https://doi.org/10.31925/farmacia.2025.6.20 **ORIGINAL ARTICLE**

BROMELAIN-ENRICHED PROTEOLYTIC ENZYMES CONCENTRATE TREATMENT IN PATIENTS WITH EXTENSIVE BURNS: UPDATED ROMANIAN CONSENSUS

SILVIU ADRIAN MARINESCU [1,11], TIBERIU PAUL NEAGU [2,11], ZORIN PETRISOR CRAINICEANU [3,12], RALUCA TEODORA TATAR [4,11]*, MIHAELA PERTEA [5,13], SORIN VIOREL PARASCA [6,11], MARIUS EUGEN CIUREA [7,14], FLORIAN DOREL BODOG [8,15], ANA MARIA OPROIU [9,11], EUGEN GABRIEL TURCU [1,11], ANA MARIA STEFANESCU [1], MIRELA TIGLIS [2,11], PANCHE TASKOV [3], RALUCA MIHAELA ALEXANDRU [4], DOINA IULIA NACEA [4,11], ILEANA CARMEN BOIANGIU [6], MILENA GEORGESCU [7], GEORGIANA ALBINA VIERIU [8], MIHAELA IULIANA ZAHARIA [9], LAURA RADUCU [10,11], CRISTIAN RADU JECAN [10,11]

[1] *"Bagdasar-Arseni" Clinical Emergency Hospital, Bucharest, Romania*
[2] *Bucharest Clinical Emergency Hospital, Bucharest, Romania*
[3] *"Pius Brinzeu" County Emergency Hospital, Timişoara, Romania*
[4] *"Grigore Alexandrescu" Children's Emergency Hospital, Bucharest, Romania*
[5] *"Saint Spiridon" County Emergency Hospital, Iaşi, Romania*
[6] *Plastic, Reconstructive and Burn Surgery Hospital, Bucharest, Romania*
[7] *Emergency County Hospital, Craiova, Romania*
[8] *Bihor County Emergency Hospital, Oradea, Romania*
[9] *Emergency University Hospital, Bucharest, Romania*
[10] *"Agrippa Ionescu" Emergency Hospital, Bucharest, Romania*
[11] *"Carol Davila" University of Medicine and Pharmacy, Faculty of Medicine, Bucharest, Romania*
[12] *"Victor Babeş" University of Medicine and Pharmacy, Faculty of Medicine, Timişoara, Romania*
[13] *"Grigore T. Popa" University of Medicine and Pharmacy, Faculty of Medicine, Iaşi, Romania*
[14] *University of Medicine and Pharmacy of Craiova, Faculty of Medicine, Craiova, Romania*
[15] *University of Oradea, Faculty of Medicine, Oradea, Romania*

**corresponding author: raluca.tatar@umfcd.ro*

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Abstract

Enzymatic debridement (ED) has emerged as a crucial method in the treatment of burns, particularly for managing mixed-depth burns. Enzymatic debridement was first introduced in Romania in 2015, and the initial national consensus followed in 2021. This revised consensus encapsulates the shared knowledge of Romanian experts and seeks to optimise its use in clinical practice. A consensus guideline was established through a modified Delphi process, comprising 46 statements on the application of ED in burn management. A multidisciplinary team representing 10 Romanian burn facilities discussed these statements. Consensus was established when at least 80% agreement was reached among the experts. The panellists reached agreement on all statements: 38 statements reflected a firm consensus of 100%, 5 a 90% consensus and 3 an 80% consensus. The recommendations issued by the Romanian consensus panel provide updated guidelines for enzymatic debridement in burn surgery that draw on the Romanian experience and the current scientific literature on the subject. These guidelines, alongside the previous consensus, can be regarded as a national reference protocol on enzymatic debridement.

Rezumat

Debridarea enzimatică (DE) reprezintă o metodă importantă în tratamentul arsurilor, în special pentru managementul arsurilor cu profunzime mixtă. Debridarea enzimatică a fost introdusă pentru prima dată în România în anul 2015, iar primul consens național a fost publicat în 2021. Prezentul consens revizuit sintetizează cunoștințele comune ale experților români și are ca obiectiv optimizarea utilizării acestei metode în practica clinică. Ghidul de consens a fost elaborat printr-un proces Delphi modificat și a cuprins 46 de afirmații referitoare la aplicarea debridării enzimatice în tratamentul arsurilor. Un colectiv multidisciplinar reprezentând 10 unități și compartimente de arși din România a analizat și a discutat aceste afirmații. Consensul a fost considerat atins atunci când s-a obținut un nivel de acord de cel puțin 80% între experți. Membrii panelului au ajuns la acord pentru toate afirmațiile: 38 au întrunit un consens ferm de 100%, 5 un consens de 90%, iar 3 un consens de 80%. Recomandările formulate de panelul de consens românesc oferă ghiduri actualizate pentru utilizarea debridării enzimatice în chirurgia arsurilor, bazate atât pe experiența clinică națională, cât și pe literatura științifică actuală din domeniu. Aceste recomandări, împreună cu consensul anterior, pot fi considerate un protocol național de referință privind debridarea enzimatică.

