White Paper

Dr. Herbert Haller
Dr. Bernd Hartmann
Dr. Frank Sander

White Paper on the Use of **SUPRA**THEL® after Enzymatic Debridement with Nexobrid®

Learn more about **SUPRA**THEL®

White Paper on the Use of Suprathel® after Enzymatic Debridement with Nexobrid®

B. Hartmann,* F. Sander*, H. Haller,**

Enzymatic debridement (ED) is used for selective eschar removal in deep burns, which preserves the healthy epidermal and dermal parts of the skin. With ED, the extent of the area requiring grafting and the donor area is smaller. After debridement, supporting the undisturbed healing of cutaneous and epidermal structures is recommended[1]. Exsiccation and other factors can deepen the burn. Therefore, a dressing that promotes the healing of epidermal structures and protects dermal structures is necessary; this can be achieved using Suprathel®[2].

WHICH WOUNDS ARE NOT SUITABLE FOR ED:

In burn injuries pretreated with silver sulfadiazine (SSD), other silver products, and iodine, ED have been described to be less successful[1]. In general, enzyme-inactivating products such as copper and heavy metals should be avoided[3].

The effectiveness of ED in scald injuries might be even lesser[4]. A 100% consensus was reached for this statement among 12 participants in the 2020 consensus[5]. Incomplete debridement can also occur, happened especially during "early" debridement and in old people.

There is no evidence for the treatment of c**hemical burns** with ED[1,4].

ED is not indicated during surgical release for **extended trunk burns in patients with established respiratory compromise, established compartment syndrome** in the extremities, **and high voltage injury**[5]. ED is **not recommended** in **diabetic feet and fresh scald injuries**[4].

ED is highly recommended for deep facial burns and shows excellent results; however, special preparations are needed to protect the sensory organs[6].

* *Zentrum für Schwerbrandverletzte mit plastischer Chirurgie am Unfallkrankenhaus Berlin, Germany;*

***HLmedConsult, Austria*

POTENTIAL SIDE EFFECTS OF BROMELAIN:

Potential cytotoxicity of ED with respect to keratinocytes and fibroblasts was confirmed but only in vitro[7]. During ED, wound fluid digested the collagen-elastin matrix Matriderm™ for up to 240 minutes. After 240 minutes, the effect was negligible. Since bromelain is generally toxic to skin cells[7], burn wound fluid dilutes its cytotoxic effects while simultaneously affecting the remaining tissues[8]. In vitro data from animal experiments indicate that bromelain can promote fibrinolysis. Inhibition of cytochrome-P450-2C8 and cytochrome-P450-2C9 results in the enhancement of effects of different drug (amiodarone, amodiaquine, chloroquine, fluvastatin, paclitaxel, pioglitazone, repaglinide, rosiglitazone, sorafenib, torasemid, ibuprofen, tolbutamide, glipizide, losartan, celecoxib, warfarin, and phenytoin). Bromelain can increase the effect of angiotensin-converting-enzyme inhibitors, fluorouracil, vincristine, benzodiazepines, barbiturates, narcotics, and antidepressant agents[9].

WOUND BED PREPARATION BEFORE ED:

Wounds should be cleaned by removing blisters and denatured keratin layers by brushing or surgical means, if necessary. Late burns with dry

eschars require mechanical removal of the dried superficial levels and prolonged presoaking for up to 12 hours[5].

PRESOAKING:

Fresh and moist wounds can be treated immediately. Otherwise, moisturizing for a minimum of 2 hours is recommended. A solution of 0.9% NaCl or another suitable disinfectant solution (e.g., polyhexanide) can be used for this purpose.

