Effective use of Biobrane as a temporary wound dressing prior to definitive split-skin graft in the treatment of severe burn: A retrospective analysis

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A B S T R A C T

Aims: To report on the use of Biobrane, a synthetic skin substitute, as a temporary wound cover in patients with severe burn. In particular we wished to examine the role of Biobrane in maintaining a healthy wound bed following surgical excision and identify factors associated with regrafting.

Methods: A retrospective case series review was performed on patients with severe burns (≥20% TBSA), admitted to the Victorian Adult Burns Service, in Melbourne, from January 2009 to June 2012. Logistic regression analysis was performed to identify factors associated with regrafting.

Results: Out of 58 patients with median %TBSA burn of 30%, 22 patients (37.9%) required regrafting of at least one area previously treated with Biobrane and split-skin graft. On univariate analysis, need for regrafting was significantly associated with increasing %TBSA (OR 1.04, 95% CI: 1.01–1.08; p = 0.02), and after multivariate analysis to adjust for this effect, hospital LOS (OR 1.04, 95% CI: 1.02–1.07; p = 0.001); total operative time (OR 1.16, 95% CI: 1.06–1.28; p = 0.002) and total number of surgeries (OR 1.69, 95% CI: 1.27–2.26, p < 0.001) remained significantly associated with regrafting. Age, gender, time to surgical debridement and Biobrane application, and anatomical region were not found to be associated with regraft.

Conclusion: At our institution, Biobrane has emerged as an alternative option to maintain a healthy wound bed after burn excision and prior to grafting. Our small number of extensive graft failures, small areas of regrafting and low infection rate following Biobrane application reflects our current experience with Biobrane. Precise indications and most appropriate methods for Biobrane use are yet to be established.

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1. Introduction

Allografts have been the gold standard for the provision of wound closure in the absence of adequate donor sites for autologous grafting of extensive burn wounds [1,2]. However, bioengineered skin substitutes also have the potential to preserve a healthy wound bed until definitive grafting is possible by providing physiological wound closure and a mechanical barrier to infection and fluid losses [1,3], and as they are not subject to rejection they can remain in place for much longer than allograft. In addition, when adequately adhered to the wound bed, a temporary skin substitute decreases colonisation by bacteria by eliminating dead space, whilst maintaining a quiescent wound bed with less clinically evident inflammation [4,5].

Biobrane is a bilaminate biosynthetic skin substitute composed of nylon mesh coated with collagen peptides bonded to a silicon membrane, designed to mimic the properties of the dermis and epidermis respectively [6]. It therefore possesses many of the features of an ideal skin substitute such as wound adherence, protection from contamination, flexibility, good water vapour transmission, low cost, and ease of application and transparency for wound observation [7,8].

Studies investigating Biobrane as a temporary wound dressing is limited, however one study concluded that there was no significant difference in the number of dressing changes, purulence or graft take when compared with frozen cadaver allografts [9].

Biobrane is increasingly used as an alternative to cadaver allograft for temporary wound dressing of uncontaminated wounds at our service. The aim of this study is to review the use of Biobrane as a temporary wound dressing before definitive split skin graft (SSG) in patients with severe burn. In particular, this study seeks to investigate the ability of Biobrane to maintain a healthy excised wound bed prior to skin grafting and identify factors which may influence graft failure and the need for regrafting.

2. Methods

The Victorian Adult Burns Service (VABS) is a state-wide adult burns service located at The Alfred Hospital, a university affiliated tertiary referral centre in Melbourne, Australia. A retrospective chart review was performed on all patients admitted to VABS from January 2009 to June 2012 who received Biobrane as temporary wound dressing before definitive SSG. Approval was obtained from our hospital’s human research and ethics committee as a low risk quality improvement project.

