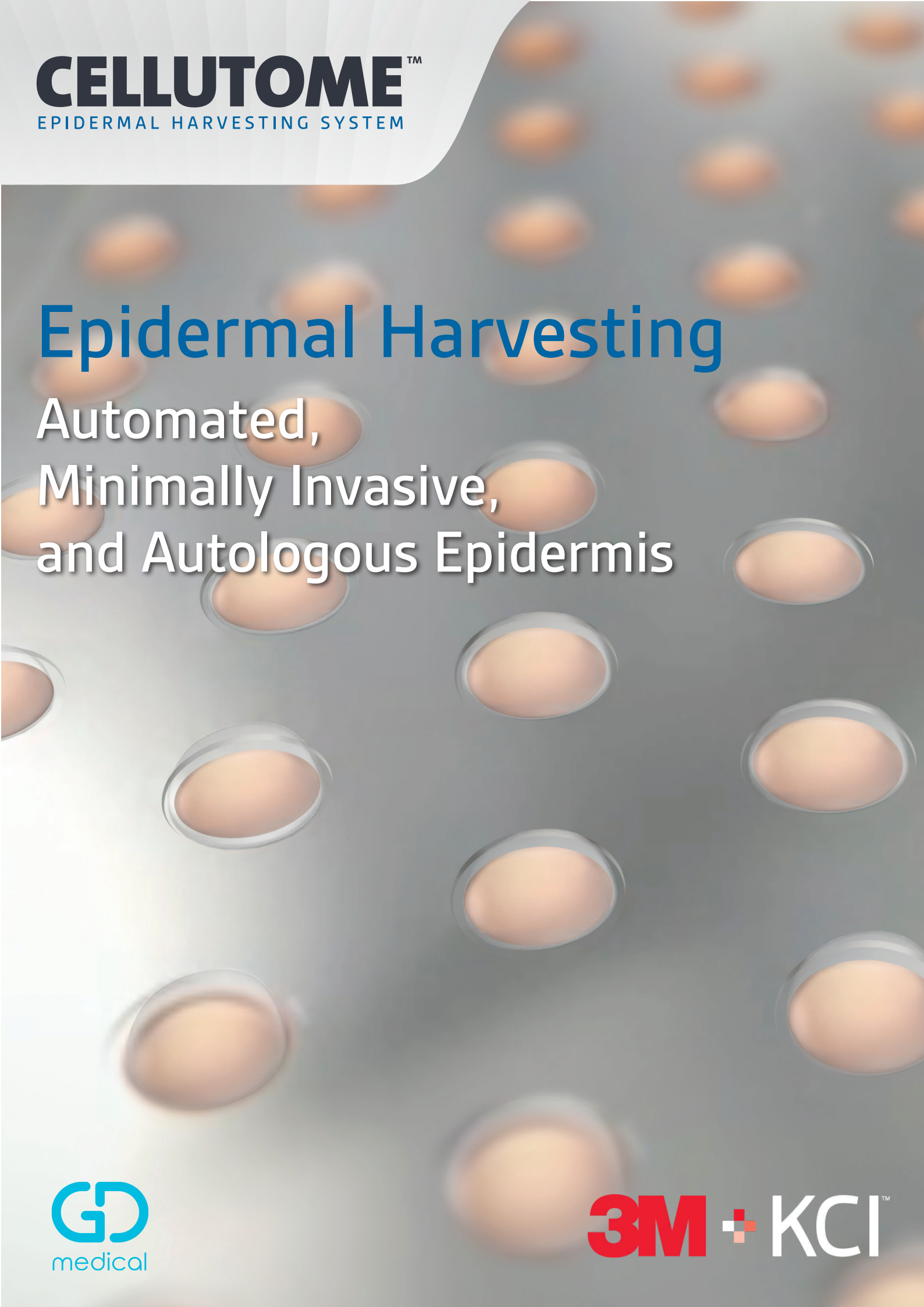
CELLUTOME™
EPIDERMAL HARVESTING SYSTEM

Epidermal Harvesting

Automated, Minimally Invasive, and Autologous Epidermis



GD medical

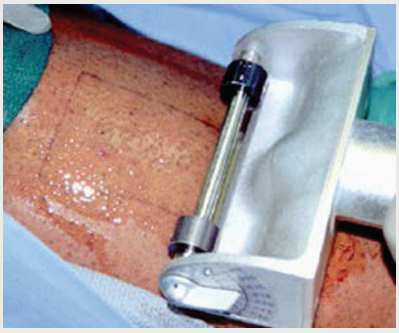
3M + KCI™

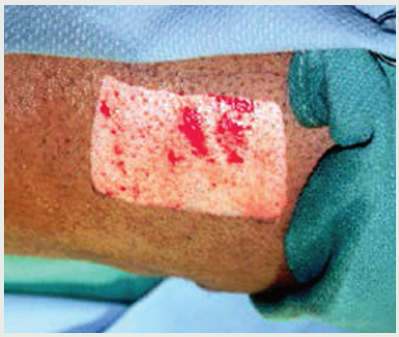
The challenges of achieving wound closure

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.



