# THE EFFICACY OF THE COMBINATION OF INTENSE PULSED LIGHT THERAPY AND PLATELET-RICH PLASMA WITH PLATELET-RICH PLASMA ALONE FOR FACIAL REJUVENATION

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MASTER OF SCIENCE
IN
DERMATOLOGY

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

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**THIS THESIS IS A PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN DERMATOLOGY**

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| **Author** | Yamin Eaint |
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## ABSTRACT

Background: Skin aging is a multifactorial process characterized by collagen degradation, reduced elasticity, wrinkle formation, and impaired skin barrier function due to intrinsic aging and extrinsic factors such as ultraviolet exposure. Non-invasive facial rejuvenation techniques have gained popularity, with platelet-rich plasma (PRP) promoting tissue regeneration through growth factors, while intense pulsed light (IPL) improves pigmentation, vascular lesions, and collagen remodeling. The synergistic potential of combining IPL with PRP may enhance overall skin rejuvenation outcomes.

Objective: To compare the clinical efficacy of combined IPL and PRP therapy versus PRP alone for facial rejuvenation, focusing on wrinkle reduction, skin viscoelasticity, trans-epidermal water loss (TEWL), overall aesthetic improvement, patient satisfaction, and adverse effects.

Methods: A randomized split-face clinical trial was conducted involving 12 healthy participants aged 25–45 years with grade 2–3 wrinkles. Participants received combined IPL + PRP treatment on one side of the face and PRP alone on the other side every four weeks for three sessions. Outcomes were evaluated at baseline and during follow-ups (weeks 4, 8, and 12) using VISIA® wrinkle analysis, Cutometer® for viscoelasticity, Tewameter® for TEWL, Global Aesthetic Improvement Scale (GAIS), patient satisfaction scores, and adverse-effect monitoring.

Results: The combination therapy demonstrated greater improvement in wrinkle scores, skin elasticity, and hydration compared with PRP alone. Participants receiving IPL + PRP showed significant collagen remodeling, improved skin tone ($p < 0.05$), and

higher satisfaction scores, while maintaining a favorable safety profile with minimal and transient adverse effects.

Conclusion: The combination of IPL and PRP is a safe and more effective approach for facial rejuvenation than PRP monotherapy. This synergistic treatment improves wrinkles, skin viscoelasticity, hydration, and patient satisfaction, supporting its use as a non-invasive, comprehensive anti-aging strategy and providing a foundation for future larger-scale studies.

**Keywords:** Intense Pulsed Light (IPL), Platelet-rich Plasma (PRP), Facial Rejuvenation, Skin Aging, Wrinkle Reduction

# TABLE OF CONTENTS

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# LIST OF FIGURES

# CHAPTER 1

# INTRODUCTION

## 1.1 Background

Skin aging is a natural and inevitable process characterized by a gradual decline in the skin's elasticity, firmness, and overall appearance. As we age, various factors contribute to this phenomenon, including genetic predisposition, sun exposure, lifestyle choices, and environmental influences. Collagen and elastin, essential proteins responsible for maintaining skin structure, diminish over time and lead to the formation of wrinkles, fine lines, and sagging. Additionally, external factors like UV radiation accelerate the aging process by causing oxidative stress and collagen degradation (1).

Physical appearance also determines one's degree of personality and sense of self-confidence. As a result, the demand of facial rejuvenation has drawn more attention, with a particular focus on investigating more effective techniques, especially for non-operative techniques (1). Rejuvenation involves the elimination and regeneration of the skin, resulting in a more structured, youthful dermal matrix and normalized epidermis (2).

Non-invasive treatments for facial rejuvenation have become increasingly popular, offering individuals a range of options without the need for surgery (3). Among them, platelet-rich plasma (PRP) demonstrates positive effects on facial rejuvenation, whether used independently or in conjunction with other treatments like laser procedures, subcision, and growth factors. Its rich concentration of growth factors contributes to notable growth potential and accelerated healing. In contrast, ablative techniques, despite causing considerable patient discomfort and downtime with potential adverse events, can be contrasted with non-ablative methods such as intense pulsed light (IPL) therapy (Gade et al.) (5). Non-ablative approaches like IPL, offer substantial benefits with fewer complications and less discomfort, significantly impacting skin tone and influencing collagen deposition.

There have been reports that intense pulsed light (IPL) therapy is beneficial in treating ageing skin. IPL therapy uses continuously applied strong pulsed photons as a low-energy, low-density, non-ablative treatment. IPL uses broad spectrum light that is not coherent and is produced by powerful Xenon lamps. It is possible to optimize the treatment parameters, such as wavelength, pulse duration, and energy, for particular tissues by narrowing the related spectrum through the use of filters. After IPL enters the tissues, hemoglobin and melanin specifically absorb it, causing photothermal effects. IPL has the ability to temporarily damage collagen through heat and stimulate the contraction and restructuring of collagen fibers. This process, known as photo-rejuvenation, leads to beneficial effects on the skin (5).

Platelet-rich plasma (PRP), derived from autologous plasma, is extensively employed in various dermatological procedures for noninvasive facial rejuvenation. The PRP concentrate contains diverse growth factors, and there is a hypothesis that these factors play a role in tissue repair, regulate genes related to cellular proliferation and differentiation, and promote angiogenesis. This cellular-level rejuvenation is thought to yield more enduring effects compared to invasive procedures (6). Its minimally invasive nature and use of the body's own healing components contribute to its appeal, making PRP a versatile and increasingly popular option in various medical and cosmetic practices (1).

It is hypothesized that intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) work in conjunction to provide a potent, safe and effective method of overall facial rejuvenation. PRP, which is made from the patient's own blood, has a high proportion of growth factors that encourage the formation of collagen and support tissue regeneration. Together with IPL, which resolves vascular issues and abnormalities in pigmentation, this combination may treat a variety of desirable cosmetic issues. PRP accelerates the skin's repair process by improving overall skin health and optimizing the results of IPL. By working together, IPL and PRP can provide patients not only a non-invasive and effective option but also more youthful and refreshed appearance.

The objective of this study is to evaluate the efficacy of pairing intense pulsed light (IPL) therapy with platelet-rich plasma (PRP) for facial rejuvenation. It’s worth noting that there is no existing research on this combined treatment. The anticipation is

that employing this method may lead to better outcomes compared to individual therapeutic approaches.

## 1.2 Research Questions

Does the combination of intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) have a better clinical efficacy than PRP alone in facial rejuvenation?

## 1.3 Objectives

1.3.1 General Objective

To compare the efficacy of the combined therapy of intense pulsed light (IPL) and platelet-rich plasma (PRP) with PRP alone in facial rejuvenation.

1.3.2 Specific Objective

1. Primary Objective

To compare the mean changes of wrinkle score between combination therapy and monotherapy groups by using Visia scan.

2. Secondary Objective

1) To compare mean changes of viscoelasticity and trans-epidermal water loss measurement between combination therapy and monotherapy groups by using Cutometer and Tewameter.

2) To compare the overall improvement and patient satisfaction between combination therapy and monotherapy for facial rejuvenation by using Global Aesthetic Improvement Scale and Participant's Satisfaction Score respectively.

3) To compare the adverse effects between combination therapy and monotherapy by using research questionnaire.

## 1.4 Research Hypothesis

The dual combination of intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) is better than PRP alone in

1. Reducing wrinkles
2. Increasing viscoelasticity
3. Decreasing trans-epidermal water loss
4. Great participants' satisfaction
5. Less adverse effects

## 1.5 Benefits

1.5.1 To utilize the dual combination of intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) in facial rejuvenation as an alternative treatment

