Epidermal Harvesting
Automated, Minimally Invasive, and Autologous Epidermis
The challenges of achieving wound closure

Stalled and non-healing chronic wounds can present a number of challenges to both the patient and physician:

• Long and expensive procedures that require trained specialists in the OR
• Prolonged and costly recovery times for patients, with multiple follow-ups
• Loss of quality of life
• Amputation

These wounds are often the result of conditions such as diabetes, obesity, autoimmune and vascular disorders. Initiating the healing of these types of wounds is extremely difficult and can result in devastating consequences for the patient if not achieved.

Physicians have adopted a number of techniques in order to encourage successful closure of chronic wounds, among them:

• Topical agents
• Hyperbaric oxygen therapy
• Stem cell therapy
• Negative Pressure Wound Therapy (NPWT)
• Autografts

Full-thickness and split-thickness autografts are invasive methods that harvest epidermis and dermis, creating a new wound that can result in donor site pain, infection, scarring and morbidity.

Epidermal Skin Grafts (ESGs) offer an alternative to invasive autografting methods (such as split-thickness skin grafts), harvesting only epidermis from the donor site, and providing a minimally invasive treatment option to achieve closure.
A historical view of epidermal skin grafting for patients with non-healing wounds

Yamaguchi et al.¹ (2004) compared epidermal sheets obtained from suction blisters and standard local wound care (debridement, bed rest, special cast, and antibiotics) for treating intractable Diabetic Foot Ulcers (DFUs).

38-patient study
• 18 patients without exposed bone
• 20 patients with exposed bone

Key results
• Patients with DFUs without exposed bone who received epidermal grafts had significantly shorter healing times compared to patients who received standard therapy (4.3 ± 0.6 weeks vs 11.6 ± 3.4 weeks, respectively; p=0.042)
• Patients with DFUs with exposed bone who received epidermal grafts did not require any amputations (0/11) compared to 8/9 patients with standard therapy (p<0.0001)

Costanzo et al.² (2008) investigated the use of autologous suction blister grafting for chronic leg ulcers.

18-patient study
• with 29 chronic, non-healing leg ulcers

Key results
• 2-6 weeks post graft, 55% of the ulcers achieved complete healing
• 12 weeks post graft, the overall healing rate was 89%
• Most ulcers demonstrated a stimulation of reepithelialization from the wound edge and increased healthy granulation tissue formation after application of the epidermal grafts
• The authors concluded that autologous epidermal grafting is a viable treatment for chronic leg ulcers

Conclusion
In these and other studies, epidermal grafting using a suction blister harvesting technique has been shown to be a viable option for the management of chronic wounds.

Amputations in patients with exposed bone DFUs

0/11
patients receiving epidermal grafts

vs.

8/9
patients receiving standard therapy

55%
of the ulcers achieved complete healing at 2-6 weeks post graft

89%
of the ulcers achieved complete healing at 12 weeks post graft
The science behind epidermal skin grafting

The advantages of epidermal skin grafting

ESG differs from full-thickness and split-thickness skin grafts in that they contain the epidermal layer of the skin, which includes all epidermal cells which have the potential to contain basal layer keratinocytes. These cells play a fundamental role in reepithelialization and wound healing. Also present are melanocytes, which produce melanin which is responsible for repigmentation of new skin.

The development and advancement of suction blister epidermal grafting technology adopted by the CELLUTOME™ Epidermal Harvesting System, has been shown in a healthy human study of 15 patients to isolate both keratinocytes and melanocytes within the microdomes (i.e. blisters), keeping the cellular structure of the epidermis intact and therefore viable for transplant.
In a healthy human study of 15 subjects, it was shown that microdomes contain viable proliferative cells with the potential to migrate and grow out to achieve reepithelialization and repigmentation. Basal keratinocytes begin to cover the wound by repopulating the areas between the microdomes.

The technology of the CELLUTOME™ System splits the dermal-epidermal junction to form microdomes, which are harvested into epidermal micrografts. These micrografts consist of undamaged epithelium with keratinocytes and melanocytes.

Growth factor secretion
Active secretion of growth factors by epidermal grafts is essential to promote the reepithelialization process by further stimulating the wound bed and keratinocyte proliferation and migration.
Epidermal skin grafting mechanism of action

Week 1-2
When the wound bed has been properly prepared and is free of necrotic tissue or infection, coverage of the wound by a superficial layer of keratinocytes may be nearing completion by the end of the first week. However, when the first wound dressing is removed, these cellular developments are microscopic and may not be visually apparent.

Week 2
Through the second week, keratinocytes should continue to proliferate and differentiate, expanding the graft to completely cover the wound area. However, this basal layer may not become visible until later stages of epidermal maturation.

