PROTOCOL DATE AND VERSION: 05 June 2024, Version 2

PROTOCOL TITLE: Manual implantation of Full-Thickness Skin Microcolumns for 'Donor-Free' Skin Renewal

SECTION A: RESEARCH TEAM AND LOCATIONS

A1. RESEARCH TEAM

Study Role	Institution/Company and Contact Information
Principal Investigator and Sponsor	**Rodney K. Chan, MD** Principal Investigator The Metis Foundation 210-569-1140 chan@metisfoundationusa.org
Key Research Personnel	**Victoria Diaz, RN** Research Project Manager The Metis Foundation 210-569-1140 diaz@metisfoundationusa.org **Kristin Anselmo, RN** Research Coordinator The Metis Foundation 210-569-1140 kanselmo@metisfoundationusa.org

A2. RESEARCH LOCATIONS

The Center for Ambulatory Surgery of America, Northeast Baptist Hospital, South Texas Aesthetic and Reconstructive Surgery Clinic

B. SOURCE OF EXTERNAL FUNDING

The Metis Foundation

C1. OBJECTIVES/STUDY DESIGN

Objectives/Hypothesis:

Objectives: The objective of this study is to validate the proof of concept regarding the approach of manual implantation of full-thickness skin microcolumns (FTSMs) as coverage for open wounds without creating an additional donor scar and while also capitalizing on the wound healing benefits offered by full-thickness skin grafts.

Hypothesis: FTSMs will provide coverage for open wounds with decreased: time to re-epithelization, pigmentation, wound contraction, and scar thickness at the donor site, while resulting in an injured site that heals better or the same as the split-thickness skin graft (STSG) control.

Study Design:

Previously three patients have been successfully treated with the use of manual FTSM for wound coverage. To provide additional proof of concept data, this study will validate manual FTSM implantation on a larger scale with a 10-patient population. This will be measured by the following hypothesized parameters: time to re-epithelization, pigmentation, wound contraction, scar thickness, pain at the donor site and injury site healing outcome. The approach to testing this hypothesis will be to perform manual FTSM harvest, placement on the injured site, covered by an inert dressing for 10 patients with open wounds necessitating tissue coverage. The rationale is that although preliminary proof of concept data has already been obtained from three patients treated with FTSM implantation, additional proof of concept data would strengthen the conclusions made based on these cases.

C2. **BACKGROUND**

Various techniques for skin replacement have been developed over the years (2). The current proposed method of orthogonal skin harvest differs from other existing technologies that harvest skin fragments, such as the Cellutome™ (KCI, An Acelity Company, San Antonio, TX) and the Autologous Regeneration of Tissue™ (ART) device (Medline, Northfield, IL). The Cellutome™ device utilizes a vacuum on the donor site to create epidermal blisters which are then raised using the device harvester and transferred to the injured site. This approach only harvests epidermis as opposed to full-thickness skin (3,4). Th ART™ device differs in that it harvests and releases skin microcolumns, a method which provides full-thickness skin but also lacks organization of the tissue or a means of facilitating tissue transfer (5). With FTSM harvest, the skin columns are implanted in a regular pattern with fixed density which will optimize epithelialization and healing.

Other skin replacement options which are utilized in clinical settings aid with wound healing but lack the advantages of incorporating full-thickness skin or organized dermal matrices. RECELL® (AVITA Medical, Valencia, CA) is a suspension of Spray-On Skin™ made from an autologous STSG which can be friable, lacks durability, fails to prevent transpiration, and most importantly does not contain any dermal components (6). Micrograft transplantation requires harvest of STSGs that are then minced into smaller pieces and placed on the injured area (7).

Temporary wound dressings provide coverage for wounds to prevent infection with antimicrobial properties and provide protection from injury as a barrier. StrataGraft™ (Stratatech, a Mallinckrodt Company, Madison, WI), made from human neonatal foreskin, provides coverage of wounds until they ready to receive definitive skin replacement (8). Xeroform® (McKesson, Irving, TX) an occlusive, antimicrobial dressing, can also provide temporary protection wounds (9). These alternatives, while not meant to provide definitive treatment by their nature, do provide benefits in temporizing a definitive approach. However, they leave the wound open for a longer period of time, and increase the risk of long-term healing complications such as scarring and contracture.

