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Effectiveness of a Regenerative Epithelial Suspension (RES), on the pigmentation of split-thickness skin graft donor sites in children: the d*RES*sing pilot randomised controlled trial protocol

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ABSTRACT

Background Paediatric donor site wounds are often complicated by dyspigmentation following a split-thickness skin graft. These easily identifiable scars can potentially never return to normal pigmentation. A Regenerative Epidermal Suspension (RES) has been shown to improve pigmentation in patients with vitiligo, and in adult patients following a burn injury. Very little is known regarding the efficacy of RES for the management of donor site scars in children.

Methods and analysis A pilot randomised controlled trial of 40 children allocated to two groups (RES or no RES) standard dressing applied to donor site wounds will be conducted. All children aged 16 years or younger requiring a split thickness skin graft will be screened for eligibility. The primary outcome is donor site scar pigmentation 12 months after skin grafting. Secondary outcomes include re-epithelialisation time, pain, itch, dressing application ease, treatment satisfaction, scar thickness and health-related quality of life. Commencing 7 days after the skin graft, the dressing will be changed every 3–5 days until the donor site is ≥95% re-epithelialised. Data will be collected at each dressing change and 3, 6 and 12 months post skin graft.

Ethics and dissemination Ethics approval was confirmed on 11 February 2019 by the study site Human Research Ethics Committee (HREC) (HREC/18/QCHQ/45807). Study findings will be published in peer-reviewed journals and presented at national and international conferences. This study was prospectively registered on the Australian New Zealand Clinical Trials Registry (available at https://anzctr.org.au/ACTRN12620000227998.aspx).

Trial registration number Australian New Zealand Clinical Trials Registry [Available at https://anzctr.org.au/ACTRN12620000227998.aspx]

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Donor Site dressed with a Regenerative Epidermal Suspension Trial is the only study to evaluate dyspigmentation on paediatric split-thickness skin graft donor site wounds treated with Regenerative Epidermal Suspension.
⇒ Dyspigmentation will be assessed using a combination of objective measures and validated scar assessment scales.
⇒ A limitation is the exclusion of children from non-English speaking backgrounds and those in the care of Department of Community Services due to the format of data collection.
⇒ Another limitation is stratification for skin colour type not possible as numbers required are too great to enable the conduct of a pragmatic study.

INTRODUCTION

Background

A split-thickness skin graft (STSG) donor site wound (DSW) may be complicated by cosmetically unacceptable hypertrophic scarring and dyspigmentation after healing.[1] Hypertrophic scars are prominent, easily identifiable and can be symptomatic with pain or itch.[2 3] In the case of scar dyspigmentation, the spectrum of abnormal colour is either hyperpigmented, hypopigmented or dyschromic (hyperpigmented areas interspersed with hypopigmentation).[4] Of the numerous trials that have evaluated re-epithelialisation of paediatric STSG donor sites,[5–9] none have specifically focused on donor site dyspigmentation. As a result, current management options for donor site dyspigmentation are guided by treatments for scar dyspigmentation.[10–12]

While donor site pain and itch are reported to settle within 3 weeks of a skin graft,[2] it is the long-term donor site morbidity of

dyspigmentation that is more difficult to manage. As the mechanistic knowledge of scar dyspigmentation continues to evolve, effective treatment for paediatric donor site dyspigmentation is lacking. Current therapeutic options for dyspigmented scars have not specifically been evaluated for paediatric donor sites (eg, conservative tanning lotions, bleaching creams, cosmetic camouflage, invasive tattoo, laser therapy, cultured or non-cultured melanocyte transplantation and surgical excision with primary closure or STSG).[10] Clinicians are faced with navigating the challenges of limited treatment options and lack of evidence regarding these options, as well as the short-term and long-term impacts of appearance-related distress on the well-being of a child.[13–16]

Regenerative Epithelial Suspension (RES, Avita Medical, Valencia, California, USA) prepared using the RECELL Autologous Cell Harvesting device has been used clinically for over two decades.[17] A skin biopsy obtained from the dermoepithelial junction is transformed by a three step enzymatic degradation to a mixture of keratinocytes (65%), fibroblasts (30%) and melanocytes (3.5%) which is aerosolised onto the wound bed; either as a replacement for STSG, or to deposit epithelial cells in the interstices of a meshed and expanded STSG.[18] RECELL requires a substantially smaller donor area than a standard STSG. As such, RES may incur less cost in the overall donor site management when compared with standard treatment.[19] In a recent systematic review and meta-analysis of randomised controlled trials evaluating the efficacy of autologous skin cell suspensions including RES, none were conducted on paediatric STSG donor sites.[20] This study aims to evaluate RES in the management of paediatric donor site scar pigmentation a year after STSG.

