

# LOW-ENERGY HELIUM-NEON LASER THERAPY INDUCES REPIGMENTATION AND IMPROVES THE ABNORMALITIES OF CUTANEOUS MICROCIRCULATION IN SEGMENTAL-TYPE VITILIGO LESIONS

Chieh-Shan Wu,<sup>1,2</sup> Stephen Chu-Sung Hu,<sup>1</sup> Cheng-Che E. Lan,<sup>1,2</sup> Gwo-Shing Chen,<sup>1,2</sup>  
Wen-Ho Chuo,<sup>3</sup> and Hsin-Su Yu<sup>1,2</sup>

<sup>1</sup>Department of Dermatology, Kaohsiung Medical University Hospital, and <sup>2</sup>Department of Dermatology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, and <sup>3</sup>Department of Pharmacy, Tajen University, Pingtung, Taiwan.

Segmental vitiligo (SV) is a special form of vitiligo occurring in a dermatomal distribution, and an abnormality involving the sympathetic nerves supplying the affected dermatome is known to underlie this disorder. Previously, we have shown that SV is associated with an abnormal increase in cutaneous blood flow and adrenoceptor responses in the affected areas. Since SV is resistant to conventional forms of therapy, its management represents a challenge for dermatologists. Low energy helium-neon lasers (He-Ne laser, wavelength 632.8 nm) have been employed as a therapeutic instrument in many clinical situations, including vitiligo management and repair of nerve injury. The purpose of this study was to evaluate the effectiveness and safety of He-Ne lasers in treating SV, and determine their effects on the repair of sympathetic nerve dysfunction. Forty patients with stable-stage SV on the head and/or neck were enrolled in this study. He-Ne laser irradiation was administered locally at 3.0 J/cm<sup>2</sup> with point stimulation once or twice weekly. Cutaneous microcirculatory assessments in six SV patients were performed using a laser Doppler flowmeter. The sympathetic adrenoceptor response of cutaneous microcirculation was determined by measuring cutaneous blood flow before, during and after iontophoresis with sympathomimetic drugs (phenylephrine, clonidine and propranolol). All measurements of microcirculation obtained at SV lesions were simultaneously compared with contralateral normal skin, both before and after He-Ne laser treatment. After an average of 17 treatment sessions, initial repigmentation was noticed in the majority of patients. Marked repigmentation (>50%) was observed in 60% of patients with successive treatments. Cutaneous blood flow was significantly higher at SV lesions compared with contralateral skin, but this was normalized after He-Ne laser treatment. In addition, the abnormal decrease in cutaneous blood flow in response to clonidine was improved by He-Ne laser therapy. Our study showed that He-Ne laser therapy is an effective treatment for SV by normalizing dysfunctions of cutaneous blood flow and adrenoceptor responses in SV patients. Thus, the beneficial effects of He-Ne laser therapy may be mediated in part by a reparative effect on sympathetic nerve dysfunction.

**Key Words:** cutaneous microcirculation, He-Ne laser, segmental-type vitiligo, sympathetic adrenoceptor response  
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Received: Oct 17, 2007 Accepted: Dec 10, 2007  
Address correspondence and reprint requests to:  
Dr Hsin-Su Yu, Department of Dermatology,  
Kaohsiung Medical University Hospital, 100  
Tzyou 1<sup>st</sup> Road, Kaohsiung 807, Taiwan.  
E-mail: dermyu@kmu.edu.tw

Low-energy helium-neon lasers (He-Ne laser, wavelength 632.8 nm) have all the normal properties of lasers, including monochromaticity, parallelism, and coherence. However, the energy output is so low that direct irradiation (biostimulation), rather than a thermal effect, is responsible for the biological alterations they

induce. By definition, low-energy lasers do not produce temperature elevations above 0.1–0.5°C in irradiated tissues [1–3]. Low energy lasers have potential therapeutic applications in rheumatoid arthritis [4], wound healing [5], postherpetic neuralgia [6,7], and recovery following nerve injury [8,9]. The continuous wave He-Ne laser has been most frequently employed in these clinical situations [10]. Recently, studies have demonstrated that low-energy lasers induce biostimulatory effects on cultured cells. He-Ne laser irradiation stimulates the release of various growth factors by macrophages and other cells and results in the proliferation of fibroblasts and keratinocytes [11–14]. We have previously shown that He-Ne laser irradiation could induce the release of basic fibroblast growth factor (bFGF) and nerve growth factor (NGF) from cultured keratinocytes, and stimulate migration and proliferation of cultured melanocytes [15]. Moreover, He-Ne lasers have been found to induce locomotion of immature melanoblasts and promote melanogenesis of differentiated melanoblasts *in vitro* [16]. These results suggest that He-Ne lasers may have biostimulatory effects on various cell types residing in the skin.

