ENZYMATIC DEBRIDEMENT WITH NEXOBRID® REDUCES SURGERY IN LASER DOPPLER IMAGING-CONFIRMED DEEP BURNS

LE COUPLAGE LASER DOPPLER- EXCISION ENZYMATIQUE AU NEXOBRID® PERMET DE RÉDUIRE LE RECOURS À LA CHIRURGIE EN CAS DE BRÛLURE

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SUMMARY. In contrast to tangential excision, enzymatic debridement with NexoBrid® selectively removes non-viable tissue, allowing some deep dermal burn wounds to still heal conservatively. In this retrospective study, we investigated the reduction in surgery and associated scarring following enzymatic debridement in definitely deep burns as proven by laser Doppler imaging. One hundred two *exclusively laser Doppler imaging-blue regions of interest* where there was no doubt at all about the surgical indication, were selected for analysis in 32 patients treated with NexoBrid®. The total surface area of the 102 *exclusively blue regions of interest* was 5,086.4cm². NexoBrid® resulted in a substantial reduction in the need for autografts as 1,986.9cm² (39%) healed with conservative treatment. This corresponded with a significant reduction in patients (56.3%) requiring surgery. *Exclusively laser Doppler imaging-blue regions of interest* treated surgically with split thickness skin grafts required significantly more time to heal compared to conservative treatment (37.8±17.5 vs. 27.0±10.5 days). A very limited rate of hypertrophic scarring (16.7%) was observed. This is the first paper demonstrating a proven and significant reduction in the extent of autografting as well as in the number of surgical procedures after selective enzymatic debridement in objectively laser Doppler imaging-defined and therefore proven deep burns. Even after extended conservative treatment with prolonged healing times following NexoBrid®, hypertrophic scar formation was limited (5/54 regions of interest, 9.3%). Also in operated patients, the incidence of hypertrophic scarring following a strict regimen of aftercare was low (12/48 regions of interest, 25%).

Keywords: burn, laser Doppler imaging, flux values, enzymatic debridement, donor site morbidity, surgery

RÉSUMÉ. *À la différence de l'excision chirurgicale tangentielle, le débridement enzymatique au Nexobrid® ne s'intéresse qu'au tissu nécrosé ce qui permet la cicatrisation spontanée de certaines brûlures intermédiaires. Dans cette étude rétrospective, nous avons évalué la diminution des interventions chirurgicales (et des séquelles y afférant) en cas d'utilisation de l'excision enzymatique sur des brûlures affirmées comme profondes par Imagerie Laser- Doppler (ILD). Nous avons analysé 102 régions d'intérêt, apparaissant bleues à l'ILD chez 32 patients traités par Nexobrid®, représentant une surface totale de 5 086,4 cm². Ceci a permis une cicatrisation spontanée de 1 986,9 cm² (39% de l'ensemble et 56,3% chez les patients ayant dû être opérés). Les patients traités par excision- greffe sont restés significativement plus longtemps que ceux ayant cicatrisé spontanément (37,8 +/- 17,5 j VS 27 +/- 10,5). L'incidence globale des cicatrices hypertrophiques était basse (16,7%). Ceci est la première publication montrant une diminution significative de la surface greffée et du nombre d'interventions chirurgicales après l'utilisation d'une excision enzymatique chez des patients souffrant de brûlures définies comme profondes par ILD. Même après une cicatrisation spontanée longue après Nexobrid®, l'incidence des cicatrices hypertrophiques reste faible (5/54 régions d'intérêt - 9,3%) quand elle s'élève à 25% après excision- greffe (12/48).*

