



INTRODUCING RECELL® INTO CLINICAL PRACTICE

# TREAT EARLY IN DEEP PARTIAL-THICKNESS *AND* FULL-THICKNESS BURNS

## Introduction

Burn injuries account for approximately 1% of the non-fatal injuries in the United States each year, which translates to nearly 500,000 patients annually requiring medical care for burns.<sup>1</sup> Approximately 10% of these cases require hospitalization.<sup>2</sup> Although mortality associated with burns has dramatically decreased, largely due to changes in patient and burn characteristics and advancements in burn care, the complex management of burn injuries can lead to prolonged hospital stays, heavy resource utilization, and patient morbidity.<sup>2,3</sup>

Treatment of burn wounds is a complex process and presents several challenges to the burn team. The standard of care for deep-partial-thickness and full-thickness burn wounds is autologous split-thickness skin grafts which has significant

drawbacks. These can lead to increased hospital length of stay for the patient.

Burn management has evolved over time, with new technologies and treatment paradigms resulting in improved outcomes.<sup>3</sup> These technologies have included cultured epithelial autografts, skin cell suspensions, and dermal substitutes.<sup>4</sup> Data with one such technology, the RECELL Autologous Cell Harvesting Device, are presented here.

The FDA approved RECELL Device used to prepare Spray-On Skin™ Cells, addresses many challenges in burn care by providing a point-of-care technology for early treatment and discharge of patients with small and large total body surface area (TBSA) partial and full-thickness burns.<sup>3</sup>

Please see inside back cover for full Important Safety Information.

## RECELL® – Delivers Spray-On Skin™ Cells

The RECELL Device is an FDA-approved technology that allows preparation of an autologous suspension of Spray-On Skin™ Cells at the point-of-care for treatment of acute thermal burn injuries, with every 1 cm<sup>2</sup> of donor skin yielding a suspension that covers up to 80 cm<sup>2</sup> of treatment area.<sup>4</sup> RECELL is indicated as a primary intervention for deep partial-thickness burns with confluent dermis, or in conjunction with widely meshed skin grafts for mixed-depth and full-thickness burns (Figure 1). Preclinical data demonstrated that the suspension includes a mixed population of skin cells, including sub-populations of

keratinocytes including basal keratinocytes, suprabasal keratinocytes and activated keratinocytes, critical for regeneration of the epidermis, fibroblasts, and melanocytes<sup>5</sup> (Figure 2). A small, thin split-thickness skin sample is incubated with a proprietary enzyme solution that promotes the breakdown of adhesions between the cells of the epidermis and the adjacent extracellular matrix. The skin sample is mechanically manipulated to disaggregate the cells, which are filtered, drawn into a syringe, and sprayed over the burn wound.<sup>6</sup> The process can be completed in as little as 30 minutes.<sup>4,6</sup>

Figure 1. Treatment of DPT Burns With Spray-On Skin Cells

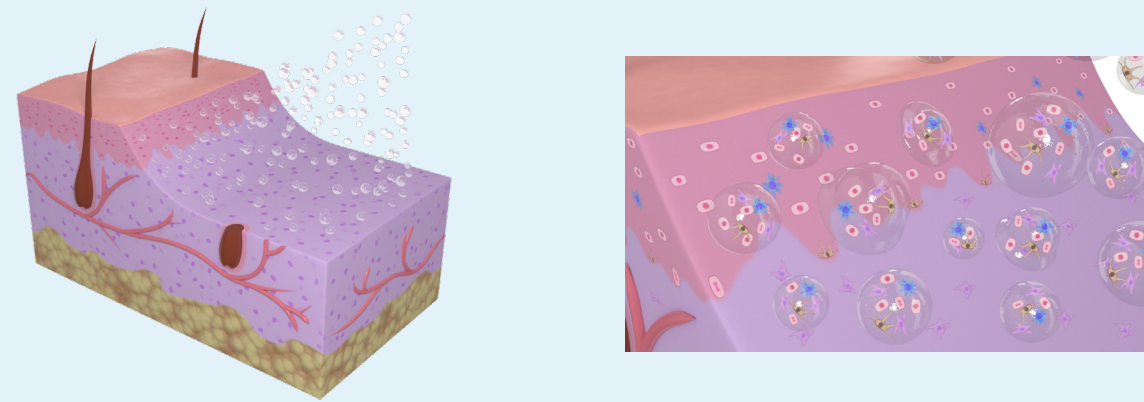
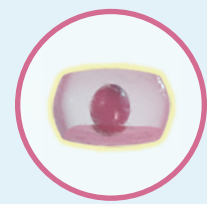


