

**A COMPARATIVE STUDY ON
EPIDERMAL GRAFTING VS SPLIT SKIN GRAFTING
IN WOUND HEALING IN OUR INSTITUTE**

A DISSERTATION SUBMITTED TO
THE TAMILNADU DR.MGR MEDICAL UNIVERSITY
In partial fulfillment of the regulations for the award of the
Degree of M.S (GENERAL SURGERY)

BRANCH-1



DEPARTMENT OF GENERAL SURGERY
STANLEY MEDICAL COLLEGE AND HOSPITAL TAMILNADU
DR.MGR MEDICAL UNIVERSITY,CHENNAI

MAY 2020

CERTIFICATE BY THE INSTITUTION

This is to certify that dissertation “**A COMPARATIVE STUDY ON EPIDERMAL GRAFTING VS SPLIT SKIN GRAFTING IN WOUND HEALING IN OUR INSTITUTE**” is a bonafide record of work done by **Dr. K. NATRAMIZH** in the Department of General Surgery, Stanley Medical College, Chennai, during her Post Graduate Course from MAY 2017- MAY 2020. This is submitted in partial fulfillment for the award of **M.S. DEGREE EXAMINATION- BRANCH I (GENERAL SURGERY)** to be held in May 2020 under the **Tamilnadu DR.M.G.R. Medical University, Chennai.**

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DECLARATION

Dr. K. NATRAMIZH solemnly declare that this dissertation titled **“A COMPARATIVE STUDY ON EPIDERMAL GRAFTING VS SPLIT SKIN GRAFTING IN WOUND HEALING IN OUR INSTITUTE”**, is a bonafide work done by me in the department of general surgery, Govt. Stanley Medical College and Hospital, Chennai under the supervision of **Prof. Dr.T.SIVAKUMAR,M.S.** This dissertation is submitted to the Tamilnadu Dr MGR Medical university, Chennai in partial fulfillment of the university regulations for the award of M.S. Degree (General Surgery), branch – 1 examination to be held in May 2020.

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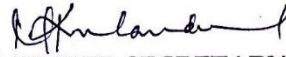
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ABSTRACT

OBJECTIVES OF STUDY

- To compare the efficacy and clinical outcome of Epidermal grafting and Split skin grafting in wound healing in our institute
- To assess time period for healing in donor site, pain score as reported by patients in numerical rating scale(0-10)

METHODOLOGY

This is a Prospective randomised study that compares the efficacy and wound healing mechanism of Epidermal grafting with Split skin grafting. The primary outcome measures proportion of wound that heals in 6 weeks and donor site healing time. The secondary outcome measures pain score and patient satisfaction. Written informed consent will be obtained from all subjects before enrollment in study. Patients will be randomly allotted into two equal groups. Group A will undergo Epidermal grafting as treatment modality for wound healing. Group B

will undergo Split skin grafting as the treatment modality for wound healing. Split skin grafting done using Humby knife and Epidermal grafting done using Epidermal harvesting system. All patients will be reviewed at 1st week, 2nd week, 4th week and 6th week post operatively.

RESULTS

In our study the following results had been arrived:

- ***DONOR SITE PAIN SCORE***

In the Epidermal grafting group, the donor site pain score is zero while in the Split Skin Grafting group, the mean donor site pain at week one is 5.4 (S.D=0.8). Donor site Pain is better in the Epidermal grafting group.

- ***DONOR SITE HEALING***

In the Epidermal grafting group, the mean donor site healing is 98.28% (S.D=1.46%) while in the Split Skin Grafting group, the mean donor site healing is 86% (S.D=4.9%). Donor site healing is better with Epidermal

grafting group. Student t-test shows a value of 8.76 with a p-value=0.00143 ($p<0.005$) which is highly significant.

- ***EPITHELIALISATION OF GRAFT***

The two groups do not significantly differ in the epithelialisation of the recipient area in the follow-up period with the p value =0.65 which is not significant.

CONCLUSION

Epidermal skin grafting has better donor site healing and no pain at donor site as compared to Split skin grafting. Epithelialisation of graft at recipient area does not significantly differ from Split skin graft.

Hence Epidermal graft is a promising alternative to the more invasive conventional surgical techniques as it is day care surgery without anesthesia and reduces the surgical burden for patients in need of wound coverage.

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INTRODUCTION

Chronic wounds are more prevalent disease with a significant healthcare burden. These wounds often do not respond to standard wound care therapy alone. It requires the use of adjuvant therapies. Epidermal grafting, previously utilized primarily for correction of Vitiligo in Dermatology, is increasingly being considered as a beneficial therapy for healing of both acute and chronic wounds. Epidermal grafting has been shown to be successful in the management of chronic wounds, with promising healing outcomes in refractory patients. It has not only been shown to be effective, but it is also associated with lower cost and morbidity when compared to traditional skin grafting techniques as well as improved healing in the donor site. This treatment modality has become more standardized, reproducible, and user friendly as well as less time consuming, through the use of the **Epidermal Harvesting System**, making its use in the clinical setting more easy and beneficial. Epidermal grafting represents a promising,

efficacious and cost-effective option for treatment of acute and chronic non-healing wounds.

Chronic wounds are common. They are difficult to treat and are a financial burden to the patients as well as the health care system. Venous leg ulcers which affects a large population, heal after six months of standard care in only 50 -75% of patients. Skin grafting techniques are often utilized to assist in wound healing in case of non healing wounds. Various forms of skin grafting exist. Traditionally skin grafting techniques are divided into full thickness skin grafts and split thickness skin grafts. Full thickness skin grafts which consist of grafts containing the epidermis and the entire dermis. Split thickness skin grafts which consist of grafts containing the epidermis and part of the dermis. Epidermal grafts which is a promising alternative to traditional techniques, consist of grafts containing the epidermal tissue alone. Full thickness skin graft are harvested by surgical excision and primary closure is done for the donor site. This modality is only possible for specific areas where there is sufficient skin laxity, limiting the applicability of

its use in other areas. Split thickness skin grafting are usually harvested by use of a dermatome which can shave a portion of skin, the depth of which can be adjusted by settings of the dermatome, leaving the deeper, reticular dermis intact. This method creates a wound at the donor site. Donor site usually carries risk of infection, scarring and poor wound healing. Full thickness skin grafting are commonly used when cosmesis is an important consideration, to prevent wound contraction in areas such as on the face. Split thickness skin grafting are commonly used in the treatment of chronic lower extremity wounds as their thinner nature requires less vascular supply and the graft take is better. In some instances, newer therapies, such as cellular and tissue-based products, have been replacing the use of skin grafting due to the limitations imparted by the high-risk nature of the procedures. In many cases, skin grafting require hospitalization and the use of a surgical operating room, administration of regional or general anesthesia and periods of immobility in certain cases, limiting their use. Epidermal grafting is a method that allows autologous skin grafting in an

outpatient setting without requiring anaesthesia minimizing the costs and morbidities when compared with split thickness and full thickness grafting.

Epidermal skin grafting was first introduced by Kiistala and Mustakallio in 1964. Traditionally, it has been performed by the suction blister technique. By this technique, it results in cleavage through the lamina lucida which is the weakest part of the skin and subject to cleavage with suction. It preserves the ultrastructure of the epidermis with only patchy hemidesmosome disruption. Traditionally, it has been used in dermatology for treatment of vitiligo. It has been shown to be effective in the management of acute surgical wounds and chronic ulcers. Its use has been limited to date because of the previously tedious and time consuming processes to produce suction blisters. A new, commercially available, automated system for epidermal harvesting, Cellutome minimizes these factors. It has been shown to be less time consuming and more standardized and reproducible than former methods. It functions by applying heat and suction concurrently to normal skin at the

donor site and induce small blisters or microdome, within 30-45 minutes. These epidermal samples are then transferred via transparent adhesive film dressing to the recipient sites, which are then wrapped in compression. Suturing or other procedures are not necessary.

Epidermal grafting has several benefits when compared to split and full thickness skin grafting. The donor site experiences less pain and scarring as compared to other modalities. The epidermis lacks pain sensory nerves. Patients experience minimal discomfort and hence do not require anesthesia for the procedure. The donor site also heals rapidly within several days. The donor site heals with very minimal or no scarring, as the dermis is left intact. Epidermal grafts are suitable for lower extremity and less vascularized wounds because the thinner graft requires less vasculature so that it remains viable. The procedure is simplified and automated and does not require more surgical training. The procedure can be performed on an outpatient basis or at the bedside without anaesthesia.

Epidermal grafting is beneficial in treatment of various patients including those with acute wounds, chronic ischemic wounds, chronic diabetic foot ulcers. Epidermal grafting was found to be a successful treatment in a case series of five patients with pyoderma gangrenosum, where the risk of pathergy often limits treatment with other modalities. Pathergy is a phenomenon whereby trauma may lead to worsening of the wound. So creation of a donor site, as would be needed for Split skin grafting, would be a contraindication. In this series, all five patients experienced substantial wound size reduction, and three out of five experienced wound closure. All donor sites healed without sequelae .

REVIEW OF LITERATURE

HISTORY OF SKIN GRAFTING

Ratner and Hauben and colleagues give excellent overviews of the history of skin grafting.

Skin grafting originated among the tilemaker caste in India approximately 3000 years ago. A common practice then was to punish a thief or adulterer by amputating the nose. The surgeons of their day took free grafts from the gluteal area to repair the deformity. From this modest beginning, skin grafting evolved into one of the basic clinical tools in the field of plastic surgery.

In 1804 an Italian surgeon named Boronio successfully autografted a full-thickness skin graft on a sheep. Sir Astley Cooper grafted a full-thickness piece of skin from a man's amputated thumb onto the stump for coverage. In 1823, Bunger successfully reconstructed a nose with a skin graft. In 1869, Reverdin rekindled worldwide interest in skin grafting with his report of successful pinch grafts. In 1872, Ollier pointed out the importance of the dermis in skin grafts, and in 1886 Thiersch

used thin split thickness skin to cover large wounds. To this day the names Ollier and Thiersch are synonymous with thin (0.005–0.01-inch) split thickness grafts.

Lawson, Le Fort, and Wolfe used full thickness grafts to successfully treat ectropion of the lower eyelid. Krause popularized the use of full thickness grafts in 1893 and known today as Wolfe-Krause grafts.

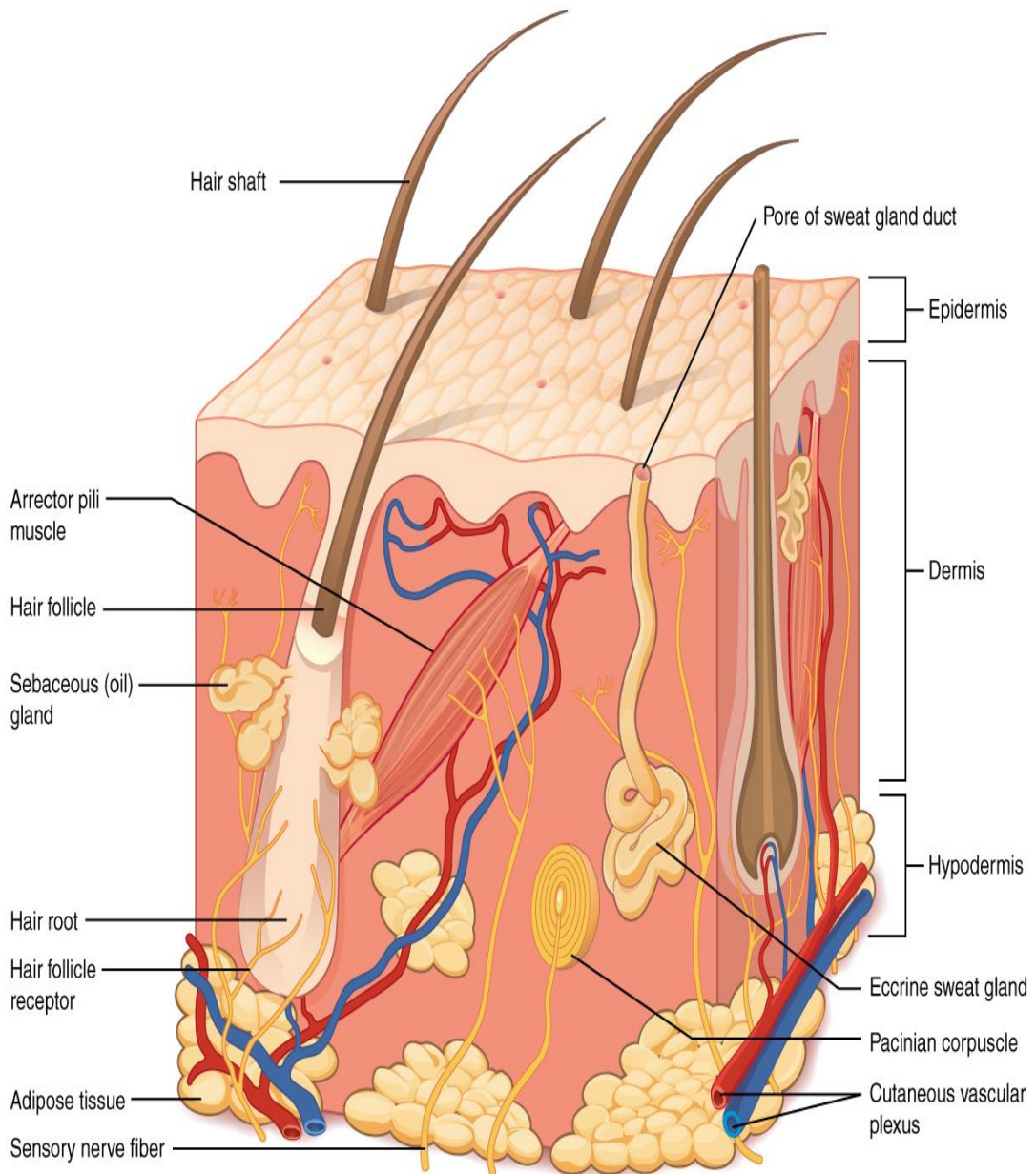
Brown and McDowell reported using thick split thickness grafts (0.01–0.022-inch) for the treatment of burns in 1942. In 1964 Tanner, Vandeput, and Olley gave us the technology to expand skin grafts with a machine that would cut the graft into a lattice pattern.

