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# Eschar removal by bromelain based enzymatic debridement (Nexobrid®) in burns: An European consensus



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## ARTICLE INFO

### Article history:

Accepted 27 July 2017

### Keywords:

Burn  
Enzymatic debridement  
Nexobrid  
Consensus  
Eschar removal

## ABSTRACT

Early debridement and/or eschar removal is regarded as a significant step in the treatment of deep partial and full thickness burns. It aims to control wound bioburden and allows early wound closure by conservative treatment or skin grafting. Preservation of viable dermis accompanied by early wound closure, is regarded as a necessary step to reduce scar related complication, e.g. functional limitations and/or unaesthetic scar formation. Aside from the classical techniques of surgical excision as tangential excision for eschar removal, hydro-surgery, maggot therapy, laser, enzymatic debridement have been described as additional techniques in the burn surgeon's armamentarium. It is widely accepted that early eschar removal within 72h improves the outcome of burn wound treatment by reducing bacterial wound colonization, infection and length of hospital stay. In contrast, the right technique for eschar removal is still a matter of debate. 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. In order to assess the role and clinical advantages of enzymatic debridement by a mixture of proteolytic enzymes enriched in Bromelain (Nexobrid®) beyond the scope of the literature

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<http://dx.doi.org/10.1016/j.burns.2017.07.025>

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and in view of users' experience, a European Consensus Meeting was scheduled. The aim was to provide statements for application, based on the mutual experience of applying enzymatic debridement in more than 500 adult and pediatric patients by the consensus panelists. Issues to be addressed were: indications, pain management and anesthesia, timing of application, technique of application, after-intervention care, skin grafting after enzymatic debridement, blood loss, training strategies and learning curve and areas of future research needs. 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 document may serve as preliminary guideline for the use of enzymatic debridement with user-oriented recommendations until further evidence and systematic guidelines are available.

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## 1. Introduction

Early eschar removal is regarded as the key step in the treatment of deep partial and full thickness burns. Xiao-Wu et al. have demonstrated that early excision within 48h of injury can significantly reduce the rate of invasive infection, sepsis and length of hospital stay [1]. In accordance, Barret and Herndon showed that a significant reduction of bacterial colonization, bacterial counts and infection rate is possible by early excision within 24h of injury compared to later excision [2].

It is widely accepted that early eschar removal within 48h may improve the outcome of burn wound treatment. Nevertheless, the complexity of burn depth assessment within this time frame due to burn depth progression and late demarcation, as well as logistical reasons sometimes postpone the ideal time of eschar removal, which may lead to additional injury and loss of viable dermis. In summary, the optimal technique for eschar removal should selectively remove nonviable burned tissue, achieve minimal blood loss, allow for optimal clinical wound bed evaluation and treatment decisions resulting in faster wound healing by means of conservative treatment or early surgical coverage by autologous skin grafting in order to improve aesthetic and functional outcome and thus the quality of life.

The choice of the optimal technique is still a matter of debate. Aside from the classical technique of surgical excision, various other techniques have been developed, applied and validated for burn eschar removal, providing a level of evidence that ranges between 2 to 5: these techniques include hydro-surgery, maggot therapy, laser, collagenase based enzymatic gel treatment, special cautery systems and Bromelain based enzymatic debridement [3–14].

It has been reported that classical surgical excisions done within the first 24h after burn injury may significantly reduce blood loss during eschar removal [15]. The procedure itself is regarded as a highly technical one, and a learning curve with training is necessary [16]. Special knives for tangential excision have to be fitted using varying thickness of skin guards to limit the thickness of excised tissue, and presence of pinpoint bleeding indicates the viable layer. Nevertheless, it is still recommended to include a thin adjacent layer of viable tissue into burn wound excision to enable safe transplant take and

total excision of the burn wound. For hydro-surgery (e.g. Versajet<sup>®</sup>), there is evidence available that burn eschar excision has the capacity to significantly reduce the amount of excised viable dermis compared to standard of care, but further superiority to tangential excision could not be demonstrated so far [5–8]. In order to debride burn wounds more superficially, Dessy et al. demonstrated that the use of lubricants and a razor may reduce the pain during debridement compared to the use of sterile gauze for scraping the roof off, but no further superiority could be shown [17]. Fu et al. compared collagenase based gel (Irujol<sup>®</sup> mono) to Vaseline treatment. They were able to show a reduction of necrotic tissue after a minimum of 14 days of application of collagenase gel in a randomized controlled trial (RCT) [12]. For the use of medical maggots, larvae and cautery knife with air spray in burn wound debridement only limited evidence is available from case series predominantly showing feasibility of these techniques without comparison to standard of care [3,13,14].

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 [4,11]. In addition, it has been shown that enzymatic debridement can reduce the rate of burn wound infection and the length of hospital stay, which is mainly due to early application and timely selective eschar removal [10].

In order to assess the role and advantages of Bromelain based enzymatic debridement (Nexobrid<sup>®</sup>) beyond the scope of the existing literature and in view of users' experience, a European Consensus Meeting was scheduled to provide statements for application.

## 2. Methods

European consensus guidelines on enzymatic debridement for eschar removal in burns were formulated by a multistep process, which included a systematic literature review (2000–2016), expert panel discussion and voting on panel statements, based on the only available approved drug Nexobrid<sup>®</sup>. Peer-reviewed literature was used as a basis for pre-formulated statements by the first and senior author (C.H. and U.K.). These statements were the basis for panelist discussions. A formal evaluation of the quality of the published evidence on

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