Week 0-1
When the wound bed has been properly prepared and is free of necrotic tissue or infection, coverage of the wound by a superficial layer of keratinocytes may be nearing completion by the end of the first week. However, when the first wound dressing is removed, these cellular developments are microscopic and may not be visually apparent.

Week 2
Through the second week, keratinocytes should continue to proliferate and differentiate, expanding the graft to completely cover the wound area. However, this basal layer may not become visible until later stages of epidermal maturation.

Appropriate preparation of the wound bed prior to grafting is essential to healing progression.

Individual results may vary depending on the patient’s circumstances and condition.
Week 3

Patches of epidermis may finally be observed across the wound after three weeks. Epithelial maturation may continue, and white patches of epidermis become increasingly visible as the grafts expand and thicken. Melanocytes within the epidermis should initiate skin repigmentation through the production of melanin, and skin tone patches begin to appear across the wound.

Week 4+

Depending on patient comorbidities, complete epithelial differentiation between grafts should have occurred, and full reepithelialization is visible.
The advantages of epidermal skin grafting

From a 15-patient healthy human study using CELLUTOME™ System

Key growth factors for reepithelialization
Analysis of secreted growth factors showed all epidermal microdomes contained proliferative cells capable of secreting critical growth factors important for modulating the wound healing response.
Growth factor levels were observed to continue to increase over time, reaching a threshold at Day 3 and then remaining constant until Day 7. Each microdome array secreted growth factors important for reepithelialization including: VEGF, TGF-β, PDGF AA, PDGF AB/BB, HGF and G-CSF.

Analysis of secreted growth factors in vitro

<table>
<thead>
<tr>
<th></th>
<th>Microdome (24 hr)</th>
<th>Microdome (48 hr)</th>
<th>Microdome (72 hr)</th>
<th>Microdome (7 days)</th>
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</thead>
<tbody>
<tr>
<td><strong>EGF</strong></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td><strong>FGF-2</strong></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TGF-β</td>
<td>+</td>
<td>+</td>
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<tr>
<td>G-CSF</td>
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<tr>
<td>PDGF-AA</td>
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<tr>
<td>PDGF-AB/BB</td>
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<td>HGF</td>
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<tr>
<td>VEGF</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>

* The signal to noise ratio for EGF was greater than 1; therefore, results for EGF were not valid.
** The signal for FGF-2 was not detectable in the positive control, HEK; therefore, the results for this analyte were not valid.

Proven reproducibility

All harvested epidermal micrografts exhibited:
- Uniform undamaged cells
- Micrograft formation at dermal-epidermal junction
- Cell outgrowth and secretion of growth factors

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Proportion of undamaged tissue

![Proportion of undamaged tissue graph](image)

- 99.5%

* 12 subjects
Minimal impact on patient experience

The impact of the epidermal harvesting procedure was measured in a study involving 15 healthy human subjects.

Fast donor-site recovery:
- Minimal pain and donor-site trauma, with no need for anesthesia
- Donor site heals within 2–4 weeks

Donor-site case studies

In a study of 15 healthy human subjects, donor sites were completely healed within 2–4 weeks.

Donorsite dermal response score

7 Strong reaction
6 Vesicular eruption
5 Erythema, edema, papules
4 Definite edema
3 Erythema and papules
2 Definite erythema, readily visible
1 Minimal erythema, barely perceptible
0 No evidence of irritation

The featured case studies are representative of the average progression of healing for the study. As with any case study, the results and outcomes should not be interpreted as a guarantee or warranty of similar results. Individual results may vary depending on the patient’s circumstances and condition.
Step-by-step
CELLUTOME™ Epidermal Harvesting

**Step 1: Patient/Wound assessment**
Begin with a thorough assessment of the patient and wound to assure comorbidities are addressed and patient has the requisite ability to heal. Established wound bed preparation and standard care treatment protocols for wounds are recommended to initially prepare the wound bed.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Wound</th>
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<tbody>
<tr>
<td>Age</td>
<td>Exposed structures</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Perfusion</td>
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<tr>
<td>Medications</td>
<td>Contamination/infection</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Necrotic/devitalized tissue</td>
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<tr>
<td>Smoking</td>
<td>Wound duration</td>
</tr>
<tr>
<td>Social support network</td>
<td>Etiology</td>
</tr>
<tr>
<td></td>
<td>Location</td>
</tr>
<tr>
<td></td>
<td>Size</td>
</tr>
<tr>
<td></td>
<td>Tissue types</td>
</tr>
<tr>
<td></td>
<td>Drainage</td>
</tr>
</tbody>
</table>

**Step 2: Harvesting & application**
No pretreatment is required at the donor site. The donor site may be warmed and/or moistened prior to applying the CELLUTOME™ System.

