Application of RECELL to Promote Healing Following CO2 Laser Treatment in Cosmetic Facelift Patients

IRB00085278

NCT05386368

IRB Approval Date: 05/04/2023

Study Title: Application of RECELL to Promote Healing Following CO2 Laser Treatment in Cosmetic Facelift Patients

Principal Investigator: Joseph Molnar, MD, PhD

Co-investigator(s): Ramon Llull, MD, PhD, Anthony DeFranzo, MD, Christopher Runyan, MD, Robert Siska, MD, Abby Peoples, BA, Caitrin Curtis, MD, Amelia Davidson, BS

Sponsor or funding source: Department of Plastic and Reconstructive Surgery, RECELL product provided by Avita Medical

Background, Rationale and Context

The RECELL system is a regenerative epidermal harvesting device that is currently FDA approved for use in treatment of partial thickness burns in adults. The system works by enzymatically processing a small sample of the patient's skin to create a regenerative epidermal suspension (RES) graft that can be sprayed onto a burn wound. Contained within the RES is a mix of keratinocytes, fibroblasts, and melanocytes.[1,2] The advantage of using the RECELL system over traditional skin grafting techniques is that, when enzymatically processed, donor tissue can be applied to re-epithelialize a significantly larger area than traditional skin grafting techniques. RES usually allows an 80:1 donor site to graft site expansion ratio.[3,4]

While RES has been most extensively used in burn treatment, it has also been used with success following CO2 laser resurfacing for the treatment of vitiligo and for enhanced healing following microdermabrasion.[5,6] A decade of precedent exists for treating patients with vitiligo through a combination of CO2 laser and regenerative epidermal suspension grafting with the goal of improved skin pigment after re-epithelialization.[7] A 2019 study assessed the healing time with and without RECELL application in 78 patients undergoing microdermabrasion for acne scare treatment. They study found a statistically significant decrease in healing time between the two groups, with the RECELL group (n = 48) healing in an average of 5.27 days and the group with microdermabrasion alone (n= 30) healing in an average of 12.3 days; healing time was defined as total epithelialization duration.[8]

With the safety and efficacy of RES demonstrated in multiple clinical contexts, our study aims to ascertain if RES can be used for cosmetic purposes to enhance healing following CO2 partial field ablation. CO2 laser resurfacing is often used as an adjunct treatment during facelift procedures to address signs of aging in the periorbital and perioral areas. The laser treatment works by a superficial layer of the skin, requiring complete reepithelialization of laser treated areas. This process results in significant post-operative erythema, pain, and downtime for the patient. During the facelift procedure, excess skin is removed and discarded. In our proposed study, this excess skin would be repurposed via processing with the RECELL system to be used as a regenerative epidermal suspension graft on CO2 laser treated areas. The excess skin removed on a facelift is a greater surface area than the required 2 x 3 skin graft that is required for the common 80:1 expansion used in burn surgery. Therefore, we should have significant amounts of excess skin that could be repurposed as a split thickness skin graft that can be used for the recell. There will not be any additional skin removed further than what is required for the

facelift. We will use an 0.008 inch Weck blade to repurpose the excess skin into a split thickness skin graft need for the recell.

Device Output Characterization
We do not have any plans for this.

Objectives
The primary objective and study endpoint will be safety. The number of skin reactions will be evaluated to measure the primary endpoint over the treated area vs placebo control.

Methods and Measures

Design
Randomized, Double Blind, Placebo Controlled

Setting
Atrium Health Wake Forest Baptist Department of Plastic and Reconstructive Surgery

Subjects selection criteria

- **Inclusion Criteria**
  Adults 22 years or older
  Patients undergoing facelift with perioral CO2 laser treatment
  Skin that is Fitzpatrick Score 1 or 2
  Subjects who are in general good health
  Subjects who fully understand the research nature of this study and sign the informed consent

- **Exclusion Criteria**
  Prior perioral CO2 laser resurfacing
  Allergy to components of preparation system
  Subjects who have cosmetic or surgical treatment in perioral area within 3 months before the study (including laser, chemical peels, fillers, botulinum toxin).
  Subjects with existing open wounds on the face
  Subjects with active cutaneous infection, acne, dermatitis or any active dermal disease on the face
  Subject with signs of hypersensitivity or inflammation on the face
  Subjects with known hypersensitivity to trypsin or compound sodium lactate solution (Hartmann's Solution)
  Subjects with known hypersensitivity to anesthetics, adrenaline/epinephrine, povidone-iodine, or chlorhexidine solutions.
  Subjects with any disease/condition that may affect wound healing such as diabetes or obesity
  Subjects with any bleeding disorder

Subjects with any existing malignancy
Subjects who are pregnant, breastfeeding, or whose urinary pregnancy test is positive before participation in the study
Subjects with any disease/condition deemed unsuitable for facelift surgery or RECELL treatment by the treating physician