2.1. Biobrane application

All patients had their wounds debrided and Biobrane applied under general anaesthetic. Deep partial thickness and full thickness burns were excised using a tangential excision technique down to a viable wound bed. Haemostasis was obtained and Biobrane was applied slightly stretched over the wound bed and attached with staples, retention tape, or a combination of both. The Biobrane was then dressed with silver-impregnated anti-microbial dressing (Acticoat – Smith & Nephew) moistened with sterile water and wrapped with gauze and crepe bandage. The Biobrane was inspected on day three to five post-operatively. If it remained adherent with no signs of infection, then the Biobrane was left intact until grafting. At this time, the Biobrane was removed and the wound inspected for any non-viable areas. The wound was lightly debrided with a curette, prior to SSG application. More recently, a Versajet hydro-debriding device has been used for this purpose.

2.2. Data collection

Medical records and the VABS data registry were reviewed to select patients who received Biobrane and SSG to the same area, with Biobrane employed for temporary wound closure following burn wound excision. The exclusion criteria were: patients who had burns <20% total body surface area (%TBSA); when Biobrane was used as definitive treatment (that is, Biobrane and SSG were not applied to the same area); or when case notes were unclear or not available. A sole data collector was used to compile the information.

All patients had demographic data collected on age, sex, type and site of burn and %TBSA. Information on time and date of burn, date of admission and date of discharge was also noted.

Data collected about the application of Biobrane included time and anatomical area. Time between first debridement and Biobrane application was noted, as well as time between Biobrane application and first SSG to the same area. If removal of Biobrane was not documented, then it was assumed that Biobrane was left intact until a subsequent wound closure manoeuvre was documented.

Other surgical data was collected such as type of SSG applied (autograft, allograft or unknown), total number of operative encounters and total operating time. In-hospital outcomes also recorded were hospital length of stay (LOS), intensive care unit (ICU) admission details, mortality and infection of Biobrane. Infection of Biobrane was defined as specific notation of infected Biobrane or pus under Biobrane in the in-patient or operative notes.

2.3. Outcomes

The primary outcome of this study was failure of the primary SSG applied to an area previously treated with Biobrane. Requirement for a secondary SSG (regraft) was considered due to primary graft failure, and may have been due to either patient, wound-related or other factors.

2.4. Statistical analysis

All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC, USA). As the primary outcome was a binary variable (need for regraft), analyses were conducted using logistic regression with results reported as odds ratios and 95% confidence intervals. To account for the confounding effect of total body surface area burned, analyses were further
adjusted by %TBSA. The association between anatomical area and need for regraft was determined by computing robust standard errors to account for the multiple anatomical regions per patient. Continuous variables were summarised using mean ± standard deviation or median (interquartile range) depending on the underlying distribution of the data. A two-sided p value of 0.05 indicated statistical significance.

3. Results

3.1. Patient demographics and characteristics

A total of 183 patients were identified over the two year study period and we excluded 125 patients for the following reasons: burns < 20% TBSA (n = 97), areas where Biobrane was applied did not receive SSG to same area (n = 26) and medical record data not available or unclear (n = 2), leaving us with 58 patients for analysis.

The overall characteristics of the 58 patients are summarised in Table 1.

3.2. In-hospital outcomes

There were three (5.2%) patients with burns >35% TBSA who died in the course of treatment; all deaths were due to multi-system organ failure. Of these, two patients died before possible regrafting and one patient died after regrafting occurred. Infection of Biobrane occurred on four patients, totalling six sites. Other in-hospital outcomes, including ICU admission details and are summarised in Table 1.

3.3. Biobrane application

The specific details regarding the application of Biobrane are shown in Table 2. The time between burn and surgical debridement varied and in two patients, this value was unknown. Biobrane was most commonly applied to burns excised from the upper limbs (72.4%).

When analysed per site, there were 168 instances where Biobrane was replaced with a SSG. The time between Biobrane application and the first application of SSG ranged between 1 and 112 days. In more than 70% of sites, the time between Biobrane application and SSG was within three weeks. In 46 sites (27.4%), the time between Biobrane and SSG was longer than three weeks. A summary of time between Biobrane and SSG is shown in Fig. 1.

In 27 sites (15 patients), Biobrane was removed and replaced with an allograft. In three of these sites, Biobrane was removed due to documented infection. An additional five patients received allograft directly after their treatment on an area not previously treated with Biobrane. Further breakdown according to area can be found in Table 2.