Vitiligo is a common pigmentary disorder characterized by depigmented macules due to the loss of melanocytes. The mechanisms underlying how melanocytes disappear from vitiliginous skin is still not completely defined. Clinically and physiologically, vitiligo can be classified into two distinct types: nonsegmental-type vitiligo (NSV), which is associated with autoimmune diseases, and segmental-type vitiligo (SV), which occurs in a dermatomal distribution and is associated with a dysfunction of the sympathetic nerves in affected skin [17,18]. The sympathetic nervous system has a profound effect on cutaneous blood flow, mainly by influencing arterioles and arteriovenous anastomoses (thermoregulatory vessels) [19]. Therefore, measurement of cutaneous blood flow and its adrenoceptor response can reflect the sympathetic nerve function of a certain skin area. Previously, we demonstrated that cutaneous blood flow and adrenoceptor responses are abnormally increased in SV lesions [18].

Conventional therapies for patients with vitiligo include topical corticosteroids, phototherapy, and photochemotherapy. Recent investigations have reported 63% effectiveness for ultraviolet-B light (UVB), 75% for NB-UVB, 45% for topical psoralens and ultraviolet-A

light (PUVA), 63% for oral PUVA, and 44% for topical steroid therapy in vitiligo treatment (including all types of vitiligo) [20–22]. Twenty to 40 sessions of PUVA treatments are usually required before initial repigmentation occurs [21]. Although these therapeutic modalities may induce varying degrees of repigmentation in vitiligo lesions, potential undesirable effects, including erythema, bullous formation, and hyperpigmentation, may occur. In particular, chronic irradiation of periocular vitiligo lesions may lead to ophthalmic damage, such as cataract and visual acuity deterioration. Furthermore, SV responds poorly to these forms of treatment, with only surgical intervention during the stable stage showing efficacy [23–26], but patients fear surgery and anesthesia. Thus, finding a safe and effective treatment for SV is an important aspect of current research.

Previous reports have shown that He-Ne laser irradiation leads to biological effects, such as an improvement in nerve injury [8,27]. We have also shown in our pilot study that a low energy He-Ne laser is effective for treating patients with SV [15]. The purpose of this study was to further evaluate whether He-Ne laser therapy is a safe and effective treatment modality for SV, and to clarify its biological effects on the repair of sympathetic nerve dysfunction.

## MATERIALS AND METHODS

### Subjects

Forty patients with facial and/or neck stable-stage SV were selected for this study. There was no history of autoimmune diseases (such as thyroid disease, Addison's disease, pernicious anemia, insulin-dependent diabetes mellitus or alopecia areata) or other systemic diseases among these patients. None of the patients had received treatment for vitiligo in the preceding 3 months. There were 17 females and 23 males, with ages ranging from 3 to 43 years (mean age, 20 ± 12 years). Assessments of cutaneous blood flow and sympathetic adrenoceptor responses were performed and analyzed in six patients who experienced obvious repigmentation (50%) after He-Ne laser treatment. In addition, 10 healthy individuals without vitiligo were enrolled as normal controls for the experiments on cutaneous blood flow. The study was approved by the Institutional Review Board of the Kaohsiung Medical University.

### ***Treatment of vitiliginous lesions with He-Ne laser irradiation***

A continuous wave He-Ne laser (OMNIPROBE™ Laser Biostimulation System, Physio Technology, Topeka, KS) with an average power output of 1.0 mW was used for treatment as previously described in our pilot study [15]. It was designed for point stimulation (irradiation point by point) once or twice a week, and the irradiating flux for each treatment point was 3.0 J/cm<sup>2</sup>. No other therapeutic interventions were employed during the course of He-Ne laser treatment.

### ***Evaluation of repigmentation***

Vitiliginous lesions in all patients were manually traced and the square centimeters of involvement counted on an overlaid grid. The lesions were recorded regularly before, during and after He-Ne laser therapy. The percentage of repigmentation after He-Ne laser treatment was defined as follows: (area of repigmented vitiligo lesion ÷ area of vitiligo lesion prior to He-Ne laser therapy) × 100%.

### ***Laser Doppler flowmetry***

Cutaneous microcirculatory assessments were performed as previously described in our pilot study [18]. A laser Doppler flowmeter (PeriFlux, PF3, Perimed, Sweden) was used for cutaneous blood flow measurement. For comparison, the blood flow of contralateral normal skin was also measured. Standard probes (PF408) were fixed on lesions and the contralateral normal skin, and measurements were made simultaneously before He-Ne laser treatment. The blood flow (blood cell flux or perfusion) was expressed in perfusion units (PUs). The flow was calculated by the product of the number of red blood cells moving in the measured volume (within the surface capillaries of the skin) and the mean velocity of these cells. The perfusion ratio (PR) is defined as: (perfusion units of lesional skin ÷ perfusion units of contralateral normal skin) × 100%. After obvious repigmentation induced by regular He-Ne laser treatment, standard probes were fixed on the lesions (residual vitiligo lesion or repigmented area) and the contralateral normal skin, and measurements were made simultaneously. All measurements were repeated three times, and the mean values of perfusion units were analyzed by Perisoft, the Perimed analysis program for PeriFlux.

