

# Efficacy of suction blister epidermal grafting with concomitant phototherapy in vitiligo treatment

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## Abstract

**Introduction:** There are many surgical methods for vitiligo treatment that have been used for over 30 years. Suction blister epidermal grafting (SBEG) is considered one of the simplest and most effective of them.

**Aim:** To determine how effective suction blister grafts with concomitant phototherapy are in vitiligo treatment.

**Material and methods:** The study was conducted on 10 patients with vitiligo that was resistant to previous treatment including phototherapy in monotherapy. Involvement of affected sites was different for every patient. We used cryotherapy for blistering at the recipient site and an automatic suction device for blistering at the donor site. The blister was separated from the donor site and fixed with dressing to the recipient site. After removing the final dressing (about 7 days after SBEG) patients started phototherapy (6 patients had UVB 311 nm and 4 had PUVA). All patients treated with UVB 311 nm were qualified for treatment in our clinic and the method was chosen according to expert recommendations from the European Dermatology Forum (EDF) Guidelines for Vitiligo where narrowband (NB) UVB is the phototherapy of choice. Three patients who had PUVA therapy were treated with this method in other clinical centers and sent to us only to undergo SBEG. One patient had previously received UVB 311 nm for 3 months, which showed no effects. Repigmentation of lesions was evaluated at 3 and 6 months after the surgical procedure.

**Results:** Ten patients (9 females with a mean age of 36.88 years and 1 man aged 39 years) were enrolled in the study. Nine patients showed progressive repigmentation at 3 and 6 months follow-up with a rate varying from 13 to 76% (mean: 44.5%) and 35 to 100% (mean: 67.5%). One patient showed 5% depigmentation at a visit after 6 months in comparison to the follow-up visit 3 months after SBEG.

**Conclusions:** With this technique, patients who did not respond to the usual treatments showed very good repigmentation over a 6-month follow-up. There were no side effects such as scarring.

**Key words:** suction blister, PUVA, UVB 311 nm, repigmentation, vitiligo, planimetry.

## Introduction

Vitiligo is an acquired skin disorder of great cosmetic significance. It affects approximately 0.1–2% of the world population, varying in different world regions [1, 2]. Topical corticosteroids or calcineurin inhibitors are the most valuable treatments for localized vitiligo [3]. Phototherapy is currently the most widely used for large vitiliginous areas and smaller lesions resistant to other therapies [4–8]. Narrow-band UVB is considered by many to be equally effective to psoralen and ultraviolet A (PUVA) and thus is used as the first choice therapy for most patients [3, 9, 10]. In spite of this multiplicity of affordable

treatment options, many physicians are still frustrated with results and prescribe no treatment at all. Because of these disappointing outcomes, several surgical methods were introduced in the hope of achieving a more encouraging response. Surgical techniques are reserved for patients with stable vitiligo that is unresponsive to conventional therapies [11–14]. A number of dermatosurgery techniques are available to promote repigmentation of vitiligo: mini- or punch grafts, split-thickness skin grafts, cultured epidermal sheets, cultured melanocyte suspensions, follicular grafts and suction blister epidermal grafts [15–26]. Each procedure has its advantages

