THE EFFICACY AND SAFETY OF PICOSECOND LASER USING COMBINATION OF 1064 AND 532 NM FOR AXILLARY HYPERPIGMENTATION

HAN LIN NAING

MASTER OF SCIENCE
IN
DERMATOLOGY

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE
MAE FAH LUANG UNIVERSITY

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ABSTRACT

Hyperpigmentation of the skin is a common dermatological condition in which the color of the skin generally becomes darker. These changes in skin coloration can be a result of various internal and external factors including hormonal changes, inflammation, injury, acne, eczema, certain medication, UV exposure, etc. Skin pigmentation and coloration are governed by the biological processes involving the production of the skin pigment called melanin produced by melanocytes in various layers of skin. Thus, alterations in melanocyte production or distribution of melanin result in skin hyperpigmentation disorders

Axillary hyperpigmentation (AH) is a common condition in dark-skinned individuals that can cause cosmetic concerns, especially in Asian populations. In a study by James et al, histopathological analysis has shown that the most common cause of AH is post inflammatory hyperpigmentation (PIH), which in turn can result from several factors. Another study by Evan et al pointed out that axillary tissue differs from other body tissues. Axillary tissue constitutes extra hair follicles, extra sweat glands, extra sebaceous glands, and higher transepidermal water loss values that cause weaker skin barriers. Moreover, the axilla is a flexural area susceptible to

constant skin friction, chemical exposure, and frequent shaving, which can damage the skin tissue and cause irritation, causing PIH.

Lasers have been using for the treatments but need to use many times and not well-satisfied. Picosecond laser is the newest technology works on pigmentation and gave an effective result with lesser treatment sessions with less side effects. In this study, we sought to determine the clinical efficacy and safety of Picosecond laser using combination of 1,064 nm and 532 nm and follow up at 4, 8 and 16 weeks. To study efficacy and safety of Picosecond laser using combination of 1,064 nm and 532 nm. 22 participants with AH were enrolled in this clinical trial study. The participants were treated with Picosecond laser using combination of 1,064nm and 532 nm compare before and after treatment. Three blinded independent dermatologists assessed results using standardized photographs according to the Global Aesthetic Improvement Scale (GAIS) evaluated paired pre- and post-treatment (week 4, 8 and 16). Melanin index was measured before and after treatment (week 4, 8 and 16) using a Mexameter (MX18, Courage and Khazaka®, Cologne, Germany). Participants also completed self-assessments using GAIS. Subjects rated their Subjective satisfactory scale at 4 weeks, 8 weeks and 16 weeks after treatment. Melanin index measured via a Mexameter was significantly improved after 3 sessions of treatment compare with baseline at before treatment (p=0.001) Physicians GAIS showed clinical improvement 16 weeks after treatment.

Keywords: Axillary Hyperpigmentation, PIH, Picosecond Laser, Transient Hyperpigmentation

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CHAPTER 1

INTRODUCTION

1.1 Background

Skin hyperpigmentation is one of the common dermatological conditions that the color of the skin gets darker. These skin changes can be result of verities of external and internal matters including inflammation, changes in hormones, acne, injury, some medications, exposed to UV, eczema, etc. (Pérez-Bernal et al., 2000). Pigmentation and coloration of the skin are influenced by the process of biology including the skin pigment production which is called melanin that produced by melanocytes in many layers of skin. Therefore, disturbing in production of melanocytes or alteration of melanin lasts in hyperpigmentation of the skin (Rossi et al., 2011).

Though, hyperpigmentation of the skin can't be considered as a harmful or lethal disease; but it can still affect life's quality of the sufferers by targeting psychological and emotional health. Many options of treatment are out there for hyperpigmentation. Most agents are basically used to apply topically as gels, ointments, or cream. Still, these options may show various side effects like irritation, skin peeling, or hypopigmentation, skin drying. The long-term treatment time varies from many months to many years can lead to poor compliance and poor satisfaction.

A common condition in someone with darker skin especially in Asian populations which may lead to cosmetic and emotional concerns is axillary hyperpigmentation (AH). James et al. (2006) revealed that post inflammatory hyperpigmentation (PIH) is the most common cause of axillary hyperpigmentation, that can come from many matters. Another study by Evan et al showed that axillary tissue is different from tissues of other body parts. (James et al., 2006) Axillary tissue contains extra sweat glands, extra sebaceous glands, extra hair follicles, then have values of transepidermal water loss higher which can lead barriers of the skin become

weaker. Besides, the axilla is a flexural area sensitive to chemical exposure, frequent shaving and skin friction that can cause damage to the skin tissue and may lead to irritation, and causing PIH.2,3 (James et al., 2006)

By staying away from causative factors, treating the underlying condition without using laser may not improve axillary hyperpigmentation to get much better. Treating such condition can't get away from the choice of the first modality which has been Q-switched laser. Since the method is useful in the treatment of skin pigmentation by selective photothermolysis effect (Anderson & Parrish, 1983). Yet, people treated with Q-switched laser may develop redness, tenderness, swelling after procedure for a while. And in darker skin type population, PIH can also be seen. Moreover, laser must be completed many times to obtain good result. At present, picoseconds (10-12) laser has been developed and managed to use for many pigmentary lesions, mostly for removing of tattoos. The advantage of picoseconds laser over Q-switched laser is a thermal-photoacoustic effect, so people should face lower pain, lower downtime and lower time required during treatment (Lee, Cho & Glen, 2010).

1.2 Research Questions

1.2.1 Does combination of Picosecond laser at the wavelengths of 1,064 and 532 nm effectively reduce melanin index (comparing after treatment with baseline) for the treatment of axillary hyperpigmentation

1.2.2 Does combination of Picosecond laser at the wavelengths of 1,064 and 532 nm have a clinical efficacy safety in treating axillary hyperpigmentation

1.3 Objectives

1.3.1 Primary Objective

Comparing melanin index reduction before and after using the combination of Picosecond laser at the wavelength of 1,064 and 532 nm in treating axillary hyperpigmentation.

1.3.2 Secondary Objective

To study safety and efficacy of picosecond laser at the wavelengths of 1,064 and 532 nm for the treatment of axillary hyperpigmentation

1.4 Research Hypothesis

1.4.1 Combination of Picosecond laser at the wavelengths of 1,064 and 532 nm have a statistical difference in melanin index reduction for the treatment of axillary hyperpigmentation.

1.4.2 Combination of Picosecond laser at the wavelengths of 1,064 and 532nm have a clinical efficacy (measured by clinical photographs and Global Aesthetic Improvement Scale) for the treatment of axillary hyperpigmentation.

1.5 Scope of Research

This study had been conducted in 22 participants female with axillary hyperpigmentation aged 20-45. Volunteers will be arranged with Picosecond laser at 1,064 nm wavelength and followed by 532 nm on the same area. Participants will be received the same procedure every 4 weeks for four times at Mae Fah Luang University Hospital, Bangkok. Skin color, smoothness, and side effects were evaluated by Fitzpatrick skin type paper, photography, Mexameter® and Global Satisfactory before and after treatments. Mexameter® used to measure melanin index prior the treatment, at every time of treatment and at week 16 which is one month after the last session. Global Satisfactory will be done at the end of study.

1.6 Conceptual Framework

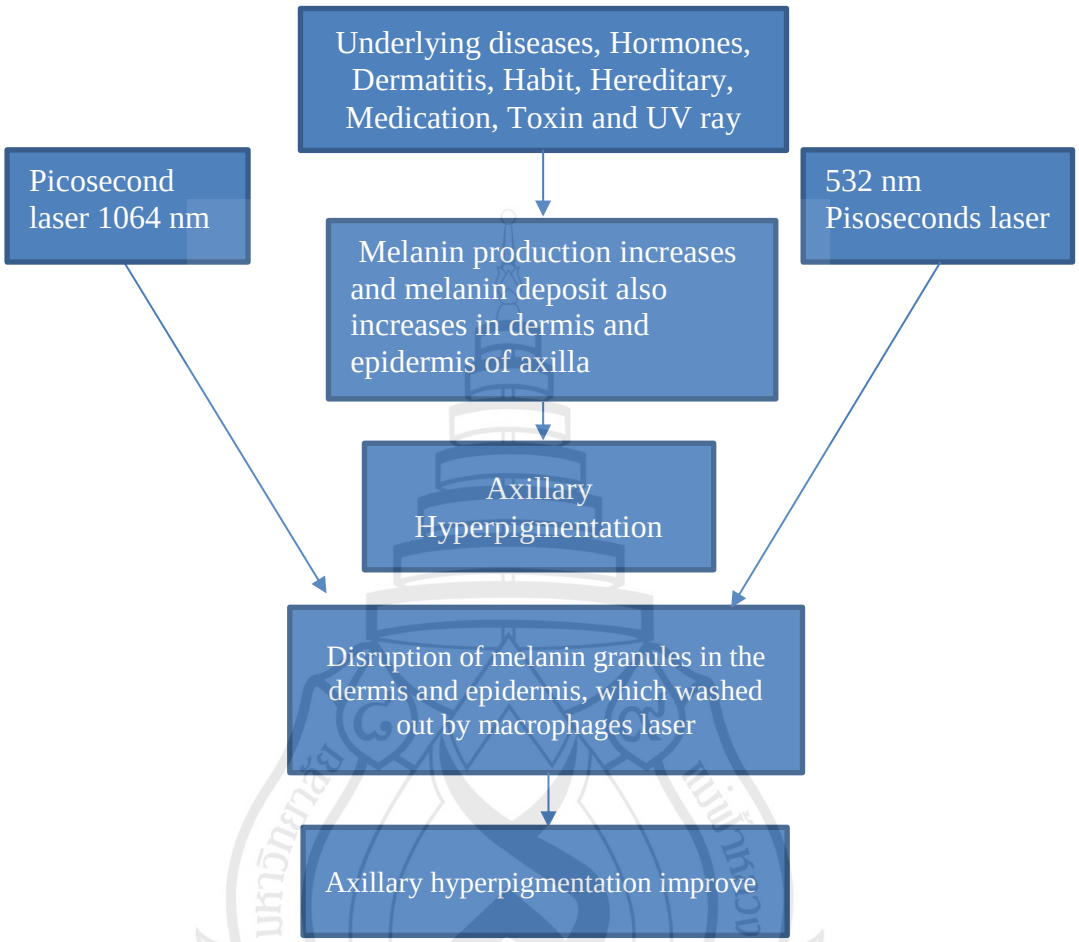


Figure 1.1 Conceptual Framework

1064 nm Nanosecond (Q-switched) laser has been the first choice if the specialist wants to treat pigmentary lesions such as dark lips in patient with dark skin because of selective photothermolysis effect. With pulse width shorter than melanin's thermal relaxation time and leads to disruption of melanin granules by photoacustic effect while surrounding tissues are safe from heat that transmitted from the melanin. Melanin granule fragments will be cleared from the area by macrophages and provides improvement of pigmentary lesions. Though, the endpoint will still have erythema and still possible to cause PIH, mainly in darker skin.

