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Review

# Surgical management of leukoderma after burn: A review

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ABSTRACT

Burns are a common and sometimes devastating injury causing a significant amount of pain, disability, and occasionally death. Burns can have serious aesthetic and functional consequences such as pigmentary changes and formation of scar tissue. Hypopigmentation or depigmentation is often a result of partial- or full-thickness burns, which is referred to as leukoderma after burn. Thus, this study is aimed at systematically reviewing the surgical options for treating leukoderma after burn in order to gain insight into the advantages, disadvantages, and future implications of each surgical technique. The surgical procedures reviewed include dermabrasion with thin split thickness grafting, epidermal cell suspension spray, suction blister epidermal minigrafting, minigrafting, cultured epithelium, non-cultured keratinocyte suspension, and chip skin grafting.



## Contents



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## 1. Introduction

Burns often lead to physical deformity and changes in cutaneous pigmentation, which vary depending on the depth of injury. Hypopigmentation or depigmentation often results from partial- or full-thickness burns, which is referred to as leukoderma after burn [1]. This is a non-vitiligo type of depigmentation because it lacks the common theory of an autoimmune etiology [2]. The nature of this process is related to injury. Such injuries include: physical or chemical trauma, burns, inflammation, infection, or radiation [3]. This disease process has increased prevalence in ethinicities with darker pigmentation, and is often found in the hands, head, and neck regions [1,4]. Secondary to the often large and aesthetically important areas of injury, there can be an associated severe psychosocial disability in this patient population [5].

It is understood that skin pigmentation involves melanin, which is synthesized in melanosome vesicles residing in melanocytes in the basal layer of the epidermis. Each melanocyte transfers melanosomes to neighboring keratinocytes via their dendritic-like processes [6]. The melanocyte and the keratinocytes that receive its melanosomes are collectively known as an epidermal-melanin unit [6]. The pathophysiology of post-burn leukoderma results from melanin loss at the basal layer of the epidermis [7]. Specifically, the formation of the epidermal-melanin unit is interfered with by scar tissue formed during the proliferation and remodeling phases of wound healing [6]. Fibrosis ultimately inhibits melanocyte migration and subsequent production of melanin in the injured area. Hypopigmentation is disfiguring, usually permanent, and in need of a curative aid [8].

Current treatment modalities include non-surgical and surgical interventions. Non-surgical therapies are temporary and involve makeup and tattooing [1]. Post-burn leukoderma is usually resistant to UV-based therapy (UV-B, psoralen plus UV-A), which does not address melanogenesis and texture deformities [9]. However, long lasting treatment requires surgical interventions that involve removing the affected area and replacing it with skin of similar texture and color. These surgical techniques aim to restore the melanocytes in the affected areas and address the two main challenges: depigmentation and textural changes [9].

Though not covered in this review, but worth noting, inflammatory hyperpigmentation can be equally as deforming. Similar to hypopigmenation, it is triggered by a host of insults (electromagnetic devices, lasers, radiofrequency devices, microdermabrasion, etc.), however the most common causes are secondary to flame or boiling water burns [7]. The dyspigmentary changes are subsequent to melanocyte injury rather than melanin loss as seen in hypopigmentation [10]. Treatments include topical agents (hydroquinone, kojic acid, arbutin, azelaic acid), lasers, and intense pulsed light [10].

Here we focus on the various surgical procedures which have been shown to improve and or treat post-burn leukoderma. We aim to give the community a guide into the intricacies and controversies of each treatment, with a focus on guiding patient management.

## 2. Methods

This review adheres to the principles outlined in the Cochrane guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines statement. A thorough literature review of the National Library of Medicine and PubMed databases was conducted. The following search was performed: (Burn OR postburn OR post burn) AND "postinflammatory", "depigmentation", "hypomelanosis", "achromic", "hypopigmentation", or "leukoderma". Only articles written in English were included for further review. Search results were cross-checked with the Scopus database using the same search terms. The search yielded 525 articles. The titles and abstracts of the articles were independently reviewed by two authors for overall relevance and content. Articles were included if they contained suitable background information, clinical presentation, epidemiology and treatments. Twenty papers met the inclusion criteria and were included in this review.

