**The Use of Negative Pressure Wound Therapy in Paediatric Hand and Feet burns: A Pilot, Prospective,
Randomised Control Trial**

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**Statement of Compliance**

**This study will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research and the Note for Good Clinical Practice.**

**STUDY INVESTIGATOR(S)**

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**1. INTRODUCTION**

Burn wound progression can be variable after the initial injury has occurred. Tissue oedema as a result of the injury can compromise microcirculation resulting in this progression. Pressure applied to this area through NPWT is known to squeeze oedema fluid out of the interstitial space. It is plausible that applying NPWT within this initial timeframe may halt or limit burn wound progression.

The use of Negative Pressure Wound therapy (NPWT) in the treatment of burns has increased over the past decade. It is common practice at the Pegg Leditschke Children’s Burns Centre, Queensland Children’s Hospital to apply NPWT post-split thickness graft to improve take of the graft and more recently it’s efficacy in acute burns has been tested using the Renasys GoTM. More recently the Renasys GoTM has been trialled in the unit for burns less than 5% TBSA within 1 week of injury. This study found improved clinical outcomes, especially when applied within 48 hours. However, parents reported a burden due to the size of the Renasys GoTM and need for recharging accessories. There is a sub cohort of burns patients – hand and feet burns – that account for a large majority of paediatic burn morbidity. It is proposed that the burden of NPWT may be acceptable in this population.

Applying NPWT could greatly improve the final outcome of a burn wound. This could have multiple implications as improved time to re-epithelialisation can impact on overall cost of treatment, requirements for scar management as well as possible reconstructive requirement in the future.

**2. BACKGROUND**

This study will primarily address the paucity of knowledge around the potential for implementation of NPWT within hand and feet (HAF) burns. HAF burns are notoriously difficult to dress due to being small surfaces with multiple joints. Therefore, the time required to apply the dressing and the ability to achieve a seal have been limitations to NPWT in these areas. This is in addition to the identified barriers of the machine being cumbersome for small, paediatric patients.

HAF burns currently cause a significant burden of care to the healthcare system. This is owing to paediatric patients having the unfortunate combination of being curious about their environment, slow withdrawal reflexes and an inability to process consequences of actions. A burn in this region may go on to have long term consequences – including reduced fine motor skills, psychological and cosmetic concerns. Therefore, it is proposed that if NPWT can reduce this morbidity – that the therapeutic gain outweighs the clinical burden of NPWT.

**3. AIM(S) OF STUDY**

This study aims to establish the feasibility and safety for the use of negative pressure wound therapy in children with hand and feet burn injuries.

**4. OBJECTIVES**

A pilot RCT of the application of Negative Pressure Wound Therapy (NPWT) on acute HAF burns in paediatric patients will be conducted to assess feasibility, safety and measurements that would be included in a larger trial (30 participants maximum).

**5. HYPOTHESIS**

**5b. Primary Hypothesis**

*H0: The use of NPWT is both feasible and safe in paediatric hand and feet burns.*

*HA: The use of NPWT is NOT feasible and/or safe in paediatric hand and feet burns.*

**5b. Secondary Hypotheses**

*H0: The use of NPWT DOES improve time to epithelialisation, pain, itch, scar formation, quality of life and need for operative management.*

*HA: The use of NPWT DOES NOT improve time to epithelialisation, pain, itch, scar formation, quality of life and need for operative management.*

**6. STUDY DESIGN**

This study is a two - armed, prospective randomized trial comparing:

1. Group 1: Standard treatment (MepitelTM and AcitcoatTM) (15 patients) OR
2. Group 2: Standard treatment plus Renasys TouchTM (15 patients)

Further information will be collected to examine impact on health-related quality of life, treatment burden and health care costs of this intervention.

**7. STUDY SETTING/LOCATION**

Pegg Leditschke Children’s Burns Centre (PLCBC), Queensland Children’s Hospital, Brisbane

**8. STUDY POPULATION**

Participants who present to the PLCBC within 48hours of sustaining a burn injury will be approached for recruitment into the trial. After obtaining informed consent, the participants will be randomised into a treatment arm.