FTSM harvest skin replacement is an alternative to the standard of care STSG. The orthogonal harvest of skin vs tangential drastically reduces procedural burden, can minimize hospitalization time, and possibly decrease the cost of care for patients in need of skin grafting. With an augmentation of initial healing at the injury and donor sites, patients would have a lesser need for physical therapy, scar revisions, or contracture releases. This would result in improved joint mobility, skin elasticity, functionality, and in turn improved quality of life.

Current standard of care for wounds too large to close on their own often involves coverage with STSGs. STSG harvest itself has several disadvantages. Procurement poses a challenge in cases where the area requiring coverage is extensive and patients lack enough intact, healthy skin to serve as a graft. Additionally, meshing can result in an aesthetically unappealing “fish-net” appearance once healed (10, 11). Because STSGs only include the upper dermis, they lack the appendages that afford skin much of its functionality such as the hair follicles, sweat glands, and reticular dermal fibroblasts contained in FTSGs, resulting in dysfunctional scars upon healing (12, 13).

C3. **STUDY ENDPOINTS**

Primary:

1. Donor site re-epithelization between day 10 to 14

Secondary:

1. Donor site
    a. Pigmentation
    b. Contraction
    c. Scar Thickness
    d. Pain
2. Injured site
    a. Re-epithelization
    b. Pigmentation
    c. Contraction
    d. Scar Thickness
    e. Pain

C4. **SUBJECT SELECTION**

Patients aged 18-85 requiring surgical treatment of open wounds of the torso or extremities requiring skin grafting will be considered for enrollment in this study through review of the electronic medical record by research staff.

Potential subjects must meet the following inclusion and exclusion criteria to be included in this study.

Inclusion Criteria

All subject enrolled must meet ALL the following criteria:

1. 18-85 years of age
2. 10-125 cm^2 open wound on the scalp, neck, torso or extremities necessitating tissue coverage
3. Sufficiently healthy skin to serve as a donor site

Exclusion Criteria

Subjects who meet ANY of the following criteria will be excluded from the study:

1. Wound area involving the face*
2. Wound area involving joints*
3. Pregnancy^
4. Prisoner
5. Active wound infection at potential treatment sites
6. Exposed muscle, joint, tendon, or bone within the wound bed

*Only areas of a wound involving the face or joints will be excluded, not the entire wound. If a large wound covers a large area of the upper extremity including the joint, the area not involving the joint may still be considered for enrollment into the study.

^Pregnancy screening is done on all women of childbearing age prior to initiation of anesthesia. This information will be reviewed as part of the screening process and prior to enrolling an individual in the study.

When a potential subject is identified a member of the research staff will approach the potential subject prior to the start of the operation and introduce the proposed study. If a potential subject expresses interest in participation in the study, the PI or designated study personnel will proceed with the informed consent process for potential enrollment.

Compensation for participation:
Participants will be compensated up to $175 total, $25 per visit for participation in this research. When patients are enrolled into the study, they will be asked to complete a form with their banking information for direct deposit payment into their personal account. The completed form will be sent to and processed by the sponsor, the Metis foundation. Participants will receive compensation upon completion of the study.