TIMING OF ED:

- After an update of the European consensus, the timing was classified as **very early** (within 12 hours of injury), **early** (between 12 and 72 hours), and **delayed** (after 72 hours)[4].
- It is suggested that ED be performed as early as possible **to prevent compartment syndrome** in patients with circumferential burns of the extremities and extensive trunk burns. However, surgery is suggested when respiratory compromise is established, as in these cases[4].
- In general, it is suggested that ED be performed within 72 hours of injury by the European consensus. Later application is possible in "selected patients" after appropriate preparation (surgical removal of superficial layers followed by treatment or prolonged pre-soaking). Complete eschar removal should be performed within the first 7 days of injury[1].

Spanish experts indicate that ED be performed within 24-48 hours of admission. They agree that it should be performed within 7 days of injury. When immediate ED is not possible, the use of Mepilex, with Prontosan® or Vaseline gauze and nitrofurazone as a temporary cover, is suggested [10].

LIMITATION OF THE AREA FOR ED:

According to the **regulatory constraints**, 15% of the total body surface area (TBSA) should be considered for ED, and larger areas should be debrided in successive interventions. Spanish experts suggest active treatment against **hypothermia** (when necessary) when presoaking and post-soaking are performed simultaneously in one patient.

Hypothermia, due to soaking, is a contradiction to **hyperthermia, a possible side effect of ED**. Therefore, soaking can be used to reduce the hyperthermic side effect of ED[10].

Areas corresponding to more than 15% of the TBSA could be debrided in one session without adverse effects[11], as described **by** Hofmaenner et al., **who** treated areas corresponding to a median of 18% (interquartile range, 15–19) of the TBSA in one session.

PAIN TREATMENT:

For ED, **proper analgesia**, sometimes in the form of general anesthesia, is necessary. This requires monitoring and ventilation facilities, at least on standby.

Regional anesthesia, including anesthesia using catheter techniques, has been suggested for the treatment of extremities[1]. Plexus anesthesia can be used for a prolonged period, covering the post-soaking period and the first dressing change[12].

Further anesthesia is usually not required. Pain levels reported during ED were low in general. Sympathicolysis with regional anesthesia can optimize wound bed perfusion and support healing.

Another option is tumescence anesthesia with long-lasting anesthetics.

Nevertheless, there have been episodic reports

about severe pain during ED despite proper anesthesia for unknown reasons.

TIMING OF APPLICATION OF NEXOBRID:
ED treatment itself should last for 4 hours as per a consensus between all expert groups. Experts do not suggest a repetition of enzyme application on the same wound. Prolonged exposure to enzymes for some more hours does not cause harm[1].

CHOICE OF DRESSINGS AFTER ED:
Expert panels agree on applying a dressing post-ED, protecting the wound from desiccation[13]. Dr. Martinez suggests covering areas with Suprathel®, which has regenerative potential for spontaneous healing, and using a hydrocolloid in regions that need grafting [10]. Dos Santos followed the same algorithm[14] for burns on the hands.
Treatment with a silicone dressing before additional debridement and grafting was linked to prolonged healing time in the Berlin study[15]. In such cases, early debridement or the use of Suprathel® as a temporary dressing can be considered.

SOAKING AFTER ED (WET TO DRY PROCEDURE):
The "**wet to dry procedure**" involves the treatment of the wound with soaked cotton material after ED and and leaving it in place until drying is suggested. When the wounds are dry, the pads are gently removed and replaced by other moistened drapes. Changing the dressing also removes adhering debris, further cleaning the wound. Experts have increased the duration of post-soaking from 2 hours to 4 hours or more.
Monclus[10] suggested **prolonging the time of post-soaking** independently from later cover or grafting of three post-soaking procedures, each accounting for a total of 8 hours. Other authors have described a post-soaking period of 4–12 hours (mostly performed overnight)[12].
The European consensus suggests post-soaking with polyhexanide, whereas Spanish experts suggest the use of polyhexanide or soapy chlorhexidine.

