

# Our experience with dermal substitute Nevelia® in the treatment of severely burned patients

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## ABSTRACT

**BACKGROUND:** This research aims to retrospectively evaluate the effectiveness and safety of dermal substitute (DS), Nevelia®, for the treatment of severely burned patients.

**METHODS:** Twenty severely burned patients were enrolled in this study between May 2017 and May 2018. After escharotomy of the wound, the treatment protocol was applied following a two-step procedure –DS implantation followed by split-thickness skin graft (STSG) application. Need for surgery, complications, hospitalisation duration and overall survival were analysed.

**RESULTS:** Mean age was 40.1±4 (18–86) years old; female/male: 5/15. Mean burn surface area was 50.1%±2 (25–96). Two patients died under hospital treatment due to the severity of their burn trauma and comorbidities. For the rest of the cases, STSG was performed after Nevelia® at mean 21.2 days. No complications due to Nevelia® were detected. The patients were discharged with a mean total recovery of 55.2±4 days.

**CONCLUSION:** This study showed that Nevelia® can be used safely and effectively in severely burned patients with low complication rates and short hospital stay.

**Keywords:** Dermal substitute; eschar management; major burn.

## INTRODUCTION

The principle of care in managing severely burned patients is primarily focused on survival. The main issues in the first hours are resuscitation and haemodynamics. After 48 hours, septic problems and eschar management eventually become a critical issue. The insufficiency of skin graft donor sites in severely burned patients is one of the major problems in the management of these patients.

Dermal substitutes (DS) are becoming an important part of burn care with an increasing interest. In the acute phase of

burn treatment, the use of DS ameliorates functional and aesthetic long-term results. DS are bio-matrices that perform the functions of the cutaneous dermal layer, including protecting the subcutaneous tissue from physical factors, acting as a barrier against infections and reducing scarring. DS, which act like matrices or scaffold and support tissue buildup, boost wound healing consequently.<sup>[1,2]</sup> The structure of DS provides flexibility and better scar tissue formation. In both acute and chronic stages, DS has a large part in healing full-thickness skin defects<sup>[3]</sup> and advanced scar quality.<sup>[4]</sup>

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Nevelia® (Symatase Aesthetics, Lyon, France) is made from specific native collagen with a large fibrous proportion to preserve cell adhesion signals and mechanical structure to support regeneration. In vitro test demonstrate an optimised colonisation as fibroblasts recognise collagen fibres. Nevelia® is indicated for dermal regeneration in cases involving skin loss, particularly in burns and trauma. This bi-layer matrix is usually used in combination with a thin split-thickness skin graft (STSG) to recreate skin resembling the normal one in terms of function and appearance. This research describes our experience in using Nevelia® for the treatment of severely burned patients.

## MATERIALS AND METHODS

This retrospective case series study was approved by the Health Sciences University, Bağcılar Education and Research Hospitals' Ethics Committee. This study included patients who were admitted to a burn care unit with severe full-thickness burn wounds [Total Body Surface Area (TBSA)  $\geq 25\%$ ] between May 2017 and May 2018. Their need for surgery, complications, hospitalisation duration and overall survival were analysed. TBSA percentage and TBSA with Nevelia® surface were measured using the Lund and Browder chart.<sup>[5]</sup>

