RECELL Terminology

Autologous[1,2]
Cells or tissues obtained from the same person (patient derived).

Autologous Skin Cell Suspension (ASCS)
A patient's own skin cells (keratinocytes, fibroblasts, and melanocytes) that are isolated, dispersed in a fluid, and applied to the patient in a single operative procedure. Generic name to describe Spray-On Skin™ Cells or RES™.

Autologous Skin Graft (Skin Autograft)[1,2]
Skin that is removed (donor site) from one point of an individual's body that is then transferred to another portion of the same individual's body. The success of a skin grafts can typically be determined within 72 hours of the surgery. If a graft survives the first 72 hours without an infection or trauma the body, in most cases, will not reject the graft. Before the surgery, the recipient and donor sites must be free of infection and have a stable blood supply.

Skin autografts can be of the following types:

- Epidermal autografts (EAG): Skin graft consisting only of the epidermal tissue.
- Split-thickness skin grafts (STSG): Skin graft consisting of the entire epidermis and portions of the dermis, typically limited to the papillary dermis and upper portion of the reticular dermis. The range of STSG thickness includes 0.008"-0.016". These skin grafts are typically used when surgical intervention for wound healing is required. Split-thickness skin grafts are often meshed using a skin graft mesher to allow for expansion (expansion ratios are dependent on amount of available skin as well as location of the body).
- Full-thickness skin grafts (FTSG): Skin graft consisting of the entire epidermis and dermis and are typically used to cover small, functionally, and cosmetically important areas. Benefits include decreased scar formation; however, the donor site must be closed with primary direct closure or with a STSG.
- Micrograft: Small island split-thickness skin grafts allowing for expansion greater than that achieved using a typical skin graft mesher. The most common type of micrograft is created using a Meek device (Humeca) allowing for up to 9:1 expansion.
- Pedicle grafts/pedicle flap: A graft which is left attached to the original site by a narrow base of tissue to provide a blood supply during grafting.
- Cultured epithelial autograft (CEA): Involves obtaining full-thickness specimens (two 2x6 cm) of healthy skin. The skin is grown in a laboratory in the presence of murine (mouse) fibroblasts that promote growth. It takes about 3 weeks to be ready for grafting and is very costly. The final product is 2-8 cells thick, so it is at risk for shearing and blistering months after the procedure. Often used in conjunction with a widely meshed skin graft.

Allogeneic[1,2]
Cells or tissue obtained from individuals of the same species.

Allograft[1,2]

A graft obtained from individuals of the same species (cadaveric tissue). In burns, human cadaver skin is used as a temporary covering on excised burn wounds. This tissue plays a major role in the surgical management of large burn wounds when autograft is not readily available. Allografts are obtained from a skin bank.

Basement Membrane[2,3]

Proteins found at the epidermal-dermal junction that help to connect the epidermis to the dermis. Following wound healing it can take several weeks and sometimes months to form and minor shearing forces may cause blistering and sometimes epidermal loss until mature.

Burn[1]

A burn is a complex injury to the skin and underlying tissues of the body and is a direct result of contact with electrical, chemical, heat, or radiation. A burn involves the destruction of skin cells, and sometimes the underlying structures of muscle, fascia, and bone. It occurs when these structures absorb more heat than their capacity to dissipate it. Burn injuries are classified by depth of burn injury (superficial, partial-thickness, or full-thickness)

Burn Depth[1]

- Superficial (i.e., first degree burns): involve only the epidermis and are erythematous and painful.
- Partial-thickness (PT) (i.e., second-degree burns): extend through the epidermis and into the dermis and can be classified as superficial partial-thickness (SPT) or deep partial-thickness (DPT) burns. Blistering is a hallmark of PT burns, with SPT burns typically pink, moist, and painful, and DPT burns typically dry, mottled, pink-and-white, and less painful. In some cases, it is difficult to distinguish between SPT and DPT burns—these burns are often referred to as an indeterminate depth burn.
- Full-thickness (FT) (i.e., third- and fourth-degree burns): Extend through both the epidermis and dermis and into the subcutaneous fat or deeper tissues, such as muscle, tendons, or bone. These burns are typically white or black, dry, and painless. Full-thickness burns may cause a range of responses in the body including nutrient and fluid shifts, electrolyte imbalance, respiratory failure, heart failure, multiple organ failure, and/or suppression of the immune system.

