An open, prospective randomized pilot investigation evaluating pain with the use of a soft silicone wound contact layer, Mepitel® One, vs. Bridal Veil and staples used on split thickness skin grafts as a primary dressing

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INTRODUCTION

Burns are, unfortunately, a common injury with as many as 450,000 people in the United States of America suffering burns that require treatment. (American Burn Association, 2011) Superficial burns are easily treated, usually with a conservative approach by topical medication, or with some type of dressing or covering that promotes the natural course of healing. For deep dermal burns, a combination of excision and grafting is preferred (Orgill, 2009). Areas of burn injury that initially appear more superficial can sometimes become deeper over a period of 48-72 hours, resulting in necrosis of the burn wound from infection or poor perfusion to the affected area (Fritz, 2008). This resulting conversion to a deeper burn then requires excision and grafting.

Skin grafts are placed over excised areas of full thickness injuries and usually attached with sutures or staples (Fritz, 2008). Staples are usually the preferred method of attachment because sutures take more time to do and require a higher level of skill (Meiring et al, 1982). While staples are useful in anchoring grafts in place, subjects often complain that they cause pain as wound healing progresses. The use of staples can also Increase the risk of infection and scarring (Chughtai et al, 2000, Smith et al, 2010). Pulling and sticking are common complaints and there is the possibility that staples can become embedded in the graft. This leads to disruption of an otherwise healed area, increased pain, and anxiety for the subject as well as anxiety for the staff. Furthermore, wound-related pain can cause psychological stress which may, in turn, delay healing (Solowiej, et al 2009). Unfortunately the pain is often mismanaged and subjects suffer more pain than is necessary (Nagy, 1999). Thus, there remains a need for less painful methods of fixing grafts to the wound bed. Other methods such as fibrin sealants are in use (Foster, et al 2008) and these alleviate the need for staples; however, successful use is dependent on appropriate technique. In some circumstances, the sealants can fail to adhere (Sierra et al 2000); this is a particular problem with moist conditions. If fibrin sealants are applied too thickly wound healing is slowed down (O'Grady et al, 2000).

When dressing changes require staple removal, patients experience varying degrees of pain and anxiety. Anxiety during dressing changes can sometimes be mistaken for pain, resulting in the potential for over-sedation, which is detrimental to the subject (Vanderbilt University, 2007). Pain is subjective and anxiety often confounds a true pain assessment in subjects who are alert. The visual analog pain scoring system is a reliable method for measuring pain in burn subjects and was used in this study (Choiniere et al, 1994, Hickerson et al, 1994, Marvin et al, 1996).

Graft take can be optimized with appropriate medical management. Use of non-adherent dressings to protect the graft is customary. Various types of netting-style dressings are used by many burn clinicians. One such type is Bridal Veil; this is a commercially available, sterile product that comes in 2.0, 3.0, and 4.0mm hexagonal mesh sizes. Grafts are fixated with staples under and sometimes over the Bridal Veil to secure them in place.

For the purpose of this study, the term Bridal Veil is used generically. Three study sites used Conformant 2® Wound Veil and one site used commercially available Bridal Veil.

Silicone net dressings have also been used successfully to prevent, lifting and adherence of skin grafts to the dressings, prevent pain, and promote healing (Terrill & Varughese, 2000, Dykes et al, 2001, Platt et al, 1996). These dressings have also been used successfully to retain secure skin tears in situ. **Mepitel® One** is a sterile, transparent, and flexible wound contact layer consisting of perforated polyurethane film coated with **Safetac®** soft silicone adhesive on one side. **Mepitel® One** is available in various sizes and can be left in place for several days (up to 14 days) depending on the wound/skin condition (Collin, 2009). This product firmly fixes to clean, intact peripheral skin, thus eliminating the need for staples.

Appropriate secondary dressings can also enhance graft take. Bolster-style dressings that provide adequate absorbency are acceptable. These dressings are also designed to apply mild pressure to the wound in order to promote uniform adherence of the graft to the wound bed, as well as to prevent shear forces from shifting the graft on the wound bed (Fritz, 2008).

