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Excimer laser treatment of vitiligo – critical retrospective assessment of own results and literature overview

Excimer-Laser bei Vitiligo – Kritische Wertung eigener retrospektiver Behandlungsergebnisse und Literaturübersicht

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Keywords
- 308-nm excimer laser
- localized vitiligo
- NB UVB
- tacrolimus

Summary

Background: In numerous studies the 308-nm excimer laser has been described as an effective therapy method for localized vitiligo. Our experience and critical evaluation of the relevant literature lead to a less enthusiastic endorsement.

Patients and methods: A total of 9 patients with localized vitiligo were evaluated in our retrospective study. The sessions took place 2–3 times per week; the energy dose was increased depending on the occurring side effects. The rate of repigmentation was evaluated in 5 grades: grade 0 = 0 %, grade 1 = 1–25 %, grade 2 = 26–50 %, grade 3 = 51–75 %, grade 4 = 76–100 %. Subjective patient satisfaction was rated "satisfied" / "not satisfied".

Results: In face and neck areas we used a cumulative energy dose of 16.6 J/ cm^2 and achieved repigmentation grade 4 in 33.3 %, grade 2 in 33.3 %, grade 1 in 11.1 % and no improvement in 22.2 % of the cases. On hands and knees we used a medium cumulative energy dose of 20.8 J/ cm^2 and did not observe any tendency towards repigmentation. Four of the patients were satisfied, while 5 were not. Side effects (erythema, blisters, crusting and perilesional hyperpigmentation) were transient in all cases. Within a medium observation period of 19.1 months, one patient had a relapse.

Conclusions: The excimer laser should be regarded as a treatment alternative in cases of localized vitiligo of the face. The treatment at other sites is clearly limited because of only partial repigmentation, considerable expense of time and money as well as the potentially higher risk of tumorigenesis.

Schlüsselwörter
- 308-nm-Excimer-Laser
- lokalisierte Vitiligo
- NB UVB
- Tacrolimus

Zusammenfassung

Hintergrund: Der 308-nm-Excimer-Laser wird in zahlreichen Studien als effektive Therapiemethode der lokalisierten Vitiligo dargestellt. Eigene Erfahrungen und eine kritische Literaturübersicht gaben Anlass, die Ergebnisse zu relativieren.

Patienten und Methodik: Insgesamt 9 Patienten mit lokalisierter Vitiligo wurden retrospektiv untersucht. Die Sitzungen erfolgten 2–3× pro Woche. Abhängig von den Begleitreaktionen wurde die Energiedichte gesteigert. Die Repigmentierungsrate wurde in 5 Grade eingeteilt: Grad 0 = 0 %, 1 = 1–25 %, 2 = 26–50 %, 3 = 51–75 %, 4 = 76–100 %. Die subjektive Patientenzufriedenheit wurde mit „zufrieden"/„nicht zufrieden" bewertet.

Ergebnisse: An Gesicht und Hals wurde mit einer kumulativen Energiedosis von 16,6 J/ cm^2 bei 33,3 % der Herde eine Repigmentierung Grad 4, in 33,3 % Grad 2, in 11,1 % Grad 1 und in 22,2 % keine Verbesserung erzielt. An Händen und Knien war bei einer mittleren kumulativen Energiedosis von 20,8 J/ cm^2 keine Repigmentierungstendenz zu sehen. Insgesamt 4 der Patienten waren zufrieden, 5 dagegen nicht. Nebenwirkungen (Erytheme, Blasen- oder

Krustenbildung, periläsionale Hyperpigmentierung) waren in allen Fällen transient. Bei einem mittleren Nachbeobachtungszeitraum von 19,1 Monaten kam es bei einem Patienten nach anfänglicher Besserung zu einem Rezidiv.
Schlussfolgerungen: Der Excimer-Laser ist für lokalisierte Vitiligoherde in Gesicht und Hals als Behandlungsalternative zu sehen. Eine meist nur partielle Repigmentierung, der hohe finanzielle und zeitliche Aufwand sowie das potentiell verstärkte Risiko einer Kanzerogenese bei höheren kumulativen Energiedosen schränken die Behandlung an anderen Lokalisationen deutlich ein.