3.4. General surgical details

The total number of operations and total operative time is presented in Table 2. Total operative time was not available for 12 patients. The longest time to Biobrane application was 161.6 h in one patient. Details regarding the surgical debridements and SSG per patient are also shown in Table 2.

3.5. Primary outcome – need for regraft

A total of 22 patients (37.9%) required a regraft of at least one area previously treated with Biobrane and autologous SSG.

<table>
<thead>
<tr>
<th>Table 2 – Summary of surgical details (N = 58).</th>
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<tbody>
<tr>
<td>Biobrane application</td>
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<tr>
<td>Biobrane applied to anatomical region</td>
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<tr>
<td>Time to first SSG after temporary dressing of Biobrane&lt;sup&gt;b&lt;/sup&gt;: days</td>
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<tr>
<td>Biobrane was replaced with allograft: days</td>
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<tr>
<td>General surgical details</td>
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</table>

Data are median (inter-quartile range) or number (%); SSG: Split-skin graft.

<sup>a</sup> Data not available for two patients (N = 56).
<sup>b</sup> Median 30.3 (IQR 28.3–48.8).
<sup>c</sup> Analysed per site (N = 168).
<sup>d</sup> Data not available for 12 patients (N = 46).

Table 1 – Characteristics and outcomes for patients treated with Biobrane as a temporary dressing at a state-wide burns service (N = 58).

<table>
<thead>
<tr>
<th>Demographic variables</th>
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<tbody>
<tr>
<td>Age: years</td>
<td>43.3 ± 18.4</td>
<td>Male gender:</td>
<td>37 (63.8)</td>
</tr>
<tr>
<td>%TBSA</td>
<td>30 (23–40)</td>
<td>Cause of burn&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Flame/flash/explosion: 49 (86)</td>
</tr>
<tr>
<td>In-hospital outcome variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection of Biobrane</td>
<td>4 (6.9)</td>
<td>Hospital length of stay: days</td>
<td>41.5 (28–73)</td>
</tr>
<tr>
<td>ICU length of stay: days</td>
<td>8.5 (2–23)</td>
<td>Death</td>
<td>3 (5.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data are mean ± standard deviation, median [inter-quartile range] or number (%); %TBSA: percentage of total body surface area; ICU: intensive care unit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;sup&gt;a&lt;/sup&gt; Data were not available for one patient (N = 57).</td>
</tr>
</tbody>
</table>
whereas 36 patients (62.1%) did not require any regrafts. There were two patients who had cases of extensive regrafting following Biobrane application. All other cases of regraft were described as “small” or “patchy” in operation reports. Table 3 shows the variables that were demonstrated at a univariate analysis to be associated with the need for regraft. They included: %TBSA (OR 1.04, 95% CI: 1.01–1.08; p = 0.02); hospital LOS (OR 1.04, 95% CI: 1.02–1.07; p = 0.001); ICU LOS (OR 1.05, 95% CI: 1.01–1.09; p = 0.02), total operative time (OR 1.16, 95% CI; 1.06–1.28; p = 0.002) and total number of surgeries (OR 1.69, 95% CI: 1.27–2.26, p < 0.001). Age and gender were comparable in both groups and were not significantly associated with regrafting. Time between burn and Biobrane application was only significantly associated with the need for regrafting in the 12–24 h group (OR 0.23, 95% CI 0.05–0.93; p = 0.04).

When adjusted for the effect of %TBSA through multivariate analysis; hospital LOS, total operative time and total number of surgeries remained significantly associated with need for regraft. ICU LOS and time between burn and Biobrane application in the 12–24 h group were no longer significant.

Age and gender remained insignificant. Details can be seen in Table 4.

Table 5 shows the rate of regraft according to area. Of the 168 sites receiving Biobrane for temporary wound closure, 43 sites (25.6%) required a regraft. The upper (35.1%) and lower limbs (32.1%) were the most common anatomical area to receive Biobrane as a temporary wound dressing. When adjusted for clustering, anatomical region was not associated with a higher rate of regraft. Of the 27 sites (16.1%) where Biobrane was replaced with an allograft, 16 sites were then regrafted with an autologous SSG.