**9. ELIGIBILITY CRITERIA**

Participants will include 30 children (15 participants standard treatment, 15 participants with standard treatment PLUS NPWT) with a new burn and the following inclusion criteria:

**9a. Inclusion criteria**

1. Age less than or equal to 16 years of age
2. Must present within 48hours of sustaining a burn injury
3. Any burn that is DPT or of greater depth on the hand or foot
4. >0.5% TBSA on one hand or foot (ie >1/2 of the hand or foot) and is SPT
5. May be in the context of a larger burn

**9b. Exclusion criteria**

1. Older than 16yrs of age
2. Clinician treatment priority contradicts randomization
3. Area <0.5% on one hand or foot and only SPT
4. Do not wish to participate
5. The child is unwell at the time of presentation

**10. STUDY OUTCOMES**

**10a. Primary Outcome**

1. **Feasibility Outcomes**
* Proportion of screened patients who are potentially eligible.
* Proportion of eligible participants who are recruited.
* Compliance with the trial interventions (measured twice-weekly while participant recruited to study).
* Completeness of data collection for primary outcomes.
* Proportion of participants lost to follow-up or withdrawn.
* Staff and patient satisfaction (collected on treatment completion).

Feasibility outcomes will be measured at the time of screening, request for consent, device removal, patient discharge or four weeks after recruitment unless otherwise stated and; if required, 3 month follow up.

Based on criteria adapted from Polit & Beck (2008), feasibility outcomes will be analysed and deemed feasible if the following criteria are met:

* Greater than or equal to 80% of patients screened will be eligible
* Greater than or equal to 80% of eligible participants will agree to enrol
* Greater than 80% of participants in the intervention groups will receive their allocated treatment (measured twice weekly while participant recruited to study)
* Less than 5% of data collection for primary outcomes will be missing
* Less than or equal to 10% of participants will be lost to follow up or withdraw from the study
* Staff and patient assessment of intervention utility and acceptability

Questionnaires will be developed to obtain qualitative and quantitative data about the feasibility of the NPWT for acute paediatric HAF burns application by staff and participants/participants parents.

**For the staff questionnaire**: A mixed method questionnaire incorporating the Likert scale will be asked using Weiner et als. (2017) model for implementation studies. This will address three criteria:

1. Acceptability – is it ethically justifiable to be using NPWT in paediatric HAF burns
2. Appropriateness – does this intervention optimise burns management and facilitate better care than is currently provided
3. Feasibility –
	1. Ease/difficulty of application and delivering the intervention
	2. Additional burden related to monitoring or encouraging patients throughout the treatment
	3. Whether there were patients unable/unwilling to adopt the treatment
	4. Time required to apply the dressing
	5. Knowledge for application of the device
	6. Any other barriers encountered that were unexpected

**For the participant questionnaire**: Once again, a mixed method questionnaire incorporating the Likert scale will be administered. However; only feasibility will be assessed as patients are unlikely to have the clinical knowledge base to address acceptability and appropriateness. The questions will address the ease/difficulty and confidence of performing, maintaining, and adhering to the intervention.

1. The ability to maintain a seal
2. Mobility with the device
3. Confidence/knowledge to manage issues if they did arise
4. General tolerance of the child of the device
5. Battery/charging issues
6. Would they use the device again

**Safety** will be assessed using data collected on adverse effects, which will be monitored throughout the study and recorded by an Adverse Events Log. The type, incidence, and severity of adverse events (Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Life-threatening; and Grade 5: Death) will be recorded. Adverse event rates will be assessed and graded by a multidisciplinary clinical team, and reported per number of days the dressing was applied, before a comparison between Intervention and Control groups is made. Events per number of days will be reported and compared to published event rates from other wound studies.

Participants will be advised to report and log any adverse event that may occur during the study. They will be provided with contact details for reporting and an adverse event log. In addition to self-report, participants will be questioned weekly about adverse events through the duration of wound care.

**10b. Secondary Outcome(s)**

**Demographic information and clinical details**

This will be collated from the caregiver and the patient’s chart. Baseline parameters will be recorded including mechanism, date and time of injury, time to presentation, management preceding presentation, immunisation status, Fitz-Patrick skin type, medical and surgical history and a set of vital signs including temperature.