### ***Sympathetic adrenoceptor response***

The  $\alpha$ - and  $\beta$ -adrenoceptor responses of the cutaneous microcirculation were measured using the method of Ekenvall and Lindblad with a slight modification, as described previously in our pilot study [18,28]. The Perilont MicroPharmacology System (Perimed) was employed for iontophoresis. Cutaneous blood flow was recorded with a laser Doppler flowmeter before, during and after the iontophoresis. The probe holders with a drug delivery electrode (PF383, Perimed) were placed on the lesion and the contralateral normal skin. Phenylephrine (1 mM; Sigma, St Louis, MO, USA), clonidine (10 mM; Sigma) and propranolol (10 nM; Sigma) were used as  $\alpha_1$ -,  $\alpha_2$ -adrenoceptor agonists and  $\beta$ -adrenoceptor antagonist, respectively. The intensity of the electric current was maintained at 200  $\mu$ A DC during the iontophoresis. After obvious repigmentation by regular He-Ne laser treatment, the standard probes were fixed on the lesions (residual vitiligo lesion or repigmented area) and the contralateral normal skin, and measurements were made simultaneously. All measurements were repeated three times.

### ***Statistical analysis***

Statistical analysis was performed using SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). Data are expressed as mean  $\pm$  standard deviation. Statistical significance was tested using paired and unpaired Student's *t* tests or one-way ANOVA. Statistical significance was defined as  $p < 0.05$ .

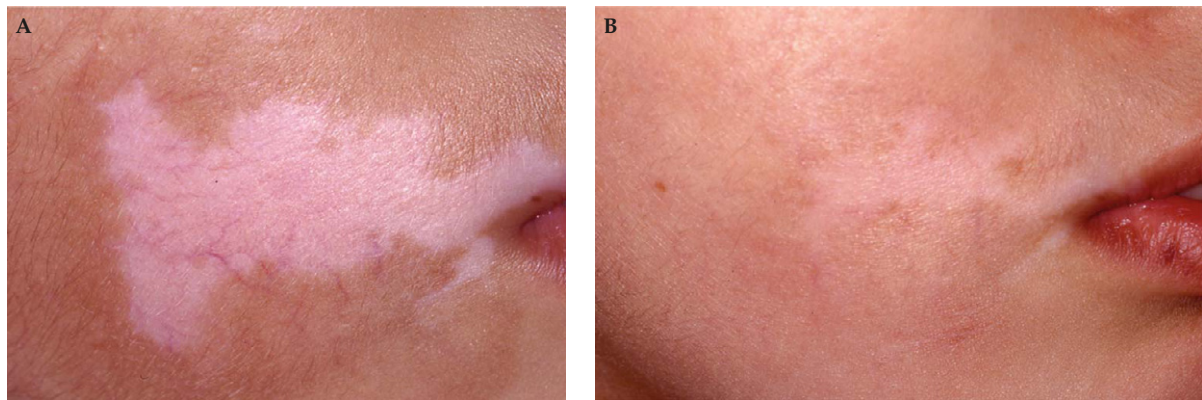
## **RESULTS**

### ***Low-energy He-Ne laser therapy is a safe and effective treatment modality for SV***

Patients with SV were treated with a He-Ne laser once or twice a week; their treatment responses are shown in Table 1. Among the 40 patients who received He-Ne laser treatment, the majority exhibited initial repigmentation at the edges (perilesional repigmentation) after receiving an average of 17  $\pm$  10 treatments. After further treatment, both perilesional and perifollicular repigmentation could be seen in most patients. Marked repigmentation (>50%) was observed in 60% of patients following successive treatments. The repigmented areas were similar in color to normal skin, and no obvious hyperpigmentation was noticed. Three patients (7.5%) experienced complete repigmentation

**Table 1.** Effectiveness of He-Ne laser treatment in 40 SV patients

Repigmentation, %	Patients, <i>n</i> (%)	Initial repigmentation, number of treatments	Total number of treatments
100	3 (7.5)	7±1	20±4
76–99	6 (15)	19±13	158±32
51–75	15 (37.5)	17±8	132±76
26–50	12 (30)	20±11	89±47
≤25	2 (5)	16±1	69±45
0	2 (5)		53±13
Total	40 (100)		



**Figure.** (A) A 5-year-old girl who had vitiligo on the right cheek for 1 year. She had undergone treatment with short-term topical PUVA combined with topical steroids in another hospital. Obvious perilesional hyperpigmentation, hypertrichosis and telangiectasia were noted, in addition to no clinical improvement. (B) After 174 treatment sessions, there was 84% repigmentation. In addition, the previous perilesional hyperpigmentation, hypertrichosis and telangiectasia gradually improved after the former treatment was stopped.

