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(54) **NONINVASIVE CUTANEOUS BLOOD FLOW ASSESSMENT AS A RESPONSE PREDICTOR FOR VISIBLE LIGHT THERAPY ON SEGMENTAL VITILIGO**

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A61B 5/02 (2006.01)
A61B 5/00 (2006.01)

(52) **U.S. Cl.**
USPC **600/504**

(58) **Field of Classification Search**
USPC 600/504
See application file for complete search history.

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(57) **ABSTRACT**

Visible light is a treatment option for Segmental Vitiligo (SV), and visible light-induced repigmentation is associated normalization of sympathetic. Currently it is difficult to predict individual patient's response to visible light therapy. Therefore, the present invention uses the Laser Doppler Flowmeter to serve as a response predictor for visible light on treating SV. The present invention recruited 14 Segmental Vitiligo patients for evaluating clinical information. First Laser Doppler Flowmeter was used to evaluate the cutaneous blood flow of SV lesion and contralateral normal skin, and then treated them with visible light irradiate, cold-stress, rewarmed, and recorded the change of skin blood flow, finally the patients received regular visible light treatment for 3 months, and patients have a sign of repigmentation after the treatment.

7 Claims, 5 Drawing Sheets

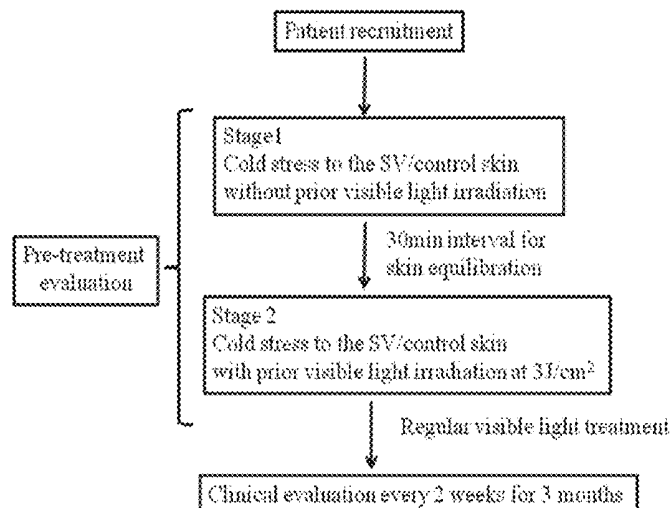


FIG. 1

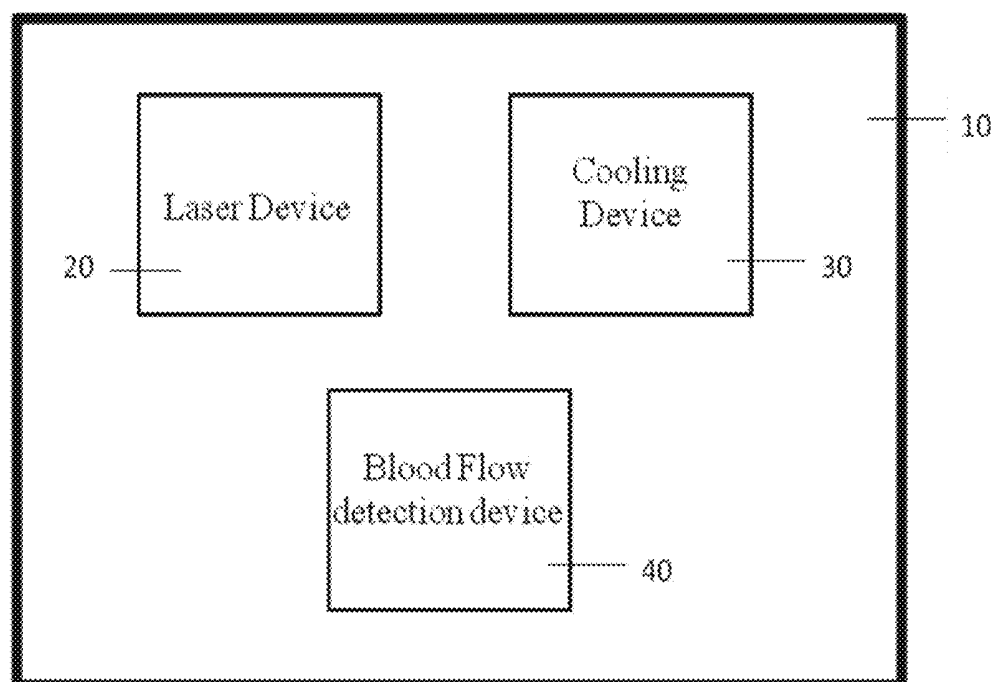


FIG. 2

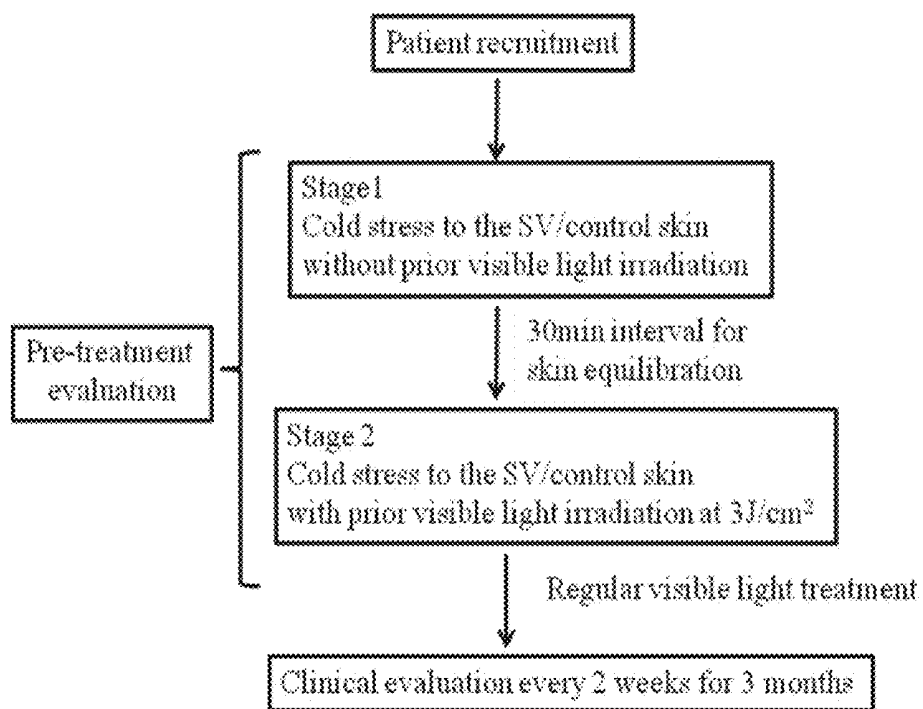


FIG. 3

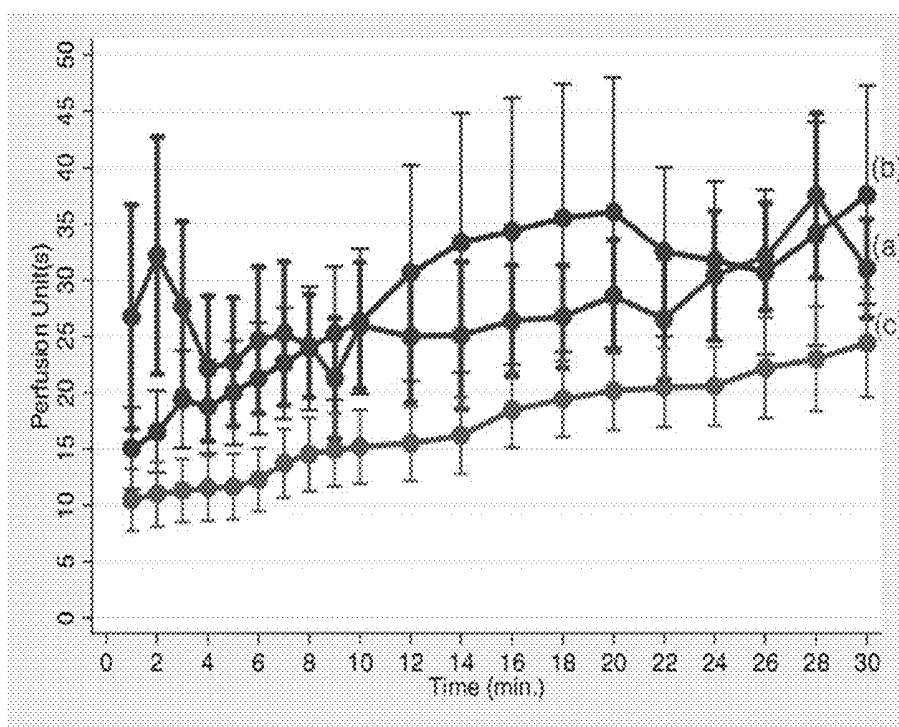


FIG. 4

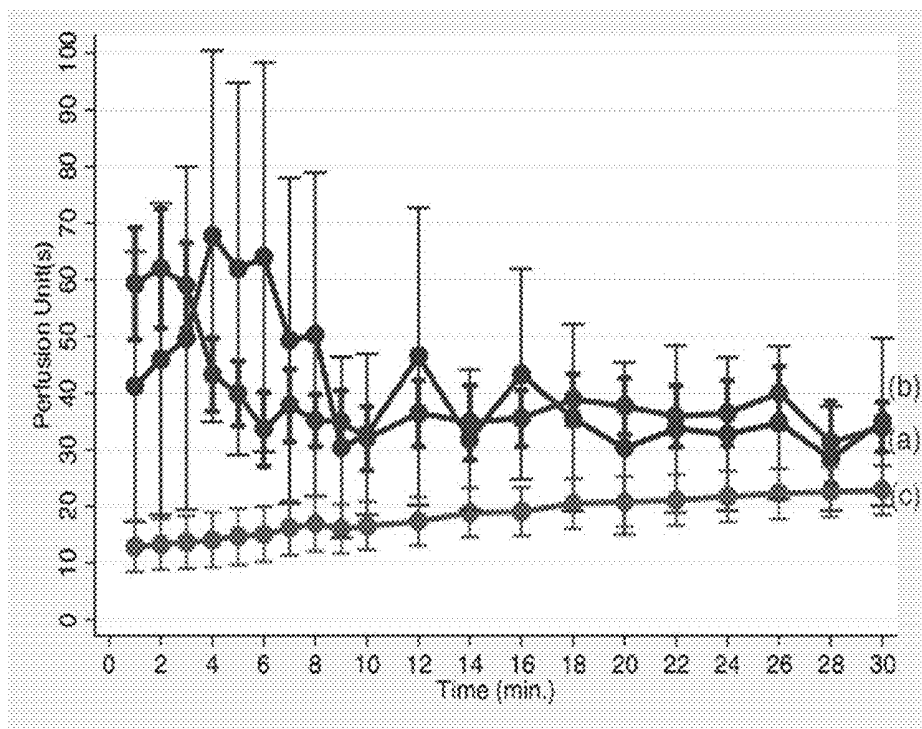
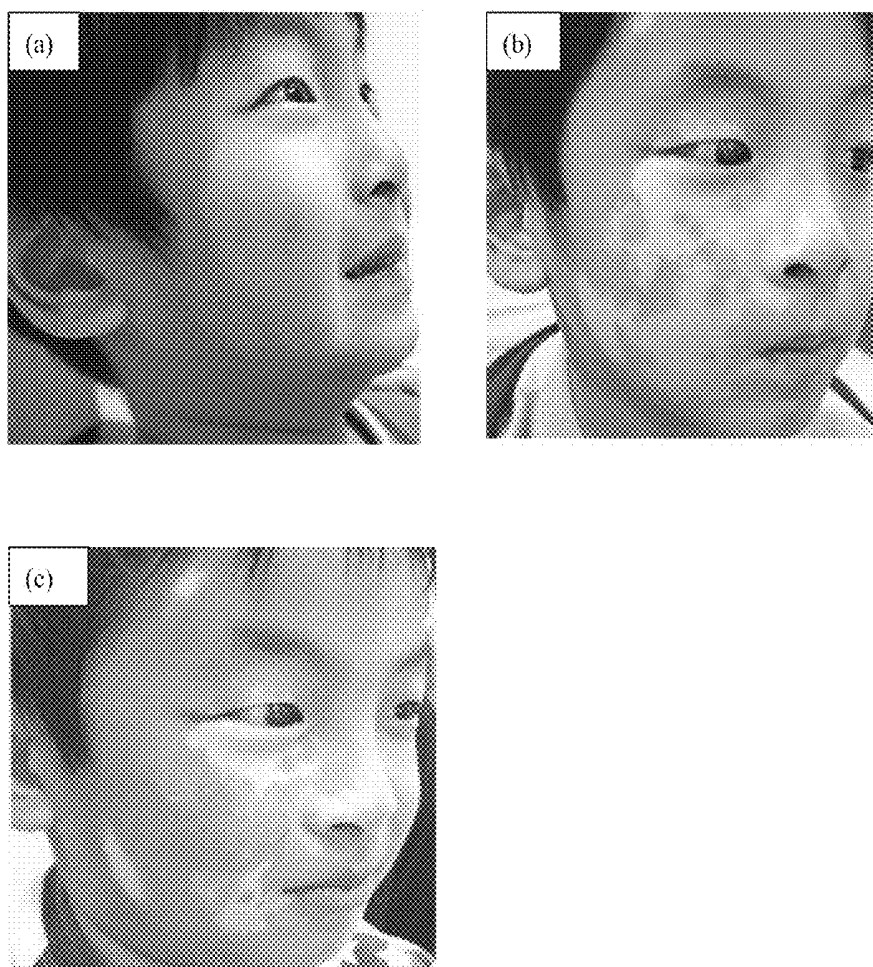