Keywords: enzymatic debridement, burn, statement, consensus

Introduction

The purpose of this national consensus document is to underline the best practices and recommendations for enzymatic debridement. Involving damaged tissue (with slough), microorganisms, biofilms, contaminants, pro-inflammatory cytokines, foreign material and proteases as a result of a burn, debridement is mandatory for the wound bed preparation. This document aims to consolidate the most recent evidence, including research and professional opinion, to establish consensus on the principles and techniques of debridement. With the ageing European population leading to increasing surgical procedures and the prevalence of hard-to-heal wounds, challenges in healthcare settings are necessitating crucial wound management. Also, at the earlier end of the spectrum of life, the immaturity of the dermo-epidermal complex in childhood raises the risk of lesions and pressure injuries, especially in the intensive neonatal and paediatric settings. For these reasons, it is necessary to establish a standardised approach to debridement that can be applied across different populations [1, 2].

Enzymatic debridement (ED) is an adjunctive method that uses specific enzymes, such as collagenase derived from *Clostridium histolyticum* and proteolytic enzymes derived from pineapple stems enriched with bromelain, to destroy devitalised tissue. Bromelain-based enzymatic debridement (BED) was approved by the European Medicines Agency (EMA) (through the pineapple stem-derived bromelain-based debridement concentrate of proteolytic enzymes NexoBrid®, MediWound Ltd, Yavne, Israel) in 2012 [4] and introduced into practice in 2013. Since then, according to PubMed, 103 papers were identified in the last decade, but with heterogeneous data, 3 RCTs and 30 retrospective studies, 69 reports about the NXB with case reports, letters, reviews, learning curve reports, consensus papers, combined modality studies, non-English language papers and *in vitro* studies [5]. Since then, more than 10,000 patients have been successfully treated with NXB for deep burns. European consensus guidelines and individual country guidelines have been published for Spain, Italy, Romania and Poland. It is currently approved for use in forty-four countries worldwide, most recently in the United States, and in pre-approval stages in Australia [1, 2, 6-12]. However, with the increased adoption of ED and ongoing research, further refinement has become essential to align national practice with the latest evidence and international guidance.

The present paper emphasises the experiences of 10 Romanian burn facilities and discusses 46 statements. Several earlier recommendations were retained because they remain important for the learning curve of ED, whereas others were updated or broadened based on new data and clinical experience. Because burn care continues to evolve, regular revisions are needed to keep practice in line with the most effective strategies [13-15].

Materials and Methods

Study design

The questionnaire was developed using a modified Delphi methodology, a well-recognised approach also employed in recent European, Spanish and Polish consensus documents. The process consisted of gathering experts in a national multi-centre nominal group with expertise in managing burn patients. The study was carried out in four stages: a) Developing and formulating the questionnaire using Delphi techniques; b) Organising the panel of experts; c) Discussion of the statements by the panel of experts in the first round; and d) Integrating and analysing the consensus statements in the second round; quantitative synthesis.

Stage one: developing and formulating the questionnaire using the Delphi technique

A series of statements was developed based on the experience of the coordinating group of experts from multinational facilities. Prior to the meeting, a non-systematic review of recent literature on bromelain in English and Romanian was conducted using PubMed and Scopus, with no time limitations. Sixty-five documents were analysed. All of them demonstrated the efficacy of the products and methods, in accordance with the European consensus update and the Italian, Spanish and Polish guidelines. The results were materialised in 46 statements based on the aforementioned European consensus on the use of bromelain and studies on its application. Eighteen statements were carried over from the Romanian 2021 consensus, while 28 were new. Statements were grouped into nine thematic categories: Indications/Contraindications (1 - 13), Mass Casualty Incidents (14 - 16), Diagnostic Criteria (17), Timing (18 - 20), Extensive Burns (21, 22), Preparation/ Application (23 - 33), Pain Management/Anaesthesia (34 - 36), Post-ED Wound Care (37 - 43) and Outcomes/Cost-Effectiveness (44 - 46).

Stage two: organising the panel of experts

The consensus involved a panel of clinical experts (n = 21), from 10 burn facilities (Bucharest, Timișoara, Iași, Craiova, Oradea), that played a key role in outlining and defining the recommendations and statements: "Bagdasar-Arseni" Clinical Emergency Hospital, Bucharest; Bucharest Clinical Emergency Hospital; "Pius Brinzeu" County Emergency Hospital, Timișoara; "Grigore Alexandrescu" Children's Emergency Hospital, Bucharest, "Saint Spiridon" County Emergency Hospital, Iași; Plastic, reconstructive and burn surgery Hospital, Bucharest; "Agrippa Ionescu" Emergecy Hospital, Bucharest; Emergency County Hospital, Craiova; Bihor County Emergency Hospital, Oradea; Emergency University Hospital, Bucharest. Members were selected for their experience in burn care, direct work in the ED and standing as opinion leaders. During the meeting,

they developed the consensus recommendations and statements to inform best practices for debridement across a variety of patient settings. The recommendations were subjected to ongoing reflection and review during the development of this manuscript.

