Official title: Single-Stage Integra Reconstruction in Burns

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Science and Merit – 2/2015

Staff Only
Project #
PI:
Submission Date(s):

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The following **9 headings/sections highlighted in blue** correspond with the criteria used to evaluate your proposal. All the **questions/requests are highlighted in yellow;** they all must be answered providing sufficient detail for a reviewer to determine whether the review criteria have been met.

****MAIN RESEARCH QUESTIONS, STUDY AIMS, SPECIFIC HYPOTHESES****

1.1 Please clearly state your overall research questions and/or study aims.

Primary Research Question:

Does combining the use of Integra®, a synthetic dermal substitute, with the application of a skin graft, known as autografting, into a one-stage procedure result in comparable outcomes to the standard two-stage procedure, so as to be a feasible, safe alternative to the standard two-stage approach?

Primary Hypothesis:

Single-stage Integra reconstruction is safe, i.e. does not result in increased infections, and effective, i.e. does not result in increased graft loss, justifying further study in small to intermediate-sized burns that could result in significantly reduced hospital stays in a specific burn population.

****1. BACKGROUND & SIGNIFICANCE****

1.2 What is the specific knowledge gap that the project intends to fill? Include a brief review of past research in this area, numbering your citations to relevant literature as well as including them in the reference section #9.1.

Integra®, a synthetic dermal substitute, has been utilized in burn care for decades.[1] Composed of a porous collagen-chondroitin 6-sulfate fibrillary mat covered with a thin sheet of silastic, it serves to cover wound beds of freshly excised burns and allow for the infiltration of fibroblasts, capillaries, and macrophages, essentially creating a "neodermis" while also acting as a barrier against infection and a blockade against heat and moisture loss.[1] Typically, 10-14 days after Integra® placement, a patient returns to the operating room, the top silastic layer of the Integra® is removed, and an autograft – a split-thickness skin graft harvested from the patient – is applied directly on top of the incorporated Integra®. The result is regarded to be a cosmetically and functionally superior result to that which would have been obtained had the wound bed itself been autografted at the time of excision, as opposed to being covered by Integra® and autografted during a second operation.

Advantages of Integra® use are several.

- There are cosmetic advantages and functional advantages to the end result when compared with grafting alone.[2,3]
- Integra® provides a temporary infection and moisture loss barrier until the definitive coverage with the split-thickness skin graft. This divides the overall reconstruction, and, therefore, the associated physiologic insult into two stages. It should be noted that this advantage did not start with the invention of Integra® – homograft and allograft (cadaver) coverage provided temporary coverage prior to the advent of Integra®.
- The neodermis allows for definitive coverage to be done with a thinner split-thickness skin graft than would otherwise be utilized to cover an Integra®-free wound bed. This allows for faster donor site healing with decreased scarring and pain. Additionally, in the setting of larger burns, the faster donor site healing means a shorter time until these donor sites can be re-harvested to cover additional burned sites.

Disadvantages of Integra® include infection risk, the need for an additional surgery, the cost of Integra® itself, and the increased hospital length of stay necessitated by waiting for the additional surgery, although this latter point has been brought into question in severely burned patients.[4]

Integra® use in single-stage procedures to cover defects without grafting has shown benefit when defects are fairly small, e.g. fingertip injurires[5], and small head and neck skin cancer resections.[6,7] Single-stage resection, Integra® placement and autografting has been successfully utilized in the setting of upper extremity avulsion injuries[8] and was utilized in the burn setting as mentioned in a 2012 letter to the editor published in *Burns*.[9] This aforementioned letter to the editor mentions a single-case. To our knowledge no trial has been performed to evaluate the potential for a single-stage Integra® reconstruction procedure in the burn population.

