Necrotizing soft tissue infections (NSTI) represent a large variety of clinical entities ranging from mild pyodermas to life threatening necrotizing fasciitis (NF). *Streptococcus spp* appears to be the most common causative organism, and aggressive treatment with surgery and antibiotics is warranted in most cases.1–3

At our burn clinic, we have used Integra® Dermal Regeneration Template ([DRT] Integra LifeSciences, Plainsboro, NJ) infrequently in the treatment of necrotizing wounds since 1999. This DRT has been reported to reduce scarring and improve skin pliability compared to wound closure by conventional meshed split-thickness skin grafts (STSG). These findings have broadened the indications for DRT to also be used in treating revised major soft tissue infections.4 Using negative pressure wound therapy (NPWT) dressings to stabilize (and conform to the shape of the wound surface) with STSG and DRT has previously been described with good results.5,6 Furthermore, NPWT is a method used to treat wounds of different stages as it decreases tissue edema, lowers bacterial count, enhances neovascularization, thus stimulating wound healing.5,9 To the authors' knowledge, this is the first published case report that describes successful treatment of a patient suffering from NF by combining DRT and NPWT. This novel protocol enabled us to manage and prepare the wound surface and apply the DRT sheets successfully. This report also shows that NPWT significantly decreased the time needed for guided dermal healing.

CASE REPORT

A Novel Concept for Treating Large Necrotizing Fasciitis Wounds With Bilayer Dermal Matrix, Split-thickness Skin Grafts, and Negative Pressure Wound Therapy

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Abstract: Treatment of necrotizing fasciitis (NF) includes radical surgical debridement often resulting in large wounds that need to be closed with methods including split-thickness skin grafts (STSG), local flaps, or guided tissue regeneration procedures. In this case report, a 45 year-old Caucasian male was surgically treated for a benign left groin hernia, developed NF, and was transferred to the authors’ burn unit. The wound was treated initially with wide debridement and with a brief delay before finally closing the wound. A collagen matrix such as Integra® Dermal Regeneration Template (Integra LifeSciences, Plainsboro, NJ) in combination with STSG and negative pressure wound treatment, can provide fast recovery resulting in pliable, functional skin.

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regeneration. Complete wound closure and patient discharge was achieved within 32 days.

Case Report
A 45-year-old previously healthy Caucasian male was surgically treated for a benign left groin hernia on an outpatient basis. Pre- and postoperative periods were uneventful. The patient began to feel ill on the night of the procedure. Thirty-six hours later he had high fever and a painful, red, and swollen left groin. He presented to the emergency department where local infection was diagnosed.

The skin of the penis and lower abdomen was erythematous, warm, and tender. A minor abscess with associated ascending cellulitis was suspected. He was started on broad-spectrum intravenous (IV) antibiotics and underwent surgical debridement and drainage (the Prolene net was removed). The wound was left open. Over the next 6 hours his condition rapidly deteriorated and he became increasingly septic. At that point (day 0), the patient was referred to the authors’ burn unit with signs of septic shock. He arrived at the ward with systolic blood pressure of 50 mmHg, highly elevated C-reactive protein 248 mg/L, creatinine 207 µmol/L, and myoglobin 6400 µg/L. White blood cell count was normal. The patient was intubated and put on plasma-expander, nor-epinephrine, dobutamine, epinephrine, cortisone, and diuretics along with tobramycin, clindamycin, and imipenem. The streptococcal test was positive and the patient was immediately taken in for surgery. Clinical findings were necrotic skin and subcutaneous tissue in the lower abdomen and left flank. Penile skin was necrotic as well as the medial part of perineum including scrotal skin. The abdominis externus/internus and latissimus dorsi muscles including fascia were completely necrotic; the serratus anterior muscle was partially necrotic. All necrotic tissue was removed until macroscopic viable tissue was found in all areas. Postoperatively, the patient stabilized rapidly.

