

# Nanocellulose-based wound dressing for conservative wound management in children with second-degree burns

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## Abstract

The initial care of burn wounds and choice of dressing are pivotal to optimally support the healing process. To ensure fast re-epithelialisation within 10–14 days and prevent complications, an optimal healing environment is essential. An innovative dressing based on nanocellulose was used for the treatment of burns in children. Children (0–16 years) with clean, partial-thickness burn wounds, 1 to 10% of the total body surface area were included. Complete re-epithelialisation was achieved within 7–17 days, with 13 patients showing re-epithelialised >95% by day 10. Satisfying results concerning time to re-epithelialisation and material handling were obtained. The possibility to leave the dressing on the wounds for 7 days showed a positive effect in the treatment of children, for whom every hospital visit may cause massive stress reactions. The nanocellulose-based dressing is a promising tool in conservative treatment of burns. Reducing the frequency of dressing changes supports a fast and undisturbed recovery; moreover, the dressing provides an optimal moist healing environment. The time to re-epithelialisation is comparable to frequently used materials, and cost reduction effect can be achieved without loss of quality. Possible pain and distress levels are kept to a minimum; therefore, flexibility and compliance of the patients and their parents are enhanced.

## KEYWORDS

burn injury, burn treatment, paediatric burns, partial thickness burns, re-epithelialisation

## 1 | INTRODUCTION

Burn injuries are among the most common type of trauma, accounting for a major health burden worldwide with a majority of cases in low- and middle-income countries.<sup>1</sup> In high-income countries, the deaths of children caused by burns have been decreasing with improved treatment options, showing a seven times lower rate compared with low- and middle-income countries. The

economic impact worldwide is enormous with burns being a leading cause of disability.<sup>1,2</sup>

The causes of thermal trauma differ depending on age and gender. In small children, hot liquids cause the vast majority of burns. Women usually get burned in domestic kitchens with hot liquids, flames, or by cook-stove explosions while men most likely injure themselves at work by fire, scalds, chemical and electrical burns, or as leisure time accidents. Non-fatal burns mostly result in

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a life-long burden such as disfigurement and disability, often resulting in stigma and rejection.<sup>1</sup> Scarring remains one of the major issues when it comes to long-term outcomes, and for that reason, it is one of the most important parameters for physical and psychological outcomes in children.<sup>3</sup> Therefore, independent of age, a fast and accurate assessment of the severity of the burn, including depth of skin involvement and percentage of total body surface area (TBSA), is of great importance for further treatment and prognosis.<sup>4</sup>

Burns are usually categorised by the depth of skin involvement. Superficial burns (I degree, I°) are characterised by an erythema of the skin, not needing any surgical intervention and spontaneous wound healing. Partial-thickness burns are subcategorised in superficial partial-thickness (IIa degree, IIa°) and deep partial-thickness (IIb degree, IIb°) dermal burns. Superficial partial-thickness burns usually show spontaneous wound healing within 14 days without any or minimal scarring and can be treated with special wound dressings, whereas in IIb° burns and full-thickness burns (III degree, III°), a prolonged wound-healing process and distinct scarring is inevitable. Therefore, the presence of IIb degree or III degree burns states an indication for surgery.<sup>4,5</sup>

Especially in severe burns, affecting large parts of the body surface, the availability of skin graft donor sites is limited, thus the decision between a conservative or operative approach is an important but challenging task. The development of new dressings for conservative wound management after burn trauma has gained increasing attention in burn research, with a great diversity also for application in deep thickness burns.<sup>5-7</sup>

A wide variety of materials are used for the conservative treatment of burns, with dressings containing silver seem to be most frequently used.<sup>3,8-12</sup> Until today, no unified “gold standard” could be determined.<sup>7</sup> However, over the past years, significant progress has been made developing new and innovative dressings.<sup>13</sup> Especially in the management of burn wounds in children, a quick and uncomplicated treatment is of great importance. A material that is easy to handle and apply in clinical practice is required.