Burn Etiologies[1]

- Scald injuries: Account for 30% of admissions with greater than 50% being children. Hot tap water is the most common cause. Many scalds could be prevented by adjusting the temperature setting on hot water heaters or placing special faucet valves.
- Flame: Most common cause in patients that are admitted to Burn Centers. Residential fires and motor vehicle crashes are frequent causes.
- Hot objects: Common causes are contact with hot metal i.e. from irons, contact with hot engine parts, hot tar (roofers), etc.
- Electrical: Account for close to 1000 deaths annually. One third of these injuries occur in the home (including small children). Commonly related to industrial or farm sites. Approximately 80 deaths result from lightning (occurring mostly during recreational activities i.e. golfing, fishing, camping etc.)
- Chemical burns: account for a small number of admissions (2%) to the hospital, however, chemical burns can occur in all age groups, with 5% occurring in children under 5 years of age.

Burn Wound Healing[1,2]

- First intention or primary closure: Process whereby the wound edges are approximated and closed with sutures.
- Secondary intention or secondary closure: Occurs when the wound closes by reformation of connective tissue and granulation tissue with subsequent re-epithelialization and wound contraction.

- Tertiary intention of delayed primary closure: Process whereby the wound is surgically closed using a skin graft of flap.

Cell Culture[2]
The process by which cells are grown outside of the body in an artificial environment (laboratory setting).

Cellular Viability[2,3]
Living cells which have the potential to contribute to the maintenance and or repair of tissue.

Cellulitis[1]
A generic term that describes a variety of bacterial infections involving the skin specifically affecting the dermis and subcutaneous fat. Signs and symptoms include redness, swelling, pain, warmth, abscess with pus formation, fever.

Colonization[1]
The presence of proliferating bacteria on a body surface, like the skin or open wounds, without a host response.

Contraction[1-3]
A late occurrence in the normal wound healing process in which cells (myofibroblasts) decrease the size of the wound by gripping the wound edges and pulling them together. Contraction results in a normal scar that is flat with discoloration.

Contracture[1,2]
A condition of shortening and hardening of muscles, tendons, or other tissues, often leading to deformity and rigidity of joints. Physical therapy, pressure, and exercise in many cases can aid in controlling contracture. If these treatments are unsuccessful surgery may be required. Techniques for contracture release include skin grafting, flap, Z-Plasty, or tissue expansion.

Debridement[1,2]
Non-surgical process of removing dead (necrotic) tissue or foreign material from and around a wound to expose healthy tissue.

Dermabrasion[1,2]
A surgical procedure to improve or minimize the appearance of scars, restore function and correct disfigurement resulting from an injury. Dermabrasion is used to smooth scar tissue by shaving or scraping off the top layers or the skin. Though dermabrasion smooths the surface of the scar it will not remove the scar. Scars are permanent, but their appearance will improve over time. The procedure may be performed in a dermatological surgeon's office or in an outpatient surgical facility.

Dermal Substitutes[1,2]
Acellular matrices or scaffolds that are used to promote new tissue growth to prepare the wound for definitive closure (autograft or allow for re-epithelialization from the wound edge/remaining epidermal elements)

Dermis[1-3]
Layer of skin below the epidermis consisting of a network of collagen fibers and elastin and is divided into two layers, the more superficial papillary dermis and the deeper reticular dermis. The main cell of the dermis is the dermal fibroblast. The dermis includes blood vessels, hair follicles, sweat glands, and sebaceous glands. It also contains mechanoreceptors to sense touch and thermoreceptors to sense heat. Once the dermis is destroyed, it will not regenerate, but heals through a repair mechanism.

Disaggregate
Process to separate or isolate the skin into cellular components achieved using enzymatic methods and mechanical force.

Enzyme[4]
A substance produced by a living organism that acts as a catalyst to bring about a specific biochemical reaction.