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and disadvantages. Minipunch grafting, though a simple outpatient procedure, is not preferred over cosmetically important sites because of the frequently associated cobblestoning [27, 28]. Split thickness grafting has the advantage that it is a simple procedure by which large areas of vitiligo can be covered in a single sitting and no special equipment is required. However, scar formation at the donor site, milia, partial loss of grafts, and thick margins of the grafts are commonly associated side effects [27]. The suction blister technique has the shortcoming that it is time consuming and only small areas can be covered in a single sitting [14, 27]. However, it is ideal for covering small, cosmetically important sites. Among these methods, the highest success rates have been achieved with split-thickness skin grafts and epidermal blister grafts. However, we consider SBEG to be less painful for the patient, easier and practically free from side effects such as scarring. Suction blisters were first introduced by Kiistala and Mustakallio in 1964 by using an angiosterrrometer [29]. Its use in replacing achromic skin was first reported by Falabella in 1971 [30]. Application of epithelial grafts nowadays is a common treatment technique for vitiligo. Unfortunately failures are still anticipated in many cases. For better results, phototherapy or photochemotherapy of donor and recipient sites can also be performed before and after grafting [11, 14, 27]. The purpose of this work is to evaluate how effective suction blister grafts with concomitant phototherapy are in treatment of resistant vitiligo cases that had failed to respond to classic phototherapy. Many studies have been performed to investigate the efficacy of vitiligo treatment modalities and a variety of assessment methods have been used to evaluate the response to therapy. Many of them rely on the subjective assessment of repigmentation by the investigator. There is still no consensus that would allow an objective and reliable evaluation of treatment results. We decided to use planimetric measurement of vitiligo

areas with a tool that is free to use – ImageJ (<https://imagej.nih.gov/ij/index.html>).

### Aim

The aim of this study was to determine how effective suction blister grafts with concomitant phototherapy are in vitiligo treatment.

### Material and methods

Ten patients (9 females with a mean age of 36.88 years and 1 man aged 39 years) were enrolled in the study (Table 1). All had stable localized vitiligo and they did not respond satisfactorily to classic phototherapy treatment although they had received this for at least 3 months. Patients under 18 years old, cases with active disease (with new crops of depigmented skin in the last 3 months), and Koebner-positive cases were excluded from the study. Full history taking, general and local examination, and photography of the lesion(s) were done for each patient. Informed written consent was obtained in all cases. The day before surgery cryotherapy was performed at the vitiligo-affected recipient site. Cryotherapy was performed with nitrous suboxide through one cycle of 10–15 s. On the day of surgery, a donor site was selected on the brachial area (with normal skin) and the area was cleaned with Kodan forte solution. The site was attached to the transparent blister-forming device and vacuum extractor apparatus to produce a high negative pressure (–0.4 bar; 6 psi) (Figure 1 A). After about 2 h of application of suction, every blister was ready (Figure 1 B). Then all bullae in the recipient site were converted into erosions by removing the roofs of the bullae with scissors. Every erosion was round and had a diameter of approximately 5–7 mm. After that suction blisters at the donor site were cut off one by one with scissors along

**Table 1.** List of all patients

Patient number	Gender	Age	Vitiligious area subjected to SBEG	Phototherapy
1	Male	39	Hand – 1 area	UVB 311 nm
2	Female	41	Elbow – 2 areas	UVB 311 nm
3	Female	42	Neck – 1 area	UVB 311 nm
4	Female	48	Face, neck – 2 areas	UVB 311 nm
5	Female	37	Calf – 1 area	UVB 311 nm
6	Female	29	Back – 1 area	UVB 311 nm
7	Female	31	Hand – 3 areas	PUVA
8	Female	41	Back – 1 area	PUVA
9	Female	23	Foot – 1 area	PUVA
10	Female	40	Hand – 1 area	PUVA



**Figure 1.** A – Vacuum extractor apparatus, B – suction blisters in the donor site and transparent blister forming device, C – bullae in the recipient site, D – suction blisters placed on the recipient site

the blister base, placed on object glass and then finally placed on the recipient site (Figures 1 C, D). Forceps and a surgical blade were used to extend the graft to its largest size so that it could cover whole erosion at the vitiliginous area. The harvested layer consisted of only epitelium with no dermal components. The donor and the recipient sites were dressed with Bactigras and gauze, which was bound in place with an adhesive plaster. The dressing was changed every day and removed completely after a week. Phototherapy was initiated immediately after removing the final dressing. UVB 311 nm was chosen as the phototherapy of choice for 6 of our patients according to expert recommendations from the EDF Guidelines. PUVA therapy was continued in 3 of 4 patients sent from other clinical centers to undergo SBEG. In one patient we changed UVB 311 nm to PUVA because of therapeutic failure after 3 months of phototherapy. All patients were followed postoperatively for 6 months. Finally, repigmentation rates were evaluated by comparing images of the lesions at 3 months and 6 months after surgery.