OBJECTIVE

The primary objective of the Institutional Review Board-approved study was to compare pain at the time of dressing removal for the use of **Mepitel® One** versus Bridal Veil and staples on deep partial or full thickness burns requiring skin grafts.

Secondary objectives were to investigate the overall costs, ease of use, adherence, tolerance, safety and efficacy of **Mepitel® One**.

METHODS

- Forty three patients who met the inclusion/exclusion criteria for the study (Table 1) were randomized to either **Mepitel® One** (Figure 1) or Bridal Veil and staples (Figure 2).
- Donor skin was harvested between 0.010 and 0.012 inch thickness. Skin was meshed at a 1:1 to 3:1 ratio. After the split-thickness skin graft was applied to the wound, **Mepitel® One** or Bridal Veil and staples was placed over the graft and over a margin of the surrounding healthy skin.
- Evaluation was performed at the initial consultation for baseline demographic data (age, gender, race, medical history) and the wound history was recorded (type of burn, site, date of injury, percentage total body surface area (TBSA), wound appearance, infection assessment).
- Skin graft assessment was performed at Day 7 (+/- 1 day) and Day 14. (+/- 1 day) If the graft had > 95% take, before the 14 days, this was considered the end of the study.
- The assessments included pain (prior, during and after product removal), dressing removal (time and pain medication or other treatments required), healing (percentage of graft take), peri-wound status, clinician input on handling, subject input on product, and adverse events.
- The time and cost of staff were estimated by referring to www.indeed.com/salary for median salaries and the start and stop time of treatment was recorded in hh:mm:ss.
- Cost data for the material used was estimated by collecting the quantities/ units used and estimating the unit cost from the GHX database (www.ghx.com), the manufacturers discount suppliers and from web vendors (the median value was reduced by 50% to more accurately reflect hospital costs).
- Photographs were taken to record the treatment status.

RESULTS

The study included 43 patients in the clinical investigation, of which three were considered either lost to follow up or withdrawn. The "intention-to-treat" (ITT) population included those patients (n=42) for whom post-treatment randomization data pertaining to the primary objective were recorded. Patient demographics and burn type are summarized in Table 2. There were no significant differences between the treatment groups in terms of the extent of burn injuries at baseline (Table 3)

TABLE 1:
Inclusion/exclusion criteria for the study

Inclusion criteria

- Subjects presenting with 1% - 25% total body surface area (TBSA) deep partial or full-thickness burns requiring skin graft
- At least 1%-10% TBSA available for grafting that could be considered for study site selection (intact, healthy peri-wound area around entire portion of this burned site)
- Both genders with age ≥ 18 years but < 70 years
- Signed informed consent

Exclusion criteria

- Subjects with chronic wounds, dermatologic skin conditions, or necrotizing disorder
- Subjects on mechanical ventilation
- Diagnosed underlying disease(s) (HIV/AIDS, cancer and severe anaemia) judged by the investigator to be a potential interference in the treatment
- Subjects treated with systemic glucocorticosteroids, except subjects taking occasional doses or doses less than 10 mg prednisolone/day or equivalent
- Use of immunosuppressive agents, radiation or chemotherapy within the previous 30 days
- Known allergy/hypersensitivity to any of the components of the investigational products
- Subjects with physical and/or mental conditions that were not expected to comply with the investigation
- Participation in other clinical investigation(s) within 1 month prior to start of the investigation
- Pregnancy

TABLE 2:
Patient demographics and burn type

Variable	Mepitel® One (n=21)	Bridal Veil and staples (n=21)
Age	38.0 (18.0) 30.0 (19.0;77.0)	42.3 (16.0) 39.0 (19.0;70.0)
Gender		
Male	16 (76.2%)	18 (85.7%)
Female	5 (23.8%)	3 (14.3%)
Type of burn injury		
Flame	10 (47.6%)	10 (47.6%)
Scald	3 (14.3%)	2 (9.5%)
Contact	8 (38.1%)	9 (42.9%)

For categorical variables, n(%) is presented. For continuous variables, mean (standard deviation) / median (minimum; maximum) are presented.