after  $20 \pm 4$  treatment courses, but needed to maintain one to two treatments per month in order to avoid redepigmentation. Six patients (15%) achieved 76–99% repigmentation after  $158 \pm 32$  treatments; 15 patients (37.5%) showed 51–75% repigmentation after  $132 \pm 76$  treatments; 12 patients (30%) displayed 26–50% repigmentation after  $89 \pm 47$  treatments; two patients (5%) achieved <25% repigmentation after  $69 \pm 45$  treatments; and two patients (5%) had no repigmentation at all. One of these patients had had vitiligo for 16 years, the other for 30 years. This is consistent with earlier reports indicating that patients with longer duration of the disease are more resistant to therapy [29]. There was no significant difference between the early-onset ( $\leq 12$  years old,  $52.8 \pm 19.7\%$ ) and late-onset ( $> 12$  years old,  $55.6 \pm 31.1\%$ ) groups in terms of treatment response. Nine patients (22.5%) were lost in follow-up due to schoolwork, busy jobs, distant residence, poor treatment response or other reasons. There was no obvious discomfort or side effects during or after He-Ne laser therapy for any of the patients.

In the Figure, we show one typical case of SV demonstrating obvious repigmentation following He-Ne laser treatment. This was a 5-year-old girl who had vitiligo on the right cheek for 1 year. She had previously accepted short-term topical PUVA combined with topical steroid treatments in another hospital. Obvious perilesional hyperpigmentation, hypertrichosis and telangiectasia were noticed, in addition to no clinical improvement (Figure A). After 174 treatment sessions, 84% repigmentation was found. In addition, the previous perilesional hyperpigmentation, hypertrichosis and telangiectasia gradually improved after ceasing former treatments (Figure B).

#### **Improvement in microcirculation at the lesional site of SV after He-Ne laser treatment**

Six patients with marked repigmentation following He-Ne laser treatment underwent microcirculatory assessments. As shown in Table 2, the pretreatment PR between lesion sites and contralateral normal skin for

**Table 2.** Perfusion ratios for SV lesions and normal skin to contralateral normal skin before He-Ne laser treatment, and for residual vitiligo lesions and repigmented lesions to contralateral normal skin after He-Ne laser treatment

	Perfusion ratio (PR)			
	Before He-Ne laser treatment		After He-Ne laser treatment	
	Lesion/Normal	Normal/Normal	Lesion <sup>#</sup> /Normal	Repigment/Normal
SV ( $n=6$ )	$2.9 \pm 0.6^*$	$1.4 \pm 0.2$	$1.6 \pm 0.2$	$1.5 \pm 0.2$
Normal controls ( $n=10$ )		$1.4 \pm 0.2^\dagger$		

\* $p < 0.01$  when compared with other groups; <sup>†</sup>PR of normal control group (high PU side/low PU side). Lesion/Normal = ratio of SV lesion perfusion units (PUs) compared with PUs of contralateral normal skin before treatment; Normal/Normal = lesion side normal skin PUs compared with PUs of contralateral normal skin before treatment; Lesion<sup>#</sup>/Normal = residual vitiligo lesion PUs compared with PUs of contralateral normal skin after treatment; Repigment/Normal = repigmented lesion PUs compared with PUs of contralateral normal skin after treatment.

**Table 3.** Comparison of sympathetic adrenoceptor responses in SV lesions before He-Ne laser treatment and residual vitiligo lesions and repigmented areas after He-Ne laser treatment\*

	Before He-Ne laser treatment ( $n=6$ )	After He-Ne laser treatment ( $n=6$ )		Normal controls <sup>†</sup> ( $n=10$ )
	Lesion, %	Residual lesion, %	Repigmented area, %	Normal area, %
Phenylephrine	$20.5 \pm 7.8$	$22.8 \pm 18.9$	$19.6 \pm 10.2$	$3.2 \pm 0.6$
Clonidine <sup>‡</sup>	$46.4 \pm 13.0$	$30.1 \pm 15.8$	$18.1 \pm 11.6$	$6.4 \pm 1.2$
Propranolol	$32.3 \pm 9.8$	$27.7 \pm 8.3$	$24.0 \pm 11.4$	$4.7 \pm 1.1$

\*Data expressed as percent of blood flow decrement measured over a 15-minute period following iontophoresis with sympathomimetic drugs; <sup>†</sup>sympathetic adrenoceptor response in 10 normal controls is also shown as a reference for comparison; <sup>‡</sup>normalization of blood flow was statistically significant in the clonidine group (one-way ANOVA,  $p < 0.05$ ).

these six patients was  $2.9 \pm 0.6$ , while the PR between lesion side normal skin and contralateral normal skin was  $1.4 \pm 0.2$ . This difference was statistically significant ( $p < 0.01$ ). After He-Ne laser treatment with obvious repigmentation, the PR between the residual lesions and contralateral normal skin decreased to  $1.6 \pm 0.2$ , and the PR between the repigmented lesions and contralateral normal skin decreased to  $1.5 \pm 0.2$ . The PRs of the residual lesions and repigmented areas of SV patients after He-Ne laser treatment were not significantly different compared to normal controls ( $1.4 \pm 0.2$ ). Hence, after He-Ne laser treatment, there was a significant normalization of cutaneous microcirculation in the SV lesional skin.