A large-scale multicentre and interdisciplinary online survey by Selig et al<sup>7</sup> focused on finding the properties for the ideal dressing. Among the most common answers, characteristics such as non-adhesion, absorbency, and antimicrobial activity could be found. Additionally, the dressings should be easily removable to guarantee a pain-free change of the material. Furthermore, a reduced frequency of dressing changes was also ranked high. Other studies considered the absorption of secretion to provide a good exudate management and ensure a moist

### Key messages

- initial care of burn wounds and choice of dressing are pivotal for the outcome
- fast re-epithelialisation within 10–14 days prevents complications and scarring
- nanocellulose-based dressings provide an optimal moist healing environment
- keeping pain and stress levels in children to a minimum is essential
- infrequent dressing changes support recovery and enhance flexibility and compliance

environment on the wound surface as an asset for optimal wound healing.<sup>14</sup> Besides, the use of the dressing in terms of reducing the time to re-epithelialisation is essential.<sup>15</sup>

The further advancement and development in this field is of great interest,<sup>5-7,10,16,17</sup> as the initial care of burn wounds and the choice of dressing are pivotal for fast and undisturbed wound healing after thermal trauma. Providing an optimal healing environment to ensure fast re-epithelialisation within 10–14 days to prevent complications such as wound infections and scarring is crucial.<sup>4,8,15,18,19</sup> To keep pain and stress levels in children to a minimum, a dressing which allows infrequent changes should be chosen. Frequent and painful dressing changes may not only cause traumatisation of the child but also disturb the wound healing process. Both factors show a bad impact on wound healing time.<sup>8,15,20-22</sup>

Reducing the frequency of dressing changes to once a week could not only increase the flexibility and compliance of the families, but could also lead to cost reduction without affecting the treatment quality. With a reduction of pain during the dressing change also the use of pain medication can be decreased.

In this study, we are testing a new material based on cellulose, which provides the characteristics of an ideal dressing for burn wounds.

Cellulose with structures in the nanometre range (up to 100 nm in diameter) is called nanocellulose. Nanocellulose is divided into three categories: microfibrillated cellulose, nanocrystalline cellulose, and bacterial nanocellulose.<sup>23,24</sup>

Bacterial nanocellulose, produced by *Komagataeibacter xylinus*, shows a high content purity and tensile strength, characterised by a nanofibre structure that confers mechanical stability and flexibility. In previous trials,

bacterial nanocellulose's high biocompatibility and hydrophilic properties gained attention as a possible new hydrogel material in wound management.<sup>25</sup> Bacterial nanocellulose is accelerating the wound healing by reducing fluid loss and facilitating the treatment by pain reduction during dressing changes.<sup>25</sup> In multiple studies, the application of cellulose-based materials in burns and chronic wound care as well as coverage of split skin graft donor sites has already been described, and the material has proven its benefits in a wide range of applications. With its unique properties, providing a moist wound environment and absorption of wound secretion, promising results have been achieved in wound management with the material positively affecting the wound healing process.<sup>14,26-28</sup>

## 2 | METHODS

### 2.1 | Recruitment

Children from the age of 0 to 16 years who presented themselves at our Department for Plastic and Reconstructive Surgery with superficial partial-thickness burn wounds (IIa°), covering a total body surface of 2 to 10% and did not meet any exclusion criteria, were considered eligible for inclusion into our study (EK Nr: 1853/2017).

### 2.2 | Exclusion criteria

Patients showing one of the following characteristics had to be excluded from the study: (a) presentation at our department >48 hours post-trauma, (b) burn wound infection, (c) I°, IIb°, and III° burn wounds, (d) TBSA <1% or >10%, (e) ongoing infections, (f) immunosuppressive therapy, (g) malignant diseases, (h) infectious diseases (HIV, hepatitis, tuberculosis), and (i) pregnant and/or breastfeeding women.

### 2.3 | Primary endpoint

The primary endpoint of our study is the number of days from the burn trauma to wound re-epithelialisation. The evaluation and photo-documentation of the wounds and their healing process is performed during every dressing change. The TBSA of the wound and percentage of wound re-epithelialisation are assessed and documented using two methods: (a) clinical judgement from one consultant and one resident plastic surgeon at each dressing change, (b) photo analysis using ImageJ. All pictures are

taken with a scale next to the burn wounds, enabling us to analyse them using ImageJ. The burn wounds were considered re-epithelialised when wound closer of >95% could be observed.

Furthermore, parameters such as number of dressing changes, ability for wound assessment through the dressing, pain levels during every dressing change, and wound infections are documented.