Mots-clés*: brûlure, imagerie laser- Doppler, excision enzymatique, chirurgie*

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Introduction

Already in 1970, Janzekovic advocated early tangential excision in combination with autologous split thickness skin grafts (STSG) for all *clinically deep* burn wounds.[1] However, this standard of care (SOC) treatment is acknowledged to be non-selective as it always additionally removes viable tissue, eventually transforming deep dermal burns into full thickness wounds. More recently, early eschar removal of deep burn wounds by means of enzymatic debridement with NexoBrid® (EDNX, MediWound, Yavne, Israel) has proven to remove non-viable tissue in a very selective and rapid manner.[2] As a result, wound healing potential (HP) is maximally preserved, allowing some deep dermal wounds to heal with conservative therapy only hereby reducing the need for surgical treatment with STSG compared to SOC.[3] Although these results seem promising, it is unclear whether this reported reduction in surgery was due to a clinical overestimation of burn depth or whether it was due to EDNX treatment or both. To objectively determine whether enzymatic debridement really reduces the need for surgery, an early and accurate diagnosis of burn depth or HP is essential.[4-6] Laser Doppler imaging (LDI) has proven to be a unique and evidence-based tool to assess burn wound HP as early as 48h post burn and this with an accuracy >95%.[6-8] This diagnostic tool has been demonstrated to be invaluable in assisting burn surgeons in the early therapeutic decision-making whether or not to operate a clinically deep burn.[6,9-11] In this article, the authors aim to investigate the exact reduction of surgery after EDNX in patients with LDI-confirmed deep burns (HP >21d) - which are a definite indication for surgery - and how this method of debridement influences the overall functional and aesthetic outcomes.

Material and methods

The Ethical Review Committee of Ghent University hospital approved this single center retrospective database analysis (protocol nr. 2019/1535).

Therapeutic path

Admission and pre-NexoBrid® procedure. All burn patients admitted to our burn center were initially clinically assessed for burn depth by a senior burn specialist. In the case of deep circumferential burns with a risk of developing compartment syndrome, patients immediately underwent an EDNX procedure to prevent a surgical escharotomy. These patients were not scanned by LDI and were therefore not included in this study. All other patients with *clinically deep burns* followed the normal burn wound treatment protocol: removal of blisters and loose skin during showering followed by the application of the enzyme alginogels Flaminal® Forte/Hydro[12] (Flen Health, Kontich, Belgium) or the hydrogel Prontosan® Wound Gel X (B.Braun, Melsungen, Germany) as wound dressings.

LDI measurements. All burn injuries - except very shallow (superficial) burns - were scanned with the MoorLDI2-BI laser Doppler (Moor Instruments, Axminster, UK), between 48h and 5d post-burn.[6] Burns with HP <14d are represented by LDI-red, burns with HP14-21d are represented by LDI-yellow combined with a pink and/or green color, and finally burn wounds with a HP >21d are represented by a blue color on the validated LDI color palette. These LDI-blue burn wounds are universally considered as a clear indication for tangential excision and skin grafting.[10,11,13]

NexoBrid® procedure. Patients with one or more *mainly LDI-blue areas* underwent EDNX treatment as a less invasive alternative to the SOC. The eligibility criteria for EDNX are presented in *Table I*.

The choice between general and regional anesthesia was made by our multidisciplinary team and discussed with the patient/legal representative prior to obtaining an informed consent as described in an earlier article.[14] The EDNX procedure itself was per-

Table I - Patient selection criteria for enzymatic debridement with NexoBrid®

Patient selection for enzymatic debridement with NexoBrid®	
Criteria for enzymatic debridement	
a)	Patients of all ages and in good general health as assessed by the anesthesiologist, pediatrician or intensive care physician
b)	Clinically deep dermal and/or full-thickness thermal burns
c)	LDI confirmed HP >21 days burns with a mainly blue color
Exclusion criteria for enzymatic debridement	
a)	Electrical or chemical burns
b)	Pregnancy or nursing
c)	History of allergy and/or known sensitivity to pineapples, papaya, bromelain or papain
d)	Pre-enrolment dressings with Flammazine or Flammacerium
e)	The patient or the legal representative refused to sign the informed consent form for enzymatic debridement and participation in the follow-up examinations

formed bedside in the burn center in three stages using our local protocol as described in the same article.[14] After making the treatment decision and obtaining an informed consent, Prontosan® soaked wound dressings were applied for at least 2h to moisten the burn eschar as start of the procedure. After initiating general or regional anesthesia, the wound was mechanically cleansed by removing the remaining keratin allowing maximum effectiveness of EDNX. Thereafter, NexoBrid® was applied for 4 hours. In the following stage, the dressings and dissolved eschar were removed by vigorously scraping over the wound bed with a tongue depressor. The wound bed was then cleansed with Prontosan® solution and wet-to-dry (WTD) Prontosan® dressings were applied for at least 2 hours. All steps of the procedure were digitally photographed with a NIKON D750 camera.