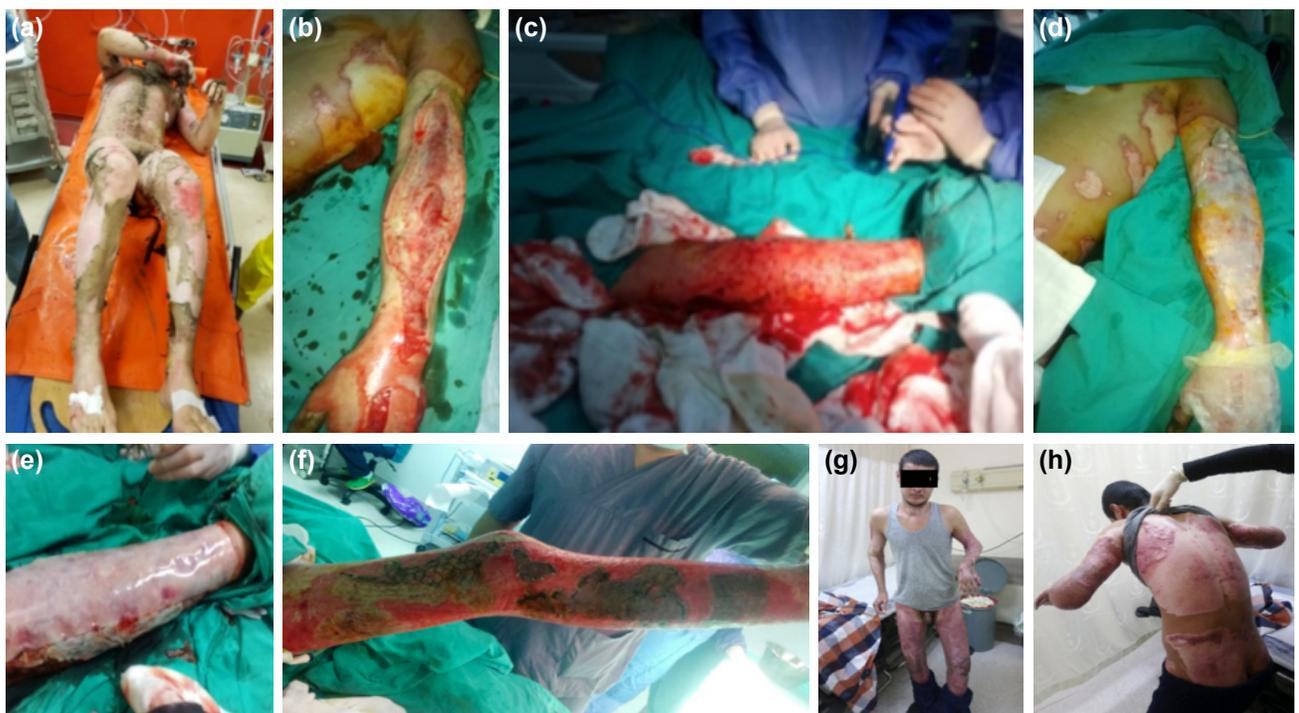
Burn patients were categorised according to a specific clinical burn management protocol designed to stabilise them within 48 to 72 hours. Later, using the SPY® Infrared Fluor-

escence Imaging System (Novodaq, Stryker, US), burn depth was measured. According to the patient's clinical state and tolerance, viable and healthy dermis were protected. Chemical eschar debridement and reepithelisation procedures were performed. In burn areas that were not too deep, self-healing procedures were followed. In areas with a third-degree burn, early eschar excision protocol was used. Then, Nevelia® was applied to the escharotomy areas.

Nevelia® was applied on the burn area using Appose™ Single-Use Skin Stapler (Medtronic, MN, USA) and was dressed with antimicrobial materials. The dressing was changed every two days. Integration of the Nevelia® to the tissues was observed during this time.

The subsequent delamination of Nevelia® (silicone leaf removal) and the timing of split-thickness skin graft application were determined on a case-to-case basis according to the availability and physiological well-being of the subject. Re-harvesting from the same donor site was necessary for some patients. Therefore, the state of re-epithelialization of the skin graft donor site was very important for them. Once delaminated, the surface of the neodermis was refreshed by dermabrasion before meshed STSG was applied and the dressing was performed.

The thickness of harvest and mesh ratio of the STSG was determined clinically on each occasion by donor site availability, and the need for the second harvest from the same



**Figure 1.** Case 1: 23 years old man (Subject 9), burned on 90% of his TBSA following a work accident. (a) The right and left limbs and the trunk were burned and underwent fascial excision. (b, c) Fasciotomy lines. No residual dermal element was left. (d, e) Nevelia® cut to shape and applied with staples. (f) Vascular invasion and collagen deposition complete by Day 20. (g, h) The autograft appearance 90 days after application over the integrated Nevelia® neo-dermis.



**Figure 2.** Case 2: 28 years old woman (Subject 19), burned on 60% of her TBSA following a house accident. (a, b) The right and left limbs and the trunk were burned and underwent fasciotomy and tangential excision. (c, d) Nevelia® cut to shape and applied with staples. Vascular invasion and collagen deposition complete by Day 20. (e, f) The autograft appearance 6 and 12 days respectively after grafting.

donor areas was anticipated. In this study, all grafts applied over Nevelia® were either applied as fenestrated sheet graft (over the dorsum of hands) or meshed 1,5–3, at all other sites. Skin grafts were dressed according to our previous standard of care, typically with paraffin gauze overlaid with saline and antibacterial-soaked gauze secured with crepe bandages. Dressings were changed with graft check at four days and then twice weekly until completely healed.