Picosecond laser owns newer mechanic comparing to Q-switched nanosecond laser i.e., releasing of the shorter pulse width. Picosecond laser can provide patients the faster improvement and lesser adverse effects.

1.7 Operational Definitions

1.7.1 Axillary hyperpigmentation is a condition in which axilla appears black, brown color. When measuring axillae with Mexameter®, the result of melanin index is 150-500 or more. It may have tone of inequality sometimes.

1.7.2 Melanin index - amount of melanin (represent dark color of the skin) measuring by Mexameter®, which value ranging from 0-999.

1.7.3 Color of the skin – Skin color and tendency to get tan or burn after exposed to UV ray can be determined by the classification of Fitzpatrick skin type. The following table shows the skin color type.

Table 1.1 Fitzpatrick Skin Type

Fitzpatrick Skin Type		
Skin type	**Typical features**	**Tanning ability**
l	Pale white skin, blue/green eyes, blond/rad hair	Always burns, does not tan
ll	Fair skin, blue eyes	Burns easily, tans poorly
lll	Darker white skin	Tans after initial burn
IV	Light brown skin	Burns minimally, tans easily
V	Brown skin	Rarely burns, tans darkly easily
VI	Dark brown or black skin	Never burns, always tans darkly

Source James et al. (2006)

CHAPTER 2

REVIEW LITERATURES BACKGOUND AND RATIONALE

2.1 Darken Axillary Skin

Skin hyperpigmentation is one of the common dermatological conditions that the color of the skin gets darker. These skin changes can be result of verities of external and internal matters including inflammation, changes in hormones, acne, injury, some medications, exposed to UV, eczema, etc. (Pérez-Bernal et al., 2000). Pigmentation and coloration of the skin are influenced by the process of biology including the skin pigment production which is called melanin that produced by melanocytes in many layers of skin. Therefore, disturbing in production of melanocytes or alteration of melanin lasts in hyperpigmentation of the skin (Rossi & Perez, 2011).

Axillary hyperpigmentation (AH) is a common condition in individuals with dark skin especially in Asian populations which may lead to cosmetic and emotional concerns. In a study by James et al, histopathological analysis has revealed that the most common cause of axillary hyperpigmentation is post inflammatory hyperpigmentation (PIH)

2.1.1 Anatomy of Axilla

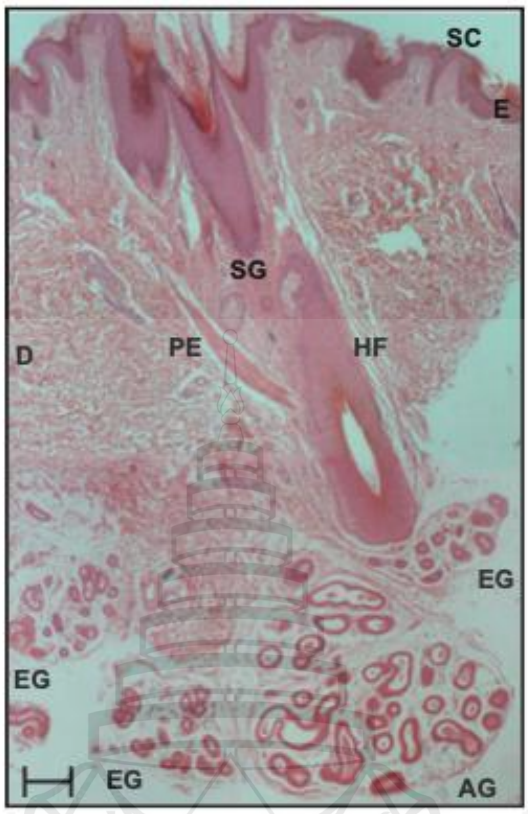
There's such a unique skin site on the body of human which seems to be axilla. (Evans et al., 2012). Apart from having huge amount of sebaceous glands and hair follicles, it's also condensed with apocrine sweat glands and eccrine glands (Evans et al., 2012) (Fig. 2.1).

There's 116 cm^2 and 65cm^2 of median surface area for axillary skin in a single axilla of men and women respectively. (Evans et al., 2012). Many reports revealed that the basic functions of the skin of axillae are markedly differ from the other parts

of the body.Therefore, transepidermal losing of water (TEWL) and corneosurfametry have shown decreased axilla's barrier integrity, equate to the volar forearm, but a Raman's recent receptive study has revealed about lactic acid (part of sweat), cholesterol and ceramide 3 levels are increased, and NMF amounts decreased, which is contrasted to the forearm. Moreover, compare to the forearm, axilla's cornified envelopes seems to be smaller showing stratum corneum's shorter turnover, but still no definite variance in maturation of corneocytes. 'Dryness of the skin' which is measured by squamometry pointed out about stratum corneum of axilla keeps more incomplete desquamated thing on the surface compared to forearm, and in turn which is concerned with reduced levels of the desquamatory stratum corneum chymotryptic enzyme in the surface layers of the skin (Evans et al., 2012).

Branches of papers were pointed the existence of differences in axillae's skin surface pH in unsimilar gender. But, Burry et al. announced that there's no pH varies in female and male axillae /sweat pH, (when there's correction of sweat pH for losing of CO_2 after secretion), while Williams et al. (2005) pointed that women's axillae's pH are lower than men's before and after cleaning with water. Variation in these reports can be allocated to dissimilarity of surfaces' pH measurement techniques, and as the upcoming result, there's area which needed to be discussed. Burry et al. (2001) as well announced there's a huge varies in the fossa and vault of the axilla's skin surface pH and made the vault has the higher sweating rates. This occurrence is said to come from the decreased time accessible for reabsorption of bicarbonate of eccrine gland duct from the sweat on the way to surface of the skin. (Evans et al., 2012)

Rhythms of circadian as well seemed to be impact pH of axillary skin. Therefore, pH of the surface of the skin of male has shown about 5.9 in the daytime and about 5.5 in night time. The above findings may show a diurnal fluctuation in stratum corneum enzyme function and sebum production (Evans et al., 2012).



Note Stratum corneum (SC), epidermis (E), dermis (D), hair follicle (HF), piloerector muscle (PE), sebaceous gland (SG), eccrine sweat gland (EG) and apocrine gland (AG). Notice the significant amount of epidermal folding. Staining is haematoxylin and eosin. Scale bar represents 100 lm. (Image kindly provided by Prof. Douglas Bovell, Glasgow Caledonian University).

Figure 2.1 Histological section of axillary skin. Longitudinal section of human axillary skin showing main anatomical features

2.1.2 Histopathology of Axillary Hyperpigmentation

SEA's populations especially women (Philippines, Thailand, and Indonesia) have the concerned problem with underarms' skin darken, but few is noted about the fact distinction between hyperpigmented and pale underarm's skin.

One of the most common complaints in patients with colored skin is PIH. (James et al., 2006) It causes from production of melanin up rises or pigments' abnormal distribution in the dermis and/or epidermis after injury from outside. Many

inflammatory starters, including ROS, thromboxane, leukotrienes and prostaglandins, are reported to cause melanocyte's activation. Basal cell layer's destruction with melanophages and incontinentia pigmenti in the dermis has also been pointed. (James et al., 2006)

On histopathologic, it's signalized melanocytic activity increasement and deposition of melanin in both the dermis and epidermis, and also an infiltration of inflammation primarily composed of macrophages and mononuclear cells. Those observations help the hypothesis of axillary hyperpigmentation as one of PIH, as the causing elements could be concerned to cause irritation continuously due to hair removal, cleansing, tight clothes, or use of antiperspirants. (James et al., 2006)

2.1.3 Treatment for the Axillary Hyperpigmentation

PIH's treatment can be prolonged and difficult. The first step for this condition is treatment of the underlying condition and prevention, then interventions for depigmentation.

Nowadays, axillary hyperpigmentation still has no standard treatment, there're still limitation to the studies of the treatment's studies. Most frequently available treatment for this condition are topical whitening agents. But flexibility in efficacy, local irritation, and prolong treatment can set back these topical agents' usage.

Treating of the pigmented skin lesion have 2 principles:

2.1.3.1 Reduce the production of new melanin

1. Avoidance and prevention
2. Agents for topical usage

Azaelaic acid, Hydroquinone, Kojic acid, Aloesin, Licorice extract, Arbutin and Ascorbic acid are the agents that can reduce the production of melanin by inhibition of tyrosinase enzyme. PIH lesions can be helped by the anti-inflammatory property of Licorice extract (Zhu et al., 2006).

2.1.3.2 Removing of the existing melanin from the axilla

Laser instrument is one of the new methods which is available and used to treat underarm whitening. The other method which has the lightening effect on the axillary skin like chemical peeling has not much used because of its poor result and

inconvenient. Nowadays, in the treatment of hyperpigmentation, energy-based devices and lasers become a better choice.