The E-Burn mobile application will be used to accurately assess **TBSA** (down to 0.1%). This is particularly important given most burns will be small surface areas.

**Burn depth** will be categorized by laser Doppler imager (LDI) scan and treating consultant review of photographs at presentation and the first dressing change (between days 3 – 5) as either ‘superficial partial thickness only’, ‘mixed depth’, or ‘deep dermal partial thickness only’. The photograph review will be blinded.

**Percentage Re-epithelialisation**

Clinical photographs will be taken at each dressing change. A panel of experienced burns clinicians will then perform a blinded review of the photographs, and assess epithelialisation. The burn will be considered healed when 95% epithelialised.

**Scar/skin assessment (At 3 months)**

If further scar management treatment is required after full re-epithelialisation of the burn injury has occurred, a referral will be made by the treating consultant to the scar management clinic. At 3 months following full re-epithelialisation of the burn injury, a face-to-face follow-up will be completed with all participants to conduct a skin and/or scar review in conjunction with Occupational Therapy.

An **Ultrasound Scan** (BT12 Venue 40 MSK, GE Healthcare) will be taken of the burn area to measure the thickness of the scar at three months. When measuring scar thickness with the GE Healthcare ultrasound, an image will be taken centrally from the site of interest (as opposed to peripherally on the scar border). An average of three measurements will be recorded and used in a blinded analysis by clinicians.

The **Brisbane Burn Scar Impact Profile** will be used to measure the intensity and frequency of sensations, such as pain, tightness and discomfort as well as health related quality of life specific to people with burn scars. This measure was developed and tested for preliminary validity in children with burn scars and is undergoing further testing with children and caregivers. In adults with burn scars the Brisbane Burn Scar Impact Profile has been found to have acceptable reproducibility, responsiveness and longitudinal validity.

A record of the patients **ROM** over joints will also be recorded, and noted the extent of reduction if present.

**Surgical Intervention**

Any surgical intervention required; including debridement, grafting and escharotomy, will be recorded. A record of the number of outpatient clinic appointments each child attends will also be recorded.

**Pain and distress**

This will be assessed at home (between dressings via parents) and during dressing changes (in clinic via clinicians).

Parents

1. Participants self report of pain intensity using the Faces Pain Scale Revised (FPS-R) (if participant was aged 3 years or over);
2. Participant’s self report (if aged over 8 years) or the parents report of the participant’s pain intensity using a Visual Analogue Scale – Pain (VAS-P);

Clinicians

1. Nurses’ observational rating of the participant’s pain and distress using the face, legs, activity, cry, consolability (FLACC) scale (<3 years old);
2. Any analgesic and/or sedative medications administered to the participant at each dressing change will be also recorded

**Itch**

Itch intensity will be self-reported for children aged 8 years and older using an 11-point NRS (0 to 10). The Toronto Pediatric Itch Scale is an observation based scale rating itch behaviours on a scale of 0 (absence of itch) to 4 (severe itch with significant disruption) and will be completed by caregivers for children aged under 5 years. Between the ages of 5 and 8, the Itch Man Scale will be used which asks patients to identify which picture on a 5 point scale (0 – 4) best represents their itch. Numeric rating scales have been recommended over visual analogue scales due to improved adherence, increased responsiveness and fewer missing values in populations of adults with pain and chronic itch.

**Resource use and costs**

A record of the resources and associated cost for each participant will be recorded from the perspective of the health service provider and costed at market rates. This will include trial interventions costs (e.g. the number of dressing changes, type and size of dressings used and scar therapy products), as well as other burn-related resource use (and costs) that may be important to a health service deciding which of the interventions to implement in their model of care for patients with burns (e.g. moulds and splinting, overheads and labour time). Labour time (e.g. occupational therapists, physiotherapist, nurses and surgeons) will be quantified for each patient (on the basis of time duration utilised and number of appointments required) and costed at the relevant state award rates for each respective discipline. Length of stay in hospital will be calculated up until the time that the patient is clinically ready for discharge, omitting any additional occasions of social admission needs.