In 1975 epithelial skin culture technology was published by Rheinwald and Green, in 1979 cultured human keratinocytes were grown to form an epithelial layer adequate for grafting wounds.

HISTORY OF EPIDERMAL SKIN GRAFTING

First introduced by Kiistala and Mustakallio in 1964. Epidermal skin grafting has traditionally been performed by the suction blister technique. This preserves the ultrastructure of the epidermis with only patchy hemidesmosome disruption. Initially it has been used in dermatology for treatment of Vitiligo but has been shown to be effective in the management of acute surgical wounds and chronic ulcers. The Epidermal Harvesting System functions by applying heat and suction concurrently to normal skin at the donor site to induce small blisters or microdome, within 30-45 minutes. These epidermal samples are then transferred using transparent adhesive film dressing to the recipient sites and are then wrapped in compression.

ANATOMY



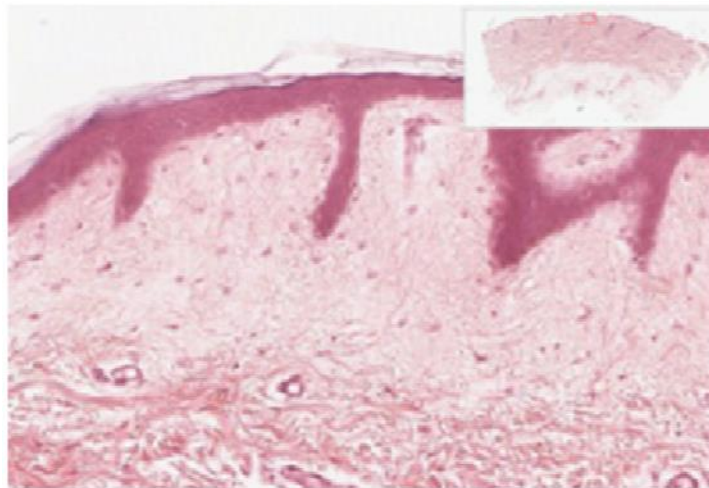
The skin covers the entire external surface of the human body. It serves as a protective barrier that prevents internal tissues from exposure to trauma, ultraviolet radiation, temperature extremes, toxins and bacteria. Other important functions include sensory perception, immunologic surveillance, thermoregulation, and control of insensible fluid loss.

The integument consists of 2 mutually dependent layers - the epidermis and dermis, which rest on a fatty subcutaneous layer, the panniculus adiposus. Embryologically the epidermis is derived primarily from surface ectoderm but is colonized by pigment-containing melanocytes and pressure-sensing Merkel cells of neural crest origin and Langerhans cells of bone marrow origin.

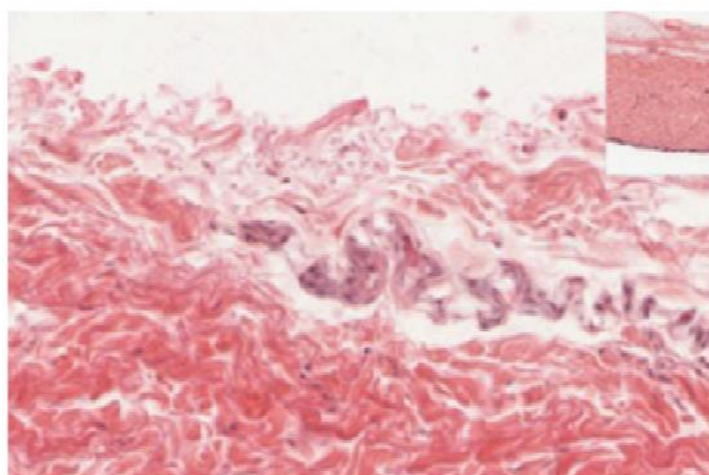
THE EPIDERMIS

The epidermis is composed of keratinized, stratified squamous epithelium. It is made of four or five layers of epithelial cells depending on its location in the body. It is

avascular. From deep to superficial, these layers are the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum. Most of the skin can be classified as thin skin. “Thick skin” is found only on the palms of the hands and the soles of the feet. It has a fifth layer, called the stratum lucidum, located between the stratum corneum and the stratum granulosum.

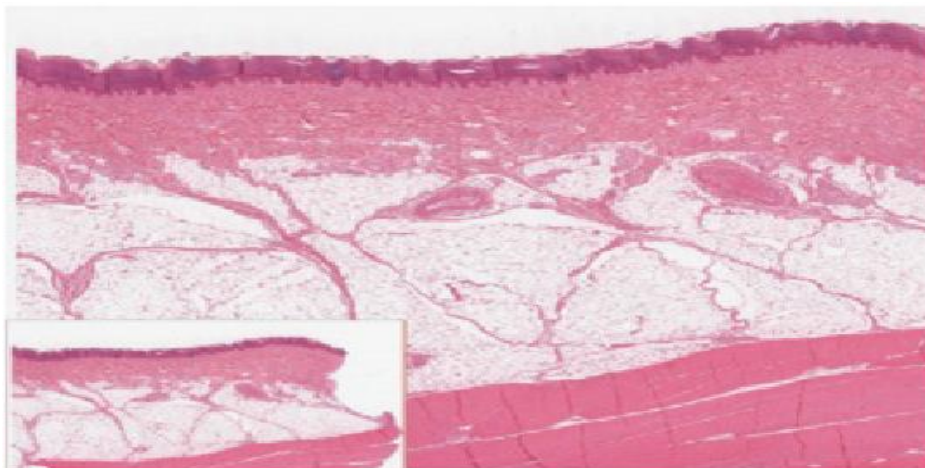


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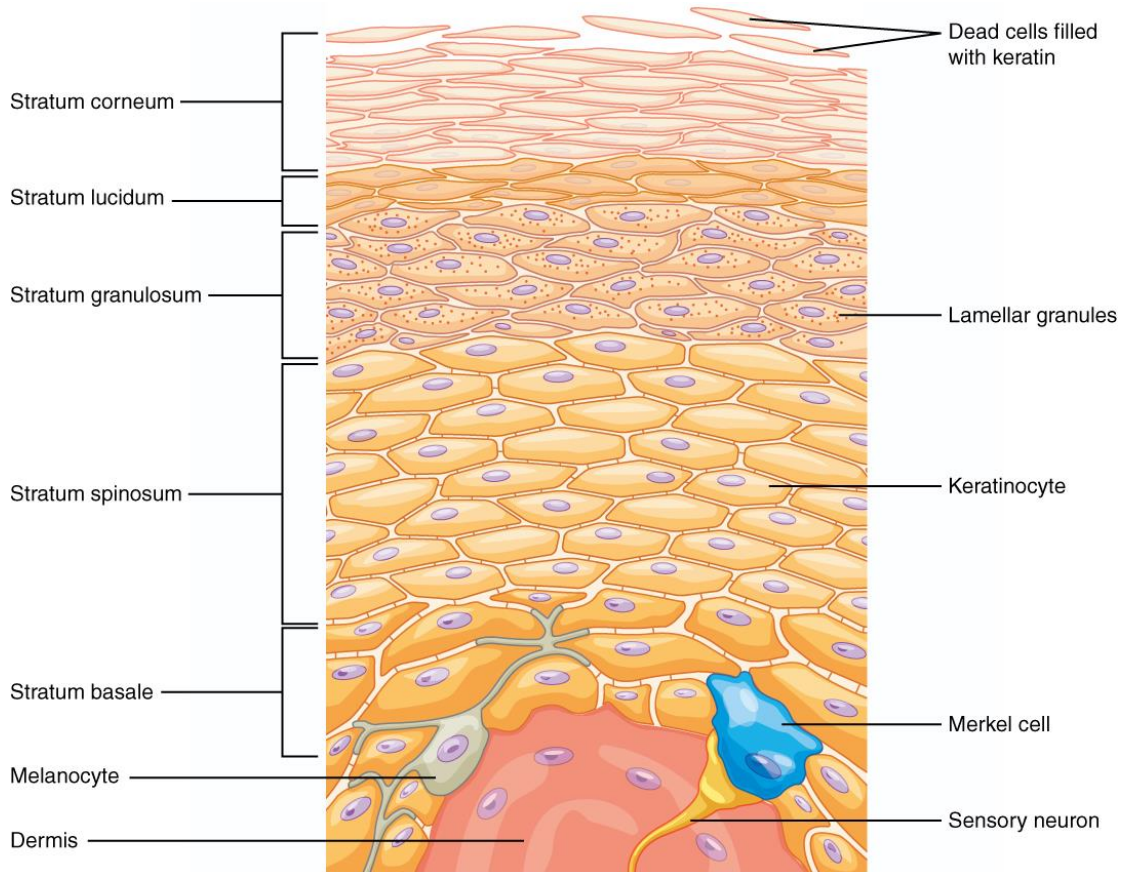
The cells in all of the layers except the stratum basale are called keratinocytes. A **keratinocyte** is a cell that manufactures and stores the protein keratin. **Keratin** is an intracellular fibrous protein that gives hair, nails, and skin their hardness and water-resistant properties. The keratinocytes in the stratum corneum are dead. It regularly slough away, being replaced by cells from the deeper layers .



STRATUM BASALE

The **stratum basale** also called the stratum germinativum. It is the deepest epidermal layer and attaches the epidermis to the basal lamina. The cells in the stratum basale bond to the dermis via the basement membrane. A finger-like projection known as the Dermal papillae increase the strength

of the connection between the epidermis and dermis; the greater the folding, the stronger the connections made .



The stratum basale is a single layer of cells cuboidal-shaped stem cell. All of the keratinocytes are produced from this single layer of cells, which are constantly going through mitosis to produce new cells. As new cells are formed, the existing cells are pushed superficially away. The **Merkel cell**, abundant on the surfaces of the hands and feet, which functions as a receptor and is responsible for stimulating sensory nerves that the brain perceives as touch. The **melanocyte** produces the pigment

melanin which gives hair and skin its color. It protects the living cells of the epidermis from ultraviolet radiation damage.

STRATUM SPINOSUM

The **stratum spinosum** is spiny in appearance due to the protruding cell processes. It joins the cells via a structure called a **desmosome**. The stratum spinosum is composed of eight to ten layers of keratinocytes. Interspersed among the keratinocytes is the Langerhans cell, a type of dendritic cells which functions as a macrophage.

The keratinocytes in the stratum spinosum begin the synthesis of keratin and release a water-repelling glycolipid that helps prevent water loss from the body.

STRATUM GRANULOSUM

The **stratum granulosum** has a grainy appearance. The cells become flatter and they produce large amounts of the proteins keratin, which is fibrous, and **keratohyalin**, which

accumulates as lamellar granules within the cells. These two proteins make up the bulk of the keratinocyte mass giving the layer its grainy appearance.

STRATUM LUCIDUM

The **stratum lucidum** is a smooth thin layer of cells is found only in the thick skin of the palms, soles, and digits. The keratinocytes in this layer are dead and flattened. These cells are densely packed with **eleiden**, a clear protein rich in lipids, derived from keratohyalin.

STRATUM CORNEUM

The **stratum corneum** is the most superficial layer of the epidermis. There are usually 15 to 30 layers of cells in the stratum corneum. This layer helps to prevent the dehydration of underlying tissues, and provides a mechanical protection against abrasion. Cells in this layer are shed periodically and are replaced by cells pushed up from the stratum granulosum and the entire layer is replaced during a period of about 4 weeks.

DERMIS

The **dermis** might be considered the core of the integumentary system. It contains blood and lymph vessels, nerves, hair follicles and sweat glands. It is composed of an interconnected mesh of elastin and collagenous fibers, produced by fibroblasts.



PAPILLARY LAYER

The **papillary layer** is made of loose, areolar connective tissue, which projects into the stratum basale of the epidermis to form finger-like dermal papillae. Within the papillary layer are fibroblasts, adipocytes and an abundance of small blood vessels.

This layer also contains lymphatic capillaries, nerve fibers, and touch receptors called the Meissner corpuscles.

RETICULAR LAYER

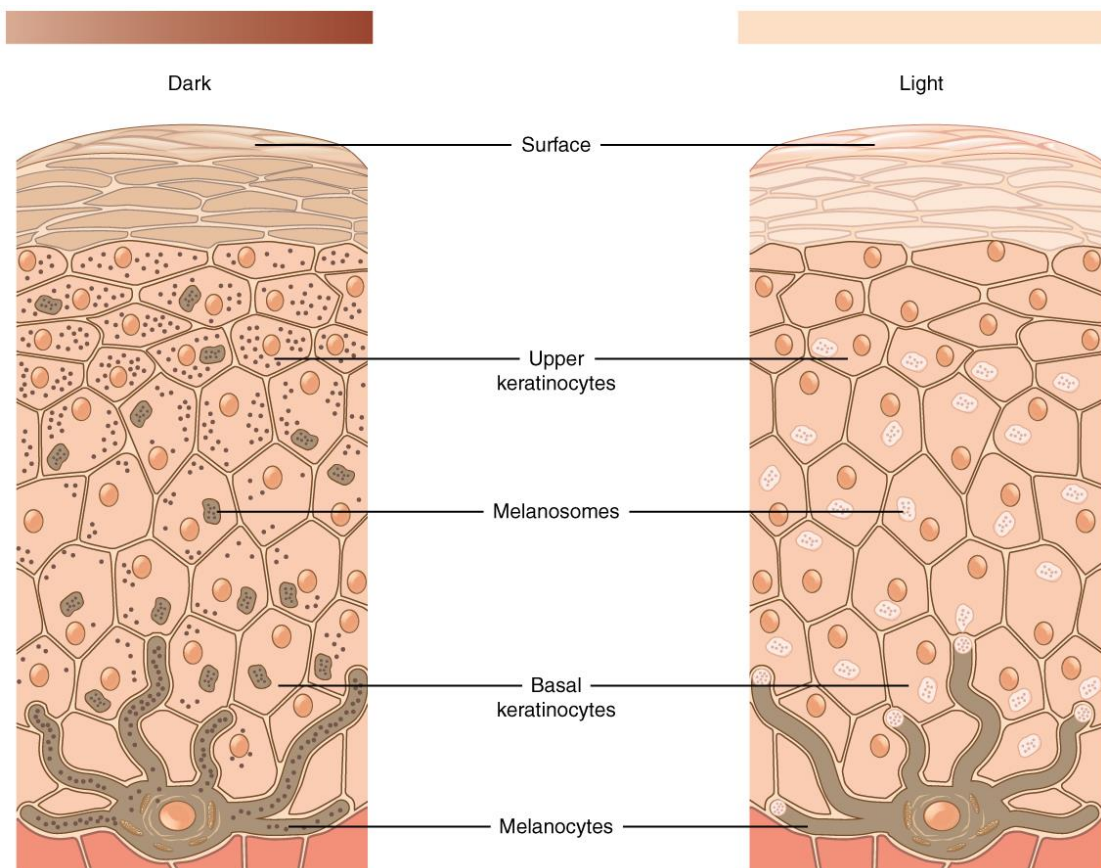
Underlying the papillary layer is the much thicker **reticular layer**, composed of dense, irregular connective tissue, which is well vascularized and has a rich sensory and sympathetic nerve supply. The **Elastin fibers** provide some elasticity to the skin, enabling movement. Collagen fibers provide structure and tensile strength. Collagen also binds water to keep the skin hydrated.