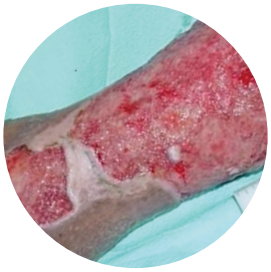


Physicians have adopted a number of techniques in order to encourage successful closure of chronic wounds, among them:

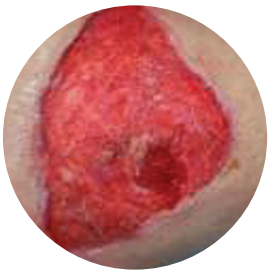
- Topical agents
- Hyperbaric oxygen therapy
- Stem cell therapy
- Negative Pressure Wound Therapy (NPWT)
- Autografts

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.

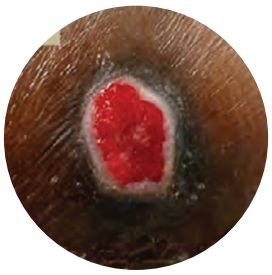
Wound types



Venous leg ulcer



Diabetic foot ulcer



Foot I&D abscess

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)

Amputations in patients with exposed bone DFUs

0/11

patients receiving epidermal grafts

vs.

8/9

patients receiving standard therapy

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

18-patient study

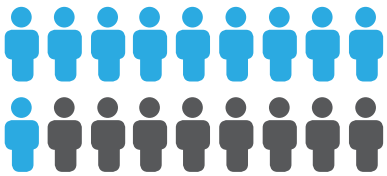
- with 29 chronic, non-healing leg ulcers

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

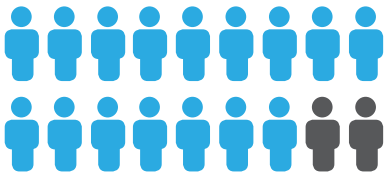
55%

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



89%

of the ulcers achieved complete healing at 12 weeks post graft



Conclusion

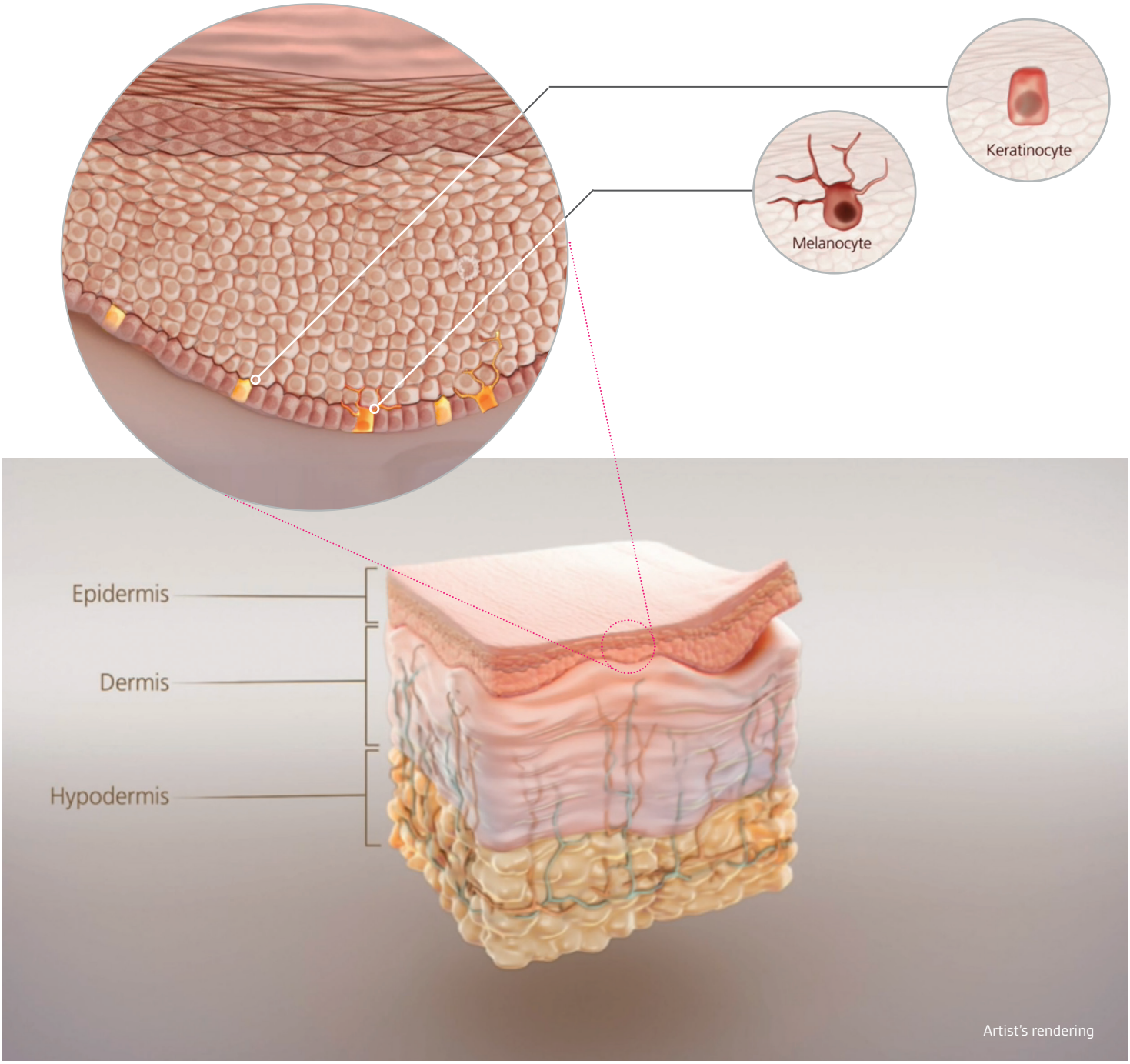
In these and other studies, epidermal grafting using a suction blister harvesting technique has been shown to be a viable option for the management of chronic wounds.