- **Sample Size**
  10 patients

Interventions and Interactions

The perioral area of the face will be treated with CO2 laser. Laser setting will be determined by the treating surgeon for each individual patient. The laser is a Lumenis Ultrapulse/Surgitouch CO2 laser, 510(k) Number K030147. A laser (light amplification by stimulated emission of radiation) based device having coherence, collimated and typically monochromatic radiation. Typically indicated to cut, destroy, remove or coagulate tissue, generally soft tissue, for general surgical purpose in medical specialties of general and plastic surgery, dermatology/aesthetic, podiatry, otolaryngology (ent), gynecology, neurosurgery, orthopedics (soft tissue), dental and oral surgery, and dentistry. The classification regulation 21 cfr 878.4810 describes a device that is carbon dioxide or argon laser intended to cut, destroy, remove or coagulate tissue by the light. This laser is typically used in our practice for skin resurfacing to reduce the signs of aging, improve skin texture, laxity and tone, and reduce scars and stretch marks. Typical settings to be used for severe facial photoaging with Total FX is: Active FX, Energy (mj) 100-125, Scan Size 6-7 mm, Density 2-3, Hertz 100-200, Repeat Delay 0.3-1.5 seconds, number of passes 2. Deep FX, Energy (mj) 12.5-22.5, Scan Size 10 mm, Density 5-20%, Hertz 300-600, Repeat Delay 0.3-1.5 seconds, Number of Pulses 1-2, number of passes 1-2. The patient would be randomized and blinded to either left perioral or right perioral RECELL application. The surgeon would also be blinded to which side received RECELL treatment or Placebo (saline spray). Randomization would occur before study initiation with subjects assigned either left perioral or right perioral RECELL treatment based on their subject enrollment number. The study team member who prepares and blinds the RECELL will create the list of subject ID numbers with subject ID number randomly assigned to either left perioral or right perioral treatment group. This will be completed prior to any patient enrollment in the study. This spreadsheet will be password protected and only accessible to study coordinators and the team member responsible for preparing RECELL.

RECELL® is a single-use, stand-alone, battery-operated, regenerative epidermal harvesting device containing enzymatic and delivery solutions, sterile surgical instruments, and actuators. The cell suspension contains a mixed population of cells, including keratinocytes, fibroblasts, and melanocytes, obtained from the disaggregation of the skin sample. The Enzyme used to process the cells is a biological agent and as such may have slight variations in color and texture. The enzyme is derived from animal tissue and has undergone filtration and terminal sterilization by gamma irradiation.

Intraoperatively, RECELL and Placebo will be provided to surgeons and assistants in opaque application devices prepared by a trained, designated study team member.

Both the treatment and placebo sides, will be dressed with a standard regenerative epidermal suspension post treatment dressing (Telfa Clear and Xeroform). Xeroform will be removed on postoperative day 1. Telfa clear will be removed on postoperative day 7. Patients will return to clinic for follow up at the following interval:

- Post Operation Day 1
- Post Operation Day 7
- Post Operation Day 14
- 1-month Post Operation
- 2-months Post Operation
- 3-months Post Operation

There is always a chance the patient may need to be withdrawn from the study. The main consideration for stopping is the dressings, as the Recell will already be sprayed. If the patient cannot tolerate the dressings, we will stop and remove them from the study. Otherwise, we will deal with complications similar to how we would deal with other laser reactions- local wound care, anti-virals, etc.

Any signs of anaphylactic events will lead to the study stopped immediately and unbinding. We will immediately wash the cell suspension off of the face with 3 liters of normal saline (NS) while treating the anaphylaxis per institutional protocol (including submuscular epinephrine).

Any high incidence of serious adverse events (any serious adverse event, including severe infection requiring return to the operating room) will warrant early unbinding and assessment of safety immediately.

Subjects will be able to withdraw from the study for any reason and at any time. We can remove the cell suspension with removal of dressings and 3 liters of NS wash.

Outcome Measure(s)

Preoperatively patient baselines will be established with standardized studio photographs, and photos using the Quantificare LifeViz® Camera, as well as in person evaluation.

Intraoperatively, the patient will be photographed in CO2 treated areas with the Quantificare LifeViz® Camera and standardized photography. This camera measures lines, closing surfaces, volume, depth, and perimeter of the skin surface for microstructure analysis. We will analyze this data to track progress throughout the study.

Postoperatively, patients will be evaluated at each visit via in person evaluation by the surgeon, as well as using standardized photography, Quantificare LifeViz® Camera photos, administration of applicable FACE-Q scales (patient completed survey), and pain score (standard 1-10 pain scale). Please find FACE-Q scales in Appendices B-H.

Please find study calendar in Appendix A.

Analytical Plan

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using Fisher's exact tests for proportions, and t-tests or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

Collection of patient-identifying information will be limited to what is necessary to conduct analysis that is accurately linked to a given subject. Other than the master 'linkage' file, patient names, and medical record numbers will be removed and subjects will be associated with an abstracted unique Study ID. DOB will only be collected in order to dynamically calculate age at operative and follow up time points. Data will be stored electronically on the Wake Forest School of Medicine's secure REDCap server, a HIPAA-compliant web platform. Information for each subject will be entered directly from EPIC to the secure REDCap database, so data will not be stored on portable storage devices (including USB drives). In addition to study informed consent, photography consent will be obtained.