Figure 2. Multiple phenotypes of cells are delivered using RECELL



### KERATINOCYTES

Keratinocytes including basal, suprabasal, and activated keratinocytes regenerate the epidermis<sup>5,9</sup>



### FIBROBLASTS

Dermal fibroblasts deposit new extracellular matrix proteins<sup>6</sup>



### MELANOCYTES

Melanocytes produce melanin to allow restoration of natural pigmentation<sup>6</sup>

## Donor Skin Availability

The use of split-thickness skin grafts effectively increases the total body surface area of open wounds through creation of the donor sites, which impose their own wound-healing burden.<sup>11</sup> This is particularly relevant for compromised patients. Solutions to overcome this challenge include grafting in stages while using temporary coverage as the donor sites heal to enable re-harvest or widely meshed grafts to expand the use of available donor skin.<sup>12,13</sup> However, these approaches present their own challenges, including donor site pain and morbidity, longer healing times, and increased risk of infection and scarring.<sup>6,13</sup>

## Donor Skin Requirements when using RECELL®

RECELL is designed to allow an up to 1:80 expansion ratio of treated area to donor skin.<sup>6</sup> Clinical trials showed that autologous Spray-On Skin™ Cells prepared with the RECELL device restored durable epidermis to viable dermis in deep partial-thickness burn wounds without the need for split-thickness skin grafting, resulting in a reduction of donor skin of 97.5%.<sup>6</sup> At 1 week, the incidence of donor site healing in the RECELL group was superior to the control group (21.8% versus 10.0%;  $P = 0.04$ , Figure 3). This result was due to the donor skin sparing properties of RECELL.<sup>6</sup> A case from this trial is shown below (Figure 4). A 48-year-old sustained a deep partial-thickness flame burn injury to his arm. The wound was excised and divided into comparable sections which were randomized to receive a 2:1 meshed split-thickness skin graft or application of Spray-On Skin Cells prepared using the RECELL System.