Photographic records were taken at every intervention (Figs. 1, 2). The punch biopsy specimens of representative areas were taken at various intervals for culture. All subjects received standard physiotherapy scar treatment, which included compression garment therapy.

## RESULTS

### Patient Characteristics

Twenty adult patients aged between 18 and 86 years old (mean age  $40.1 \pm 4$ ) shown in Table 1 were enrolled in this study. Five out of 20 patients were female. Burn incidents had occurred mostly at work and home (45% and 40%, respectively). Seventy percent of the patients were in a closed area and were exposed to inhalation injuries. Full-thickness burn wounds covered 25%–96% of TBSA with a mean surface of  $50.1 \pm 2\%$ . The mean surface receiving Nevelia® was  $8.25 \pm 1\%$  of TBSA (on third-degree burn area).

### Nevelia® application

The colonisation of Nevelia® and mean duration time for the STSG acceptance was  $21.2 \pm 3$  days. Other than two integration failure, no adverse event or complications related to the use of Nevelia® were seen. Patients were discharged with a mean recovery of  $55.2 \pm 4$  days (Table 2).

Among the 20 patients, failure was seen in two patients who had DS Nevelia®. These two cases had burn wound in 92% and 96% of their TBSA with multiple comorbidities. The clinical status of these two patients was critical, and they died from their injuries. Their wound healing was poor, probably because of multiorgan insufficiency.

## DISCUSSION

Patients with severe full-thickness burn wounds require artificial materials due to the deprivation of sufficient donor tissue. Identifying efficient, safe and cost-effective skeleton materials can be stressful. Autologous skin graft is the most preferred material in burn wound coverage; however, especially in extensive full-thickness burn wounds, having limited donor sites can complicate the process. Another distressing point is the presence of donor tissue morbidities regarding having additional wounds and scars. This issue required various skin substitutes for the treatment of acute full-thickness burn wounds.<sup>[6]</sup>

**Table I.** Subject demographics and mechanisms of burn injury

Subject No.	Age	Gender	Burned areas	Mechanisms of burn injury	% TBSA burn	DS area/TBSA (%)
1	68	Male	Lower limbs	The explosion of Liquid Petroleum Gas (LPG) bottle. Enclosed space, inhalation injury.	50	8
2	18	Male	Lower limbs	Working place fire with petrol indoors.	25	3
3	64	Male	Lower limbs and trunk	Working place fire with petrol indoors. Enclosed space, inhalation injury.	50	7
4	39	Male	Upper limbs, lower limbs and trunk	Working place fire. Enclosed space, inhalation injury.	40	5
5	32	Female	Head, upper limbs, lower limbs and trunk	Heroin intoxication. House fire started by cigarette falling into the carpet. Enclosed space, inhalation injury.	92	4
6	86	Female	Lower limbs and trunk	House fire secondary to LPG oven. Enclosed space, inhalation injury.	40	6
7	41	Male	Lower limbs and trunk	Working place fire. Enclosed space, inhalation injury.	40	5
8	62	Male	Upper limbs and trunk	Garden fire explosion.	30	10
9	23	Male	Upper/lower limbs, trunk	Working place fire with the explosion of the water boiler.	90	23
10	38	Male	Upper/lower limbs, trunk	Self-immolation with petrol indoors. Enclosed space, inhalation injury.	96	18
11	25	Male	Upper/lower limbs	Working place fire with gasoline and motor oil. Enclosed space, inhalation injury.	40	4
12	20	Male	Upper/lower limbs, trunk	Working place fire with gasoline. Enclosed space, inhalation injury.	75	10
13	25	Male	Lower limbs	Bonzai intoxication. House fire started by cigarette falling into the carpet. Enclosed space, inhalation injury.	32	16
14	40	Male	Upper/lower limbs, trunk	Working place burn with high voltage electricity.	32	6
15	32	Male	Upper limb, trunk	Bonzai intoxication. House fire started by cigarette falling into gasoline.	33	8
16	23	Female	Upper limb, trunk	House fire secondary to deodorant gas.	30	6
17	32	Male	Upper/lower limbs	Working place fire secondary to the electrical fault. Enclosed space, inhalation injury.	40	4
18	45	Male	Upper limb, trunk	Alcohol intoxication. House fire started by cigarette falling into the carpet. Enclosed space, inhalation injury	41	7
19	28	Female	Upper limb, trunk	Alcohol intoxication. House fire started by cigarette falling into the carpet. Enclosed space, inhalation injury	60	9
20	53	Female	Upper/lower limbs, trunk	Suicide attempt by opening the home natural gas. Home fire secondary to electrical spark. Enclosed space, inhalation injury.	45	6