4. Discussion

This study was a retrospective case series review of all patients admitted to VABS over a two year period who received Biobrane as temporary dressing before definitive SSG. The aim was to determine whether Biobrane served as a reliable tool in the treatment of deep burn requiring excision and in particular, its ability to maintain a healthy wound bed until SSG was applied and identify factors that may contribute to a patient requiring a regraft. Upon analysis, we found that a higher rate of regraft was associated with larger burns, hospital LOS, total operative time and total number of surgeries. Gender, age, time to surgical debridement and Biobrane application, and anatomical region were not found to be linked with regraft in this study.

The properties of Biobrane are well known and currently, comprehensive research exist surrounding its ability to definitively treat partial thickness wounds [8]. However, research exploring the use of Biobrane for temporary wound closure is limited, despite evidence that this application is common across the United Kingdom [10]. Greenwood [3] suggests that Biobrane is a viable alternative to allograft, as it is widely available and cadaver skin banks are not established in every major city. At the VABS, we have a cadaver skin bank in our state; however due to issues surrounding cost, graft

### Table 3 – Univariate analysis of need for regraft (N = 58).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Need for regraft</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>%TBSA</td>
<td>Yes (n = 22)</td>
<td>36.0 (30–60.0)</td>
<td>1.04 (1.01–1.08)</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>72.5 (46.0–95.0)</td>
<td>30.5 (23.0–45.0)</td>
<td>1.04 (1.02–1.07)</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>20.5 (6.0–26.0)</td>
<td>6.5 (0–14.5)</td>
<td>1.05 (1.01–1.09)</td>
</tr>
<tr>
<td>Total operative time^b</td>
<td>23.0 (10.4–26.9)</td>
<td>8.4 (4.9–10.6)</td>
<td>1.16 (1.06–1.28)</td>
</tr>
<tr>
<td>Total number of surgeries</td>
<td>6.5 (4–8)</td>
<td>3 (2–4)</td>
<td>1.69 (1.27–2.26)</td>
</tr>
<tr>
<td>Age</td>
<td>43 (33–55)</td>
<td>39 (23–59.5)</td>
<td>1.0 (0.98–1.03)</td>
</tr>
<tr>
<td>Gender – male</td>
<td>54.5%</td>
<td>69.4%</td>
<td>0.53 (0.18–1.58)</td>
</tr>
<tr>
<td>Burn to surgical debridement and Biobrane application^c</td>
<td>10 (47.6)</td>
<td>9 (25.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>12–24 h</td>
<td>4 (19.1)</td>
<td>16 (45.7)</td>
<td>0.23 (0.05–0.93)</td>
</tr>
<tr>
<td>&gt;24 h</td>
<td>7 (33.3)</td>
<td>10 (28.6)</td>
<td>0.63 (0.17–2.36)</td>
</tr>
</tbody>
</table>

^a Reference category.
95% CI: 95% confidence interval; %TBSA: percentage of total body surface area; LOS: length of stay; ICU: intensive care unit; SSG: split-skin graft.
^b Data are median (inter-quartile range) or proportions.
^c Data not available for 12 patients (N = 46; Yes = 25, No = 21).
^d Data not available for two patients (N = 56).
rejection, disease transfer and limited availability [2,11], Biobrane is the preferred temporary wound dressing for uncontaminated excised wounds in our unit. The use of Biobrane has been incorporated into our unit’s surgical treatment algorithm (Fig. 2). Biobrane may be considered an expensive wound closure option, however, a recent study suggests it is more cost and time-effective than cadaveric allograft when used as a temporary wound closure method [12].