Post-NexoBrid® treatment until wound healing. After the EDNX procedure, all patients were treated according to a standardized protocol consisting of the application of glycerol-preserved allografts (Euro Skin Bank, The Netherlands) in the case of large burns, or of Flaminal® Forte/Hydro,[12] or of Prontosan® Wound Gel X in the case of smaller burns, as a wound dressing until the autografting procedure and/or wound closure (defined as closure of >95% of the involved surface area). Prior to application of autografts, the wound bed was generally scrubbed but, if necessary, a tangential excision was performed until a vital wound bed was achieved. In the earlier period of EDNX treatment, there was some lack of experience with this new technique of enzymatic debridement and the final decision on surgery depended on various parameters such as: wound bed evaluation, estimation of residual wound HP, time or organizational constraints, and both patient and surgeon preferences. Later on, the decision became more standardized as described in our previous paper.[15]

Patients underwent regular wound assessments combined with high-quality digital photography.

Follow-up until scar maturation. After hospital discharge, all patients were seen in the outpatient clinic until complete wound closure, as confirmed by the burn surgeon and documented by photographic imaging. After wound closure, the patients were still regularly seen for follow-up for customized anti-scar therapy (hydration by moisturizers, pressure- and silicone therapy). During clinical examination, performed by two burn experts with more than 30 years of experience in burns (HH and SM), scar scales like the POSAS scale[16,17] were not used. However, each burn scar was evaluated on a similar basis: the vascularization, pigmentation, thickness, relief, pliability and surface of the burn scar were looked at and documented by means of digital photographs.

Eligibility criteria for this study (Table II)

The LDI-blue areas were further analyzed only if all the required data was collected and the treatment, healing, and follow-up process was fully documented.

Table II - Patient selection criteria

Patient selection for retrospective study	
Inclusion criteria	
a)	Patients of all ages that had an LDI scan between 2 and 5 days post burn injury showing LDI-blue areas
b)	The LDI scan was followed by enzymatic debridement under general or regional anesthesia
c)	The whole procedure from admission to treatment and follow-up was documented and photographed
d)	Informed consent from patient or legal representative was obtained
Exclusion criteria	
a)	Patients of all ages that did not have an enzymatic debridement under general or locoregional anesthesia but the standard of care with tangential excision of the burn eschar
b)	No LDI scan before enzymatic debridement or performed before 48 hours or after 5 days post burn injury
c)	The patient or the legal representative of the patient refused to sign the informed consent form for retrospective study

Drawing of the regions of interest (ROIs)

First, all burned surfaces with a *mainly blue color* on LDI, were meticulously analyzed as to color code, flux values and exact surface area in cm² with the help of a computer program designed by Moor Instruments (moorLDI-BI Burns Software V4.0.1). These zones consisted of a majority of LDI-blue, sometimes combined with smaller LDI-yellow and -green parts in the middle or close to the border of the LDI-blue zones. Due to their smaller size and proximity to the LDI-blue zones, a separate treatment of these closely associated LDI-yellow and -green parts is not possible (*Fig. 1*, top LDI scan A). As a result, these *mainly LDI-blue areas* are always entirely considered as an indication for surgery[14] and were therefore enzymatically debrided.

Still, to avoid all uncertainty concerning the study results, even more specific so-called 'regions of interest' (ROIs) with an *exclusively* blue color on LDI and mean perfusion values of <200 perfusion units (PU) were drawn within these *mainly LDI-blue*

areas with the same software. These *exclusively LDI-blue ROIs* (*Fig. 1*, bottom LDI scan B) were analyzed separately. According to the validated color code,[10,11] these ROIs represent truly (proven) deep burns where there is no doubt at all concerning the indication for surgery.