At present, there are numerous DS products available commercially. Most of these products have been extensively tested and examined in both pre-clinical and clinical settings.<sup>[7-10]</sup> In the last 1-year period, we have applied Nevelia® to several escharotomy areas of some of our severely burned patients.

Many of the present biocompatible DS can mimic the basic properties of the extracellular matrix in human skin by providing some structural integrity, elasticity and vascular bed. It reduces evaporative water loss, and the exudation of protein-rich fluids prevents wound desiccation and suppress micro-

**Table 2.** The number of days for the DS integration, the length of stay, adverse events suffered by each subject, classified as those related to the burn injury and its pathophysiological evolution, and those related to the DS

Subject No.	Total days of DS to integrate	Failure of DS integration	Comorbidities/ clinically relevant situation	Burn-related AE	Length of stay (days)	Result
1	21	–	Hypertension	Lower airway inhalation injuries, Pneumonia	83	Discharged with recovery
2	22	–	–	–	28	Discharged with recovery
3	20	–	Hypertension	–	66	Discharged with recovery
4	21	–	–	–	46	Discharged with recovery
5	21	Failure of DS integration in one of six areas.	Drug abuse	Significant lower airway inhalation injuries Pneumonia Pseudomonas, Acinetobacter, candida Acute renal injury requiring dialysis ileus, abdominal compartment syndrome,	23	Death
6	21	–	Alzheimer, hypertension	Pneumonia Pseudomonas, Acinetobacter in the wound, candida in the blood Small graft breakdowns on the trunk and lower limb	125	Discharged with recovery
7	20	–	–	–	64	Discharged with recovery
8	23	–	Kidney transplant (5 years ago)	Lower airway inhalation injuries Significant wound healing delay Pseudomonas, acinetobacter in the wound,	72	Discharged with recovery
9	23	–	–	Significant lower airway inhalation injuries, Pneumonia, ventilation support. Ileus, abdominal compartment syndrome, Pseudomonas, Acinetobacter in the wound	98	Discharged with recovery
10	16	Failure of DS integration in one of six areas.	–	Significant lower airway inhalation injuries, pneumonia, ventilation support. Abdominal compartment syndrome, open abdomen by Bogota bag Acute renal injury requiring dialysis	16	Death
11	23	–	–	Significant lower airway inhalation injuries, pneumonia.	35	Discharged with recovery
12	21	–	–	–	75	Discharged with recovery
13	22	–	Drug abuse	–	62	Discharged with recovery
14	20	–	–	–	45	Discharged with recovery
15	21	–	–	–	43	Discharged with recovery
16	20	–	–	–	32	Discharged with recovery
17	21	–	–	–	62	Discharged with recovery
18	23	–	Alcoholism. Child a cirrhosis due to alcohol.	Lower airway inhalation injuries	45	Discharged with recovery
19	23	–	Drug abuse and alcoholism.	–	50	Discharged with recovery
20	22	–	Alcoholism	Lower airway inhalation injuries, pneumonia, she needed mechanical ventilation support.	51	Discharged with recovery

bial proliferation. However, these products lack the epithelial layer, and in most cases, the use of such products will generally be followed by the inoculation of the split-thickness skin autograft for permanent coverage in a two-step procedure. We applied a split-thickness skin autograft after a mean of 21.4 days from the application of Nevelia®.

In severe burns, various options are available after the clinicians perform early escharotomy. These options include allograft usage, DS, keratinocyte autoculture or antimicrobial dressing material application. Allograft usage may pose problems because of rejection and infection. Antimicrobial dressing material application generally does not provide the patient with enough protection from bacteraemia. Keratinocyte autoculture has not progressed to qualify for routine clinical usage.