HYPODERMIS

The **hypodermis** is a layer below the dermis and serves to connect the skin to the fibrous tissue of the bones and muscles. The hypodermis consists of well-vascularized, loose, areolar connective tissue and adipose tissue, which functions as a mode of fat storage and provides insulation and cushioning.

PIGMENTATION

The color of skin is influenced by a number of pigments, including melanin, carotene, and hemoglobin. Melanin is produced by cells called melanocytes. Melanocytes are found scattered throughout the stratum basale of the epidermis. The melanin is transferred into the keratinocytes via a cellular vesicle called a **melanosome**.



Melanin occurs in two primary forms. Eumelanin exists as black and brown. Pheomelanin provides a red color. The accumulation of melanin in keratinocytes results in the darkening of the skin. This increased melanin accumulation protects the DNA of epidermal cells from Ultra violet ray damage and the breakdown of folic acid.

It requires about 10 days after initial sun exposure for melanin synthesis to peak. Melanosomes are temporary structures that are eventually destroyed by fusion with lysosomes.

Wrinkling of skin occurs due to the destruction of the cellular structure of the skin. Freckles appear when there is an irregular accumulation of melanocytes in the skin. Moles are larger masses of melanocytes and they should be monitored for changes that might indicate the presence of cancer.

TERMINOLOGY

A graft taken from one part of an individual's body and is transferred to a different part of the body of that same individual is Autograft. A graft from genetically identical donor and recipient individuals is Isograft. A graft taken from another individual of the same species is Allograft. A graft taken from an individual of one species that is grafted onto an individual of a different species is Xenograft.

PROPERTIES OF SKIN GRAFT

Skin grafts have been used to resurface superficial defects. Whether intended for temporary or permanent cover, the transplanted skin protects the host bed from trauma and also provides an important barrier to infection.

Thin split thickness skin grafts have the best take as it requires less vascularity. Full thickness grafts require a well vascularized recipient bed until graft perfusion has been reestablished. Full thickness grafts contract less upon healing, resist trauma better, and generally look more natural after healing than Split thickness skin grafting.

The biologic events that take place in a skin graft and its bed are reviewed by Rudolph and Klein. An ungrafted wound bed is essentially a healing wound which will undergo the typical processes of granulation, contraction, and reepithelialization to seal its surface. These processes are altered by the presence of the graft.

The biochemical changes in a skin graft after placement on a wound bed were studied by Marckmann and noted similarities with normal skin in its response to physical or chemical injury and aging.

EPIDERMIS HEALING

Medawar studied the behavior and fate of healing skin autografts. His findings can be summarized as follows.

HISTOLOGIC ASPECTS

During the first 4 days postgraft - graft epithelium doubles in thickness and shows crusting and scaling of the graft surface. Three cellular processes taking place are
-swelling of the nuclei and cytoplasm of epithelial cells

- epithelial cell migration toward the surface of the graft
- accelerated mitosis of follicular and glandular cells.

Between the fourth and eighth days after grafting, epithelial thickness may increase up to sevenfold, with rapid cellular turnover. At the same time the surface layer of epithelium exfoliates and is replaced by upwardly migrating cells of follicular epithelium at an accelerated rate. By the end of the fourth week postgraft the epidermal thickness has returned to its normal pregraft state.

HISTOCHEMICAL ANALYSIS

In the first few days postgraft, the RNA content of graft epithelial cells changes little . By the fourth day postgraft RNA content increases greatly in the basal layers. The RNA level returns to normal by tenth day. Over the first 2 to 3 days enzymatic activity progressively decreases in split-thickness skin grafts, but as new blood vessels enter the dermis–epidermis junction, the enzyme levels rebound.

DERMIS

CELLULAR COMPONENT

The source of fibroblasts in a skin graft remains obscure. Early investigators believed that these cells came from large mononuclear cells in the blood. Grillo theorized that they originated from local perivascular mesenchymal cells.

Converse and Ballantyne studied cell viability in rat skin grafts by assaying levels of diphosphopyridine nucleotide diaphorase.

FIBROUS COMPONENT

Medawar stated that most of the collagen in an autograft persists through the 40th day after grafting. Hinshaw, Miller, and Cramer concluded that split-thickness and full thickness skin autografts undergo considerable collagen turnover. In their experiments the dermal collagen became hyalinized by the third or fourth day postgraft and by the seventh day all of the collagen was replaced by new small fibers. The replacement continued through the 21st postgraft day and all the old dermal collagen had been completely replaced by 6 weeks. In the first 2-3 weeks

postgraft, the rates of collagen turnover and epithelial hyperplasia peaked simultaneously.

Klein and Peacock used hydroxyproline to determine the collagen content of grafted wounds. Changes in hydroxyproline and monosaccharide content of grafted beds paralleled those of other healing wounds. Independent studies by Hilgert and Marckmann confirmed these findings. Although Hilgert's cycle lasted 10 days and Marckmann's 14–21 days.

On the basis of studies involving tritiated proline-labeled mature collagen, Udenfriend and Rudolph and Klein agreed that 85% of the original collagen in a graft is replaced within 5 months postgraft. The collagen turnover rate of grafts is 3 to 4 times faster than that of unwounded skin.

Elastin fibers in the dermis account for the resilience of skin. While the elastin content of the dermis is small, the elastin turnover rate in a healing graft is considerable. Elastin fiber integrity is maintained through the third postgraft day, but by postgraft day 7 the fibers are short, stubby, and have begun to fragment. Elastin degeneration continues through the third

postgraft week until new fibers can be seen beginning to grow at 4–6 weeks postgraft. This replacement process is the same in full- and split thickness skin grafts.

EXTRACELLULAR MATRIX

The extracellular matrix plays a vital role in cell to cell communication. The extracellular matrix in the skin consists of insoluble proteins of fibroblast origin and smaller soluble proteins produced by either fibroblasts or keratinocytes.

EPITHELIAL APPENDAGES

The number of sweat glands transplanted during grafting and of the extent of sympathetic reinnervation to the graft determines the sweating ability of the grafted skin. A skin graft will sweat much like its recipient site. Thus a graft that is placed on the abdomen will sweat in response to physical activity, whereas an identical graft placed on the palm will sweat in response to emotional stimuli.

Although both full and split thickness skin grafts demonstrate sebaceous gland activity, thin split thickness grafts do not contain functional sebaceous glands and typically appear

dry and brittle after take.

Hair follicles are subjected to the same hyperplastic stimuli as the rest of the graft. On the fourth day postgraft the original hair sloughs off and the graft becomes hairless. Soon after the graft follicles begin to produce new hair, and very fine, baby-like hair is seen growing out of the graft by 14th postgraft day.

Full-thickness skin grafts produce hair while split thickness skin grafts produce little or no hair. Inadequate revascularization will damage the graft hair follicles and result in decreased hair density. When graft take is interrupted for any reason, subsequent hair growth will be sparse, random, and lacking in pigment.

GRAFT TAKE

The large array of physiologic events usually seen in a healing skin wound are altered and modified by placement of a graft. The success of a graft depends primarily on the extent and speed at which vascular perfusion is restored.

Given equal clinical and technical conditions, two qualities

of a skin graft influence its fate. The first determinant is the blood supply of the skin from which the graft was obtained. A graft harvested from a highly vascular donor site will predictably heal better. The second factor is the metabolic activity of the skin graft at the time of application, which will dictate its tolerance to the inevitable period of ischemia.

Skin graft take occurs in three phases. The first phase consists of plasmatic imbibition and lasts 24–48 hours. This is followed by an inosculatory phase and a process of capillary ingrowth.

PLASMATIC IMBIBITION

Hinshaw and Miller and Pepper believed that plasmatic imbibition is nutritionally important. Clemmesen Converse, and Peer thought that it merely prevents the graft from drying out and keeps the graft vessels patent in the early postgraft period.

- The graft is ischemic for an undetermined period of time that varies according to the wound bed 24 hours for a graft placed on a bed that is already proliferative; 48 hours for a graft covering a fresh wound.

- Grafts placed on poorly vascularized beds will be ischemic for a longer time. Thick Full thickness skin graft seem to tolerate ischemia for up to 3 days while thin Full thickness skin graft survive for up to 5 days. Split thickness grafts take well even after 4 days of ischemia.

- Grafts gain weight during the phase of plasmatic imbibition, adding as much as 40% to their pregraft weight through fluid movement from bed to graft. The origin of graft edema is believed to be the same as that of inflammatory edema.

INOSCULATION AND CAPPILARY INGROWTH

At the end of 48 hours, a fine vascular network is established in the fibrin layer between the graft and its recipient bed. Capillary buds from the blood vessels in the recipient bed make contact with the graft vessels. Blood flow is established and the skin graft becomes pink.

REVASCULARISATION

Three theories have been put forth to explain graft revascularisation

Connection of graft and host vessels.

The first theory holds that after the inosculatory event, the definitive vasculature of a graft consists of the blood vessels originally present within the graft. Circulation is restored in a graft via the original skin graft vessels by inosculation.

Clemmesen, working on a porcine model, injected India ink into the host vessels of the autograft. No ink was seen within the graft on the first postgraft day, but on day 2 a number of graft vessels contained India ink, suggesting communication between the host and graft vessels. After the second day many graft vessels contained India ink. Initially a fine fibrin mesh linked the graft to the bed. After the first 4 days this meshwork became lined with endothelial cells and linked up with the vessels of the graft.

Haller and Billingham too noted that the pattern of vessels in the healed graft was the same.

Formation of new vascular channels. The second theory of graft revascularization is that the graft is perfused through new vessels going from the recipient bed into the transplanted graft.

Converse and Rapaport studied skin grafts in humans and noted the inosculatory event after which there was active invasion of the graft by host vessels to produce the definitive vasculature of the graft.

Converse concluded on the basis of a study on rat model using diaphorase activity that the final vasculature of a graft stemmed from ingrown vessels from the host bed. Degenerative changes in the original graft vasculature were apparent in the first 4 days postgraft, as evidenced by progressive loss of diaphorase activity during this time. With subsequent vessel ingrowth there was return of diaphorase activity.

Wolff and Schellander measured ATP activity to evaluate return of circulation in porcine skin grafts correlated well with the pattern of new vessel ingrowth.

Zarem et al theorized based on the study on mice that preexisting graft vessels served only as nonviable conduits

through which the endothelium of the ingrowing vessels progressed. The original graft vessels degenerated concomitantly and at the same rate, leaving only those vessels growing from the recipient bed as the graft's definitive vasculature.

Combined old and new vessels. Smahe and Tsukada proposed a third hypothesis of graft revascularization. In any graft, old vessels may be recycled and new ones may grow to variable degrees. These events occurs as consecutive stages in the interaction between the graft and its bed.

The two methods of skin graft revascularization - primary and secondary.

Primary revascularization Under the scanning electron microscope it can be seen that no real circulation to the graft exists for the first 6 to 7 days postgrafting. There is only sluggish flow in the graft and this manifests as cyanotic discoloration and is particularly noticeable in full-thickness skin grafts.

In the normal course of events circulation in a skin graft is reestablished through inosculation. Blood enters the graft through these newly formed vascular connections and the graft turns pink. A pink color is generally considered a sign of probable graft survival.

The old vessels of the graft are dilated and denervated. Blood vessels from the recipient bed attach to both arteries and veins of the graft. Blood and tissue fluids moving into the graft are trapped there and unable to return to the bed because of inadequate reverse circulation.

The newly formed vascular connections differentiate into afferent and efferent vessels between 4 and 7 days postgraft, and other vessels retain their capillary like character or simply disappear. At this point, blood flow is restored within the graft.

Secondary revascularization When vascular connection between the bed and the graft are delayed, secondary revascularization occurs. The longer a graft remains ischemic, the longer the vasoactive substance remains in the tissue. A great numbers of new capillaries grow into the graft and

granulation tissue accumulates under the graft. This phenomenon is known as secondary revascularization.

The mechanism of secondary revascularization is that the vascular connections between the graft bed and the graft inhibit the formation of capillary buds. If the graft is not well applied to the bed and vascular connections are not established. Within the graft itself the vessels may be functionally deficient and may not reach the required level of biologic activity for the inosculatory event. If anastomoses fail to develop in time, the ischemic period is extended and capillary proliferation in the bed continues. If blood vessels reach the graft in time, the graft will survive and if not, the graft will fail.

The two causes of delayed wound healing are insufficient vascular proliferation in the host bed and wound contamination. Anastomoses may not form at the right time due to increased distance between the graft and its bed from interposed necrotic material, hematoma, seroma, or air bubbles.