Fig. 5



NONINVASIVE CUTANEOUS BLOOD FLOW ASSESSMENT AS A RESPONSE PREDICTOR FOR VISIBLE LIGHT THERAPY ON SEGMENTAL VITILIGO

FIELD OF THE INVENTION

The invention relates to predict a response for visible light therapy on Segmental Vitiligo (SV) via a noninvasive method.

DESCRIPTION OF PRIOR ART

Vitiligo is a depigmentary disorder with that acquired melanocyte is destroyed. With different disease types and courses, the skin of patient could appear big or small spots, the attack rate is about 1-2% thereof. Although the majority of SV do not cause damage and other clinical symptoms for patient body, patients feel annoyed with pigment difference of the skin for appearance.

Vitiligo can be classified into two distinct types in clinical manifestation and physiological response: (1) segmental vitiligo; and (2) non-segmental vitiligo. The first type occurs is associated with sympathetic dysfunction and distributes over the dermatomal position or the quasi-dematomal position, which causes significant effects on cutaneous blood flow. The second type is associated with immunity dysfunction, which belongs to autoimmune disease. Previous study with Laser Doppler Flowmeter showed that SV skin is associated with sympathetic dysregulation. However the same feature was not observed on non-segmental vitiligo skin. More specifically, the cutaneous blood flow and the adrenoceptor response in the SV lesion were significantly higher as compared to their contralateral normal skin.

For curing Vitiligo patients, low-energy Helium-Neon laser or visible-light have been used widely. However SV patients have to spend a lot of time treating, but there is not a judgment standard to predict the therapy outcome prior to treatment. The present invention can serve as a non-invasive predictor of the response to the light therapy, and serve as a standard to evaluate SV treating time with visible-light in clinical.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a device for evaluating SV treatment effect by visible-light.

FIG. 2 is a schematic diagram of the evaluation processes for the SV treatment with light.

FIG. 3 is a perfusion-time chart for 50% SV patients through with/without prior visible light irradiation.