Stage three: discussion of the statements by the panel of experts in a first round

The in-person meeting (January 21st, 2025, Bucharest) allowed centres to share their experience with ED. The meeting had two parts: first, a presentation on the latest scientific evidence. This was followed by a discussion of the 46 pre-prepared statements. Furthermore, representatives from the various burn units were able to share their personal experience on using and applying ED while addressing the different changes in the declaration wording. Representatives from burn units were required to respond to the statements using one of the provided options. Based on the analysis and scoring of the responses, the first set of recommendations was drawn up.

Stage four: integrating and analysing the second-round consensus statements; quantitative synthesis

In a second round of consensus, each statement was discussed again to verify each centre's response, and the final consensus of this article is the result of the sharing and discussion of the statements made in this second meeting.

After revision and merging, the 46 statements were distributed electronically for binary 'Yes/No' responses. To avoid bias, responses were anonymised to prevent panellists from influencing one another. Agreement was analysed descriptively, with consensus defined as ≥ 80% (≥ 8/10 votes). Each centre cast one vote. Special attention was given to mass-casualty scenarios – prompted by Romania's tragic "Colectiv" nightclub fire in 2015 [16-18]. Beyond this local experience, the possibility of large-scale burn incidents remains a global concern, whether due to industrial accidents, natural disasters, or regional armed conflicts. These situations highlight the importance of preparedness and the inclusion of enzymatic debridement in disaster response planning.

Results and Discussion

After presenting their experience regarding ED, each statement was discussed, and the final results were the outcome of sharing and discussing the initial statements and their subsequent adaptation based on the experience and knowledge acquired during the consensus-building process (Table I). Participating burn units have a combined experience of 1500 patients treated in the ED for burn injuries.

Table I

Consensus declaration on the application and care of bromelain-based enzymatic debridement on burns

Scope	Item No.	Statement	Consensus
Indications and contraindications of ED	1	Enzymatic debridement in the treatment of burns should be used only by experienced plastic surgeons who have undergone appropriate training. (10/10)	ED is considered a safe and effective method, but its use requires both theoretical knowledge and practical experience. Using ED safely and effectively requires both proper training and surgical expertise. This measure aligns with international recommendations that emphasise proper preparation before clinical application.
	2	ED is indicated for the treatment of thermal burns. (10/10)	The consensus reflects the robust clinical evidence supporting the use of ED in thermal burns. This is consistent with European guidelines and clinical studies showing that ED can reduce surgical workload while preserving viable tissue. The entire agreement suggests widespread familiarity with ED's utility in the management of thermal injuries. Careful patient selection remains important to ensure that the ED is used where it offers the most significant benefit.
	3	Enzymatic debridement is not recommended for use in the treatment of chemical or electrical burns. (8/10)	Although this statement reached consensus, there has been a lengthy discussion regarding its use in electrical burns, for which some experts have begun applying ED. More experience is still needed in these situations, as there is currently no solid evidence to support ED use in chemical burns.
	4	ED is best indicated for mid- to deep dermal burns with mixed patterns and should be avoided in superficial burns. (10/10)	The optimal indication for ED is mid- to deep dermal burns, particularly those with mixed depth patterns. By contrast, ED should not be used for superficial burns, as these typically heal spontaneously through epithelialisation. This ensures that the technique is applied only when it provides a clear benefit.
	5	ED can be applied to full-thickness burns. (10/10)	ED can also be applied to full-thickness burns. While definitive closure in such cases will ultimately require grafting, enzymatic treatment can facilitate wound bed preparation and minimise surgical trauma. This expands its role beyond partial-thickness injuries.
	6	Enzymatic debridement is a safe method for removing eschar in adult patients. (10/10)	Clinical experience confirms that ED is a safe tool for eschar removal in adult patients. Because ED is selective, it protects healthy tissue, reduces the risk of functional or cosmetic harm, and can be used effectively alongside surgery.