We also found that the PU was not the same between the two sides in normal controls (the PR between the high PU side and the low PU side was  $1.4 \pm 0.2$ ). It was not possible to predict which side would have the higher PU, and it is not related to hand dominance. The physiologic significance of this PU difference is unclear.

### **Improvement in adrenoceptor response of the SV lesional site after He-Ne laser treatment**

As shown in Table 3, the six SV patients with marked repigmentation were given iontophoresis with phenylephrine ( $\alpha_1$ -agonist), clonidine ( $\alpha_2$ -agonist), and propranolol ( $\beta$ -blocker) before He-Ne laser treatment, resulting in a marked decrease in blood flow at the lesional sites. The average decreases in blood flow were  $20.5 \pm 7.8\%$  (phenylephrine),  $46.4 \pm 13.0\%$  (clonidine), and  $32.3 \pm 9.8\%$  (propranolol). Following He-Ne laser treatment with significant repigmentation, there was a partial normalization of blood flow. At residual vitiligo lesion sites, the average decreases were  $22.8 \pm 18.9\%$  (phenylephrine),  $30.1 \pm 15.8\%$  (clonidine) and  $27.7 \pm 8.3\%$  (propranolol). At the repigmentation sites, the average decreases were  $19.6 \pm 10.2\%$  (phenylephrine),  $18.1 \pm 11.6\%$  (clonidine), and  $24.0 \pm 11.4\%$  (propranolol). The normalization of blood flow was statistically significant in the clonidine group (one way ANOVA,  $p < 0.05$ ), but not in the phenylephrine or propranolol groups. Hence, He-Ne laser treatment

caused a normalization of sympathetic adrenoceptor responses to clonidine ( $\alpha_2$ -agonist), and may have reparative effects on adrenoceptor dysfunction.

## DISCUSSION

Vitiligo is an acquired disorder of pigmentation in which depigmentation of skin and hair occurs due to a loss of melanocytes from the epidermis. SV occurs in an asymmetric dermatomal distribution. Due to its earlier onset, recalcitrant course, and decreased association with autoimmune diseases, SV is regarded as a special form of vitiligo [24,30]. After various forms of therapy, repigmentation of vitiligo lesions may occur. This involves the proliferation of inactive melanocytes in the outer root sheath of the hair follicle, followed by their upward migration to the adjacent epidermis to form perifollicular pigment islands [31].

Low energy He-Ne laser treatment has been shown to be a safe and effective treatment modality for patients with vitiligo [15]. In a study involving 18 vitiligo patients, Mandel et al (1997) reported that after 6–8 months of He-Ne laser therapy, marked repigmentation was seen in 63.9% of patients and some follicular repigmentation was seen in 34.4% of patients [32]. In this study, initial repigmentation was noticed after an average of 17 He-Ne laser therapy sessions. Marked repigmentation (>50%) was observed in 60% of patients following successive treatments and three patients (7.5%) showed 100% recovery. Thus, our results confirm that He-Ne laser irradiation is effective in treating SV. The effectiveness of He-Ne laser treatment is comparable with that of conventional therapies for vitiligo (Table 4) [20–23,26,29,33–35].

The low energy He-Ne lasers used in this study are categorized as class 2 lasers. They are considered to be safe, but the doctor and patient should not stare directly into the light beam. No obvious adverse effects were found in our patients or reported in the literature [36]. Unlike therapy with ultraviolet light, He-Ne laser treatment did not result in erythema, bullous formation, or hyperpigmentation. In addition, long-term He-Ne laser treatment of periocular vitiligo lesions did not lead to any impairment in visual acuity, even if no eye protection equipment was worn during therapy.

The pathogenesis of SV remains obscure. Since depigmentation occurs in a dermatomal distribution, an

abnormality involving the segmental nerves supplying the affected dermatome may underlie this disorder. Previously, we demonstrated a nearly threefold increase in cutaneous blood flow at SV lesions compared with contralateral normal skin, which was associated with a significant increase in the cutaneous adrenoceptor responses in SV lesions [18]. This suggests that a dysfunction of the sympathetic nerves supplying the affected dermatome exists in the affected skin, and may play a role in the pathogenesis of SV. Sympathetic nerves control blood flow through the skin, and are responsible for the vasoconstriction response in cutaneous vessels. Therefore, damaged sympathetic nerves may lead to vasodilatation and an increase in cutaneous blood flow in SV lesions. In addition, it is conceivable that sympathetic nerve dysfunction may result in abnormal and excessive cutaneous adrenoceptor response in the lesional skin. However, further investigations are required to clarify the association between the abnormalities in cutaneous microcirculation, dysfunction of sympathetic nerves, and loss of functional melanocytes in SV.