PAIN

Pain was measured using a visual analog scale (VAS) ranging from 0 (no pain) to 100 (worst possible pain) and was compared between the **Mepitel® One** group and the Bridal Veil and staples group at post-op day 7 (+/- 1 day). Pain level was obtained at the beginning of the dressing change and there was no significant difference between the groups (p=0.1690). Pain level at the mid-point of dressing removal was significant between the groups, with the removal of **Mepitel® One** being less painful (p=0.0118) and at the end of the dressing change, there was no significant difference between the groups, (p=0.0791), although with a trend to **Mepitel® One** being less painful. Overall, it was observed that the pain value was very low for the group receiving **Mepitel® One** at all time points (Figure 3).

Of the 43 subjects enrolled, 12 were pre-medicated prior to removal of dressings and study product. There were 10 subjects pre-medicated in the Bridal Veil + staples group and 2 subjects pre-medicated from the **Mepitel® One** group.

In at least 4 cases, titration of intravenous medication was necessary to complete the dressing change for the staple removal. This would imply that the pain levels during this procedure were so high that an extra dose of pain medication was necessary in order to tolerate the entire procedure with some level of relief from pain.

The two subjects medicated in the **Mepitel® One** group were treated only with oral analgesics with no titration of medication necessary.

Overall, removal of Bridal Veil and staples appears to require a much larger amount and stronger type of narcotic to meet the pain needs of subjects during dressing removal as compared to subjects having **Mepitel® One** removed. This is important to consider in terms of length of stay, nursing time, and possible narcotic-related complications.

DRESSING REMOVAL

Dressing removal was assessed in terms of attachment of product to the graft and separation of graft from the wound bed. **Mepitel® One** showed no separation of the graft from the wound bed while 15% showed separation of the graft from the wound bed with the removal of Bridal Veil and staples. (Figure 4).

GRAFT TAKE AND HEALING

Graft take was defined as > 95% take and was assessed at post-op day 7 (+/- 1 day) after the removal of the dressing. There was no significant difference noted in graft take assessment between the two groups (p=0.1449). Graft take for **Mepitel® One** was 100% and for Bridal Veil and staples 99%.

TABLE 3:
Burn injury assessment at baseline

Variable	Mepitel® One (n=21)	Bridal Veil and staples (n=21)	P-value
% TBSA	7.27 (5.41) 5.00 (1.00; 18.00)	5.83 (4.38) 4.00 (1.00; 15.00)	0.3828
% partial	3.69 (5.30) 1.00 (0.00; 16.00)	3.26 (3.99) 2.00 (0.00; 14.00)	0.6906
% deep partial	1.25 (2.32) 0.00 (0.00; 8.00)	0.38 (0.986) 0.00 (0.00; 3.50)	0.2287
% full thickness	2.33 (2.33) 2.00 (0.00; 9.00)	2.19 (2.96) 1.00 (0.00; 10.00)	0.4402

PERI-WOUND STATUS

Peri-wound status was assessed at the time of grafting and at the time of dressing removal (post-op day 7 (+/- 1 day). Variables assessed were turgor, dryness, flakiness, maceration, blistering, erythema and warmth. With the exception of one subject that developed an infection of the graft site (Bridal Veil and staples), all other subjects maintained a healthy peri-wound status. Some dryness and flakiness were reported in the majority of subjects in both groups, but this is to be expected with normal graft healing. No maceration, erythema or blistering occurred in either group with the exception of the subject that developed infection and this subject had mild erythema and warmth of the peri-wound skin.

CLINICIAN INPUT

Clinician input was given on the dressing's conformability to the grafted site, ability to stay in place, ease of use, transparency, and the overall experience with the dressing. This input was gathered at the time of grafting, and post-op day 7 (+/- 1 day), and post-op day 14 (+/- 1 day), if applicable. Both groups had similar evaluations for most categories, with some categories being more favorable for **Mepitel® One** (Figure 5). In terms of overall experience, **Mepitel® One** was rated as 'good' and 'very good' in 39% and 61% of assessments, whereas Bridal Veil and staples were rated as 'good' and 'very good' in 75% and 5% of assessments.