Furthermore, these studies, while encouraging, were performed with standard Integra®. A thinner version of Integra®, which is half of the thickness of standard Integra®, has been developed for ease of use in trickier anatomic areas, such as the axilla, where increased flexibility would be useful. We believe this decreased thickness would be useful in a single-stage reconstruction, as skin grafts initially receive nutrients prior to incorporation and new blood vessel growth via imbibition. While single-stage reconstruction with Integra® has been demonstrated with standard thickness Integra®, we believe this decreased thickness would increase the likelihood of graft survival due to the decreased distance of nutrient diffusion.

1.3 What preliminary results do you have that support your proposal?

Our burn center has examined the use of Integra® with autografting in a single-stage procedure in the setting of chronic wounds. In 2009, patients with chronic wounds refractory to treatment for more than 3 months in our wound clinic were considered for treated with Integra®. Six patients underwent a single-staged composite graft (Integra® + autograft). Of these six patients, all six had graft "take" classified as "good" at one week. Five of the six had graft take classified as "good" at one month, with the remaining patient's graft take classified as "fair". This was in the setting of chronic wounds, which are notoriously difficult to heal, typically due to patient comorbidities which impair vascularity of the wound beds.

1.4 What is the importance of the research to the scientific community?

Demonstrating the safety and feasibility of single-stage Integra® reconstruction could lead the way towards changing the standard of care for a significant population of burn patients, potentially reducing the hospital stays of thousands of patients each year.

****2. APPROACH****

Some questions in this section do not apply to all study designs; please mark Not Applicable as appropriate

2.1 Describe the study design (e.g., "This is a randomized controlled trial to test the effect of a guided imagery intervention on sleep quality"). Please see this List of Study Designs.

This is a prospective, descriptive, pilot case series involving patients with significant burns who are candidates for reconstruction with Integra®. Should they choose to participate in the trial, the majority of a patient's wounds would be treated in accordance with standard cares of the Regions Hospital Burn Center. However, a small area of the wound would, at the time of excision, have the smallest sheet of thin Integra® (125 cm^2) placed and be immediately autografted with a 3:1 meshed split-thickness skin graft. Of note, 125 cm^2 represents approximately 0.7% of an average sized patient's total body surface area, so for even the smallest burns in our proposed trial, this area would represent a small portion of the patient's area of injury. The remaining injury areas would be covered with standard-thickness Integra® only. The donor graft, a 4 cm x 10 cm sheet of skin, would be meshed in a 3:1 ratio to be expanded to cover the 125 cm^2 sheet of thin Integra®. The patient's post-operative care would be largely unchanged, although the patient would have a donor site of 40 cm^2 that would be dressed and managed in the usual fashion.

Post-operatively, the patient's care would be largely unchanged. Progress of graft "take" at the single-stage 125cm^2 site would be monitored regularly. Eventually, 10-14 days later, the patient would return to the operating room for eventual auto-grafting over their standard Integra®. If autograft "take" at the single-stage site was poor, the area would be re-grafted. If graft "take" at the single-stage site was adequate, the area would not require additional surgery. Thus, the total number of surgeries would not be expected to change, as the patient will require two trips to the operating room regardless of trial enrollment. The 125 cm^2 site would be monitored daily after dressing "take-down" (typically post-operative day 5) while hospitalized and then on a standard post-operative schedule for sloughing or graft loss, infection, hematoma or underlying blood collection, seroma or underlying fluid collection, and time to 95% healed. This last variable is measured by determining the post-operative day at which 95% of the surface area of the graft is covered with epidermis. Because we are meshing the 40 cm^2 sheet of skin in a 3:1 fashion, the resultant graft will look like a thin fence of skin with open diamond-shaped interstices that will slowly each fill in from the peripheral surrounding skin as the graft heals. It is these interstices that give the typical meshed appearance of healed skin grafts. When 95% of the open areas have filled in, that day is determined to be the time to 95% healing. Similarly, an adjacent area of identical size, which will be treated in the standard fashion, will be monitored serially and will serve as a control. Since patients will serve as their own controls, a direct comparison between reconstruction strategies will be enabled.