2.2 Picoseconds Laser and Uses

2.2.1 In dermatological scene, picosecond laser technology has become much interest. A 755nm laser, which is the 1st picosecond laser, has been approved by the United States Food and Drug Administration (FDA) in 2012, used to treat pigmentary lesions and for tattoo removal. Because of the lesser duration of pulse which is only 10-12 sec, picosecond laser becomes an upgrading laser technology.

Brauer et al. (2015) published results which is good with the picosecond laser at 755nm added diffractive lens array for treatment of acne scar. Pigmentation and skin texture were better.

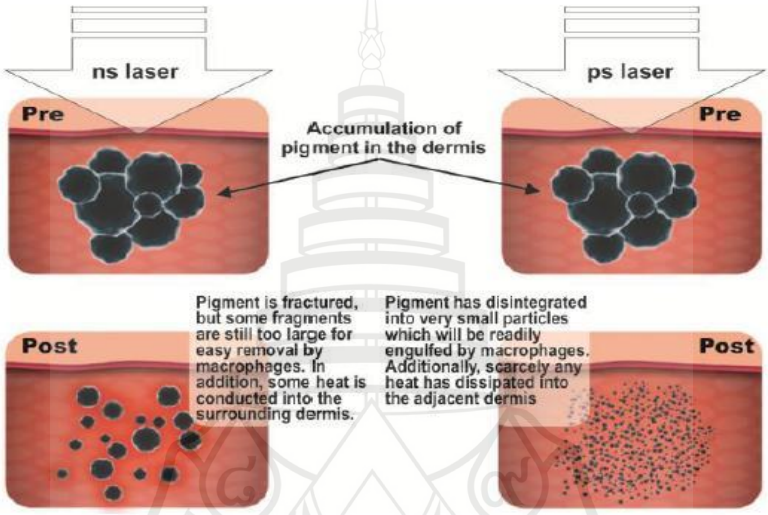
Berstein et al. (2017) have discussed about picosecond laser with 532 and 1064nm embracing a hand piece with 10x10 holographic beam-splitting property observed to effect more during facial acne scars' treatment. There was well toleration of the patients with very little downtime to no downtime.

Weiss et al. (2017) created a blinded trial researching a novel diffractive lens array's effectiveness for facial wrinkles by using a 755nm Picosecond alexandrite laser. And observed that it's highly effective and safe for skin rejuvenations also wrinkles.

On paper "Effects of a fractional picosecond 1,064 nm laser for the treatment of dermal and mixed type melasma", pointed out about combining the 1,064nm fractional picosecond laser with standard 4% hydroquinone is significantly better and effective than treating with 4% hydroquinone alone in mixed or dermal type melasma and shows a safety profile of good. (Chalermchai & Rummaneethorn, 2018)

Pulse duration 10^{-12} seconds owning picosecond lasers, are the updated lasers providing efficacious and fast in removing of tattoo (Goh et al., 2015). In 1998, Ross et al. first compared the use of Picosecond and nanosecond lasers treating for human's tattoos which are black in color, the used measurements were seemed to be tied but announced that removing of tattoo with picoseconds pulse duration was more

effective (Ross et al., 1998). Analysis macroscopically about interactions between laser and tattool for 1064 nm nanosecond Nd:YAG and picoseconds lasers in mimicking of tissues revealed that fracture of particles by picoseconds were more equally spread all over the zones of injury caused by photoacousting than those of nanosecond (Ahn et al., 2017) (Fig.2.2)



Source Cho Blair et al. (2010)

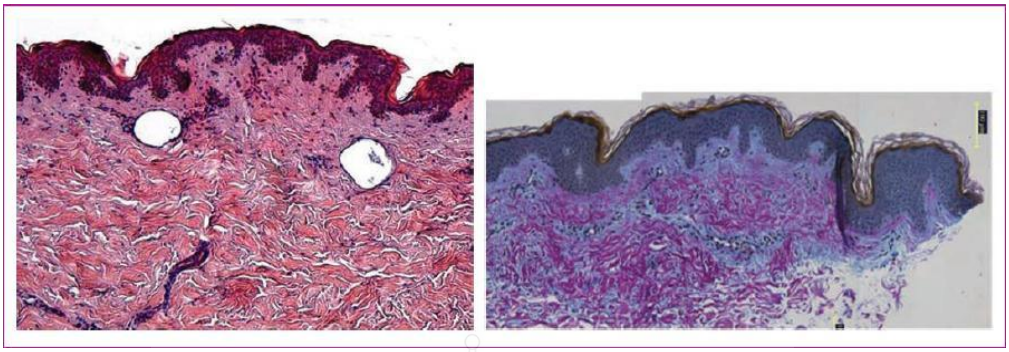
Figure 2.2 The Effect on accumulations of pigment compared between the conventional nanosecond and picoseconds lasers

There are some studies about treating pigmented lesions by picoseconds lasers. The retrospective study by Ohshiro et al. (2016) stated that the novel picoseconds lasers both the 755 nm alexandrite and 1064 nm Nd:YAG are efficacious for the treatment of dermal pigmented lesions. Patients in the study obtained successful lightening without immediate whitening phenomenon (IWP) and PIH. It implies the IWP, which is usually followed by PIH in Asians, does not need to be obtained achieve clinical clearance in picoseconds laser treatment of dermal pigmented lesions. For epidermal pigmented like tattoo, when compare between Nd:YAG 1064 nm nanosecond and picoseconds, conventional high-energy

nanosecond pulses produced clearing comparable with lower energy picoseconds pulses (Ross et al., 1998).

Picosecond laser also create laser induced optical break down (LIOB) in the dermis (Habbema et al., 2013). LIOB creation stimulates a healing response and skin remodeling which result in skin rejuvenation, improvement in appearance of facial acne scars and facial wrinkles (Brauer et al., 2015; Weiss et al., 2015). Kevin Schomacker and Jayant D. Bhawalker explained that LIOB occurs when the pulse intensity is high enough to strip electrons from the exposed material, generate plasma. The plasma absorbs the remaining laser energy, which rapidly heats and expands the plasma, forming a cavitations' bubble. Collapse of the cavitations' bubble generates strong local mechanical forces that can further disrupt tissue in the local area (Schumacker & Lomax (2015). Habbema et al. (2013) used 0.15mJ of focused 1064 nm laser with 10 um diameter, the pulse intensity was estimated to be 380 GW/cm^2.The study demonstrates subsurface dermal injury with intact epidermis and the healing led to new collagen growth, showing skin rejuvenation (Habbema et al., 2013).

(Left panel: H&E stain section of skin tissue showing vacuoles in the upper dermis caused by LIOB. The tissue section was taken immediately after laser irradiation. Right panel: tissue section stain with Herovici stain to show new collagen formation from healing of LIOB damage. The sample was biopsied 30 day after laser irradiation).



Source Habbema et al. (2013)

Figure 2.3 Microscopic of Picoseconds 1064 nm Nd:YAG

2.3 Picosecond Laser's safety and Side Effects

Comparing to nanosecond lasers, picosecond laser spread energy at very short duration of pulse. Therefore, pulses of picosecond laser can create faster photothermal reactions and carry effects of photoacoustic to surrounding tissues targeted chromophores in a great extent.

Unnecessary outcomes like post inflammatory hypo or hyperpigmentation and scarring can be caused after treated with laser. Because of those possible side effects, treated by lasers were effective less or once became avoided utterly, and leading patients with not enough choices of treatment.

Mier et al. (2016) carried out a review about removing of tattoo by picosecond laser. Writers pointed out that a strong photoacoustic effect can be caused by picosecond laser which is effective for removing of various colors of tattoos. Picosecond laser's ability of removing tattoos in multicolor was identified for yellow, red, purple, and green tattoos. Yet, the results were not compared directly with the findings of the Q-switched lasers. As an updated mechanic, picosecond laser is taking place in aesthetic dermatology, and their application for other problems concerning beauty, other than tattoos.

Ohshiro et al. (2016) made a trial researching the points of picosecond laser in treating dermal melanocytosis in Asians. Pointed out that both 755nm and 1064nm of picosecond lasers are handy in the removing of dermal melanocytosis with less adverse effects.

755 nm picosecond laser's effectiveness for the pigmented lesions' which are benign' like Nevus of Ota, was well noted by Chan et al. (2008). Was showed out that there's association of picosecond laser and PIH at a lower risk in Asians.

On paper "Effects of a fractional picosecond 1,064 nm laser for the treatment of dermal and mixed type melasma" researched on comparison of 1,064 nm fractional picosecond laser plus 4% hydroquinone cream and 4% hydroquinone cream. Pointed that the mean mMASI score at the Week 12 was clearly lowered in the area treated with picosecond laser. No differences were observed in the mean Mexameter melanin index, participant satisfaction score, and DLQI score. (Chalermchai & Rummaneethorn, 2018)

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Design of Study

Before, After, experimental, comparative study.

3.2 Population for Study

The study was held among female volunteers, aged 20-45 years, skin types III-V according to Fitzpatrick and have the problem of axillary hyperpigmentation who're able to get treating at Mae Fah Luang University Hospital, Bangkok

3.3 Determination of Sample Size

By using 2 standard deviations and mean from the foregoing paper, the sample was planned. Based on paper of Chalermchai & Rummaneethorn (2008) "Effects of a fractional picosecond 1,064 nm laser for the treatment of dermal and mixed type melasma", Journal of Cosmetic and Laser Therapy 2018.