1.5.2 To provide a data base for further research studies

## 1.6 Conceptual Framework

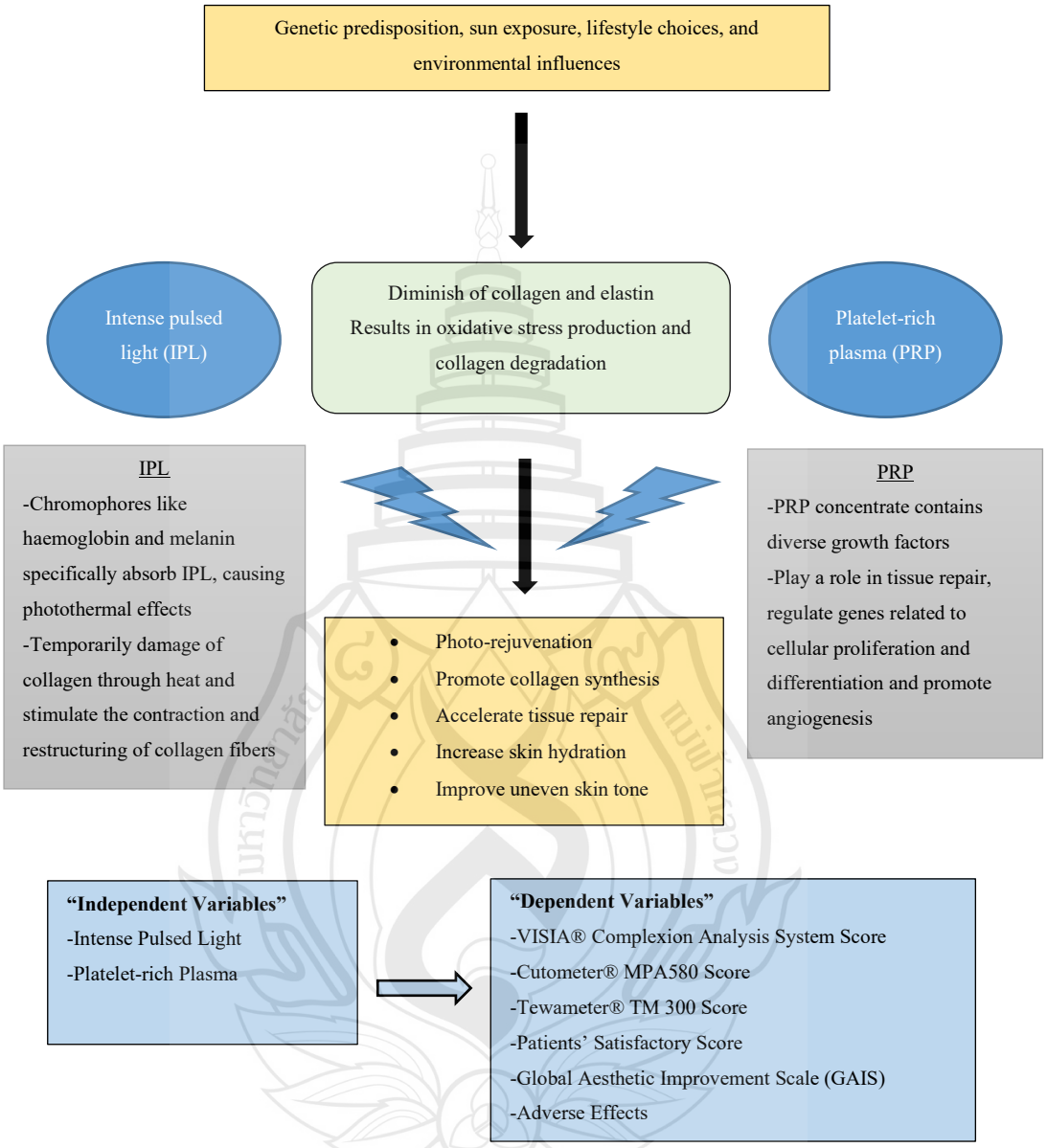



**Figure 1.1** Conceptual Framework

## 1.7 The Scope of Research

The study included 12 male and female participants, aged 25- 45, exhibiting wrinkles, with grade 2 or 3 according to wrinkle severity rating scale (WSRS) and participants who want to undergo facial rejuvenation. These individuals will undergo a

series of treatments involving both intense pulsed light (IPL) therapy (split-face) and platelet-rich plasma (PRP) (full face) every four weeks for three sessions at Mae Fah Luang University Hospital in Bangkok. Evaluation of changes and side effects will be conducted at each treatment session by using Visia scan, Cutometer, Tewameter, Global Aesthetic Improvement Scale (GAIS) and the Patients' Satisfactory Score. Follow-up assessments will be performed at 4th week, 8th week and 12th week.

## 1.8 Operational Definitions

1.8.1 Face rejuvenation refers to a set of cosmetic or medical procedures designed to enhance the appearance of the face by addressing signs of aging, skin damage or other aesthetic concerns.

1.8.2 Intense pulsed light (IPL), absorbed by specific tissue chromophores like hemoglobin and melanin, is a non-invasive procedure that uses a broad spectrum of light to target various skin concerns and contribute to overall skin rejuvenation.

1.8.3 Platelet-rich plasma (PRP), obtained from patient's own blood after processing it to concentrate the platelets, is used to stimulate tissue repair, collagen production and angiogenesis.

1.8.4 Skin aging is influenced by both intrinsic and extrinsic factors. Intrinsic factors include genetic predispositions, hormonal changes, and metabolic processes, while extrinsic factors involve environmental influences such as UV radiation, pollution, and lifestyle choices.

1.8.5 Photo-rejuvenation is a non-invasive procedure that uses light energy, penetrates the skin, stimulate collagen production and promote a more even skin tone.

1.8.6 Oxidative stress occurs when there's an imbalance between the production of free radicals and the body's ability to counteract or detoxify their harmful effects, leading to cellular damage and inflammation.

1.8.7 Split-face study typically involves a comparison of two different treatments or interventions on opposite sides of an individual's face. This method allows researchers or practitioners to assess and compare the effectiveness or outcomes of the

treatments by observing differences between the treated and untreated sides of the face within the same person.

1.8.8 Efficacy refers to the ability or capacity of something to produce the desired result or effect, often measured by its effectiveness and efficiency in achieving a specific purpose or goal.

1.8.9 Combination means a set or arrangement formed by selecting and grouping elements or objects without considering the order. It involves choosing items from a larger set, resulting in various possible arrangements.

1.8.10 Compare means to examine the similarities and differences between two or more things in order to highlight their characteristics or qualities.

1.8.11 Satisfaction reflects to the state of contentment, fulfillment or happiness derived from a particular situation, experience, product or service: Score 0= not satisfy, Score 1= mildly satisfy, Score 2= moderately satisfy, Score 3= greatly satisfy

1.8.12 Adverse effects mean negative or harmful consequences resulting from a treatment, intervention, drug or exposure: Grade 1= Mild, Grade 2= Moderate, Grade 3= Severe, Grade 4= Very sever or Life threatening, Grade 5= Death

1.8.13 Wrinkle Severity Rating Scale (WSRS): Grade 1= no visible nasolabial fold (NLF) continuous skin line, Grade 2= shallow but visible NLF with a slight indentation, Grade 3= moderate deep NLF; visible at normal appearance, Grade 4= very long and deep NLF; prominent facial feature <2mm visible fold if stretched, Grade 5= extreme deep long NLF; 2-4mm V shaped fold if stretched

## 1.9 Limitations

1.9.1 Extended follow-up cannot be done due to limitations in the time of study.

1.9.2 Performing a tissue biopsy is not feasible due to concerns related to volunteers' cosmetic considerations and privacy.

# CHAPTER 2

# LITERATURE REVIEW

## 2.1 Structure and Function of Normal Skin

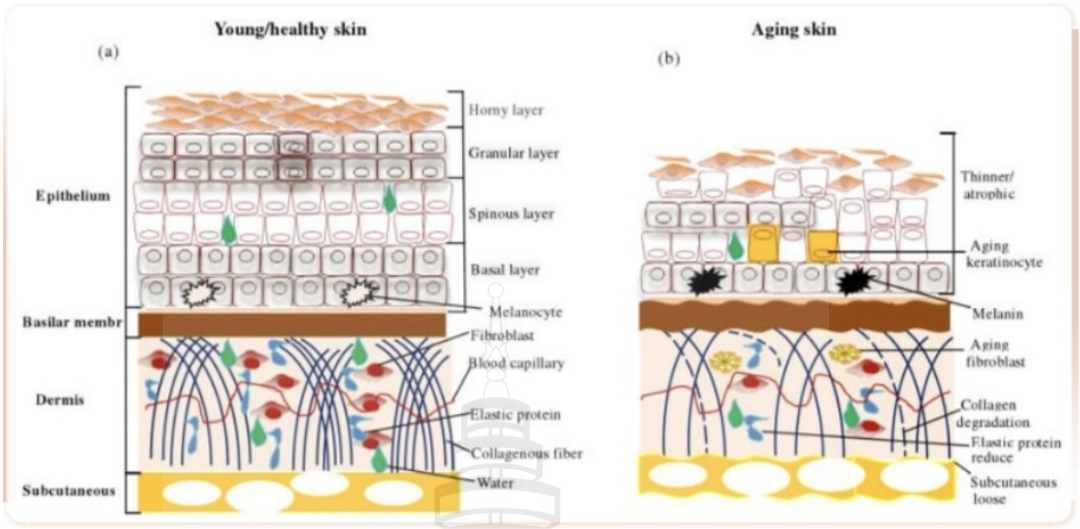
The functional integrity of the skin is determined by the supportive structures within, and the developmental process. The skin, organized into three distinct layers, undergoes a dynamic maturation process to establish its complex structure and fulfill its diverse functions.

1. Epidermis serves as a protective barrier to the external environment, functioning as a center for immune surveillance and activation. Its role is crucial in preventing and combating infections.

2. Dermis constitutes the primary structural component of the skin, predominantly composed of collagen. Serving as a central interface to the skin's vasculature and nervous system, it closely interacts with the epidermis and coordinates the overall skin function.

3. Hypodermis, located beneath the collagen-rich dermis, features subcutaneous adipose tissue playing a crucial role in energy balance. Additionally, it has recently been recognized for its involvement in facilitating communication with the epidermis and contributing to immune surveillance.

The skin is responsible for various vital functions, such as withstanding trauma, shielding against ultraviolet light, warding off infections, perceiving the environment, regulating temperature, and managing energy metabolism. These diverse systems within the skin undergo development at distinct rates. Similar to the developmental process of other organs, skin development follows a stepwise progression, transitioning from more pluripotent cells to increasingly specialized and differentiated cells, each with specific functions.




**Source** (7)

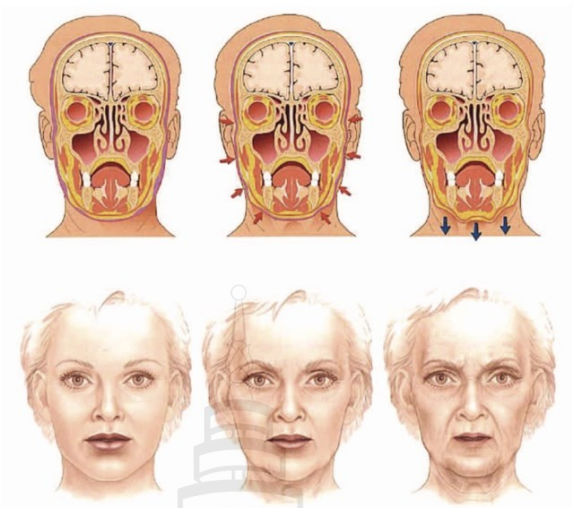
**Figure 2.1** (a) Schematic diagram of skin structure, (b) Schematic diagram of skin structure after aging. This picture is a comparison of the changes between young skin and aging skin

## 2.2 Skin Aging

Skin aging is a complex process influenced by both intrinsic and extrinsic factors. Intrinsic factors, driven by genetic factors and the passage of time, cause a gradual deteriorations in the skin's structural proteins like collagen and elastin. Extrinsic factors, such as sun exposure, pollution, and lifestyle choices, contribute to premature aging by accelerating the formation of fine lines, wrinkles, and age spots (6). Over time, the skin's ability to repair and regenerate diminishes, resulting in a loss of firmness and elasticity.