Introduction

Phototherapy has for years been an essential component in the conventional treatment of vitiligo. The use of narrowband UVB therapy (NB UVB) in the generalized forms is limited in localized vitiligo by the UV-burden of normally pigmented perilesional skin. At the same time it is often not possible to achieve the necessary high doses needed for repigmentation in the diseased areas. The excimer (**exc**ited d**imer**) laser used in vitiligo treatment emits light of the wavelength 308 nm and is thus similar to the 311 nm of the established NB UVB therapy. With the laser especially small and hard to access areas can be treated with significantly higher doses in comparison.

Since Báltas et al. first reported a successful excimer laser treatment in a female patient with localized vitiligo on the elbow, numerous studies examined the effectiveness (Table 1) and altogether assess it positively in the regions such as face, neck, trunk and proximal limbs [1–15].

In this paper the existing largely very positive studies concerning vitiligo treatment with the excimer laser will be discussed critically and will be relativized on the basis of our own results.

Patients/Materials and Methods

We examine retrospectively the results of 6 female and 3 male patients (age: 26–69 years, average 49.3 years) with localized vitiligo and skin types II-IV according to Fitzpatrick who were treated with the excimer laser in the time period from 08/2001 to 09/2004 and followed-up.

Two cases showed a progressive course, the other patients had stable lesions for over 6 months. Five of the 9 patients had previously attempted other treatments without success (PUVA, topical steroids, NB UVB). The vitiligo lesions existed at least 1.5 months, in the longest case since 20 years, the mean duration of the disease was 6.7 years. Five of the 9 patients had lesions in the face (perioral, forehead, chin, cheeks) and neck. Four patients presented with lesions on the distal limbs (hands, knees).

Therapy was performed with a xenon-chloride excimer laser (Stella 1.0 Tuilaser, Germany, wavelength 308 nm, pulse duration 60 ns, frequency 200 Hertz, spot size 1.41 cm^2). Patients and physician wore protective glasses during the procedure.

Sessions were performed 2 to 3 times weekly. Depending on side effects either the dose was increased or in the case of blisters or crusts therapy was interrupted on the average for 5–7 days.

Photodocumentation was performed before and after therapy. In cases of beginning repigmentation the course was also documented photographically (camera: Canon EOS 300, objective: Macro Lens EF 100 mm (1:2.8), film: Revue DIA 100 Sunshine).

Repigmentation was rated through objective appraisal of the photographic material through 2 physicians not participants in this study. Repigmentation was rated analogous to Taneja et al. on the basis of a 5-point scale: grade 0 = 0 %, grade 1 = 1–25 %, grade 2 = 26–50 %, grade 3 = 51–75 %, grade 4 = 76–100 % [15]. Subjective patient satisfaction was rated as "satisfied"/"not satisfied".

Due to the retrospective design of the study no untreated control lesions to rule out spontaneous repigmentation were included, neither were consistent treatment parameters employed.

Results

On the face and neck we treated a total of 9 vitiligo lesions in 5 patients. We achieved an improvement of grade 4 in 3 lesions (33 %) (Figure 1) and in a further 3 (33 %) grade 2 (Figure 2). One lesion (11 %) showed a modest repigmentation (grade 1), the other 2 (22 %) did not respond to treatment (grade 0).

On hands and knees none of the 4 patients showed signs of repigmentation, so that no further differentiation of the individual lesions was performed.

The achieved repigmentation was judged by 4 patients as cosmetically satisfactory, by the other 5 as unsatisfactory.

The treatment frequency was between 12 and 39, on the average 23.3 sessions. The dose varied from 100 mJ/cm^2 at the begin of therapy up to a maximal dose of 6000 mJ/cm^2. The cumulative dose ranged from 4.8 J/cm^2 to 37.8 J/cm^2 with an average of 18.2 J/cm^2.

As the most frequent side effect transient erythema occured in 8 patients, further in 8 % of treatment sessions on average blistering and crusting occurred. Perilesional hyperpigmentation was observed in 4 patients; all regressed in the course of 6–8 weeks.

The average follow-up time was 19.1 months. In this observation period one case developed a relapse in an initially repigmented lesion on the neck.

Discussion

The effectiveness of 308-nm excimer laser therapy is like NB UVB phototherapy attributed to immunonodulatory mechanisms (induction and secretion of cytokines, T-cell mediated apoptosis) [17, 19]. Further it is assumed that inactive melanocytes in the outer root sheath of the hair follicles are stimulated to proliferate and migrate by the irradiation and thus produce repigmentation [16, 19].

