

Eschar Removal by Bromelain based Enzymatic Debridement (Nexobrid®) in Burns: An European Consensus



Christoph Hirche¹, Antonella Citterio², Henk Hoeksema³, Ján Koller⁴, Martina Lehner⁵, José Ramón Martínez⁶, Stan Monstrey³, Alexandra Murray⁷, Jan A. Plock⁸, Frank Sander⁹, Alexandra Schulz¹⁰, Benjamin Ziegler¹, Ulrich Kneser¹

¹BG Trauma Center, Hand-, Plastic and Reconstructive Surgery, Burn Center, University of Heidelberg, Ludwigshafen, Germany
²Anesthesiology, Plastic and Reconstructive Surgery, Burn Unit, Ospedale Niguarda, Milano, Italy
³Burn Unit, Department of Plastic Surgery, Ghent University Hospital, Gent, Belgium
⁴Burn Department, University Hospital Bratislava, Ruzinov Hospital Univerzitná nemocnica Bratislava, Bratislava, Slovak Republic
⁵Department for Plastic, Aesthetic and Reconstructive Surgery, University Hospital St. Pölten, St. Pölten, Austria
⁶Burn Unit, Hospital Universitario La Paz, Madrid, Spain
⁷Burn Unit, Stoke Mandeville Hospital, Aylesbury, Buckinghamshire, United Kingdom
⁸Division of Plastic Surgery and Hand Surgery, Burn Center, University Hospital Zurich, Zurich, Switzerland
⁹Burn Center with Plastic Surgery, Unfallkrankenhaus Berlin, Berlin, Germany
¹⁰Department of Plastic Surgery, Hand Surgery, Burn Center, University of Witten/Herdecke, Cologne-Merheim Medical Center, Germany.



Introduction:

There is increasing evidence that Enzymatic Debridement is a powerful tool to remove eschar in burn wounds, reducing blood loss, the need for autologous skin grafting and the number of wounds requiring surgical excision, reduce rate of burn wound infection and the length of hospital stay.

Method:

In order to assess the role and advantages of Bromelain based Enzymatic Debridement (Nexobrid®) beyond the scope of the existing literature and in view of users' experience, a European Consensus Meeting was scheduled to provide statements for application and user orientated guidelines to contribute to successful treatment (Frankfurt, Germany, January 2017), hosted by BG Trauma Center Ludwigshafen, Germany.

Multistep process:

- Systematic literature review (2000-2016) applying Oxford Level of Evidence Classification System
- Pre-formulated statements on various issues
- Expert panel discussion and voting on panel statements (Austria, Belgium, Germany, Italy, Slovak Republic, Spain, Switzerland and United Kingdom) with plastic surgeons, burn surgeons, non-physician panelist), one vote per center per statement
- Standard of Care (SOC): surgical excision with tangential knives and/or hydro surgery were regarded as surgical standard of care (SOC) and if applicable compared to Enzymatic Debridement.

Results:

Sixty-eight (68) consensus statements were provided for the use of Enzymatic Debridement. The degree of consensus was remarkably high, with a unanimous consensus in 88.2% of statements, and lowest degree of consensus of 70% in only 3 statements. This consensus may serve as preliminary guidelines for the use of Enzymatic Debridement with user-orientated recommendations until further evidence and systematic guidelines are available.

Conclusion:

This consensus may serve as preliminary guidelines for the use of Enzymatic Debridement with user-orientated recommendations until further evidence and systematic guidelines are available.



Statements:

1. Indications and setting	
• ED should only be applied by experienced burn teams after adequate training in ED.	100%
• Enzymatic Debridement (ED) with Nexobrid is a safe and reliable alternative tool for early eschar removal in adults.	100%
• ED can be applied in pediatric patients and is performed with satisfying results but this is currently considered as off label use.	100%
• In case of a moist burn eschar, ED can be applied to all burned surfaces.	100%
• ED is advantageous in treatment for hands, feet and face.	100%
• Contact of ED to the eyes and the tympanum should be avoided.	100%
• ED preserves viable dermis more efficiently compared to SOC.	100%
• ED as the only procedure for debridement should be limited to thermal burns, i.e. scald/flare/contact burns.	100%
• In additional trauma, such as high voltage injury, blast injury or crush burn, surgical techniques should be applied in order to release muscular compartment pressure and provide nerve decompression.	100%
• ED cannot be recommended for eschar removal in chemical burns.	100%
• Pretreatment with silver sulfadiazine or betadine should be avoided.	100%
• Standard burn wound and depth assessment is sufficient prior to ED.	90%
• Frequent photography and wound documentation is strongly recommended to provide wound documentation for all members of the burn team.	90%
• ED can be regarded as a useful tool in case of limited OR capacity.	70%
• ED can be safely applied in up to 15% BSA in one session (label).	100%
• Up to 30% BSA can be treated by ED based on individual decision, but this is considered as off-label use.	100%
• ED can be applied for early eschar removal in circumferential extremity burns to prevent surgical escharotomy as SOC but not to replace fasciotomy.	100%
• The extremity should be monitored and surgical escharotomy and/or fasciotomy should be performed if signs of deterioration appear.	100%
2. Pain Management and Anesthesia	
• Adequate pain management is essential before, during and after ED.	100%
• Regional anesthesia is recommended for ED at the isolated (upper) extremity.	70%
• Analgesics-based intravenous sedation or general anesthesia is recommended for ED at the trunk and if different regions are treated at the same time.	100%
3. Timing of application	
• ED can be applied immediately after initial assessment and wound preparation.	100%
• Later application (>72 hours from injury) is possible in selected patients after appropriate preparation.	100%
4. Application of ED	
• Preparation of the wound by blister removal and superficial debridement of keratin remnants is necessary prior to ED (before or after pre-soaking).	100%
• A moist wound environment is essential prior to ED, because ED does not work in dry wounds.	100%
• A moist wound environment can be achieved by a pre-soaking phase of at least 2 hours in acute burns <72 hours from injury.	90%
• Pre-soaking might not be required, if a moist wound environment is present prior to ED.	100%
• Pre-soaking is not recommended in an emergency indication for the prevention of burn induced compartment syndrome.	100%
• An additional mechanical cleaning step can be performed at the end of the pre-soaking phase .	100%
• The enzymes should be applied for 4 hours.	100%
• 2g/1% BSA should be applied in adult patients in order to achieve an active agent layer of approximately 1.5-3mm thickness.	100%
• Even distribution of the enzymes over the entire wound area is required.	100%
• The application of a moist dressing for at least 2 hours is recommended.	100%
• Prolonged application up to 18 hours can improve the results of ED.	100%
• ED requires sterile occlusive dressings with minimal dead space.	100%
• The dressing during ED includes:	100%
o An adhesive local barrier (e.g. paraffine/vasaline vaseline gauze or ointment) , or stoma paste) is necessaryshould be applied 2-3 cm outside the treated area in order to prevent leakage of the active agent	
o Occlusive film	
o Bulky, protective dressing	
• Complete eschar removal should be achieved within 7 days of injury.	100%
• Re-application of ED after initial failure is currently not recommended.	100%
• Wound assessment should be performed within 2 hours after ED.	100%
• Post-ED wound bed color and bleeding patterns play a key role in diagnosing the resulting depth of the burn wound.	90%
• A uniform red or pink post ED wound bed represents high chances for spontaneous healing.	100%
• A uniform white post ED wound bed with pin-point punctate bleeding has good chances for spontaneous healing with acceptable results.	100%
• A post ED wound bed with large diameter red circles or oval patterns is associated with prolonged healing and skin grafting should be considered in these wounds.	100%
• Exposed fat post ED is a clear indication for skin grafting.	100%
5. Post-interventional care of wounds after enzymatic debridement – wound management	
• Debris and the residues of the enzymes and dissolved dermis should be removed by scraping.	100%
• After ED, it is necessary to keep a moist environment to avoid desiccation.	100%
• Pseudo-eschar is a specific layer sticking to the wound that may develop several days after ED.	100%
• If an occlusive layer remains >14 days, re-debridement should be taken into consideration.	100%
• Granulation tissue may develop in prolonged spontaneous healing after ED starting at day 14.	100%
• Hypergranulation is a sign of insufficient reepithelization.	100%
• Granulation tissue requires topical treatment followed by secondary healing or surgical treatment.	100%
• Topical steroids can be recommended to avoid hypergranulation.	100%
6. Post-interventional care of wounds after enzymatic debridement – wound management	
• ED reduces the number and surface of skin grafting procedures.	100%
• ED should be regarded as a debridement tool, and autologous skin transplantation or other reconstructive procedures including application of dermal substitutes or flaps should be performed if stable healing cannot be expected.	100%
• ED may allow good results even after a prolonged healing time.	100%
• Autologous skin grafting should be advisable at latest after 21 days if there is no progress in epithelization.	70%
• Delayed healing might result in unstable scarring and insufficient functional and aesthetic results.	100%
• When ED is applied in deep dermal burns, dermal replacement matrices may be used.	100%
7. Scar prevention	
• Scar treatment (Massage, ointment, compression garments, silicon, etc.) should immediately start after healing.	100%
8. Blood loss	
• ED reduces blood loss compared to SOC.	100%
• ED might induce relevant blood loss in patients with coagulopathy or therapeutic anticoagulation.	90%
9. Training strategies	
• ED requires standardized protocols and significant experience in the field of burn care and surgery.	100%
• ED requires clear communication and multi-professional training.	100%
• Logistic requirements of ED have to be considered prior to implementation.	100%

Blue highlighted: Consensus between 80-90%; red highlighted: consensus ≤70%