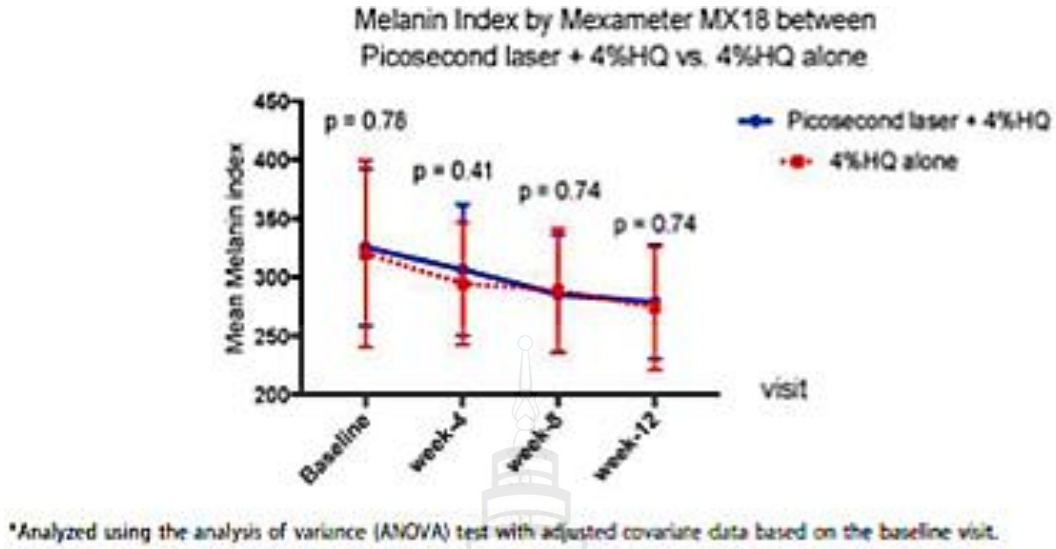


Figure 3.1 The melanin index by Mexameter® MX18 between Picosecond laser +4% HQ vs 4% HQ alone

Before treatment, Mexameter Melanin index, MMI $n_1 = 32$, mean MMI before = 325.275, $SD_1 = 64.07133\mu$

After treatment with Picosecond laser, $n_2 = 32$, MMI-after = 277.7406, $SD_2 = 53.64865$

$\alpha = 0.05$ (two-tail)

$Z_{0.025} = 1.96$

$\beta = 0.10$

$Z_{0.10} = 1.28$

$N = 32$

$SD = 64.07133$

$SD_2 = 53.64865$

Pool Variance $(\sigma^2) = (n_1-1)SD_1^2+(n_2-1)SD_2^2/n_1+n_2-2$

$\sigma^2 = [31(64.07133)^2 + 31(53.64865)^2] / 32 + 32 - 2$

$= 3484.4$

$\mu_1 = 325.275,$

$\mu_2 = 277.7406$

μ_d = 325.275-277.7406

= 47.5

N = $(z_{\alpha/2}+z_{\beta})^2 \sigma_d^2 / \mu_d^2$

= $(1.96+1.28)^2 (3484.4) / (325.275-277.7406)^2$

= 16.21 (17)

Estimation of losing the follow up visiting at 20%, then n = 17 / (1-0.20) = 21.25. Therefore, around 22 subjects

3.4 Selection Criteria

3.4.1 Inclusion Criteria

3.4.1.1 Healthy, female with axillary hyperpigmentation and willingly to volunteer in the program

3.4.1.2 20-45 years old with skin type III to V according to Fitzpatrick

3.4.1.3 Volunteers who can receive the procedure every four weeks for three months, who are able to follow up four weeks after the latest session of treatment

3.4.1.4 Volunteers with potential of childbearing who can agree to do birth control within the trial time

3.4.1.5 Volunteers will be needed to agree on a form of consent for photographing and treatment

3.4.2 Exclusion Criteria

3.4.2.1 Lactation/ Pregnancy

3.4.2.2 Subjects who is on Amiodarone, Minocycline, Amlodipine, oral pills continuously

3.4.2.3 Subjects being treated with any other laser treatment 3 months prior to this trial

3.4.2.4 Subjects with previous scarring, keloid, and poor wound healing histories

3.4.2.5 Volunteers with previous records of receiving photosensitive drugs, having history of photosensitive skin

3.4.2.6 Subjects with open wound or active skin disease in an area of treatment

3.4.2.7 Medical illness like pre-malignancy and malignancy, immunosuppressant, coagulopathy, and poor control diabetic mellitus

3.4.3 Discontinuation Criteria

3.4.3.1 Participant wants to discontinue the program from any reason.

3.4.3.2 Participant has serious complication from the program.

3.4.3.3 Participant receives other treatment for underarm whitening during study.

3.4.3.4 Pregnancy, serious illness or die

3.4.3.5 Participant fails in follow up appointment.

3.4.4 Study Location

Mae Fah Luang University Hospital, Bangkok

3.5 Materials and Equipments

3.5.1 PicoWay Laser

PicoWay Specifications

Laser Type	Nd:YAG	Frequency Doubled Nd:YAG
Wavelengths	1064 nm	532 nm
Maximum Energy	400 mJ	200 mJ
Pulse Duration	450 ps	375 ps
Peak Power	0.9 Gigawatts	0.53 Gigawatts
Spot Sizes	2, 3, 4, 5, 6, 7, 8, 9, 10 mm	
Repetition Rate	Single, 1, 2, 3, 4, 5, 10 Hz	
Delivery System	Articulated arm with zoom handpiece	
Warm Up Time	2 minutes	
User Interface	Touchscreen with GUI	
Size	42" H x 18" W x 27" D / 107 cm H x 46 cm W x 69 cm D	
Weight	275 lbs. / 125 kgs.	
Power Requirements	200-240 VAC, 50/60 Hz, 30 A, 4600 VA Single	

SYNERON CANDELA

(A) Instrument (B) Specification

Figure 3.2 PicoWay Laser and its Specification

The picosecond laser system is a new mechanic managed for lessen the pain and skin discoloration after laser which is due to thermal effects (Chalermchai & Rummaneethorn, 2018). Picosecond laser system is a laser system with many exceedingly short durations of pulse at only 300 to 500 ps.Compared to previous laser technologies, picosecond laser can be managed to deliver higher pulse energy due to shorter pulse duration with a lesser thermal effect. At the same power, the photoacoustic stress caused by picosecond lasers gives larger melanin fragmentation and higher energies nanosecond lasers'thermal stress. Similarly, treating with shorter durations of pulse available sufficient outcomes that can be received with lesser powers, so lessen the danger of causing the scars, so minimize damages of thermal burn to the structures of the surrounding skin. Recently, 532, 755 and 1064 nm are accessible wavelengths for picosecond (Chalermchai & Rummaneethorn, 2018)

In this study, the parameter will be set as: 1064 nm wavelength, frequency 10 Hz, spot size 5mm, fluency 0.2-0.8 J/cm^2 and repeat 5 passes/treatment. After that,

532 nm wavelength, fluency 0.6-0.7 J/cm^2, spot size 2mm, one pass along the same area.

3.5.2 Ultrasound Gel

3.5.3 Mexameter® from Courage-Khazaka used to measure the melanin's amount which stands in for the skin's darker color and hemoglobin which stands in for the skin's red color by reflectance. Value ranges from zero to 999 for erythema, melanin therefore little vary may be known.

3.5.4 Anesthetic cream to use topically

3.5.5 Form of consent

3.5.6 Record sheet and questionnaire for volunteers

3.5.7 Ethical Approval Document

3.6 Study Procedures

3.6.1 Volunteers were enrolled for the trial by using inclusion and exclusion criteria

3.6.2 Volunteers were educated, informed the study's information, together with study procedure, objectives, pretreatment instruction, post-treatment information, study's advantages, and odds-on side effects.

3.6.3 Volunteers were recruited to the study after giving information about consent form.

3.6.4 In clinical record form, volunteers' full physical examination was recorded.

3.6.5 Volunteers were taken photographs before the study (as baseline) and at Week 4, Week 8 and Week 16 accordingly.

3.6.6 Mexameter® MX18 were used to record volunteers' melanin indexes.

3.6.7 Volunteers' axillae were numbed by EMLA® cream (lidocaine 2.5% and prilocaine 2.5%) and after 45 minutes, the numbing cream were cleaned.

3.6.8 Volunteers were assigned to treat with picosecond lasers.

3.6.9 Volunteers were informed about the appointment's schedule which were 4th, 8th and 16th week after the first time of laser.

3.6.10 Complications and effects of laser would be recorded and evaluated.

3.6.11 Statistical assessment of the records were done.

3.6.12 Study records were summed up and reported.

3.7 Follow Up

4 weeks after each treatment

3.8 Data Collection and Outcome Measurement

3.8.1 Volunteers will be tested physically, and data will be noted.

3.8.2 Universal records, such as age, gender, drug allergy history, underlying disease will be noted.

3.8.3 After volunteers had undergone treatment, date will be noted at Week 0, Week 4, Week 8 and Week 16 respectively.

3.8.4 Other two physicians, who were not concerned to this thesis will run the neutral conclusion contained photos and side effects consideration at Week 0, Week 4, Week 8 and Week 16 after treatment. All data will be inspected.

3.9 Clinical Evaluation

3 specialists subdued from any concerning data, reviewed all cases, and perform assessment to the volunteers'taken photographs. Compare before and after results and score 0-2. (0 = no improve, 1 = improve < 50%, 2 = improve > 50%)

3.10 Subject Assessment

Volunteers' satisfactions were recorded by the following scale:

0 = unsatisfied

1 = little satisfied

2 = moderately satisfied

3 = very satisfied

To measure the adverse effects, volunteers were informed to note down the following symptoms:

1. Pain score, grading from no pain (0) to severe pain (10)
2. Duration (days) of redness or burning sensation
3. Others, such as post inflammatory hyperpigmentation or hypopigmentation, swelling, infections, formation of the scar and scaling.

3.11 Outcome

3.11.1 Primary Outcome

Evaluation of the melanin index in procedure of treating axillary hyperpigmentation by combination of Picosecond laser at the wavelengths of 1,064 and 532 nm.

3.11.2 Secondary Outcome

3.11.2.1 Evaluation of the clinical efficacy of axillary hyperpigmentation by combination of Picosecond laser at the wavelengths of 1,064 and 532 nm.