2.2.1 Aging of Deeper Layers

The aging process also impacts various components of the facial structure, encompassing the skin, soft tissues like subcutaneous fat, muscle, and fascia, as well as the structural foundation provided by bone and teeth. These elements collectively contribute to the dynamic phenotypic presentation of the face across the lifespan (8).



**Note** In the young face (left), the subcutaneous fat deposits (yellow) are masked by the fullness provided by extracellular colloidal fluids (purple). With advancing age, progressive loss of facial fullness causes the subcutaneous fat deposits and underlying soft tissue and skeletal structures to become more evident (center); involutional exposure of fat deposits in the jowl and chin gives the impression of descent (right).

**Source** (8)

**Figure 2.2** Coronal sections illustrating the loss of facial fullness that occurs with age

2.2.2 Dermal Aging

The skin's dermis is like a support system made of collagen, which keeps the skin firm and structured. As the skin ages, the dermis thins, causing dry and pale skin, fine wrinkles, and sagging with less elasticity. Sweat and oil glands become less active, making the skin dry. This is because of decreased peroxisome proliferator-activated receptor gamma (PPAR-γ), heading to less oil production. Sometimes, sebaceous gland hyperplasia can occur as sebaceous glands increase in size (9).

As people age, the number and variety of certain skin cells, called dermal fibroblasts, decrease. This change is more noticeable in the papillary dermis, where there is a decrease in these specific fibroblasts. All these changes affect how the skin works and make it more likely to have age-related skin issues, like delayed healing of wounds (10).

Furthermore, the dermal elastic fibers in the skin go through changes. These fibers, made of elastin and fibrillin, have a special arrangement in the skin. In the upper papillary dermis of the skin, there are fibers called oxytalan fibers that help keep the outer layer (epidermis) connected to the layer beneath (dermo-epidermal junction or DEJ). In aging skin when exposed to sunlight, these fibers break down, and enzymes like matrix metalloproteinase (MMPs) and neutrophil elastases degrade the elastic fibers in the upper skin layer (11). This leads to disorganized elastic fibers building up in the reticular dermis of the skin, creating a condition known as solar elastosis.

2.2.3 Photo-aging

Photo-aging results from prolonged exposure to ultraviolet (UV) radiation, mainly causing skin issues like wrinkles, sagging, roughness, discoloration, expanded blood vessels, and pigment spot formation. The impact of UV light on the skin depends on its wavelength, categorized into A, B, and C types. UV-A (320–400 nm) has lower energy but deeply penetrates the skin, primarily affecting the dermis. It accelerates collagen breakdown, leading to tissue damage and gradual degeneration of the skin's supporting structure. UV-A hinders the production of hyaluronic acid (HA) by reducing the synthesis of hyaluronic acid synthase, altering the composition of skin proteoglycans. On the other hand, UV-B affects keratinocytes in the skin's outer layer, potentially causing DNA damage and mutations, releasing cytokines, and leading to aging, inflammation, apoptosis, and even skin cancer.

## 2.3 Management of Skin Aging

2.3.1 UV Protection

Sunlight plays a crucial role in life. They may, however, accelerate the aging process of our skin and cells. For this reason, it's critical that we should protect our skin from the sun by wearing appropriate clothing and applying sunscreen. Additionally, staying in the shade is helpful. This is the simplest and most effective method for delaying the effects of age and preventing premature skin aging.

2.3.2 Lifestyle Modification

1. Balanced Diet: rich in antioxidants, vitamins and minerals to support the skin health

2. Hydration: Keep the skin well-hydrated by drinking enough water and using moisturizers to maintain the skin elasticity

3. Skincare Routine: Establish a consistent skincare routine with products that suit with our skin types

4. Regular Exercise: Physical activity promotes healthy circulation, contributing to vibrant skin. It also helps reduce stress, which can impact aging.

5. Adequate Sleep: Make sure to get quality sleep which may leads to skin repair and rejuvenation.

6. Avoid Smoking: Smoking accelerates skin aging, leading to wrinkles and dullness. Quitting can have positive effects on skin health.

7. Limit Alcohol: Excessive alcohol consumption can dehydrate the skin, contributing to premature aging (12).

2.3.3 Dermatologic Interventions to Counteract Mechanism of Skin Aging

**Table 2.1** Clinical properties of skin aging with their respective aging mechanism and counteract strategies

| **Clinical properties** | **Histological/ Molecular changes** | **Strategy** |
|---|---|---|
| Roughness | SC compaction↑<br>Epidermal thickness↓<br>Epidermal HA↓ | Microdermabrasion<br>Superficial chemical peels<br>Microneedling, fractional laser, FRFM<br>AHA, RA, EFG, peptides, estrogen, biopolymers (PDRN, PN)<br>Moisturization, LMWHA, acetylated HA |
| Solar lentigines | Elongation of RRs<br>Mutations of KC/MC genes | TCA peels<br>Laser (CO2, Er: YAG, ablative fractional laser)<br>FRFM |

**Table 2.1** (continued)

| Clinical properties | Histological/ Molecular changes | Strategy |
|---|---|---|
| | MC No. ↑, Melanogenesis | Selective photothermolysis<br>IPL, low-fluence Q-swiched Nd:YAG laser |
| Wrinkles | Epidemal thickness ↓ | Microdermabrasion, superficial chemical peels RA |
| | ROS → Inflammatory cytokines ↑ | Microneedling, fractional laser, FRFM |
| | →MMPs ↑ | Antioxidants, exosomes, GFs, PRP, SVF |
| | → Degradation of ECM protrins | Biopolymers (PDRN, PN)<br>Laser, IPL, RF, HFUS<br>Synthetic polymers (PLA, PCL, PDO) |
| | More dermal changes in photoaged skin | Photoprotection |
| Sagging | ROS →MMPs↑ | Antioxidants, biopolymers, synthetic polymers, GFs, HFUS |
| | Elastic fiber degeneration | Fibroblast stimulation by EBDs |
| | Collagen degradation | Biopolymers, synthetic polymers, PRP, SVF<br>Fat injections, fillers |
| | Remaining disorganized elastic fibers | Ablative fractional lasers, FRFM |
| Inelasticity | Solar elastosis | Repeated chemical peels, topical RA<br>Ablative fractional laser, FRFM |
| | Neutrophil elastase↑ | Antioxidants |
| Edema | Vascular leakage ↑ | Massage and drainage (mechanical, US, RF, shock wave, acoustic wave) |

**Table 2.1** (continued)

| Clinical properties | Histological/ Molecular changes | Strategy |
|---|---|---|
| | → Fluid retention | |
| | Intervascular distance ↑ (loosely woven collagen network) | Fibroblast stimulation (EBDs, injectables) |
| | Ecstatic vessels with atrophic walls | Selective photothermolysis, FRFM |
| Telangiectasia | Collagen and elastic fibers ↓ | Fibroblast stimulation (EBDs, injectables) |
| Redness | Perivascular inflammation | Antioxidants, PRP, exosomes, PDRN, PN |
| Purpura | Neurogenic inflammation | HFUS |
| | | Botulinum toxin, mild cryotherapy |

**Note** Abbreviation: AHA, alpha-hydroxy acid; EBD, energy-based device; ECM, extracellular matrix; EGF, epidermal growth factor; FRFM, fractional radiofrequency microneedling; GF, growth factor; HA, hyaluronic acid; HFUS, high-frequency ultrasound; II, interleukin; IPL, intense pulsed light; KC, keratinocyte; LMWHA, low-molecular weight hyaluronic acid; MC, melanocyte; MMP, matrix metalloproteinase; PCL, polycaprolactone; PDO, polydioxanone; PDRN, polydeoxyribonucleotide; PLA, poly (lactic acid); PN, polynucleotide; PRP, platelet-rich plasma; RA, retinoic acid; RF, radiofrequency; ROS, reactive oxygen species; RR, rete ridge; SC, stratum corneum; SVF, stromal vascular fraction; TCA, trichloroacetic acid; TNF, tumor necrosis factor; US, ultrasound.

**Source** (10)

## 2.4 Skin Rejuvenation Background

In recent times, there has been a growing annual demand for facial rejuvenation. Numerous studies are utilizing bibliometric analysis to create visual maps of facial rejuvenation research, aiming to identify research hotspots and emerging trends in the field. From 2017 to 2021, there has been a notable surge in annual publications,

reaching a total of 2,478, constituting 39.9% of the overall publications during that period. As per the author's analysis keywords, key research focuses in the condition encompass facial photoelectric therapy, aging signs and treatment in the mid-face, the use of autologous fat transfer for facial rejuvenation, facial plastic surgery, cosmetic injections for facial enhancement, and rhytidectomy along with related anatomy (13).

As people learn more about how faces age and want to look younger, researchers are always finding new ways to treat aging. This not only brings more options for treatment but also speeds up the progress of facial rejuvenation. Exploring why faces age, creating strategies to stay youthful, finding safe and effective treatments, and understanding how current treatments work are still the main goals in the development of facial rejuvenation.

Nowadays, combination therapies for facial rejuvenation are trending, time saving and increasing patient satisfaction as in these studies such as CO2 laser + IPL (5), non-ablative fractional laser + IPL (14), CO2 laser + PRP (15). They were also found to be safe, tolerable with minimal downtime and few adverse effects. Likewise, it is supposed to be safe rejuvenation effect with reduced downtime in the combination therapy on face.