### 2.1. *Dermabrasion with thin split thickness skin grafting*

Dermabrasion followed by split-thickness skin grafting has been used in the treatment of post-burn leukoderma. Dermabrasion is used to remove damaged/scarred tissue and to prepare the site for grafting with donor skin containing intact melanocytes which could remodel and repigment the burned area. The procedure begins by superficially stripping the depigmented area using a diamond burr or electric dermatome until uniform punctate bleeding is noted [1,8,11–13]. The thickness used typically varies between 4 and 8 thousands of an inch [1,8,11–13]. Some have used a flash scanned carbon dioxide laser to ablate the depigmented area, which results in a smoother surface with less bleeding [1,14]., The treated area is then grafted with split thickness donor skin procured from the abdomen, back, thigh, and buttock under general anesthesia [8,12–14].

The majority of studies using this technique have yielded satisfactory results [1,8,11,13,15,16]. A subjective assessment by Khan et al. evaluated the color match of the recipient site, and was reported as "good" in 13 patients and "excellent" in 2 patients, totaling 15 operations [1,8,11,13,15,16]. This procedure may be coupled with other reconstructive techniques, such as z-plasty, scar release, and grafting, increasing the

utility of this technique [1]. A reported advantage is the lack of scarring seen at the donor or recipient sites [1,8,11–14]. However, hyperpigmentation at the recipient site has been known to occur [1,8,13]. Other potential drawbacks include the risk incurred with general anesthesia, an unanticipated hospital stay, the cost of the procedure and the safety precautions utilized while working with the carbon dioxide laser [1,12–14].

### 2.2. *Epidermal cell suspension spray*

Iman et al. evaluated the efficacy of treating post-burn hypopigmentation using an autologous epidermal cell suspension spray [17]. In this study, 28 patients were divided into two groups. In the first group (n=18), the epidermal cell suspension was sprayed on the wound surface after dermabrasion of hypopigmented skin. In the second group (n=10), the epidermal cell suspension was injected into the hypopigmented area without removal of the hypopigmented skin. Biopsies were taken and processed under sterile conditions using NaBr4N and Trypsin to separate the epidermis from the dermis [17]. In both groups, an amniotic membrane and gauze dressing was applied to prevent autograft cell loss and contamination. The mean time between burn and therapeutic intervention for cell spray and cell injection was 1.77 and 1.9 years, respectively. Both treatment groups experienced mild repigmentation, as measured by both clinical score and the measured amount of melanocyte counts per field on a 400× magnification, but the difference between the groups was not statistically different in either case [17].

### 2.3. *Suction blister epidermal minigrafting*

Suction blister epidermal minigrafting for the treatment of post burn leukoderma dates back to 1971 [17]. This method involves an apparatus consisting of a suction pump, compressor unit, manometer, vacuum bottle, hoses, and suction cups [17]. In 2007, Burm et al. consolidated the units into a portable suction pump with a built-in manometer and suction cups that have an independent one-way valve [18]. A mild sedative can be used to acquire the minigraft using this technique [19]. The inner aspects of the thigh and/or abdomen are recommended as donor sites [17–19]. The cups are properly placed onto the donor skin and brought to a negative pressure of 150-300 mmHg to induce the formation of bullae which can later be harvested. [17–19]. The hypopigmented skin may be frozen with liquid nitrogen [19] and removed in 24-48 h with superficial dermabrasion [18]. Grafts obtained from the harvested bullae are placed on the dermabraded skin in an overlapped fashion to prevent achromic fissure formation [17–19].

The studies utilizing this technique reported a majority of patients being satisfied with the results and had 100% take of the graft with “adequate repigmentation” as objectively observed by study investigators [17–20]. There was an absence of scarring or surface irregularity seen in the donor or recipient sites [17–19]. This technique is particularly inexpensive and multiple samples can be obtained from a relatively small donor site [17]. The suction technique can be used to create a larger graft, however, the amount of skin that can be treated is limited. Hyperpigmentation of the recipient area has been noted in a few cases [17,19]. Some studies have suggested that superficially dermabrading the area to remove the hyperkeratotic epidermis may smoothen out the irregular scars better than using liquid nitrogen [17–19].