3.11.2.2 Evaluation of the volunteers' satisfaction for the treatment of axillary hyperpigmentation by combination of Picosecond laser at the wavelengths of 1,064 and 532 nm.

3.12 Data Analysis

3.12.1 Descriptive Data Analysis

3.12.1.1 Volunteers' recorded information will be investigated by descriptive statistical analysis for providing of descriptive information like means, medians, modes, percentages, standard deviations, and ranges.

3.12.1.2 Volunteers'satisfaction will be analyzed by descriptive statistical analysis.

3.12.1.3 Volunteers'side effects will be analyzed by descriptive statistical analysis.

3.12.2 Inferential Data

The data will be statistically analyzed by paired t-test for normal distribution data. Contrastingly, Wilcoxon signed-rank test will be used to analyze the nonparametric data. The significance levels of p-value < 0.05 is acceptable.

3.12.2.1 Comparing Global Aesthetics Improvement score before-and-after at 4^{th}, 8^{th}, 16^{th} weeks will be assessed by Repeated Measurement analysis of variance (ANOVA).

3.12.2.2 Comparing mexameter melanin index at before, and after 4^{th}, 8^{th}, 16^{th} weeks will be analyzed by using Repeated Measurement ANOVA. (Chalermchai, & Rummaneethorn, 2018).

CHAPTER 4

RESULTS

4.1 Baseline Characteristic

Twenty-two participants with Axillary hyperpigmentation were enrolled in the study. Twenty participants completed the study, all are female, and two participants lost to follow up at 8th week visit due to their personal reasons. Their age ranges from 20-45 years.

All participants were performed Picosecond laser using combination of 1,064nm and 532 nm and completed sixteen weeks follow up in this clinical study.

All participants had not been treated by any procedure to treat Axillary Hyperpigmentation such asQ-switch Nd Yag laser,Transamin injection on affected area.

The details of the demographic data were shown in table 4.1.

Table 4.1 Participants' demographic characteristic Characteristics of the volunteers (n=20)

Characteristics		**n**
Gender	**Female**	
Age Group (20-45)	Mean+/-SD	26.2 +/-1.361

4.2 Mean Melanin Index

Table 4.2 Statistical analysis of Mean Melanin Index at overall, right, and left side axillae on baseline, follow-up 4th, 8th, and 16th week (n=20)

	Overall	Right axillae	Left axillae
Baseline	207.29±60.32	203.87±58.90	210.71±66.68
Week 4	204.19±51.38	207.43±48.72	200.96±57.43
Week 8	203.38±51.54	203.02±50.37	203.73±54.83
Week 16	188.59±51.88	191.05±49.17	186.13±55.96
P-value	**0.001***	**0.041**	**0.002***

Note Data presented by mean±SD

P-value determine by Repeated measure ANOVA

* Statistically significant at the 0.05 level

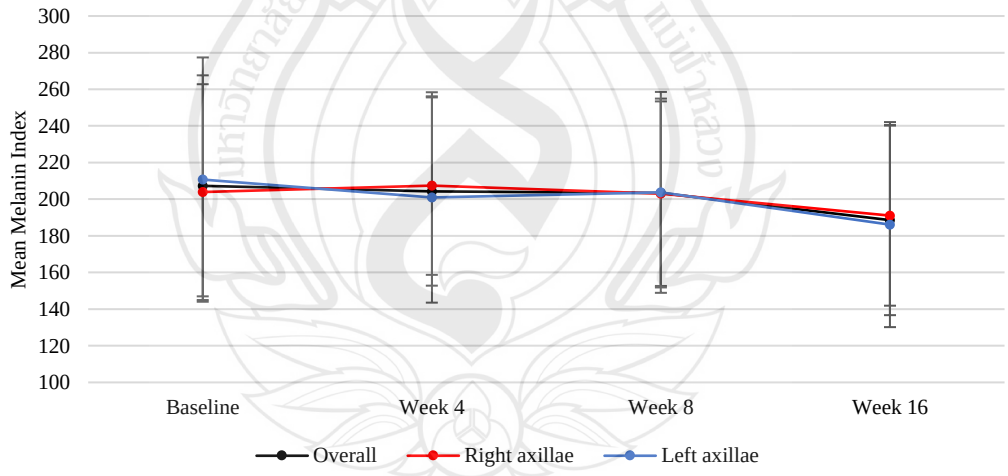


Figure 4.1 Line graph showing Mean Melanin Index at overall, right, and left side axillae in each visit

According to the statistical analysis results from table 4.2 and figure 4.1, mean of Mean Melanin Index at overall axillae on baseline was 207.29±60.32, 4th week 204.19±51.38, 8th week 203.38±51.54, and 16th week 188.59±51.88. The mean of Mean Melanin Index in each visit statistically significant decreased at the level of 0.05 ($p<0.001$). Considering the split-axillae of participants indicated that mean of Mean Melanin Index at right side axilla on baseline was 203.87±58.90, 4th week 207.43±48.72, 8th week 203.02±50.37, and 16th week 191.05±49.17, and left side axillae on baseline was 210.71±66.68, 4th week 200.96±57.43, 8th week 203.73±54.83, and 16th week 186.13±55.96. The mean of Mean Melanin Index at right and left side axillae in each visit statistically significant decreased at the level of 0.05 ($p=0.041$ and $p=0.002$, respectively). Therefore, the multiple comparison analysis is shown in table 4.3.

Table 4.3 Multiple comparison of Mean Melanin Index at overall, right, and left side axillae between baseline, follow-up 4th, 8th and 16th week (n=20)

Time	Pair comparison	Overall		Right side axillae		Left side axillae	
		Mean difference (%change)	P-value	Mean difference (%change)	P-value	Mean difference (%change)	P-value
Baseline	Week 4	-3.10 (-1.50%)	1.000	3.56 (1.75%)	1.000	-9.75 (-4.63%)	0.740
Baseline	Week 8	-3.91 (-1.89%)	1.000	-0.85 (-0.42%)	1.000	-6.97 (-3.31%)	0.743
Baseline	Week 16	-18.70 (-9.02%)	0.006*	-12.82 (-6.29%)	0.397	-24.58 (-11.67%)	0.011*
Week 4	Week 8	-0.82 (-0.40%)	1.000	-4.41 (-2.13%)	0.950	2.78 (1.38%)	1.000
Week 4	Week 16	-15.60 (-7.64%)	0.034*	-16.37 (-7.89%)	0.009*	-14.83 (-7.38%)	0.232
Week 8	Week 16	-14.78 (-7.27%)	<0.001*	-11.96 (-5.89%)	<0.001*	-17.60 (-8.64%)	0.017*

Note Multiple comparison determines by the Bonferroni method

* The mean difference is significant at the 0.05 level

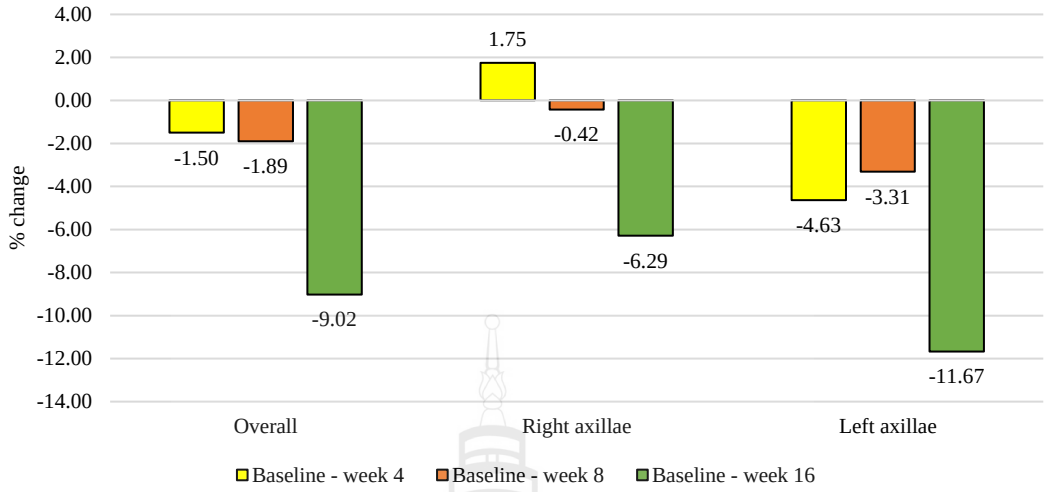


Figure 4.2 Bar graph showing percent change value of Mean Melanin Index on follow-up 4th, 8th, and 16th week compare with baseline

According to the multiple comparison result from table 4.3, It found that Mean Melanin Index on overall axillae at 16th week lower than baseline, 4th and 8th week statistically significant at the level of 0.05 ($p<0.05$). In comparison to the follow-up 16th week, the mean change of Mean Melanin Index on overall axillae at baseline, 4th and 8th week was -18.70 (% change -9.02), -15.60 (% change -7.64), and -14.78 (% change -7.27) respectively. For right side axillae, the Mean Melanin Index at 16th week lower than 4th and 8th week statistically significant at the level of 0.05 ($p<0.05$). In comparison to the follow-up 16th week, the mean change of Mean Melanin Index on right side axillae at 4th and 8th week was -16.37 (% change -7.89), and -11.96 (% change -5.89) respectively. For left side axillae, the Mean Melanin Index at 16th week lower than baseline and 8th week statistically significant at the level of 0.05 ($p<0.05$). In comparison to the follow-up 16th week, the mean change of Mean Melanin Index on right side axillae at baseline and 8th week was -24.58 (% change -11.67), and -17.60 (% change -8.64) respectively.