Subject Recruitment Methods

Patients who are scheduled to undergo elective facelift surgery with perioral CO2 laser resurfacing will be identified in the Plastic Surgery Clinics at both Janeway Tower and Vest Mill office locations. Any patient meeting inclusion criteria will be recruited during preoperative planning. Patients will have study information provided by a qualified study team member. There will be no compensation provided for this study, but the laser will be offered at no cost for participants.

Informed Consent

Informed consent will be obtained by approved study personnel after study purpose, duration, interventions, benefits and risks are thoroughly discussed with the subject. After the entire consent has been reviewed and all questions have been answered, potential subjects will be given the option to participate. A copy of the signed and dated consent form will be given to each enrolled subject and one placed on the chart. The original will be kept with research study records. In addition, a consent for photography and photograph use in research and publication will be obtained and placed in the chart prior to study participation. Please see a copy of Informed Consent in Appendix I.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to conduct outcomes research and related research to improve facelift and CO2 laser resurfacing outcomes. All database data will be entered into the Wake Forest School of Medicine's secure REDCap server. To help ensure subject privacy and confidentiality, a linkage file will be maintained containing each patient's medical record number and unique REDCap ID. Patient names will not be maintained in this file. The linkage file will be stored separately from the data available to researchers and will be kept secure, with access limited to designated study personnel. Data access will be limited to study staff. Data and records will be kept locked and secured, with any

computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study however patient photographs may appear in publications with patient consent.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Additional safety assessment will include a full medical history and physical before proceeding with study activities.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Adverse events would include the inability to tolerate dressings, deeper burns - including blistering burns or full-thickness burns - which would be managed with local wound care as we would manage any other burn in our burn center. We will record any viral outbreaks and any need for antivirals (such as HSV outbreaks from burn or recell). Given the fact that we are doing a controlled burn, the adverse outcome for "burns," will be blistering burn, signifying a deeper than expected burn from the laser.

We will assess for adverse events at each follow-up visit. Follow-up visits will include photography and assessment for adverse events.

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

We will report all adverse events to the FDA as described in 21 CFR 312.32**.**

Risk Analysis

Given that Recell is a product that speeds up wound healing, we do not anticipate that it will lengthen the wound healing course for the laser.

References

1. Hirobe T. Keratinocytes regulate the function of melanocytes. *Dermatologica Sin*. 2014;32(4):200-204. doi:10.1016/J.DSI.2014.05.002
2. Wood F, Giles N, Stevenson A, Rea S, Fear M. Characterisation of the cell suspension harvested from the dermal epidermal junction using a ReCell® kit. *Burns*. 2012;38(1):44-51. doi:10.1016/J.BURNS.2011.03.001
3. Holmes IV J, Molnar J, Carter J, et al. A Comparative Study of the ReCell® Device and Autologous Spit-Thickness Meshed Skin Graft in the Treatment of Acute Burn Injuries. *J Burn Care Res*. 2018;39(5):694-702. doi:10.1093/JBCR/IRY029
4. Holmes J, Molnar J, Shupp J, et al. Demonstration of the safety and effectiveness of the RECELL ® System combined with split-thickness meshed autografts for the reduction of donor skin to treat mixed-depth burn injuries. *Burns*. 2019;45(4):772-782. doi:10.1016/J.BURNS.2018.11.002
5. Lommerts JE, Meesters AA, Komen L, et al. Autologous cell suspension grafting in

segmental vitiligo and piebaldism: a randomized controlled trial comparing full surface and fractional CO2 laser recipient-site preparations. *Br J Dermatol*. 2017;177(5):1293-1298. doi:10.1111/bjd.15569
6. Ren J, Liu J, Yu N, et al. The use of noncultured regenerative epithelial suspension for improving skin color and scars: A report of 8 cases and review of the literature. *J Cosmet Dermatol*. 2019;18(5):1487-1494. doi:10.1111/jocd.13071
7. Van Geel N, Wallaeys E, Goh BK, De Mil M, Lambert J. Long-term results of noncultured epidermal cellular grafting in vitiligo, halo naevi, piebaldism and naevus depigmentosus. *Br J Dermatol*. 2010;163(6):1186-1193. doi:10.1111/j.1365-2133.2010.10014.x
8. Chen Q, Yu N, Liu Z, et al. The Clinical Efficacy of ReCell® Autologous Cell Regeneration Techniques Combined with Dermabrasion Treatment in Acne Scars. *Aesthetic Plast Surg*. 2020;44(2):535-542. doi:10.1007/s00266-019-01481-8

Appendix

A. Study Calendar
B. Preoperative Scale
C. FACE-Q POD 1 Scales
D. FACE-Q POD 7 Scales
E. FACE-Q POD 14 Scales
F. FACE-Q 1 Month Scales
G. FACE-Q 2 Month Scales
H. FACE-Q 3 Month Scales
I. Informed Consent – Created following final protocol approval
J. Photography Consent – standard departmental photography consent