Figure 3. Incidence of definitive closure of donor sites<sup>6</sup>

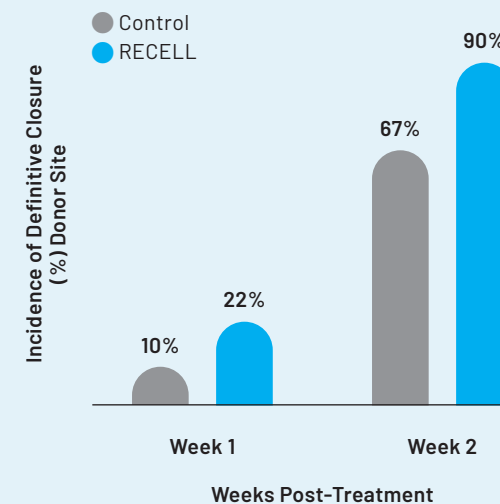
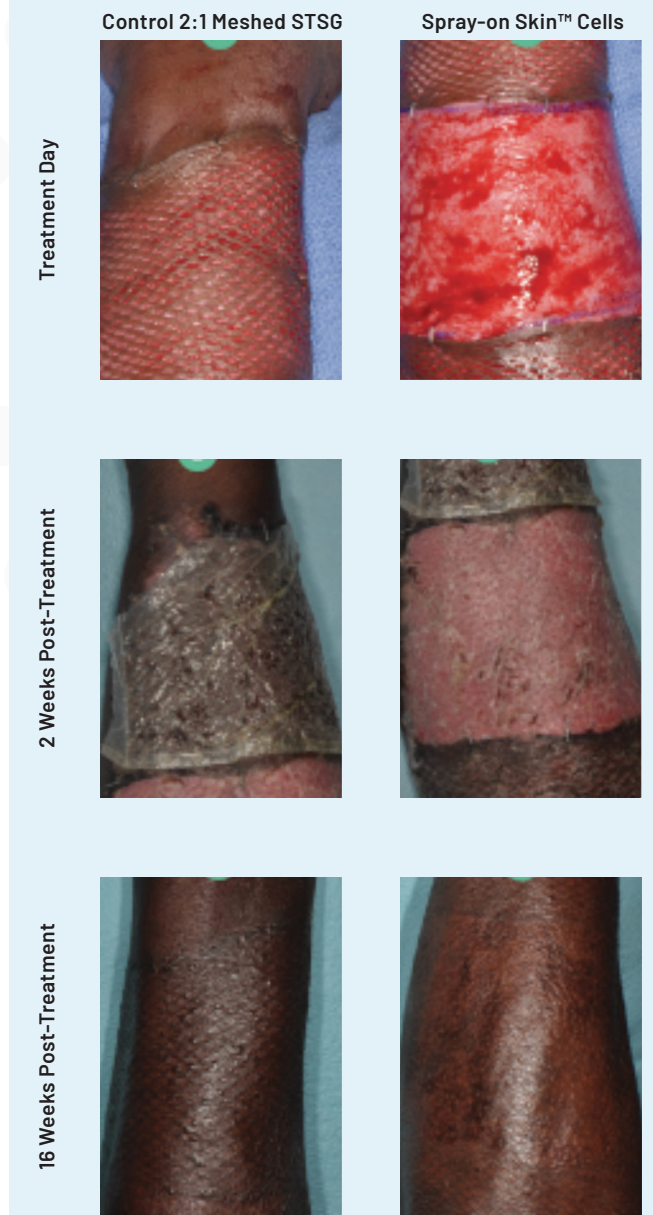
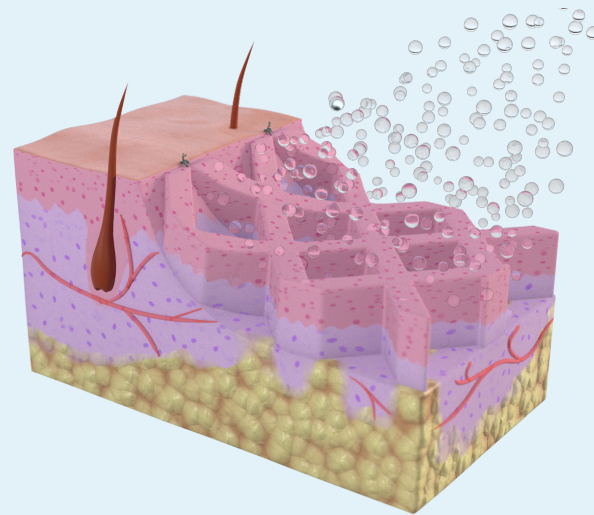


Figure 4.

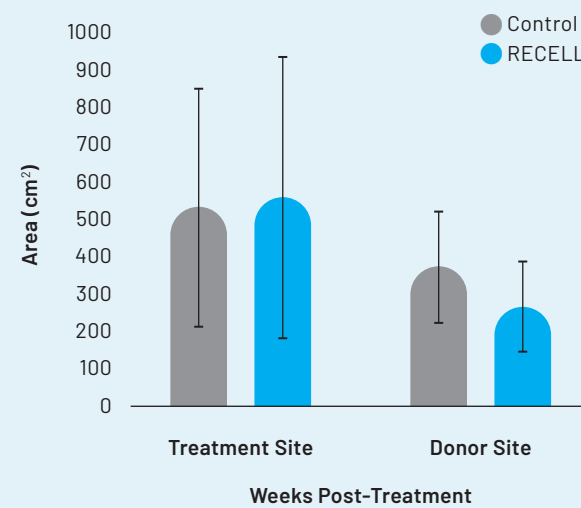


In full-thickness burn injuries, application of Spray-On Skin Cells (Figure 5) in combination with a widely meshed split-thickness skin graft resulted in on average 32% less use of donor skin compared to traditional autograft.<sup>4</sup> There was a significant reduction in the area of donor skin needed for the RECELL and meshed graft arm (Figure 6).<sup>4</sup> A case from this trial is shown below (Figure 7). A 9-year-old patient was treated with either 3:1 meshed graft or RECELL plus 4:1 meshed graft. Both sites were 80% to 99% closed within 1 week. The treatment including RECELL reduced donor site requirements by 40%.<sup>4</sup>