2.2 How are you identifying eligible subjects or records? (e.g., clinic visit, search of Epic, registry, etc.)

	Not Applicable

Eligible patients will be adults (Age 18 or older) admitted to the Regions Hospital Burn Center with thermal burns that will be reconstructed with Integra®. There is not a firm protocol in place for Integra® use – this is decided at the level of the burn attending physician on a case-by-case basis.

2.3 What is the study population of interest and what are the study inclusion/exclusion criteria?

Inclusion criteria – English-speaking adult burn patients greater than 18 years old, admitted with burn injuries eligible for Integra® reconstruction at the discretion of the burn attending physicians.

Exclusion criteria – patients with isolated hand or face burns – these burns are treated with sheet grafts (unmeshed); the 3:1 mesh grafts would not be used on these cosmetically sensitive areas. If they have hand and/or face burns *in addition* to other areas, they will not be excluded. However, the study itself will not be performed on the hands or face. Additionally, patients unable to present to our clinic for routine follow-up due to geographic limitations or otherwise will be ineligible.

2.4 If you are not using the entire population of interest, what is the method for obtaining a subset or sample of this population?

X	**Not Applicable**

2.5 Will you need to perform "preparation for research" activities prior to consenting subjects for research?

X	**No**
	Yes
	Not Applicable

If you answered yes above, appropriate preparation for research activities prior to consenting subjects must include the following process to determine inclusion/exclusion criteria:

1) Study staff will work with the PI to determine the methods used in identifying potential subjects for the research. For example, this may include creating an Epic Workbench report of patients who are in the hospital and meet minimum criteria for the research.

2) Study staff may access medical records of all potential subjects' identified (i.e., Workbench) to determine eligibility criteria using information that already exists in the medical record. During this process, no identifiable information may be recorded and any documentation made of a potential subject's information that would disqualify them will be destroyed.

   If an eligible patient is not being cared for by the PI, study staff must approach the patient's provider to determine if it is appropriate to proceed with the consent process.

3) If additional testing needs to be done to see whether a patient meets criteria for entry into the study, the PI or staff will need to consent the patient first.

4) If the preparation activity confirms a patient is a possible subject, PI/staff approaches the patient to begin the consent process.

2.6 Describe the steps in your recruitment process.

	Not Applicable

Patients meeting inclusion criteria will be approached prior to their excision and Integra® placement procedure. The risks and benefits of the study will be discussed so that informed consent could be obtained.

2.7 Describe any interventions that are used in this study.

	Not Applicable

Enrolled patients will undergo a single-stage reconstruction of 125 cm^2 of their burn – thin Integra® will be placed with an immediate split-thickness skin graft placed at the time of the first surgery. The remainder of their injury will be treated

according to the routine standard of care – first-stage excision and Integra® placement with second-stage autografting 10-14 days later.

2.8 Provide a brief, sequential, bullet-point description of the all the data collection activities you will conduct from start to finish (e.g., chart review, patient survey, follow-up visits, data pull from the electronic medical record, etc.) and who will conduct each. Please see our Example of Data Collection Steps.

After enrollment, we will collect

-Age, gender, %BSAB, mechanism of injury, location of burns

-presence of burn cellulitis

-Post-burn day of Stage 1 of reconstruction (excision, Integra® placement, and 125 cm^2 auto-graft)

-location of 125cm^2 single-stage reconstruction site

-percentage of graft coverage at first dressing takedown, typically post-operative day 5 and then daily

-post-burn day of Stage 2 of reconstruction (auto-grafting over remaining Integra®, re-grafting of initial 125 cm^2 study area if necessary.

-time to 95% healing of single-stage grafted area and time to 95% healing of control 125 cm^2 wound auto-grafted during second reconstruction procedure adjacent to the single-stage graft.