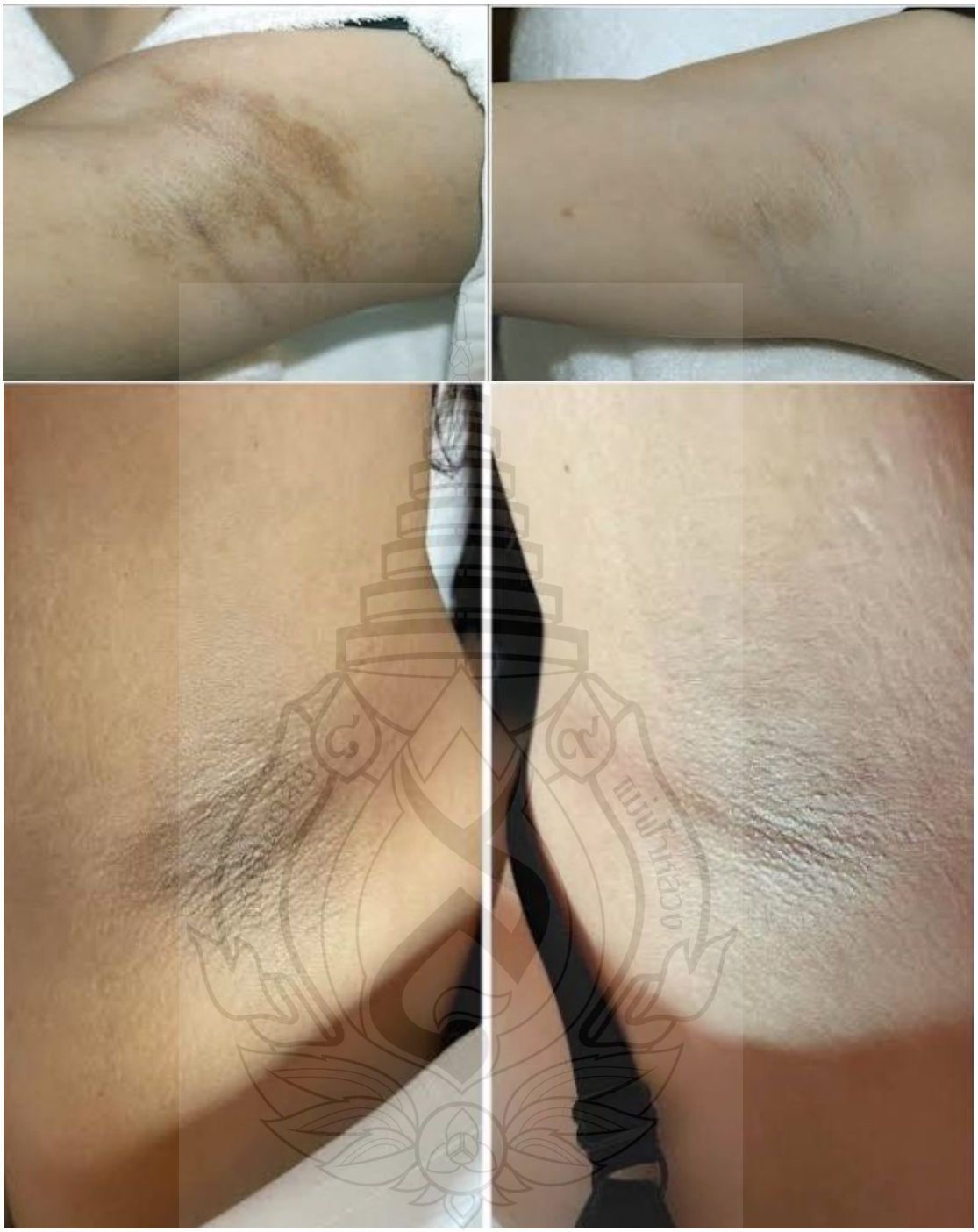


Figure 4.3 Before (Left) and after (Right) the treatment of axillary hyperpigmentation by Picosecond Laser

4.3 Global Aesthetics Improvement Score (GAIS)

Table 4.4 Statistical analysis of GAIS on follow-up 4th, 8th, and 16th week **(**n=20)

Time	Median (IQR)	GAIS, n(%)			
		0	**1**	**2**	**3**
Week 4	1 (0, 1)	6 (30.0)	14 (70.0)	-	-
Week 8	2 (1, 2)	-	6 (30.0)	14 (70.0)	-
Week 16	3 (2, 3)	-	-	6 (30.0)	14 (70.0)
P-value	**<0.001***				

Note IQR: Interquartile range, P-value determine by Friedman test

* Statistically significant at the 0.05 level

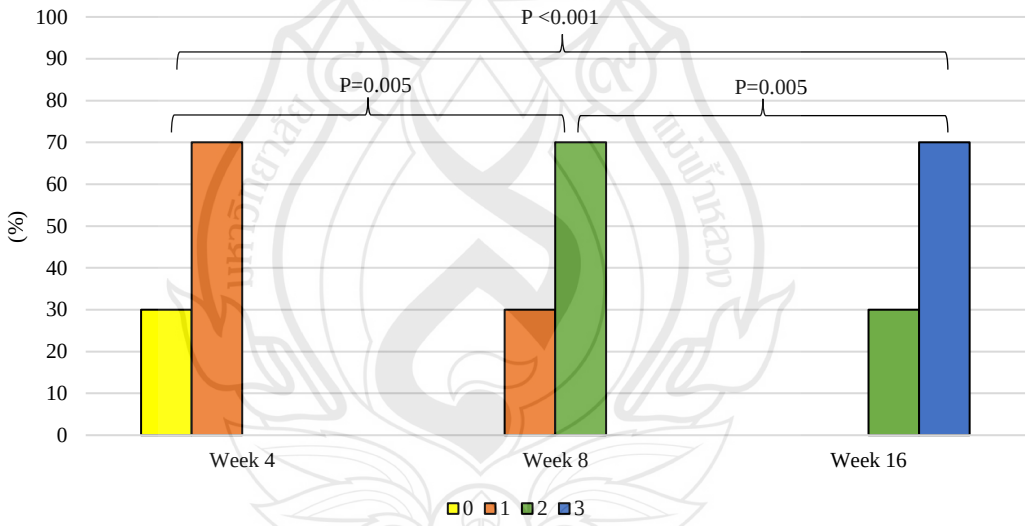


Figure 4.4 Bar graph showing GAIS on follow-up 4th, 8th, and 16th week

According to the statistical analysis results from table 4.4 and figure 4.3, median of GAIS on 4th week was 1(IQR 0, 1), 8th week 2(IQR 1, 2), and 16th week 3(IQR 2, 3). The median of GAIS in each visit statistically significant increased at the level of 0.05 ($p<0.001$). Therefore, the multiple comparison analysis is shown in table 4.5.

Table 4.5 Multiple comparison of GAIS between follow-up 4th, 8th and 16th week (n=20)

Time	Pair comparison	P-value
Week 4	Week 8	0.005*
Week 4	Week 16	<0.001*
Week 8	Week 16	0.005*

Note Significance values have been adjusted by the Bonferroni correction for multiple tests.

* Statistically significant at the 0.05 level

According to the multiple comparison result from table 4.5, It found that GAIS at 16th week higher than 4th and 8th week and at 8th week higher than 4th week statistically significant at the level of 0.05 ($p<0.05$).

4.4 Patient Satisfaction

Table 4.6 Statistical analysis of patient satisfaction score on follow-up 4th, 8th, and 16th week **(**n=20)

Time	Median (IQR)	Patients' Satisfaction, n(%)			
		Unsatisfied (0)	little satisfied (1)	moderately satisfied (2)	very satisfied (3)
Week 4	1 (0, 1)	8 (40.0)	12 (60.0)	-	-
Week 8	2 (2, 2)	-	2 (10.0)	18 (90.0)	-
Week 16	3 (3, 3)	-	-	1 (5.0)	19 (95.0)
P-value	**<0.001***				

Note IQR: Interquartile range, P-value determine by Friedman test

* Statistically significant at the 0.05 level

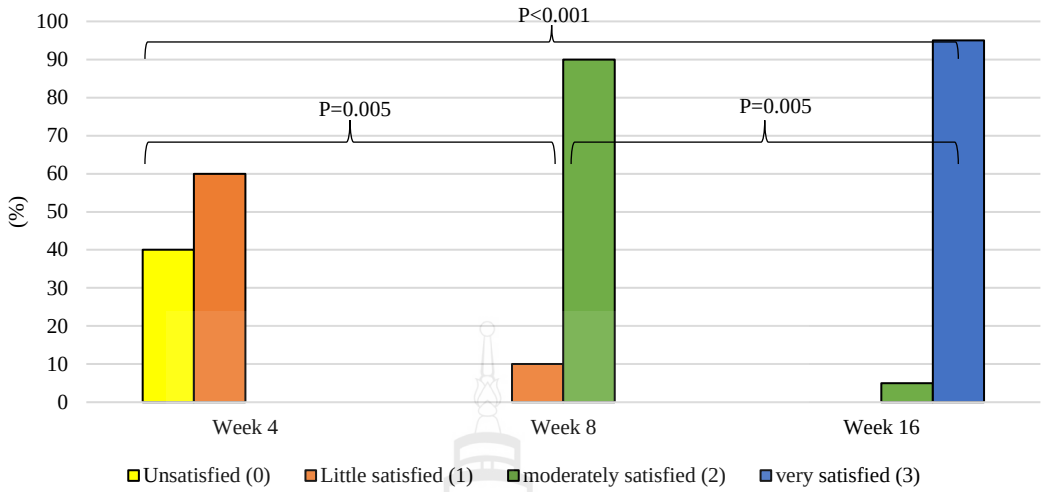


Figure 4.5 Bar graph showing patient satisfaction score on follow-up 4th, 8th, and 16th week

According to the statistical analysis results from table 4.6 and figure 4.4, median of patient satisfaction score on 4th week was 1(IQR 0, 1), 8th week 2(IQR 2, 2), and 16th week 3(IQR 3, 3). The median of patient satisfaction score in each visit statistically significant increased at the level of 0.05 ($p<0.001$). Therefore, the multiple comparison analysis is shown in table 4.7.