Objectives

1. *Primary:* to compare the effectiveness of RES versus no RES on donor site scar pigmentation in children receiving a STSG; measured using the DSM II ColorMeter Lightness (L*) parameter at 12 months post skin graft.
2. *Secondary:* to evaluate the effectiveness of RES versus no RES on donor site: erythema, re-epithelialisation time, pain, itch, health-related quality of life (HRQoL), scar severity (including sensation, thickness), treatment satisfaction, dressing application ease, intervention fidelity, healthcare resource use, recipient site engraftment and pigmentation (Melanin Index (MI), pigmentation(b*)) at 12 months post skin graft.

METHODS AND ANALYSIS

Study design

The d*RES*sing (donor site dressed with a *R*egenerative *E*pidermal *S*uspension) Trial is a prospective, two-arm, parallel group, single-centre, randomised pilot trial with a 1:1 allocation ratio. An active control group (No RES) will be used in lieu of a placebo (ie, no treatment at all) as all donor sites are covered with an inert dressing which is part of standard practice at the study centre. The Consolidated Standards of Reporting Trials extension for randomised pilot and feasibility trials was followed for the design of this study (figure 1).[21 22]

Participants

Setting

This study will be conducted at the Pegg Leditschke Children's Burn Centre at the Queensland Children's Hospital, Brisbane, Australia, where more than 1200 new patients with acute burn injuries are treated annually. The hospital serves a catchment of 1.73 million km^2 inclusive of a population of approximately 5 million inhabitants.[23]

Eligibility criteria

All patients who present to the study site will be screened for eligibility by the clinical staff. The inclusion and exclusion criteria are illustrated in table 1.

Recruitment

Eligible participants will be asked to consider enrolment into the trial, prior to a scheduled date for the STSG. Informed consent will be obtained from the attending guardian; see online supplemental file S1. The majority of STSGs are performed as elective procedures within a week of clinic review. This time allows parent/guardian and child (where old enough) to become fully conversant with the trial, and to have any questions answered. On the day of STSG once suitability of the wound for STSG is confirmed by the attending burn surgeon, the participant will be randomised to one of the two intervention groups. For children whose parent/guardian have declined to participate in the study, standard healthcare will be delivered, and permission sought for demographic data collection (figure 1).

Patient and public involvement statement

Participants or the public will not be involved in the design nor conduct of this study. At various timepoints during the enrolment, participants and parent/guardian will be asked to rate their treatment satisfaction with the assigned intervention. On the final 12-month follow-up, participants and parent/guardian who agree will be offered an email copy of the published results from this trial once these become available.

Interventions

Participants eligible for STSG will be allocated to either:

1. *Group A*: RES (intervention group).
2. *Group B*: no RES (active control group).

The details of the initial donor site dressing application at baseline are tabulated in table 2.

Operative procedures

All STSGs will be completed under general anaesthesia using sterile conditions. The attending surgeon will determine the size of donor skin required to cover the burn wound in square centimetres (cm^2). To assess the size of donor site required to prepare the RES, the E-Burn application[24] will be used to provide surface area in cm^2.