Grafts that heal by secondary intention are smooth, fibrotic, tight, and have a slick, silvery sheen on the surface.

Large grafts often heal both by primary and secondary revascularization.

Histologically the epidermis and papillary dermis are destroyed by necrosis in the full-thickness graft that heals by secondary revascularization. The papillary dermis is replaced by a thin layer of connective tissue and it is covered by a flattened epidermis. The reticular dermis is normal histologically. Hinshaw and Miller noted accelerated collagen turnover in pig autografts which healed by secondary revascularization.

SKIN GRAFT TECHNIQUES

DONOR SITE SELECTION AND GRAFT HARVEST

- The selection of a graft donor site is based on these factors
- whether a full thickness skin graft or a split thickness skin graft is to be used
 - whether the intended donor site matches the recipient bed in colour
 - potential morbidity of graft harvest at that site.

An appropriate colour match is particularly important in

head and neck reconstruction with skin grafts. Any skin graft taken below the clavicles and applied above the clavicle will result in a lifelong colour mismatch. Both full and split thickness skin grafts can be harvested above the clavicle. Skin graft harvested from the submental is a good source of graft. For Full thickness defects above the clavicle, tissue expansion is recommended to recruit an adequate volume of Full thickness skin grafts.

Graft reconstruction of the nasal tip requires specialized skin of similar thickness and pore size. The glabella provides skin of such thickness. The donor sites for nasal tip grafting have included the concha, nasolabial fold, pre and postauricular skin, the neck, and supraclavicular areas.

Donor sites should be carefully chosen to avoid hair bearing skin and to camouflage the resulting scar to minimize morbidity from graft harvest. Tiem advocates a bilaminar harvest also known as the trapdoor technique, whereby an epithelial flap is raised, a dermal graft is taken, and the superficial layer is replaced in its original site.

Beck and colleagues compared the trapdoor technique with standard elliptical excision in patients (60 graft sites). Although both techniques were successful and had minimal complications, “the elliptical method [was associated with] less discomfort, texture change, numbness, and itching. The scars were concealed better and less noticeable.”

Common full thickness graft donor sites are the groin, postauricular area and clavicular region. Split skin grafts are usually harvested from the outer thigh.

GRAFT SIZING AND EXPANSION

Skin grafts sizing is usually decided using preformed templates of easily available materials, such as cardboard and latex. The cutout is then applied over the donor site, traced with a marking pen. A graft of the outlined area is resected.

A wound is reepithelialized from the edges toward the center. With graft expansion, larger areas can be covered with smaller sections of skin.

Various techniques to expand skin for grafting have been described including - Pinch grafts, Relay transplantation, Meshing, Meek island grafts, Microskin grafts and the Chinese technique of intermingling autografts and allografts.

A pinch graft breaks up a whole graft of skin into tiny pieces to increase the edge area. Pinch grafts are reported to be effective in treating small to medium sized wounds.

Relay transplantation consists of cutting a graft into strips. After 5 to 7 days, the original strips are removed and transplanted, leaving the epithelial explants in place. This process may be repeated up to 4 times.

Meshing is the term used for cutting slits into a sheet of graft and this causes stretching of the graft. Advantages of the Meshed grafts

- meshed grafts will cover a larger area than non meshed grafts
- the contour of the meshed graft can be adapted to fit in a regular recipient bed
- blood and exudate can drain freely

- in the event of localized bacterial contamination, only a small area of meshed graft will be affected
- meshed graft offers multiple areas of potential reepithelialization.

The main disadvantages of meshed grafts are the considerable surface area that must heal by secondary intention. Pulling the graft lengthwise to narrow the skin perforations to slits before transplantation lessens these problems.

The Meek technique involves a special dermatome. Meek grafts are useful alternatives to meshed grafts when donor sites are limited and are particularly well suited for grafting granulating wounds and unstable beds.

Intermingled transplantation of autograft and allograft, successfully in China since 1973, mostly in the treatment of large burns. This technique has significantly less scar contracture.

GRAFT FIXATION

Graft fixation occurs in two phases.

Phase 1 - begins immediately after grafting. It lasts about 72 hours. During this time the graft remains adherent to the bed by the formation of fibrin bond.

Phase 2 - coincides with the onset of fibrovascular ingrowth and vascular anastomoses between the graft and the host.

Foam gauze is used for securing skin grafts to wounds on the shoulder and face. Lyofoam is a semipermeable, nonwoven polyurethane foam dressing. The foam is easy to apply directly on the graft and is biologically inert and it retards bacterial colonization.

Another simple and versatile and rapid technique opted by Johnson, Fleming and Avery consisting of staples and latex foam dressing to secure skin grafts. Wolf and coworkers confirmed the effectiveness of rubber foam with staple fixation in various patterns to provide even pressure distribution on skin grafts.

Amir et al modify a cutoff disposable syringe to affix the silk threads of their graft dressings. Cheng and colleagues use a disk cut from the bottom of an IV infusion bottle on which multiple radial slits are made in the perimeter for tying the sutures holding the graft.

Modern bolster technologies of skin graft fixation replace sutures and staples with either fibrin glue or octyl-2-cyanoacrylate. Fibrin glue does not interfere with healing and at the same time does not promote wound infection. Fibrin glue produces better esthetic results. A thin layer of fibrin glue improves graft take in the head and neck and mobile body parts.

CELLUTOME EPIDERMAL HARVESTING

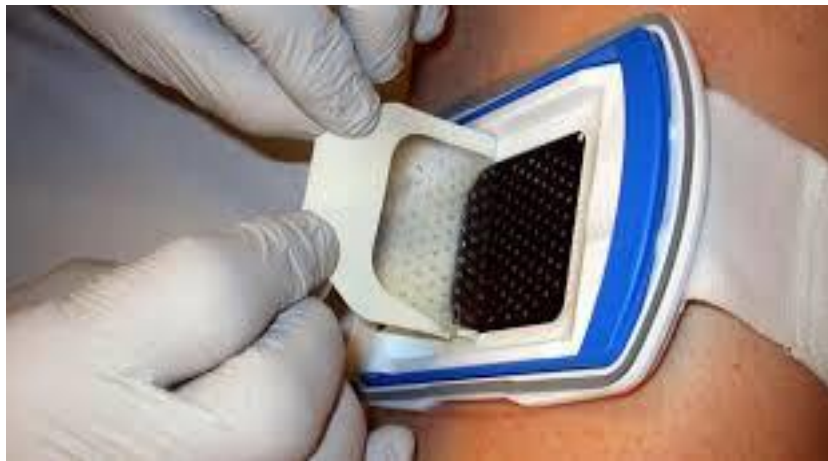
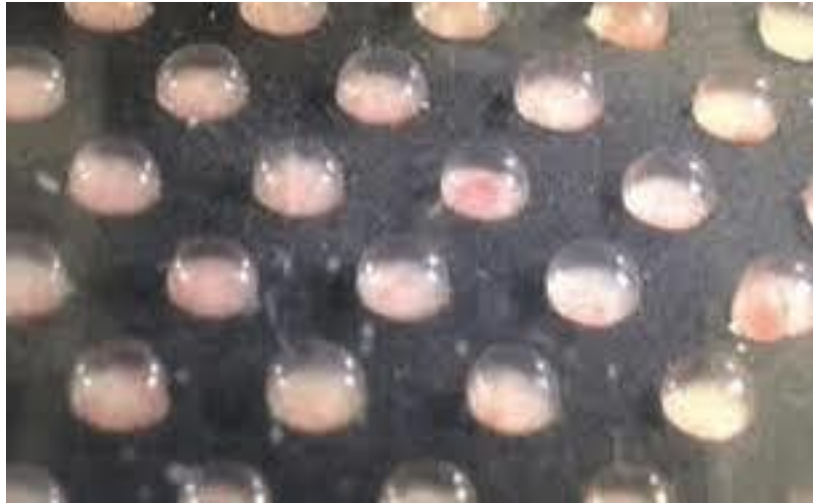
A new and automated system for epidermal harvesting, the CELLUTOME has been utilized for the treatment of acute and chronic wounds. The system consists of

- Control unit
- Vacuum head
- Harvester that is applied to intact skin on the donor site





This system simultaneously warms the skin at a temperature of 40 degrees Celsius and administers a negative pressure of 200 mmHg to harvest. This works on the principle of thermal suctioning. Both a smaller harvester that creates 42 epidermal microdomes and a larger harvester that creates 128 epidermal microdomes. The harvesting time ranges from 15 to 60 minutes, on average lasting 30 minutes depending on various host factors. The epidermal grafts are then transferred to the recipient site via transparent adhesive film dressing and secured in place with compression wraps. The donor site is covered with a transparent film dressing.



These small microdomes are cleaved consistently through the lamina lucida. This method retains the original structure of the keratinocyte. The proliferative activity of the basal keratinocytes that secrete various factors important for wound healing is maintained. The factors secreted are vascular endothelial growth factor (VEGF), transforming growth factor-alpha (TGF-a),

platelet-derived growth factor (PDGF), hepatocyte growth factor (HGF) and granulocyte colony stimulating factor (G-CSF) .

This Epidermal Harvesting System has also been used successfully on several patients with chronic wound including wounds due to venous insufficiency, pyoderma gangrenosum, sickle cell disease, post-surgical wounds, and traumatic wounds and patients with auto immune connective tissue disorder.

MECHANISM

Skin grafts take through three phases. The first phase is plasmatic imbibition phase - when the transplanted tissue absorbs wound fluid and gains up to 40% weight during the first 24 hours . The second phase is the inoscularity phase, where anastomoses between donor and recipient skin are formed, and occurs two to three days post grafting . The third phase is the revascularization phase, where there is vascular proliferation within both the donor and recipient tissues .

A new phase proposed in epidermal grafting is called the keratinocyte activation phase. After engraftment, the keratinocytes are “activated”. Keratinocytes become proliferative and they express cell-matrix adhesion proteins- beta 1 integrin. In a study by Yamaguchi et al., all grafts took well and after engraftment, immunohistochemical analysis was performed for Ki67, a marker of cell proliferation and beta 1 integrin. Beta 1 integrin has been shown to be a marker of cell-matrix adhesion and is upregulated at the edge of a wound healing site. They found an upregulation of Ki67 and beta 1 integrin in epidermal graft and split thickness skin graft treated wounds, as compared to low expression in Full thickness skin graft. The expression of beta 1 integrin was found in more layers for wounds treated with epidermal grafts as compared to Split thickness skin graft. These results support that the activation of keratinocytes may be mediated by the interaction between epidermis and dermis, leading to production of important growth factors in wound healing.

The importance of an epithelial-mesenchymal interaction in wound healing between the grafted epidermis and recipient dermis has been demonstrated in the treatment of palmoplantar wounds . Palmoplantar skin is more resilient with high levels of keratin 9. On the other hand, grafts applied from nonpalmoplantar sites result in poor cosmetic outcomes and grafts from these sites tend to be less durable and more at risk for erosions and ulcerations. The ideal graft for these sites would be one with similar features to palmoplantar epidermis, and previous studies have shown that culture of palmoplantar fibroblasts with nonpalmoplantar keratinocytes resulted in expression of keratin 9 . Therefore, it was postulated that the dermal cells can interact with the epidermal cells in such a way as to transform their protein expression to behave more like that of the recipient site.

In further evaluation, Yamaguchi et al. treated palmoplantar wounds with epidermal sheets and Split thickness skin graft, both derived from non palmoplantar sites . The Split thickness skin graft retained its non palmoplantar phenotype

with hyperpigmentation and hyperkeratosis whereas the epidermal graft demonstrated adoption of palmoplantar phenotype with hypopigmentation. This was supported on histology as the areas treated with Split thickness skin graft showed acanthosis and elongation of saw-tooth rete ridges. Those treated with epidermal graft showed thick stratum corneum and acanthosis similar to normal palmoplantar epidermis. As well, immunohistochemistry was performed for keratin 9, which was negative in the epidermis of wounds treated with Split thickness skin grafting and positive in wounds treated with epidermal grafting. This demonstrates the direct interaction between epidermis and dermis, leading to transformation of the donor site to be more consistent with the recipient site.

Keratinocyte activation and epithelial - mesenchymal interaction contributes to the success of Epidermal grafting by production of appropriate growth factors and pro-healing cytokines. The major effect of healing is through stimulation of epithelialization from the edge of the ulcer and is thought to be

mediated by growth factors produced by grafted keratinocytes .
In a study by Costanzo et al. of 29 chronic, non-healing ulcers on the lower extremities treated with autologous epidermal grafting, they observed an increase in re-epithelialization from the wound edge.

OBJECTIVES

- To compare the efficacy and clinical outcome of Epidermal graft and Split skin grafting in wound healing in our institute

- To assess time period for healing in donor site, pain score as reported by patients in numerical rating scale(0-10)

MATERIALS AND METHODS

METHODOLOGY

This is a Prospective randomised study that compares the efficacy and wound healing mechanism of Epidermal grafting with Split skin grafting. The primary outcome measures proportion of wound that heals in 6 weeks and donor site healing time. The secondary outcome measures pain score and patient satisfaction. Written informed consent will be obtained from all subjects before enrollment in study. Patients will be randomly allotted into two equal groups. Group A will undergo epidermal grafting as treatment modality for wound healing. Group B will undergo Split skin grafting as the treatment modality for wound healing. Split skin grafting done using Humby knife and Epidermal graft done using epidermal harvesting system. All patients will be reviewed at 1st week , 2nd week, 4th week and 6th week post operatively.

SAMPLES OF SLPIT SKIN GRAFTING PATIENTS

Split skin grafting is done using humby's knife under spinal/regional anesthesia.