### 2.4 | Pain score assessment

As pain management is an essential part of the treatment process, the pain and distress levels at every dressing change were obtained using the *Büttner Scale*<sup>29</sup> for children under the age of 8 years. The Visual Analog Pain Scale (VAS 1–5) score was used for children above the age of 8.

### 2.5 | Adverse events

If adverse events, for example, infections or reactions to the used dressing occur, the dressing regime is changed according to the standard of care at our department and previously collected data are used until that time. In cases where all inclusion criteria were met, the final decision whether the patient will be included in the study or not was made by the plastic surgeon in charge.

#### 2.5.1 | Procedure

Children and their parents usually present themselves at the children emergency outpatient clinic. After cleaning and disinfection of the burn wounds, which in a great number of cases had not been accurately treated by the parents but covered with, for example, toothpaste or flour, an assessment of the affected area is made. The depth of the burn wounds is evaluated clinically by an experienced resident plastic surgeon and a consultant plastic surgeon.

All the enrolled patients and their legal representatives have given written informed consent before inclusion into the study. When the patient met all the inclusion criteria and there was no reason for exclusion, the nanocellulose wound dressing was applied directly on the burn wound in accordance with the manufacturer's instructions. To ensure fixation and maintain a moist wound environment, a fatty gauze was put in-between the nanocellulose and a dry cover up dressing as well as a bandage for fixation. The application process is illustrated in Figure 1. To ease the removal and reduce pain trauma to the wound beds, the dressing can be soaked in sterile water prior to removal. When soaked, the adherence of

**FIGURE 1** Application process of the nanocellulose dressing: (a) assessment of the wound, disinfection; (b) application of the nanocellulose dressing; (c) application of the fatty gauze to maintain a moist environment



**FIGURE 2** Study procedure time table: day 0—admission to the hospital and primary care of the wounds; day 3—first visit, dressing change, evaluation of the wound; day 10—second visit, dressing change, evaluation of the wound, termination of study if wound close >95%; day 17—final wound control



the material decreases and can be removed easily. When soaked, the adherence of the material decreases and it can be removed easily. Furthermore, the more advanced the healing process, the easier it is to remove the material.

The dressing is left in place for 3 days. On day 3, the first dressing change, wound assessment, and photo documentation with and without the dressing are performed. Wounds are disinfected and debrided when necessary. Pain and distress levels are evaluated as described earlier. If the wound healing is accurate and there are no signs of infections, a new dressing is applied as stated.

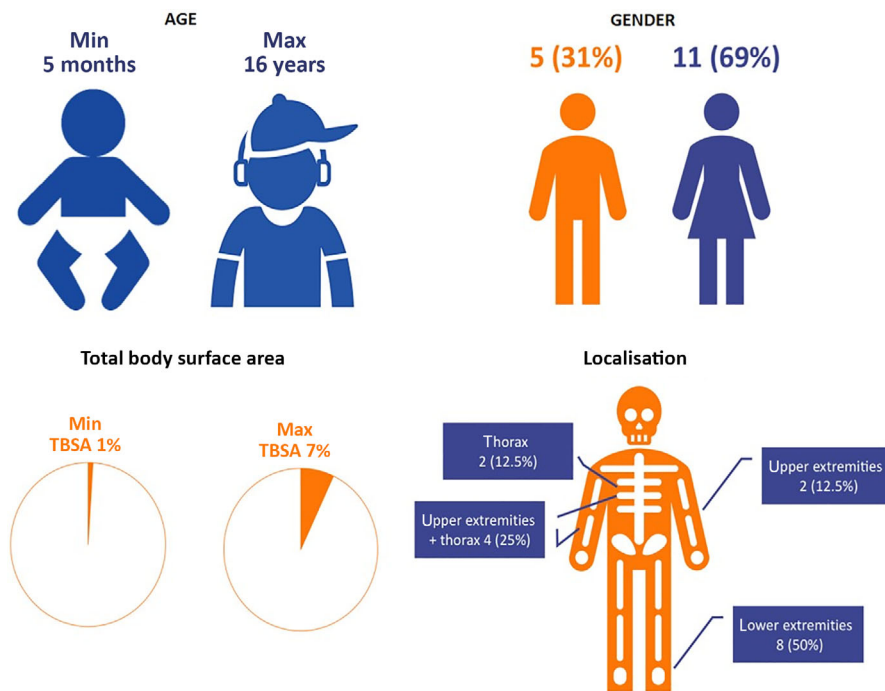
Follow-up visits then take place on day 10 and day 17 after trauma, following the same working steps as on day 3 (Figure 2). At each check-up, the burn wounds are again assessed by an experienced resident plastic surgeon and a consultant plastic surgeon. In case of wound closer or occurrence of adverse events, the study is terminated and follow-up appointments are arranged following our standard of care in burn patients.