WOUND ASSESSMENT AFTER ED:

Assessment based on the following factors should be performed within 2 hours of treatment:

Condition of the wound bed and chance of healing, according to the 2017 Consensus	**Chance of spontaneous healing**
Red or pink	High chance of spontaneous healing
White wound bed with pin-point punctate bleeding	Good chance of healing with acceptable results
Red circles or oval patterns of large diameters	Prolonged healing time; grafting should be considered
Exposed fat	Grafting necessary

GRAFTING AFTER ED:

The **European consensus** suggests traditional grafting, when necessary, after at least 2 days 1. According to Spanish experts, grafting with autologous skin should not be performed before 3–5 days have passed due to increased secretion from the wound. After ED, **wounds often produce large amounts of fluid and debris**. Therefore, tight dressings can cause retention and "swimming off" of the dressing.

This condition is excellently described as a "slimy coat, which consists of exudation from the increased bed swelling and dissolved eschar"[12]. The presence of debris in the wound can increase the risk of infection. Exudation and debris can reduce graft take and increase the risk of dressing dislocation. Increased production of fluid containing debris can occur actively over hours and even for days.

INCOMPLETE REMOVAL OF DECAYED MATERIAL AFTER NEXOBRID TREATMENT

Rosenberg described that in 75% of cases, a single application of Debrase® was sufficient to remove all necrotic tissue in mixed burns[16]. Schulz reported the complete removal of necrotic tissue, not requiring further action, in 90 % of cases[17]. In Berlin, a retrospective evaluation of 56 patients with 104 wounds described residual necrosis in 33% of the wounds or 14% of the regions[15].

As the microscopic completeness of necrotic tissue removal is challenging to evaluate in a clinical situation, one can assume that a small proportion of necrotic tissue can remain, which is not visible on simple inspection. Self-cleaning over a specific period or actions to clean the wound before definitive closure with grafts or dressings might be necessary. Necrotic tissue can be found at different times, even when no necrotic tissue was visible before.

Necrosis observed immediately after ED:

The European consensus suggests "additional eschar removal by hydrosurgery or standard of care"[1] if non-vital tissue is found after ED, to achieve complete eschar removal within 7 days. There are no further suggestions for grafting in this context.

Residual necrosis observed after some days during the first dressing change:

This type of necrotic tissue is generally addressed as **pseudoeschar**. The European consensus defines pseudoeschar as "a specific layer sticking to the wound that may develop several days after treatment"[1]. The experts' therapeutic advice is to leave it in place and "consider" surgical debridement after more than 14 days.

The risk of infection may advocate early surgical removal.

Late necrosis detected after more than 1 week during a dressing change:

Such late pseudoeschar formation was attributed to the use of SSD creams by Palao[18]. Nevertheless, the Berlin group described late pseudoeschar development under silicone dressings when no early pseudoeschar had been visible. Grafting after surgical removal of this late necrosis was linked with prolonged healing time.

EXPERIENCE FROM BERLIN:

The "Zentrum für Schwerbrandverletzte mit Plastischer Chirurgie Berlin" is one of the biggest burn centers in central Europe and has longstanding experience with ED. They investigated 56 patients, of whom 42 were treated with Suprathel®[15]; the others with silicone dressings.

Even when no necrotic tissue was detected directly after ED, necrotic tissue or pseudoeschar

could be found later. The origin of this necrotic tissue is unclear. It may be derived from thermal injury, toxic or delayed effects of the enzymes used, or burn wound progression. Di Lonardo et al. observed that the lytic action of bromelase spared partially damaged dermis[19] and stated that it might develop into a neo-eschar by desiccation.

ED complete:

When **ED was completed**, a **dermal layer with regenerative potential** (no visible subcutaneous fat or vessels) with **no necrotic tissue** can be found **during the first dressing change**; the chance for undisturbed healing under Suprathel® without the need for further operative procedures is high. The expected total healing time was approximately 27 days, with an estimated percentage of spontaneous healing of 75%. Healing after grafting (25%) due to different factors occurs within the same time frame[15]. In these patients, a reduction in grafting and donor areas can be confirmed.