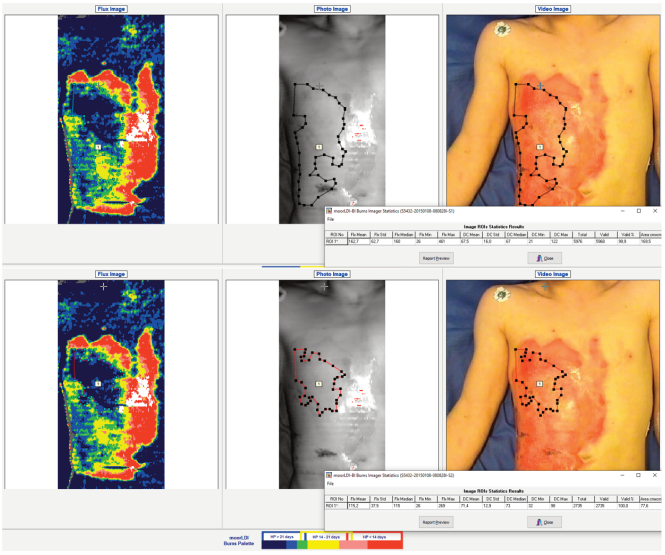

Fig. 1 - Example of mainly (top) and exclusively (bottom) LDI-blue ROI

Data collection

All data were anonymized and collected in a secured electronic datasheet by the burn surgeons (KC, IDD and ND) and the burn care coordinator (HH): 1. age, height, and weight of the patient, 2. date, cause, location, depth, and extent of the burn trauma, 3. date and outcome of the LDI scan, 4. date of the EDNX procedure, 5. need for additional surgical procedures, 6. time until wound closure, and 7. data of scar aftercare: pressure garments, hydration therapy, additional (surgical) procedures, development of hypertrophic scars (HTS), etc.

Statistical analysis

All statistical analyses were performed using SPSS Statistics 25 (SPSS, Chicago, IL, USA). We tested for normality of all recorded parameters using the Kolmogorov-Smirnov test and equality of variances was assessed using Levene's test. Characteristics among groups were compared and analyzed using the Chi-squared test, Fisher's Exact test, Wilcoxon signed rank test and independent samples t-test. Outcomes were subsequently analyzed using (binary) logistic regression as well as ROC-curve analysis. A priori, a two-sided value of $p<0.05$ was considered statistically significant.

Results

Between January 2015 and November 2019, 530 patients were admitted in our intensive care burn center. Four hundred sixty-six of them (88%) underwent LDI examination for burn depth assessment. Eighty-four patients had enzymatic debridement with NexoBrid® for their LDI-proven deep burns. Thirty-two patients with deep burns on LDI who were treated with EDNX met all the eligibility criteria for this study (*Table III*).

This resulted in a total of 87 *mainly LDI-blue areas* with an entire surface of 7,119.1cm² with a clear indication for surgery. Of the total surface area, 3,505.7cm² (49.2%) was treated conservatively while 3,613.4cm² (50.8%) was covered with autologous STSGs (*Fig. 2*). Within these *mainly LDI-blue*

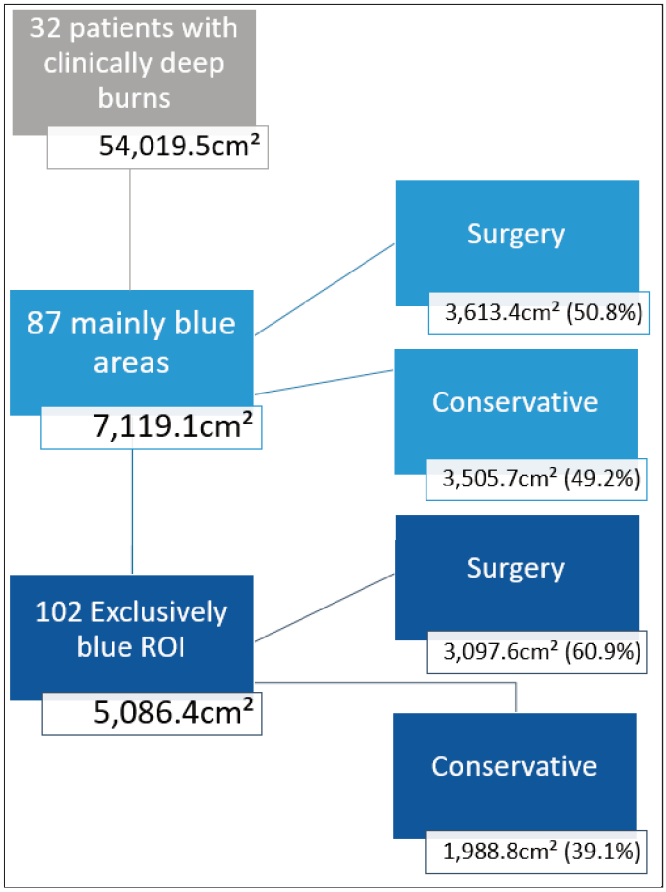

Fig. 2 - Overview of treatment decisions for mainly LDI blue areas and exclusively blue ROIs