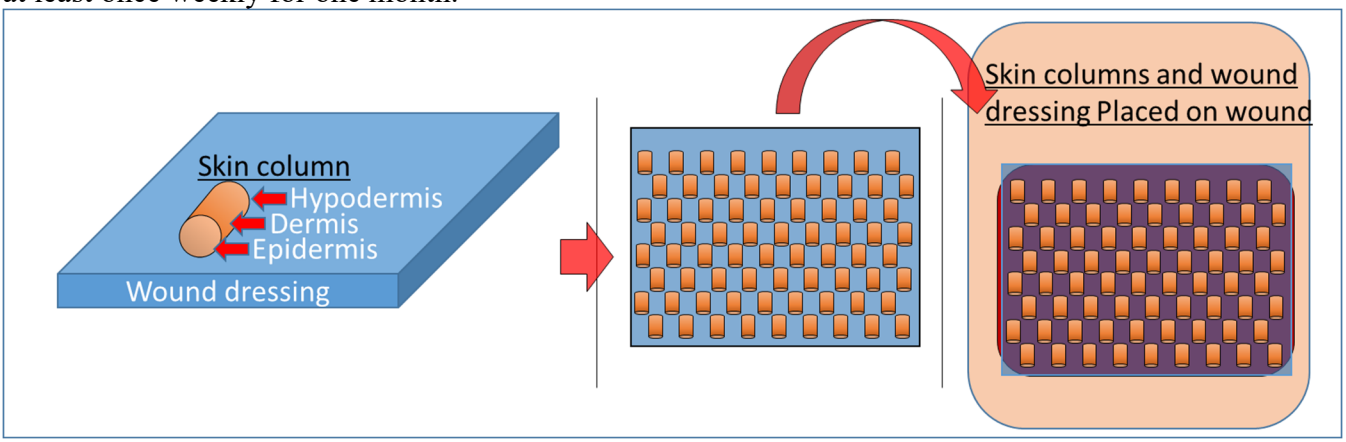
D. STUDY PROCEDURES/RESEARCH METHODS

Informed consent of patients to be enrolled will be performed in a quiet and private area of the hospital to ensure confidentiality. Designated study staff will discuss and explain elements of the study to include detailed review of protocol procedures, discussion of the investigational device, potential risks and benefits of participation, and voluntariness of participation. The designated study staff will also be available to answer questions for the potential subject.

A copy of the Institutional Review Board (IRB)-approved informed consent document will be left with the patient to be enrolled and ample time will be given for their review and decision making. If the patient decides to participate, the IRB-approved consent document will be signed and dated appropriately by all persons required on the document. The original signed consent document will be kept in the study files; a copy will be given to the patient and a copy will be placed in the subject's medical record.

Study procedures will not begin until eligibility is determined, and the informed consent process is completed. Patients who sign the informed consent form are considered to be enrolled. If a patient signs the consent but is not randomized into the study, the patient is considered a screen failure.

After enrollment and completion of informed consent, the patient will be considered an enrolled patient. Up to 10 patients with open wounds of the torso or extremities requiring skin grafting will be enrolled into this study. The study area will be 10 to 125 cm^2. If a patient has multiple non-contiguous wounds that qualify for the study, up to two areas may be enrolled into the study. All other non-study areas will be treated per standard of care procedures/per the operating physician's discretion. The FTSMs will be harvested under sterile conditions in the operating room with a 1.5mm standard biopsy punch from a donor site deemed appropriate by the operating physician based on available healthy tissue; most commonly, the site is located on the thigh. Donor site location and rationale for this decision will be documented. Following FTSM harvest, they will be manually placed onto an inert dressing by experienced study personnel in the operating room. The FTSM on the inert dressing will then be applied to the open wound and covered with a non-occlusive dressing. Additional secondary dressings of the physician's choice will also be utilized. Wounds will be assessed at the first dressing takedown by the primary care team and study members. Study members will be notified by treating staff of any concerns including but not limited to infection, increased pain, or wound break-down. Study members will assess wounds at least once weekly for one month.



Patients will be scheduled for visits with study team members to perform wound assessments and collect data. Every effort will be made to ensure that these visits coincide with the surgical follow-up for subject convenience and to encourage continued study involvement. As such if a patient remains inpatient the visits will be conducted at the hospital. Assessments will continue until 6 months post-operatively or until complete re-epithelialization of the donor site, depending on which occurs first. If complete re-epithelialization occurs prior to 6 months, patients will be encouraged but not required to follow-up to 6 months (Table 1). Compensation will be offered to patients for the additional time and effort required to participate in the study.