Early surgical excision is associated with decreased incidence of wound infection, metabolic disturbance and the systemic inflammatory response commonly caused by sepsis, as well as shorter LOS [13,14]. In many cases, immediate autografting of all excised wounds is not possible due to insufficient donor sites, or not advisable, due to patient instability and peripheral vasoconstriction [3,15]. Biobrane has emerged as a valuable tool in allowing immediate wound closure, which is vital to prevent wound desiccation, prevent infection and decrease fluid losses following total excision of large burns [15,16]. Delayed wound closure with resulting ongoing inflammation in the wound bed can also result in poor scar quality and contractures [15].

Rate of regraft in our study was assessed both as per patient and per site. The rate for patients was 37.9% and the rate by sites was 25.6%. In the existing literature, an acceptable rate of regrafting in the >20% TBSA cohort has not been consistently reported. One prospective case series has reported a regraft rate of 19% after SSG dressed with cotton gauze and antimicrobial solution in 27 patients [17].

Neither Purdue et al. [9] nor El-Khatib et al. [18] reported on regraft rates in their studies when comparing Biobrane with another skin substitute. When compared to alternative techniques for wound coverage in severe extensive burns, Vloemans et al. [19] described extensive regrafting in 48 of 70 (37.2%) cases after sandwich grafting with glycerol-preserved allograft (GA) and MEEK-meshed grafts, compared to two (3.4%) cases in our study. A small study of 14 patients by Khoo et al. [20] investigated the same sandwich technique with GA and found four patients had complete healing, however another four (28.6%) required a regraft. The same study describes the need for regraft in 6 of 29 patients (37.5%) after tangential excision of deep burns and GA prior to primary SSG.

At our service, when Biobrane does not adhere to the burn wound, it is removed and replaced with allograft (see Fig. 2). In most cases, this allograft must be replaced with autologous SSG due to eventual rejection [15,21]. There were three patients whose only instances of “regraft” were when Biobrane was removed, replaced with allograft and then with autograft; these patients were not included in the regraft group, despite the fact that this may have indicated a failure of Biobrane. Failure of Biobrane wound adherence was not an outcome measure in this study, however there were 15 patients (27 sites) where Biobrane was removed and replaced with allograft. The presence of infection, which may also prompt Biobrane removal, was noted in 6.9% of patients or 3.6% of sites. This rate is lower than that reported by Purdue [9], who reported an infection rate of 15.4% of sites in a prospective study. Data regarding prophylactic antibiotics was not collected in either study. In theory, risk of infection when Biobrane is applied to a surgically excised burn wound should be minimal as Biobrane, the wound and the procedure are aseptic.

Although hospital LOS, total operative time and total number of surgeries were associated with regraft, these are outcomes rather than predictors. Whilst these associations remain unchanged after adjusting for %TBSA, our sample size was not large enough to assess the independent association of each of these factors on regraft or clinical outcomes.

Of note, in our study, time between burn and Biobrane application does not appear to impact rate of regraft, however in the majority of patients time to application was within 72 h. This suggests that there is a wide window of opportunity where Biobrane is effective and therefore delay to wound excision is not necessarily a contraindication to the use of Biobrane, in contradistinction to its use in partial thickness burn wounds, where colonisation of the wound may preclude its successful use days after injury. The anatomical region

<table>
<thead>
<tr>
<th>Area</th>
<th>SSG application after temporary Biobrane</th>
<th>Sites requiring regraft</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head or neck</td>
<td>7 (4.2)</td>
<td>3 (42.9)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Chest or abdomen</td>
<td>36 (21.4)</td>
<td>7 (19.4)</td>
<td>0.32 (0.09–1.16)</td>
<td>0.08</td>
</tr>
<tr>
<td>Back or buttocks</td>
<td>12 (7.1)</td>
<td>3 (25.0)</td>
<td>0.44 (0.08–2.62)</td>
<td>0.37</td>
</tr>
<tr>
<td>Upper limb</td>
<td>59 (35.1)</td>
<td>16 (27.1)</td>
<td>0.50 (0.12–1.99)</td>
<td>0.32</td>
</tr>
<tr>
<td>Lower limb</td>
<td>54 (32.1)</td>
<td>14 (25.9)</td>
<td>0.47 (0.11–1.99)</td>
<td>0.30</td>
</tr>
</tbody>
</table>

* Data are number (%); 95% CI: 95% confidence interval; SSG: split-skin graft.
**Fig. 2 – VABS algorithm for patients with severe burn treated with Biobrane as a temporary dressing.**
which Biobrane was applied to did not affect the rate of regraft. However, this analysis did not take into account %TBSA which was closed with Biobrane or %TBSA which was eventually treated with a SSG. In our study, of the majority of graft failures were described as “small” or “patchy” areas of loss, which is typical when large areas are grafted [15].