areas, 102 specific ROIs (mean of 3.2±3.0 (SD) ROI per patient) with an *exclusively blue color on LDI* were selected as definitely deep burns to precisely determine the reduction in surgery after EDNX treatment. This corresponded to a total - *exclusively LDI-blue ROIs* - surface of 5,086.4cm² (71.4% of the *mainly LDI-blue areas*) definitely requiring surgical treatment. Of the total surface of *exclusively LDI-blue ROIs* treated with EDNX, 39.1% (1988.8cm²) healed with conservative treatment while 60.9% (3,097.6cm²) needed additional wound coverage with autologous STSGs. This corresponded to a significant reduction ($p<0.001$) to only 18 patients (18/32, 56.3%) still requiring surgical treatment. To highlight the reduction in surgical extent, we further analyzed these 18 patients who ultimately required surgery for part of their *exclusively LDI-blue areas*. The total surface of *exclusively blue ROIs* in these 18 patients was 3,894.5cm^2. Following the EDNX procedure, a 20.5% (796.9cm^2) reduction of the initial surface area necessitating surgery was noted ($p=0.043$).

Overall, the mean LDI flux values were significantly different ($p<0.001$) between the *exclusively LDI-blue ROIs* treated conservatively (145.7PU) and the ROIs eventually treated with skin grafting (119.5PU) (*Table III*). Usually, LDI flux values represented by the blue color on the LDI color palette are a clear indicator whether surgical treatment is required. In the case of EDNX treatment, it is important to mention that this is less evident as this type of debridement better preserves the still present HP of the burn wound. The mean healing time of the 102 *exclusively LDI-blue ROIs* after the EDNX procedure was 32.1±15.2d. The LDI-blue ROIs treated with STSG required significantly longer time to heal ($p<0.001$), compared to the conservatively treated wounds (37.8±17.5d vs. 27.0±10.5d). The mean time between the EDNX and the first autografting procedure was 14.3±7.4d.

After complete wound healing, all but five - 4 conservatively and 1 surgically treated - patients (27/32, 84%) followed the standard protocol for the treatment of their burn scars, consisting of hydration

Table III - Overview of the (demographic) data and outcomes

Data overview	
No. of patients (of which minors)	32 (7)
Mean age (±SD)	36.8 (± 24.5) years
Cause of burn injury (n=32)	Contact burn 2 (2 adults) Flame burn 15 (1 adolescent and 14 adults) Flash burn 1 (1 adult) Scald 14 (6 children and adolescents, 8 adults)
Mean total %TBSA (±SD)	11.5 (± 8.7) %
Mean clinically deep burned: - %TBSA (±SD) - surface area per patient (±SD)	9.9 (± 7.6)% 1,688.1 (± 1,505.3) cm²
Mean *mainly LDI-blue* surface area (n=87) Mean *mainly LDI-blue* flux values (n=87)	222.5cm² 142.4 PU
Mean surface per *exclusively LDI-blue ROI* (±SD) Mean total surface *exclusively LDI-blue ROI* per patient (±SD) Mean flux value (PU) per *exclusively LDI-blue ROI* (n=102) (±SD)	49.9 (± 54.9) cm² 159.0 (± 219.3) cm² 133.3 (± 40.1) PU
Location ROI (n=102)	Scalp 1 Neck 1 Thorax/abdomen/back 19 Shoulder/arm 23 Wrist/hand/fingers 10 Perineal 2 Hip/leg/ankle 38 Foot 8
Mean time between burn injury and EDNX procedure (±SD)	3.0 (± 1.1) days
Conservative vs. surgery after EDNX - n=102 ROI -cm² -Surface area/ROI (±SD) -Mean flux values -Healing time (±SD)	54/48 1,988.8/ 3,097.6 cm² 36.8 ± 38.3 cm² / 64.6 ± 66.4 cm² (p=0.013) 145.7/119.5 PU (p<0.001) 37.8 ± 17.5 / 27.0 ± 10.5 days (p<0.001)
Mean healing time *exclusively LDI-blue ROI* (n=102)	32.1 ± 15.2 days
Mean total follow-up time (±SD)	537.3 (± 549.5) days