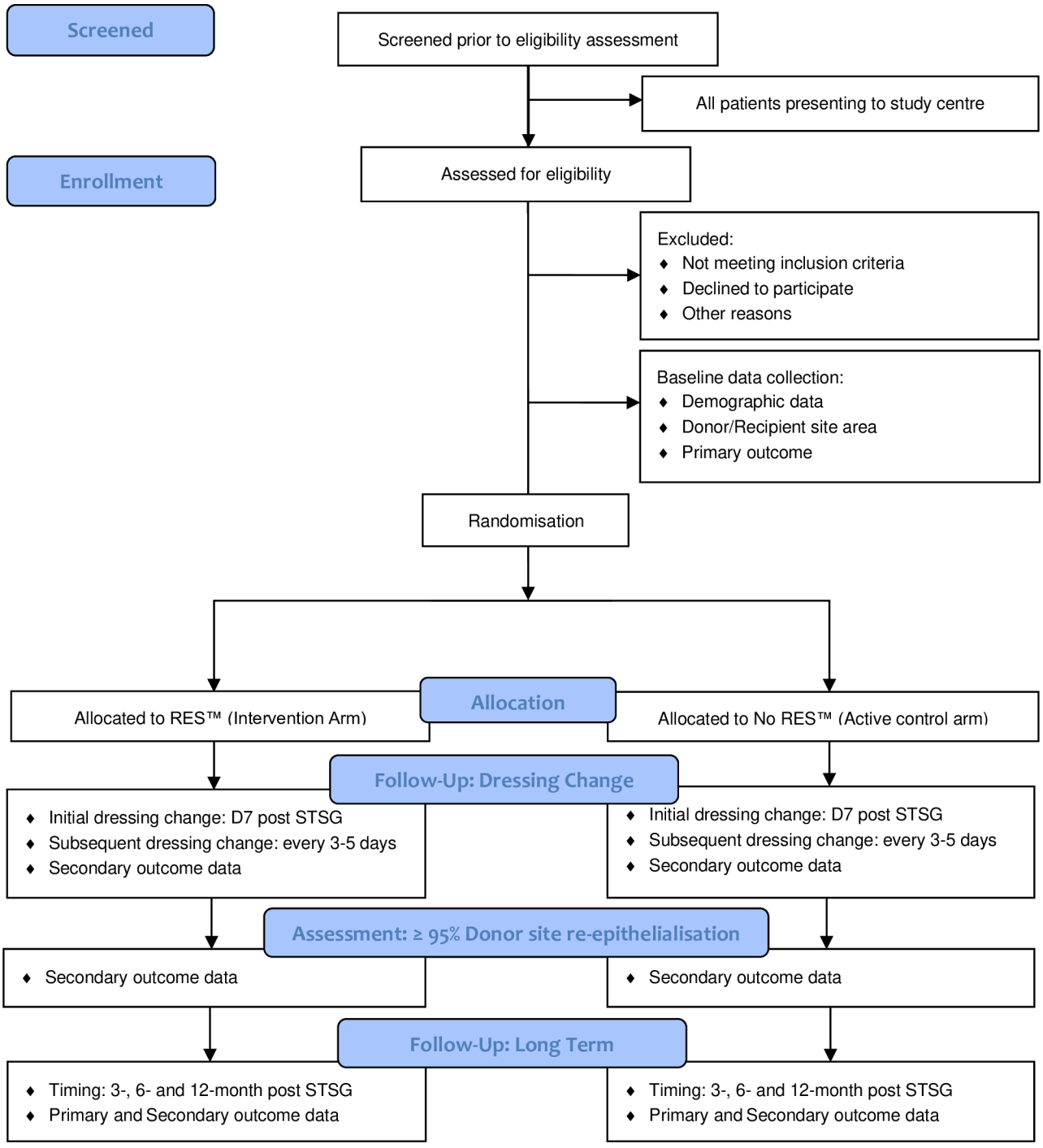

Figure 1 Donor site dressed with a Regenerative Epidermal Suspension Trial Consolidated Standards of Reporting Trials (CONSORT) flow diagram. RES, Regenerative Epithelial Suspension; D7, day 7; STSG, split-thickness skin graft.

The E-Burn mobile application software is freely available, allows for total body surface area burned calculation by painting a body image (dimensions determined by the patient height, age, and weight) using an adjustable brush, specification of burn depth and is used globally and at the study site.[24 25]

Liquid paraffin will be applied to the donor site to act as a lubricant for optimal donor skin harvest with a pneumatic dermatome at a depth of 0.018 cm (0.007 in).[26] This falls within the recommended harvest depth for optimal cell yield to prepare the RES. A three step-degradation process will transform the donor skin sample into a RES. Skin will be harvested from the anterolateral thigh. Only the first 'swipe' donor site located on the anterolateral thigh will be assessed per participant. The variability of donor site scar hypertrophy depends on factors such as anatomical location, age, ethnicity, Fitzpatrick skin type as well as the extent of interventions administered in the DSW.[27] To minimise potential bias, the donor site location will be standardised to the