The mechanisms by which He-Ne laser treatment induces repigmentation of vitiligo lesions are still unclear, although several hypotheses have been proposed. Previously, we have demonstrated that He-Ne laser irradiation can induce the release of basic fibroblast growth factor (bFGF) and nerve growth factor (NGF) from cultured keratinocytes and stimulate the migration and proliferation of cultured melanocytes [15]. bFGF is a melanocyte growth factor, whereas NGF promotes melanocyte survival in skin. Thus, by stimulating the release of these two cytokines, He-Ne laser therapy may induce perilesional and perifollicular repigmentation in SV patients. In addition, there have been reports indicating that He-Ne laser therapy has reparative effects on the microcirculation and nerve cells [9,37–39]. Since we have shown that SV is associated with dysfunctions of the cutaneous microcirculation and sympathetic nerves, it is possible that He-Ne laser therapy may lead to improvements in these abnormalities. In this study, the increase in microcirculation at SV lesional sites was normalized after He-Ne laser therapy. In fact, the residual lesions and repigmented areas of SV patients after He-Ne laser treatment showed no significant differences in PR compared with normal controls. In addition, the assay of sympathetic adrenoceptor function in residual lesions and repigmented areas demonstrated progressive

**Table 4.** Comparisons of the effectiveness of the He-Ne laser and common vitiligo therapies

Treatment mode	Topical steroids [21,35]	Topical 0.1% tacrolimus [33,35]	UVB/NB-UVB [20,22,29,35]	PUVA [34,35]	Surgical treatments [26,35]	He-Ne
Effectiveness	41–54%	41–58%	57–67%	45–69%, but poor in SV (2.4%) [23]	56–90%	60% in our study in SV
Advantages	Easy & convenient application	Easy & convenient application	Suitable for lesions involving large BSA, easy application	Suitable for lesions involving large BSA	Suitable for intractable lesions	Simple, convenient, safe & effective
Contraindications or limitations	Steroid allergy	Tacrolimus allergy	Photoallergy, history of skin cancer; not suitable for periorbital or genital lesions	Pregnancy, breast-feeding, photoallergy, history of skin cancer; not suitable for periorbital or genital lesions; need psoralen pretreatment	Active stage; phobia of anesthesia or surgery	None
Possible adverse effects or potential risks	Skin atrophy, purpura, rosacea-like dermatitis, telangiectasia, folliculitis or acne	Pruritus, burning sensation, local infection, acne	Hyperpigmentation, pruritus, xerosis, photoaging, carcinogenesis	Nausea, vomiting, GI upset after psoralen intake, hyperpigmentation, bulla formation, focal hypertrichosis & hyperkeratosis, pruritus, xerosis, photoaging, carcinogenesis	Scar formation, Koebner phenomenon, uneven color	None

BSA = body surface area; GI = gastrointestinal.

improvement (namely, the percent of lesional PU after iontophoresis decreased in the following order: before treatment > residual vitiligo after treatment > repigmented area after treatment). The phenylephrine and propranolol groups showed improvement, but only the clonidine group showed statistical significance. Thus, the beneficial effect of He-Ne laser therapy on vitiligo lesions may be mediated partially by reparative effects on the cutaneous microcirculation and damaged sympathetic nerves. One possible explanation for this phenomenon may be that a He-Ne laser, through biostimulation, regulates the local physiologic condition of the lesion and creates an environment favorable for melanocyte survival. Normalization of PR is an important indicator of the biostimulatory regulation of cutaneous microcirculation [38]. However, we also found that, even in the repigmented lesion, the sympathetic adrenergic responses had not completely recovered. This may be the reason why the three patients with complete repigmentation still needed maintenance therapy twice a month to prevent recurrence. The duration of He-Ne laser therapy required to completely repair the dysfunction of sympathetic nerves, and the effect of a He-Ne laser on individual  $\alpha$ - and  $\beta$ -adrenoceptors, require further study.

Our results confirmed the effectiveness and safety of He-Ne lasers in treating SV, and showed that this may be mediated in part by an improvement of sympathetic nerve dysfunction. The effectiveness of He-Ne laser treatment is comparable to that of conventional therapies for vitiligo. He-Ne laser irradiation is an easier treatment modality to administer, less expensive and has no adverse effects compared with other conventional therapies. Hence, we conclude that He-Ne lasers can effectively treat SV and have reparative effects on damaged sympathetic nerve function.