Still there is no consensus about the choice of evaluation methods and outcome parameters used in surgical vitiligo studies. These results are thus non-

comparable data. Most methods are based on visual assessment, which may lead to a highly subjective outcome. We found only three studies that mention the use of a more objective measurement tool. The planimetric measurement used by Boersma *et al.* [31] was in our opinion the most accurate, and we used the same method in our study.

## Results

In this study, 10 patients (9 female and 1 male) with stable vitiligo were evaluated for response following suction blister grafting, with pre- and post-graft phototherapy. The age of our male patient was 39 and female patients' medium age was 36.88. Responses to treatment at different follow-up evaluations are presented in Table 2. Nine patients showed progressive repigmentation at 3 and 6 months follow-up with a rate varying from 13 to 76% (mean: 44.5%) and 35% to 100% (mean: 67.5%) (Figures 2 A, B). Repigmentation rates between the first and second follow-up visit varied from 14% to 100%. One patient showed 5% depigmentation at a visit after 6 months in comparison to the follow-up visit 3 months after SBEG. One patient presented the Koebner phenom-

**Table 2.** Response to treatment after 3 and 6 months

Patient number	Recipient vitiligious area surface before SBEG (A) [mm <sup>2</sup> ]	Recipient area vitiligious surface 3 months after SBEG (B) [mm <sup>2</sup> ]	Recipient area vitiligious surface 6 months after SBEG (C) [mm <sup>2</sup> ]	A-B [mm <sup>2</sup> ] (and % of repigmentation area)	A-C [mm <sup>2</sup> ] (and % of repigmentation area)	B-C [mm <sup>2</sup> ] (and % of repigmentation area)
1	540	207	105	333 (52)	435 (81)	102 (51)
2.1	262	169	60	93 (36)	202 (77)	109 (65)
2.2	165	143	103	22 (13)	62 (38)	40 (28)
3	405	293	0	112 (28)	405 (100)	293 (100)
4.1	764	270	40	494 (65)	724 (95)	230 (85)
4.2	4642	1258	183	3384 (73)	4459 (96)	1075 (85)
5	941	226	118	715 (76)	823 (88)	108 (48)
6	820	432	152	388 (48)	668 (82)	280 (65)
7.1	253	149	59	104 (41)	194 (77)	90 (60)
7.2	384	212	164	172 (45)	220 (57)	48 (23)
7.3	144	81	70	63 (44)	74 (51)	11 (14)
8	1695	573	215	1122 (67)	1480 (88)	358 (63)
9	2685	749	265	1936 (72)	2420 (90)	484 (65)
10	209	126	133	83 (40)	76 (35)	-7 (-5)

**Figure 2.** A – Patient 4, area 2 (neck) – before SBEG, B – patient 4, area 2 (neck) – 6 months after SBEG (after transferring 40 suction blisters)

enon in the donor area but vitiliginous patches repigmented 2 months after starting phototherapy. We observed a significantly better repigmentation rate in patients with concomitant UVB 311 nm therapy than PUVA, which was 82.125% after 6 months and 69.4% after 6 months, respectively.