Scope	Item No.	Statement	Consensus
	7	Enzymatic debridement can be used safely in paediatric patients. (9/10)	ED can be applied safely in children when performed with appropriate precautions. Its selectivity helps preserve viable tissue, which is especially important in this age group to avoid unnecessary excision and long-term functional or aesthetic damage. Correct dosing and close monitoring remain essential to ensure both safety and efficacy. Recent clinical evidence has further supported paediatric use, and NexoBrid® has now received formal approval for children, following studies demonstrating its safety and effectiveness in this population.
	8	ED is highly recommended for facial burns. (8/10)	The use of ED is particularly valuable in the management of facial burns. ED is particularly valuable in areas with delicate structures, such as the eyelids or lips, as it minimises unnecessary excision and improves functional and cosmetic outcomes.
	9	ED is recommended for perineal and genital burns. (8/10)	Because these areas are difficult to treat surgically, the selectivity of ED is an advantage, helping preserve function and potentially improving both healing and quality of life.
	10	ED is indicated for burns of the hands and feet. (9/10)	Hands and feet are critical functional regions, where preserving viable tissue is essential for good outcomes. By limiting unnecessary excision and reducing the need for grafting, ED supports both function and recovery. While there is solid evidence for use in the hands, data on the feet—particularly the soles—remain more limited.
	11	The use of enzymatic debridement is not recommended when there is clinical evidence of local infection. (10/10)	Active infection reduces enzymatic efficacy and may delay healing. In such cases, infection should first be controlled with appropriate antimicrobial measures before ED is considered.
	12	ED is useful for circumferential burns, where early application can prevent burn-related compartment syndrome and the need for escharotomies. (10/10)	In circumferential burns, early ED can relieve pressure and reduce the risk of developing compartment syndrome. This approach often decreases the need for escharotomies and contributes to safer patient management.
	13	ED applied as early as possible might prevent burn-induced compartment syndrome in extensive trunk burns, but cannot replace surgical release in case of established respiratory distress. (10/10)	In extensive trunk burns, early ED may help reduce the likelihood of compartment syndrome. However, if respiratory distress is already present, surgical release remains the only effective treatment. Careful monitoring and timely decisions are essential.
Mass casualty incidents	14	Enzymatic debridement can be particularly useful in mass-casualty burn disasters. (10/10)	During mass-casualty events, the ability to treat multiple patients quickly is critical. ED is portable, relatively easy to use, and reduces operating room time, surgical workload and transfusion requirements. These features make it a valuable tool for disaster response.
	15	Any specialised burn facility should stock and have available a minimal quantity of the drug to provide emergency treatment in the case of a mass casualty incident. (10/10)	Preparedness at the hospital level is essential. Because procurement may be delayed by bureaucracy, weekends, or manufacturer availability, every facility that treats burn patients should maintain a minimal stock of ED for emergencies.
	16	Romania should maintain a National emergency supply for mass-casualty incidents, including enzymatic debridement agents. (10/10)	At the national level, ED should be part of disaster preparedness planning. Establishing an emergency stockpile would ensure rapid access during major burn events and align Romania with international readiness standards.
	17	Laser Doppler Imaging is a helpful tool for identifying burns that require ED, but clinical assessment is sufficient. (10/10)	Laser Doppler Imaging can assist in determining burn depth and selecting cases for ED. However, experienced clinical assessment remains the primary and sufficient method for decision-making.
Diagnostic	18	Classifications of ED application timing are early (< 72 h) or delayed (> 72 h). (10/10)	Early use (within 72 hours) is associated with greater efficacy and reduced inflammation, whereas later application requires thorough preparation to ensure optimal enzyme activity. This distinction provides a clear framework for clinical practice.

Scope	Item No.	Statement	Consensus
Timing of enzymatic debridement	19	Enzymatic debridement can be performed immediately after clinical evaluation of burn depth and wound cleansing. (10/10)	Once burn depth is assessed and the wound is cleansed correctly, ED can be applied immediately. Prompt use maximises benefits, accelerates eschar removal and optimises wound bed preparation.
	20	Enzymatic debridement can be applied up to 7 days from the injury in the presence of moist eschars: late application requires adequate wound preparation through mechanical removal of the superficial layers and pre-soaking with wet dressings. (10/10)	ED remains effective up to 7 days post-injury if moist eschar is present. In delayed cases, superficial necrotic layers should be mechanically removed and dry eschars softened with moist dressings to ensure proper enzymatic activity.
The use of ED in large burns	21	Sequential ED procedures for larger TBSA are possible with up to 15% TBSA *per* session. (10/10)	In extensive burns, ED can be performed in stages. Treating up to 15% TBSA *per* session is considered both safe and effective. This gradual approach allows for better physiological tolerance while ensuring adequate wound management.
	22	ED of more than 15% TBSA/session requires adequate monitoring and hemodynamic support and is considered as an off-label use. (10/10)	When more than 15% TBSA is treated in a single session, close monitoring and hemodynamic support are essential. Such use is outside the approved indication and should be reserved for specific situations, for example in disaster scenarios.
Preparation and application	23	Coagulopathy has to be treated prior to ED. (10/10)	Pre-existing coagulopathies must be corrected before ED. Failure to do so increases the risk of bleeding, particularly if larger vessels are exposed during treatment.
	24	Orifices of the face require special protection measures to prevent contact with the product, and an ophthalmologic exam is recommended before and after application. (10/10)	When treating facial burns, natural orifices such as the eyes, nose and mouth should be carefully protected to prevent accidental exposure. An ophthalmologic exam before and after the procedure is advisable to ensure ocular safety.
	25	In early use of enzymatic debridement, standard wound cleansing and saline flushing immediately before application, without prolonged pre-soaking, are sufficient for effective debridement. (10/10)	For fresh burns (within 72 h), ED can be applied after routine cleansing and saline flushing. Prolonged pre-soaking is unnecessary, which simplifies the process without reducing effectiveness.
	26	Hydrogel dressings can be used as an effective moisturiser for dry eschar to improve pre-soaking. (10/10)	In cases of dry eschar, hydrogel dressings can facilitate rehydration and enhance the effectiveness of pre-soaking, thereby ensuring more uniform product activity.
	27	Pretreatment with silver sulfadiazine or betadine should be avoided. (10/10)	Topical agents such as silver sulfadiazine or povidone-iodine should not be applied before ED. They interfere with enzymatic activity and reduce efficacy.
	28	Shortening the product application time to < 4 h is not recommended. (10/10)	The product should remain in place for at least 4 hours. Shorter application times risk incomplete debridement and unpredictable outcomes.
	29	Careful removal of blisters and epidermis remnants is a prerequisite for enzymatic debridement. (10/10)	Before applying ED, blisters and epidermal remnants must be removed. If left intact, they act as barriers to enzyme penetration and compromise the results.
	30	The use of an antiseptic solution is necessary in both early and late applications when treating contaminated wounds. (10/10)	When wounds are contaminated, antiseptic irrigation should be performed before ED, whether early or late. This reduces bacterial load without impairing enzymatic activity [1-7].
	31	In adult and paediatric patients, the recommended application is approximately 5 g *per* 2.5% TBSA, corresponding to approximately 450 cm^2, or a 3 mm-thick layer. (10/10)	The recommended dosage is about 2 g of product *per* 1% TBSA (≈ 180 cm^2), applied as a uniform layer of around 3 mm. This standard applies to both adults and children.