Necrotizing fasciitis was confirmed by histology and judged to be secondary to a beta-hemolytic group A streptococcal infection. The patient was treated with hyperbaric oxygen for 3 hours and surgically debrided from minor amounts of necrotic tissue (day 1). The patient returned to our burn unit (day 2) and was again surgically debrided from minor amounts of necrotic tissue (Figure 1A); the wound surface totaled approximately 1400 cm² (7.8% body surface area). The wound was covered with an open-cell polyurethane foam (V.A.C. GranuFoam®, KCI Europe Holding B.V., Amstelveen, the Netherlands), which was stapled to the wound margins. A suction tube with spread holes was placed within the foam and an adhesive film dressing (OpSite™, Smith & Nephew Wound Management, Hull, United Kingdom) was draped over the sponge and extended approximately 5 cm into healthy skin (Figure 1B). Negative pressure was then continuously created with a regular suction device with adjustable pressure levels and a shut-off alarm. The negative pressure level was then adjusted until the foam contracted into the wound cavity and then further adjusted to desired levels (100 mmHg-125 mmHg). The patient remained stable.

On day 5, the wound was inspected without any progressing infection or necrosis evident. The perineal wound was closed with local skin flaps and meshed (1:1.5). The DRT was stapled in place over the remainder of the wound. The penis was covered with STSG (0.012-in), and the exposed left testicle was buried within the left inner-thigh area to be uncovered later when the perineum healed. The polyurethane foam was applied directly onto the silastic layer of the DRT and negative pressure was applied continuously. The wound was examined at day 6, 8, and 12. Splinting was not necessary, as the negative pressure dressing secured the DRT throughout treatment. The patient was mobilized on day 7 with continua-
ous negative pressure. The day-16 examination revealed the awaited peach colored appearance of regenerated neodermis; the silastic membrane was peeled off. STSGs (0.006-in) were harvested, meshed 1.5:1, and stapled over the neodermis. The STSGs were covered with petroleum jelly gauze and polyurethane foam to re-commence the NPWT as had been done previously. At day 18, the wound was examined and the STSG was found to be healing well. The wound was thereafter treated with petroleum jelly gauze. The transplanted wound matured subsequently and the patient was discharged to home on day 32. The patient returned to full-time work 6 months after the initial surgery. Follow-up photos were taken on day 65 and 131. A 3-mm punch biopsy was obtained from the neodermis for histology and immunohistochemical staining at day 16, 18, 32, and 131. The patient gave informed consent for this case report.

**Histological preparation and staining.** The full-thickness punch biopsies were fixed in 4% neutral buffered PFA overnight, washed in PBS, dehydrated through a graded ethanol-xylene series, and embedded in paraffin. Cross sections (7-μm thick) were stained using hematoxylin and eosin (H&E) and studied with respect to dermal regeneration and re-epithelialization.

**Immunohistochemistry targeting collagen I.** A polyclonal rabbit anti-cow collagen I antibody was used to target the DRT. Biotinylated anti-IgG antibodies were used as secondary antibodies. Sections were rinsed in phosphate buffered saline (PBS), and non-specific protein binding was blocked with 2% normal goat serum diluted in PBS. The sections were then incubated with primary antiserum at a final concentration of 1/500 for 30 minutes at room temperature. The sections were rinsed in PBS and incubated with a biotinylated secondary antibody (2 g/mL) for 30 minutes. After washing, the bound antibody was localized with an avidin-peroxidase Vectastain® VIP-kit (Vector Laboratories, Burlington, CA) with hydrogen peroxide as peroxidase substrate. Negative control included the omission of the primary antibody.

Sections were examined with an Olympus BX41 light microscope and images were captured with an Olympus DP70 CCD camera.

**Results**

At day 16, examinations revealed the awaited appearance of regenerated neodermis (Figure 2). The DRT take rate was estimated to be approximately 95% (visual inspection). Histology of the biopsy obtained at day 16 showed that fibroblasts had thoroughly populated the matrix and that the dermal tissue regeneration was progressing (Figure 3).

Immunohistochemical staining targeting bovine collagen showed that the DRT was still present in the regenerating tissue (Figure 4). At day 18, an estimated 95% take rate of the STSGs was apparent. The transplanted wound matured subsequently. Immunohistochemistry revealed

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**Figure 2.** Day 16, orange/peach color of regenerated dermal tissue underneath the silastic membrane.