The science behind epidermal skin grafting

The advantages of epidermal skin grafting

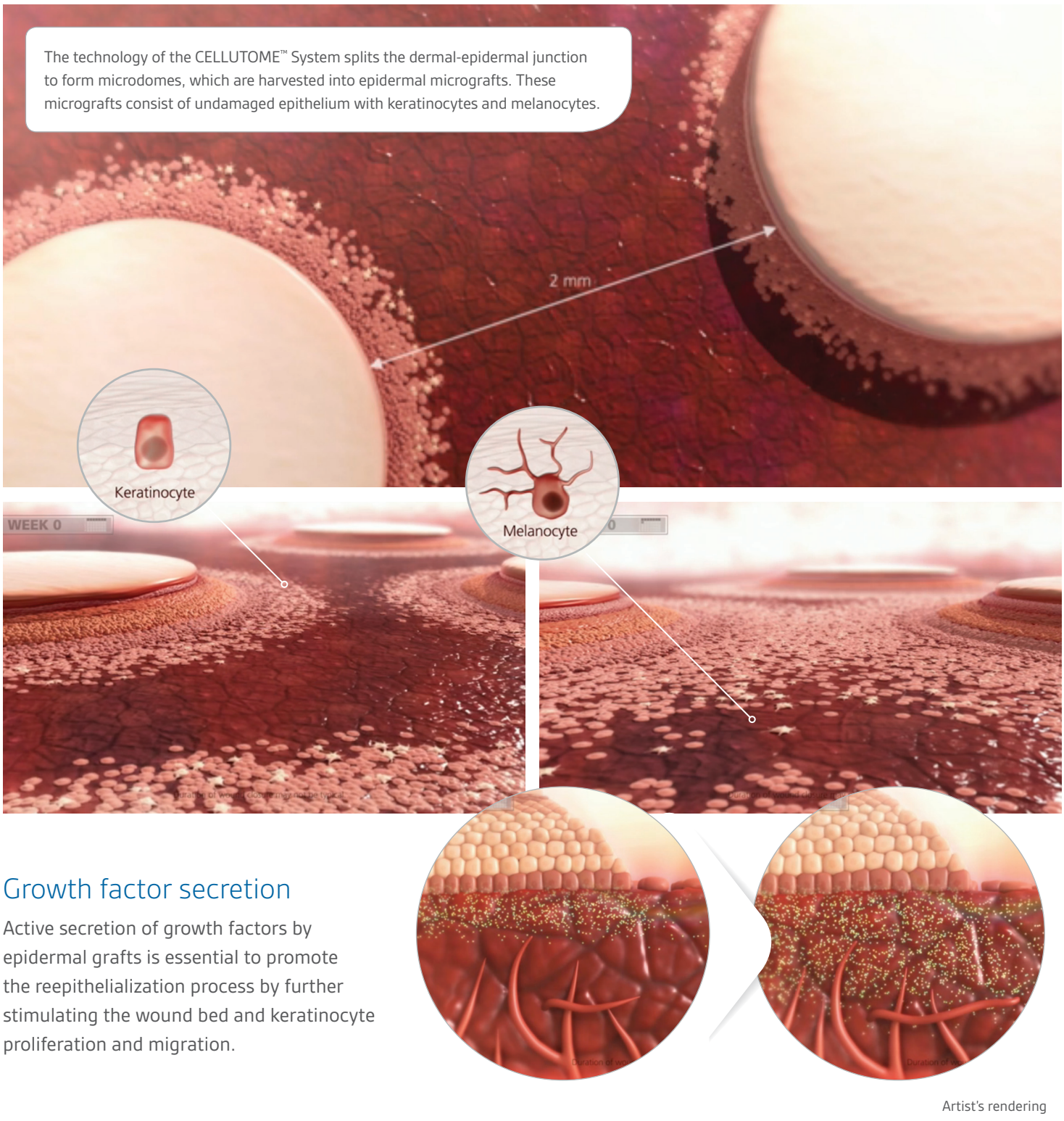
ESG differs from full-thickness and split-thickness skin grafts in that they contain the epidermal layer of the skin, which includes all epidermal cells which have the potential to contain basal layer **keratinocytes**. These cells play a fundamental role in **reepithelialization** and **wound healing**. 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.[3]

Basal keratinocytes begin to cover the wound by repopulating the areas between the microdomes.