by moisturizers and pressure garments combined with silicone therapy and/or polyurethane inlays for at least one year. Seven patients (4 adults and 3 children; 7/32, 21.9%), corresponding to 17 *mainly LDI-blue areas and exclusively LDI-blue ROIs* (17/102, 16.7%) developed HTS despite maximal anti-scar therapy. More specifically, in 12 of these ROIs, the HTS developed after surgical treatment of the burn wounds (12/48 ROIs, 25%), while in the 5 other ROIs, it was following conservative treatment (5/54 ROIs, 9.3%). This difference was statistically significant (p=0.033). There was also a significant difference in healing time in ROIs with and ROIs without HTS (38.8±10.7d vs. 30.7±15.6d respectively, p=0.044). Other factors related to HTS were significantly lower LDI flux values of the ROIs with HTS compared to the ROIs without (116.5±19.1cm² vs. 135.1±44.7cm² respectively, p=0.003) (*Table IV*). None of the patients with HTS developed a functional disability related to the burn scars and none of them required any additional surgical procedure.

Discussion

In this study we investigated the exact reduction in the number of surgical procedures as well as the extent of autografting after EDNX treatment in LDI-confirmed deep burns with a clear indication for surgery. Furthermore, we evaluated the influence on the overall functional and aesthetic outcomes.

The observed reduction in surgery after EDNX

In our burn center, LDI is used for accurate burn depth assessment on a regular basis in >85% of the patients,[18,19] which already results in a significant reduction in unnecessary surgical procedures compared to burn centers advocating early and aggressive surgical treatment of all clinically deep burns.[20] Our protocol to operate only the truly deep burns was reflected in this study by the fact that LDI was able to reduce the mean surface area of *clinically deep burns* – many of which would have been operated in burn centers without LDI - per patient from 1,688cm² to only 222.5cm² (7,119.1cm²/32 patients) *mainly LDI-blue areas* per patient requiring STSGs. In this study, 3,613.4cm² of the total *mainly LDI-blue* surface area (50.8%) was eventually covered with autologous STSGs after EDNX treatment. In order to accurately determine the reduction in surgery caused by EDNX, the authors focused on the *exclusively LDI-blue ROIs* (159cm² per patient) where there is no doubt on the clear indication for surgery. The current study was therefore able to undeniably demonstrate that EDNX not only contributed to a reduction in the extent of autografting, but also led to a reduction in the number of surgical procedures. Of the 102 *exclusively LDI-blue ROIs* requiring surgery according to LDI, 39.1% of the total surface area healed with conservative treatment only. This corresponds to a significant reduction to only 18 patients (18/32, 56.3%) still requiring an operation after EDNX. These results are not comparable with those from the literature since this is the first

Table IV - Comparison LDI-blue ROI with and without hypertrophic scarring

Data overview			
	Hypertrophic scars	**No Hypertrophic scars**	p-value
ROI (n=102)	17 (16.7%)	85 (83.3%)	N/A
Mean age (±SD)	25.7 (± 22.2) year	39.8 (± 23.7) year	p=0.28
Skin color (patients)	Fitzpatrick Type III 5 (1 child, 4 adults) Fitzpatrick Type IV 1 (1 child) Fitzpatrick Type V 1 (1 child)	Fitzpatrick Type III 25 (4 children/adolescents, 21 adults) Fitzpatrick Type IV 5 (1 child, 4 adults)	N/A
Mean % TBSA burned (±SD) Mean % TBSA clinically deep (±SD)	18.9 (± 7.0)% 16.7 (± 5.3)%	11.0 (± 8.9)% 9.4 (± 7.8)%	N/A
Mean surface per ROI	38.8 (± 35.1) cm²	51.5 (± 58.0) cm²	p=0.37
Flux value (±SD) (PU)	116.5 (± 19.1) PU	136.7 (± 42.4) PU	p=0.003
Surgery vs conservative treatment	12 / 5	36 / 49	p=0.033
Healing time (±SD)	38.8 ± 10.7 days	30.7 ± 15.6 days	p=0.044
Mean total follow-up time (±SD)	649.0 (± 503.6) days	544.2 (± 576.2) days	N/A

N/A = not applicable

study about LDI-confirmed deep burns, while the burn wounds in the other mentioned papers were only *clinically* deep burns.[3,21-24]