Table 1 d*RES*sing Trial eligibility criteria

Inclusion criteria	Exclusion criteria
1. Age: ≤ 16 years 2. Requires a split thickness skin graft 3. Children (where applicable) and accompanying parent/guardian must be willing and able to complete all the follow-up evaluation required by the study protocol. 4. Maximum donor site area is 320 cm^2 and recipient site area is 400 cm^2	1. Non-English-speaking background 2. In the care of the Department of Community Services 3. Requires a full thickness skin graft 4. Donor site will be local to the recipient site 5. Hypersensitivity to trypsin or sodium lactate. 6. Previous adverse reaction to general anaesthesia.

cm^2, centimetre squared ; d*RES*sing, donor site dressed with a *R*egenerative *E*pidermal *S*uspension.

anterolateral thigh for all participants in this trial. Topical application of local anaesthesia (bupivacaine 0.25% with epinephrine 1:200 000 AstraZeneca Pty Ltd, North Ryde, NSW, Australia), calculated at a maximum safe dose (2 to 2.5 mg/kg) will facilitate pain relief and haemostasis at the newly created donor site.[28 29] A saline-soaked gauze will be temporarily applied to the donor site with or without the addition of epinephrine (1 mg/1000 mL NaCl) and/or a temporary pressure dressing. Thereafter, the donor site will be dressed with either: RES or No RES followed by an inert, impregnated, tulle gras dressing (CUTICERIN). A sequential outer secondary dressing will follow: ALLEVYN foam dressing that will be affixed to normal skin with Hypafix, a conformable, adhesive retention tape (table 2). The STSG will be secured to the recipient site with, ARTISS or HistoAcryl based on surgeon preference. The application of RES (for intervention arm participants) onto recipient site prior to STSG placement will also be as per the treating surgeon. Thereafter, a standard dressing will be applied.

Postoperative care

Postoperative simple analgesia will be prescribed as required. A handout will be given to the accompanying parent/guardian containing basic dressing advice and when to seek medical attention prior to the scheduled outpatient clinic review date. The first outpatient review date will be 1 week after STSG and subsequently, every 3–5 days until the DSW is ≥95% re-epithelialised. Scar assessments and other outcome measures will be completed in the outpatient clinic at 3, 6 and 12 months after the date of STSG. All outcome measurement timepoints are illustrated in table 3. An investigator who has completed a minimum of 6 months training for scar assessments including colorimetry under the supervision of study centre occupational therapists with expertise in burn scar assessment will perform scar assessments.

Monitoring

Adverse effects for the proposed interventions are expected to be minimal. Potential donor site adverse effects include infection (cellulitis, impetigo, sepsis), haematoma, pruritus, allergic reaction to dressings, local inflammation and hypergranulation. Potential recipient site adverse effects such as infection, graft loss, hypergranulation and contracture will be managed with a standardised unit protocol. Careful monitoring of participant medical records, self-reports by parent/guardian (and participants where appropriate) and treating clinicians will be conducted to identify adverse events. A Safety

Table 2 d*RES*sing Trial initial dressing application

Initial donor site dressing application		
Perioperative	General anaesthesia at start of procedure for both groups.	
Operative	Sterile preparation of donor site and recipient site 2D imaging and area calculation of both recipient site and donor site	
	RES	No RES
	RES prepared with RECELL device RES applied to donor site wound CUTICERIN affixed to healthy skin over RES	CUTICERIN placed on donor site and affixed to healthy skin
Outer dressing	ALLEVYN followed by Hypafix	
Postoperative	Routine postoperative management First dressing change at 7 days after split-thickness skin graft. Subsequent dressing changes every 3–5 days until ≥95% re-epithelialised or referred for redo-skin graft.	

2D, two dimensional; d*RES*sing, donor site dressed with a Regenerative Epidermal Suspension; RES, Regenerative Epithelial Suspension.

Table 3 d*RES*sing Trial assessment timeline

	Outcome measurement timepoints				
	Baseline data	Follow-up visit			Study completion
Outcome data/measure	At STSG under GA	COD at 7 days post STSG then every 3–5 days until ≥95% re-epithelialisation	3 months	6 months	12 months
Eligibility screen	×				
Informed consent	×				
Donor/recipient site area	×				
Allocation	×				
Sociodemographic data	×				
Height/weight	←	—	—	—	→
Group A RES	←	—			
Group B No RES	←	—			
2D Image	←	—	—	—	→
Donor site scar thickness sonography			←	—	→
Scar colorimetry	×		←	—	→
NRS-P proxy, NRS-P	←	—			
NRS-I proxy, NRS-I	←	—			
BBSIP, CHU9D			←	—	→
Treatment satisfaction, NRS-TS		←	—	—	→
Ease of dressing application	←	—			
Masked review: donor/recipient site and scar imaging					×
Donor site intervention fidelity	←	—			
Adjunct interventions	←	—			
Other outcomes	←	—			
Peri-procedural analgesia/sedation/anaesthesia	←	—	—	—	→
Anti-pruritic medication		←	—	—	→
Scar management		←	—	—	→

