transplantation and new pathway creation by microvascular techniques.[33]

SUMMARY

Combined with advanced dermal substrates, spray-on skin and the development of fractional lasers are probably the most critical recent technologies in burn care and reconstruction. Regenerative medicine advances are leading to self-assembling whole skin substrates, which will revolutionize the treatment of skin injuries shortly. Emerging technologies in other fields of medicine spill over into burn treatment and reconstruction. Interdisciplinary cooperation is essential in driving the developments forward and making them available to burn patients. Close cooperation with development institutions and engineering entities is instrumental.

In desperate need are long-term outcome studies of all these described interventions. Only large national and possibly international data collections like the breast cancer and reconstruction database will eventually be able to determine the value of individual burn care and reconstruction treatments.[34]

CLINICS CARE POINTS

- Consider burn eschar removal on hands, feet, face, and neck by enzymatic debridement.
- Consider coverage with dermal regeneration substrate of burns that reach past dermal elements.
- Employ advanced epidermal skin substitutes for pain control and scar prevention.
- Employ autologous cell spray to decrease donor sites and improve outcomes.
- Employ state-of-the-art diagnostic tools to determine burn depth and perfusion of tissue.
- Abstain from traditional skin grafting of burns with remaining dermal element and scar excision. Instead, use autologous cell spray and scar remodeling techniques like lasers and microneedling to modify and remodel the existing scar, often while preserving sensation and contour and pigmentation.

DISCLOSURE

The author has nothing to disclose.

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