SUBJECT INPUT

Subject input was received on the comfort of the dressing, conformability, and overall experience with the dressing. Most categories were similar in responses between the two groups, however, the majority of the subjects in the **Mepitel® One** group (57.9%) felt the comfort of the dressing was very good, 47.4% felt the conformability was very good, and 78.9% of the subjects in the **Mepitel® One** group felt the overall experience was very good (Figure 6).

ADVERSE EVENTS

Various adverse events were reported in both treatment groups. A minimum number of these were considered as typical complications that develop in patients with burn injuries. As such, one subject in the Bridal Veil and staples group developed infection of the skin graft which was subsequently resolved with antibiotic therapy. No serious adverse events were reported in either treatment group.

Figure 1: Mepitel® One used on a split thickness skin graft. Graft take was excellent, the peri-wound skin remained intact and healthy, and the dressing was easily removed without any adherence

Figure 2: Bridal Veil and staples used on a split thickness skin graft. Despite the use of staples, Bridal Veil easily bunched in places. The staples pulled and tugged at the netting, causing discomfort

Figure 3: Pain of dressing removal 7 days post-operative measured using the VAS system

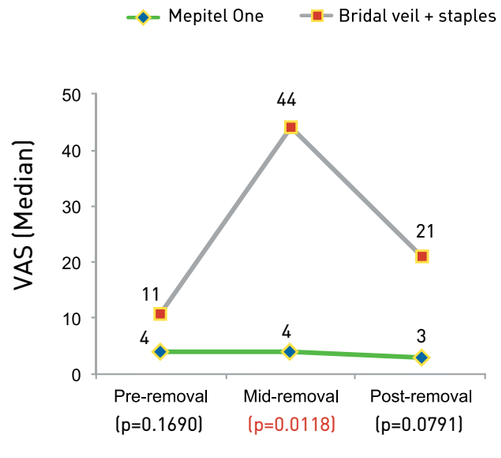
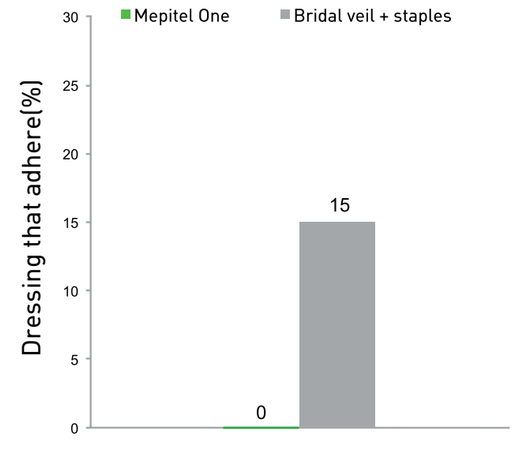


Figure 4: Separation of graft from wound bed.



OVERALL COSTS

For the total of all costs, including time and unit costs, there were no statistically significant difference between the two treatment groups. However, there was a trend for lower costs with **Mepitel® One** (p=0.1709).

There was a highly significant difference for the total staff costs in favor of **Mepitel® One** (p=0.0064).

The time required for dressing application was comparable for both the **Mepitel® One** and Bridal Veil and staples treatments (p=0.3152).

Less time was used for **Mepitel® One** for dressing removal. There was a statistically significant difference in favor of **Mepitel® One** from the time dressing removal started to the time dressing removal ended (minutes) (p= 0.0005). Bridal Veil and staples required 75% more time to remove than **Mepitel® One**.