Pseudoeschar:

In all patients showing **early and late pseudoeschars**, debridement and grafting were performed on day 7. The corresponding healing time was 23 days in the Suprathel® group, which was shorter than that in the silicone group, regardless of grafting.

When a **late pseudoeschar presents after initial complete debridement, grafting** after the removal of all necrotic tissues is suggested.

Completely debrided wounds with regenerative potential **without early pseudoeschar can be treated conservatively with Suprathel® or grafted based on the extent** of injury or bacterial growth, most of the **other wounds benefit from early debridement and grafting.**

When a wound **shows residual necrosis after ED, debridement and grafting are indicated, even after a short treatment period with Suprathel® to avoid a prolonged healing period. The area to be transplanted could not be reduced in** patients who underwent later operation. Conservatively treated patients did not undergo transplantations.

WHAT CAN BE A STANDARD SCHEDULE FOR AND AFTER ED:

Wound cleaning	1 h
Presoaking	0-4 h
Application of ED	4 h
Removal of debris	0.2 h
Evaluation: wound depth, residual necrosis, staging of wound (1-4)[18]	Residual necrosis Yes/No
1st wet to dry procedure	4 h
2nd wet to dry procedure	Till the next morning
Complete removal of residual necrosis (Versajet, Weck)	
First dressing	Jelonet and Polyhexanide
First dressing change on day 3 or 4	

WHAT CAN BE A STANDARD SCHEDULE FOR AND AFTER ED:

Evaluation: Pseudoeschar (YES or NO)	Early pseudo eschar Y/N
Removal of necrotic tissue + dressing (Suprathel®) or grafting	Day 3 or 4
Dressing on day 7 (Infection: YES or NO)	Day 7 or 8 Late Pseudoeschar Y/N
Leaving the dressing in place or debridement and grafting	

Conclusion:

Burn wound treatment after ED with Suprathel® results in a shorter healing time as compared to that with silicone membranes, both in spontaneously healed and operated wounds. Necrotic tissues should be removed early.

Suggested indications for surgery after ED

Based on the wound status:

- **Visible fat** or no dermal remnants indicate grafting after 4 days, as suggested by the European consensus.
- **Visible residual necrosis after ED** must be removed, as this contributes to a prolonged healing period.

Based on the wound progress:

- **Early pseudoeschars** represent necrosis that was not visible in the first evaluation after ED. If they are not visibly superficial, it is recommended to remove them to avoid a prolonged healing period and infection.
- **Late pseudoeschars** represent necrosis that was not visible before or was not removed in the prior evaluations. It has to be treated in the same way as mentioned above.
- **Wounds not healed within 3 weeks without a tendency for repair** should be considered for grafting, although Hoecksema et al. successfully challenged the rule of 21 days[20]. Although a prolonged healing duration can be expected without grafting, higher rates of hypertrophic scars were not found.

RECOMMENDATIONS FOR SUPRATHEL® AFTER ED

The European consensus summarized their experience after treating more than 500 patients but did not recommend any special dressing after the ED procedure. In this consensus, the participants **recommended dressings or templates that provide comfort and reduce pain and the frequency of dressing changes**[1]. Suprathel® has all of these properties. In other publications, some authors from this consensus explicitly confirmed that Suprathel® is an appropriate dressing after ED[12].

In the Spanish consensus, Suprathel® is described as the preferred dressing after ED because of its properties. Furthermore, seven experts from the central Spanish burn units who have treated >350 patients with ED recommended Suprathel®[10]. At the 18th European Burns Association Congress (EBA) in 2019, multiple posters showing positive results with Suprathel® after ED were presented.

WHEN NOT TO USE SUPRATHEL®:

In cases where pain could not be sufficiently controlled by analgesia during ED, Suprathel® should not be expected to reduce pain sufficiently. There is a high possibility that pain cannot be cont-

rolled by the pain-reducing effects of Suprathel® alone.

WHY USE SUPRATHEL®?