Table 1. Schedule of Events

	Week (+/- 1 Day)						**Month (+/- 1 month)**
Research Procedures	**0**	**1**	**2**	**3**	**4**	**6**	**6**
Assessment of Eligibility	X						
Informed Consent	X						
Screening, Medical History, Physical Exam	X						
Medical Chart Review	X		X*	X*	X*	X*	X*
Vital Signs	X	X	X*	X*	X*	X*	X*
FTSM Placement and Coverage with Non-occlusive Dressing	X						
Removal of Dressing		X**					
Hospital or Outpatient Follow-up		X	X*	X*	X*	X*	X*
Wound Imaging	X	X	X*	X*	X*	X*	X*
Assess for Adverse Events	X	X	X*	X*	X*	X*	X*

*Follow-up will occur for up to 6 months or until wounds are re-epithelialized, whichever comes first. If wounds are re-epithelialized prior to 6 months, patients will be encouraged but not required to follow-up past complete re- epithelialization.
**Dressing removal will likely occur within the first week, usually between day 3-7. Date of dressing removal will be documented for each patient. Dressing replacement will be left to the discretion of the treating surgeon.

Research Procedures:
Data will be collected at each weekly assessment. Data to be collected includes:

Digital photography: Standard digital photographs will be taken at each assessment to document wound healing progression.

SilhouetteStar® (optional): The SilhouetteStar® (Aranz Medical, Christchurch, New Zealand) enables the user to account for contour of the wound and distance between the wound and the camera using three laser lines that align at a known distance from the wound. The accompanying software can then calculate area, depth, and thickness for any selected area within the image automatically. This modality is used to measure the primary endpoint of re-epithelialization as well as contraction.

Patient and Observer Scar Assessment Scale (POSAS): The POSAS consists of two numeric scales, one to evaluate the opinion of the patient and one to evaluate the opinion of an observer, resulting in a subjective scar score. The patient scale evaluates color, pliability, thickness, relief, itching, and pain. The observer remarks on

vascularization, pigmentation, pliability, thickness, and relief. This scale has proved to be an accurate, reliable subjective measurement of scarring (19-22).

3D Camera (optional): The Antera 3D® (Miravex, Dublin, Ireland, or similar device) collects 3 dimensional (3D) images of the wound areas and surrounding healthy skin. The collected 3D images allow capture of topographic features as well as wound texture, scar, erythema, and pigmentation.

Data Collection

Data collection will consist of data collection sheets. All information collected about subjects during the study will be kept strictly confidential and will be maintained in a secure, locked file and accessed only by study staff. Upon completion of the study, records will be archived in a password-protected file on a Metis server.
All information collected about subjects during the study will be kept strictly confidential. Subject names will not appear in any reports or published articles. Materials that identify subjects as individuals including medical records will not be released without the subject's explicit permission as required by law.

Subjects will be made aware that their medical records, which identify them as individuals, may be inspected by the designated IRB and/or other applicable regulatory authorities.

Managing Data and/or Human Biological Specimens for this Study:
To protect subject confidentiality, subjects will be identified using an assigned sequential study identification number that will be used on study documents. The key linking subjects' identities will be electronically stored by the research team on a password-protected, secured database, separate from other study data. All information collected about subjects during the study will be kept strictly confidential and will be maintained in a secure, locked file accessible only by study staff. Signed informed consent forms will be kept no fewer than three years, and no longer than 6 years for signed HIPAA authorizations. Upon completion of the study, records will be archived in a password-protected file on a secured network server. Thereafter, the key linking subject identifiers to study identification numbers will be destroyed, rendering the data permanently de-identified. Subject names will not appear in any reports or published articles. Electronic data to include, but not limited to, information gathered from the electronic medical records and stored data entries will be stored on a password-protected file. Locked subject study records will only be accessed by personnel assigned to the protocol.