**11. STUDY PROCEDURES**

**11a. Recruitment of participants**

Members of our Burns Team and ED staff will notify researchers of eligible participants for the trial and provide the participant with a participant information form. An investigator will then be available to discuss patient participation in more detail and if the patient/family is interested in participation, they will be asked to sign a consent form. The study follow-up time periods will match standard outpatient burns review times (e.g. Dressing changes until re-epithelialisation, and at 3 months where possible).

**11b. Randomisation**

Randomisation will be by an investigator of the team and completed using a computer- generated block randomisation. Allocation will be via the REDCap software randomisation module.

Due to the nature of the study, double blinding will not be possible as treating therapists will be aware of the treatment modality. Assessors of wound re-epithelialisation and scar thickness will be blinded to the intervention.

**11c. Study procedure**

**Group 1 – Control Group:**

Patients in the control group will receive routine care (Acticoat™ and Mepitel™).

**Group 2 – Renasys Touch™/Acticoat™ and Mepitel™ Intervention Group:**

Patients in the treatment group will have their wounds dressed with the same dressing combination as the control group: Acticoat™ (Smith and Nephew) and Mepitel™ (Molnlycke). In addition, NPWT Renasys Touch™ (Smith and Nephew) will also be applied. An experienced burns clinician or burns nurse will apply the negative pressure dressing and provide appropriate parental and child education. Parents will be given an information sheet that is provided to all patients receiving NPWT at the Queensland Children’s Hospital, Brisbane.

**Procedure and Dressing Changes for both groups:**

1. Dressings (+/- negative pressure depending on group allocation) will be **changed post first dressing application** at PLCBC or post debridement in ED. Standard dressings to be changed every 3-5 days, NPWT to be removed initially after 4 – 7 days.

2. **Distraction techniques** during change of dressings will be used as appropriate for each participant as per PLCBC routine standard of care.

3. **Analgesia** will be provided as per unit policy.

5. Patients in NPWT **NPWT ARM ONLY** to continue NPWT until first dressing change. After the removal of the NPWT, treatment will be continued with standard dressings (Mepitel™ and Acticoat™).

6. All patients to continue with standard silver protocol dressings (under NPWT for Intervention group) unless requires skin grafting or infection.

7. Data will still be collected for patients who require grafting or infection, and these will be included in the final analysis.

**11e. Safety considerations/Patient safety**

A safety log containing adverse events and patient complaints will be kept on all patients. Adverse events will be graded and reported in all results. The CHQ HREC will be contacted of any adverse events.

Regular team meetings will be held. Principal investigators will review study progress at these meetings, address pertinent issues and identify further actions to be taken. The principal investigators will ensure via this regular review process that data is managed appropriately (i.e. stored in a de-identified fashion) and that appropriate steps are taken with regard to data cleansing and dissemination of results.

**11g. Data management & Storage**

Data will be stored in a de-identified manner. Each child involved in the study will be de-identified and allocated a unique identifier.

**12. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS**

**12a. Sample size and statistical power**

As this is a feasibility pilot study, we predict 30 participants will be sufficient to determine safety and acceptability of the proposed intervention and outcome measures. Brickett and Day 1994 suggest that a pilot sample of approximately 10 are sufficient to perform a pilot study.

**12b. Statistical methods**

Depending on the distribution of data will determine the choice of parametric or non-parametric analysis. If a significant difference between the groups is found, post hoc analyses will be then conducted using the Mann–Whitney U tests to determine which groups are significantly different from each other.

Pain will be analysed with multilevel generalized linear mixed effects modelling with a log link function and gamma distribution to determine differences between the treatment groups at timepoints and over time.

The statistical method used for the study objectives/hypotheses may include t-test, chi-squared and/or multivariate modeling. An ITT analysis is preferred as it compares all subjects in the groups to which they were originally randomly assigned (despite withdrawal, treatment failure or cross-over). The QUT Research Methods Group will be engaged to perform all quantitative analysis.

**13. ETHICAL CONSIDERATIONS**

The study will be conducted in full conformance with principles of the “Declaration of Helsinki”, Good Clinical Practice (GCP) and within the laws and regulations of the country in which the research is conducted.

This study will undergo a full human research ethics committee review with the Children’s Health Queensland Human Research Ethics Committee (CHQ HREC)