FIG. 4 is a perfusion-time chart for 50% SV patients through with/without prior visible light irradiation.

FIG. 5 shows a patient with segmental vitiligo over right face prior to visible light therapy (FIG. 5a). Three months after regular therapy (FIG. 5b). Nine months after regular therapy (FIG. 5c).

SUMMARY OF THE INVENTION

The present invention relates to a device for evaluating treatment effect of visible light on therapy Segmental Vitiligo (SV), the device comprising:

- (a) a laser device for irradiating an lesion area with a visible light;
- (b) a cooling device for cooling the affected area with a cool-stress after an irradiation of the visible light; and

- (c) a blood flow detection device for measuring a blood flow of the affected area after the cool-stress.

The present invention relates to an evaluating method for visible-light therapy Segmental Vitiligo (SV), comprising the following steps of

- (a) evaluating a blood flow of an affected area and a normal skin after a cool-stress
- (b) after irradiating a visible-light, cooling and evaluating the blood flow of the affected area; and
- (c) after a visible-light treatment, evaluating to determine treatment time.

DETAILED DESCRIPTION OF THE INVENTION

In the past, Segmental Vitiligo patients have to spend a lot of time on the visible-light therapy, but the treatment outcome has not been predicted. Therefore, the present invention provides a device for evaluating the treatment effect for Segmental Vitiligo (SV) with light therapy (FIG. 1). In an embodiment, a device for evaluating Segmental Vitiligo (SV) treatment effect of a visible-therapy comprising a laser device for irradiating an affected area with a visible light, a cooling device for cooling the affected area with a cool-stress after an irradiation of the visible light, and a blood flow detection device for measuring a blood flow of the affected area after the cool-stress.

According to the device of the present invention for evaluating the effect of Segmental Vitiligo (SV) treatment of the visible-light therapy, the laser device emits a visible light of red light with a wavelength of 633 ± 5 nm is preferred.

According to an embodiment of the present invention for evaluating Segmental Vitiligo treatment effect per the visible-light therapy, the preferred cooling device served to cool the affected area by the cool-stress after an irradiation of the visible light, wherein the temperature range is $0^{\circ}\text{C.} \sim 4^{\circ}\text{C.}$ with which to determine the function of autonomic nerves.

According to an embodiment of the present invention for evaluating Segmental Vitiligo treatment effect per the visible-light therapy, the blood flow detection device is Laser Doppler flowmeter (PeriFlux System 5000, Perimed, Sweden), the blood flow in the capillary of SV affected area and control normal skin are measured by the blood flow detection device.

The present invention further provides an evaluating method for visible-light therapy for Segmental Vitiligo (SV), comprising the steps as following:

- (a) evaluating a blood flow of an affected area and a normal skin after a cool-stress
- (b) after irradiating a visible-light, cooling and evaluating the blood flow of the affected area; and
- (c) after a visible-light treatment, clinically evaluating to determine treatment time.

In an embodiment, the affected area and normal skin were exposed to a cold-water packing at $0^{\circ}\text{C.} \sim 4^{\circ}\text{C.}$ for 10 minutes per the cool-stress function of autonomic nerves of the patient skin was determined. In this stage, visible-light irradiation was not performed. In an embodiment, without irradiating by the visible light, the blood flow of the affected area (FIG. 3a) and the control skins (FIG. 3c) showed inconsistent changes (sporadic increase and decrease between two sequential recordings). After the first step was finished, the tested skins were remained equilibration for 30 minutes prior to the next stage. The second stage of pre-treatment evaluation, the affected skin of the Segmental Vitiligo patients receive a visible light irradiation and then place on the cold-water packing at $0^{\circ}\text{C.} \sim 4^{\circ}\text{C.}$ for 10 minutes. After cooling the affected area, the blood flow is recorded by Doppler Flowmeter. In the preferred embodiment, after irradiated by a

visible light, the blood flow variation of the affected area showed more consistent. In the third stage, patients received a continuous red visible-light with a wavelength of 633 ± 5 nm three times per week, and for three months. The irradiating flux for each affected area is 3.0 J/cm^2 every time, and the power output is measured by a power meter (POW-105, Lasotronic).