Managing Data and/or Human Biological Specimens for Future Research:
No human specimens will be banked for future research. All other data collected in the study will be stored as above. If this data is used for future studies, no new consent will be obtained as the patient will have already signed a consent form for use of the data. Subjects may withdraw from the study at any time. Subjects will not be contacted prior to any future use of the collected data. No genetic testing will be performed on the specimens, and the specimens themselves will not be banked. Research staff alone will have access to the data files in the future. Data will be stored for five years following completion of the study in a deidentified fashion. After five years of completion of the study, the data will be destroyed.

Data Analysis
The following endpoints will serve as outcome assessments to be measured for statistical analysis:
- Donor site re-epithelialization (primary endpoint)
- Donor site:
    - Pigmentation
    - Contraction
    - Scar Thickness
    - Pain
- Injured site:
    - Re-epithelialization

- o Pigmentation
- o Contraction
- o Scar Thickness
- o Pain

Means and standard deviations or medians and inter-quartile ranges will be used as summary statistics for continuous variables, and they will be analyzed using Student's t-test and ANOVA or Mann-Whitney Test, whichever is most appropriate. Data may be log-transformed for normalization. Factors that are measured over time will be analyzed using repeated measures ANOVA. Post-hoc multiple comparisons will be adjusted using Bonferroni-Holms method. Significance for results will be established when p-values are less than 0.05.

Statistical Considerations:
Patients with missing clinical assessment data will be excluded from analysis of that specific assessment. Assuming data for all other assessments is present, these data will be included appropriately. Outlier data points will be assessed on a case-by-case basis to determine if the data represents an error in data collection or a true value and will be included in final analysis accordingly. Patients with insufficient data may be replaced per the discretion of the investigator.

Sample Size:
The sample size is 10 patients.

Study Arms:
There is 1 arm to the study:

This study will have one prospective group to validate the proof of concept in manual FTSM placement on a larger scale of 10 patients.

Sample Size Justification:
Although skin replacement via FTSMs has been performed on 3 patients with success, we plan to perform manual FTSM harvest and placement on 10 additional patients in order to strengthen this preliminary data. This data will serve as a basis for potential follow up studies.

Data Analysis Plan:
The primary endpoint of re-epithelialization and secondary endpoint of contraction will be measured using the software accompanying the SilhouetteStar®. Pigmentation will be measured by ImageJ (NIH, Bethesda, MD). Scar thickness will be measured via POSAS. All measurements will be performed on both the injury and donor sites. Patient and Observer Scar Assessment Scale (POSAS) will be used for subjective data on re-epithelialization, scar thickness, pigmentation and pain.

D1. RISK/ SAFETY INFORMATION

Risks of harm, measures to reduce the risks of harm and benefits of participation

Risks of Harm:
All potential risks and benefits will be discussed with the potential subject during the consent process to include the possibility of no direct benefit to the participating subject and the possible benefit to the military scientific community as well as the public at-large. As an ongoing process, the subject will be monitored for safety and all attempts to mitigate risks will be taken. Risks are outlined by procedure/intervention below.

Research Procedure Name: Manual harvest of FTSM and application to the injured site
Research Procedure Description: FTSM will be harvested from the donor site with a series of punch biopsies. These microcolumns will be placed on the injured site and will be covered with an inert dressing followed by application of a non-occlusive dressing.

Research-related Risks: Pain, numbness, swelling, bleeding, infection, or scarring where tissue is harvested. Loss of skin or graft failure.

Research Procedure Name: Data collection
Research Procedure Description: Access to medical records to review and collect data
Research-related Risks: Potential loss of confidentiality

Research Procedure Name: Digital photography, PHI
Research Procedure Description: Photographs of study treatment sites, information from medical records
Research-related Risks: Confidentiality breach

Measures to Minimize Risks of Harm:
Research Procedure Name: Manual harvest of FTSM and application to the injured site
Measures to Minimize Risks of Harm: Providers with operative experience will be available to harvest and place FTSMs to increase safety and efficiency, minimizing time under anesthesia.

Research Procedure Name: Data collection
Measures to Minimize Risks of Harm: Use of password protected electronic files, securing of paper documents in a locked cabinet in a badge access area, removal of subject PHI by redacting identifiable information, limiting of access to the database study personal, and no transmission of identifiable data to any outside source.