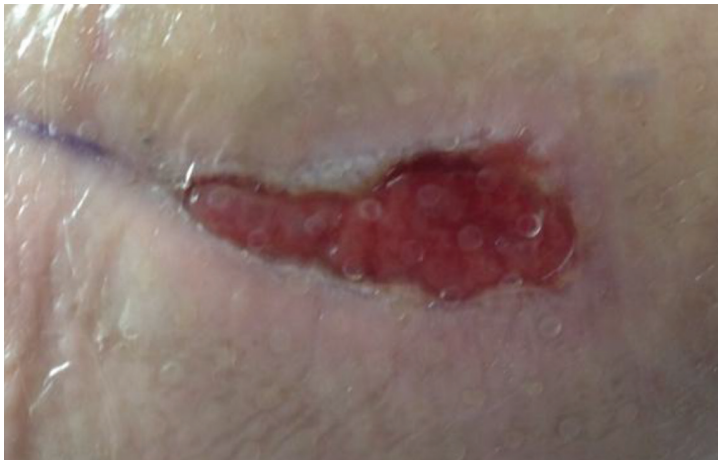
Growth factor secretion

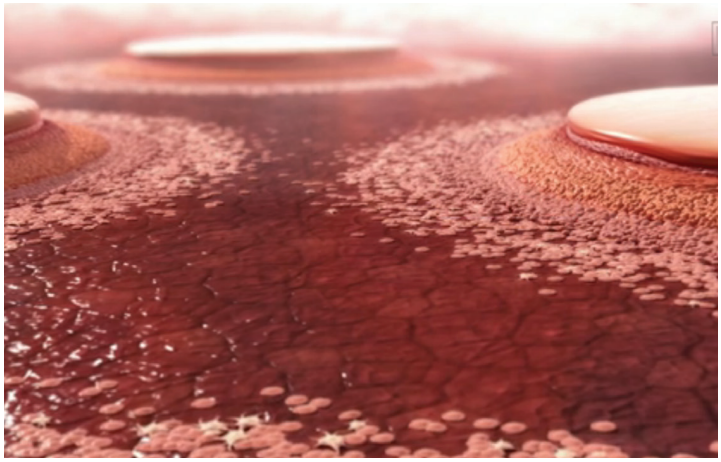
Active secretion of growth factors by epidermal grafts is essential to promote the reepithelialization process by further stimulating the wound bed and keratinocyte proliferation and migration.

Artist's rendering

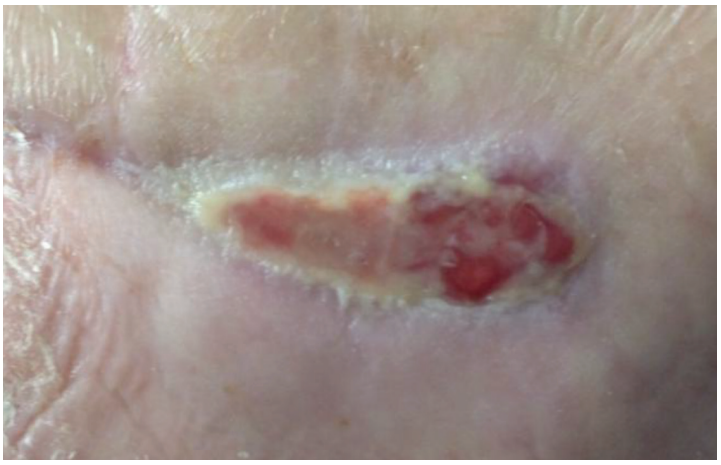
Epidermal skin grafting mechanism of action

Week 1-2





Week 2-3



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.

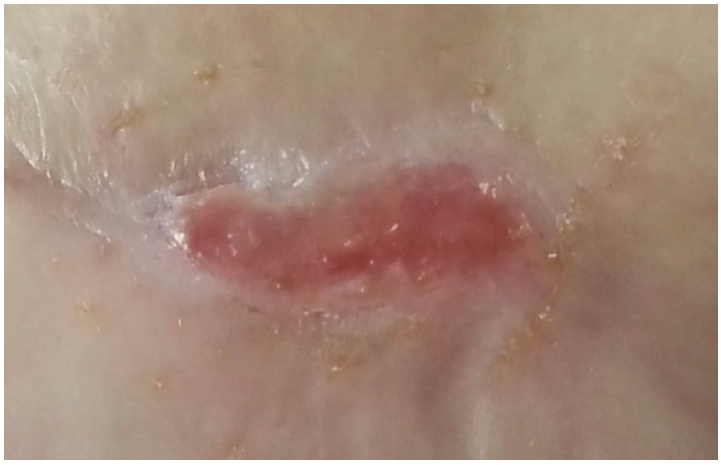
Week 2

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.