-single-stage graft site complications (infection, hematoma, seroma, sloughing of graft)

-adjacent (control) wound complications (infection, hematoma, seroma, sloughing of graft)

2.9 Provide a timeline for the main study activities. Please see our Example Timeline

October, 2016 – IRB submission

December, 2016 – February, 2016 – patient enrollment

March, 2016 – April, 2016 – Data Collection/Analysis

May, 2016 – June, 2016 – Abstract/Manuscript preparation

2.10 Describe your plans for ensuring data security

Once a patient is enrolled they are assigned a unique identification number that is assigned to that patient for the duration of the study. The master database linking the patient name with the unique identification number is stored on one password-protected, secure computer in the Critical Care Research Center. The center is a a locked office with limited accessibility. All paper files are stored in locked cabinets at all times. Research staff are fully trained in the elements of patient privacy and confidentiality.

2.11. List the KEY variables that will be collected to support the study aims outlined in item 1.1. KEY variables include those used for:

1) achieving the study aims (outcomes, predictors, potential confounders),

2) identifying the study population (for inclusion/exclusion criteria),

3) describing the study population

Please see an Example of a Completed Table and an Example Data Dictionary.

Variable Name	Data Source (patient survey, EMR, claims, registry)	Purpose (sample identification, description, grouping variable, study endpoint, predictor, covariate)	Measurement Scale (binary, continuous)
Age	EMR/Registry	Description	Continuous
Gender	EMR/Registry	Description	Binary

Percentage of Body Area Burned (%BSAB)	EMR/registry	Description	Continuous
Burn Location(s)	EMR	Description	Descriptive
Presence of Burn Cellulitis	EMR	Confounder	Binary
Post-Burn Day of Stage 1 (Tangential Excision/Integra® Placement with 125 cm^2 of auto-grafting)	EMR	Covariate	Continuous
Location auto-grafted	EMR	Description	Descriptive
Complications of Integra®	EMR	Covariate	Descriptive
Time to 95% healing of single-stage skin graft	EMR	Study Endpoint	Continuous
Complications of Stage 1 Auto-graft (infection, hematoma, seroma, sloughing)	EMR	Study Endpoint	Descriptive
Post-Burn Day of Stage 2 (auto-grafting remaining Integra areas)	EMR	Covariate	Continuous
Location of control auto-graft	EMR	Description	Descriptive
Time to 95% healing of control skin graft	EMR	Study Endpoint	Continuous
Complications of control skin graft (infection, hematoma, seroma, sloughing)	EMR	Study Endpoint	Descriptive

2.12 Provide operational definitions of any variables listed above that aren't adequately described by the variable name above, and provide a brief background of any validated measurement scales listed above.

n/a

2.13 If you are collecting data elements besides those listed in Table 2.10 above, provide a justification for gathering the additional data.

Reminder: For chart review studies, a data collection form must be uploaded with your application listing variables collected and how they are recorded (chart review studies). Provided are links to two example chart review tools: **Word Chart Review Example** and **Excel Chart Review Example**

****3. ANALYSIS****

3.1 Describe the statistical methods that will be used to address the study aims. For each aim, this will usually include:

- Description of the sample used for the particular analysis
- The variables included in the specific analysis and their role in the analysis
- Numeric summaries computed (e.g., mean, standard deviation, proportion, correlation)
- A summary of data exploration and presentation activities (e.g., generating scatter plots, summary tables)
- Description of statistical tests (e.g., independent samples t-test, Mann-Whitney test), and models constructed (e.g., logistic regression)

Please see our Examples of Statistical Methods.

Describe here:

Note: Please reference the area/pages of an established protocol if you are not writing your own analysis plan.

This is a descriptive pilot study. Means and standard deviations will be computed to describe continuous variables and percents for binary or categorical variables. Patient demographics (age, sex) will be tabulated to characterize the population.

Aim 1 will be to describe the time to 95% healing of the single-stage reconstructed skin graft as well as to determine the frequency of complications of infection, seroma, hematoma, sloughing, and graft loss. Aim 2 will be to compare that to the same characteristics of the adjacent (control) 125 cm^2 skin graft.

Frequency charts for incidences of complications between the single-stage and control skin grafts will be compared with chi-square tests. Times to 95% healing will be compared with t-tests.

Sample size:

3.2 What is the estimated sample size(s) for the primary study analyses (per group for studies with different arms or comparison groups)?