A) HUMBY'S KNIFE



B) DONOR SITE GRAFT HARVESTING



C) GRAFT FIXED TO RECIPIENT SITE



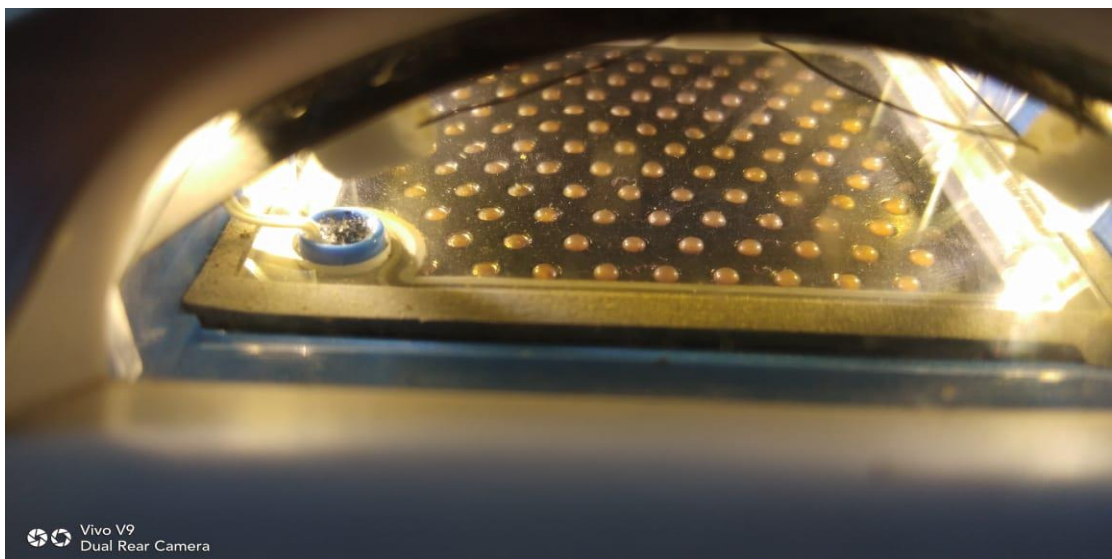
D) HEALED DONOR SITE

EPIDERMAL SKIN GRAFTING

Epidermal skin grafting is done using cellulome epidermal skin harvester 'without anesthesia' on day care basis



A) EPIDERMAL HARVESTING SYSTEM



B) EPIDERMAL GRAFT HARVESTING USING CELLUTOME



C) HARVESTED EPIDERMAL SKIN



D) RECIPIENT AREA



E) GRAFT FIXED TO RECIPIENT SITE



F) HEALED RECIPIENT SITE AT 4th WEEK



G) DONOR SITE AT 1ST WEEK



H) RECIPIENT AREA



I) RECIPIENT AREA



J) RECIPIENT SITE AT 4 WEEKS

ANALYSIS AND DISCUSSION OF STUDY

AGE DISTRIBUTION

The mean age of the participants is 44.12 years (S.D=11.89 years) in the epidermal grafting group while the mean age of the participants is 41.64 years (S.D=12.55 years) in the split skin graft group. The following figure shows the comparison of the age distribution between the two groups.

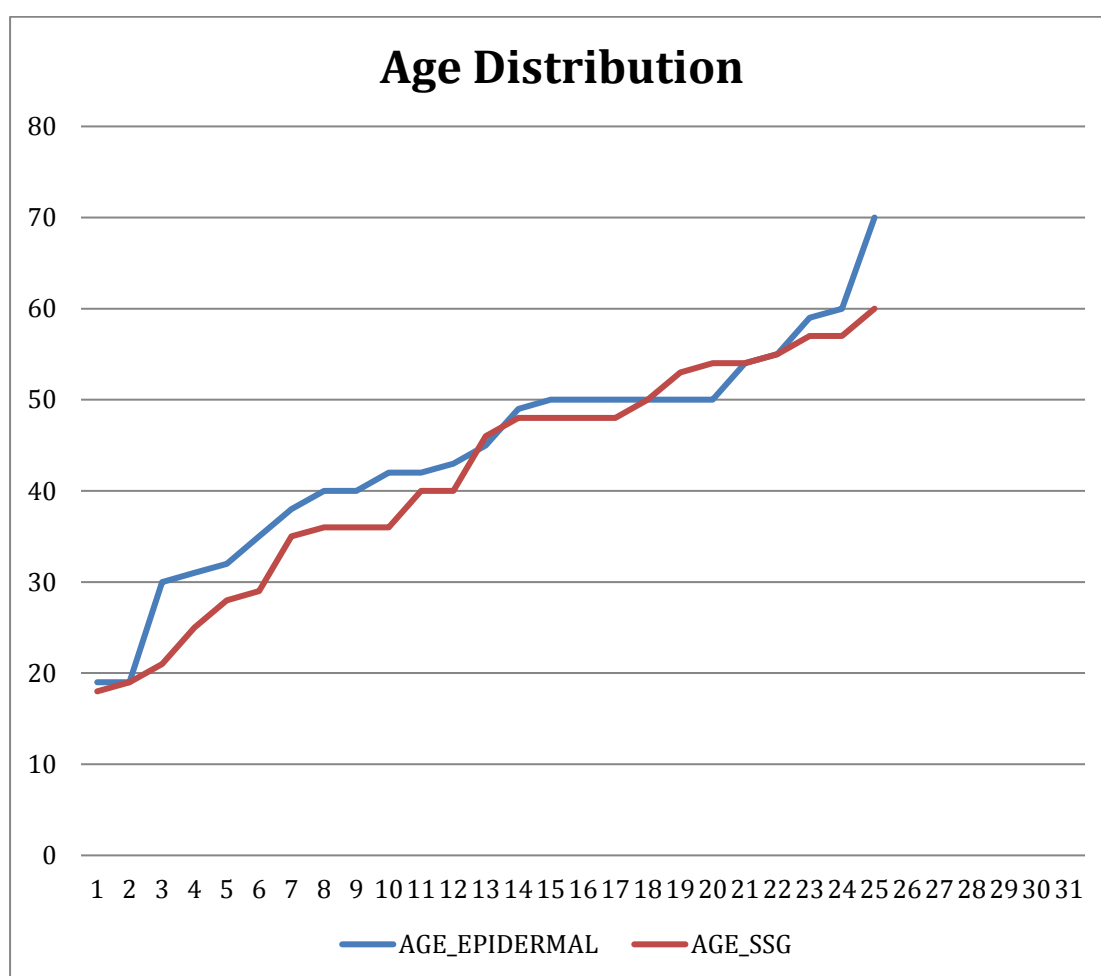


Figure 1: Age distribution of the two groups

GENDER DISTRIBUTION

In the epidermal grafting group, the number of males was 18 (72%) and females were 7 (28%). In the Split Skin Grafting Group, the number of males was 20 (80%) and females were 5 (20%).

	Epidermal Grafting Group		Split Skin Grafting Group	
	Male	Female	Male	Female
Frequency	18	7	20	5
Percentage	72	28	80	20

Table 1: Gender Distribution

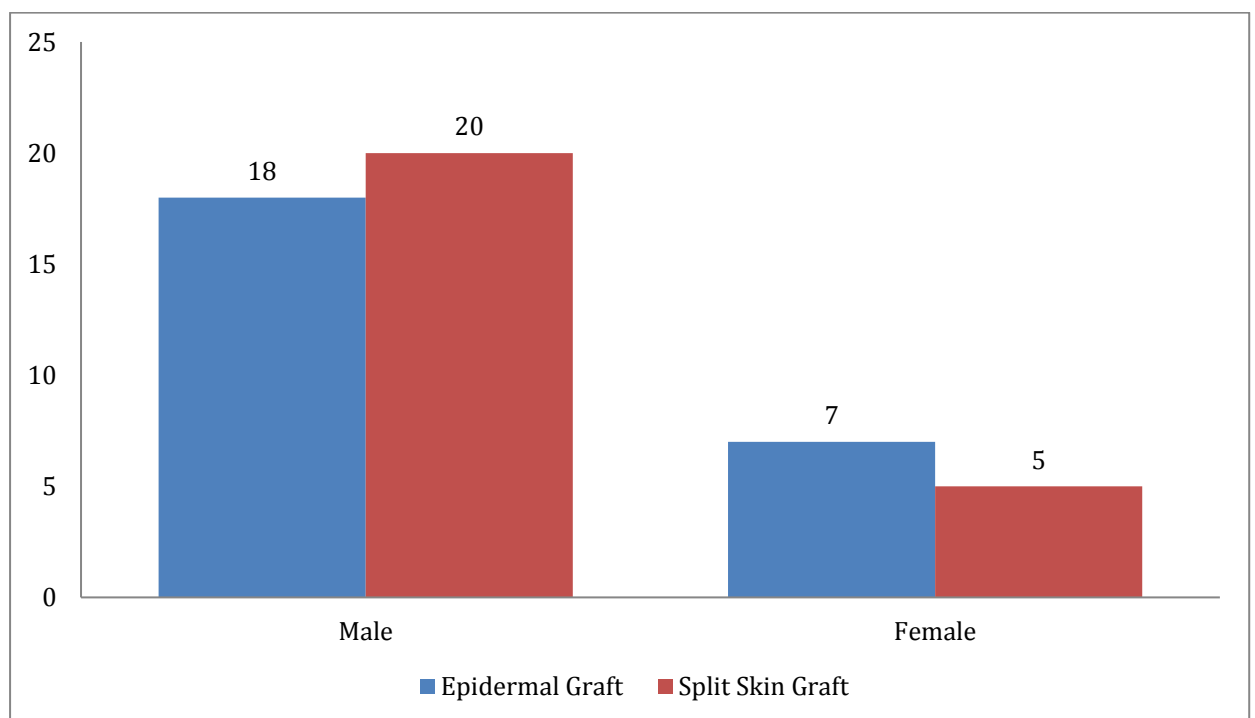


Figure 2: Gender Distribution

DIAGNOSIS

The following tables show the diagnosis of the patients in the two groups.

Epidermal Grafting Group

Diagnosis	Frequency
Post Infective Raw Area-Left Thigh	2
Post Infective Raw Area – Left Leg	7
Post Infective Raw Area –Right Foot	3
Post Infective Raw Area -Back	1
Post Infective Raw Area –Left Foot	2
Post Infective Raw Area –Left Side Neck	1
Post Infective Raw Area –Right Leg	2
Post Traumatic Raw Area –Right Leg	2
Post Traumatic Raw Area –Left Forearm	1
Post Traumatic Raw Area –Left Leg	2
Post Traumatic Raw Area –Left Arm	1
Post Traumatic Raw Area –Left Foot	1

Table 2: Diagnosis of Epidermal Group

Split Skin Grafting Group

Diagnosis	Frequency
Post Infective Raw Area –Left Thigh	2
Post Infective Raw Area – Left Leg	7
Post Infective Raw Area –Right Foot	3
Post Infective Raw Area -Back	1
Post Infective Raw Area –Left Foot	2
Post Infective Raw Area –Left Side Neck	1
Post Infective Raw Area –Right Leg	2
Post Traumatic Raw Area –Right Leg	2
Post Traumatic Raw Area –Left Forearm	1
Post Traumatic Raw Area –Left Leg	2
Post Traumatic Raw Area –Left Arm	1
Post Traumatic Raw Area –Left Foot	1

Table 3: Split Skin Grafting Group

COMORBIDITIES

Around 48% in the epidermal grafting group and around 52% in the split skin grafting group did not have any comorbidity. The following table shows the comorbidity among the two groups.

Comorbidity in Epidermal Grafting Group	Frequency (percentage)
Nil	12 (48%)
Diabetes Mellitus=II	10 (40%)
Hypertension and Diabetes Mellitus-II	1 (4%)
Hypothyroidism and Diabetes Mellitus-II	1 (4%)
Tuberculosis and Diabetes Mellitus-II	1 (4%)

Table 4: Comorbidity in Epidermal Grafting Group

Comorbidity in Split Skin Grafting Group	Frequency (percentage)
Nil	13 (52%)
Diabetes Mellitus=II	11 (44%)
Hypertension and Diabetes Mellitus-II	1 (4%)

Table 5: Comorbidity in Split Skin Grafting Group

DURATION OF WOUND (IN WEEKS)

The mean duration of wound in weeks is 3.24 weeks in the epidermal grafting group (S.D=0.86 weeks) while the mean duration of wound in the split skin grafting group is 3.4 weeks (S.D=1.01 weeks).