**Donor site prep (1-2 minutes)**
**CELLUTOME™ Harvester placement (1-2 minutes)**
**Press RUN (1 minute)**
**Blister assessment (at 30 minutes)**

This is an ideal time to prep the wound to ensure it is completely clean. Transfer the harvested microdomes using ADAPTIC TOUCH™ Non-Adhering Silicone Dressing.

**Step 3: Follow-up**
For at least 1 week, ESGs should not be disturbed in any way and the non-adhering silicone dressing should not be removed, although secondary dressings can be changed within 1 week, if needed.

**7 days**
**14 days**

At the first few weekly dressing changes, debridement should not be performed, unless there is any negative change in the wound bed appearance, such as excessive maceration, infection or necrosis.

This is an overview only. For complete safety information and instructions for use, see CELLUTOME™ Epidermal Harvesting System Instructions for Use.
Given its thinness, graft proliferation may occur, but may not be visible for up to 3 weeks after application.

**Criteria for a graftable wound bed**
- Adequate granulation tissue formation to support living cell therapy
- Controlled drainage
- Controlled bioburden
- Shallow wound bed free of surrounding infection and necrotic tissue

**Secondary dressings**
- Compression and bolstering materials
- Compression wraps
- Offloading devices such as total contact casting (depending on the wound etiology and location)

NPWT can also be used to improve graft/wound bed contact.

**Graft acquisition** (2-3 minutes)
**Graft application** (2-3 minutes)
**Recipient/donor site bandaging** (2-4 minutes)

To create double-density ESGs, cut the transfer dressing and reorient it over the harvest, so that all microdomes are on the dressing, which can then be applied over the wound.

Secondary dressings can, and should, be used over the wound after application of ESGs to protect the grafts.

**Wound Prep Strategy**
- Delayed 1st intention

The use of NPWT and other active therapies may be used to prepare the wound bed.

**Debridement** (Initial triage, or diagnostic)

**Step-by-step approach to using CELLUTOME™ Epidermal Harvesting System to harvest epidermal grafts**

use, see CELLUTOME™ Epidermal Harvesting System Instructions for Use.
The CELLUTOME™ Epidermal Harvesting System

CELLUTOME™ Harvester
- Disposable
- Single-patient use
- Provides structure for formation of microdomes

CELLUTOME™ Control Unit
- Reusable
- Creates and regulates suction (negative pressure: -400 to -500mmHg) and warming (37°C to 41°C) required to raise epidermal microdomes

CELLUTOME™ Vacuum Head
- Reusable
- Delivers negative pressure and warming from CELLUTOME™ Control Unit to CELLUTOME™ Harvester

ADAPTIC TOUCH™ Non-Adhering Silicone Dressing
- Used to capture microdomes prior to cutting and transfer micrografts to recipient site
- Aids in maintaining proper graft orientation
- Non-adhering
- Wide-meshed to allow drainage

KERRAFOAM™ Gentle Border
KERRAFOAM™ Gentle Border to cover donor site
Our technology

CELLUTOME™ System technology helps with the formation of microdomes through an automated process of gentle suction and heat at the donor site to create a viable epidermal micrograft over a period of approximately 30-40 minutes.

A dressing is used to transfer the epidermal micrograft to the recipient site from the donor site.
Bring the benefits of epidermal harvesting to your patients and practice

- Automated, precise and reproducible process
- Minimally invasive procedure with an average harvesting time of 45 minutes
- Can be performed in the office/outpatient setting
- Does not require anesthesia
- Minimal patient discomfort with procedure
- Minimal scarring at donor site
- Operation technique and postoperative care are simplified and convenient
- Cost-effective alternative to skin substitutes
- Easy to integrate into existing clinical practice
- Comprehensive training from an Acelity representative in less than one hour
- Can be performed by any suitably trained physician
**CELLUTOME™ Epidermal Harvesting System Ordering Information**

<table>
<thead>
<tr>
<th>Item</th>
<th>Part Number</th>
<th>Unit of Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>CELLUTOME™ System Kit</td>
<td>CT-KIT</td>
<td>Each</td>
</tr>
<tr>
<td>(Control Unit and Vacuum Head)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0cm x 5.0cm Harvester</td>
<td>CT-H50</td>
<td>Case of 5</td>
</tr>
<tr>
<td>2.5cm x 2.5cm Harvester</td>
<td>CT-H25</td>
<td>Case of 5</td>
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</table>
Reference:


NOTE: Specific indications, contraindications, warnings, precautions and safety information exist for KCI products and therapies. Before use, physicians must review all risk information and essential prescribing information which can be found in the CELLUTOME™ Epidermal Harvesting System Instructions for Use. This material is intended for healthcare professionals.

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