**Figure 3.** Representative routine histological sections of the DRT applied 11 days earlier stained with H&E. The matrix is thoroughly populated by fibroblasts and the dermal tissue regeneration is progressing.
Figure 4. Immunohistochemical staining of the DRT, applied 11 days earlier, for cow collagen I indicating the presence of the DRT in the regenerating dermal tissue. A) Stained DRT on wound surface (original magnification x20). B) Negative control (omission of primary antibody, origin).

Figure 5. Representative routine histological sections of DRT applied 13 days earlier, subsequently over-grafted with STSG, stained with H&E. The dermal regeneration is almost complete and the STSG has attached and is healing.

Figure 6. Immunohistochemical staining for cow collagen I indicating the presence of the DRT (applied 27 days earlier) in the regenerating dermal tissue. A) No presence of stained DRT in the interface between regenerating dermal tissue and the STSG (original magnification x10). B) Negative control (omission of primary antibody; original magnification x10).
that dermal regeneration was almost complete and the STSG had attached (Figure 5). The clinical appearance and physical function of the grafted wound were considered excellent; the skin was smooth and pliable.

Histology revealed rapid and thorough fibroblast and capillary infiltration into the DRT, eventually revealing a neodermis. The DRT functioned as a scaffold for guided dermal regeneration. It was somewhat surprising that immunohistochemistry could not target the DRT after day 18 (Figure 6A, B). The patient returned to full-time work 6 months after the initial surgery. Follow-up photos on day 65 (Figure 7) and 131 (Figure 8) reveal a pliable and aesthetically acceptable result. Routine histology from skin biopsy obtained at day 131 revealed normal skin (Figure 9).

**Discussion**

Necrotizing fasciitis (NF) affects the tissue through thrombosis of skin microcirculation, which results in necrosis, liquefaction of fat, and destruction of muscles. In the presented case, the large underlying muscles of the abdomen and the left flank were also involved, resulting in profound NF. For such defects, wound coverage is usually achieved by using meshed STSG. This provides effective wound closure and imposes limited morbidity. However, there are several drawbacks both in terms of function (ie, wound contracture and hypertrophic scarring) and cosmetic result (meshed grafts usually leave an unsightly “fish-net” appearance). Also, transplanting a skin graft directly onto a wound with little or no dermal component usually renders a poor result.

In the novel protocol described in the presented case, the affected area was initially treated with debridement and antibiotics to control infection. Additionally, the patient had one occasion of HBO treatment according to existing protocols. Continuous negative pressure was used both before and after the wound was covered with the DRT and subsequently the STSG. The first period of
NPWT continued from days 2 to 5 to stimulate the healing process with rapid granulation to ensure that infection was properly treated and that no new necrosis had formed. After the application of the DRT, there was no need for the patient to be immobilized to ensure graft take (the DRT and later on the thin STSG), as the negative pressure dressing kept the grafts fixed for the duration of the treatment (day 5–18). Three months after discharge, the patient had a good cosmetic and functional result. No sign of hypertrophic scarring was seen in the area covered with the DRT. The final clinical appearance and physical function of the grafted wound were regarded as excellent with smooth and pliable skin.

Despite more than 2 decades of clinical use, the take rate of the DRT engraftment remains lower than with autografts and the ideal technique for optimizing take rate remains controversial. Although the original report by Burke et al noted take rates of 95% to 100% of the over grafted ultra-thin STSG on artificial dermis, subsequent authors have not been as successful. Improvements in take rate have been reported with the use of NPWT in combination with the DRT in traumatic cases. In this retrospective study of the DRT used in small, uncomplicated wounds, nearly 100% take rates were achieved. In larger wounds, there are several difficulties in scaling the entire area, including the borders, to maintain a vacuum seal. As the DRT integration progresses, fibroblasts deposit native collagen as the collagen component of the dermal layer is degraded. Normally, dermal regeneration usually takes place over 3–6 weeks if local conditions remain optimal, and an additional 4 days is necessary for epidermal take. In the present case, proper dermal regeneration was achieved after 13 days with good take of the epidermal layer within 3 days after skin grafting.

**Conclusion**

We believe that this is a safe way to proceed when the initial debridement is properly performed. Initial wide debridement with a short delay to wound closure with a collagen matrix, such as the DRT, and a negative pressure device provides rapid recovery and excellent results for the patient in addition to being a safe procedure. The authors believe further study of this concept in different traumatic conditions is necessary.

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