BBSIP, Brisbane Burn Scar Impact File; CHU9D, Child Health Utility 9D; COD, change of dressing; 2D, two dimensional; GA, general anaesthesia; NRS-I, numeric rating scale - itch; NRS-I Proxy, numeric rating scale - itch proxy; NRS-P, numeric rating scale - pain; NRS-P Proxy, numeric rating scale-pain proxy; NRS-TS, treatment satisfaction numeric rating scale; RES, Regenerative Epidermal Suspension; STSG, split-thickness skin graft.

Monitoring Group comprising three independent clinicians will receive regular reports of progress and adverse events, and their reviews will be fed back to the investigatory team. All adverse events will all be reported to the clinical health service and the overseeing Human Research Ethics Committee (HREC). Discontinuation or alteration of treatment will be at the discretion of the treating clinical team and will be closely monitored throughout the study and all deviations reported.

Study outcomes

Primary outcome: donor site scar pigmentation—L*

Constitutional ('intrinsic') skin colour differs from facultative ('inducible') skin colour following sunlight exposure[30] Pigmentation will be measured objectively with the DSM II ColorMeter using the CIELab (Lightness [L*], erythema [a*], pigmentation [b*])[31] and narrow band spectrophotometry (Erythema Index (EI), MI) colour space systems.[32] The Lightness (L*) index will be the primary approach for the measurement of pigmentation (primary outcome). In a study of 55 patients with burn scars, for pigmentation and erythema, DSM II parameters (L*, MI, a*, EI) had acceptable to excellent inter-rater reliability.[33 34]

The DSM II is a small hand-held device that combines narrow-band spectrophotometry and tristimulus reflectance colorimetry in a single measurement of skin 4 mm in diameter.[31] From the experience of the investigators the first DSM II measurement is often different to the two subsequent measurements. Hence, an average of three measures will be taken for the donor site and compared with normal skin on the contralateral limb. This will provide a difference measurement which will be used as the study measure.

Secondary outcome: donor site scar pigmentation (other)

The secondary approach for the measurement of pigmentation will be the MI and pigmentation b* indices. Parent/guardian proxy reports of donor site scar pigmentation will also be evaluated with the colour item of the Brisbane Burn Scar Impact Profile (BBSIP).[35–38]

Secondary outcome: erythema

Scar erythema, identified as redness, represents vasodilatory changes and inflammatory responses during natural progression of scar formation.[39] Scar erythema will measured with Erythema (a*) (primary approach) and EI (secondary approach). Scar erythema will also be evaluated subjectively with the pigmentation item of the BBSIP measure. Both donor and recipient site scar erythema will be measured with these parameters using the same procedures as for scar pigmentation.

Secondary outcome: time to re-epithelialisation (TTRE)

The number of days required for the DSW to attain ≥ 95% re-epithelialisation will be determined by: (1) non-masked clinical judgement from the attending surgeon (primary approach) and (2) masked burn specialist panel assessment of two-dimensional (2D) donor site re-epithelialisation (secondary approach). Digital 2D photographs will be taken of a participant's donor site at time of the skin graft and every dressing change until the wound is ≥ 95% re-epithelialised. Recipient site engraftment will be assessed using the same approach, with this endpoint defined as number of days after skin graft until ≥98% engraftment based on the expertise of the treating surgeon.

Secondary outcome: pain

An 11-point numeric ratings scale for pain (NRS-P 0=no pain, 10=worst possible pain) will be used. This scale has not been validated for children under 8 years of age. Therefore, self-reports will be used for children over 8, and parent/guardian proxy reports (NRS-P Proxy) for children under 8.[40–44] The first pain assessment will be at 4 hours post-skin graft once the participant has recovered from the general anaesthesia and is about to be discharged home. At 24 hours post skin graft, the parent/guardian will receive a text message that allows them to complete an observer report of the participant's pain at that time (NRS-P Proxy) and where applicable, a self-report from the participant (NRS-P). Thereafter pain measures (where applicable) will be taken during dressing changes. As a large proportion of the potential cohort at the study site are non-verbal toddlers,[45] the proxy pain report (NRS-P Proxy) for all participants will be completed by the parent/guardian for the entire cohort as the primary approach for pain. The donor site will be exposed first to prevent the influence of pain associated with the STSG graft dressing change.