Suprathel® is a bioactive dressing. Polymers from polyhydroxy acids, mainly based on polylactic acid, have been successfully used in burn treatment for nearly 20 years. There is significant evidence for various clinical benefits of Suprathel® such as pain reduction, reduced workload, short healing time, and low complication rates. This provides excellent cosmetic results in superficial, deep partial-thickness, and even small full-thickness burns[2,21–28]. It has a lower infection rate than Mepitel and Flaminal and reduces burn wound progression[29].

It acts as an energy source for cells by providing external lactate and pyruvate, which fuels energy metabolism in the cells[30,31]. Simulating a hypoxia-like state in wounds without oxygen reduction releases multiple growth factors with effects on fibroblasts, keratinocytes, the extra-cellular matrix, and endothelial cells[32,33]. By supporting wound healing, it reduces burn wound conversion and the need for grafting[29,34].

PRECAUTIONS DURING SUPRATHEL® TREATMENT:

- We suggest the application of disinfectants over the inner dressing (Suprathel® and separation layer) with polyhexanide gel or similar compounds.
- When dressings above the wounds are still wet after 14 days, check for hypergranulation or infection based on the residual necrotic tissue.
  - o In the case of developing hypergranulation, consider the use of a topical corticoid ointment.
  - o In severe cases, surgical debridement might be necessary.
- When the time of healing is prolonged (> 3 weeks), consider using autografts. Spontaneous healing under Suprathel® can only work in areas with enough dermal remnants; otherwise, the wound will heal from the margins over a long time. The longer the healing time due to diminished resources for epithelialization, the worse will be the scar quality.
- Perform compression using elastic bandages over the primary dressing to avoid edema for mation and dislocation of Suprathel®, especially in strongly exudative wounds. This also works as scar prophylaxis.

HOW LONG CAN SUPRATHEL® TREATMENT BE CARRIED ON AFTER ED?

The European consensus suggests checking for the need of autografts after a treatment period of 3 weeks to reduce scarring.

Hoeksema demonstrated that even after extended treatment, the rate of hypertrophic scars was not elevated with the use of topical corticosteroids[20]. The healing duration observed was 32, 7 days on average, ranging from 22 to 57 days.

Nevertheless, a prolonged healing period should be avoided, as it has psychological and social consequences.

REFERENCES

1. Hirche C, Citterio A, Hoeksema H, et al. Eschar removal by bromelain based enzymatic debridement (Nexobrid®) in burns: An European consensus. Burns. 2017;43(8):1640-1653. doi:10.1016/j. burns.2017.07.025.
2. Uhlig C, Rapp M, Hartmann B, et al. Suprathel-an innovative, resorbable skin substitute for the treatment of burn victims. Burns. 2007;33(2):221-229. doi:10.1016/j.burns.2006.04.024.
3. Schulz A, Fuchs PC, Hans N, et al. Inhibition of Bromelain Activity during Enzymatic Debridement of Burn Wounds Pretreated with Frequently Used Pro-