Only in 3 of the so far published studies was a total repigmentation (100 %) through the excimer laser in a total of 8 patients reported, this corresponds to 0.03 % of treated patients [1–4, 6–15]. The other studies state as best result a repigmentation between 75–100 %. Comparing excimer laser to conventional treatment modalities the former achieves the worst results. For example, topical use of corticosteroids of class 3 (in the German classification according to Niedner) results in 56 %, NB UVB in 63 % and the excimer laser only in 28.6 % a repigmentation of >75 % [1–15, 20].

A recent study out of Korea, however, which directly compares excimer laser and NB UVB shows in 14 patients a significantly quicker and better repigmentation through excimer laser therapy.

The high (49 %) proportion of patients [1, 3, 4, 9, 11, 12, 14, 15] who were

Table 1: Overview of all studies.
Tabelle 1: Gesamtüberblick Studienlage.

Author	No. of pat.	No. of tr. sessions/ duration of tr.	Localisation/ number of lesions	Cumulative dose (J/ cm^2)	Repigmentation	Observation period	Remarks
Báltas et al. [1]	6	2×/ week 6 months	limbs face	57.1 31.5	limbs and face: 75 % ⇒ repigm. >75 %, 25 % ⇒ repigm. <50 %	stable for 3 months	– repigm. after 8th week
Báltas et al. [2]	1	2–3×/ week 6 months	elbows	70.8	almost complete repigm.	stable for 12 months	– repigm. after 3rd month
Choi et al. [3]	69	20–30 tr.	140 lesions: face/neck limbs: acral parts/joints trunk	 11.3 14.9 19.8 12.5	face/neck: 33.3 % ⇒ repigm. >75 % 53.9 % ⇒ repigm. >50 % 69.2 % ⇒ repigm. >25 % limbs: 10.5 % ⇒ repigm. >75 % 15.8 % ⇒ repigm. >50 % 42.1 % ⇒ repigm. >25 % acral parts/joints: 0 % ⇒ repigm. >75 % 0 % ⇒ repigm. >50 % 2.9 % ⇒ repigm. >25 % trunk: 12.5 % ⇒ repigm. >75 % 31.3 % ⇒ repigm. >50 % 62.5 % ⇒ repigm. >25 %	n.m.	– plateau after 20 sessions – various initial doses depending on location
Esposito et al. [4]	24	5–58 tr. 2×/ week 9 months	whole body	n.m.	29 % ⇒ repigm. >75 % 25 % ⇒ repigm. 25–75 % 25 % ⇒ repigm. <25 % 21 % ⇒ repigm. 0 %	stable for 12 months	– various initial doses depending on location – worse response in older lesions

Table 1: Continued.
Tabelle 1: Fortsetzung.

Author	No. of pat.	No. of tr. sessions/ duration of tr.	Localisation/ number of lesions	Cumulative dose (J/ cm^2)	Repigmentation	Observation period	Remarks
Hadi et al. [6]	32	30 tr. sessions or achievement of 75 % repigm.	55 lesions: 21 face 5 head/neck 4 genital 5 trunk 15 limbs 5 hands/feet	n.m.	face: 71.5 % ⇒ repigm. >75 % 76.2 % ⇒ repigm. >50% head/neck: 60 % ⇒ repigm. >75 % 80 % ⇒ repigm. >50% genital: 50 % ⇒repigm. >75 % 75 % ⇒ repigm. >50% trunk: 40 % ⇒ repigm. >75 % 40 % ⇒ repigm. >50% limbs: 46.7 % ⇒ repigm. >75 % 60 % ⇒ repigm. >50% hands/feet: 0 % ⇒ repigm. >75 % 20 % ⇒ repigm. >50%	4 pat. stable for 18 months	– skin type and localisation important – duration of lesions not relevant – small lesions respond better
Hofer et al. [7]	14	1–3×/ week for 6 or 12 weeks	whole body	n.m.	60 % ⇒ repigm. grade 1.7 with tr. 1×/ week 79 % ⇒ repigm. grade 2.4 with tr. 2×/ week 82 % ⇒ repigm. grade 3.3 with tr. 3×/ week	stable for 12 months	– begin of repigm. correlates with number of sessions, not with tr. frequency – grade 0: repigm. 0 %, 1: 1–5 %, 2: 6–25 %, 3: 26–50%, 4: 51–75%, 5: 76–100%

Table 1: Continued.
Tabelle 1: Fortsetzung.