Figure 5: Clinical evaluation of the overall wound treatment at 7 days post-operative

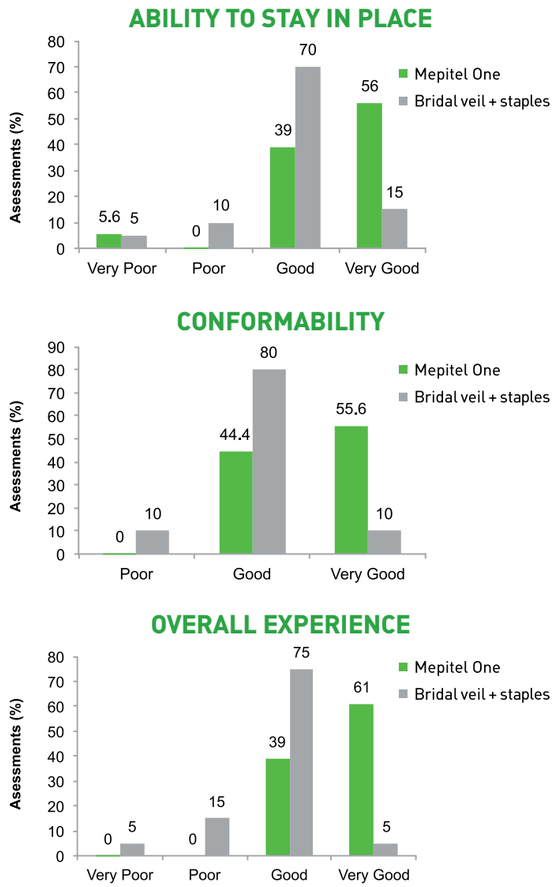


Figure 6: Subject evaluation of the overall wound treatment at 7 days post-operative

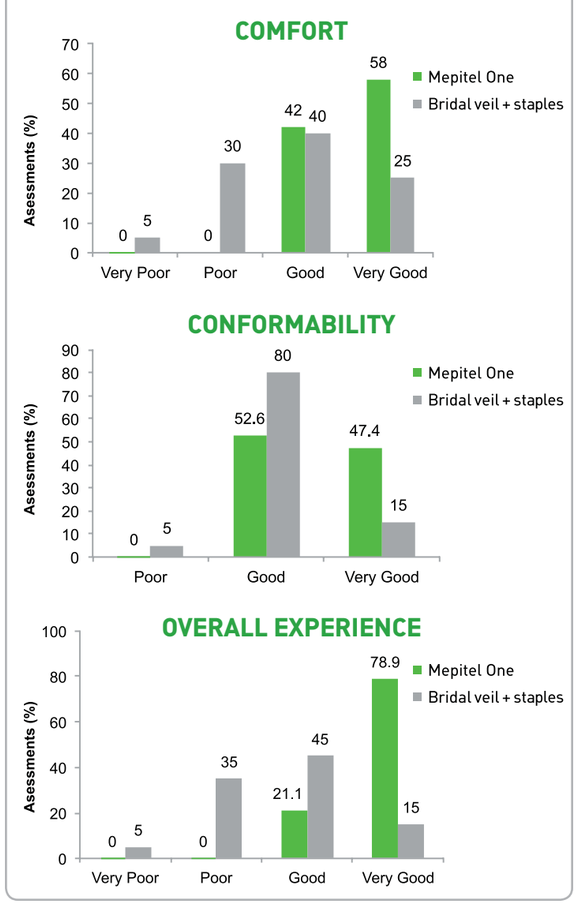


Figure 7:
Total of costs (USD)