## 2.5 Intense Pulsed Light (IPL) Therapy

2.5.1 Background Knowledge

Drs. Goldman, Fitzpatrick, and Eckhouse introduced intense pulsed light (IPL) therapy in 1992, initially for treating leg telangiectasias. They conducted experiments on rabbit ear veins as part of the development process (4). The FDA in the United States has granted approval for the use of intense pulsed light in treating various conditions such as telangiectasias, photo-rejuvenation, facial wrinkles, hyperpigmentation, lentigines, ephelides, melasma, rosacea, acne vulgaris, poikiloderma of Civatte, port-wine stains, hemangiomas, leg veins, venous malformations, and the removal of unwanted hair (16). Additionally, IPL has recently been introduced in ophthalmology to address dry eye disease caused by meibomian gland dysfunction (17).

2.5.2 Mechanism and Functions

IPL therapy is beneficial because it can be used in more ways to treat different skin types and conditions. IPL devices work by sending light into the skin, which gets absorbed and turns into heat. This heat targets specific chromophores in the skin like hemoglobin, water, and melanin, causing them to be destroyed. This process, called selective photo-thermolysis, forms the foundation of IPL technology (16). IPL is safe and works well for treating skin issues like pigmented and vascular disorders, hair removal, and signs of aging. Dermatologists commonly use IPL to address various medical and cosmetic concerns (18).

What sets IPL devices apart is their utilization of flashlamps and bandpass filters to generate pulsed light with diverse wavelengths, durations, fluence and spot size.

1. Wavelength

Flashlamps produce light covering a range from about 400 to 1400 nm. By using cut-off filters, the wavelength of light can be changed, targeting specific tissues through selective photo-thermolysis. When choosing a wavelength, healthcare providers consider other chromophores in the treatment area. This is crucial, especially when treating patients with darker skin, as it's important to ensure safety and prevent skin discoloration. Picking longer wavelengths that penetrate deeper and protect the epidermis layer can be beneficial for darker skin patients, while the opposite might be true for those with lighter skin (19).

2. Pulse Duration

The duration of a pulse is determined by the thermal relaxation time (TRT) of the chromophore, which is the time it takes for the heated tissue's temperature to drop to 37% of its highest point (20). If the target is heated for longer than its TRT, it can affect surrounding tissue and potentially lead to scarring or hypopigmentation of the skin. Having an appropriate time gap between pulses helps prevent the skin temperature from going above 70 degrees. Some IPL devices offer single pulses, while others can do multiple pules in a row. Waiting around 10 to 12 milliseconds between pulses helps the skin cool down. For patients with darker skin, a TRT of 20-40 milliseconds is recommended. The time is also adjusted based on the size of the target and the chromophore; larger ones, like hair follicles, need more time to cool down (4).

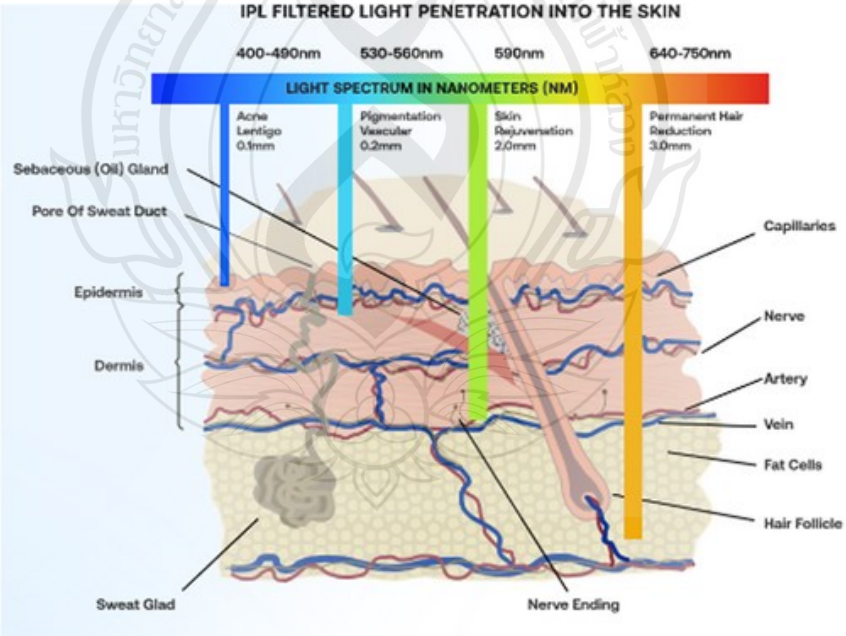
3. Fluence (J/cm2)

Fluence, measured in J/cm2, indicates how much energy is given per unit area. IPL can provide up to 40 J/cm2 of fluence. If a target is deep in the skin or doesn't absorb light well, higher fluence might be used. However, it's crucial to know that using higher fluence can lead to more side effects, especially in people with darker skin (21).

4. Spot Size

Spot size refers to the diameter of the light emitted by the flashlamp. A larger spot size helps light penetrate deeper by reducing scattering. Therefore, if the spot size is smaller, higher fluences are needed to effectively reach deeper skin targets.

Additionally, cooling devices help deliver higher fluences while safeguarding the skin's top layer from damage (epidermal bypass) by directing thermal energy to deeper tissue (22). Internal cooling systems like chilled tips, as well as external methods like ice packs or cold ultrasound gel applied before treatment, these all play a role. The cold gel reduces friction, disperses surface heat, and enhances the light penetration and absorption by reducing the difference in refractive index between air and skin.




**Source** (23)

**Figure 2.3** The choice of light wavelength allows the clinician to target a particular layer of the skin while sparing structures in deeper layers, such as hair follicles

2.5.3 Pros and Cons

IPL has benefits like treating multiple skin issues at once, being user-friendly, and requiring minimal downtime when the right settings are chosen skillfully. It's widely accessible in laser therapy clinics, and the costs are relatively lower compared to other treatments, both ablative and non-ablative treatments.

While side effects of IPL are usually rare and mild, the most common issues are pain and redness. Other possible effects include swelling, blistering, bruising, crusting, changes in skin color, white hairs, scarring, keloid formation, and infection. When used by untrained providers with incorrect settings or too much heat, it can cause skin damage and complications (4, 24).

2.5.4 Safety and Efficacy Profile in Skin Rejuvenation

(24) study demonstrated that IPL was effective for addressing periorbital skin aging, with over half of the patients experiencing moderate to significant improvement. (25) observed significant improvement in all 40 Japanese patients with facial solar lentigines after a single IPL treatment. Using ablative fractional laser (AFL) treatment along with IPL significantly reduced wrinkles and pore size while improving skin texture and elasticity in Chinese individuals with photoaged skin. Importantly, it didn't harm the skin barrier and there were no severe side effects although post inflammatory hyperpigmentation (PIH) occurred after AFL treatment which was disappeared within 30 days (5). The combination of IPL and non-ablative fractional laser (NAFL) on the same day was safe and produced a noticeable rejuvenating effect on the skin. This outcome was similar to what has been observed in other combined therapies, and importantly, it did not extend the recovery time for each specific treatment (14).

## 2.6 Platelet-rich Plasma (PRP)

2.6.1 Background History

Platelet-rich plasma (PRP), first generation of autologous platelet concentrates (APCs), shows significant promise as therapeutic tools in regenerative medicine, offering a rich reservoir of cytokines, growth factors, and other biologically active

substances. APCs' utilization is on the rise in various dental applications like periodontal surgery, orthopedics, sports medicine, and aesthetic dermatology (26).

The roots of this therapy can be traced back to transfusionology, where platelet concentrates were initially employed to address thrombocytopenia. In 1954, the term "platelet-rich-plasma" (PRP) was first coined to describe these platelet concentrates used in transfusion (27). (28) During that period, the preparation employed was termed "Platelet-derived wound healing factors" (PDWHF). The introduction of the term "platelet-rich plasma" (PRP) in the field of regenerative dentistry and medicine started in 1998, as the product found application in maxillofacial surgery for bone reconstruction (29).

2.6.2 PRP's Constituents and Their Roles

There are researches that PRP comprises approximately 578 distinct proteins. These proteins and growth factors possess the ability to enhance stem cell activity, fostering proliferation, differentiation, and regeneration of cells. Consequently, this contributes to skin rejuvenation and the production of hyaluronic acid (30). By activating fibroblasts and promoting the synthesis of collagen and other components of the extracellular matrix, PRP emerges as an appealing choice for skin rejuvenation and reducing scars. The utilization of PRP as a standalone treatment for skin rejuvenation, acne scars, periorbital rejuvenation, lipofilling, and in conjunction with fractional CO2 and other resurfacing methods is experiencing a notable surge (31).

**Table 2.2** Growth Factors present in PRP and their roles

| Growth factor | Role |
|---|---|
| PDGF | Mitogen for fibroblasts and smooth muscle cells, promotes angiogenesis and collagen production |
| TGF-β | Increases collagen content |
| VEGF | Promotes angiogenesis |
| EGF | Promotes cell growth, differentiation, Angiogenesis, and collagen production |
| Pro and anti-inflammatory cytokines (IL-4, IL-8, IL-13, IL-17) | Stimulate fibroblasts and collagen synthesis |

**Source** (31)

2.6.3 Classification of Platelet Concentrates

Four primary categories of preparations can be distinguished based on their cell content and fibrin architecture (32).

1. Pure Platelet-Rich Plasma (P-PRP) or leucocyte-poor PRP products are formulations that lack leucocytes and exhibit a low-density fibrin network upon activation.

2. Leucocyte and PRP (L-PRP) products are formulations containing leucocytes and featuring a low-density fibrin network upon activation. This category has the highest number of existing commercial or experimental systems, with numerous automated protocols developed in recent years. These protocols necessitate specific kits to ensure minimal handling of blood samples and maximum standardization of preparations.