Author	No. of pat.	No. of tr. sessions/ duration of tr.	Localisation/ number of lesions	Cumulative dose (J/ cm^2)	Repigmentation	Observation period	Remarks
Kawalek et al. [9]	8	24 tr. in 10 weeks	20 lesions: 8 proximal 12 limbs	n.m.	A: 50 % ⇒ repigm. >75 % B: 20 % ⇒ repigm. >75 %	n.m.	– A: tacrolimus, B: placebo – quicker and better response in combination
Leone et al. [10]	37	2×/ week 6 months	whole body	12.5-43	49 % ⇒ repigm. >75 % 43 % ⇒ repigm. >50 %	n.m.	– localisation important
Ostovari et al. [11]	35	2×/ week, max. 25 tr.	52 lesions: 14: "UV-sens." 38: "UV-resist."	2.6-15.3	"UV-sens": 57.1 % ⇒ repigm. >75 % "UV-resist.": 15.8 % ⇒ repigm. >75 %	stable for 1 month	– age, sex, skin type, MED and duration of lesion without influence – localisation important
Passeron et al. [12]	14	2×/ week	43 lesions: 20: "UV-sens." 23: "UV-resist."	A: 1.9-17.4 B: 3.3-20.2	A: 70 % ⇒ repigm. >75 % B: 20 % ⇒ repigm. >75 % "UV-sens.": A-77 % ⇒ repigm. >75 % B-57 % ⇒ repigm. >75 % "UV-resist.": A-60 % ⇒ repigm. >75 % B-0 % ⇒ repigm. >75 %	n.m.	– A: tacrolimus, B: placebo – quicker and better response in combination
Spencer et al. [13]	48	4–30 tr 3×/ week,	whole body	n.m.	16.7 % ⇒ repigm. <25 % 37.5 % ⇒ repigm. 25-50 % 20.8 % ⇒ repigm. >50 % 25 % ⇒ repigm. >75 %	n.m.	better response in: – proximal lesions – fresh lesions – skin type III-VI

Table 1: Continued.
Tabelle 1: Fortsetzung.

Author	No. of pat.	No. of tr. sessions/ duration of tr.	Localisation/ number of lesions	Cumulative dose (J/ cm^2)	Repigmentation	Observation period	Remarks
Spencer et al. [14]	18	3×/ week max. 6 or max. 12 tr.	23 lesions: 11 proximal 12 limbs	n.m.	after 6 tr.: 9 % of all lesions ⇒ repigm. >75 % after 12 tr.: 18 % of all lesions ⇒ repigm. >75 %	only 1 pat. observed: stable for 18 months	–
Taneja et al. [15]	18	2×/ week max. 60 tr.	hands/feet face/neck	73.1 9.3	hands/ feet: 0 % ⇒ repigm. >50 % after 60 tr. 20 % ⇒ repigm. 26–50 % after 50 tr. 100 % ⇒ repigm. 0–25 % after 50 tr. face/ neck: 100 % ⇒ repigm. >75 % after 40 tr. 100 % ⇒ repigm. 50–75 % after 30 tr.	n.m.	– worse result in old lesions – between 40th and 60th treatment further improvement in only 30 %
			axillae	18.4	axillae: 100 % ⇒ repigm. 0–25 % after 20 tr. 100 % ⇒ repigm. 25–50 % after 40 tr. 33 % ⇒ repigm. > 75 % after 60 tr.		

pat.: patients
tr.: treatments
repigm.: repigmentation
max.: maximal
n.m.: not mentioned
UV-sens.: UV-sensitive (face, neck, trunk)
UV-resist.: UV-resistent (limbs)