In the present invention, the blood flow variation of the affected treated with the aforementioned steps (a) and (b) severed as a standard to predict the ongoing visible-light in clinical therapy. In a preferred embodiment, patients accept the visible light irradiation treatment before the blood flow variation is steady increase, and show a sign of repigmentation.

Thus, in the present invention, evaluation on blood flow of the skin after a visible-light irradiation can predict the response of the SV therapy.

EXAMPLE

Example 1

A Device for Evaluating Visible-Therapy Segmental Vitiligo (SV) Treatment Result

The present invention provides a device (10) for evaluating the Segmental Vitiligo treatment effect by a visible-light therapy (e.g. FIG. 1). The device comprising a laser device (20), a cooling device (30) and a blood flow detection device (40). The laser device is used for irradiating the affected area with the visible light, and the wavelength range is 633 ± 5 nm. The cooling device is used for cooling the affected area with the cool-stress at $0^\circ \text{ C.} \sim 4^\circ \text{ C.}$ after visible light irradiation which determines a function of autonomic nerves of patients. The blood flow detection device is Doppler Flowmeter (PerFlux System 5000, Perimed, Sweden) is used for measuring the blood flow of the affected area after the cool-stress. Theoretically the blood flow is determined by the numbers of red blood cells moving in the measured volume as well as the average velocity. Analyzed by the analysis program kit (Perisoft, PeriFlux, PF3, Perimed), the data that stands for the mean values is displayed as Perfusion Unit (PU).

Example 2

An Evaluating Method for Visible-Therapy Segmental Vitiligo

The present invention provides an evaluating method for visible-light therapy on Segmental Vitiligo (SV) (e.g. FIG. 2). The present invention first recruited 14 Segmental Vitiligo patients for evaluating clinical information (Table 1), and then provided a method for SV visible-light therapy comprising three steps.

- evaluating a blood flow of an affected area and a normal skin after a cool-stress
- after irradiating a visible-light, evaluating a blood flow of the affected area by the cool-stress; and
- after a visible-light treatment of clinically evaluating to determine treatment time.

In the example, blood flow of the affected areas and the control skins were recorded and then placed in the cold-water packing at $0^\circ \text{ C.} \sim 4^\circ \text{ C.}$ for 10 minutes. Via the cool-stress, function of autonomic nerves of the patient skin was determined. In this step, visible-light irradiation was not performed. Subsequently, the blood flow was recorded by Doppler Flowmeter. FIG. 3a and FIG. 3c show the affected area

and the control skins without irradiating by the visible light, the blood flow of the affected area skins show inconsistent changes (sporadic increase and decrease between two sequential recordings). After the first step was finished, the tested skins were remained equilibration for 30 minutes before the next step continued.

In an embodiment, the second step of pre-treatment evaluation, the tested skins of the patients receive the visible light irradiation then place on the cold-water packing at $0^\circ \text{ C.} \sim 4^\circ \text{ C.}$ for 10 minutes. After cooling the affected area, the blood flow was recorded by the Doppler Flowmeter. FIG. 3b showed that blood flow patterns of 50% SV patients become progressively stable after irradiated by visible light. In the FIG. 4 shows the other 50% SV patients should not response to visible light irradiation. Thus the results can sever as a standard to determine treating time of patients by visible-light in clinical therapy.

In an embodiment, the third step was to evaluate the time for visible-light treatment on SV patients. Patients were treated with a continuous red visible-light with a red light wavelength of 633 ± 5 nm three times per week for three months. The irradiating flux for each affected area was 3.0 J/cm^2 every time, and the power output was measured with a power meter (POW-105, Lasotronic). FIG. 5 shows a patient with segmental vitiligo over right face prior to visible light therapy (FIG. 5a). Three months after regular therapy (FIG. 5b). Nine months after regular therapy (FIG. 5c).

TABLE 1

Clinical information of 14 segmental vitiligo patients recruited in the present invention.