3. Pure platelet-rich fibrin (P-PRF) or leucocyte-poor platelet-rich fibrin preparations lack leucocytes and feature a high-density fibrin network. These products solely exist in a highly activated gel form and cannot be injected or utilized similarly to traditional fibrin glues.

4. Leucocyte and platelet-rich fibrin (L-PRF), or second-generation PRP products, are formulations containing leucocytes and featuring a high-density fibrin network.

2.6.4 Factors Influencing the Production of PRP

Several factors impact the production of PRP which include: (33)

1. Blood Draw: To prevent unintended platelet activation, most utilize large bore needles (>22G) during blood collection.

2. Centrifugation: The gravity can naturally separate blood components over time, but this process is too slow for most needs. Additionally, prolonged storage may harm the substances in the blood. To speed up the separation, a centrifuge is used, which enhances the effect of gravity, providing a force thousands of times stronger.

Relative Centrifugal Field (RCF): Cellular components in blood can be separated through a method called differential centrifugation. This process adjusts the force to settle specific cellular elements while keeping others suspended. In centrifugation, the force needed to separate two phases is known as the relative centrifugal field.

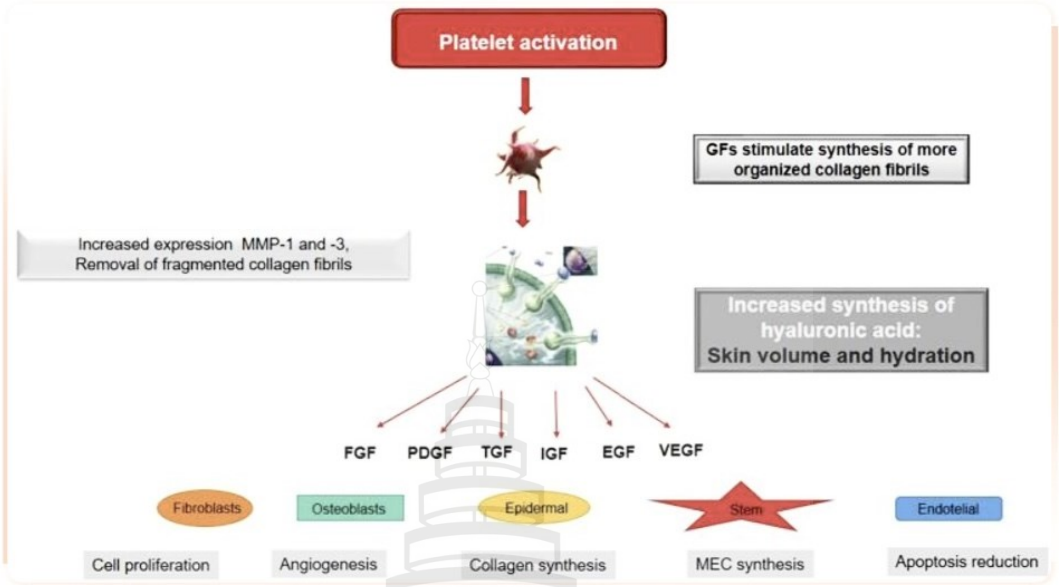
3. Temperature: Maintaining the right temperature is vital during processing to prevent platelet activation. A manual suggests a range of 21°C-24°C for blood centrifugation to obtain PRP.

4. Anticoagulants: Selecting an anticoagulant is crucial to maintain optimal functionality, integrity, and morphology of platelets. Most authors advise to use anticoagulants like citrate and sodium citrate dextrose. The authors studied the impact of sodium citrate and acid citrate dextrose (ACD-A) on platelet aggregation, pH, and extracellular calcium concentration. ACD-A is preferred for collecting platelets through apheresis, while 3.2% or 3.8% trisodium citrate is commonly used for diagnostic platelet assessments (34).

5. Activation of PRP: PRP can be activated externally using thrombin, calcium chloride, or mechanical trauma. When PRP is utilized in soft tissue, collagen serves as a natural activator, eliminating the need for external activation (35).

2.6.5 Mechanism of Action of PRP in Facial Rejuvenation

When platelets get activated either endogenous or exogenous way, they release growth factors that bind to specific cells like stem cells, fibroblasts, and skin cells. This triggers a process leading to effects such as cell growth, blood vessel formation, collagen synthesis, and reduced cell death (33). Aging skin accumulates fragmented collagen, hindering new fiber growth and disrupting the extracellular matrix. Activated platelet groups increase the expression of matrix metalloproteases (MMP-1 and -3), enhance the removal of damaged collagen fragments and stimulate the production of new, well-organized collagen fibers. They also encourage the synthesis of hyaluronic acid, increasing skin volume and hydration (36).




**Source** (26)

**Figure 2.4** Mechanism of action of autologous platelet concentrates in facial rejuvenation

White blood cells, called leukocytes, play a helpful role in wound healing by preventing infections. They also assist in creating new blood vessels (angiogenesis) and producing a supportive matrix. Since leukocytes can cause inflammation, having fewer of them in PRP reduces the chances of inflammation, resulting in improved outcomes for facial rejuvenation. (37) discovered that PRP with fewer white blood cells offers measurable enhancements in skin bio-stimulation (anabolic function). Additionally, leucocyte-rich PRP often contains red blood cell contamination, which is undesirable for facial rejuvenation. This contamination can lead to the release of reactive oxygen species (ROS), impacting platelet function by changing pH and causing inflammation.

2.6.6 Safety and Efficacy Profile

PRP is suggested to be safe, having a low-risk profile. Reported common side effects are pain during injections, redness, swelling, and bruising. PRP offers numerous advantages in facial rejuvenation and is utilized in various conditions, including atrophic acne scars, pigmentation issues and facial wrinkles. PRP, whether used alone or in conjunction with other methods like laser treatment, fat grafting or subcision, exhibits positive effects on facial rejuvenation (6).

In a recent randomized, split-face trial conducted by (38) intradermal PRP demonstrated noteworthy enhancements in both coarse and fine skin texture, as evaluated by participants who were unaware of the treatment. Similar positive outcomes were observed in a prospective study involving 11 females (39). Monthly PRP injections have been reported to result in substantial improvement in skin firmness and elasticity with minimal side effects, particularly in patients with actinic elastosis in the lower eyelid area (40).

The effectiveness of using PRP alone to rejuvenate aging facial skin was assessed in 518 patients across three studies. Two studies involved a single session, while one study involved two to four sessions based on the patient's age. Common injection areas were the infraorbital region, nasolabial folds, and crow's feet, with additional treatment areas such as the forehead/malar region, preauricular region, and jaw region.

In the study by (15), patients reported greater improvement in wrinkles, texture, and elasticity when CO2 laser was combined with PRP, as opposed to PRP alone. (41) found substantial improvement when combining fractional CO2 laser treatment with PRP for treating atrophic acne scars. Assessment using Goodman and Barons' grading system showed no significant difference between the right and left sides. The authors concluded that PRP treatment significantly reduces downtime and inflammation caused by laser treatment. (42) demonstrated that combining PRP with erbium laser yielded superior efficacy compared to 12 sessions of single plasma-rich therapy within the same timeframe.

2.6.7 Pitfalls

There are some studies which indicate that as individuals age, their tissue regeneration capability diminishes gradually together with decreased expression of growth factor receptors and reduced collagen production by fibroblasts. (43) confirmed that young fibroblasts exhibit a positive response to PRP treatment. Conversely, with increasing age, tissue regeneration ability weakens, and the expression of cell growth factor receptors diminishes, leading to reduced effectiveness of PRP. These factors lead to PRP might be a more effective option for regenerative treatments in younger patients.

## 2.7 Combination Therapy for Facial Rejuvenation and Other Benefits

Combination therapy, utilizing multiple treatments simultaneously, often proves more effective than mono-therapy by targeting various aspects of a condition for enhanced results. According to the studies, (15) showed PRP and ultra-pulsed fractional CO2 together might alleviate the erythema, pigmentation, and coarse pores produced by laser therapy in addition to substantially reducing face wrinkles and texture. Adding PRP to fat grafts had various benefits, including increased fat grafting survival, decreased bruising and inflammation, and simpler application because PRP has liquefying effect. In addition, PRP not only has a rejuvenating effect but also acts as a booster for fat transplants (44). The study (45) revealed that a combination therapy for atrophic acne scars involving dermaroller and PRP was safer and more effective than dermaroller alone in terms of improving both the clinical outcome and the dermatology life quality index score.

When combined with IPL, ablative fractional carbon dioxide laser treatment dramatically reduced pore size and wrinkles on Chinese people's photoaging skin, while also improving skin elasticity and texture. Furthermore, the combined therapy was successful in curing widespread erythema, telangiectasia, and hyperpigmentation brought on by photoaging. Moreover, the combined therapy did not compromise the integrity of the skin barrier (5). One common consequence in acne patients is post-inflammatory erythema, also known as post-acne erythema. It was reported that the combination of RF therapy, IPL therapy, and red and blue light therapy proved to be more successful in treating facial post-acne erythema than any other treatment method, according to the findings. The mean erythema index significantly reduced ($p<0.01$) after treatment (46).

Furthermore, the combination of intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) is assumed to be a powerful, tolerable and synergistic approach for comprehensive face rejuvenation. PRP, derived from the patient's own blood, is rich in growth factors that stimulates collagen production and promotes tissue regeneration. When coupled with IPL, which targets pigmentation irregularities and vascular concerns, this combination may address a wide range of positive aesthetic issues. PRP

enhances the skin's natural healing response, amplifying the effects of IPL by promoting faster recovery and boosting overall skin health. The collaboration of IPL and PRP will provide a holistic solution, offering patients a non-invasive yet effective strategy for achieving a more youthful and revitalized facial appearance.