Scope	Item No.	Statement	Consensus
	32	It is recommended that the application technique should respect the label indications. (10/10)	The application technique should follow the manufacturer's label instructions. Adherence ensures reproducibility, safety and regulatory compliance.
	33	Repeated application of ED to the same area is recommended only in exceptional cases. (10/10)	Reapplication in the same area is rarely necessary. In most cases, a single session is sufficient when wound preparation and technique are adequate. Repeat use should be considered only in select, carefully evaluated cases.
Pain management and anaesthesia	34	Adequate pain management is necessary during all stages of treatment. (10/10)	Pain control is a cornerstone of ED. Analgesia should be tailored to the individual and maintained from wound preparation through to dressing changes, ensuring comfort and cooperation.
	35	Regional anaesthesia is recommended for the ED of the isolated (upper/lower) extremity. (9/10)	For burns of the upper or lower limb, regional anaesthesia provides consistent and reliable pain relief. It enables safe, uninterrupted treatment, particularly for large areas.
	36	Local anaesthesia for ED can be useful in minor burns. (9/10)	In small burns, local anaesthesia may be a practical option. While seldom used in daily practice, it can be sufficient for limited areas.
Wound management after ED	37	Immediate post-ED wound bed colour, bleeding patterns and 3D morphology should be assessed by an experienced plastic surgeon, who should establish a further management plan. (10/10)	Immediately after ED, the wound should be assessed by an experienced plastic surgeon. Wound bed colour, bleeding patterns and morphology must be evaluated to inform subsequent management.
	38	Maintaining a moist wound bed until full coverage is paramount and should be achieved through post-debridement soaking for > 2 h and the use of specialised occlusive dressings. (10/10)	A moist wound environment must be maintained until coverage is achieved. This can be achieved through post-debridement soaking for at least 2 hours and the use of occlusive dressings, which support healing and reduce desiccation.
	39	Special dressings (silicone, hydrocolloid, or membrane dressings) or allografts are recommended if epithelialisation is expected or to prepare the wound for grafting. (10/10)	When epithelialisation is anticipated, dressings such as silicone, hydrocolloid, or membranes are recommended. In other cases, allografts can be applied to prepare the wound bed for grafting.
	40	Antibiotic administration is similarly indicated as in surgical excision. (10/10)	Antibiotic indications after ED are the same as after surgical excision. They should be used when there are clinical signs of infection or systemic involvement, but not routinely.
	41	Full-thickness wounds require autologous skin grafting. (10/10)	In full-thickness burns, ED is not sufficient for closure. These wounds require autologous skin grafting for definitive coverage.
	42	Deep dermal burn wounds may benefit from early autografting. (9/10)	Some deep dermal burns may progress slowly. In such cases, early grafting can shorten healing and improve functional and cosmetic results.
	43	Autologous skin grafting should be considered after 14 - 21 days if there is no significant progress in epithelialisation. (10/10)	If epithelialisation does not progress within 2 - 3 weeks after ED, grafting should be planned. Delaying further increases the risk of complications and scarring.
Outcomes and cost effectiveness	44	Prolonged conservative treatment after ED may result in unstable scarring, with intensive wound care, and regular reconsideration should be given for autografting. (10/10)	If conservative care is prolonged, scars may remain unstable. Regular reassessment is necessary, and grafting should be reconsidered if healing is delayed.
	45	Scar treatment and prevention of hypertrophic scars are performed according to established standard protocols in burn care (*e.g.*, compression garments, silicone and avoidance of UV radiation). (10/10)	Scar prevention after ED follows the same principles as standard burn care. Compression garments, silicone therapy and UV protection remain essential.