If necessary, a visit outside the schedule is possible at any time. The study is discontinued in case of adverse events (skin irritation, excessive itching, allergic reactions, withdrawal of consent, systemic infections). In such cases, the treatment is continued using our standard dressings (following our standard procedure in paediatric burns).

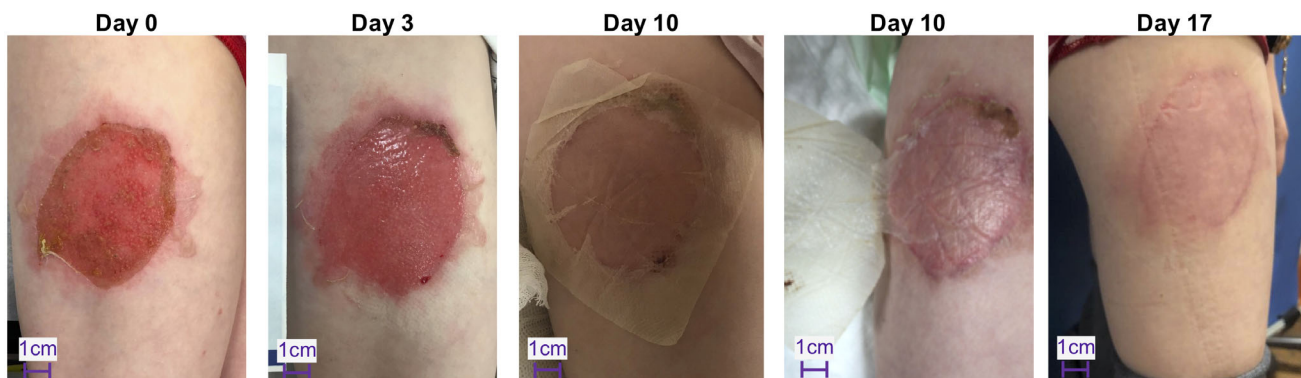
### 3 | RESULTS

All children presenting to the outpatient clinic of the Department for Plastic and Reconstructive Surgery of the Medical University of Vienna were assessed for eligibility of inclusion into this study. In total, 16 participants could be included into our trial. All children suffered their burn wounds from hot water, mostly pulling down a cup of coffee or tea off the table, pouring the hot liquid all over their bodies.

Demographics show an age distribution between 5 months and 16 years with an average of 4 years and



**FIGURE 3** Demographic data of included patients, age min 5 months to max 16 years; gender 5 males (31%), 11 females (69%); TBSA ranging from 1% to 7%; localisation thorax 2 (12.5%), upper extremities 2 (12.5%), upper extremities and thorax 4 (25%), lower extremities 8 (50%)



**FIGURE 4** Wound healing progress from initial presentation (day 0) at our clinic with a 2% burn wound in a 3-year-old child on the outer thigh, to dressing changes and wound assessment (day 3, day 10), to final follow-up visit (day 17). On day 10, the material is transparent and easily removable due to full re-epithelialisation of the wound

50% of the children being under 2 years of age. Overall, 5 boys and 11 girls were included in our study. The TBSA ranged from 1% to 7% (average 3.5% TBSA), with burns or scalds affecting all body parts. However, as in most cases, burns resulted from unintentional self-harm, mainly the front of the patients' bodies was affected. Data are illustrated in Figure 3.