In relation to removal of Biobrane, Greenwood and associates suggests re-evaluation of patient status after 48 h if they are admitted to ICU following excision of burns and application of Biobrane [3]. It is also suggested that swift definitive wound closure by SSG is warranted as soon as the patient is stable and inotropes are not required [3]. Greenwood reported that Biobrane is left in situ for 3-6 days [3]. Overall, the median time between Biobrane application and subsequent SSG in our study was 12.5 days (IQR 6–25). This longer “in-situ” time is consistent with El-Khatib et al. [18], who suggested Biobrane has the potential to be left on for up to 10 days. In our study, 46 sites received a SSG longer than 3 weeks after Biobrane application.

Biobrane can become incorporated into tissue and require excision if left for long periods of time [16,22]; however it seems that the timing of this occurrence varies. This incorporation may be delayed in massive burns. Increasing time in situ may be associated with infection of the adherent Biobrane, which acts as a foreign body. Kagan et al. [15] suggests reapplication every 5–7 days to prevent these complications. We did not electively change Biobrane during the period of this study.

In general, drawing conclusions regarding the use of Biobrane as a temporary wound dressing is difficult due to the lack of existing literature and published clinical protocols. In addition, a standardised operative record is required to reflect the increasing use of these products. This was particularly evident in our study as the main limitations were due its retrospective nature and in particular, poor clinical documentation. Specific information regarding burn depth was also not reported on due to the variability in patient reporting methods. Underlying medical conditions which may affect graft-take such as diabetes mellitus [23] were not taken into account for this study.

There is a need for further research regarding the short-term efficacy of surgical protocols in patients with major burn. Investigation into long-term outcomes such as scar quality, contracture and need for further reconstruction is also warranted. We recommend other burn services publish their surgical management algorithms and specify their protocols for utilisation of skin substitutes. This will allow for conclusions and refinement of surgical practices.

Our recommendations for practice with regard to Biobrane as a temporary wound dressing are as follows:

1. Biobrane is useful in patients with severe burns (>20% TBSA) but in particular, those with massive burns or who are at increased risk of graft loss if primary grafting is performed at the same procedure as wound excision. That is patients with:
   a. haemodynamic instability,
   b. hypothermia or coagulopathy after excision,
   c. advancing age or significant comorbidities,
   d. excised wounds of doubtful viability.
2. Temporary physiological wound coverage with Biobrane allows for early total excision of deep dermal and full-thickness burns.
3. Biobrane should be assessed for wound bed adherence after 48–72 h.
4. If Biobrane is not adhering, it should be removed and replaced with allograft if there are signs of infection. If the wound bed appears quiescent, Biobrane can be left in situ.
5. If Biobrane is adherent, it can be left in situ until donor sites are available or the patient is stable for grafting. Elective replacement of Biobrane may be indicated to prevent incorporation when grafting is delayed for weeks.

5. Conclusion

Adequate wound coverage following the excision of severe burns still poses a significant challenge, however at our institution, Biobrane has emerged as an alternative option to maintain a healthy wound bed after burn excision and prior to grafting. Our small number of extensive regrafts, small areas of regrafting and low infection rate following Biobrane application reflects our current experience with Biobrane. It can exist as a reliable alternative in the management of severe burn to cadaver allograft, or when compared with other wound closure options such as MEEK-mesh sandwich grafting.

We conclude that Biobrane is able to act as a temporary dressing in the severe burn population and age, gender or anatomical region do not influence the rate of subsequent graft failure and regraft.

Conflict of interest

None.

References