### 2.4. *Minigrafting*

When utlizing the minigrafting technique, the depigmented area is first prepared by creating a 1 mm diameter mini-punches spaced 4 mm apart, with a depth that reaches the partial-thickness dermis layer. The skin is then harvested from the patient and sectioned into smaller transplantable grafts. A total of 63 patients with post-burn leukoderma have been treated with this technique [21,22]. As part of the recovery process to stimulate melanocytes in the Lahiri et al. study, all patients were given a daily dose of 0.6 mg/kg of 8-methoxsalen and exposed to the sunlight for 15–30 min [21].

Thin minigrafting technique is able to overcome donor-site scarring associated with typical skin grafting methods when the harvest skin graft is less than 0.25 mm thick [22]. Fabella et al., reports complete repigmentation in 5 out of 6 patients following the minigraft technique [23]. Lahiri et al., classifies repigmentation into four groups. Group 1 is 0-30% repigmentation, group 2 is 30-50% repigmentation, group 3 is 50-70% repigmentation and group 4 was 70-100% repigmentation. In this study a lesion is synonymous to an area of post-burn leukodermia skin. Out of 114 lesions amongst 60 patients, 49.1% of lesions had achieved 70-100% repigmentation; 34.2% of lesions had achieved 50-70% repigmentation; 10.5% of lesions achieved 30-50% repigmenation, and lastly, only 6.1% of lesions were classified as having 0-30% repigmetation. Cobblestoning tends to be the most common side-effect, however in most cases it tends to disappear with time due to color blending between graft and surrounding skin [22]. In resistant cases, electofulgration is used. Other less common side effects include depigmenation of the graft, and keloid formation [21].

### 2.5. *Cultured epithelium*

Utilizing cultured epithelial autografts is a relatively new technique to treat hypopigmented lesions, and deep burns [21]. A split-thickness skin biopsy from the buttock is used derive a sheet of cultured epithelial cells [21]. The recipient area is dermabraded until pinpoint bleeding is observed after which the sheet of cultured epithelial cells is applied under a saline soaked gauze and padded dressing for 5 days. After dressing removal, the surface is inspected and redressed with Fixomul for several days [21]. One group treated a 5 year old with a leukodermic lesion that resulted from a burn 4 years prior [21]. Upon culturing the epithelium, pigment was seen macroscopically and the presence of melanocytes were confirmed by histochemistry and electron microscopy. Notable repigmentation was observed 6 weeks postoperatively, with complete repigmentation after 2 years [24]. Advantages of this technique include the ability to expand a large quantity of pigmented autograft from a small donor site in a relatively short period of time. Due to the expansibility of cultured autologous cells, there may be no limit to the area that can be