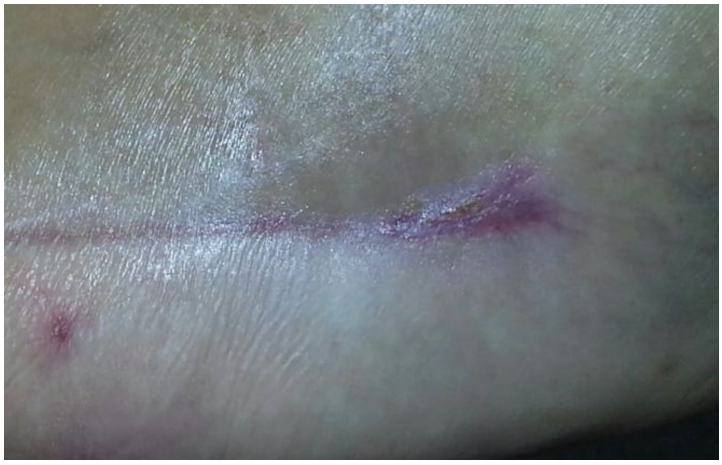
Appropriate preparation of the wound bed prior to grafting is essential to healing progression.

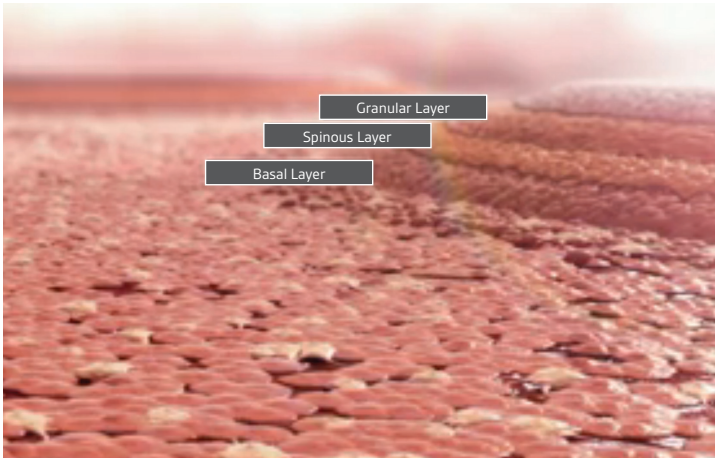
Individual results may vary depending on the patient's circumstances and condition.

Week 3-4



Week 5





Artist's rendering

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-∂, PDGF AA, PDGF AB/BB, HGF and G-CSF.

Analysis of secreted growth factors *in vitro*

	Microdome (24 hr)	Microdome (48 hr)	Microdome (72 hr)	Microdome (7 days)
*EGF	–	–	–	–
**FGF-2	–	–	–	–
TGF-∂	+	+	+	+
G-CSF	+	+	+	+
PDGF-AA	+	+	+	+
PDGF-AB/BB	+	+	+	+
HGF	+	+	+	+
VEGF	+	+	+	+

* The signal to noise ratio for EGF was greater than 1; therefore, results for EGF were not valid.

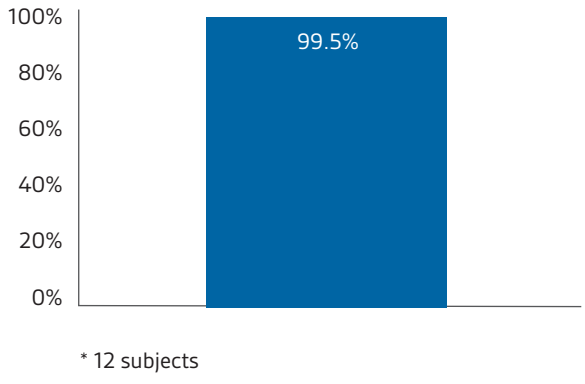
** The signal for FGF-2 was not detectable in the positive control, HEK; therefore, the results for this analyte were not valid.

Proven reproducibility

All harvested epidermal micrografts exhibited:

- Uniform undamaged cells[4]
- Micrograft formation at dermal-epidermal junction[4]
- Cell outgrowth and secretion of growth factors[4]

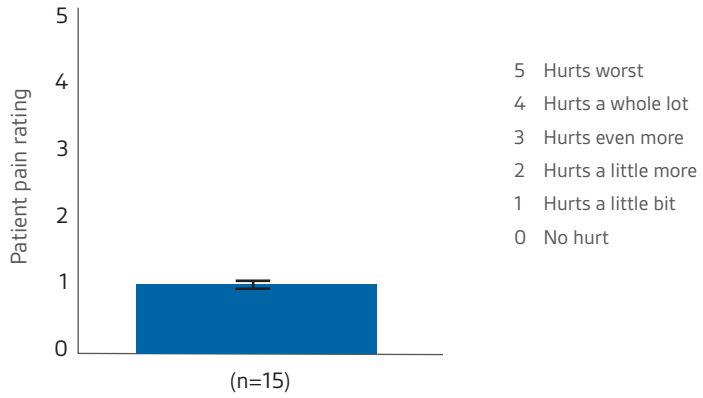
Proportion of undamaged tissue[4,*]