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## REFERENCES

1. Basford JR. Low-energy laser therapy: controversies and new research findings. *Laser Surg Med* 1989;9:1-5.

2. Yu W, Naim JO, Lanzafame RJ. The effect of laser irradiation on release of bFGF from 3t3 fibroblast. *Photochem Photobiol* 1994;59:167-70.
3. Babapour R, Glassberg E, Lask GP. Low-energy systems. *Clin Dermatol* 1995;13:87-90.
4. Goldman JA, Casay H, Bass N, et al. Laser therapy of rheumatoid arthritis. *Lasers Surg Med* 1980;1:93-101.
5. Lyons RF, Abergel RP, White RA, et al. Biostimulation of wound healing *in vivo* by a helium-neon laser. *Ann Plast Surg* 1987;18:47-50.
6. Kemmotsu O, Sato K, Furumido H, et al. Efficacy of low reactive-level laser therapy for pain attenuation of post-herpetic neuralgia. *Laser Ther* 1991;3:71-5.
7. Yaksich I, Tan LC, Previn V. Low energy laser for treatment of post-herpetic neuralgia. *Ann Acad Med Singapore* 1993;22 Suppl:441-2.
8. Khullar SM, Bordin P, Barkvoll P, et al. Preliminary study of low-level laser for treatment of longstanding sensory alternation in the inferior alveolar nerve. *J Oral Maxillofac Surg* 1996;54:2-7.
9. Mohammed IF, Al-Mustawfi N, Kaka LN. Promotion of regenerative processes in injured peripheral nerve induced by low-level laser therapy. *Photomed Laser Surg* 2007;25:107-11.
10. Pötinen PJ. Indications for LLLT and results. In: Pötinen PJ, ed. *Low Level Laser Therapy as a Medical Treatment Modality*. Tampere: Art Urpo Ltd., 1992:116-41.
11. Abergel RP, Lyon RF, Castel JC, et al. Biostimulation of wound healing by lasers: experimental approaches in animal models and in fibroblast cultures. *J Dermatol Surg Oncol* 1987;13:127-33.
12. Haas AF, Isseroff RR, Wheeland RG, et al. Low-energy helium-neon laser irradiation increases the motility of cultured human keratinocytes. *J Invest Dermatol* 1990;94:822-26.
13. Yu HS, Chang KL, Yu CL, et al. Low-energy helium-neon laser irradiation stimulates interleukin 1 alpha and interkeukin-8 release from cultured human keratinocytes. *J Invest Dermatol* 1996;107:593-6.
14. Young S, Bolton P, Dyson M, et al. Macrophage responsiveness to light therapy. *Lasers Surg Med* 1989;9:497-505.
15. Yu HS, Wu CS, Yu CL, et al. Helium-neon laser irradiation stimulates migration and proliferation in melanocytes and induces repigmentation in segmental type vitiligo. *J Invest Dermatol* 2003;120:56-64.
16. Lan CC, Wu CS, Chiou MH, et al. Low-energy helium-neon laser induces locomotion of the immature melanoblasts and promotes melanogenesis of the more differentiated melanoblasts: recapitulation of vitiligo repigmentation *in vitro*. *J Invest Dermatol* 2006;126:2119-26.
17. Koga M. Vitiligo: a new classification and therapy. *Br J Dermatol* 1977;97:255-61.
18. Wu CS, Yu HS, Chang HR, et al. Cutaneous blood flow and adrenoceptor response increase in segmental-type vitiligo lesions. *J Dermatol Sci* 2000;23:53-62.
19. Fox RH, Edholm OG. Nervous control of the cutaneous circulation. *Br Med Bull* 1963;19:110-4.