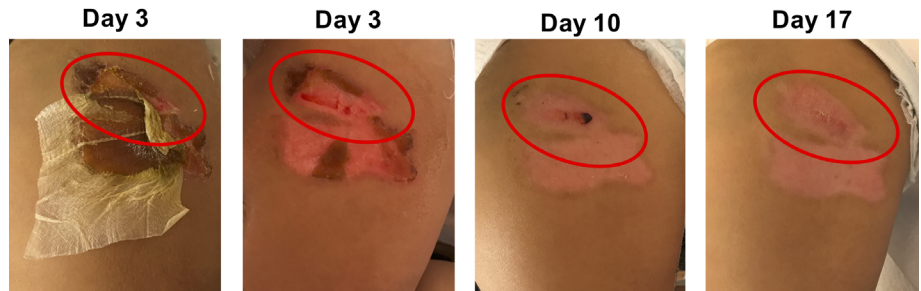
After inclusion into the study, the treatment followed the standard procedure as described in Section 2. Children mostly were excluded because the extent of burn was not according to the inclusion criteria (TBSA >1% to <10%) or was not substantial enough (I° burns), showing an erythema only. The first follow-up visit was scheduled 3 days post-trauma to

ensure that there occurred no further progression to a deeper degree of burn, which might result in an indication for surgery. One of 16 children had to be excluded from the study for that very reason and got further surgical treatment.

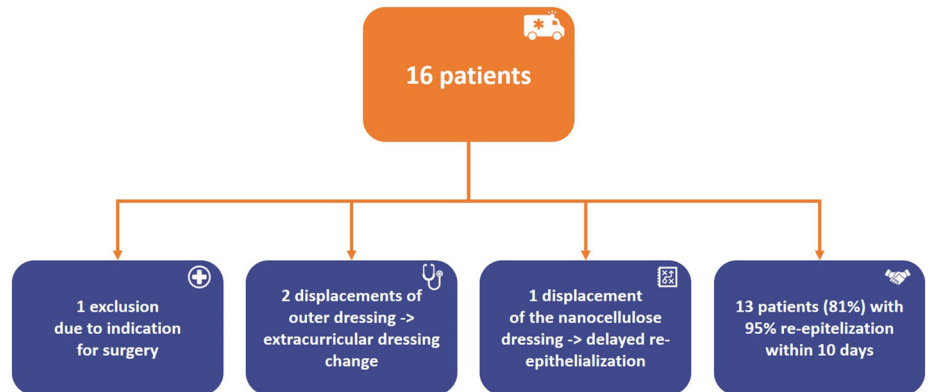
### 3.1 | Primary outcome

At every follow-up visits (days 3, 10, and 17 post-trauma), wounds were assessed by a resident plastic surgeon and a consultant plastic surgeon, both experienced in the management of burn wounds, evaluating the wound healing process. There were no inconsistencies in the wound

**FIGURE 5** Wound healing process (day 3 to day 17) after a 1% burn in a 1-year-old child on the outer thigh: delayed wound healing due to displacement of the dressing within the first 3 days



**FIGURE 6** Distribution of the initially included 16 patients: 1 exclusion due to indication for surgery; 3 deviations from the study protocol due to displacements of the dressing; 13 patients >95% re-epithelialisation within 10 days



assessment between the two surgeons. Photo documentation with a scale was performed and secondary outcome factors such as pain levels, possibility of assessment of the wounds through the dressing and signs of infections were recorded.

Time to re-epithelialisation occurred within 7–17 days with 75% showing >95% healing progress on day 10. Wound healing over time is shown in Figure 4.

One patient showed delayed re-epithelialisation on a small part of the burn wound (10%) due to obvious wearing off of the nanocellulose dressing (Figure 5).

Dislocation of the dressing was a common occurrence concerning the cover up dressing, consisting of fatty gauze and a dry bandage on the very top. Due to the adhering properties of the nanocellulose dressing after application on the wound, slight dislocation occurred in only one case. Two patients presented early to the scheduled follow-up appointment due to loss of cover up dressing. In one of these patients, the nanocellulose dressing was removed as well, because the wound showed re-epithelialisation rate of >95% by day 7. Another patient missed his 10-day post-trauma follow-up visit and presented by day 13 showing 100% re-epithelialisation of his burn wound.