# CHAPTER 3

# RESEARCH METHODOLOGY

## 3.1 Study Design

This study is a randomized split-face human experimental study (clinical trial) to compare the efficacy of the combination treatment of intense pulsed light (IPL) and platelet-rich plasma with platelet-rich plasma alone for facial rejuvenation.

## 3.2 Study Population

Twelve healthy male and female participants, aged 25-45 years, exhibiting wrinkles with grade 2 or 3 according to wrinkle severity rating scale (WSRS) and participants who want to undergo facial rejuvenation with written informed consent.

## 3.3 Study Location

Mae Fah Luang University Hospital, Bangkok, Thailand

## 3.4 Sample Size Calculation

The sample size is determined by using the data obtained from the reference paper of “Ablative fractional carbon dioxide laser combined with intense pulsed light for the treatment of photoaging skin in Chinese population” (5)

According to this study, skin wrinkles measurement by skin scan for AFL + IPL statistically significant before (16.96 ± 6.16) and 4 months after treatment (11.14 ± 4.31). For IPL alone, the results were at baseline (15.68 ± 8.04) to (15.00 ± 6.92) after 4 months of treatment.

Calculate the sample size by two means dependence. From the formula,

Set $\alpha$= 0.05 (two tailed), $Z_{0.025}$ =1.96

$\beta$= 0.2, $Z_{0.20}$= 0.8= 0.84

$n_1$= 28, $n_2$= 28

$\mu_1$= 16.96 – 11.14= 5.82

$\mu_2$= 15.68 – 15= 0.68

$S_1$= 4.31, $S_2$= 6.92

$$n = \frac{\left(Z\alpha_{/2} + Z_\beta\right)^2 \sigma_d^2}{(\mu_d)^2}$$

$$\sigma_d^2 = S_p^2 = \frac{[S_1^2(n_1 - 1) + S_2^2(n_2 - 1)]}{(n_1 + n_2 - 2)}$$

$$S_p^2 = \frac{(4.31)^2(28 - 1) + (6.92)^2(28 - 1)}{28 + 28 - 2}$$

$$S_p^2 = 33.2313$$

$$n = \frac{(1.96 + 0.84)^2 \times 33.2313}{(5.82 - 0.68)^2}$$

$$= 9.8613 \sim 10$$

Expected dropout rate is 20%, n= 10 + 2= 12

So, participants (n = 12) should be recruited.

Recruitment of research participants: according to inclusion and exclusion criteria, an invitation made by doctors or nurses, advertisement with posters.

## 3.5 Inclusion Criteria

3.5.1 Healthy male and female participants between 25-45 years old

3.5.2 Subjects who have wrinkles grade 2 or 3 according to wrinkle severity rating scale (WSRS) and also want to undergo facial rejuvenation

3.5.3 Volunteers who agree the facial rejuvenation with the combination of Intense Pulsed Light (IPL) therapy and Platelet Rich Plasma (PRP)

3.5.4 Subjects who can give informed consent and visit every appointment to Mae Fah Luang Hospital, Bangkok

## 3.6 Exclusion Criteria

3.6.1 Medications: the use of photosensitive drugs such as doxycycline antibiotic or isotretinoin for acne treatment or topical retinoids in the previous 4 weeks, systemic corticosteroids or oral retinoids in the previous 6 months

3.6.2 Patients who had undergone soft tissue filling, chemical peel, botulinum toxin injection, mesotherapy, dermabrasion or other resurfacing surgeries

3.6.3 Healing response: Candidates for treatment with medical conditions that significantly compromise healing response such as using Aspirin for heart disease

3.6.4 Active Infections/ Immunosuppression: Active infections and immunosuppression as in Autoimmune conditions compromise the healing ability of the body.

3.6.5 Open Lesions: Treatment should only be applied to intact, healthy skin, with the exception of acne-affected skin.

3.6.6 Patients on contraception usage, pregnancy and breastfeeding women

3.6.7 History of light-induced seizures, skin photosensitivity disorders, hypertrophic scars or keloid formation

3.6.8 Patients who have suffered from mental disease, uncontrolled diabetes or hypertension, alcoholism or drug abuse

3.6.9 Patients who have history of deep vein thrombosis, malignancy, bleeding tendency or coagulation disorder

3.6.10 Patients who have history of lidocaine and lidocaine and prilocaine allergy

3.6.11 Person to be treated is unwilling or unable to follow post-treatment care instructions.

## 3.7 Withdrawal Criteria

3.7.1 Participants who want to drop out from the study for any reason

3.7.2 Two third of participants who have serious complications form the study such as bleeding do not stop after withdrawing blood, light induced seizures, pain shock or other condition like getting pregnant during study time

## 3.8 Variables of Study

3.8.1 Independent variables – Intense Pulsed Light (IPL), Platelet-rich Plasma (PRP)

3.8.2 Dependent variables - VISIA® Complexion Analysis System score, Cutometer® MPA 580 Score, Tewameter® TM 300 Score, Patients Satisfactory Score, Physician Global Aesthetic Improvement Scale (GAIS), Adverse Effects

## 3.9 Materials and Method

3.9.1 Cynosure® Palomar Icon™ IPL Machine

**Source** (47)

**Figure 3.1** Palomar Icon IPL machine with different types of handpiece

The Palomar IconTM Aesthetic System's indications for usage are grounded on the chromophores' (water, hemoglobin and melanin) ability to selectively absorb light emissions.

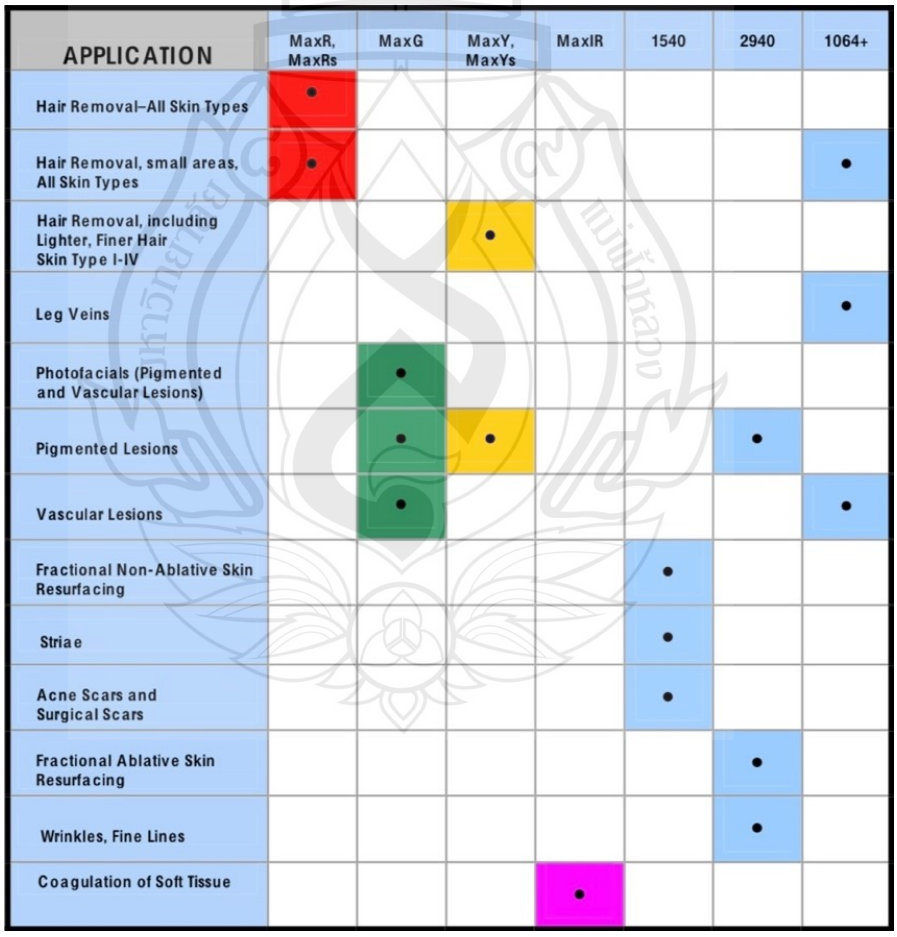
According to the handpiece, Palomar Icon Handpieces can treat wrinkles, striae, acne scars, surgical scars, unwanted hair, leg veins, benign pigmented lesions like solar

lentigines and actinic bronzing, and vascular lesions. They can also provide fractional ablative and non-ablative skin resurfacing.

When assessing the needs for treatment, number of considerations need to be made, such as:

1. Fitzpatrick Skin Type
2. Amounts of target chromophore and competing chromophores
3. Any active sun or lamp exposure
4. Ethnicity
5. Thickness of skin
6. Overall skin health prior to initiating a pulsed-light or laser treatment.

Even more by, side effects will be reduced and treatment outcomes will be maximized.




**Source** 2500-0014-A Palomar Icon™ Treatment Guide

**Figure 3.2** Suggested application chart: Treatment Guide and Palomar Icon™ Operator's Manual for specific information on the use of each Handpiece

In this study, a handpiece of MaxG$^{TM}$ with wavelength range of 500 – 670 & 870 – 1200 nm, single pulse mode, spot size of 10 x 15 mm, pulse duration of 20 ms and fluence of 20 J/cm2 will be used for facial rejuvenation.


**Source** (48)

**Figure 3.3** Palomar MaxG$^{TM}$ handpiece

3.9.2 Platelet-rich Plasma (PRP) Tube


**Source** (49)

**Figure 3.4** Fresh Blood Concentrated PRP Tube with ACD + Gel (15ml)

Fresh Blood Concentrated PRP Tube with ACD + Gel is the tube that meets standards which has passed quality research and is popular in medical schools and hospitals in Korea.