Epidermis[1]
Outermost layer of the skin responsible for providing a protective barrier to the external environment. Cells in the epidermis include keratinocytes, melanocytes, and Langerhan's cells. The epidermis is capable of regenerative healing, from keratinocyte stem cells found at the dermal-epidermal junction.

Escharotomy[1]
A procedure that involves making an incision through eschar (dead tissue) to the subcutaneous layer. It is usually a painless procedure, because it is performed through a full-thickness injury. An escharotomy may be needed to release the constriction caused by deep-partial thickness or more likely full-thickness burns that are circumferential around the chest, arm or leg.

Fasciotomy[1]
A procedure that involves making a surgical incision through the fascia to release pressure in the muscle compartment. Swelling in the muscle compartment can cause ischemia and damage to the muscle and nerves. This procedure helps normalize blood flow in the muscle compartment. Most commonly performed after severe electrical injury.

Fibroblast[1-3]
Cells in the dermis that deposit extracellular matrix proteins.

Flaps[1]
- Rotational flap: Healthy soft tissue is rotated into the defect on a fulcrum point. Rotation flaps provide the ability to mobilize large areas of tissue with a wide vascular base for reconstruction.
- Free flap: Microsurgical technique that involves the transfer of a segment of soft tissue from a distant donor site.

Granulation Tissue[1-3]
Tissue that forms on the surface of a wound comprising newly formed blood vessels.

Hemostasis[1]
To stop bleeding. Hemostasis should be achieved prior to autografting or applying RES™.

Homograft[1]
A tissue graft from a donor of the same species as the recipient, see allograft.

Infection[1]
The invasion of a host by a disease-causing agent, that may or may not lead to obvious disease.

Inflammation[1.3]
A localized protective response to tissue injury or destruction. Acute inflammation is characterized by redness, swelling, pain, and heat.

Inhalation Injury[1]
Fire has been associated with 3 different types of inhalation injuries. More than a hundred known toxic substances are present in fire smoke. When inhalation injuries are combined with external burns the chance of death can increase significantly. The three types of inhalation injuries are:

- Damage from Heat Inhalation: True lung burn occurs only if you directly breathe in a hot air/flame source, or have high pressure force the heat into you. In most cases, thermal injury is confined to the upper airways, because the trachea usually shields the lung from thermal loads. However, secondary airway involvement can occur after inhalation of steam as it has a greater thermal capacity than dry air. When hot air enters the nose, damage to the mucous membranes can readily transpire as the upper airway acts as a cooling chamber.
- Damage from Systemic Toxins: Systemic Toxins affect our ability to absorb oxygen. If someone is found unconscious or acting confused in the surroundings of an enclosed fire, systemic toxins could be a possible cause. Toxin poisoning can cause permanent damage to organs including the brain. Carbon Monoxide poisoning can appear symptomless up until the point where the victim falls into a coma.
- Damage from Smoke Inhalation: Upper airway edema is the earliest consequence of inhalation injury. Upper airway edema is commonly seen during the first 6 to 24 hours after injury. Early obstruction of the upper airway is managed with intubation. Initial treatment consists of removing the patient from the gas and allowing him to breathe air or oxygen.

Keratinocyte[1-3]
Primary cell of the epidermis responsible for skin healing.

Melanocyte[1-3]
Cell found in the epidermis that produces melanin, which is responsible for normal pigmentation.

Point-of-Care
Providing treatment in a single operative setting, rather than sending skin samples to laboratory for processing, necessitating additional intervention.

Pressure Garments[1]
Garments that prevent and control the formation of hypertrophic scars by applying counter pressure to the wounded area. Normal undamaged skin is made up of connective tissues in the dermis that form a three-dimensional mesh or collagen fibers aligned parallel to the skin's surface. The skin applies pressure against its underlying layers. Under normal circumstances, the pressure that the skin puts upon the body ensures that injured skin is replaced to its original state without scarring. When burns destroy the skin and the papillary dermis normal pressure by these layers no longer exists. Without this pressure, hypertrophic scars will form irregularly causing possible deformities.