The mean overall healing time in this study was 32.1±15.2d. Burns treated with STSGs required significantly more time to heal, compared to conservatively treated wounds (37.8±17.5d vs. 27.0±10.5d respectively). This is mainly attributed to the rather long time interval between EDNX and the autografting procedure to maximize the chances of a successful conservative approach and to obtain adequate wound bed preparation without the need for additional tangential excision before applying skin grafts. The mean healing time of the conservatively treated group was comparable to that of the EDNX group in the RCT of Rosenberg and colleagues (27.0 vs. 29.9d respectively).[3]

In burn wounds, spontaneous healing <21d is considered a prerequisite to avoid HTS.[4,25] In our study, the overall mean healing time was markedly prolonged but this allowed 39.1% of all *exclusively LDI-blue* surface areas treated with EDNX to heal spontaneously without the need for STSGs. Only 5 *exclusively LDI-blue ROIs* (9.3%) developed HTS after conservative therapy, which was significantly less compared to the surgically treated ROI (25%). None of the conservatively treated ROIs required additional surgical scar correction. These findings obviously contradict common understanding of scar formation in deep burn wounds and challenge the 21d golden rule of HTS[4] at least in EDNX treated burn wounds. This can at least be partially explained by the selectivity of the enzymatic debridement,[2] removing all non-vital tissue while maximally preserving residual epithelial cells of the skin appendages. This allows for spontaneous re-epithelialization while avoiding deepening of the burn wound caused by tangential excision.[26] The low rate of HTS in conservatively treated ROIs, despite the longer mean healing times, also contrasts with the paper by Cubison and colleagues.[4] In their group of patients treated conservatively with a healing time between 26 and 30 days, the percentage of HTS was 75% (6/8 patients).[4]

Nevertheless, in the *exclusively LDI-blue ROIs* which were treated surgically in our study, the HTS rate was significantly lower than reported in the paper of Cubison et al.[4] (88%, 28/32 patients). This substantial difference compared to our outcomes could be explained by the strict scar management protocol used in our center: moisturization of the scar several times per day, wearing pressure garments at least 23 hours per day (with a controlled pressure of >24mmHg) in combination with silicone sheets or polyurethane inlays for at least 12 hours per day. All of this during at least 1 to 2 years in patients with healing times over 18 days and in patients treated surgically. Additionally, considering the extraordinarily low incidence of HTS in the vast majority of patients treated with EDNX, it is the opinion of the authors that NexoBrid® has an anti-hypertrophic scar effect that has not yet been fully elucidated.

As generally recognized, the assessment of the need for surgical treatment after enzymatic debridement proved to be difficult. Recently, our burn center concluded that the wound bed should be clinically evaluated twice: immediately after removing NexoBrid® to assess the viability of the wound bed and after the WTD period to reach a more complete decision.[15] During these evaluations, wound bed characteristics such as incomplete debridement, visible and/or translucent fat lobules, visible and/or coagulated blood vessels and a dermal step-off in the wound bed combined with a higher range (4−5) in the newly developed wound bed color code, should lead to an early and reliable decision for skin grafting. For burn centers using LDI, mean flux values below 119.5PU - in addition to the above-mentioned wound bed evaluation - are a clear indicator for surgical therapy.[15]

Conclusion

This is the first paper demonstrating a proven and significant reduction in extent of autografting as well as in the number of surgical procedures after rapid selective enzymatic debridement. This was investigated not only in (subjectively) clinically assessed deep burns but more importantly in objectively LDI-defined and therefore proven deep burns. Even after extended conservative treatment with prolonged healing times, HTS formation was limited (5 of 54

ROI, 9.3%). Also in operated patients, the incidence of HTS was low (12/48 ROI, 25%), provided that a strict aftercare regimen is followed. The decision for skin grafting can be guided by a combination of LDI flux values and specific post-EDNX wound bed characteristics.