We plan to evaluate this procedure in 10 patients.

3.3 The sample size selected was (check all that apply):

	Based on data likely to be available during a specific time period (often based on data available in past periods)
	To conduct one or more specific analyses with adequate statistical power
	To achieve a specified level of precision in one or more key estimates
x	Other (explain): **This is a descriptive study**

3.4 Explain your choice of the sample size selection you listed above:

This is a pilot study – we believe we can enroll 10 patients in a 6 month timeframe and present our results at a regional and/or national conference to proceed with a multi-institutional study.

3.5 Describe your assumptions concerning data available for analysis (e.g. How many subjects will be randomized, possibly lost to follow-up or a procedure? What do you expect for survey response rates, and how much missing data do you expect?). Include information as it pertains to your study (human or animal).

We don't believe any patients will be lost to follow-up, as we will be excluding patients based on this limitation. We expect to have sufficient follow-up data on at least 90% of patients as our post-surgical clinic follow-up rates are above 90%.

Power analysis

NOTE: If you are doing a descriptive study (i.e., aside from computing confidence intervals you are not using statistical tests, inferential statistical testing for group comparisons, or statistical models), please complete 3.6 and skip 3.7-3.8.

If you are conducting statistical tests, using statistical inference to compare groups, or are building statistical models, please skip 3.6 and complete 3.7-3.8. **Please see our Example Power Analysis.**

3.6 Provide a measure of the precision of your estimates for key study endpoints, (e.g., 95% confidence intervals on proportions or means), using actual expected estimates.

This study will be descriptive.

We believe that there will be no increase in graft loss or delayed time to healing, but do not have a precision measure of this information. Our results will be precisely described our findings.

3.7 What level of differences observed in your primary endpoints would be considered clinically or practically significant?

3.8 What is the power for your primary analysis (and the set of assumptions underlying it: hypothesis addressed, expected pattern of effects with justification for these expectations, analysis used, variables in the analysis, effect sizes, sample sizes, alpha level, one or two-sided test)?

3.9 What are the limitations of the proposed approach and analysis?

The limitations are precisely that this is a descriptive pilot study based on a total of 10 patients. While we will characterize our data accurately, this will not be a large enough study, nor will we be auto-grafting a large enough area to extrapolate single-stage reconstruction of large burns. However, should the procedure be deemed safe and effective, it would serve as a springboard to a multi-institutional study involving single-stage reconstruction of small burns, with the definition of "small" to be determined.

3.10 Please name the people who completed the analysis section of this application.

Sam Miotke, MD

3.11 Please name the people who will summarize data and conduct statistical analysis.

Sandi Wewerka, MPH

****4. RESEARCH TEAM****

List your study team and degrees.	**List what each person will do:** Identify study subjects; Data entry; Chart abstraction; Statistical analysis; Study recruitment Interview patients; Draft and revise manuscripts	**List each person's experience** Explain each person's previous research experience with the tasks assigned or what other background/experience relates to the task they are assigned.	**Time Estimate** Please estimate the number of hours or % effort each person will spend on the study
Sam Miotke, MD, MS	Identify subjects, data entry, chart abstraction, statistical analysis, study recruitment, draft and revise manuscripts	Burn Research Fellow; UMN Surgery Resident (PGY-5), currently in second year of research time.	5%
William Mohr, MD, FACS	Identify subjects, draft and revise manuscripts	Decades of experience in burn and trauma surgical research	2%
Nicole Kopari, MD	Identify subjects, draft and revise manuscripts	Years of experience in burn and trauma surgical research	2%
Sandi Wewerka, MPH	Data analysis, draft and revise manuscripts	Decades of research and study coordinator experience	2%

****5. DISSEMINATION****

5.1 What are your plans for publication, including target journals?

Journal of Burn Care and Research

Burns

5.2 What plans do you have to share results or translate results to care delivery at HP or for HP personnel?

This is a pilot study. The results will be discussed at a burn conference as well as, ideally, at the American Burn Association annual meeting as well as the Midwest Regional Burn meeting.