The continuous wearing of pressure garments prevents the thickening, buckling, and nodular formations seen in hypertrophic scars. A soft pliable elastic scar develops which allows for normal joint movement. The external pressure applied by the garments decreases inflammatory response and the amount of blood in the scar, reducing itching and prevents collagen from synthesizing. Additionally, pressure garments provide protection against injury. It is important that burn patients begin wearing pressure garments while the scar is active and immature. Scar tissue is highly responsive in the early stages, so an early application of pressure garments is imperative.

Pressure garments should be worn at least 23 hours a day, removing them for bathing and cleaning of the garments only. Most patients will need to wear pressure garments for 12 to 18 months.

Regeneration[1-3]
The ability to renew or regrow lost or damaged tissue; scarless healing.

Repair[1-3]
The wound healing process resulting in imperfect healing.

RES™
Regenerative Epidermal Suspension comprising a mixed population of cells obtained from the disaggregation of a skin sample (0.006-0.008”). The cell population includes keratinocytes, fibroblasts, and melanocytes, which each has unique and complementary roles in the wound healing process. Same as Spray-On Skin™ Cells or ASCS.

Scar[1-3]
The result of the body's natural response to wound healing. Scars vary in nature and may be non-descript or may be painful, discolored, or raised.

- Hypertrophic scars: Hypertrophic scars are red, thick and raised; however, they differ from Keloid scars in that they do not develop beyond the site of injury or incision. Additionally, hypertrophic scars will improve over time. This time however can be reduced with the help of steroid application or injections.
- Keloid scars: Overgrowth of scar tissue. The scar will grow beyond the site of the injury. These scars are generally red or pink and will become a dark tan over time. They occur when the body continues to produce collagen a tough fibrous protein, after the wound has healed. Keloid scars are thick, nodular, ridged and itchy during formation and growth. Extensive keloids may become binding and limit your mobility. Additionally, clothing rubbing, or other types of friction may irritate them. Dark-skinned people are more likely to develop keloids than those with fair skin and the possible occurrence of Keloids reduces with age.

  Keloids may be reduced in size by cryotherapy (freezing), external pressure, cortisone injections, steroid injections, radiation or surgical removal. If injections and external pressure such as pressure garments are inadequate, the scar tissue can be cut away, this is generally an outpatient surgery performed under local anesthesia and you should be able to return to work or school within a few days. Your doctor may recommend that you wear pressure garments over the area for up to a year to prevent the Keloids from re-occurring. It is possible that this procedure will need to be repeated every few years because Keloids tend to re-occur.

Skin Graft Mesher[1]
Donor skin is passed through this tool making perforations (small slits) that allow for expansion of the skin to cover a larger surface area of the body. The tool is set to mesh at pre-determined ratio (2:1, 3:1, 4:1, etc).

Surgical Excision[1]
- Tangential: The principle of tangential excision is to remove only nonviable tissue, sparing as much viable dermis as possible in the case of the deep dermal burn. This technique utilizes a blade held at a very acute angle with the skin surface (Goulian or Watson knife).

  The endpoint of excision is brisk punctuate bleeding and a completely viable wound base with as much dermis as possible, as viable dermis is an excellent base for grafting. Viable dermis is white and shiny in color. One or two large bleeders can make the wound look red, so careful inspection and considerable experience is needed to assess the adequacy of the wound bed.

  Injured fat is particularly difficult to diagnose. Any fat that is dark yellowish-brown in color should be removed. Healthy fat is light yellowish in color and shiny. It is easy to under-excise, leaving a poor bed for graft take. In addition, it is easy to excise too much tissue, thereby removing potentially viable dermis.
- Fascial: Excision of the burn wound to fascia is used in cases of very large full-thickness burns or with very deep burns that extend well into the fat or underlying tissues. Excision is performed using a combination of sharp dissection, constant tension, and electric cautery. The vessels encountered at the fascial plane are fewer in number and larger in size than encountered in a tangential excision and

easier to control with cautery and ligatures. If performed in the first several days, the edema fluid separates fascia from overlying subcutaneous tissue, making excision very easy.