Table 4.7 Multiple comparison of patient satisfaction score between follow-up 4th, 8th and 16th week (n=20)

Time	Pair comparison	P-value
Week 4	Week 8	0.005*
Week 4	Week 16	<0.001*
Week 8	Week 16	0.005*

Note Significance values have been adjusted by the Bonferroni correction for multiple tests

* Statistically significant at the 0.05 level

According to the multiple comparison result from table 4.7, It found that patient satisfaction score at 16^{th} week higher than 4^{th} and 8^{th} week and at 8^{th} week higher than 4^{th} week statistically significant at the level of 0.05 ($p<0.05$).

4.5 Side Effect

There were no serious adverse effects or delayed adverse effects occurred during the study plan and follow-up period, and no patients withdrew from the study due to an adverse event.

15 of participants (75%) developed transient hyperpigmentation at 4^{th} and 8^{th} week after treatment and became better in the last visit (16^{th} week).

No participant showed severe thermal damage, or any injury of facial skin on the treated site, such as edematous or blister.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Discussion

Axillary Hyperpigmentation is a lesion concerning of pigmentation and hard to get the completely perfect result from just a short treatment. Using picosecond lasers may be one of the useful methods. Frequencies and time needed for giving treatments depending on specialist's clinical approval and patients' outcomes. Very little reports proving lessen time and high pulse revealed as well as safety, efficacy compared to standard methods of choice.

During this thesis, there was some cases that participants suffered from fleeting hyperpigmentation at every session of treatment. Some increasing of MI can be found in all 3 sessions. But fleeting hyperpigmentation became clinically improved after visiting at 8 weeks from the very last treatment session, and melanin indexes also decreased slightly. GAIS scores found to be become better in the last visiting follow up (Week 16)

At the same time, 532-nm laser which targets components of vessels seemed to bring out some added good results plus better effects that lasts longer in the treatment of pigmentary lesion. Then, some current studies have proved that endothelial cells can enhance pigmentation of the skin through the activation of endothelin receptor.

Good points concerning this trial are:

1. One of the new clinical trials researching the ways of treatment for Axillary Hyperpigmentation by combining 1,064nm and 532nm of Picosecond laser.
2. Reveals Picosecond laser's better results by combining 1,064nm and 532nm wavelengths for Axillary Hyperpigmentation.

3. Can use to develop as the reference paper for the treatment of Axillary Hyperpigmentation in the future.

5.2 Conclusion

By combining 1064nm and 532nm of picosecond laser for the treatment of Axillary Hyperpigmentation, can be a nice choice with less side effects. But must be noted that fleeting hyperpigmentation can still be observed after each session of treatment.

5.3 Suggestions

Due to limitation of the time in the trial, which is 16 weeks only, so the study's results are not yet perfectly observed.

Desired recommendation for the trial may be study in populations which is loaded than now, and the follow up for long term may need to be performed to observe the time that can allow the effect shows and how much the rate of recurrence can be.

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APPENDICES

APPENDIX A

ETHICAL APPROVAL DOCUMENT

บันทึกข้อความ

หน่วยงาน ส่วนบริหารงานวิจัย สถาบันวิจัยและนวัตกรรม มหาวิทยาลัยแม่ฟ้าหลวง โทรศัพท์ 7170 (จันทรา)

ที่ อว 7742(1)/1743 **วันที่** 25 พฤษภาคม 2565

เรื่อง ขอแจ้งผลการพิจารณาโครงร่างการวิจัยและเอกสารที่เกี่ยวข้อง

เรียน นาย Han Lin Naing

ตามที่ ท่านได้ส่งโครงร่างการวิจัย เรื่อง ประสิทธิภาพและความปลอดภัยของ Picosecond laser โดยใช้การรวมกันของ 1064 และ 532 nm ในการรักษารักแร้ดำ (The efficacy and safety of Picosecond laser using combination of 1064 and 532 nm for axillary hyperpigmentation) รหัสโครงการวิจัย EC 22018-20 นั้น

บัดนี้ คณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ได้ทบทวนแล้ว จึงขอแจ้งผลการพิจารณา ดังนี้

รับรอง (approval)

ทั้งนี้ ขอความอนุเคราะห์ผู้วิจัยหลักลงลายมือชื่อและวันที่หลังทำความเข้าใจข้อปฏิบัติเมื่อผ่านการรับรองจากคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ในหน้าที่ 2 และ 4 ของหนังสือรับรองด้านจริยธรรมการวิจัย (COA) ที่ได้แนบมานี้ และส่งไฟล์สแกนของเอกสารที่ชัดเจนหลังลงลายมือชื่อและวันที่กลับมายังอีเมล์ rec.human@mfu.ac.th พร้อมระบุที่อยู่ที่สะดวกรับหนังสือรับรองด้านจริยธรรมการวิจัยฉบับจริง โครงร่างงานวิจัยและเอกสารแนบฉบับที่ได้รับรองแล้ว จากนั้นเจ้าหน้าที่จะดำเนินการจัดส่งเอกสารดังกล่าวไปให้ท่าน หรือท่านสามารถติดต่อรับหนังสือรับรองการพิจารณาด้านจริยธรรมการวิจัยได้ที่สำนักงานคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ชั้น 4 อาคารบริการวิชาการ (AS) หมายเลขโทรศัพท์ 0-5391-6551 หรือ 0-5391-7170-1

จึงเรียนมาเพื่อโปรดดำเนินการ

ขอแสดงความนับถือ

(นายกานต์กุญช์ บำรุงชาติ)

หัวหน้าส่วนบริหารงานวิจัยฯ กรรมการและผู้ช่วยเลขานุการ

คณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง

APPENDIX B

INFORMATION SHEET

1. Title

THE EFFICACY AND SAFTETY OF PICOSECOND LASER USING COMBINATION OF 1,064 AND 595 nm FOR AXILLARY HYPERPIGMENTATION

2. Primary Objective

To compare the reduction of melanin index before and after using combination of wavelengths 1,064 and 532-nm for the treatment of the axillary hyperpigmentation

3. Background

Hyperpigmentation of the skin is a common dermatological condition in which the color of the skin generally becomes darker. These changes in skin coloration can be a result of various internal and external factors including hormonal changes, inflammation, injury, acne, eczema, certain medication, UV exposure, etc. (Pérez-Bernal et al., 2000). Skin pigmentation and coloration are governed by the biological processes involving the production of the skin pigment called melanin produced by melanocytes in various layers of skin. Thus, alterations in melanocyte production or distribution of melanin result in skin hyperpigmentation disorders (Rossi & Perez, 2011).

Hyperpigmentation is not considered a harmful or lethal disorder; however, it can affect the quality of life of patients by affecting their emotional and psychological health. Various treatment options are available for hyperpigmentation. These agents are primarily applied by topical route in the form of creams, gels, or ointments. However, these topical treatments pose various side effects such as skin drying, irritation, peeling, or hypopigmentation. The prolonged treatment durations ranging from several months to years may lead to poor patient compliance and satisfaction.

The challenge of effective therapy to treat hyperpigmentation remains unresolved that lays emphasis onthe need for novel treatment options. This article thus focuses on the therapeutic targets as well the various conventional, novel and emerging therapies being approached for the better, effective, and timely management of hyperpigmentation.

Axillary hyperpigmentation (AH) is a common condition in dark-skinned individuals that can cause cosmetic concerns, especially in Asian populations. In a study by James et al, histopathological analysis has shown that the most common cause of AH is post inflammatory hyperpigmentation (PIH), which in turn can result from several factors.[1](James et al. 2006)Another study by Evan et al pointed out that axillary tissue differs from other body tissues.[2](James et al. 2006) Axillary tissue constitutes extra hair follicles, extra sweat glands, extra sebaceous glands, and higher transepidermal water loss values that cause weaker skin barriers. Moreover, the axilla is a flexural area susceptible to constant skin friction, chemical exposure, and frequent shaving, which can damage the skin tissue and cause irritation, causing PIH.[2,3](James et al. 2006)

Avoiding causative agents, treating the underlying condition and non-laser method may not improve axillary hyperpigmentation to be lighter. Q-switched nanosecond laser has been the first modality for treating this condition. Because this modality is effective in treating pigmented skin lesion by selective photothermolysis effect (Anderson & Parrish, 1983). However, people who undergo Q-switched nanosecond (10^{-9}) laser treatment usually face with tenderness, redness, swelling at lips after laser procedure for a while. It also can induce post-inflammatory hyperpigmentation especially in darker skin type population. Besides, the procedure has to be done in many sessions to get good result. Nowadays, picoseconds (10^{-12}) laser has been developed and used for pigment lesion, especially in tattoo removing. The advanced benefit for picoseconds laser over Q-switched nanosecond laser is a thermal-photoacoustic effect, so people should get less downtime, less pain and may less time consume for treatment (Lee, Cho & Glen, 2016).

4. Study Location

Mae Fah Luang University Hospital, Asoke, Bangkok

5. Procedure

All participants were recruited for screening examination by using inclusion and exclusion criteria

All participants were informed and educated about all information of the study, including objectives, study method, pre-and post-treatment instruction, benefits of the study, and possible adverse effects.

Participants were given an informed consent form, and enrolled to the study.

Full physical examination were recorded in clinical record.

Standardized photographs of all participants were taken prior to the study(as baseline) and at each follow up visit at 4th, 8th and 16th weeks

The melanin index were recorded by using Mexameter® MX18

Numbed the subjects' axilla by applying EMLA® cream (lidocaine2.5% and prilocaine 2.5%) covered by an occlusive dressing for 45 minutes before being washed off.

All enrolled participants were randomly assign to undergo picosecond laser

All participants would be given a schedule of appointment at 4th, 8th, 16th weeks after treatment.

Effects and complications of Picosecond laser would be evaluated and recorded.

Statistical evaluation of all data were done.

The study results were summarized and reported.