****6. ENVIRONMENT****

6.1 Where will the study be conducted? Why is the proposed location appropriate for study?

The study will be conducted at the Regions Hospital Burn Center, where patients are treated.

6.2 How will the results of this study impact the health of HealthPartners members and the community? Be specific as to whether and how you see any clinical application as a result of this study.

This could lead to changes that eventually affect standard of care of a not insignificant portion of burn patients, decreasing costs and shortening hospital stays while maintaining safety and effective clinical outcomes.

6.3 Does the treatment strategy (drug or service) proposed in the study commit HP to covering or continuing to provide the treatment or program support after the study is completed?

No

****7. OTHER REVIEW****

7.1 Has this study been submitted for other review and/or received approval/rejection previously, including but not limited to: Federal, collaborative agency, previous HealthPartners (rejected), or other funding sources (e.g., nonprofit foundation review)?

X	**No**
	Yes (Provide dates of submission and status of review [approved, pending, or rejected])

7.2 Does this study require review by HealthPartners Radiation Safety Officer?

X	**No**
	Yes Please state that you have spoken to the Radiation Safety Office (651-254-3322) and have their support for this study.

If a research protocol is to involve the use of ionizing or non-ionizing radiation, the principal investigator (PI) should contact the Institutional Radiation Safety Officer (RS0) for Regions Hospital and HealthPartners clinics.

Regions Radiation Safety Office: 651-254-3322.
Frank E. Zink, Ph.D., Radiation Safety Officer for X-Ray Use
Yuanlin Peng, Ph.D., Radiation Safety Officer for Radioactive Materials

****8. DATA ACCESS REQUEST****

These questions must be completed if you are accessing HP/Regions data or if you study involves a HealthPartners Institute programmer. You will need to work with an Institute programmer to complete this form. Please contact Ann Hanson (952-967-5263) or Teri Defor (952-967-7304) for assistance.

If you are not proposing the access HP/Regions data (e.g. Animal Study), you may check "N/A" below.

8.1 What is the name of the programmer helped you complete this section?

8.2 Will you need to add a programmer to your study team?

X	**No**
	Yes

8.3 Considering your inclusion/exclusion criteria described in 2.3, what specific data will you need?

8.4 What years of data are needed?

This is a prospective study

8.5 Will any of the study data be shared or transferred to others within HealthPartners?

Yes, all members of the study team will have access to the data.

8.6 Will any study data be shared or transferred to others outside of HealthPartners?

X	**No**
	Yes - mark which method you will use to share study data: [ ] E-transfer [ ] Secure website/portal [ ] Other secure, encrypted method. Describe below.

8.7 Data Sources (please mark all known data sources)

Mark (X)	Data Source	Mark (X)	Data Source
	EWIS – Claims Data		Registries (chronic condition, disease)
	RDW (Research Data Mart) – historical medical, dental, state death data		Inpatient Case Management data (i.e., Care Guide, Care Partner)
	Claims/Mumps/Cache		Paper Medical Chart
X	EPIC (Electronic Medical Record)		Provider's own source (own patient's chart, provider or department/hospital registry)
	EDR (Electronic Dental Record)		Geriatric department data (i.e., transitional, long term care database)
	EDR Reporting		Data directly from contracted clinics
	New Subject Survey		VDW (Virtual Data Warehouse)
	MEDIPAC System (Regions Billing System)		Consolidated Network Provider (CPN)
	Physician Services Department Data		Health Behavior Group Data (e.g., 10,000

			steps, HRA)
	MN State Death Data		MN State Birth Data
	Misys/Sunquest (Lab production system)		Clarity (Epic Reporting Database)
	Other (Please describe):		

8.8 Exclusion Lists: Institute programmers are required to review and apply the following privacy requirements to study patients and their wishes regarding access to medical record information.