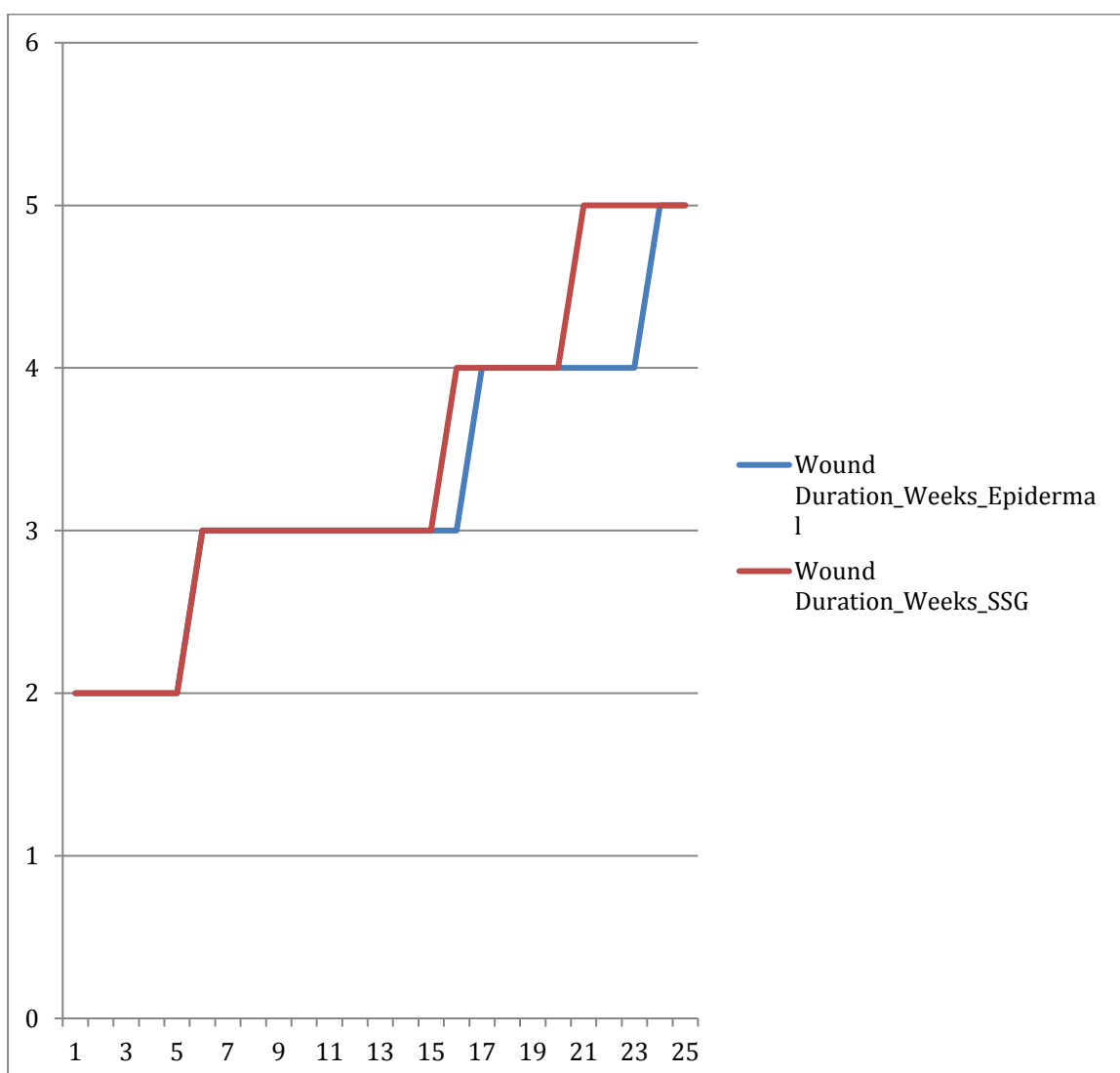


Figure 3: Duration of wound in weeks

DONOR SITE PAIN AT WEEK ONE USING THE VISUAL ANALOGUE SCALE

In the epidermal grafting group, the donor site pain score is zero while in the Split Skin Grafting Group, the mean donor site pain at week one is 5.4 (S.D=0.8). Donor site Pain is better in the epidermal grafting group.

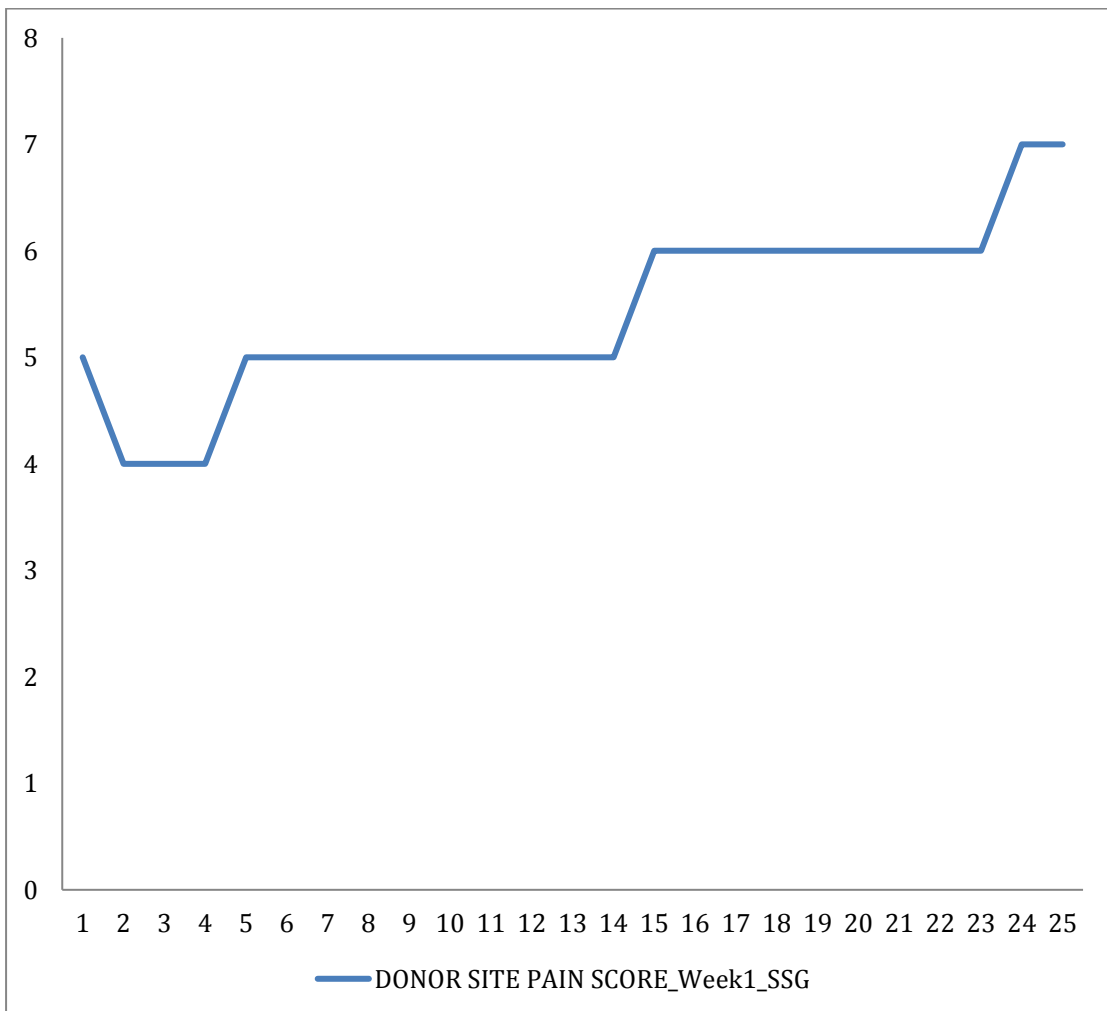


Figure 4: Donor site pain score in SSG group on week one

DONOR SITE HEALING AT WEEK TWO

In the epidermal grafting group, the mean donor site healing is 98.28% (S.D=1.46%) while in the Split Skin Grafting Group, the mean donor site healing is 86% (S.D=4.9%). Donor site healing is better with epidermal grafting group. Student t-test shows a value of 8.76 with a p-value=0.00143 ($p < 0.005$) which is highly significant.

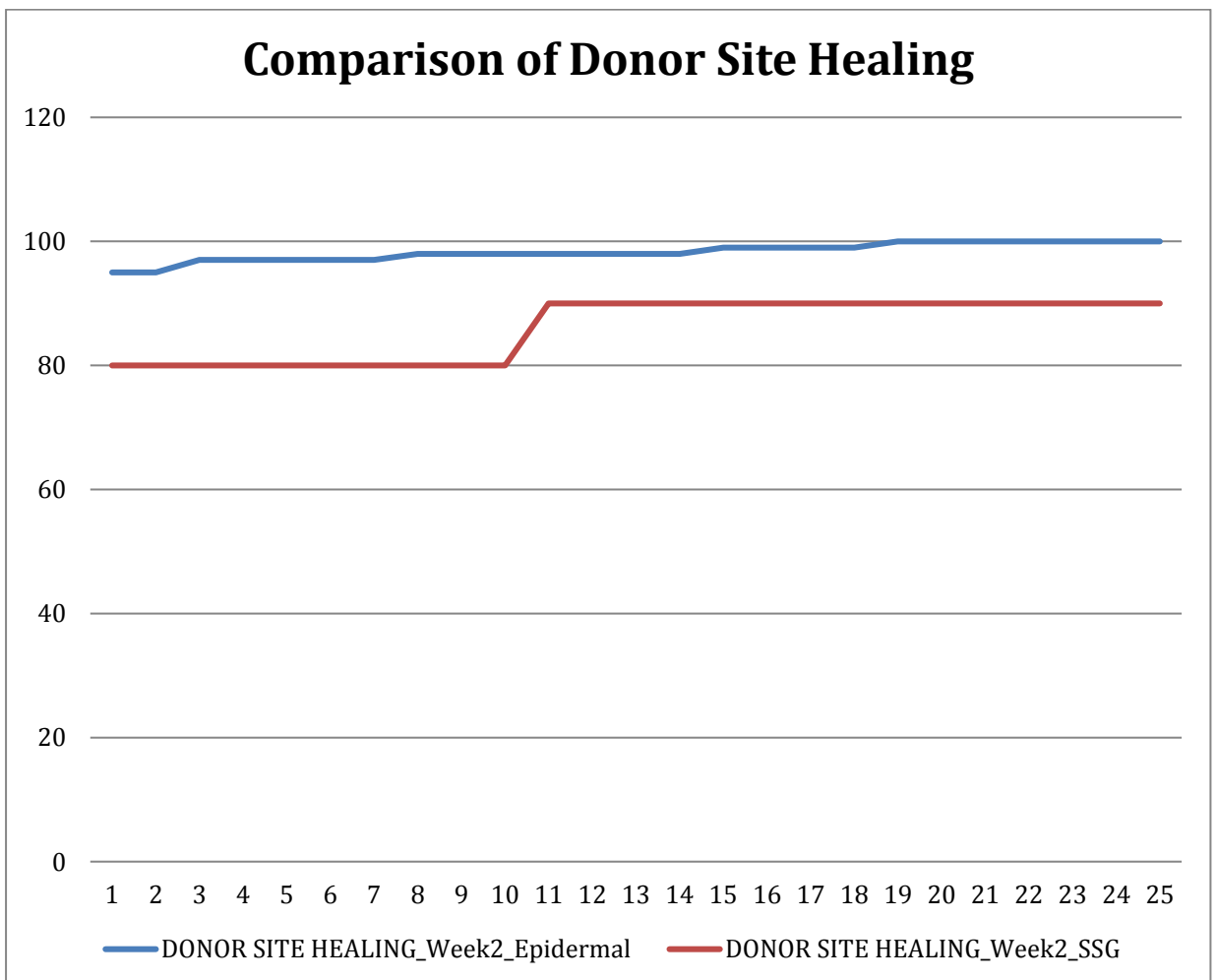


Figure 5: Comparison of Donor Site Healing among the two groups

EPITHELIALISATION OF GRAFT AREA AT 6TH WEEK

The following figures show the epithelialisation of the graft area in first week, fourth week and sixth week. The two groups do not significantly differ in the epithelialisation of the recipient area in the follow-up period.

Epithelialisation of the graft area Mean Percentage (S.D)	Week 1	Week 4	Week 6	ANOVA p-value
Epidermal Grafting Group	47.2 (7.2)	95 (4.47)	100	6.19 P=0.65 Not Significant
Split Skin Grafting Group	89.8 (4.3)	94.4 (4.54)	100	