**Table 1 – Overview of studies regarding surgical management of post burn leukoderma.**

| Type of procedure | Author (year) | No. of patients | Age | Gender | Location of depigmentation | Race/ethnicity | Results |
|---|---|---|---|---|---|---|---|
| Dermabrasion with thin split thickness skin grafting | Driscoll, 2015 | 11 | Mean age 14 | 5M, 6F | Face (3), trunk (1), upper extremity (4), lower extremity (3) | Asian (1), African American (5) Caucasian (3), Hispanic (2) | 95% |
| | Al-Qattan, 2011 | 8 | 15–40 | 16M, 7F | Forearm (2), dorsum of hand (3), dorsal aspect of digits (3) | Saudi Arabian | Satisfactory results– slight mismatch in pigmentation or texture |
| | Kahn, 1996 | 21 | Mean age 33; 12–54 | Not specified | Fingers, hands, wrists (19), face (1), anterior chest (1) | Black (4), Asian (2), Hispanic (15) | Color match excellent (34%), good (62%) |
| | Onur, 1990 | 18 | 5–35 | 4M, 14F | Facial (8), extremities (9), neck (1) | Not specified | Good color similarity to surrounding skin, flat surface and homogenous pigmentation satisfactory |
| | Açikel, 2000 | 13 | 20–22 | 13M | Face (2), trunk (4), extremities (7) | Fitzpatrick IV (8), Fitzpatrick III (5) | Color match excellent (38.5%), good (46%), fair (15%) |
| | Taki, 1985 | 32 | 13–65 | 14M, 18F | Arm, leg, thigh, scapular region, abdomen, hand, foot | Not specified | 95 to 100%, color match (range from mostly good to hyperpigmented) |
| | Kahn, 1991 | 11 | Mean 33 | 3F | Not specified | Black (2), Asian (2), Hispanic (7) | Skin graft take (excellent in 15), color match (excellent in 2, good in 13) |
| | Falabella, 1978 | 3 | 35, 14, 15 | 5F, 1M | Face, hands, legs | Caucasian (3) | Satisfactory repigmentation |
| Epidermal cell suspension spray | Imam, 2013 | 18 (cell spray group) | 28.5±9.9 | 18M | Extensor surface of hand (9), ankle (2), leg (2), wrist (1), fingers (2), trunk (1), forearm (1) | Not specified | Complete depigmentation (score 0) to mild pigmentation (score 2) |
| Suction blister epidermal minigrafting | Suvanprakorn, 1985 | 3 post inflammatory leukoderma | 31–38 (PIL) | 3F (PIL) | Not specified | Not specified | 100% |
| | Burm, 2007 | 23 | Not specified | Not specified | Face (6), arms (5), hands (11), ankle (1) | Asian | Excellent repigmentation |
| | Falabella, 1971 | 4 | 18 (2), 25, 30 | 2M, 2F | Arm, face, extremities, hand | Caucasian (2), African American (2) | Moderate to complete repigmenation |
| | Falabella, 1984 | 6 | 18, 24, 20, 22, 45, 35 | 3F, 3M | Leg, thorax, arm | Caucasian (5), Mestzo (1) | Adequate repigmentation |
| Punch minigrafting | Lahiri, 1997 | 60 total (Post burn leukoderma cases not specified) | 6–67 | 21M, 39F | Not specified | Not specified | 70–100% in 56 lesions of 31 patients |
| | Fuji, 2007 | 3 | 61, 62, 16 | 1M, 2F | Hand (2), forearm (1) | Not specified | Excellent color and texture that match surrounding skin |
| | Falabella, 1986 | Total 6 (3 with PBL) | 23, 42, 32, 25, 30, 20 | 1F | Thigh, nose/malar area, hand, foot, chin | Black (2), Mestizo (2), Brunette (2) | Complete repigmenation |
| Cultured epithelium | Stoner, 2000 | 1 | 5 | | Calf | Not specified | Complete repigmenation after 2 years |

*(continued on next page)*

**Table 1 (continued)**

| Type of procedure | Author (year) | No. of patients | Age | Gender | Location of depigmentation | Race/ethnicity | Results |
|---|---|---|---|---|---|---|---|
| Noncultured keratinocyte-melanocyte suspensions | Henderson, 2011 | 1 | 26 | M | Face, chest, lower extremities | African American | 90-100% |
| | Mulekar, 2011 | Total 10 (3 lost to follow up) | 11-65 | 9F, 1M | Extensor surface of hand (4), leg (3), wrist (1), metatarsus (2) | Not specified | 90-100% |
| Chip skin grafting | Harashina, 1985 | 12 | 12-54, mean 28 | 6M, 6F | Extremities (8), face (3), trunk (1) | Oriental | Adequate repigmentation w/in 3 months |

treated. Among the concerns regarding this technique are the discomfort and potential scar formation resulting from dermabrasion of the leukodermic site prior to the administration of the cultured epithelium (Table 1).