APPENDIX C

INFORMED CONSENT FORM

ชื่อโครงการวิจัย

THE EFFICACY AND SAFETY OF PICOSECOND LASER USING COMBINATIONOF 1064 AND 532 NM FOR AXILLARY HYPERPIGMENTATION

ประสิทธิภาพและความปลอดภัยของ.....

PICOSECOND LASER โดยใช้การรวมกันของ 532 และ 1064nm ในการรักษารักแร้ดำ

.....

ข้าพเจ้า นายนางสาว/นาง/ .....

ที่อยู่.....

ได้อ่านรายละเอียดจากเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัยวิจัย ฉบับวันที่ .....

ข้าพเจ้าได้รับสำเนาเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัย และสำเนาเอกสารแสดงเจตนายินยอมเข้าร่วมในโครงการวิจัยที่ข้าพเจ้าได้ลงนามและลงวันที่ ทั้งนี้ก่อนที่จะลงนาม ข้าพเจ้าได้รับการอธิบายโดยละเอียดจากผู้วิจัยถึงวัตถุประสงค์ วิธีการวิจัย ความไม่สุขสบายหรือความเสี่ยงที่อาจเกิดขึ้น ประโยชน์ที่คาดว่าจะได้รับจากการวิจัย และทางเลือกอื่น

ข้าพเจ้ามีเวลาและโอกาสเพียงพอในการซักถามข้อสงสัย โดยผู้วิจัยได้ตอบคำถามต่าง ๆ ด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าเข้าใจเป็นอย่างดีแล้ว

ข้าพเจ้ารับทราบจากผู้วิจัยว่าหากเกิดอันตรายใด ๆ จากการวิจัย ข้าพเจ้าจะได้รับการรักษาพยาบาล ตามที่ระบุในเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัย

ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากโครงการวิจัยเมื่อใดก็ได้ การถอนตัวนี้ไม่มีผลต่อการรักษาพยาบาลและสิทธิอื่น ๆ ที่ข้าพเจ้าจะพึงได้รับต่อไป

ผู้วิจัยรับรองว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ การรายงานหรือสรุปผลการวิจัยจะไม่ระบุชื่อนามสกุลของข้าพเจ้า การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่าง ๆ ที่เกี่ยวข้อง จะกระทำด้วยเหตุผลทางวิชาการเท่านั้น

ข้าพเจ้าได้อ่านข้อความข้างต้นและมีความเข้าใจดีทุกประการแล้ว ยินดีเข้าร่วมในการวิจัยด้วยความสมัครใจ จึงได้ลงนามในเอกสารแสดงความยินยอมนี้

..... ลงนามผู้เข้าร่วมในโครงการวิจัย

ชื่อ-สกุล ..... ผู้เข้าร่วมในโครงการวิจัย

(.....) ตัวบรรจง

วันที่ .....เดือน .....พ.ศ. .....

การจัดการกับตัวอย่างทางชีวภาพ(ถ้ามี ถ้าไม่มีให้ตัดออก)

☐ มี แต่ไม่มีการขอเก็บตัวอย่างชีวภาพที่เหลือไว้เพื่อการวิจัยในอนาคต

☐ มี และขอเก็บตัวอย่างชีวภาพที่เหลือไว้เพื่อการวิจัยในอนาคต แต่จะมีการขออนุญาตอาสาสมัคร และขออนุมัติจากคณะกรรมการจริยธรรมการวิจัย อีกครั้ง

ข้าพเจ้า ☐ ยินยอม ให้เก็บตัวอย่างชีวภาพที่เหลือไว้เพื่อการวิจัยในอนาคต

☐ ไม่ยินยอม ให้เก็บตัวอย่างชีวภาพที่เหลือไว้เพื่อการวิจัยในอนาคต

..... ลงนามผู้เข้าร่วมในโครงการวิจัย

ชื่อ-สกุล ..... ผู้เข้าร่วมในโครงการวิจัย

(.....) ตัวบรรจง

วันที่ .....เดือน .....พ.ศ. .....

ข้าพเจ้าได้อธิบายโดยละเอียดถึงวัตถุประสงค์ วิธีการวิจัย ความไม่สุขสบายหรือความเสี่ยงที่อาจเกิดขึ้นประโยชน์ที่คาดว่าจะได้รับจากการวิจัย และทางเลือกอื่น ให้ผู้เข้าร่วมในโครงการวิจัยได้ทราบและมีความเข้าใจดีแล้ว พร้อมทั้งลงนามในเอกสารแสดงเจตนายินยอมด้วยความสมัครใจ

ลงนาม ..... ผู้วิจัย

(Mr.Han Lin Naing)

ลงนาม ..... พยายาน

(.....) ชื่อ-สกุล ตัวบรรจง

วันที่ .....เดือน .....พ.ศ. .....

APPENDIX D

RESEARCH PROFILE (CONFIEDNTIAL)

ID

General Information (Only official)

1. Date
2. Name
3. Hospital number
4. Address
5. Tel
6. Email
7. Sex O Male. O Female
8. Pregnancy O Yes O No
9. Occupation -
10. Underlying disease:
11. Photosensitivity or drug induced photosensitivity:
12. Personal medication and supplement:
    a. Chemo-radiotherapy
    b. Active inflammatory skin disease, open wound in the treatment area
    c. History of malignant of premalignant lesions in the treatment area
13. History of food or drug allergy:
14. Current treatment :
15. History of following treatment before the study
    a. O Yes …….Identify
    b. O No
    - Ablative and/or Non-ablative Laser Treatment (within 1 month)
    - Microdermabrasion
    - Intense Pulse Light therapy
    - Chemical Peeling

APPENDIX E

PHYSICIAN RECORD FORM

RESEARCH RECORD: (RESEARCHERS' PART)
THEEFFICACY AND SAFETY OF PICOSECOND LASER USING COMBINATION OF 1,064 AND 532 nm FOR AXILLARY HYPERPIGMENTATION

Volunteer number.....

Tasks at the first visit

Date ...../...../.....

Please use √ symbol

Check list for the first visit		
Process	**Yes**	**No**
The volunteer has his or her armpit shave 1 day before the treatment		
Physical examination of Axillary Hyperpigmentation indicates they are fit to the selection criteria		
The volunteer has completed research profile		
All of the profile data is fit to selection criteria		
Assure that the volunteer can understand information in appendix and how to care his or her axilla after treatment		
The volunteer has written the informed consent form		
The researcher asked the volunteer for any curiosity		
The researcher answered the volunteer's questions		
Photography of the axilla were performed		
Mexameter® MX18 was performed		

1. The Global Aesthetic Improvement Scale

Score	State	Descriptions
3	Very much improved	Optimal cosmetic result
2	Much improved	Marked improvement in appearance but not completely optimal for this patient. A touch-up would slightly improve the result.
1	Improved	Obvious improvement in appearance from the initial condition, but A touch-up or re-treatment is indicated.
0	No Change	The appearance is essentially the same as the original condition.
-1	Worse	The appearance is worse than the original condition

Volunteer Number

The form for evaluate the volunteer follow the GAIS scale

1st Physician –

Area/Time	Clinical evaluation follow the GAIS score		
	4th Week	8th Week	16th Week
Right			
Left			
Mean GAIS			

Volunteer Number

The Form for evaluate the volunteer follow the GAIS scale

2nd Physician-

Area/Time	**Clinical evaluation follow the GAIS score**		
	4th Week	8th Week	16th Week
Right			
Left			
Mean GAIS			

Volunteer Number

The form for evaluate the volunteer follow the GAIS scale

3rd Physicial –

Area/Time	**Clinical evaluation follow the GAIS score**		
	4th Week	8th Week	16th Week
Right			
Left			
Mean GAIS			

Volunteer Number

2. Mexameter® MX 18

Melanin index (MI)	Left			Right			Mean
	1st	2nd	3rd	1st	2nd	3rd	
Initial MI(Baseline)							
4th Week MI							
8th Week MI							
F/U MI (at 16th Week)							

APPENDIX F

SUBJECT'S SATISFACTION QUESTIONAIR

(แบบสอบถามความพึงพอใจ)

Volunteer Number

1. Unsatisfactory factors after the treatment (อาการที่ไม่พึงพอใจ)

Please check the following signs and symptoms after each of the treatment by using √ symbol (คุณมีอาการใด ๆ ตามตารางหรือไม่(

Record of side effects after the treatment				
Symptoms	Yes (มี)	**No (ไม่มี)**	**Duration (นานแค่ไหน)**	**Remark**
Pain (เจ็บ)				
Swollen (บวม)				
Redness (แดง)				
Bruise (ช้ำ)				
Hyperpigmented (สีผิวเข้มขึ้น)				
Others (อื่น ๆ)				

Volunteer Number

2. Please score the satisfactory scale according to your desire and satisfaction after each week of the treatment (คุณสามารถให้คะแนนพึงพอใจตามที่คุณต้องการหลังจากการรักษาแต่ละสัปดาห์)

Week	Subject's satisfactory scale (0-3)
4^{th} week	
8^{th} week	
16^{th} week	

0 = Unsatisfied, No improvement of axillary hyperpigmentation (0 คะแนน=ไม่พอใจ อาการรักแร้ดำไม่ดีขึ้นเลย)

1 = Kind of Satisfied, A little improvement of axillary hyperpigmentation (1 คะแนน= มีความพึงพอใจ เห็นการเปลี่ยนแปลงของรักแร้ดำ)

2 = Satisfied, Much improvement of axillary hyperpigmentation (2 คะแนน= พึงพอใจ อาการของรักแร้ดำดีขึ้นเห็นได้ชัด)

3 = Very satisfied, Much improvement of axillary hyperpigmentation with the evenness of the skin (3 คะแนน= พึงพอใจมาก อาการรักแร้ดำดีขึ้นมากและผิวดูเรียบขึ้น)

3. Will you undergo the same treatment in the future (ในอนาคต คุณคิดที่จะทำการรักษานี้อีกหรือไม่)

O Yes O No