Spray-On Skin™ Cells

Regenerative Epidermal Suspension (RES™) comprising a mixed population of cells obtained from the disaggregation of a skin sample (0.006-0.008"). The cell population includes keratinocytes, fibroblasts, and melanocytes, which each has unique and complementary roles in the wound healing process. Same as ASCS, and preferred terminology to describe cellular suspension.

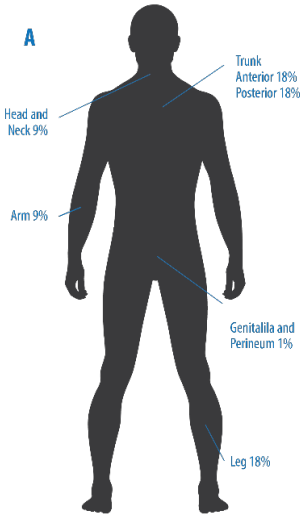
Temporary Wound Coverings[1,2]

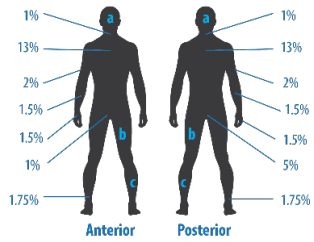
Dressings created to function as an outer barrier protection to prevent infections, or dehydration prior to a wound undergoing permanent closure. These coverings are often used when a burn patient has a large total body surface burn and limited donor skin is available. Additionally, temporary wound coverings or used as a "test" graft for questionable skin graft sites, to help prepare the wound bed for definitive closure, or as an additional protective covering on skin grafts that have been widely meshed and stretched for maximum coverage. Temporary wound coverings can be allografts, xenografts, or biosynthetic.

Total Body Surface Area (TBSA)[1]

Common terminology used to describe the extent of burn injury. This can be calculated by various methodologies described below.

- Rule of Nines: Estimates the TBSA that has been burned in multiples of nine (i.e., the head=9%, each arm=9%, the anterior chest and abdomen=18%, the posterior chest and back=18%, each leg=18%, and the perineum=1%). For children, percentages are adjusted because they have proportionally larger heads and smaller legs (i.e., the head=18% and each leg=13.5%) (See Figure).
- Lund-Browder Chart: Generally regarded as the most accurate method for estimating TBSA because it compensates for the variation in body shape with age (each arm=10%, each anterior trunk and posterior trunk =13%, and the percentage calculated for the head and legs varies based on the patient's age) (See Figure).
- Palm Size: The patient's palm, which equates to approximately 1% TBSA, is used to estimate small or scattered burns.





BODY PART	AGE					
	0 YR	1 YR	5 YR	10 YR	15 YR	ADULT
	RELATIVE % OF BODY-SURFACE AREA					
a=1/2 of Head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
b=1/2 of Thigh	3 3/4	4 1/4	4	4 1/2	4 1/2	4 3/4
c=1/2 of Lower Leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3

Source: adapted from Orgill Excision and Skin Grafting of Thermal Burns, N Engl J Med 2009; 360:893-901.

Tumescence Infiltration[1]

A technique or procedure commonly performed in the operating room that involves a solution made of saline which may include epinephrine that can be injected into the burn wound or donor site area prior to excision or harvest. The result is local vasoconstriction to help minimize blood loss as well as used around certain anatomical areas to “bleb or pump” up the tissues for easier harvesting.

Xenograft[1,2]

A tissue that has been grafted from species to another. Xenografts can be temporary dressings that are removed (most common is porcine), or as an advanced wound dressing or dermal substitute to promote tissue generation (epidermal and/or dermal).

[1]Herndon, D.N., *Total Burn Care*. 4th ed. 2012, New York, NY: Saunders Elsevier.
[2]Albanna, M. and Holmes, J.H., *Skin Tissue Engineering and Regenerative Medicine*. 1st ed. 2016, Cambridge, MA: Elsevier.
[3]Clark, A.F., *The Molecular and Cellular Biology of Wound*. 2nd ed. 1995, New York, NY: Plenum Press.
[4]Campell, N.A., Reece, J.B., and Mitchel, L.G., *Biology*. 5th ed. 1999, Menlo Park, CA: Benjamin/Cummings.