Table 6: Comparison of epithelialisation across first, fourth and sixth weeks

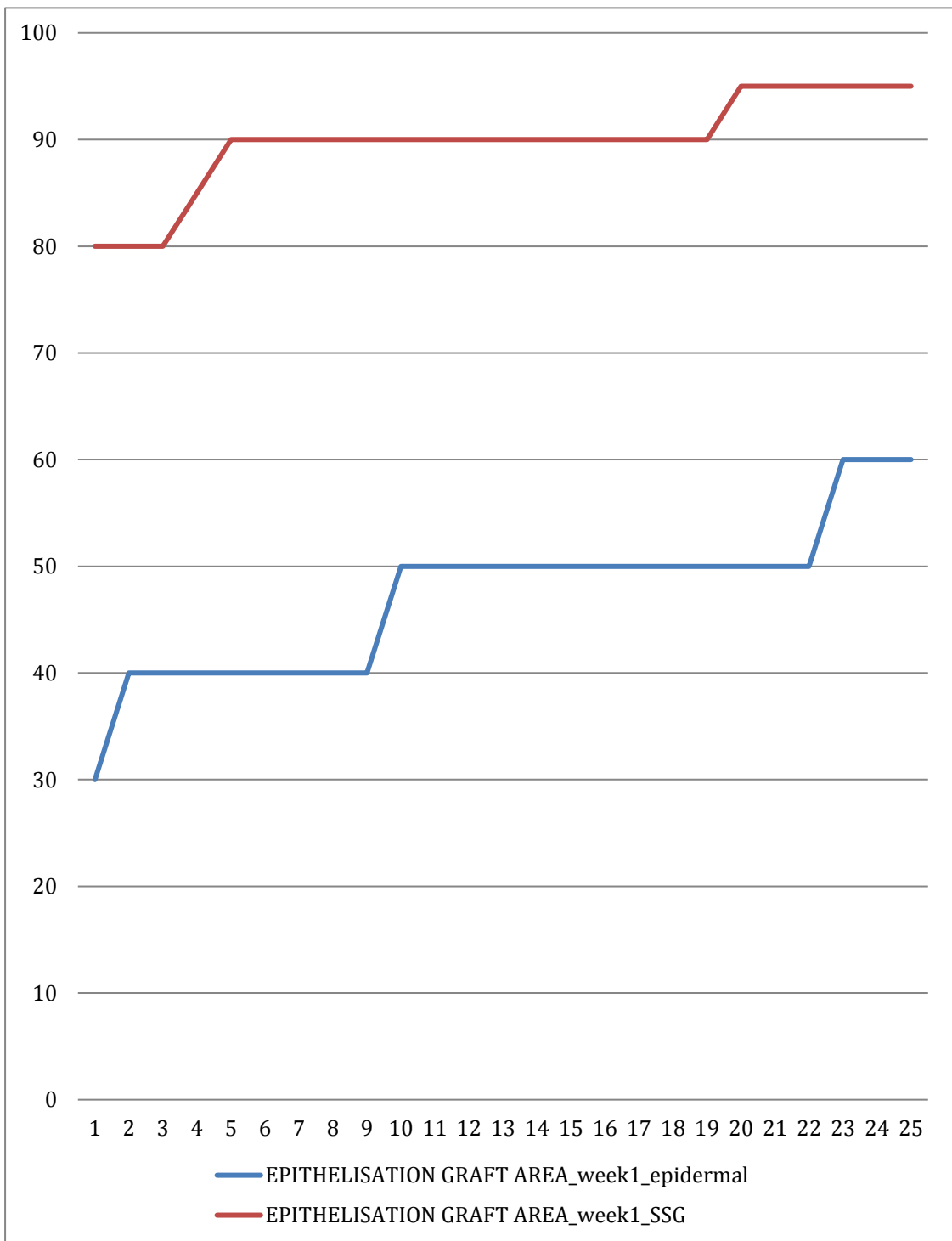


Figure 6: Comparison of epithelisation by first week

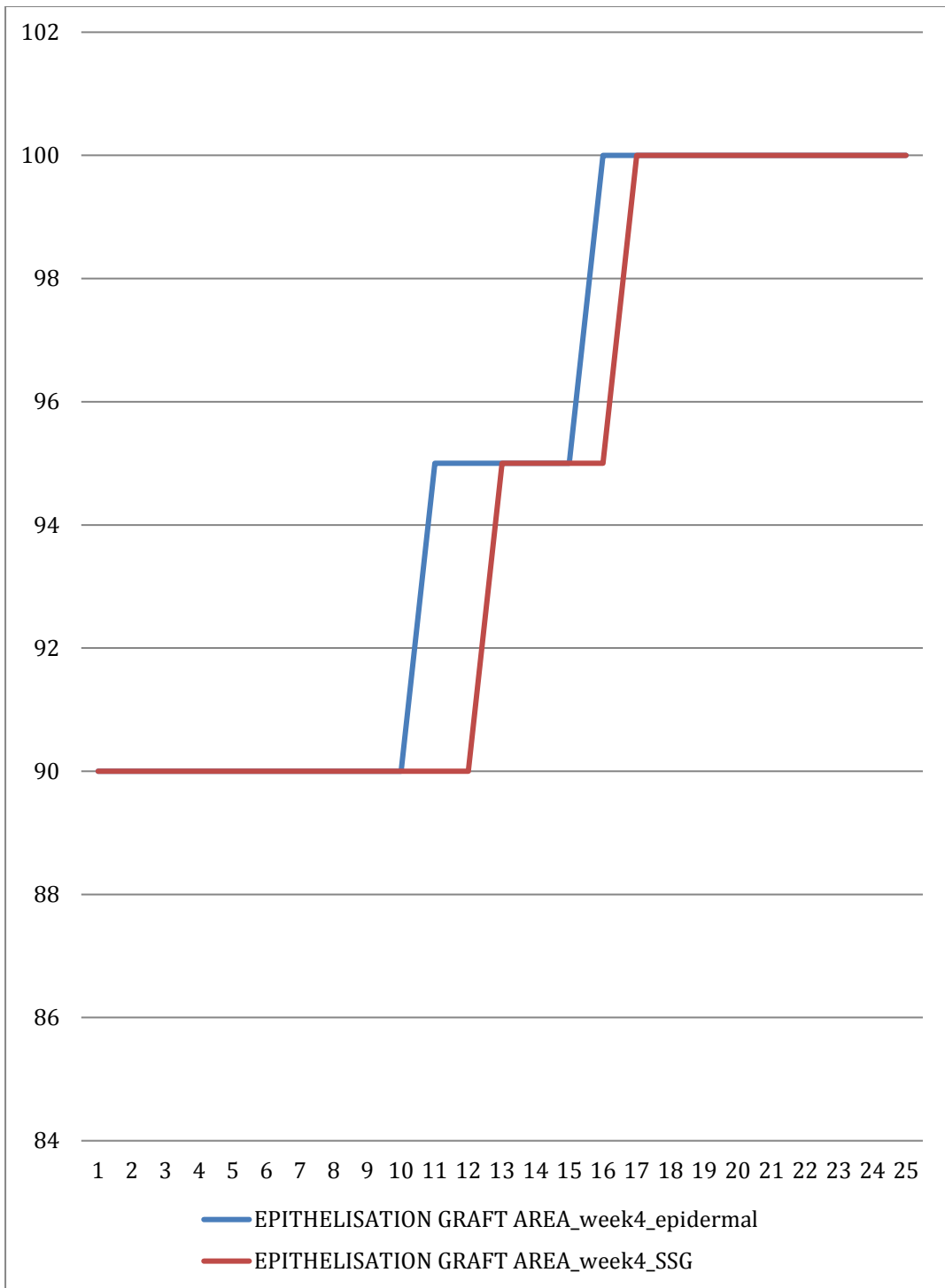


Figure 7: Comparison of epithelisation by fourth week

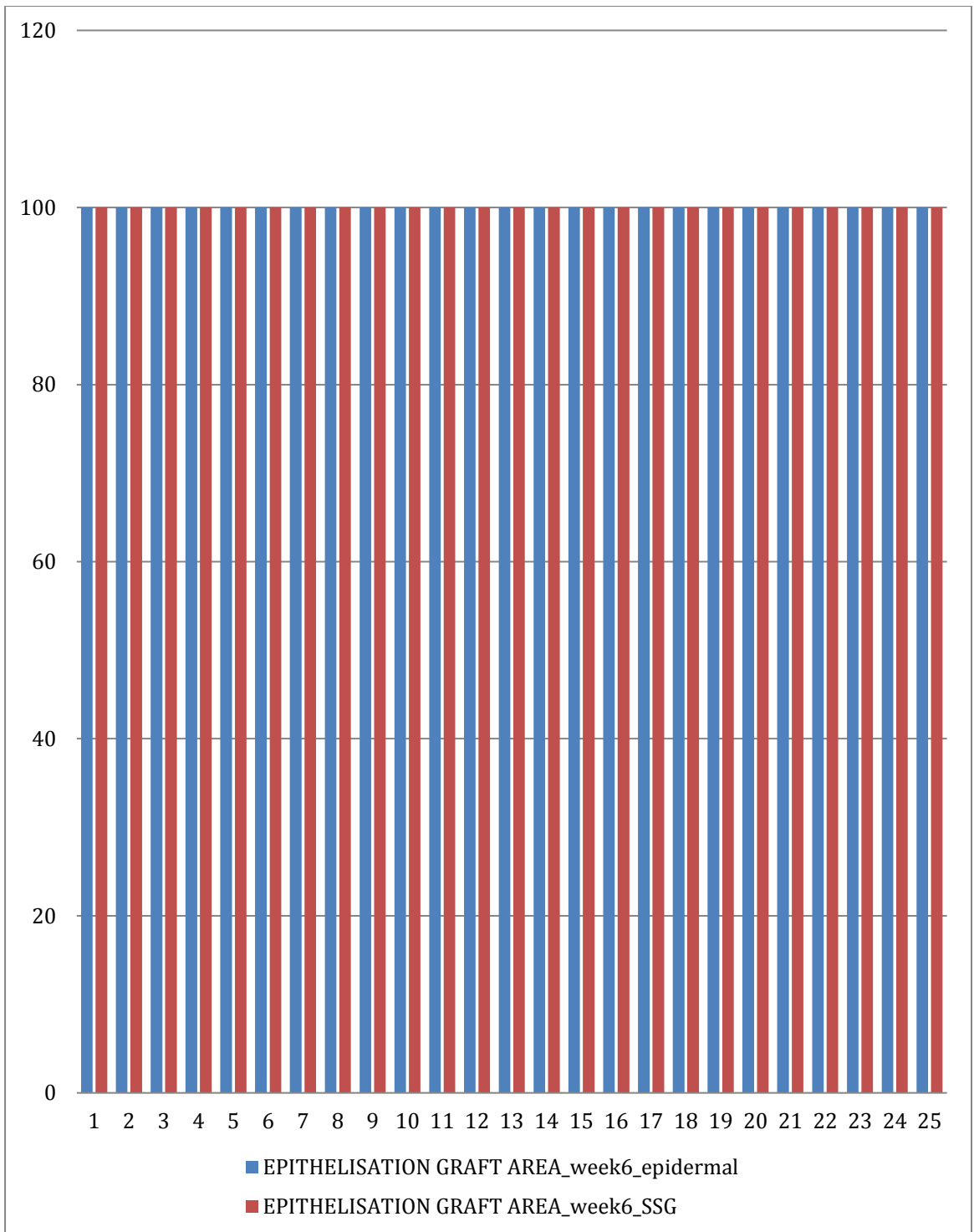


Figure 7: Comparison of epithelisation by sixth week

RESULTS

In our study the following results had been arrived:

- **DONOR SITE PAIN SCORE**

In the epidermal grafting group, the donor site pain score is zero while in the Split Skin Grafting Group, the mean donor site pain at week one is 5.4 (S.D=0.8). Donor site Pain is better in the Epidermal grafting group.

- **DONOR SITE HEALING**

In the Epidermal grafting group, the mean donor site healing is 98.28% (S.D=1.46%) while in the Split Skin Grafting Group, the mean donor site healing is 86% (S.D=4.9%). Donor site healing is better with Epidermal grafting group. Student t-test shows a value of 8.76 with a p-value=0.00143 ($p < 0.005$) which is highly significant.

- **EPITHELIALISATION OF GRAFT**

The two groups do not significantly differ in the epithelialisation of the recipient area in the follow-up period with the p value =0.65 which is not significant.

CONCLUSION

Epidermal skin grafting has better donor site healing and no pain at donor site as compared to split skin graft. Epithelialization of graft at recipient area does not significantly differ from split skin graft.

Hence epidermal graft is a promising alternative to the more invasive conventional surgical techniques as it is day care surgery without anesthesia and reduces the surgical burden for patients in need of wound coverage.

REFERENCES

1. Rice JB, Desai U, Cummings AK, et al.: Burden of venous leg ulcers in the United States. *J Med Econ.* 2014, 17:347–56. 10.3111/13696998.2014.903258
2. Kanapathy M, Smith OJ, Hachach-Haram N, et al.: Protocol for a systematic review of the efficacy of epidermal grafting for wound healing. *Syst Rev.* 2016, 5:92. 10.1186/s13643-016-0268-7
3. Yamaguchi Y, Hosokawa K, Kawai K, et al.: Involvement of keratinocyte activation phase in cutaneous graft healing: comparison of full-thickness and split-thickness skin grafts. *Dermatol Surg.* 2000, 26:463–9. 10.1046/j.1524-4725.2000.99280.x
4. Serena TE: The increasing role of epidermal grafting utilizing a novel harvesting system in chronic wounds. *Wounds.* 2015, 27:26-30.

5. Kiistala U, Mustakallio KK: In-vivo separation of epidermis by production of suction blisters. *Lancet*. 1964, 2:1444-5.
6. Constanzo U, Streit M, Braathen LR: Autologous suction blister grafting for chronic leg ulcers. *J Eur Acad Dermatol Venereol*. 2008, 22:7–10. 10.1111/j.1468-3083.2007.02148.x
7. Van Geel N, Wallaeyns 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, 163:1186–93. 10.1111/j.1365-2133.2010.10014.x
8. Ramos JV, Schmidt M, Wu SC: Epidermal skin grafts for the treatment of chronic lower extremity ulcers. *Podiatry Manage*. 2013, 32:95-104.
9. Gabriel A, Sobota RV, Champaneria M: Initial experience with a new epidermal harvesting system: overview of epidermal grafting and case series. *Surg Technol Int*. 2014, 25:55–61.

10. Hanafusa T, Yamaguchi Y, Katayama I: Intractable wounds caused by arteriosclerosis obliterans with end-stage renal disease treated by aggressive debridement and epidermal grafting. *J Am Acad Dermatol.* 2007, 57:322–6. 10.1016/j.jaad.2007.04.011
11. Hachach-Haram N, Bystrzonowski N, Kanapathy M, et al.: The use of epidermal grafting for the management of acute wounds in the outpatient setting. *J Plast Reconstr Aesthet Surg.* 2015, 68:1317-8. 10.1016/j.bjps.2015.04.019
12. 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, 151:1019-28. 10.1111/j.1365-2133.2004.06170.x
13. Yamaguchi Y, Sumikawa Y, Yoshida S, et al.: Prevention of amputation caused by rheumatic diseases following a novel therapy of exposing bone marrow, occlusive dressing and subsequent epidermal grafting. *Br J*

- Dermatol. 2005, 152:664–72. 10.1111/j.1365-2133.2005.06401.x
14. Richmond NA, Lamel SA, Braun LR, et al.: Epidermal grafting using a novel suction blister-harvesting system for the treatment of pyoderma gangrenosum. JAMA Dermatol. 2014, 150:999-1000. 10.1001/jamadermatol.2014.1431
 15. Tausche AK, Skaria M, Bohlen L, et al.: An autologous epidermal equivalent tissue-engineered from follicular outer root sheath keratinocytes is as effective as split-thickness skin autograft in recalcitrant vascular leg ulcers. Wound Repair Regen. 2003, 11:248–52.
 16. Osborne SN, Schmidt MA, Derrick K, Harper JR: Epidermal micrografts produced via an automated and minimally invasive tool form at the dermal/epidermal junction and contain proliferative cells that secrete wound healing growth factors. Adv Skin Wound Care. 2015, 28:397–405. 10.1097/01.ASW.0000470024.81711.b8

17. Osborne SN, Schmidt MA, Harper JR: An automated and minimally invasive tool for generating autologous viable epidermal micrografts. *Adv Skin Wound Care*. 2016, 29:57–64. 10.1097/01.ASW.0000476072.88818.aa
18. Hachach-Haram N, Bystrzonowski N, Kanapathy M, et al.: A prospective, multicentre study on the use of epidermal grafts to optimise outpatient wound management. *Int Wound J*. 2016, 10.1111/iwj.12595
19. Kanapathy M, Hachach-Haram N, Bystrzonowski N, et al.: Epidermal grafting versus split-thickness skin grafting for wound healing (EPIGRAAFT): study protocol for a randomised controlled trial. *Trials*. 2016, 17:245. 10.1186/s13063-016-1352-y
20. Hertle MD, Kubler MD, Leigh IM, Watt FM: Aberrant integrin expression during epidermal wound healing and in psoriatic epidermis. *J Clin Invest*. 1992, 89:1892–901. 10.1172/JCI115794

21. Labropoulos N, Tassiopoulos AK: Chronic venous ulcers. *Hawaii Med J.* 2000, 59:246–7.
22. Yamaguchi Y, Kubo T, Tarutani M, et al.: Epithelial-mesenchymal interactions in wounds: treatment of palmoplantar wounds by nonpalmoplantar pure epidermal sheet grafts. *Arch Dermatol.* 2001, 137:621–8.
23. Yamaguchi Y, Itami S, Tarutani M, et al.: Regulation of keratin 9 in nonpalmoplantar keratinocytes by palmoplantar fibroblasts through epithelial-mesenchymal interactions. *J Invest Dermatol.* 1999, 112:483–8. [10.1046/j.1523-1747.1999.00544.x](https://doi.org/10.1046/j.1523-1747.1999.00544.x)
24. Falanga V: Classifications for wound bed preparation and stimulation of chronic wounds. *Wound Repair Regen.* 2000, 8:347–52.
25. Ratner D: Skin grafting. From here to there. *Dermatol Clin* 16(1):75, 1998.
26. Hauben DJ, Baruchin A, Mahler D: On the history of the free skin graft. *Ann Plast Surg* 9:242, 1982.