Identifying a successful material that will be helpful during the eschar management period is very important. In recent years, DS has played important roles in burn treatment protocols. After escharotomy, an effective DS is very helpful in building a protection cover for the body. If DS is effective, then, the survival percentage of the patient increases.

There is still a possibility of harvest morbidity that may be inadequate in donor sites in wide burn areas. As indicated in the literature,<sup>[11]</sup> the use of Nevelia® allows us to harvest thinner split-thickness skin autografts and thus donor sites heal faster. These materials are also helpful in improving the elasticity of the skin after split-thickness skin graft application.

Despite the potential and need for DS, further research is required to strengthen the scientific evidence of the potential impacts and to develop new technologies and products.<sup>[12,13]</sup> However, these substitutes have significant limitations when used in the presence of infections or full-thickness defects.<sup>[14]</sup> In our case series, integration failed only in two of the 20 cases. These two cases had burn wound in 92% and 96% of their TBSA and had many comorbidities. Their clinical status was critical, and they died from their injuries. Their wound healing was poor, probably due to multiorgan insufficiency.

DS appear as a key research strategy to improve sufficient scaffolds to obtain long-lasting and scarred artificial skin for stem cells, regenerative medicine applications and tissue engineering.<sup>[15,16]</sup> Integra® Dermal Regeneration Template (Integra Life Science, NJ, USA) is a widely used for covering excised full-thickness burn wounds and has proven to be particularly valuable in patients with large burns and limited autograft donor sites.<sup>[11,17]</sup> Integra® consists of the following two layers: a DS made of porous bovine collagen and chondroitin-6-sulfate glycosaminoglycan and an epidermal substitute made of a synthetic silicone polymer. The dermal layer serves as a matrix for infiltration by fibroblasts and other cells from the wound bed. De Angelis B et al. reported that Nevelia® had early regenerative properties in epidermal proliferation

and dermal regeneration when compared with that of Integra. The study also showed that Nevelia® revealed more pronounced angiogenesis against Integra®, which was evaluated with  $\alpha$ -SMA immunohistochemistry.<sup>[10]</sup> In the present study, we found good integration and wound healing process with Nevelia®.

## Conclusion

The findings of the present study provide favourable results of incorporating Nevelia® in our daily practice for the treatment of severely burned patients. Authors conclude that Nevelia® is safe as well as easy to use. Additionally, graft loss over Nevelia® is unusual.

**Conflict of interest:** None declared.

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## OLGU SERİSİ - ÖZET

### Ağır yanık hastalarının tedavisinde deri eşdeğeri Nevelia® deneyimimiz

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**AMAÇ:** Bu araştırma, ağır yanık hastalarının tedavisinde deri eşdeğeri, Nevelia®'nin etkinliğini ve güvenliğini geriye dönük olarak değerlendirmeyi amaçlamaktadır.

**GEREÇ VE YÖNTEM:** Mayıs 2017–Mayıs 2018 tarihleri arasında çalışmamıza 20 ağır yanıklı hasta alındı. Eskarektomiden sonra yara tedavi protokolü iki aşamalı bir prosedürle uygulandı. Deri eşdeğeri implantasyonunu kısmi kalınlıkta deri grefti takip etti. Ameliyat ihtiyacı, komplikasyonlar, hastanede kalış süresi ve genel sağkalım analiz edildi.

**BULGULAR:** Yaş ortalaması 40.1±4 (18–86), kadın/erkek: 5/15 idi. Ortalama yanma yüzey alanı %50.1±2 (dağılım, 25–96) idi. Yanık travmalarının ve yandaş hastalıklarının ciddiyeti nedeniyle iki hasta kaybedildi. Olgularda greft, Nevelia® uygulamasından ortalama 21.2 gün sonra yapıldı. Nevelia® kaynaklı herhangi bir komplikasyon gelişmedi. Hastalar ortalama 55.2±4 günde taburcu edildi.

**TARTIŞMA:** Bu çalışma Nevelia®'nin düşük komplikasyon oranları ve kısa hastanede yatış süresi ile ağır yanık hastalarında güvenli ve etkili bir şekilde kullanılabileceğini göstermiştir.

**Anahtar sözcükler:** Ağır yanık; eskar yönetimi; deri eşdeğeri.

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