Scope	Item No.	Statement	Consensus
	46	ED may help reduce resource utilisation (blood products, surgical procedures, OR room capacity, human resources). (10/10)	By reducing the need for surgical excision, transfusions and operating room use, ED can ease the strain on hospital resources. This is particularly relevant in high-volume centres or mass-casualty scenarios.

The panel reviewed 46 statements covering indications, contraindications, technical aspects, pain control, wound management after ED, and broader issues such as preparedness for mass casualties and resource allocation. In the end, 38 statements reached complete agreement (100%), 5 statements were supported by 90% of voters and 3 statements reached the minimum threshold of 80% (Figures 1 and 2).

The strongest agreement was observed for the role of ED in thermal, deep dermal and full-thickness burns, as well as for statements regarding application technique and post-ED management. There was also a unanimous consensus on key safety points: ED should be performed only by trained plastic surgeons, proper wound preparation and infection control are essential, and pain management must be tailored to each stage of treatment.

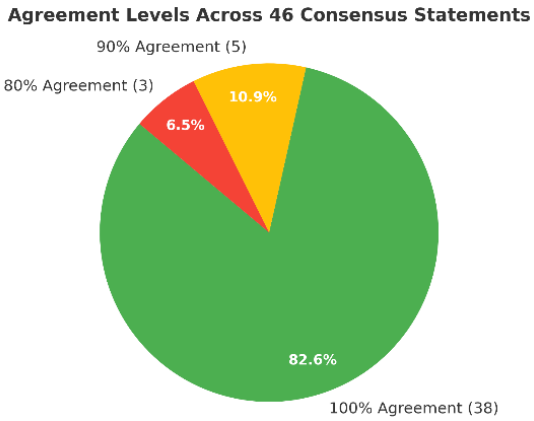

Figure 1.
Distribution of consensus levels across the statements

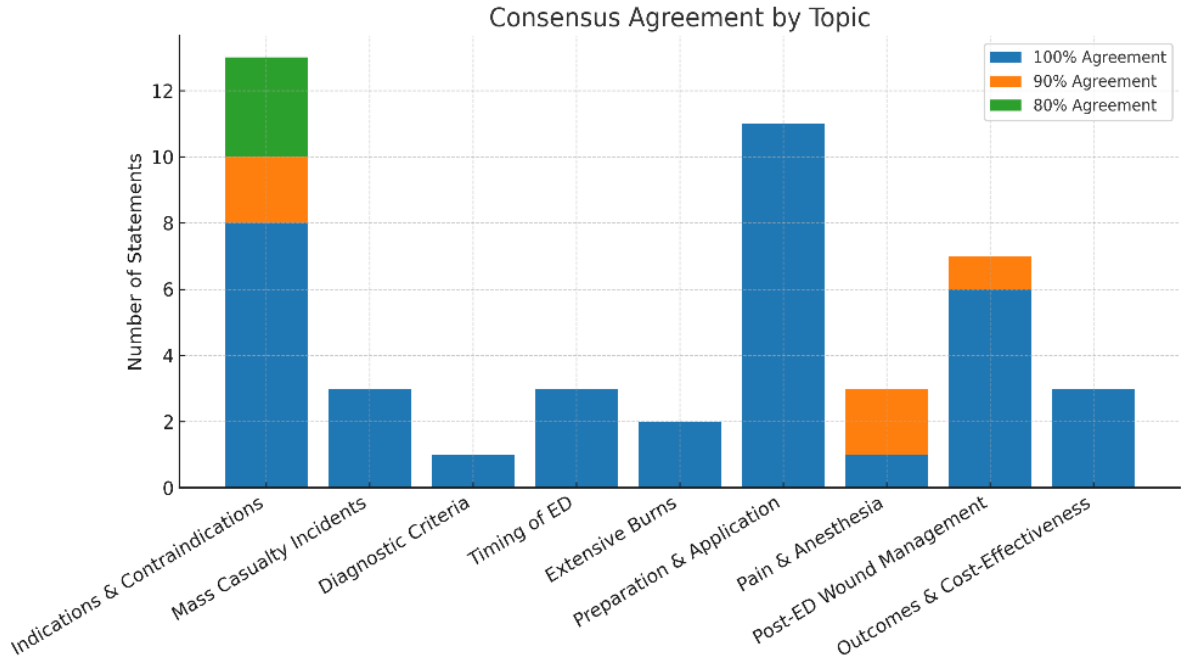

Figure 2.
Consensus agreement by topic

Areas with slightly lower agreement reflected either limited experience or ongoing debate. These included the use of ED in electrical burns, the use of ED in sensitive functional or cosmetic regions, and the value of local anaesthesia for minor burns. Here, although the majority supported the statements, some panellists preferred a more cautious approach until further evidence became available.