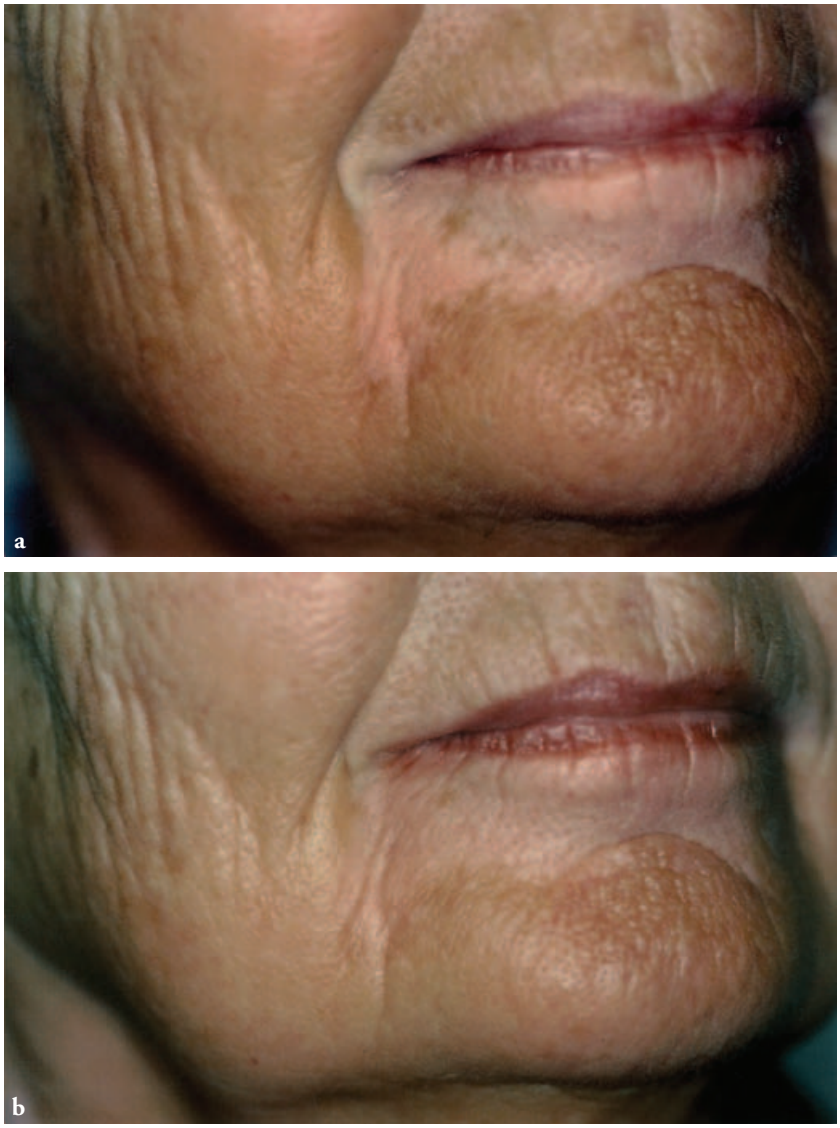

Figure 1: (a) Vitiligo before treatment, (b) Result after 37 treatment sessions: repigmentation grade 4.
Abbildung 1: (a) Vitiligo vor Therapiebeginn, (b) Zustand nach 37 Behandlungen-Repigmentierung Grad 4.

unsuccessfully treated with other forms of phototherapy (PUVA, NB UVB among others) and who showed improvement with excimer laser therapy also speaks for the effectiveness of this laser type. In our study only one female patient had previous unsuccessful NB UVB and here laser therapy could achieve a repigmentation grade 2.

All authors report consistently that response to therapy is very dependent on the location of the lesion, a fact which we can also confirm. One reason for the poor response on the hands could be the generally low density of hair follicles, as repigmentation usually originates from melanocytes of the hair follicles [16, 19].

It is also possible that the better results in other publications result from the application of higher cumulative energy doses [1, 2, 15].

Despite the partial successes we do not consider excimer laser therapy as advisable without limitation for lesions on the distal limbs. The use of high cumulative energy doses necessarily increases the risk of iatrogenic UV-damage. It must also be considered that a repigmentation of 25–50 % as Taneja et al. achieved in 20 % of their patients after 50 sessions often displays an inhomogenous picture which does not satisfy the expectaions of patients, not to speak of the cost/effectiveness relationship. Patients should be thoroughly informed as to realistic results. One of the key criteria is patient satisfaction with the treatment result. Choi et al. consider an improvement of 50 % as cosmetically acceptable. Such repigmentation rates can by comparative analysis of so far published studies with large patient collectives be found after an average of 25.2 sessions in 37.3 % of the cases [3, 4, 9, 11, 15]. Four of our patients, even with only partial repigmentation, were satisfied, the 5 others were not.