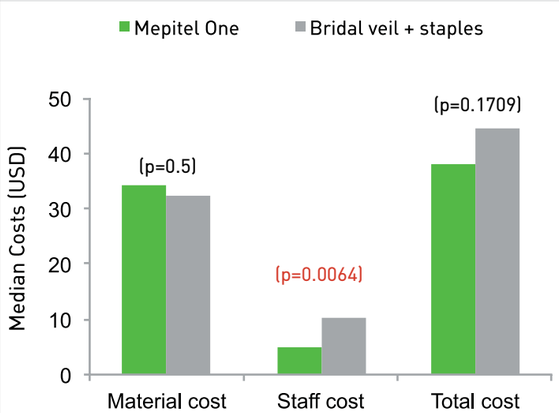
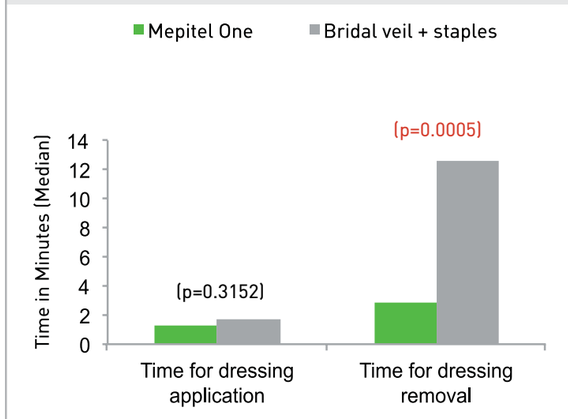


Figure 8:
Time for dressing application and removal



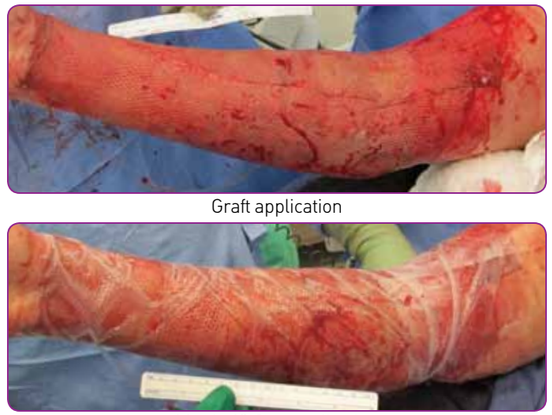
DISCUSSION

This study set out to evaluate the pain experienced at dressing removal for **Mepitel® One** compared to Bridal Veil and staples when used as a primary dressing over split thickness skin grafts. The performance of the dressings was also assessed by both the clinicians and patients.

- **Mepitel® One** was shown to be less painful than the common standard of care (Bridal Veil and staples) at the time of dressing removal, and this difference was statistically significant (p=.0.0188).
- **Mepitel® One** was comparable to the method of treatment (Bridal Veil and staples) regularly used at the participating centers in all of the clinician and patient assessments, and performed better in terms of stay on ability, conformability, comfort, ease of use and the overall experience of the patients.
- **Mepitel® One** showed lower overall costs although these were not statistically significant.
- The time taken for dressing removal was greatly reduced with **Mepitel® One**.

The following case studies give further insight into the performance of the two treatment regimes that were evaluated in the study.

CASE STUDY 1: Mepitel® One



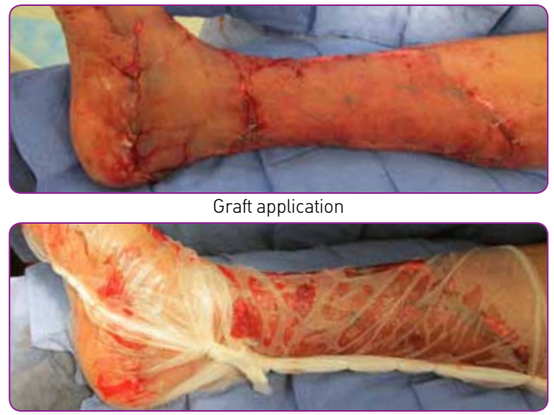
Graft application

Mepitel® One application

Post-op Day 7 prior to removal

Post-op Day 7 removal

CASE STUDY 2: Bridal Veil and Staples



Graft application

Bridal Veil application

Post-op Day 7 prior to removal

Post-op Day 7 removal

CONCLUSION

The results of this study indicate that **Mepitel® One** should be considered as a clinically acceptable primary dressing for placement over skin grafts in the treatment of burns. **Mepitel® One** demonstrated less pain, better ease of use and a better overall experience for patients than the comparator treatment involving the use of staples. When the total costs were evaluated **Mepitel® One** was also less expensive and took much less time to remove, a major benefit to both patient and clinician.

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