Finally, the group emphasised ED's potential to reduce pressure on hospital resources and to support disaster preparedness. All participants agreed on the need for both hospital-level and national emergency stocks, recognising ED as a method that can ease the work-load of surgical teams, operating theatres and blood banks during crises. The final statements are presented in Tables II - X.

Table II

Indications and contraindications of ED

Item No.	Statement	Agreement
1	ED should only be used by experienced plastic surgeons after appropriate training.	100%
2	ED is indicated for the treatment of thermal burns.	100%
3	ED is not recommended for chemical or electrical burns.	80%
4	ED is best indicated for mid- to deep-dermal burns with mixed patterns and should be avoided on superficial burns.	100%
5	ED can be applied to full-thickness burns.	100%
6	ED is a safe debridement tool for eschar removal in adult patients.	100%
7	ED can be used safely in paediatric patients.	90%
8	ED is highly recommended for facial burns.	80%
9	ED is recommended for perineal and genital burns.	80%
10	ED is indicated for burns of the hands and feet.	90%
11	ED is not recommended when there is clinical evidence of local infection.	100%
12	ED is useful for circumferential burns; early application can prevent burn-related compartment syndrome and reduce the need for escharotomies.	100%
13	In extensive trunk burns, early ED might help prevent compartment syndrome, but cannot replace surgical release if respiratory distress is established.	100%

Table III

Mass casualty incidents

Item No.	Statement	Agreement
14	ED can be instrumental in mass-casualty burn disasters.	100%
15	Every specialised burn facility should stock a minimal quantity of ED for emergencies.	100%
16	Romania should maintain a national emergency supply that includes ED agents.	100%

Table IV

Diagnostic criteria

Item No.	Statement	Agreement
17	Laser Doppler Imaging is helpful to identify burns requiring ED, but clinical assessment is sufficient.	100%

Table V

Timing of Enzymatic Debridement

Item No.	Statement	Agreement
18	ED timing is classified as early (< 72 h) or delayed (> 72 h).	100%
19	ED can be used immediately after clinical depth evaluation and wound cleansing.	100%
20	ED can be applied up to 7 days from injury in the presence of moist eschars; late use requires mechanical preparation and pre-soaking with wet dressings.	100%

Table VI

Use of ED in extensive burns

Item No.	Statement	Agreement
21	Sequential ED is possible for larger TBSA, with up to 15% TBSA *per* session.	100%
22	ED > 15% TBSA *per* session requires monitoring and hemodynamic support and is considered off-label.	100%

Table VII

Preparation and application

Item No.	Statement	Agreement
23	Coagulopathy must be treated prior to ED.	100%
24	Facial orifices require protection from product contact; an ophthalmologic exam is recommended before and after application.	100%
25	In early use, standard wound cleansing and saline flushing immediately before application are sufficient; prolonged pre-soaking is not required.	100%
26	Hydrogel dressings can be used to moisturise dry eschar and improve pre-soaking.	100%
27	Pretreatment with silver sulfadiazine or povidone-iodine should be avoided.	100%
28	Shortening the application time to < 4 h cannot be recommended.	100%
29	Careful removal of blisters and epidermal remnants is a prerequisite for ED.	100%

Item No.	Statement	Agreement
30	An antiseptic solution is necessary when contaminated wounds are present, whether applied early or late.	100%
31	Recommended dose: 2 g *per* 1% TBSA (≈ 180 cm²), applied as a 3 mm thick layer (adults and children).	100%
32	The application technique should follow the label instructions.	100%
33	Repeated application to the same area should be reserved for exceptional cases.	100%

Table VIII

Pain management and anaesthesia

Item No.	Statement	Agreement
34	Adequate pain management is necessary during all stages of treatment.	100%
35	Regional anaesthesia is recommended for the ED of an isolated extremity.	90%
36	Local anaesthesia may be helpful in minor burns.	90%

Table IX

Post-ED wound management

Item No.	Statement	Agreement
37	An immediate post-ED assessment of wound bed colour, bleeding patterns and 3D morphology should be performed by an experienced plastic surgeon to inform the management plan.	100%
38	Maintaining a moist wound bed until full coverage is achieved is paramount (post-debridement soaking for > 2 h and use of occlusive dressings).	100%
39	Special dressings (silicone, hydrocolloid, membrane) or allografts are recommended if epithelialisation is expected or if grafting is anticipated.	100%
40	Antibiotic administration after ED follows the same indications as after surgical excision.	100%
41	Full-thickness wounds require autologous skin grafting.	100%
42	Deep dermal burns may benefit from early autografting.	90%
43	Consider autologous skin grafting after 14 - 21 days if epithelialisation shows no significant progress.	100%