### 2.6. *Noncultured keratinocyte-melanocyte suspensions*

Autologous noncultured melanocyte-keratinocyte transplantation has been used in the treatment of leukoderma after burn and vitiligo [9,22,23].The technique involves removal of a superficial sample of donor skin. The epidermis of the donor skin is isolated in an effort to properly sequester melanocytes and keratinocytes. The recipient area is dermabraded, and the keratinocyte-melanocyte suspension is then applied to the denuded area and allowed to mature [9,22]. Both Henderson et al. and Mulekar et al. reported impressive results using autologous non-cultured melanocyte-keratinocyte transplantation. At six months after-treatment an average of 90–100% confluent repigmentation was objectively seen [9,22]. The patients also reported an improvement in skin texture [9]. This technique has the advantage of using a donor to recipient ratio of 1:10 in a single session [9,22]. This procedure can also be performed on any area of injury, including uneven surfaces [22]. The technique is quicker and costs less than the cultured epithelial suspension technique [22]. Of those that reported post-operative swelling and pain, symptoms tend to resolve on their own [9].

### 2.7. *Chip skin grafting*

Chip skin grafting involves abrading the leukodermic area and the surrounding scars using an electric dermabrader until uniform dermal bleeding is visualized [24]. A thin split-skin graft is obtained from a donor area and cut into small pieces creating mud-like skin chips. The chips are then spread evenly over the abraded recipient area and covered with nonadhesive ointment gauze [24]. Chip skin grafting is similar to punch micrografting in that melanocytes from the grafts migrate towards the leukodermic skin [24]. There is a notable decrease in donor site disability and disfigurement when compared to sheet or punch grafting as this method utilizes very thin grafts [24]. Harashina et al. objectively saw “adequate repigmentation” utilizing chip skin grafting in all patients within 3 months. This particular study only included people of Asian race, therefore larger studies broader skin types are warranted. The preparation of chip skin grafts have been argued to be easier and faster when trying to obtain the same quantity of graft via a punch method.

## 3. Discussion

Current treatment modalities for post-burn leukoderma include non-surgical and surgical interventions. Non-surgical therapies are temporary, involving the use of makeup and tattooing. Permanent treatment requires surgical treatments that remove the affected area and replace it with skin of similar texture and color. The aim of these treatments is to restore the melanocytes in the affected areas. The surgical treatments include dermabrasion with thin split thickness skin grafting, epidermal cell suspension spray, suction blister epidermal

minigrafting, punch micrografting, cultured epithelium, noncultured keratinocyte-melanocyte suspensions, and chip skin grafting.

Dermabrasion with thin split thickness skin grafting is a fairly simple and versatile approach [1,8,11–13]. In a study by Kahn et al. after grafts were placed on the area of interest, sixty two percent of patients (n=21) reported good color match and twelve patients reported excellent color matches [1,8,11,13,15,16]. The ability to couple this technique with other procedures, and its lack of scarring in donor and recipient sites are its greatest advantage [1,8,11–14]. Additionally, the size of the donor site is limited in its use for large areas of hypopigmentation [1]. Unfortunately, due to the procedure's use of general anesthesia and possible hospitalization, this therapy can be costly [1,12,13].

The epidermal suspension spray for repigmentation of the hypopigmented post-burn leukoderma areas [25] involves general anesthesia and preparing under sterile conditions. The previously prepared suspension is then sprayed onto the dermabraded recepient site [25]. Although this method used a meticulous metric of melanocyte counts per field at 400× magnification, the clinical results were not satisfying to the patients nor the clinicians [25]. The lack of favorable clinical results may be attributed to the difficulty in attaching epidermal cell suspension onto the skin. Future studies utilizing an enhanced attachment method for the epidermal cells may be warranted.

Suction blister epidermal minigrafting involves the use of a contraption to create suction blisters on both the hypopigmented and normal regions; these blisters are frozen with liquid nitrogen and removed. The majority of patients that underwent this procedure had moderate to complete repigmentation [17–20]. Additionally, this intervention lacked scarring or surface irregularity in both the donor and recipient sites [17–19]. Contrary to dermabrasion with thin split thickness skin grafting, this procedure is particularly inexpensive and requires minimal anesthesia [17]. Disadvantages include the possibility of post-treatment hyperpigmentation in darker skin types as noted in [14]; however, the hyperpigmentation was not reported in a later study by Falabella [19] Additionally, the infeasibility of treating large surface areas [19] much like dermabrasion with thin split thickness skin grafting. Additionally, the method itself requires more time to complete; secondary to a 4–5 day incubation period [17,19].