Minimal impact on patient experience

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

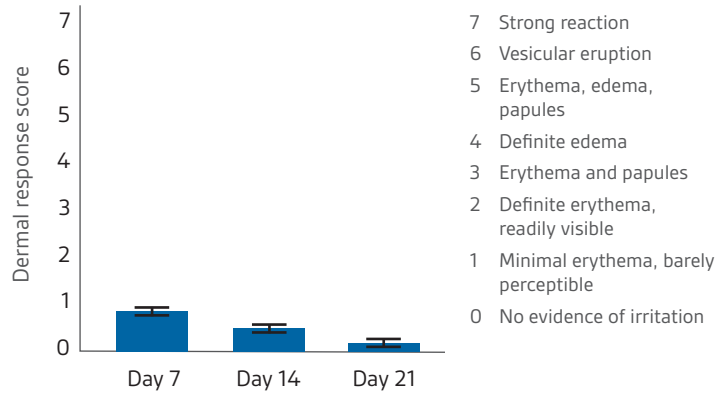
Patients undergoing epidermal harvesting experienced minimal pain[4]



Fast donor-site recovery:

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

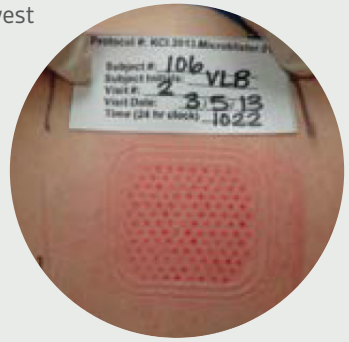
Donor-site dermal response score[4]



Donor-site case studies‡

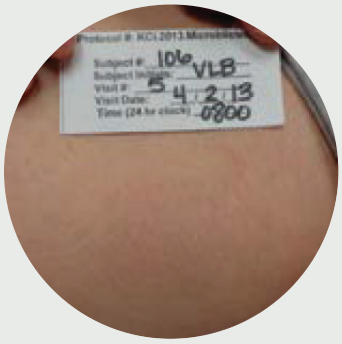
In a study of 15 healthy human subjects, donor sites were completely healed within 2–4 weeks.

At harvest



14 days

21 days

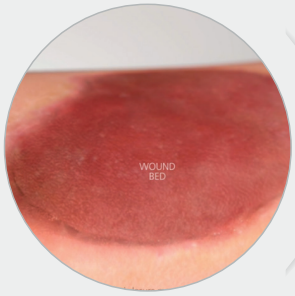


‡The featured case studies are representative of the average progression of healing for the study. As with any case study, the results and outcomes should not be interpreted as a guarantee or warranty of similar results. Individual results may vary depending on the patient's circumstances and condition.

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.



Patient

- Age
- Nutrition
- Medications
- Comorbidities
- Smoking
- Social support network

Wound

- Exposed structures
- Perfusion
- Contamination/infection
- Necrotic/devitalized tissue
- Wound duration
- Etiology
- Location
- Size
- Tissue types
- Drainage

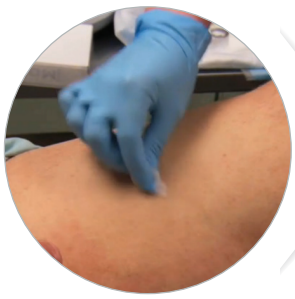
Begin ongoing patient optimization

Step 2: Harvesting & application

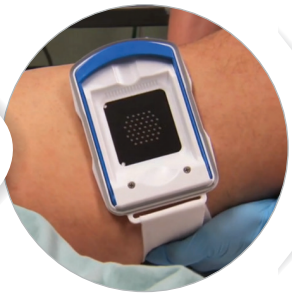
No pretreatment is required at the donor site. The donor site may be warmed and/or moistened prior to applying the CELLUTOME™ System.

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

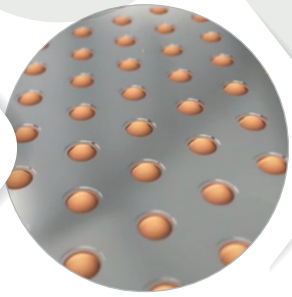


Donor site prep (1-2 minutes)



CELLUTOME™ Harvester placement (1-2 minutes)

Press RUN (1 minute)

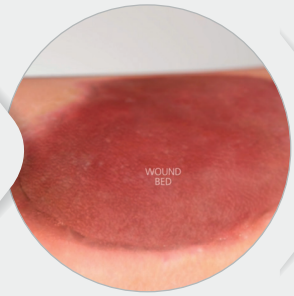


Blister assessment (at 30 minutes)

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



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.