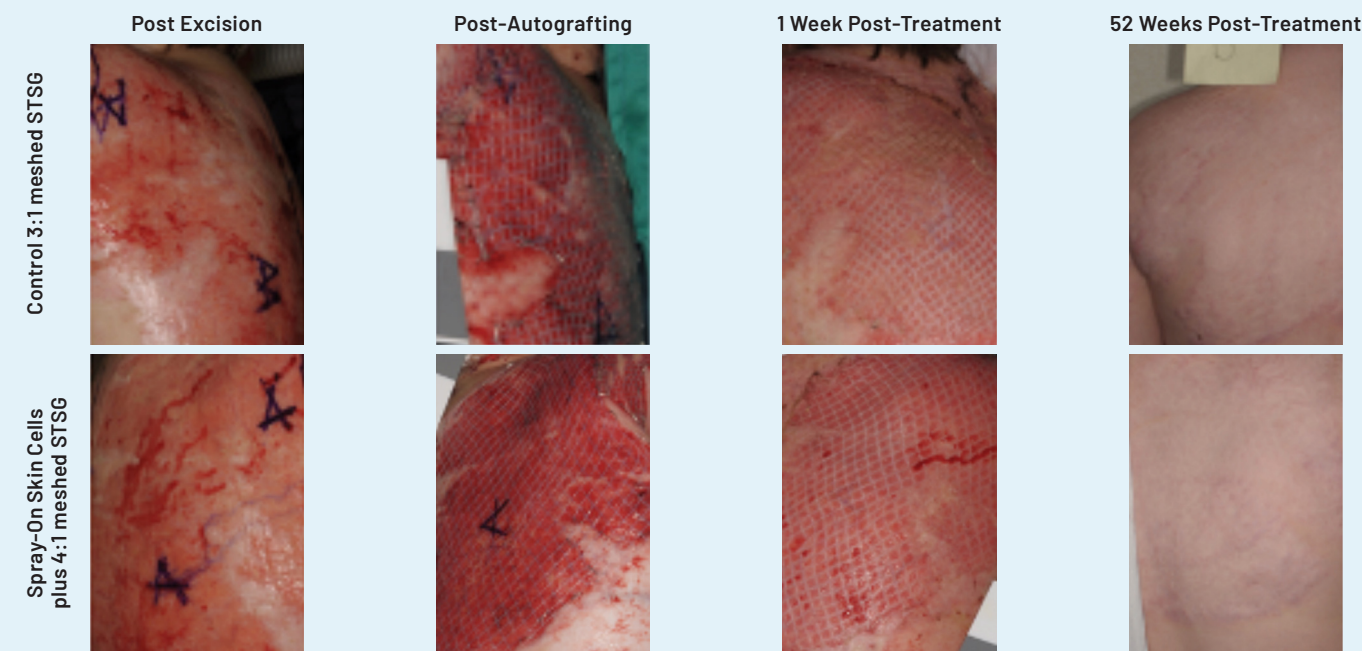
**Figure 5. Treatment of FT Burns With meshed STSG and Spray-On Skin™ Cells**