Product Details

1. Properties: Medical Materials
2. Model Number: OY-012
3. Material: Glass

4. Color: Red

5. Certificate: CE ISO

6. Packaging: Independent packaging

7. Additive: ACD (Acid-citrate-dextrose) + gel

3.9.3 Centrifuge Machine

Properties

1. Compact design for separation of blood samples and other routine applications in emergency and small laboratories

2. Two large LED displays for speed/RCF and time

3. Possibility of programming RCF

4. Reduced temperature increase in the chamber by means of continuous air cooling through air channel in the lid

5. Safety ensured by steel body, lid and chamber, lid locking system and motor over temperature protection


**Source** (50)

**Figure 3.5** NF200 Bench Top Centrifuge

**TECHNICAL SPECIFICATIONS**

| | |
|---|---|
| Maximum Speed | 5.000 rpm |
| Maximum RCF | 2.822xg |
| Tube Capacity | 12x15 ml. |
| Control System | Programmable Microprocessor Control |
| Speed Set Range | 1.000-5.000 rpm |
| Speed Set Step | 10 rpm |
| Timer Set Range | 1-99 Minutes and Hold Position |
| Timer Set Step | 1 minute |
| Motor | Induction Motor |
| Body, Lid And Chamber | Epoxy-Polyester Powder Coated Steel |
| Power Supply | 230 V / 50-60 Hz (115 V / 60 Hz ) |
| Power Consumption | 150 W |
| External Dimensions (WxDxH) mm. | 280x360x260 |
| Packing Dimensions (WxDxH) mm. | 350x420x480 |
| Net / Packed Weight, kg. | 12 / 16 |

**Source** (51)

**Figure 3.6** Technical specifications of NF200 Bench Top Centrifuge

3.9.4 VISIA® Complexion Analysis System

Using a multispectral imaging and analysis system, the VISIA® Complexion Analysis System (Canfield, Fairfield, NJ) is an equipment for scanning the skin of the face and capturing important visual data. Under the same settings, it can identify features such as brown spots, red areas, wrinkles, roughness, pores, UV spots, and porphyrins.

**Source** (52)

**Figure 3.7** VISIA® Skin Complexion Analysis System

3.9.5 Tewameter® TM 300

The Tewameter® TM 300 (formerly the Tewameter® TM Hex) is the most popular measuring tool in the world for transdermal water loss (TEWL) measurement because of its "open chamber" concept. It is a fundamental tool for all kinds of applications and a crucial parameter for evaluating the skin's ability to act as a moisture barrier that can be damaged, even slightly, and early detection is possible.

**Source** (53)

**Figure 3.8** Tewameter® TM 300

3.9.6 Cutometer® MPA 580

It uses negative pressure to evaluate the elasticity of the upper layer of the skin. The suction method forms the basis of the measuring principle. This machine's measurement approach makes it possible to gather data regarding the mechanical and elastic characteristics of the skin's surface as well as to measure skin aging objectively.


**Source** (54)

**Figure 3.9** Cutometer® MPA 580

3.9.7 Local Anesthetic Cream

3.9.8 Informed Consent Form

3.9.9 Patients' Satisfactory Record Form

3.9.10 Adverse Effects Record Form

## 3.10 Study Procedure

3.10.1 Preparation

1. Participants will be chosen based on approved parameters.

The goal of the study, each step of the protocol, the potential side effects of the treatment, and the benefits will be addressed by the researcher. For Thai participants who do not understand in English, my Thai colleagues will help me in explaining them.

2. History taking will be done and an informed consent form must be signed by participants.

3. The subjects' information is well documented.

3.10.2 Treatment Process

1. Prior to the procedure, Visia scan, Cutometer and Tewameter will be used to measure the parameters of each participant whose face has already been washed with water and soap.

2. Cutometer and Tewameter will be put on both cheeks and right and left side of forehead to measure the skin elasticity and TEWL respectively.

**Source** (55)

**Figure 3.10** Landmarks for Cutometer and Tewameter measurement

3. Standardized photos will be taken by using a digital camera from Visia scan in the same light, posture, and setting prior to the treatment (baseline) and at each follow-up session on 4th, 8th and 12th weeks. All photograph data will be documented by using a code number and the eyes will be obscured to make confidentially.

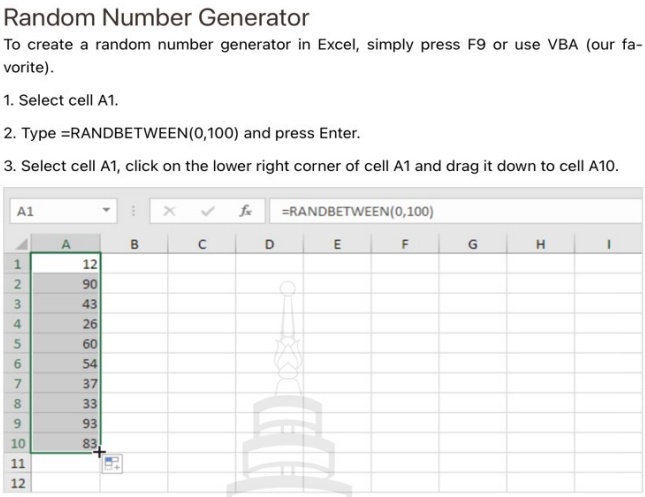
**Source** (56)

**Figure 3.11** Visia scan showing 3 views: Left 45°, Center 0° and Right 45°

**Source** (57)

**Figure 3.12** Standardized face photos taken by Visia scan (Left 45°, Center 0° and Right 45°)

4. Using a random number table generated by Excel, IPL will be performed to the left side of the face of the odd-numbered patients and to the right side of the face of the even-numbered patients.




**Source** (58)

**Figure 3.13** Random number generated by Excel

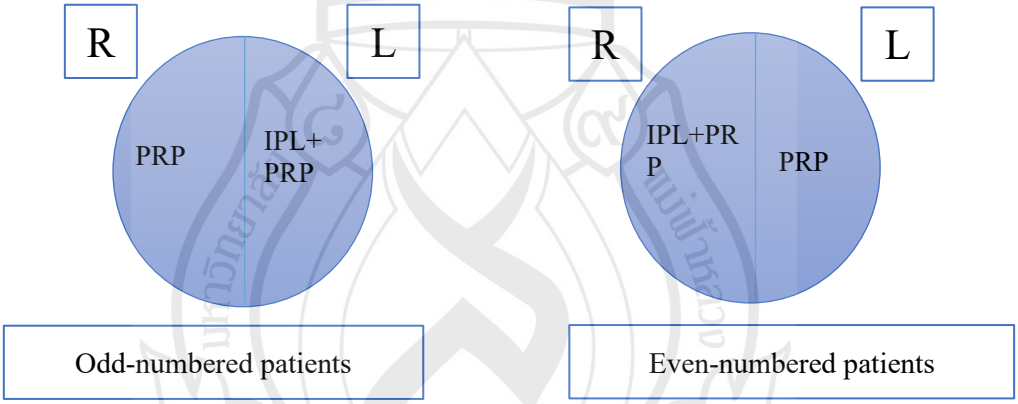



**Figure 3.14** IPL treated sides: left side of odd-numbered patients, right side of even-numbered patients

be applied to face for 30 minutes before the treatment and then cleansed with water.

As a first procedure,

1. Cooled gel (1-2 mm thick) will be applied to the treated areas to avoid IPL induced damage to the epidermis of the skin and an eye shield will also be placed.

2. IPL (MaxGTM handpiece, Palomar IconTM, Cynosure®) with range 500 – 670 & 870 – 1200 nm of wavelength, single pulse mode, 20 ms of pulse duration, 10 x 15 mm of spot size and 20 J/cm2 of fluence will be used.

3. Then, applied gel will be removed and all treated areas will be covered with ice pack while waiting for PRP preparation to avoid certain complications.

As a second procedure,

The patient's blood (10 ml) will be extracted by venipuncture and collected in a tube that contains anticoagulants (ACD) and cell separator gel under aseptic technique in blood collecting room at Mae Fah Luang University Hospital, Bangkok by the investigator. The PRP tube is an in-house kit that is used in MFU hospital.

PRP preparation protocol at Mae Fah Luang University Hospital, Bangkok is as follows:

Blood collection, PRP preparation and injection is performed by using aseptic technique.

1. Draw blood 15 ml.

2. Transfer the blood into a PRP tube and centrifuge it.

3. Speed and duration are 3,000 rpm for 5 minutes.

4. Carefully extract the desired PRP layer, ensuring that red blood cells are not included.

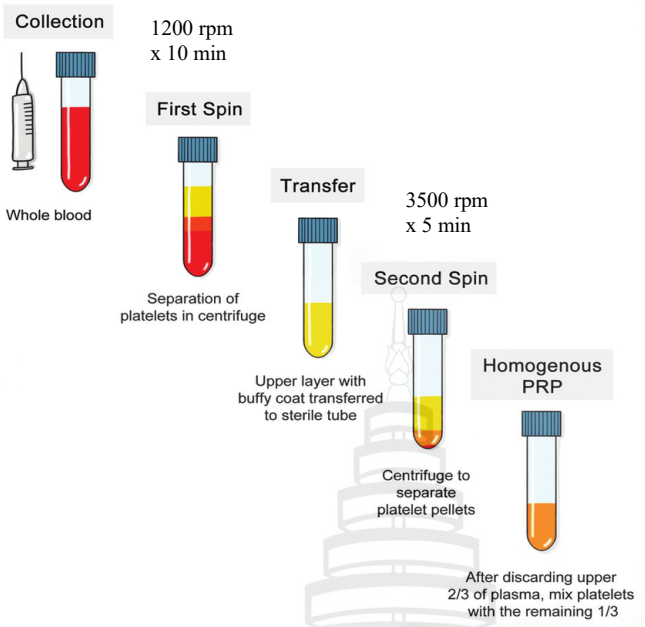
As for the investigator, PRP preparation is according to this reference paper (59)

1. Double centrifugation technique will be used. The first spin will be 1200 rpm for 10 min and then, the supernatant plasma containing platelets and buffy coat will be transferred into another sterile tube (without anticoagulant).