Gender/Age	Sickness Duration	Anatomic Location	Poliosis	Maximum Diameter (cm)
Female/31	1 yr	face	(+)	2
Male/63	1 yr	face	(-)	1.5
Female/27	1 yr	face	(-)	2
Male/5	1 yr	leg	(-)	1.5
Male/10	5 yr	face	(-)	1
Female/19	7 yr	face	(-)	2
Male/6	2 yr	face	(+)	4
Female/11	6 yr	face	(+)	4.5
Female/31	1 yr	face	(-)	1
Female/11	1 yr	neck	(-)	2
Female/30	1 yr	face	(-)	1
Female/9	2 yr	face	(-)	1.5
Male/39	3 yr	face	(-)	2
Male/8	1 yr	face	(-)	2.5

What is claimed is:

- A device for evaluating visible-light therapy effect on Segmental Vitiligo (SV) treatment, the device comprising:
 - a laser device for irradiating an lesion area with a visible light;
 - a cooling device for cooling the affected area with a cool-stress after an irradiation of the visible light; and
 - a blood flow detection device for measuring a blood flow of the affected area after the cool-stress, wherein a temperature of the cooling device during the cool-stress is from 0° C. to 4° C.
- The device as claimed in claim 1, wherein the laser device emits the visible light of red visible light with a wavelength of 633 ± 5 nm.
- The device as claimed in claim 1, wherein the blood flow detection device is Laser Doppler flowmeter.
- An evaluating method for visible-light therapy on Segmental Vitiligo (SV), comprising the following steps of:

evaluating a blood flow of an affected area and a normal skin after a cool-stress;
 after irradiating a visible-light, cooling and evaluating the blood flow of the affected area; and
 after a visible-light treatment, clinically evaluating to 5
 determine treatment time,
 wherein a temperature of the affected area during the cool-stress is from 0° C. to 4° C. and a cool-stress time is 10 minutes.

5. The evaluating method as claimed in claim 4, wherein 10
 the blood flow of the affected area is determined by Laser Doppler flowmeter.

6. The evaluating method as claimed in claim 4, wherein the visible-light irradiated the affected area is a red visible-light with a wavelength of 633±5 nm. 15

7. The evaluating method as claimed in claim 4, wherein a frequency of visible-light treatment of the affected area is three times a week, for three months with an irradiating flux for each treatment point of 3.0 J/cm².

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专利名称(译)	无创性皮肤血流评估作为节段性白癜风可见光治疗的反应预测因子		
公开(公告)号	US8652061	公开(公告)日	2014-02-18
申请号	US13/214340	申请日	2011-08-22
[标]申请(专利权)人(译)	高雄医学大学		
申请(专利权)人(译)	高雄医学大学		
当前申请(专利权)人(译)	高雄医学大学		
[标]发明人	YU HSIN SU LAN CHENG CHE YU WEI TAI		
发明人	YU, HSIN-SU LAN, CHENG-CHE YU, WEI-TAI		
IPC分类号	A61B5/00 A61B5/02		
CPC分类号	A61N2005/007 A61B5/444 A61N2005/0662 A61B5/4848 A61N2005/067 A61N2005/0628 A61N5/0616 A61B5/0261 A61B5/0059		
代理人(译)	KING , ANTHONY		
优先权	100105244 2011-02-17 TW		
其他公开文献	US20120215120A1		
外部链接	Espacenet USPTO		

摘要(译)

可见光是节段性白癜风 (SV) 的治疗选择，可见光诱导的再色素化与交感神经的正常化有关。目前，很难预测个体患者对可见光疗法的反应。因此，本发明使用激光多普勒流量计作为治疗SV的可见光的响应预测器。本发明招募了14名节段性白癜风患者用于评估临床信息。FirstLaser Doppler流量计用于评估SV病变和对侧正常皮肤的皮肤血流量，然后用可见光照射，冷应激，复温处理，记录皮肤血流变化，最后患者接受常规可见光照射治疗3个月，患者在治疗后有再色素的迹象。