Research Procedure Name: Digital photography, PHI
Measures to Minimize Risks of Harm: To protect privacy, subject's images will be labeled with an assigned subject number, visit number, and date. Identifying features such as eyes, mouth, tattoos will be redacted to protect the identity of the subjects

D2. MONITORING AND REPORTING OF ADVERSE EVENTS/SERIOUS ADVERSE EVENTS

Monitoring
Data collected on the subjects will be entered into a data spreadsheet that will be verified routinely by designated study personnel for accuracy and completeness. The trial will be conducted in compliance with any applicable laws and regulations. Designated study staff, for accuracy and completeness, will verify data collected. All regulatory and subject files will be maintained in accordance with any applicable regulations.

The principal investigator will be responsible for the protocol safety monitoring. The PI will make study documents (e.g., consent forms, data pulls) and pertinent hospital or clinical records readily available for inspection by the IRB and oversight staff for confirmation of the study data.

Adverse Events
There are no adverse events that are anticipated in this patient population.

Unexpected adverse events and unanticipated problems
All unanticipated problems involving risks to subjects or others will be promptly reported to the IRB by email. A complete written report will follow the initial notification.

D3. CONFIDENTIALITY

Privacy for Subjects

Discussion of the study with the potential subject and the informed consent process will be done in a quiet and private area of the patient care setting to ensure privacy.

Subjects will be made aware that their research records, which identify them as individuals, may be inspected by applicable regulatory authorities, to ensure the integrity of the data and/or to protect research participants.

Confidentiality Procedures for Research Records, Data

To protect subject confidentiality, subjects will be identified using an assigned study ID number that will be used on study documents. The key linking subjects' identities will be electronically stored by the research team on a password protected secured database, separate from other study data. All information collected about subjects during the study will be kept strictly confidential and will be maintained in a secure, locked file accessible only by study staff. Signed informed consent forms will be kept no fewer than three years, and no fewer than 6 years for signed HIPAA authorizations. Upon completion of the study, records will be archived in a password-protected file on the Metis Foundation network server. Thereafter, the key linking subject identifiers to study ID numbers will be destroyed, rendering the data permanently de-identified. Subject names will not appear in any reports or published articles.

Electronic data to include, but not limited to, information gathered from the electronic medical records and stored data entries will be stored on a password protected file. Locked subject study records will only be accessed by research personnel assigned to the protocol.

D4. INTENDED USE OF DATA

The data from this study will be used to provide proof of concept from previous data that FTSMs applied to injured sites requiring tissue coverage will decrease time to re-epithelization, pigmentation, contraction scar thickness and donor site pain prior to the utilization of this same approach in a prospective, randomized trial. This will provide a basis for which follow up studies can be done to evaluate this method in other clinical wound settings.

References:

1. United States. The U.S. Army in Multi-Domain Operations 2028. 2018. <https://purl.fdlp.gov/GPO/gpo114669>.
2.Nyame, T.T., H.A. Chiang, and D.P. Orgill, *Clinical applications of skin substitutes.* Surg Clin North Am, 2014. **94**(4): p. 839-50.
3.Serena, T., et al. *Use of a novel epidermal harvesting system in resource-poor countries.* Adv Skin Wound Care, 2015. **28**(3): 107-112.
4.Vinceneux Talvande, B., et al. *Use of Cellutome for the healing of venous or mixed ulcers.* Int Wound J, 2018. **15**(6): 993-999.
5.Jaller, J.A., et al., *Evaluation of Donor Site Pain After Fractional Autologous Full-Thickness Skin Grafting.* Adv Wound Care (New Rochelle), 2018. **7**(9): p. 309-314.
6.Peirce, S.C. and G. Carolan-Rees, *ReCell((R)) Spray-On Skin System for Treating Skin Loss, Scarring and Depigmentation after Burn Injury: A NICE Medical Technology Guidance.* Appl Health Econ Health Policy, 2019. **17**(2): p. 131-141.
7.Hackl, F., et al., *Epidermal regeneration by micrograft transplantation with immediate 100-fold expansion.* Plast Reconstr Surg, 2012. **129**(3): p. 443e-452e.
8.Centanni, J.M., et al., *StrataGraft skin substitute is well-tolerated and is not acutely immunogenic in patients with traumatic wounds: results from a prospective, randomized, controlled dose escalation trial.* Ann Surg, 2011. **253**(4): p. 672-83.
9.Barillo, D.J., et al., *The antimicrobial spectrum of Xeroform((R)).* Burns, 2017. **43**(6): p. 1189-1194.
10.Brusselaers, N., et al., *Skin replacement in burn wounds.* J Trauma, 2010. **68**(2): p. 490-501.