**Figure 6. Relative Reduction in Donor Skin Use with RECELL vs Meshed Graft<sup>4</sup>**



**Figure 7. Patient Case: Healing outcomes With 3:1 vs 4:1 Mesh Grafts plus RECELL<sup>®4</sup>**

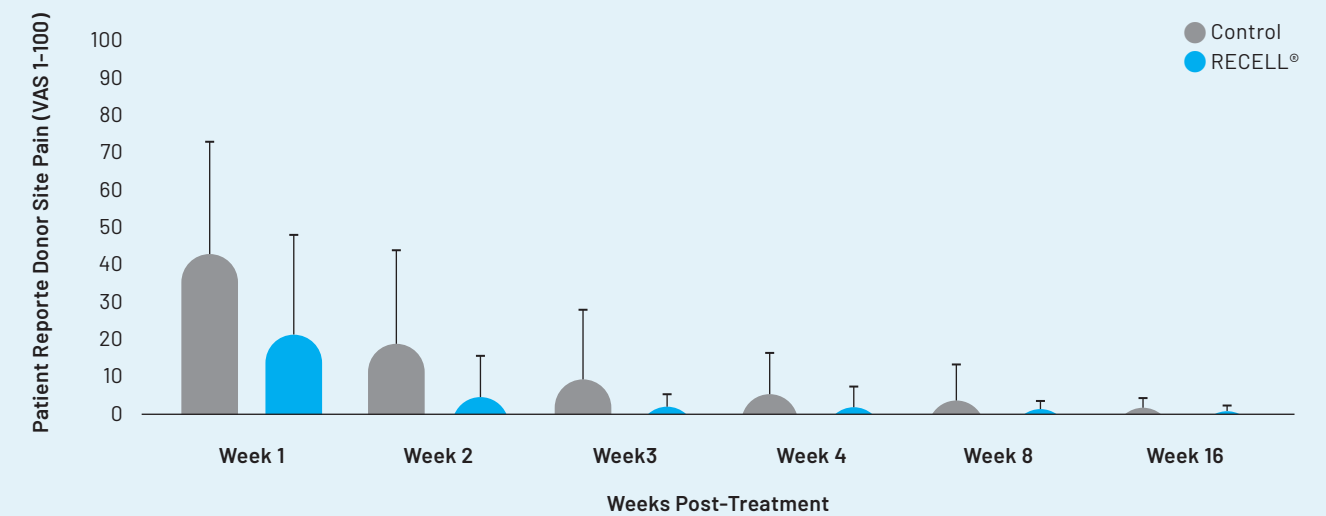


### Experience of Pain for RECELL treated patients

Reduction in pain and pain management is a priority for all patients, particularly those with burns.<sup>6</sup> Burn specialists are focused on managing donor site pain and pain associated with multiple dressing changes. As seen in a recent study the

use of RECELL has allowed for smaller donor sites, resulting in less donor site pain over the first 16 weeks (Figure 8), patients reported significantly less pain at the RECELL donor site compared with Controls ( $P \leq .05$  at each time point).<sup>6</sup>

**Figure 8. Patient reported donor site pain<sup>6</sup>**



### Length of Stay

Factors discussed influence length of stay, including the size and depth of the burn injury, initial decision time point for treatment, number of surgical procedures needed to close the wound, donor skin availability, and the need for pain management for both the wound itself and the donor site.<sup>11,14</sup>

Length of stay for burn injuries is correlated with the size of the burn area, typically 1 day for every 1% (TBSA).<sup>14</sup> Reducing hospital length of stay is especially important when trying to relieve strain on critical care beds by discharging patients early.

A hospital-perspective model was developed to evaluate cost-effectiveness of RECELL versus standard of care (split-thickness skin graft) for deep partial-thickness burns and RECELL with meshed skin graft for full-thickness burns. This model determined that the use of RECELL led to a 14-17.3% reduction in overall costs, driven by a 32-37% reduction in the number and duration of procedures needed for definitive closure, 15% reduction in hospital length of stay, and 22% reduction in rehabilitation needs.<sup>3</sup>

This information is based on peer reviewed health economic data and not on comparative head to head studies.