The long term results must also be critically analyzed. Only a few authors followed the treatment results over a longer time period. The improvement remained stable in the course of one month [11], 3 [1], 12 [2, 4, 7] up to a maximum of 18 months [6, 14]. In our collective we noted a relapse after 11 months in one patient.

The combination of excimer laser or NB UVB phototherapy with calcineurin inhibitors appears promising. A repigmentation rate >75 % was achieved in 2 studies in 50 % and 70 %, respectively, in lesions co-treated with tacrolimus and only in 20% in excimer monotherapy [9, 12]. Repigmentation under combined therapy also occurred in 19 % and 17 %, respectively, quicker as with excimer laser therapy only. It must be considered, however, that the current prescribing information explicitly warns against the combination of tacrolimus with UV-therapy, hence the combination should only occur in the framework of studies.

Passeron et al. also compared dependence of response rates on localisation. Lesions on localisations which traditionally respond less well to light exposure ("UV-resistant" = limb, especially distal sites) responded with a 75 % repigmentation in 60% to the combination with tacrolimus, none however to excimer laser monotherapy [12]. This data suggest superiority of combination therapy with tacrolimus. This must be confirmed through larger studies with long-time follow-up.

In conclusion we consider excimer laser therapy for vitiligo on the basis of the reported results, the cost/effectiveness analysis and the side effects advisable only for limited lesions of the face. This also explains our low patient numbers, as we restrictively offer this therapy modality to select patients. <<<

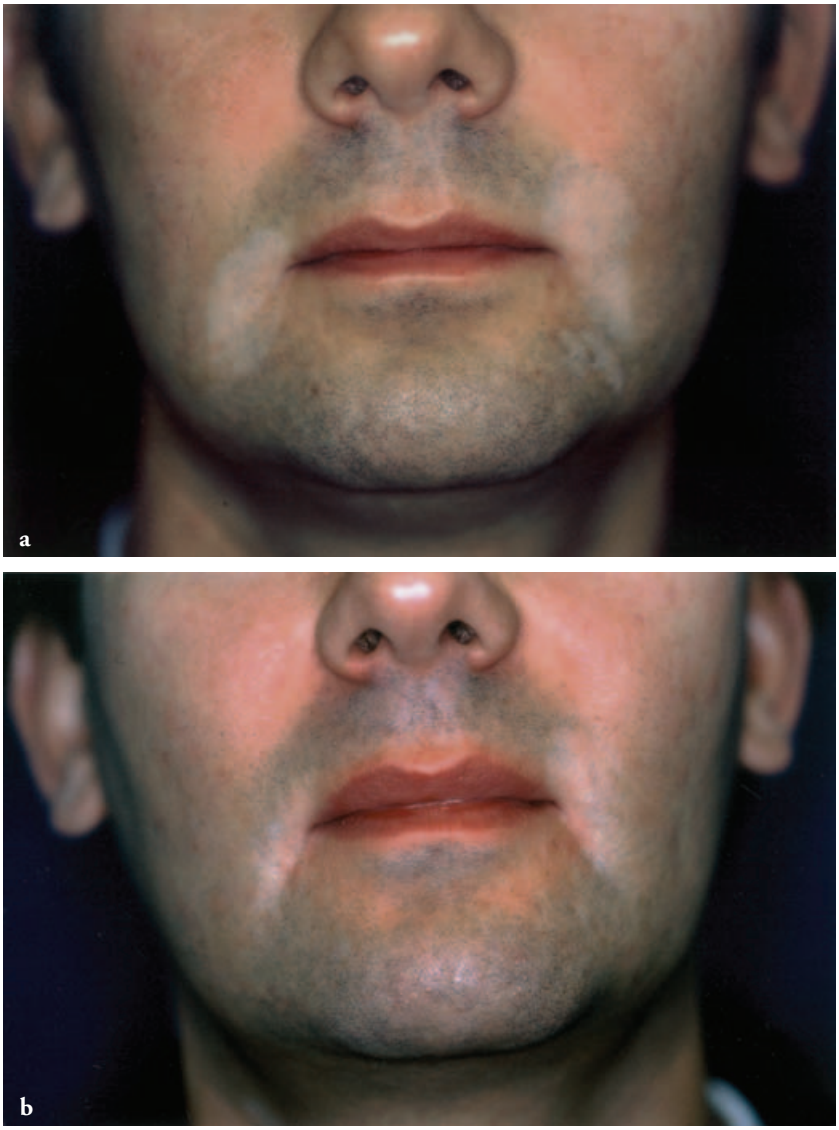

Abbildung 2: (a) Vitiligo vor Therapiebeginn, (b) Zustand nach 33 Behandlungen-Repigmentierung Grad 2.
Figure 2: (a) Vitiligo before treatment, (b) Result after 33 treatment sessions: repigmentation grade 2.