27. Brown JB, McDowell F: Massive repairs with thick split skin grafts; emergency “dressing” with homografts in burns. *Ann Surg* 115:658, 1942.
28. Tanner JC Jr, Vandeput J, Olley JF: The mesh skin graft. *Plast Reconstr Surg* 34:287, 1964.
29. Rheinwald JG, Green H: Serial cultivation of strains of human epidermal keratinocytes: the formation of keratinizing colonies from single cells. *Cell* 6:331, 1975.
30. Green H, Kehinde O, Thomas J: Growth of cultured epidermal cells into multiple epithelia suitable for grafting. *PNAS* 76:5665, 1979.
31. Vistnes LM: Grafting of skin. *Surg Clin North Am* 57:939,1977.
32. Grabb WC: Basic techniques in plastic surgery (skin grafts).
33. In: Grabb and Smith’s *Plastic Surgery*, 3rd ed, Boston, Little Brown, 1979.
34. Rudolph R, Klein L: Healing processes in skin grafts. *Surg Gynecol Obstet* 136:641, 1973.

35. Smahel J: The healing of skin grafts. *Clin Plast Surg* 4:409,1977.
36. Marckmann A: Reaction of skin autotransplantation. Studies on the microcirculation and the biochemical composition in dermis (thesis). Copenhagen, Munksgaard, 1966.
37. Medawar PB: The behaviour and fate of skin autografts and skin homografts in rabbits. *J Anat* 78:176, 1944.
38. Medawar PB: A second study in the behaviour and fate of skin homografts in rabbits. *J Anat* 79:157, 1945.
39. Medawar PB: The experiimental study of skin grafts. *Br Med Bull* 3:79, 1945.
40. Scothorne RJ, Tough JS: Histochemical studies of human skin autografts and homografts. *Br J Plast Surg* 5:161, 1952.
41. Van Winkle W: The fibroblast in wound healing. *Surg Gynecol Obstet* 124:369, 1967.

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001
INFORMED CONSENT

DISSERTATION TOPIC:

**“A COMPARITIVE STUDY ON EPIDERMAL GRAFTING Vs SPLIT SKIN
GRAFTING IN WOUND HEALING IN OUR INSTITUTE”**

PLACE OF STUDY: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI
NAME AND ADDRESS OF PATIENT:

I, _____ have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I will continue to receive the medical treatment as usual.

I understand that I will not get any payment for taking part in this study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full co-operation for this study.

Name and Address of the Volunteer:

Signature/Thumb impression of the Volunteer

Date:

Witnesses:

(Signature, Name & Address)

Date:

Name and signature of investigator: (Dr.K.NATRAMIZH):

PROFORMA

Name :

Age :

Sex :

IP NO:

D.O.A:

Wt:

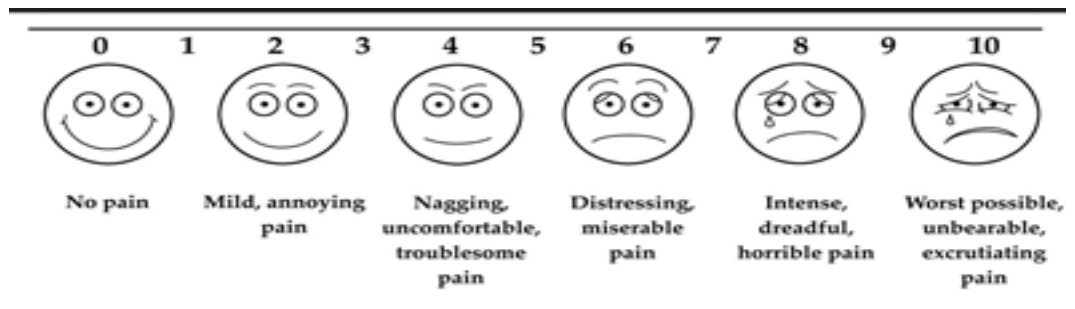
Ht:

Comorbidities:

Diagnosis:

Method of grafting:

Donor site pain score at 1st week:
(visual analogue score)



Donor site healing at 2nd week:

Epithelialization of graft at recipient area:

- at 1st week =
- at 4th week=
- at 6th week=

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001
INFORMED CONSENT

DISSERTATION TOPIC:

“A COMPARITIVE STUDY ON EPIDERMAL GRAFTING Vs SPLIT SKIN
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PLACE OF STUDY: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI
NAME AND ADDRESS OF PATIENT:

நான், _____

எனதுசொந்தமொழியில்ஆய்வுவிவரங்களைபற்றிதெரிவிக்கப்பட்டது.

நான்முற்றிலும்ஆய்வுவிவரங்களைபுரிந்துகொண்டேன்.

ஆய்வுபங்கெடுத்துக்கொண்டுள்ளநான்,

சாத்தியமானஅபாயங்கள்மற்றும்பயன்களைஅறிந்துஇருக்கிறேன்.

நான்எந்தநேரத்திலும்ஆய்வுஇருந்துதிரும்பமுடியும்மற்றும்அதன்பின்னர்,

நான்வழக்கம்போல்மருத்துவசிகிச்சைபெறதொடரும்என்றுபுரிந்துகொள்ள.

நான்இந்தஆய்வில்பங்குஎடுத்துஎந்தபணம்பெறமுடியாதுஎன்றுபுரிந்து.

நான்ஆட்சேபிக்கிறேன்மாட்டேன்இந்தஆய்வின்முடிவு,

எந்தமருத்துவஇதழில்கிடைக்கும்என்றால்,

என்தனிப்பட்டஅடையாளவெளிப்படவில்லைவழங்கப்படும்.

நான்இந்தஆய்வுபகுதியாகஎடுத்துசெய்யவேண்டும்என்றுஎனக்குநான்இந்தஆய்வு

வுஎன்முழுஒத்துழைப்புநீட்டிக்கஎன்றுஉறுதியளிக்கிறேன்.

பெயர்மற்றும்தொண்டர்முகவரி:

தொண்டர்கையொப்பம் / பெருவிரல்ரேகை

நாள்:

சாட்சிகள்:

(கையொப்பம், பெயர்மற்றும்முகவரி)

நாள்:

பெயர்மற்றும்புலன்விசாரணைகையொப்பம்: (டாக்டர்)

MASTER CHART

EPIDERMAL GRAFTING

S.NO	NAME	AGE	SEX	DIAGNOSIS	CO MORBIDITIES	WOUND DURATI ON	DONOR SITE PAIN SCORE 1 ST WK (VAS)	DONOR SITE HEALING 2 ND WK	EPITHELISATION GRAFT AREA		
									1 ST WK	4 th WK	6 TH WK
1.	MURUGASEN	40	M	PTRA -RT LEG	NIL	3 wks	0	98%	50	95	100
2	ARUMUGAM	60	M	PIRA- LT LEG	NIL	3 wks	0	95%	60	95	100
3	SURESH	50	M	PIRA-LT THIGH	DM2	3 wks	0	100%	40	90	100
4	VIJAYALAKSHMI	50	F	PIRA-LT LEG	HT/DM	4 wks	0	98%	50	90	100
5	HARIKRISHNAN	38	M	PIRA-RT LEG	NIL	3 wks	0	100%	40	95	100
6	MANUSAMY	54	M	PIRA-RT FOOT	DM2	3 wks	0	97%	50	90	100
7	RAMANI	43	F	PIRA- LT LEG	DM2	5 wks	0	98%	50	100	100
8	MARY	40	F	PIRA-LT FOOT	DM2	4 wks	0	99%	40	100	100
9	SANTHANALAKSHMI	70	F	PIRA-RT FOOT	DM2	3 wks	0	100%	50	90	Lost follow up

10	LINGASEN	50	M	PIRA-LT LEG	DM2	3 wks	0	98%	50	95	100
11	ASHOK	19	M	PTRA-LT ARM	NIL	2 wks	0	99%	60	100	100
12	NAIMUDEEN	45	M	PIRA-LT THIGH	DM2/HYPO THY	4 wks	0	97%	40	95	100
13	RAJKUMAR	59	M	PIRA-BACK	DM2	4 wks	0	100%	50	100	100
14	MUKESH	19	M	PTRA- RT LEG	NIL	2 wks	0	97%	60	100	100
15	VIJAYAKUMAR	55	M	PIRA-RT FOOT	NIL	3 wks	0	99%	50	90	100
16	SASIKUMAR	32	M	PIRA-LT FOOT	DM2	3 wks	0	98%	40	100	100
17	BUVANESHWARI	49	F	PIRA-RT LEG	DM2	5 wks	0	99%	50	90	100
18	MURUGAN	35	M	PTRA-LT FOREARM	NIL	3 wks	0	100%	50	100	100
19	VADIVELU	50	M	PTRA-LT LEG	NIL	2 wks	0	100%	50	90	100
20	BANU	42	F	PIRA-LT LEG	NIL	4 wks	0	97%	40	90	100
21	SRINNIVASAN	50	M	PIRA-LT SIDE NECK	DM2/TB	4 wks	0	98%	30	100	100
22	RENU	42	F	PIRA-LT LEG	DM2	4 wks	0	98%	50	90	100
23	MANI	50	M	PIRA-LT LEG	EPI	3 wks	0	97%	40	90	100
24	PARTHIBAN	30	M	PTRA-LT FOOT	NIL	2 wks	0	95%	40	100	100
25	SEKAR	31	M	PTRA-LT LEG	NIL	2 wks	0	100%	50	100	100

SPLIT SKIN GRAFTING

S.NO	NAME	AGE	SEX	DIAGNOSIS	CO MOR	WOUND DURATI	DONOR SITE PAIN SCORE	DONOR SITE HEALING	EPITHILISATION GRAFT		
									1 ST WK	4th WK	6th WK
1.	ANANDHARAMAN	60	M	PIRA- RT FOOT	DM2	4 wks	6	90	95	95	100
					/HT						
2	LOGANADHAN	50	M	PIRA- LT LEG	DM2	3 wks	6	90	90	90	100
3	VARATHARAJAN	54	M	PIRA- LT FOOT	DM2	5 wks	7	80	90	90	100
4	DHAMODHARAN	36	M	PTRA- RT FOOT	NIL	2 wks	5	90	90	100	100
5	RANI	46	F	PIRA- LT FOOT	DM2	3 wks	7	80	95	100	100
6	RAJAN	21	M	PTRA- RT LEG	NIL	2 wks	5	90	95	95	100
7	RAMACHANDRAN	48	M	PIRA- LT FOOT	DM2	4 wks	5	90	90	95	100
8	KASTHURI	48	F	PIRA- LT FOOT	DM2	3 wks	6	80	90	90	100
9	GIRI	18	M	PTRA- RT	NIL	2 wks	6	90	95	100	100
				GLUTEAL							
				REGION							
10	THIYAGARAJAN	40	M	PIRA- RT FOOT	NIL	5 wks	4	80	90	95	100
11	VEERAMUTHU	40	M	PIRA- RT FOOT	DM2	4 wks	5	90	90	90	100
12	SIGAMANI	55	M	PIRA- LT LEG	NIL	5 wks	6	80	80	90	100

13	VIMALA	36	F	PIRA- LT LEG	NIL	3 wks	5	90	90	100	100
14	NAGARAJ	57	M	PIRA- RT LEG	DM2	5 wks	6	90	80	90	Lost follow up
15	DHAWOOTH	57	M	PIRA- RT FOOT	DM2	3 wks	5	80	90	90	100
16	DINESH KUMAR	19	M	PTRA- RT FOOT	NIL	2 wks	4	90	95	100	100
17	SHANTHAKUMAR	35	M	PTRA- RT LEG	NIL	3 wks	6	90	90	100	100
18	MEERAN	29	M	PTRA- LT FOOT	NIL	3 wks	5	90	90	100	100
19	GANESH	48	M	PIRA- LT LEG	DM2	3 wks	5	80	85	90	100
20	NALINI	28	F	PIRA- LT GLUTEAL REGION	NIL	3 wks	6	80	90	90	100
21	IYAPPAN	54	M	PIRA- RT LEG	DM2	4 wks	6	80	90	90	100
22	RAMESH	48	M	PIRA- RT LEG	NIL	4 wks	5	90	90	90	100
23	VELANGANNI	36	F	PIRA- RT LEG	NIL	3 wks	5	90	95	100	100
24	PREMACHANDRAN	53	M	PIRA- RT LEG	DM2	5 wks	5	80	80	90	100
25	SATHISH KUMAR	25	M	PTRA- LT FOOT	NIL	2 wks	4	90	90	100	100

***PIRA – POST INFECTIVE RAW AREA, PTRA- POST TRAUMATIC RAW AREA
RT- RIGHT, LT- LEFT**

DM- DIABETED MELLITUS, HT- HYPERTENSION, EPI-EPILEPTIC, HYP THY- HYPO THYROID.