Secondary outcome: itch

All parent/guardian will complete a proxy observation itch report (NRS-I Proxy) for all participants. Itch intensity self-report (NRS-I), where applicable, will be completed by participants ≥8 years old. Itch intensity will be assessed using an 11-point Numeric Rating Scale of itch intensity (NRS-I, 0=no itch to 10=worst imaginable itch), at each dressing change until ≥95% donor site re-epithelialisation is confirmed by the attending burns surgeon. At 3, 6 and 12 months post STSG, all parent/guardian will complete the NRS-I Proxy item of the BBSIP.[35 36] In a study of 413 children who were grafted within 2 weeks of a burn injury, the proxy report by parent/guardian for itch using an NRS had excellent correlation with Itch Man scores (0.896, 95% CI 0.87 to 0.91).[46]

Secondary outcome: ease of dressing application

After each dressing application, a short questionnaire of clinicians' opinions regarding ease of application, conformability of the dressing, length of dressing change and any additional comments as free text will be obtained until donor site is ≥95% re-epithelialised.

Secondary outcome: treatment satisfaction

Assessment of treatment satisfaction will assist in identifying barriers and enablers of the interventions from both the parent/guardian and clinician perspective.[47] An 11-point Numeric Rating Scale (0=not satisfied to 10=extremely satisfied) will measure both parent/guardian and clinician satisfaction with each intervention group, with a section for additional comments.

Secondary outcome: donor site scar height

The portable B-mode ultrasound Venue 40 MSK (GE Healthcare, Fairfield, Connecticut, USA) will measure donor site scar height up to level of epidermis. Ultrasound measurement of scar height has previously been validated at the study site in children with burn scars.[48] An average of three measurements will be taken from the donor site scar only. The study site scar relocation protocol will be followed at each scar assessment.

Secondary outcome: HRQoL

Scar-specific HRQoL: scar-specific HRQoL will be measured with the BBSIP instrument, previously validated for children (0–18 years) and parent/guardian.[35 36] The BBSIP measures the intensity and frequency of sensations, such as pain, tightness and discomfort as well as HRQoL specific to people with burn scars. A parent/guardian will complete the BBSIP for all participants.

Paediatric HRQoL: The Child Health Utility 9D (CHU-9D) will also be used to assess HRQoL. The CHU-9D includes nine items: worry, sadness, pain, fatigue, annoyance, schoolwork/homework, sleep, daily routine and ability to join in activities.[49–52] The CHU9D is validated for use with children aged 7–17 years including validation with an Australian adolescent population.[53] A parent/guardian proxy report will be completed for all participants.

Other outcomes

Healthcare resources used for the management of donor sites for each participant will be collected over a 12-month period, from the perspective of a health service provider. This will include resource utilisation required for interventions (eg, donor site dressings), scar management, hospitalisation based on setting (eg, emergency

department, inpatient, outpatient) and this will include clinician labour as well.

Sociodemographic data (eg, age, sex, ethnicity, Fitzpatrick skin type,[54] anatomical location of donor site) will be collected from all participants at baseline on the day of STSG by primary investigator. A study-specific intervention fidelity checklist for the donor site will be completed at each dressing application until donor site reaches ≥95% re-epithelialisation. This will include prewound preparation; dressing application and a post dressing application follow-up information sheet for care of the donor site dressing.

Data management

Sample size estimate

This pilot study will recruit a sample size of 20 participants per group with 40 participants in total based on the available population within a 12-month period. The sample size is intended to provide effect estimates suitable for informing a subsequent larger trial.[55]

Randomisation

Randomisation and allocation will be completed with the Research Electronic Data Capture (REDCap, 2019, Vanderbilt University, USA) software.[56] To balance the small group sizes for this trial, block randomisation will be used. The randomisation sequence will be generated by an experienced biostatistician and then uploaded onto REDCap by a person not involved with the study, thereby maintaining concealment of the randomisations sequence from the investigators, clinicians and participants. Randomisation will occur, once the attending surgeon confirms the criterion for inclusion is fulfilled. This separates the randomisation from enrolment and further reduces the risk of selection bias.