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References

1 Báltas E, Csoma Z, Ignácz F, Ignácz F, Dobozy A, Kemény L. Treatment of vitiligo with the 308-nm xenon chloride excimer laser. Arch Dermatol 2002; 138: 1619–1620.
2 Baltás E, Nagy P, Bónis B, Novák Z, Ignácz F, Szabó G, Bor Z, Dobozy A, Kemény L. Repigmentation of localized vitiligo with the xenon chloride laser. Br J Dermatol 2001; 144: 1266–1267.
3 Choi KH, Park JH, Ro YS. Treatment of vitiligo with 308-nm xenon-chloride excimer laser: therapeutic efficacy of different initial doses according to treatment areas. J Dermatol 2004; 31: 284–292.
4 Esposito M, Soda R, Costanzo A, Chimenti S. Treatment of vitiligo with the 308 nm excimer laser. Clin Exp Dermatol 2004; 29: 133–137.
5 Grema H, Raulin C. Der Excimer-Laser in der Dermatologie und ästhetischen Medizin. Hautarzt 2004; 55: 48–56.
6 Hadi SM, Spencer JM, Lebwohl M. The use of the 308-nm excimer laser for the treatment of vitiligo. Dermatol Surg 2004; 30: 983–986.
7 Hofer A, Hassan AS, Legat FJ, Kerl H, Wolf P. Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients. Br J Dermatol. 2005; 152: 981–985.
8 Hong SB, Park HH, Lee MH. Short-term effects of 308-nm xenon-chloride excimer laser and narrow-band ultraviolet B in the treatment of vitiligo: a comparative study. J Korean Med Sci 2005; 20: 273–278.
9 Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. Dermatol Surg 2004; 30: 130–135.
10 Leone G, Iacovelli P, Paro Vidolin A, Picardo M. Monochromatic excimer light 308 nm in the treatment of vitiligo: a pilot study. J Eur Acad Dermatol Venerol 2003; 17: 531–537.
11 Ostovari N, Passeron T, Zakaria W, Fontas E, Larouy JC, Blot JF, Lacour JP, Ortonne JP. Treatment of vitiligo by 308-nm excimer laser: an evaluation of variables affecting treatment response. Lasers Surg Med 2004; 35: 152–156.
12 Passeron T, Ostovari N, Zakaria W, Fontas E, Larouy JC, Lacour JP, Ortonne JP. Topical tacrolimus and the 308-nm excimer laser: a synergistic combination for the treatment of vitiligo. Arch Dermatol 2004; 140: 1065–1069.
13 Spencer JM, Hadi S. Successful treatment of vitiligo with the 308 nm excimer laser. Lasers Surg Med Suppl 2002; 14: 34.
14 Spencer JM, Nossa R, Ajmeri J. Treatment of vitiligo with the 308-nm excimer laser: a pilot study. J Am Acad Dermatol 2002; 46: 727–731.
15 Taneja A, Trehan M, Taylor CR. 308-nm excimer laser for the treatment of localized vitiligo. Int J Dermatol 2003; 42: 658–662.
16 Yu HS. Melanocyte destruction and repigmentation in vitiligo: a model for nerve cell damage and regrowth. J Biomed Sci. 2002; 9: 564–573.
17 Ongenae K, van Geel N, Naeyaert JM. Evidence for an autoimmune

pathogenesis of vitiligo. Pigment Cell Res 2003; 16: 90–100.
18 Kemp EH, Waterman EA, Weetman AP. Autoimmune aspects of Vitiligo. Autoimmunity 2001; 34: 65–77.
19 Cui J, Shen LY, Wang GC. Role of hair follicles in the repigmentation of vitiligo. J Invest Dermatol 1991; 97: 410–416.
20 Njoo MD, Spuls PI, Bos JD, Westerhof W, Bossuyt PMM. Nonsurgical repigmentation therapies in vitiligo: Meta-analysis of the literature. Arch Dermatol 1998; 134: 1532–1540.