Thus, a total number of 13 patients showed full re-epithelialisation by day 10 post-trauma (Figure 6). On day 17, there was a follow-up visit to monitor the accurate wound care. For aftercare treatment, we recommended the application of fatty ointments three

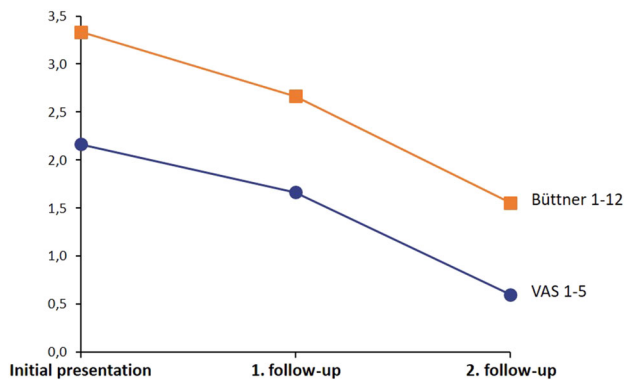
times a day and to avoid sun exposure for at least 1 year.

Parameters such as number of dressing changes, possibility of wound assessment through the dressing, pain levels during every dressing change, and wound infections were documented at every visit.

Besides the three cases reported earlier, no unscheduled dressing changes were performed. With progression of the re-epithelialisation, the dressing becomes more transparent, allowing to evaluate the healing process without removing.

The used pain-intensity scores were adapted depending on the age of the child. We used the *Büttner* scale<sup>29</sup> for children under 8 years and the VAS-score for all children above. In the course of the study, the pain scores showed a significant decrease compared to the initial presentation and first follow-up. Pain values were surprisingly low throughout the course the study. The children showed a rather homogeneous distribution of pain levels for each dressing change. Although pain was worse at the beginning of the treatment, it decreased during the healing progress of the burn wounds, as expected (Figure 7). Furthermore, children old enough reported a slight ease of pain after application due to the cooling effect of the dressing.

The material we used in our study was easy to handle in clinical routine when performing dressing changes. With the material being flexible, it can be further adjusted after applying it on the burn wounds;



**FIGURE 7** Decrease of pain levels due to progress in wound healing over the course of the study. From the initial presentation at our department to the second follow-up visit on day 10 post-trauma

however, the material sticks to the wound and surrounding skin independently, which is of advantage in small children. After full re-epithelialisation, it can be peeled off easily.

Very satisfying results concerning time to re-epithelialisation and material handling were obtained. The possibility to leave the dressing on the wounds for 7 days shows a very positive effect in the treatment of children for whom every hospital visit may cause massive stress reactions even if pain levels are kept to a minimum. Overall, the included children showed great acceptance for this new dressing and experienced an uneventful recovery.

### 3.2 | Adverse events

No adverse events such as infections or allergic reactions to the used material were recorded for the course of the study. Delayed re-epithelialisation due to displacement of the dressing occurred in one patient.

## 4 | DISCUSSION

The initial care of burn wounds and the choice of dressing are pivotal for an optimal healing process, as providing the best possible healing environment enables fast and undisturbed wound healing. Prolonged healing time does not only result in an increased burden for the patient and costs for the health system, but also raises the probability of hypertrophic scarring.<sup>3,8,15,18,19,30</sup>

In this study, we tested a new promising material based on nanocellulose to treat IIa degree burns in children aged 5 months to 16 years. Over the past years, many research groups focused on defining characteristics

for the optimal dressing for advanced burn wound management.<sup>7,17,27</sup> The dressing we used in our study presents unique and favourable characteristics such as providing a moist environment during the healing process while being permeable for air and liquids and absorbing wound exudates. In a study by Wei et al,<sup>31</sup> they performed basic experiments comparing wound healing environments, stating that wound healing in a moist environment was superior to a dry environment. The moist environment leads to promotion of growth factor production, stimulation of cell proliferation and acceleration of cell migration. In addition, a reduction of pain levels during the healing process and dressing changes had also been detected in wounds healing in a moist surrounding.<sup>31</sup> Tang et al<sup>9</sup> detected that burn wounds could even progress to a deeper degree, leading to a subsequent damage of the burned skin if the loss of fluids exceeds a certain threshold. Therefore, an optimal dressing must not only be able to absorb wound secretion but also maintain a moist environment throughout the healing process to assist and support fast re-epithelialisation.<sup>9</sup>