### Treating Sooner Decreases Length of Stay

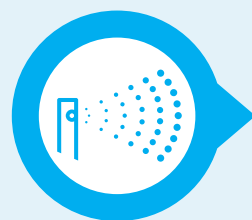
Deep-partial thickness burns may heal on their own but it is not uncommon for these burns to convert to full-thickness injuries, therefore they are often referred to as indeterminate burns. The "wait and see" approach is a methodology whereby this type of burn are assessed upon presentation to the burn center and given time to demarcate before a decision is made about closing the wound with conventional autografting (often around day 7-10 after burn). This can delay re-epithelialization and increase the chance of hypertrophic scarring, infection risk, and the number of dressing changes required.<sup>15,16</sup> Based on standardised questions posed to surgeons experienced in the use of RECELL<sup>17</sup>, the benefits of treating early with RECELL vs. utilizing the wait and see approach include donor site reduction and resulting decreased pain. Some of these burn experts have shortened initial treatment time to within 24 to 48 hours instead of waiting 10 days for wounds to declare (Figure 8). Early treatment may prevent the requirement for autografting.<sup>13</sup> As stated earlier the aim is to close the wound as fast as possible, but surgeons would like to minimise the requirement to skin graft (due to donor site morbidities) where possible. RECELL is a technology that allows the surgeon to take a small piece of the patient's skin to prepare a Spray-On Skin™ cell suspension for immediate application. Therefore commencing the healing process shortly following admission, avoiding the "wait and see approach" and its resultant delays in achieving definitive closure.

Figure 9. Algorithm of Care with RECELL®



**Day 0**

Admission



**24-72 Hours**

Excision and application of Spray-On Skin™ Cells



**Discharge the Next Day**

Day 1 post surgery

### Summary and Conclusion

Burn treatment is complex, with a number of challenges. Using RECELL in combination with wider meshed grafts in larger TBSA burns, can lead to fewer surgeries and less donor skin requirements than previous standards of care.<sup>3,6</sup> RECELL is a point-of-care device that affords the ability to treat patients earlier (within 72 hours of the burn), with a small skin sample to cover up to eighty times the area<sup>9</sup>, instead of waiting for the burn to demarcate. Burn surgeons are now able to treat

these patients with RECELL and burns with smaller TBSA are often discharged the next day.<sup>17</sup> This summary highlights the reduced number of surgeries, reduced donor site size and reduced donor site pain. By providing a point-of-care technology, that allows application of the patients own skin cells from a small sample of their own skin, RECELL enables early treatment and discharge of patients with both small and large TBSA burns.

### Notes


### IMPORTANT SAFETY INFORMATION

**INDICATIONS FOR USE:** The RECELL® Autologous Cell Harvesting Device is indicated for the treatment of acute thermal burn wounds. The RECELL device is used by an appropriately-licensed healthcare professional at the patient's point of care to prepare autologous RES® Regenerative Epidermal Suspension for direct application to acute partial-thickness thermal burn wounds in patients 18 years of age and older or application in combination with meshed autografting for acute full-thickness thermal burn wounds in pediatric and adult patients.

**CONTRAINDICATIONS:** RECELL is contraindicated for: the treatment of wounds clinically diagnosed as infected or with necrotic tissue, the treatment of patients with a known hypersensitivity to trypsin or compound sodium lactate (Hartmann's) solution, patients having a known hypersensitivity to anesthetics, adrenaline/epinephrine, povidone-iodine, or chlorhexidine solutions.

**WARNINGS:** Autologous use only. Wound beds treated with a cytotoxic agent (e.g., silver sulfadiazine) should be rinsed prior to application of the cell suspension. RECELL is provided sterile and is intended for single-use. Do not use

if packaging is damaged or expired. Choose a donor site with no evidence of cellulitis or infection and process skin immediately. A skin sample should require between 15 and 30 minutes contact with Enzyme. Contact in excess of 60 minutes is not recommended. RECELL Enzyme is animal derived and freedom from infectious agents cannot be guaranteed.

**PRECAUTIONS:** RECELL is not intended for use without meshed autograft for treatment of full-thickness burn wounds. The safety and effectiveness of RECELL without meshed autograft have not been established for treatment of partial-thickness burn wounds: on the hands and articulating joints, >320 cm<sup>2</sup>, in patients with wounds totaling >20% total body surface area (TBSA). The safety and effectiveness of RECELL with autografting have not been established for treatment of full-thickness burn wounds: on the hands and articulated joints, and in patients younger than 28 days of age (neonates).