ducts. J Burn Care Res. 2018;39(3):413-422. doi:10.1097/BCR.0000000000000609.
4. Heitzmann W, Fuchs PC, Schiefer JL. Historical perspectives on the development of current standards of care for enzymatic debridement. Med. 2020;56(12):1-8. doi:10.3390/medicina56120706.
5. Schulz A, Fuchs PC, Rothermundt I, et al. Enzymatic debridement of deeply burned faces: Healing and early scarring based on tissue preservation compared to traditional surgical debridement. Burns. 2017;43(6):1233-1243. doi:10.1016/j. burns.2017.02.016.
6. Schulz A, Fuchs PC, Oplaender C, et al. Effect of Bromelain-Based Enzymatic Debridement on Skin Cells. J Burn Care Res. 2019;40(4):444-450. doi:10.1093/jbcr/irx011.
7. Ferrara JJ, Dyess DL, Luterman A, et al. The suppressive effect of subeschar tissue fluid upon in vitro cell-mediated immunologic function. J Burn Care Rehabil. 1988;9(6):584-588.doi:10.1097/00004630-198811000-00002.
8. EMA. Anhang 1: Zusammenfassung der Merkmale des Arzneimittels. :1-71. https://www.ema.europa.eu/en/documents/product-information/nexobrid-epar-product-information_en.pdf.
9. Martínez-Méndez, José-Ramón, Jordi Serracanta Domènech, Enrique Monclús-Fuertes, Dolores Pérez del Caz, Eugenia López-Suso, Juan de Dios García Contreras and J-MP-P. Guía clínica de consenso en el uso de desbridamiento enzimático en quemaduras con NexoBrid® Consensus guideline about the use of the enzimatic debridement Material y método. Chir Plast Ibero-Latinoamericana. 2017;43(2):193-202.
10. Hofmaenner DA, Steiger P, Schuepbach RA, et al. Safety of enzymatic debridement in extensive burns larger than 15 % total body surface area. Burns. 2020:1-9. doi:10.1016/j.burns.2020.10.012.
11. Schulz A, Perbix W, Shoham Y, et al. Our initial learning curve in the enzymatic debridement of severely burned hands—Management and pit falls of initial treatments and our development of a post debridement wound treatment algorithm. Burns. 2017;43(2):326-336. doi:10.1016/j.burns.2016.08.009.
12. Mu M, Ziegler B, Fischer S, et al. In view of standardization: Comparison and analysis of initial management of severely burned patients in Germany, Austria and Switzerland. Burns. 2015;41(1):33-38. doi:10.1016/j.burns.2014.08.021.
13. Verdaguer e BJDSBSJA-SJ, Dos Santos BP, Serracanta J, Aquuilera-Saez J, Verdaguer e BJ, Verdaguer e BJDSBS JA-SJ, et al. Designing an algorithm for the use of Suprathel® following enzymatic debridement with Nexobrid® in burn injuries in hands. EBA 2019 e-poster. 2017. doi:https://doi.org/10.26226/morressier.5d1df08674846b60c6f392da.
14. Sander F, Omankowsky A, Radtke F, et al. Do Dressing Materials Influence the Healing Time after Enzymatic Debridement? 2019:4. doi:https://doi.org/10.26226/morressier.5d1df08674846b60c6f39307.
15. Singer AJ, McClain SA, Taira BR, et al. Rapid and selective enzymatic debridement of porcine comb burns with bromelain-derived Debrase®: Acute-phase preservation of noninjured tissue and zone of stasis. J Burn Care Res. 2010;31(2):304-309. doi:10.1097/BCR.0b013e3181d0f4d4.
16. Loo YL, Goh BKL, Jeffery S. An Overview of the use of Bromelain-Based Enzymatic Debridement (Nexobrid®) in Deep Partial & Full Thickness Burns: Appraising the Evidence. J Burn Care Res. 2018;(April):1-9. doi:10.1093/jbcr/iry009.
17. Palao R, Aguilera-Sáez J, Serracanta J, et al. Use of a selective enzymatic debridement agent (Nexobrid®) for wound management: Learning curve. World J Dermatology. 2017;6(2):32. doi:10.5314/wjd.v6.i2.32.
18. Di Lonardo A, Nardini V, De Rosa M, et al. Enzymatic escharolysis with Nexobrid® on partial thickness burn wounds: Pre-and post-debridement histological assessment. Ann Burns Fire Disasters. 2018;31(1):23-27.
19. Hoeksema H, , K. Claes , K. De Meyere ND, Sommeling C, et al. Annals of Burns and Fire Disasters. Ann Burn Fire disasters,. 2017;Abstracts(Sept.):60. https://www.eba2017.org/en/Abstracts_20_901.html.
20. Schwarze H, Küntscher M, Uhlig C, et al. Suprathel®, a New Skin Substitute, in the Management of Partial-Thickness Wounds. Ann Plast Surg. 2008;60(2):181-185. doi:10.1097/SAP.0b013e318056bbf6.
21. Uhlig C, Rapp M, Dittel KK. Neue Strategien zur Behandlung thermisch geschädigter Hände unter Berücksichtigung des Epithelersatzes Suprathel®. Handchirurgie Mikrochirurgie Plast Chir. 2007;39(5):314-319. doi:10.1055/s-2007-965234.
22. Schwarze H, Küntscher M, Uhlig C, et al. Suprathel®, a new skin substitute, in the management of partial-thickness burn wounds: Results of a clinical study. Ann Plast Surg. 2008;60(2):181-185. doi:10.1097/SAP.0b013e318056bbf6.
23. Blome-Eberwein SAM, Patrick Pagella RN C, Deborah Boorse RN C, et al. Results from Application of an Absorbable Synthetic Membrane to Superficial and Deep Second Degree Burn Wounds. Am Burn Assoc Annu Conf Boston, MA. 2014. http://www.silon.