In our study, no adverse events such as infections were detected. However, as the risk of infection in burn wounds is comparatively high, another essential characteristic of a burn dressing includes antimicrobial activity.<sup>7</sup> Some studies claim that the use of silver-containing dressings, which are supposed to provide an anti-infective effect, would delay wound healing due to mild toxicity.<sup>11,16,32</sup> To overcome these limitations in silver-containing dressings, recent studies found an alternative based on nanocellulose material where the same material that was used in this study had been soaked with antiseptic solutions, which could be useful in prevention infections or in the treatment of infected wounds.<sup>33,34</sup> As burn wounds being prone to infections, the application of nanocellulose combined with antiseptic substances is of great interest for further investigation. Furthermore, in an *in vivo* clinical study, the material based on nanocellulose has already shown to be a promising tool for skin graft donor site treatment in burn patients.<sup>14</sup>

A study conducted by Wasiak et al<sup>6</sup> showed the biggest advantages for an optimal wound healing relate to the time to full re-epithelialisation, the frequency and number of dressing changes, and pain and stress levels experienced during every change of dressing. Our observations during this study showed a comparable time to full re-epithelialisation to prior studies when Suprathel or Mepilex Ag were used,<sup>16</sup> with an average time to re-epithelialisation of 10 days, thereby showing a consistency with our data. According to previous studies, the time period to obtain an optimal outcome and significantly reduce the risk of scarring in burn wounds is between 10 and 14 days.<sup>8,15,18</sup>

Assessing wounds adequately and the appropriate and objective recording of data are always challenging and limited in studies including small children. Especially, with regard to pain, scores and stress levels during every dressing change. We tried to solve this problem by using a material conferring a benefit in treatment of children suffered from burn wounds. With its non-adherent properties and the possibility to leave the dressing in place for a whole week, disturbance of the re-epithelialisation process and thereby trauma on the wound beds on dressing removal can be decreased. Moreover, distress levels can be limited by extending the frequency of dressing changes up to 7 days. By trying to decrease pain levels during dressing changes using a material that can be easily removed, wound healing might be further accelerated compared to other dressing materials.<sup>3</sup> Several studies declared that the reduction of the frequency of dressing changes, and therefore also a decrease of occurrence of high pain and distress levels lead to a significant, positive impact concerning re-epithelialisation rates in children. High stress levels could lead to a dysregulation of biomarkers and thereby to an impairment of the healing process.<sup>12,19-22</sup>

Even when leaving the dressing in place for 7 days, no adverse events related to the used material had been detected, potentially underlining its high biocompatibility. Additionally, the material we used in our study was easy to handle in clinical practice performing dressing changes. It showed a cooling effect after application which is a great benefit after suffering a burn injury compared to other frequently used materials in acute burn wound treatment. With the material being flexible, it can be further adjusted after applying it on the burn wounds. Anyhow, the material would stick to the wound and surrounding skin independently, another advantage in treatment of small children. During the healing process, the material gets slightly transparent allowing an assessment of the healing progress without removing the dressing completely. After full re-epithelialisation, it can be peeled off easily. As the liquid component of the dressing would be absorbed by a dry cover up bandage, an extra layer of fatty gauze must always be applied in between. This additional work-step can be time consuming. An “all-in-one” wound dressing would help to spare time and material. As mentioned earlier, the cover up bandage tended to slip in some patients. Consequently, we have applied an extra fixation with patches where necessary.

The tested wound dressing based on nanocellulose might be a promising tool in conservative wound treatment after burn injuries. With reducing frequency of dressing changes a fast and undisturbed recovery of the burned skin can be achieved. The time to re-

epithelialisation is comparable to frequently used materials in burn wound management, however, still providing an optimal moist healing environment. Thereby not only possible pain and distress levels in children are reduced to a minimum and their challenging treatment is facilitated, but enhanced flexibility and compliance of the patients and their parents as well as a cost reduction effect without loss of quality could be observed.

Considering all of these characteristics, a valid alternative to frequently used dressings in burn wound treatment might have been found. Since this study is limited by its closely defined patient population, further studies with a larger number of cases are required to validate our findings.

### ACKNOWLEDGEMENT

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### CONFLICT OF INTEREST

All authors hereby declare that they have no conflicts of interest.

### DATA AVAILABILITY STATEMENT

No data are available

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