**SPECIAL PATIENT POPULATIONS:** The safety and effectiveness of RECELL have not been established for treatment of acute thermal partial-thickness burn wounds in pediatric patients younger than 18 years of age.

**References:** 1. American Burn Association. Burn incidence and treatment in the United States: 2016. <https://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet/>. Accessed December 18, 2020. 2. McDermott KW, Weiss AJ, Elixhauser A. Burn-related hospital inpatient stays and emergency department visits, 2013: Statistical brief #217. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006. 3. Kowal S, Kruger E, Bilir P, et al. Cost-effectiveness of the use of autologous cell harvesting device compared to standard of care for treatment of severe burns in the United States. *Adv Ther*. 2019;36(7):1715-1729. 4. Holmes IV JH, Molnar JA, Shupp JW, 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. 5. Wood FM, 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;38:44-51. 6. Holmes IV JH, Molnar JA, Carter JE, et al. A Comparative study of the RECELL device and autologous split-thickness meshed skin graft in the treatment of acute burn injuries. *J Burn Care Res*. 2018;39(5):694-702. 7. Hirobe T. Keratinocytes regulate the function of melanocytes. *Dermatol Sin*. 2014;32(4):200-204. 8. Freedberg I, Tomic-Canic M, Komine M, et al. *Keratins and the Keratinocyte Activation Cycle* *J Invest Dermatol* 116:633-640, 2001. 9. Instructions for Use. RECELL® Autologous Cell Harvesting Device. 10. Singer AJ, Clark RAF. Cutaneous wound healing. *New England Journal of Medicine*. 1999; 341(1):738-746. 11. Rowan MP, Cancio LC, Elster EA, et al. Burn wound healing and treatment: review and advancements. *Crit Care*. 2015;19:243. 12. Jeschke MG, van Baar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. *Nat Rev Dis Primers*. 2020;6(1):11. 13. Finnerty CC, Jeschke MG, Branski LK, Barret JP, Dziewulski P, Herndon DN. Hypertrophic scarring: the greatest unmet challenge after burn injury. *The Lancet*. 2016;388(10052):1427-1436. 14. Kruger E, Bilir P, Kowal S, et al. Relationship between patient characteristics, length of stay and number of procedures for severe burn patients: analysis of the American burn association national burn repository. Poster presented at: ISPOR 2018; May, 2018; Baltimore, MD. 15. Kagan RJ, Peck MD, Hickerson WL, et al. Surgical management of the burn wound and use of skin substitutes. White paper for the American Burn Association. <http://www.oc.im.ehu.es/Fundamentos/fundamentos/Textos/American%20Burn%20Association.pdf>. Accessed November 4, 2020. 16. Wood F, Martin L, Lewis D, Rawlins J, McWilliams T, Burrows S, Rea S. A prospective randomised clinical pilot study to compare the effectiveness of Biobrane® synthetic wound dressing, with or without autologous cell suspension, to the local standard treatment regimen in paediatric scald injuries. *Burns*. 2012 Sep;38(6):830-9. doi: 10.1016/j.burns.2011.12.020. Epub 2012 Feb 8. PMID: 22322141. 17. Research conducted in August 2020, interviewed four surgeons who were experienced in using RECELL, Dr Carson, Dr Kahn, Dr Kopari and Dr Sood. Standardised questions posed to experts in the burn field.

Incorporation of RECELL<sup>®</sup> into the standard of care leads to:



**Reduction in length of stay<sup>3</sup>**

In <20% TBSA burns, clinicians are now able to treat patients with RECELL 2-3 days after burn injury and discharge the next day



**No more "wait and see" approach<sup>17</sup>**

Treating early provided favorable healing outcomes



**Reduction in donor size and pain<sup>6</sup>**

1:80 expansion ratio requires less donor skin, resulting in less pain



**Increased use in smaller burns<sup>17</sup>**

An evolution from using RECELL in larger burns to smaller burns

**TREAT EARLY.**  
FIND YOUR REASON TO RECELL.