14 days

Artist's rendering

This is an overview only. For complete safety information and instructions for

approach to using System to harvest epidermal grafts[5]

Debridement
(Initial triage, or diagnostic)

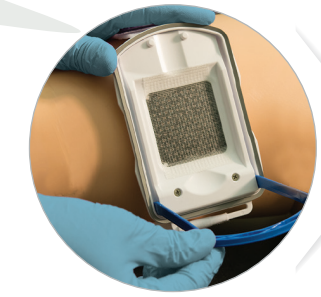
Wound Prep Strategy
Delayed 1° intention

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

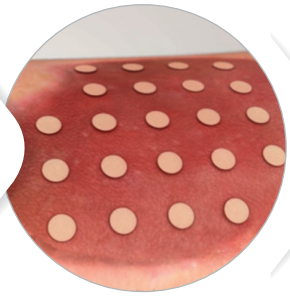
Criteria for a graftable wound bed

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

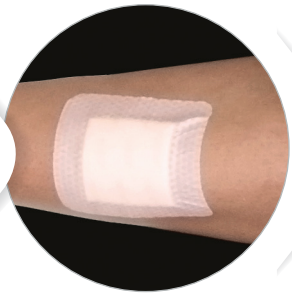
To create double-density ESGs, cut the transfer dressing and reorient it over the harvest, so that all microdomes are on the dressing, which can then be applied over the wound.



Graft acquisition
(2-3 minutes)



Graft application
(2-3 minutes)



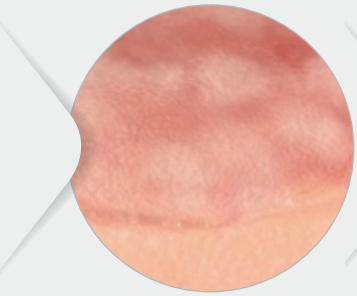
Recipient/donor site bandaging
(2-4 minutes)

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

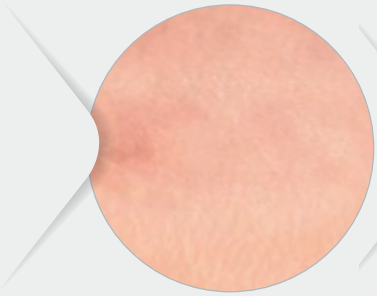
Secondary dressings

- 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.



21 days



Given its thinness, graft proliferation may occur, but may not be visible for up to 3 weeks after application.

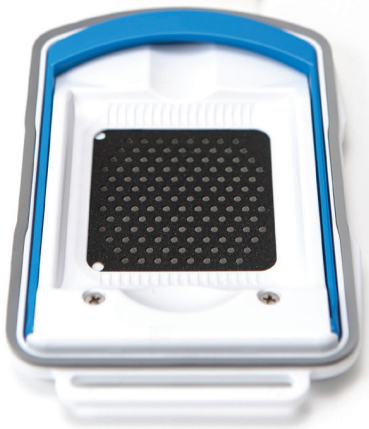
Artist's rendering

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



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

CELLUTOME™ Control Unit

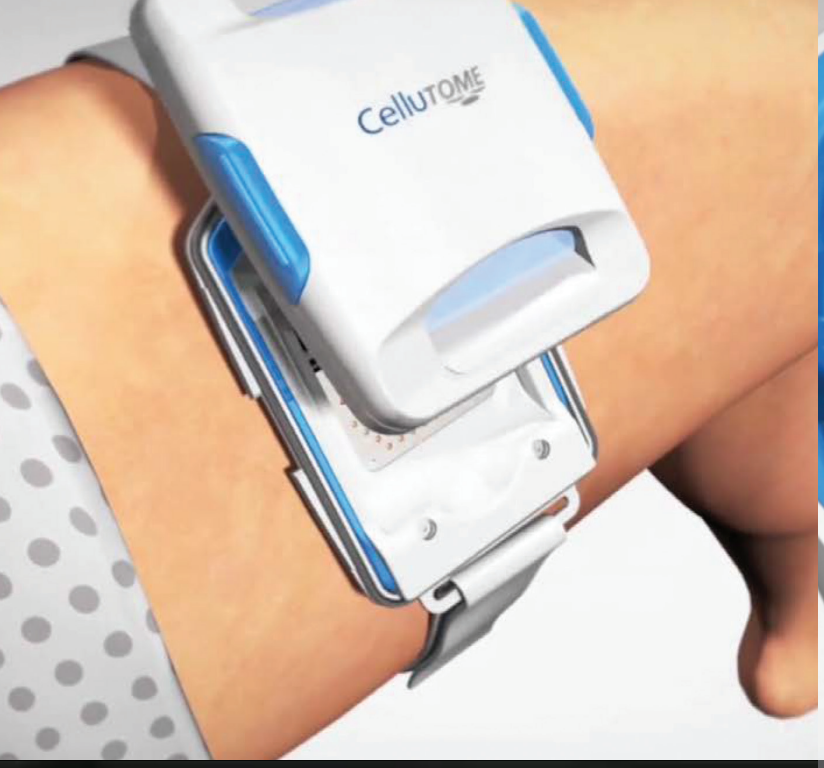
- Reusable
- Creates and regulates suction (negative pressure: -400 to -500mmHg) and warming (37°C to 41°C) required to raise epidermal microdomes