Masking

On completion of data collection, re-epithelialisation and pigmentation of each participant's donor site will be assessed by a burn specialist panel (including surgeons, nurses and occupational therapists). The panel assessing pigmentation will not be the same as the panel for re-epithelialisation. When there is a difference in assessment, the panel will review the images until consensus is reached. Both participants and burns specialist panel will be masked to the assigned intervention for each donor site. This may not be entirely possible if a surgeon within the specialist burns panel has been responsible for the clinical management of participants as they may recognise the donor site of their patients. An experienced sonographer familiar with sonographic assessments of scar thickness will complete masked assessments of donor site scar thickness.[48]

Data collection, storage

Data collection will occur as outlined in table 3. Questionnaires will include items measuring pain and itch, treatment satisfaction, dressing application ease, a sociodemographic data, BBSIP, CHU-9D and intervention fidelity measures. Data will also be collected in the form of digital images, clinical characteristics, colorimetry and sonography. Data collection will be completed using the REDCap software. Confidential participant data will be kept in a locked filing cabinet at the study site and backed up on the secure QUT Research Data Storage Service. In accordance with the National Health and Medical Research Council guidelines for clinical trials, all data will be stored for 15 years after completion of the study.

Statistical analysis

Exploratory analysis will be conducted, and descriptive statistics reported. The primary approach to analysis will be using an intention-to-treat approach. A two-tailed p value <0.05 will be considered statistically significant. SPSS (IBM Corporation) and Stata (StataCorp) software will be used for analysis where appropriate.

Pigmentation and erythema will be analysed with a three-step approach. The mean of three measurements for each DSM II parameter (L*, MI*, a*, EI*) will be calculated for both the scar and normal site (anatomical location contralateral to the scar at the same level in normal, unaffected skin). Second, 2D images from normal and scar site will be classified using the colour parameter of the Manchester Scar Scale (MSS).[57] Each pair of scar/normal images will be assigned a category: 'perfect match', 'slight mismatch', 'obvious mismatch' and 'gross mismatch'.[58] Third, the absolute mean differences between scar and normal skin site across control and treatment groups will be analysed using generalised estimating equations. This is an anchor-based approach[59 60] that will incorporate the MSS colour parameter as an 'anchor' to classify the 2D scar site image with their corresponding colorimetry measurements. Scar pigmentation will be deemed acceptable (perfect or slight mismatch) and not acceptable (obvious and grossly mismatched). The proportion in each group with an acceptable outcome will be analysed using χ^2.

The TTRE and engraftment data will be analysed with a survival analysis model, with re-epithelialisation time as the main outcome and the intervention group as the explanatory variable. As this is a pilot study, the effect of other variables such as burn depth will not be included in the analysis due to the constraints of a small sample size. All remaining secondary outcomes data will be analysed using an approach appropriate for longitudinal data: primarily using generalised estimating equations with an alternative of mixed model regression analysis if this is deemed necessary, with an appropriate link function depending on the nature of the data. A thematic content analysis using a deductive approach[61–63] will be used to interpret the open comment responses regarding the ease of dressing application and treatment satisfaction questionnaires.

ETHICS AND DISSEMINATION

Ethics approval was confirmed on 11 February 2019 by the study site HREC (HREC/18/QCHQ/45807). This study was prospectively registered on the Australian New Zealand Clinical Trials Registry (available at https://anzctr.org.au/ACTRN12620000227998.aspx). Verbal and written informed consent for participation will be obtained from all eligible participants (where applicable) and their accompanying parent/guardian. All amendments to the protocol will be communicated to the study centre HREC and the Australian New Zealand Clinical Trials Registry. Study findings will be published in peer-reviewed journals and presented at national and international conferences.

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Contributors Initiated collaborative project: RMK, BG, ZT, SMM. Project conceptualisation: RMK, BG, ZT, SMM, AB, CAM, BP. Designed data collection tools: RMK, ZT, AB, ZD. Wrote statistical plan: DV, ZD. Drafted manuscript: AB. Critical review and editing of final draft manuscript: all authors. Final version of manuscript approval: all authors.

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Competing interests Co-investigators of the study are paediatric burns surgeons (RMK, CAM, BP) treating participants at the study site. However, these surgeons will not have any role in the participant recruitment, allocation to groups. The BBSIP was developed by two of the authors (ZT, RMK) and is used as standard of care at the study site.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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