Mark X	Exclusion List
	HealthPartners Institute Exclusion List which excludes persons from all medical research. This should be used for all studies. Applies to all data used internally and externally.
	Gramm-Leach-Biley Opt-Out List: (if known; sometimes this can be determined after a study starts). Applies to identifiable data being sent externally.
	Consent for Treatment-Payment-Operations (TPO) Opt-Out List: (if known; sometimes this can be determined after a study starts). Applies to identifiable data being sent externally.

8.9 Data Elements (Please mark all elements that will be used/ accessed during the study):

Mark (X)	Data Elements
X	Name
	Address
	Telephone Number (any)
	Fax Number
	Certificate/license number (i.e., DEA number, professional license number)
	Email address
	Device identifier or serial number
	URL or IP address (web addresses)
X	Full face photos, biometric identifiers, or other images
	Health Plan beneficiary number (or family contract number)
	Date of Birth
	Vehicle identification or serial number
X	Medical Record number (or any personal record identifier)

8.10 Data Content (Please mark all content areas that apply to your study

Mark (X)	Data Content
X	Demographic: age and gender
	Health Plan enrollment information (i.e., dates, coverage)
	Diagnoses - Medical
X	Procedures - Medical
	Mortality Data
	Lab Results
	Prescriptions/ Medications

	Dates of Service (treatment)
	Facility or Provider Identifier / Characteristics (e.g., specialty, FTE, Clinic)
	Birth Certificate Data
	Pathology / Tissue Type
	Financial data
X	Provider notes
	Vitals – height, weight, BP, etc
	Social history – tobacco use, etc.
	Other Clinical data
X	Other: please describe: Wound and graft photographs

****9. REFERENCES****

9.1 Please list below or attach a list of numbered references to support your literature review in section 1 above.

1. Heimbach D, Luterman A, Burke J, Cram A, Herndon D, Hunt J, Jordan M, McManus W, Solem L, Warden G, Zawacki B. Artifical dermis for major burns: a multi-center randomized clinical trial. Ann Surg 1988;208(3):313-9.

2. Nguyen DQA, Potokar TS, Price P. An objective long-term evaluation of Integra® (a dermal skin substitute) and split thickness skin grafts, in acute burns and reconstructive surgery. Burns 2010: 36: 23-28.

3. Branski LK, Herndon DH, Pereira C, Micak RP, Celis MM, Lee JO, Sanford AP, Norbury WB, Zhang X, Jeschke MG. Longitudinal assessment of Integra® in primary burn management: a randomized pediatric clinical trial. Crit Care Med 2007;35:2615-23.

4. Ryan CM, Schoenfeld DA, Malloy M, Schulz III, JT, Sheridan RL, Tompkins RG. Use of Integra® artificial skin is associated with decreased length of stay of severely injured adult burn survivors. J Burn Care Rehabil 2001;23:311-7.

5. Jacoby SM, Bachoura A, Chen NC, Shin EK, Katolik LI. One-stage Integra® coverage for fingertip injuries. HAND 2013;8:291-5.

6. Burd A, Wong PSY. One-stage Integra® reconstruction in head and neck defect. JPRAS 2010;63:404-9.

7. De Angelis B, Gentile P, Tati E, Bottini DJ, Bocchini I, Orlandi F, Pepe G, Di Segni C, Cervelli G, Cervelli V. One-stage reconstruction of scalp after full-thickness oncologic defects using a dermal regeneration template (Integra®). BioMed Research International 2015:1-11.

8. Demiri E, Papconstantinou A, Dionyssiou D, Dionyssopoulos A, Kaidoglou K, Efstratiou I. Reconstruction of skin avolusion injuries of the upper extremity with Integra® dermal regeneration template and skin grafts in a skingel-stage procedure. Arch Orthop Trauma Surg 2013;133:1521-6.

9. Kosutic D, Beasung E, Dempsey M, Ryan L, Fauzi Z, O'Sullyvan B, Orr D. Scingle-layer Integra® for one-stage reconstruction of scalp defects with exposed bone following full-thickness burn injury: a novel technique. Burns 2012; 38: 143-5.