Punch micrografting has demonstrated effectiveness in a study of 60 cases– half of the study group reported more than 70% repigmentation and 83.3% of the treated post-burn leukodermia lesions had at least 50% improvement in repigmentation [26–28]. This procedure involves the creation of punches evenly spaced apart on the recipient regions and skin harvesting from donor sites that fit into the punched out recipient regions. The use of a small donor area to cover a large defect makes this technique particularly attractive [26]. Maximizing the melanocyte's ability to migrate in a centrifugal manner may account for the effectiveness of this technique [26]. However, cobblestoning has been noted in several cases [26,27]. Eventually this negative effect appears to resolve over time, or can be treated successfully with electofulgruration [27].

Autologous cultured epithelium yielded favorable results in a 5 year old burn victim with post-burn leukoderma. Complete repigmentation was noted at the burn site within 2 years [21]. As little as a 1 $cm^2$ split-thickness skin biopsy may be required to prepare the epidermal sheets. Dermabrasion occurs immediately prior to surgery with subsequent placement of the cultured epithelium over the recipient area. This technique may have slight discomfort with minimal scarring. Larger prospective studies are needed to verify the reported success of this case report.

In utilizing noncultured autogolous cell suspensions, the epidermis is spread from full thickness skin and applied to a dermabraded hypopigmented area. This modality was favorable with an average reported repigmentation of 90–100% after 6 months of treatment [9,22]. This technique can use small donor sites to treat a 10× larger hypopigmented area [9,22]. However, the ability to expand small donor sites is not feasible and is therefore not as versatile as the cultured approach. However, with smaller regions of injury, this intervention is cost-effective when compared to the cultured epithelial suspension method [22].

Chip skin grafting revealed adequate repigmentation in leukodermic areas in a study of 12 patients [24]. The technique utilizes a skin-graft mesher and blade to prepare the graft. The skin chips are directly applied to the abraded recipient region and covered with nonadhesive ointment gauze. Harashina et al. found that chip skin grafting resulted in less donor site disability, disfigurement and was easier to prepare when compared to punch grafting [24]. However, there are a lack of studies applying this technique to a variety of patient populations. Further studies are warranted to illustrate this technique's applicability to different patient populations.

## 4. Conclusion

Of the seven surgical techniques reviewed for the treatment of post-burn leukoderma only four of the techniques were analyzed in multiple reports. Six studies demonstrated that dermabrasion with thin split thicknesss skin grafting provides satisfactory repigmentation results [1,7,10,11,13,15,16]; four studies suggest that suction blister epidermal minigrafting is an inexpensive technique with adequate amount of repigmentation [14,18–20]; three studies demonstrate that punch minigrafting provides above average repigmentation results [21–23]; and two studies report that noncultured keratinocyte suspension provides consistently excellent repigmentation results [8,25]; Of the four techniques, only punch minigrafting and noncultured keratinocytes suspensions demonstrated the greatest improvements in repigmentations; however noncultured keratinocytes suspension perhaps has the most potential benefits with the fewest side effects. The three remaining surgical techniques: epidermal cell suspension spray [17], cultured autograft epithelium [24], and chip skin grafting [27] were single study or case reports. More studies are needed to confirm the reported benefits of epidermal cell suspension spray, cultured autograft epithelium and chip skin grafting. Surgical interventions need to address depigmentations and textural changes associated with post-burn

leukoderma. Other concerns include addressing the effects of treatment to the donor, and the accompanied distressing side-effects to the recipient. The ergonomics of treatment modality as well as low cost methods should be considered. The main limitation of this review is that the surgical studies of post-burn leukoderma were mostly case reports and single-center investigations. Larger head-to-head, randomized, and observer-blinded studies are needed to eliminate observational bias and to determine if one surgical technique is superior to another via direct comparison.

## Grant information

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**Collaborator:** United States Department of Defense.

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