BIBLIOGRAPHY

1 Janzekovic Z: A new concept in the early excision and immediate grafting of burns. J Trauma, 10: 1103-8, 1970.
2 Rosenberg L, Krieger Y, Silberstein E et al.: Selectivity of a bromelain based enzymatic debridement agent: a porcine study. Burns, 38: 1035-40, 2012.
3 Rosenberg L, Krieger Y, Bogdanov-Berezovski A et al.: A novel rapid and selective enzymatic debridement agent for burn wound management: a multi-center RCT. Burns, 40: 466-74, 2014.
4 Cubison TC, Pape SA, Parkhouse N: Evidence for the link between healing time and the development of hypertrophic scars (HTS) in paediatric burns due to scald injury. Burns, 32: 992-9, 2006.
5 Bombaro KM, Engrav LH, Carrougher GJ et al.: What is the prevalence of hypertrophic scarring following burns? Burns, 29: 299-302, 2003.
6 Hoeksema H, Van de Sijpe K, Tondu T et al.: Accuracy of early burn depth assessment by laser Doppler imaging on different days post burn. Burns, 35: 36-45, 2009.
7 Shin JY, Yi HS: Diagnostic accuracy of laser Doppler imaging in burn depth assessment: systematic review and meta-analysis. Burns, 42: 1369-76, 2016.
8 Wang R, Zhao J, Zhang Z et al.: Diagnostic accuracy of laser Doppler imaging for the assessment of burn depth: a meta-analysis and systematic review. J Burn Care Res, 41(3): 619-625, 2020.
9 Pape SA, Skouras CA, Byrne PO: An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. Burns, 27: 233-9, 2001.
10 Pape SA, Baker RD, Wilson D et al.: Burn wound healing time assessed by laser Doppler imaging (LDI). Part 1: Derivation of a dedicated colour code for image interpretation. Burns, 38: 187-94, 2012.
11 Monstrey SM, Hoeksema H, Baker RD et al.: Reprint of: Burn wound healing time assessed by laser Doppler imaging. Part 2: Validation of a dedicated colour code for image interpretation. Burns, 38: 195-202, 2012.
12 Hoeksema H, Vandekerckhove D, Verbelen J, Heyneman A, Monstrey S: A comparative study of 1% silver sulphadiazine (Flammazine(R)) versus an enzyme alginogel (Flaminal(R)) in the treatment of partial thickness burns. Burns, 39: 1234-41, 2013.
13 Claes KEY, Hoeksema H, Robbens C et al.: The LDI Enigma Part II: Indeterminate depth burns, man or machine? Burns, 47(8): 1773-1782, 2021.
14 Claes KEY, Amar S, Hoeksema H et al.: Pain management during a bromelain-based selective enzymatic debridement in paediatric and adult burn patients. Burns, 48(3): 555-567, 2022.
15 Claes KEY, De Decker I, Monstrey S et al.: Helpful hints in deciding what and when to operate after enzymatic debridement. Burns, 49(1): 80-90, 2023.
16 Draaijers LJ, Tempelman FR, Botman YA et al.: The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. Plast Reconstr Surg, 113: 1960-5; discussion 66-7, 2004.
17 van der Wal MBA, van de Kar AL, Tuinebreijer WE et al.: The modified patient and observer scar assessment scale: a novel approach to defining pathologic and nonpathologic scarring? Plast Reconstr Surg, 129: 172e-74e, 2012.
18 Claes KEY, Hoeksema H, Vyncke T et al.: Evidence based burn depth assessment using laser-based technologies: where do we stand? J Burn Care Res, 42(3): 513-525, 2021.
19 Claes KEY, Hoeksema H, Robbens C et al.: The LDI Enigma, Part I: So much proof, so little use. Burns, 47(8): 1783-1792, 2021.
20 Xiao-Wu W, Herndon DN, Spies M, Sanford AP, Wolf SE: Effects of delayed wound excision and grafting in severely burned children. Arch Surg (Chicago, Ill : 1960), 137: 1049-54, 2002.
21 Schulz A, Shoham Y, Rosenberg L et al.: Enzymatic versus traditional surgical debridement of severely burned hands: a comparison of selectivity, efficacy, healing time, and three-month scar quality. J Burn Care Res, 38: e745-e55, 2017.
22 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, 43: 1233-43, 2017.
23 Krieger Y, Bogdanov-Berezovsky A, Gurfinkel R et al.: Efficacy of enzymatic debridement of deeply burned hands. Burns, 38: 108-12, 2012.
24 Cordts T, Horter J, Vogelpohl J et al.: Enzymatic debridement for the treatment of severely burned upper extremities - early single center experiences. BMC Dermatol, 16: 8, 2016.
25 Deitch EA, Clothier J: Burns in the elderly: an early surgical approach. J Trauma, 23: 891-4, 1983.
26 Gurfinkel R, Rosenberg L, Cohen S et al.: Histological assessment of tangentially excised burn eschars. Can J Plast Surg, 18: e33-6, 2010.