11.Tam, J., et al., *Reconstitution of full-thickness skin by microcolumn grafting.* J Tissue Eng Regen Med, 2017. **11**(10): p. 2796-2805.
12.Tam, J., et al., *Fractional Skin Harvesting: Autologous Skin Grafting without Donor-site Morbidity.* Plast Reconstr Surg Glob Open, 2013. **1**(6): p. e47.
13.Wong, V.W., et al., *Stem cell niches for skin regeneration.* Int J Biomater, 2012. **2012**: p. 926059.
14.Manstein, D., et al., *Fractional photothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury.* Lasers Surg Med, 2004. **34**(5): p. 426-38.
15.Rettinger, C.L., et al., *Accelerated epithelialization and improved wound healing metrics in porcine full-thickness wounds transplanted with full-thickness skin micrografts.* Wound Repair Regen, 2017. **25**(5): p. 816-827.
16.Hassanpour, S.E., et al., *Comparison of three different methods of dressing for partial thickness skin graft donor site.* World J Plast Surg, 2013. **2**(1): p. 26-32.
17.Jain, A., A. Agarwal, and C. Shamshery, *An effective pharmacological management of postburn hypertrophic scar pain.* J Anaesthesiol Clin Pharmacol, 2014. **30**(1): p. 111-2.
18.Masella, P.C., et al., *Evaluation of Six Split-thickness Skin Graft Donor-site Dressing Materials in a Swine Model.* Plast Reconstr Surg Glob Open, 2013. **1**(9): p. e84.
19.Draaijers, L.J., et al., *The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation.* Plast Reconstr Surg, 2004. **113**(7): p. 1960-5; discussion 1966-7.
20.Truong, P.T., et al., *Reliability and validity testing of the Patient and Observer Scar Assessment Scale in evaluating linear scars after breast cancer surgery.* Plast Reconstr Surg, 2007. **119**(2): p. 487-94.
21.van de Kar, A.L., et al., *Reliable and feasible evaluation of linear scars by the Patient and Observer Scar Assessment Scale.* Plast Reconstr Surg, 2005. **116**(2): p. 514-22.
22.van der Wal, M.B., et al., *The modified patient and observer scar assessment scale: a novel approach to defining pathologic and nonpathologic scarring?* Plast Reconstr Surg, 2012. **129**(1): p. 172e-174e; author reply 174e.
23.Bird, M.L., et al., *Accuracy, Validity, and Reliability of an Electronic Visual Analog Scale for Pain on a Touch Screen Tablet in Healthy Older Adults: A Clinical Trial.* Interact J Med Res, 2016. **5**(1): p. e3.
24.Scott, J. and E.C. Huskisson, *Graphic representation of pain.* Pain, 1976. **2**(2): p. 175-84.
25.Belmont, P., McCriskin, B., Sieg, R., Burks, R., Schoenfeld, A., *Combat wounds in Iraq and Afghanistan from 2005 to 2009.* J Trauma Acute Care Surg, 2012. **73**:3-12.
26.Kauvar, D., Wolf, S., Wade, C., Cancio, L., Renz, E., Holcomb, J., *Burns sustained in combat explosions in Operations Iraqi and Enduring Freedom (OIF/OEF explosion burns).* Burns, 2006. **32**:853–7