20. Westerhof W, Nieuweboer-Krobotova L. Treatment of vitiligo with UVB radiation *vs* topical psoralen plus UVA. *Arch Dermatol* 1997;133:1525–8.
21. Plott RT, Wagner FR. Modern treatment approaches to vitiligo. *Cutis* 1990;45:311–6.
22. Njoo MD, Bos JD, Westerhof W. Treatment of generalized vitiligo in children with narrow-band (TL-01) UVB radiation therapy. *J Am Acad Dermatol* 2000;42:245–53.
23. El-Mofty AM, El-Mofty M. Vitiligo: a symptom complex. *Int J Dermatol* 1980;19:237–44.
24. Koga M, Tango T. Clinical features and course of type A and type B vitiligo. *Br J Dermatol* 1988;118:223–8.
25. Hann SK, Lee HJ. Segmental vitiligo: clinical findings in 208 patients. *J Am Acad Dermatol* 1996;35:671–4.
26. Mulekar SV. Long term follow-up study of segmental and focal vitiligo treated by autologous, noncultured melanocyte-keratinocyte cell transplantation. *Arch Dermatol* 2004;140:1211–5.
27. Rochkind S, Rousso M, Nissan M, et al. Systemic effects of low-power laser irradiation on the peripheral and central nervous system, cutaneous wounds and burns. *Lasers Surg Med* 1989;9:174–82.
28. Ekenvall L, Lindblad LE. Is vibration white finger a primary sympathetic nerve injury? *Br J Ind Med* 1986; 43:702–6.
29. Scherschun L, Kim JJ, Lim HW. Narrow-band ultraviolet B is a useful and well-tolerated treatment for vitiligo. *J Am Acad Dermatol* 2001;44:999–1003.
30. Kovacs SO. Vitiligo. *J Am Acad Dermatol* 1998;38:647–66.
31. Fitzpatrick TB. Mechanisms of phototherapy of vitiligo. *Arch Dermatol* 1997;133:1591–2.
32. Mandel AS, Haberman HF, Pawlowski D, et al. Non PUVA nonsurgical therapies for vitiligo. *Clin Dermatol* 1997;15:907–19.
33. Lepe V, Moncada B, Castaneda-Cazares JP, et al. A double-blind randomized trial of 0.1% tacrolimus *vs* 0.05% clobetasol for treatment of childhood of vitiligo. *Arch Dermatol* 2003;139:581–5.
34. Grimes PE. Psoralen photochemotherapy for vitiligo. *Clin Dermatol* 1997;15:921–6.
35. Forschner T, Buchholtz S, Stocjlesh E. Current state of vitiligo therapy—evidence-based analysis of the literature. *JDDG* 2007;5:467–76.
36. Pötinen PJ. The physics of laser. In: Pötinen PJ, ed. *Low Level Laser Therapy as a Medical Treatment Modality*. Tampere: Art Urpo Ltd., 1992:17–44.
37. Walsh LJ. The current status of low level laser therapy in dentistry. Part 1. Soft tissue applications. *Aust Dent J* 1997;42:247–55.
38. Shevrygin BV, Rybalkin SV, Pekli FE, et al. Correction of microcirculatory disorders with low-energy laser radiation in children with vasomotor rhinitis. *Vestnik Otorinolaryngologii* 2000;2:31–3.
39. Mel'man EP, Del'tsova EI. Effect of helium-neon laser radiation on restoration of the structure of the microcirculatory bed and neurocytes of the small intestine following experimental ischemia. *Arkh Anat Gistol Embriol* 1987;92:39–45.

# 低能量氦氖雷射可促使分節型白斑病灶 色素恢復並改善其交感神經機能異常

吳介山<sup>1,2</sup> 胡楚松<sup>1</sup> 藍政哲<sup>1,2</sup> 陳國熏<sup>1,2</sup> 卓玟禾<sup>3</sup> 余幸司<sup>1,2</sup>

<sup>1</sup>高雄醫學大學附設醫院 皮膚科

<sup>2</sup>高雄醫學大學 醫學院醫學系 皮膚科學

<sup>3</sup>大仁科技大學 藥學系

分節型白斑是一種特殊型的白斑，其病灶分布於單側的神經節段上，目前的研究認為是由於病灶交感神經機能異常所致，我們過去的研究發現分節型白斑病灶有皮膚血流量上升及交感神經腎上腺接受器亢進的異常表現。臨床上其頑固的治療反應對皮膚科醫師而言是一項艱鉅的挑戰。低能量氦氖雷射 (波長 **632.8 nm**) 在臨床上已被廣泛運用於治療許多疾病，其中包括白斑治療與神經損害的修復在內。本研究之目的在評估以低能量氦氖雷射治療分節型白斑的療效與安全性，並進一步探討其對病灶交感神經機能異常的修復作用。我們選取 **40** 位病灶位於頭頸部的穩定期分節型白斑患者，低能量氦氖雷射以點治療的模式 ( $3.0 \text{ J/cm}^2$ ) 每週治療 **1-2** 次；另外在 **6** 位經氦氖雷射治療後有明顯色素回復的分節型白斑患者以雷射都卜勒血流測定儀測定病灶治療前後皮膚血流量的差異，並以離子電泳導入擬交感神經藥劑觀察病灶皮膚血流量的變化，藉以評估其交感神經腎上腺接受器機能在治療前後的變化，所有檢查均同時監測正常側對稱部位作為比較。平均在 **17** 次治療後，即可發現病灶開始出現色素恢復的現象，而在持續接受治療的患者中 **60%** 可以觀察到有顯著的治療效果 (色素恢復  $> 50\%$ )，而且所有接受治療者完全沒有任何不適反應或副作用出現；同時在 **6** 位規則治療的分節型白斑患者發現治療前異常上升的病灶皮膚血流量已恢復正常，而交感神經腎上腺素接受器對於 **clonidine** 的異常反應亦有逐漸恢復正常的趨勢。由以上的結果我們相信：低能量氦氖雷射不僅可以有效地治療分節型白斑，其對於病灶部位異常的交感神經機能亦可能有相當程度的修復或調控的作用。

**關鍵詞：**皮膚微循環，低能量氦氖雷射，分節型白斑，交感神經腎上腺接受器  
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通訊作者：余幸司醫學博士

高雄醫學大學附設醫院皮膚科

高雄市807三民區自由一路100號