Table X

Outcomes and cost-effectiveness

Item No.	Statement	Agreement
44	Prolonged conservative treatment after ED may result in unstable scarring; autografting should be reconsidered.	100%
45	Scar prevention/treatment should follow standard burn protocols (compression garments, silicone, UV avoidance).	100%
46	ED may reduce resource use (blood products, surgery, OR time, staffing).	100%

Prioritising safety and achieving the treatment goals are essential during debridement. Care must be taken to minimise unintentional exposure to or harm to viable structures, such as nerves and blood vessels. The health professional should have a solid understanding of human anatomy and, based on their clinical skills and area of practice, be able to discriminate among tissue types across anatomical sites to reduce the risk of injury [19]. The greater the removal of microbial and non-microbial elements, including exotoxins, endotoxins, enzymes and foreign substances, while minimising harm to surrounding healthy tissue, the fewer the obstacles to healing [20], thereby enhancing the effectiveness of debridement in facilitating healing without causing delays or interruptions.

Approved in Europe in 2013 to achieve more individualised burn eschar removal while being less invasive and more efficient, NexoBrid® and, by extension, the enzymatic debridement have attracted significant attention and adoption among plastic surgeons worldwide over the past 5 years [21, 22]. Since the last consensus established in 2020 [9], when experience with approximately 350 patients was shared, an additional 400 patients have been treated, based on the Romanian consensus document.

Forty-six statements were formulated, reaching important topics like: indications, pain management and anaesthesia, significant surface indication, time of application for various indications, preparation and application, post-interventional wound management, skin grafting, outcome, scar and revision management, skin grafting, outcome, scar and revision management, patient's perspective, logistic aspects and training strategies. The degree of consensus was high: 38 statements received complete agreement (100%), 5 were supported by 90% of voters and 3 met the minimum threshold of 80%. A new perspective on the potential of outpatient treatment has attracted considerable interest, highlighting further benefits of the concept compared with actual skin grafting, which, in 2017, during the European

Consensus meeting, generated considerable controversy [2].

Although many advantages have been described for the treatment of severely burned patients, particularly the earlier and less traumatic removal of necrotic tissue, we acknowledge the limitations of enzymatic debridement as defined by European surgeons, and this should be kept in mind in further discussions aimed at improving success rates. Berner *et al*. reported their experience with patients diagnosed with diabetic foot disease, for which enzymatic debridement was used, with eschar and wound deepening necessitating surgery and skin grafting. The authors recognised their limited experience, but, particularly in diabetic foot wounds, they continued to recommend avoiding the enzymatic debridement, primarily because of micro-angiopathy and bleeding patterns [23]. Another limitation concerns high-voltage injuries with deep muscle damage and increased compartmental release, as the enzyme is limited to the eschar. Additionally, the sald burns have not yielded the same results as the flame burns when using ED; therefore, this technique is not recommended in the early phase of scald burns. All panellists agreed that the use of ED on large surfaces should be discussed intensively, as water loss is not negligible in light of resuscitation/volume management. That is why the profile of the ideal patient with extensive burns for ED must be established, previously to early eschar removal and the systemic effect of bromelain [21, 24-28]. Fischer *et al*. demonstrated the feasibility and safety of Enzymatic Debridement for the prevention of operative escharotomy in circumferential deep burns of the distal upper extremity [29]. These findings reinforce the notion of an early time point for ED use, after pre-soaking. Laser Doppler Imaging (LDI) is considered by the panellists to be the most useful imaging method, owing to its ability to predict regions that may benefit from early grafting after enzymatic debridement, as described by Jan SN *et al*. [30]. Although, the "Colectiv" tragedy is still kept alive in the Romanian burns panel, no consensus has been reached regarding the limited operations room capacity. In any ED case, additional issues may arise, such as the possibility of transplantation and the need for large volumes of blood products, although Rosenberg *et al*. reported a reduced need for blood products after EED in general [19].

Conclusions

This second Romanian consensus builds up on the first document published in 2021 and incorporates updated knowledge in line with recent European standards. The statements confirm that ED is a safe and effective method in carefully selected cases, particularly in mixed-depth burns and in functionally or cosmetically sensitive regions. At the same time, the panel clearly outlined the limits of ED: it is not recommended for chemical or electrical injuries, in the presence of infection, or for more than 15% TBSA *per* session without strict monitoring. Beyond its clinical aspects, ED was also recognised for its organisational advantages. By reducing the need for surgical excision, transfusions and operating room time, it helps preserve critical resources, particularly in high-demand situations such as mass casualty incidents. These updated recommendations can serve as a practical reference for burn centres, units and compartments across Romania, while keeping alignment with broader European practice. Continued research and clinical experience, including contributions from Romanian teams, will be essential for further refining these guidelines, particularly with respect to long-term outcomes.

Conflict of interest

The authors declare no conflict of interest.

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