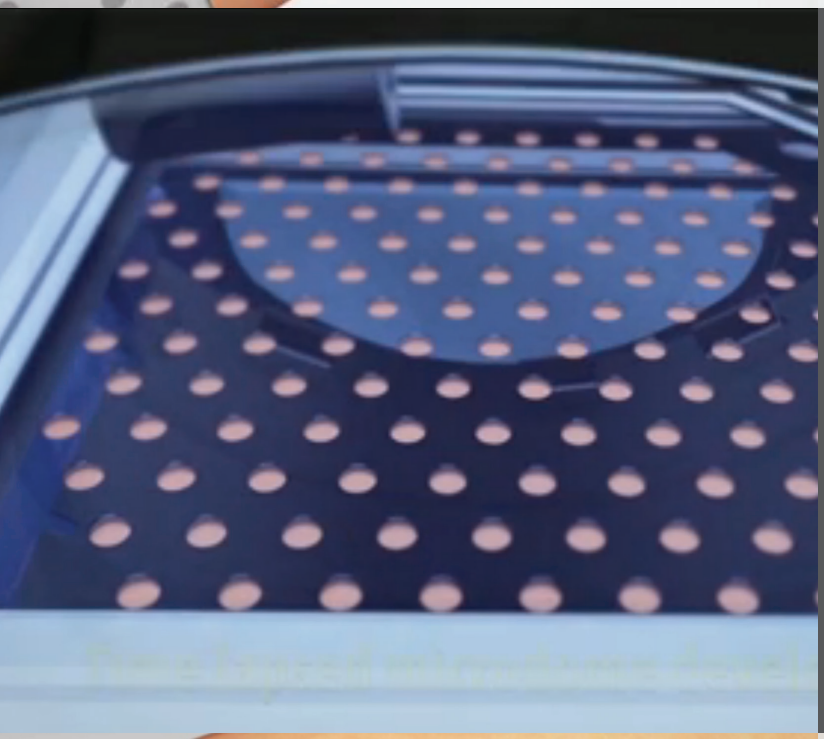
KERRAFOAM™ Gentle Border

KERRAFOAM™ Gentle Border to cover donor site

CELLUTOME™ Vacuum Head

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

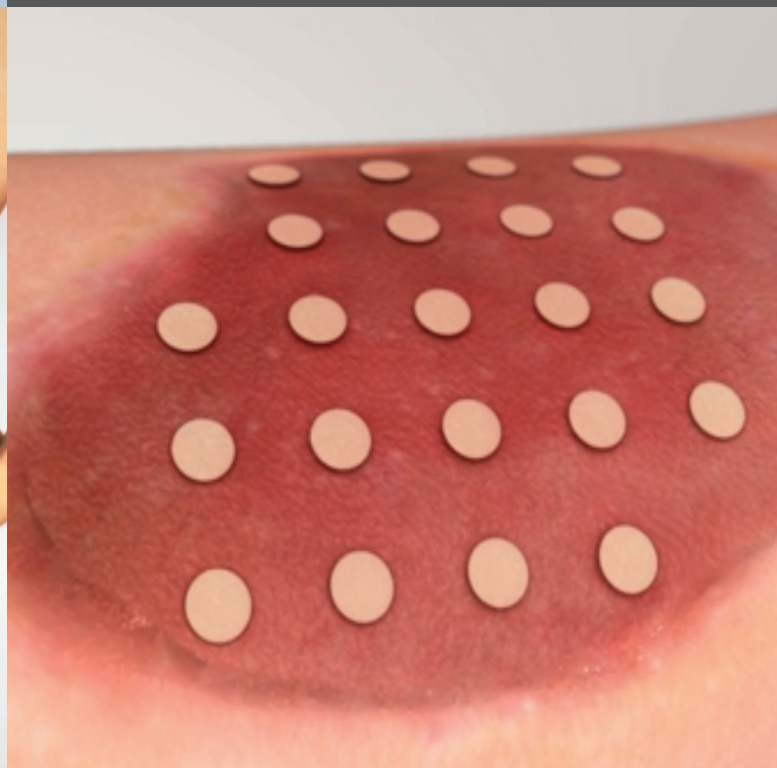




Our technology

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

Item	Part Number	Unit of Measure
CELLUTOME™ System Kit (Control Unit and Vacuum Head)	CT-KIT	Each
5.0cm x 5.0cm Harvester	CT-H50	Case of 5
2.5cm x 2.5cm Harvester	CT-H25	Case of 5

CELLUTOME™
EPIDERMAL HARVESTING SYSTEM

Reference:

1. Yamaguchi Y, Yoshida S, Sumikawa Y et al. Rapid healing of intractable diabetic foot ulcers with exposed bones following a novel therapy of exposing bone marrow cells and then grafting epidermal sheets. *Br J Dermatol.* 2004 November 1;151(5):1019-1028.
2. Costanzo U, Streit M, Braathen LR. Autologous suction blister grafting for chronic leg ulcers. *J Eur Acad Dermatol Venereol* 2008 January 1;22(1):7-10.
3. Osborne SN, Schmidt MA, Harper JR. An Automated and Minimally Invasive Tool for Generating Autologous Viable Epidermal Micrografts. *Advances in Skin and Wound Care*. February 2016;29(2):57-64.
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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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