## Discussion

Currently, several medical treatments for vitiligo are available, including topical and systemic corticosteroid, photochemotherapy using PUVA, narrow-band UVB, human placental extracts, antioxidants, and low-energy laser irradiation [32, 33]. Despite the availability of these therapeutic options, many patients with vitiligo fail to achieve satisfactory results. For patients whose vitiligo has been nonresponsive to medical treatments and has been stable, surgical therapies are viable alternatives. Autologous skin grafts can be obtained from uninvolved skin using several dermatosurgery techniques [1]. Each method has its pros and cons. The mini-graft is simple and non-expensive, but it has the highest rate of adverse effects, with a 35% risk of cobblestone appearance at the recipient site and hypopigmentation and keloid formation at the donor site [34, 35]. Thin split-thickness grafting has the highest mean success rate (87%) according to a systematic review by Njoo *et al.* [27]. Transplantation of melanocytes cultured in vitro from a small piece of donor skin is very expensive and requires special and advanced laboratory facilities that are currently available only at a few academic centers [9]. Suction blister grafting is accomplished by suction of pigmented epidermis from the dermis and its transfer to achromic areas. When the epidermal grafts remain in contact with the denuded surface of the recipient vitiliginous area for about a week, the melanocytes readily migrate to the graft bed, resulting in repigmentation. Therefore, this procedure is actually “melanocyte transfer” and the epidermis obtained through suction blisters is only a carrier [36, 37]. In most studies in the literature, 1 week after the surgical procedure phototherapy was used to induce proliferation of melanocytes at the recipient sites [38–40]. However, in two studies the authors proved that it is not necessary for obtaining repigmentation in vitiliginous areas [41, 42]. The repigmentation rate in all these studies, according to the review by Njoo *et al.*, was 87%, whereas Ozdemir *et al.* reported rates of 25–65% [27, 43]. In a study simi-

lar to ours, Maleki *et al.* evaluated 10 patients with refractory vitiligo who were treated with a suction blister graft and subsequent PUVA therapy and reported over 90% repigmentation in 7 patients [44]. In our study, blister grafting with concomitant phototherapy showed repigmentation over 90% at the 6 months follow-up in 3 patients and over 70% in 6 patients, which according to the most popular criteria for the repigmentation rate (> 90% = complete, 71–90% = good) is a very good result. Although phototherapy alone failed to help the same patients with the same dosage, it succeeded here in restoration of pigmentation in a short time (after 3 months mean 44.5% and after 6 months mean 67.5%). We observed the Koebner phenomenon in the donor area of 1 patient with stable vitiligo like a few authors before [45, 46], but like Kim and Kang [47] we believe that it is not problematic. We compared in detail our results to another study conducted by Maleki *et al.* [42] in which no concomitant phototherapy was performed after SBEG. He evaluated 10 lesions in 10 patients and graded repigmentation rates as ‘complete’ (> 90%), ‘good’ (71–90%), ‘moderate’ (51–70%) and ‘poor’ (< 50%). We evaluated 10 patients with 14 vitiliginous areas and for this comparison graded same repigmentation rates. The results are shown in Table 3. Interestingly, repigmentation rates in our patients are worse than the group of Maleki *et al.* that was not subjected to phototherapy after the surgical procedure. It may be the result of ethnic differences, but to confirm that another study on our patients should be performed where the control group does not have concomitant phototherapy.

## Conclusions

The advantages of this technique include low cost, absence of scarring at donor or recipient sites and the possibility of reusing the donor site. Furthermore, it does not have the limitations of other tissue grafts (minigrafts, pinch grafts, or thin or ultrathin split thickness grafts), which often lead to mismatch in texture and color, not acceptable at cosmetically prominent sites. The disadvantages are that it is time-consuming and not suitable for large areas, which have to be operated on a few times to achieve repigmentation. In summary, the results of our study indicate that SBEG combined with phototherapy can provide rapid, safe, effective treatment for small, stable vitiligo.

**Table 3.** Comparison of repigmentation rate in Maleki *et al.* study vs. our patients

Follow-up visit [months]	Response to treatment							
	Mild		Moderate		Good		Complete	
	Maleki <i>et al.</i>	Our study	Maleki <i>et al.</i>	Our study	Maleki <i>et al.</i>	Our study	Maleki <i>et al.</i>	Our study
3	0%	57%	20%	21%	20%	22%	60%	0%
6	0%	36%	20%	43%	10%	14%	70%	7%

**Conflict of interest**

The authors declare no conflict of interest.

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