com/wp-content/uploads/2014/09/ECPB2014-Results-from-Application-of-an-Absorbable-Synthetic-Membrane.pdf. Accessed December 20, 2020.

24. Glik J, Kawecki M, Kitala D, et al. A new option for definitive burn wound closure – pair matching type of retrospective case–control study of hand burns in the hospitalised patients group in the Dr Stanislaw Sakiel Centre for Burn Treatment between 2009 and 2015. Int Wound J. 2017;14(5):849-855. doi:10.1111/iwj.12720.
25. Held M, Rothenberger J, Engelke AS, et al. Evaluation of commonly used temporary skin dressings and a newly developed collagen matrix for treatment of superficial wounds. Adv Ski Wound Care. 2015;28(12): 551-554. doi:10.1097/01.ASW.0000473136.66014.69.
26. Kaartinen IS, Välisuo PO, Alander JT, et al. Objective scar assessment - A new method using standardized digital imaging and spectral modelling. Burns. 2011;37(1):74-81. doi:10.1016/j.burns.2010.03.008.
27. Behr B, Megerle KO, Germann G, et al. New concepts in local burn wound therapy. Handchirurgie Mikrochirurgie Plast Chir. 2008;40(6):361-366. doi:10.1055/s-2008-1039062.
28. Blome-Eberwein SA, Amani H, Lozano D, et al. 501 Second-Degree Burn Care with a Lactic Acid Based Biodegradable Skin Substitute in 229 Pediatric and Adult Patients. In: Journal of Burn Care & Research.Vol 39.;2018:S223-S223. doi:10.1093/jbcr/iry006.423.
29. Lampe KJ, Namba RM, Silverman TR, et al. Impact of lactic acid on cell proliferation and free radical-induced cell death in monolayer cultures of neural precursor cells. Biotechnol Bioeng. 2009;103(6):1214-1223. doi:10.1002/bit.22352.
30. Herz H, Blake DR, Grootveld M. Multicomponent investigations of the hydrogen peroxide- and hydroxyl radical-scavenging antioxidant capacities of biofluids: The roles of endogenous pyruvate and lactate. Free Radic Res. 1997;26(1):19-35. doi:10.3109/10715769709097781.
31. Miller BF, Fattor JA, Jacobs KA, et al. Lactate and glucose interactions during rest and exercise in men: Effect of exogenous lactate infusion. J Physiol. 2002;544(3):963-975.doi:10.1113/jphysiol.2002.027128.
32. Philp A, Macdonald AL, Watt PW. Lactate--a signal coordinating cell and systemic function. J Exp Biol. 2005;208(Pt 24):4561-4575. doi:10.1242/jeb.01961.
33. E. Schriek; M. Sinnig. The Use of Caprolactone Dressing in Pediatric Burns - A Gold Standard? ABA 2018. 2018.
34. E. Schriek; M. Sinnig. The Use of Caprolactone Dressing Pediatric Burns - A Gold Standard ? ABA 2018. 2018.