2. The second spin will be 3500 rpm for 5 min to obtain a platelet concentrate.

3. The lower one-third is PRP and upper two-third will be platelet-poor plasma (PPP).

4. PPP will be removed and the platelet pellets will be suspended in a minimum quantity of plasma (3 mL)




**Source** (59)

**Figure 3.15** Platelet-rich plasma preparation steps

5. Later, the treatment areas will be disinfected by using iodine, and then the iodine will be removed by using 75% alcohol.

6. PRP will then be injected to both cheeks and forehead.

7. A 30 gauged needle will be used for intradermal injections by mesotherapy technique (point by point) by the investigator under guidance of Aj Tanomkit and the injections will be spaced about 1 cm apart.

**Source** (60)

**Figure 3.16** PRP injection sites

8. Immediately after injection, gentle pressure with gauze will be applied for 5 minutes, and then compressed with normal saline swabs for 5 minutes.

9. All post treatment complications such as pain, swelling, burn, numbness and other side effects will be assessed.

10. Then, the investigator's own moisturizer and sunscreen will be applied to participants' face as post-treatment care.

11. All post treatment care such as avoiding sun exposure, applying sunscreen (at least SPF 45) and moisturizer will be advised to all subjects.

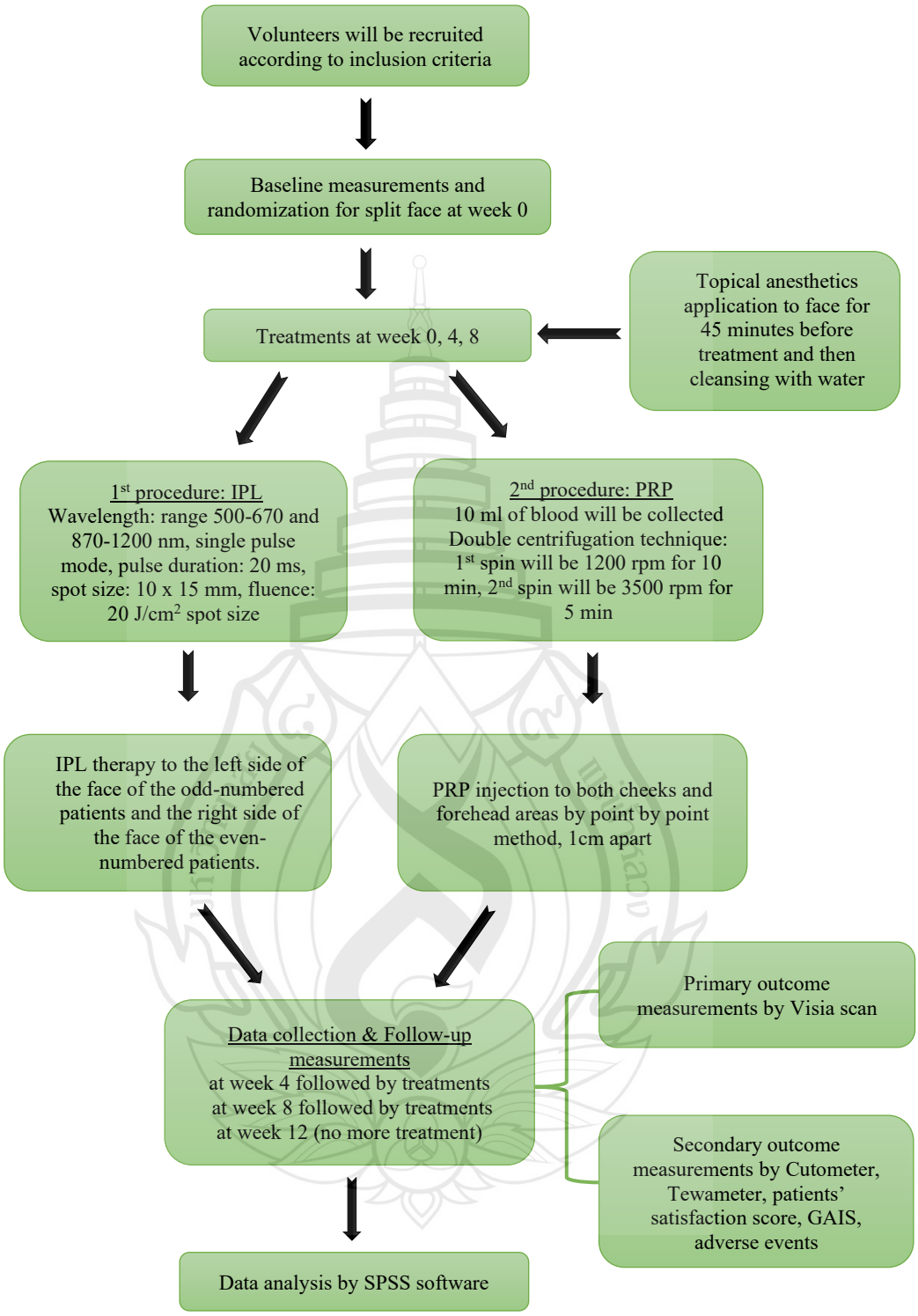



**Figure 3.17** Schematic overview of study procedure

3.10.3 Follow-up Visit Process (on 4th, 8th and 12th weeks)

1. PRP and IPL treatments will be done on week 0, 4 and 8 (3 sessions) together with follow-up measurements. Measurements only will be done on week 12, no more treatment.

2. At each follow up visit, all subjects will be assessed by cutometer, tewameter and visia scan.

3. All subjects will be taken a photograph under identical camera setting as baseline (photographic facial position: Left 45°, Center 0° and Right 45°).

4. If any adverse reaction occurs, they will be evaluated.

5. Moreover, every treatment session, the patients will be called to inquire about any side effects such as blistering and erythema during the next 24 to 48 hours.

After completion of the research, untreated side of the participants will be provided with same treatment.

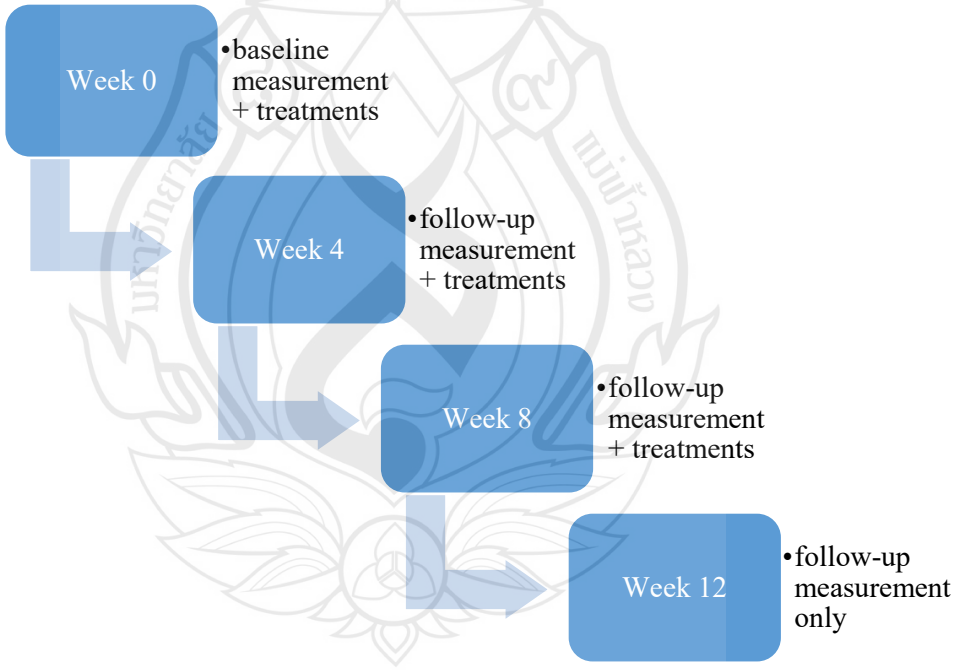



**Figure 3.18** Outline of measurements and treatment plan

## 3.11 Outcome Measurement and Data Collection

3.11.1 Primary Outcome Measurement

Wrinkle measurement from baseline to 4th, 8th and 12th weeks will be evaluated by using VISIA visual assessment.

3.11.2 Secondary Outcome Measurement

1. Viscoelasticity and trans-epidermal water loss measurement from baseline to 4th, 8th and 12th weeks will be evaluated by using Cutometer and Tewameter.

2. Overall improvement and patient satisfaction on both sides of the face will be assessed by using Global Aesthetic Improvement Scale by researcher and two independent physicians and Participant's Satisfaction Score respectively and then the rates of satisfaction and improvement will be compared.

3. The adverse effects on both sides of the face will be recorded by using research questionnaires followed by data comparison for their incidence.

Patients' Satisfactory Score

Satisfactory scores will be collected at 12th week

Score 0 = not satisfy

Score 1 = mildly satisfy

Score 2 = moderately satisfy

Score 3 = greatly satisfy

**Table 3.1** Physician Global Aesthetic Improvement Scale (GAIS) at 12th week

| | Rating | Description |
|---|---|---|
| 1 | Very much improved | Optimal cosmetic result in this subject |
| 2 | Much improved | Marked improvement in appearance form the initial condition, but not completely optimal for this subject |
| 3 | Improved | Obvious improvement in appearance from initial condition, but a re-treatment is indicated |
| 4 | No change | The appearance is essentially the same as the original condition |
| 5 | Worse | The appearance is worse than the original condition |

The adverse events following the treatments will be evaluated by observing the immediate complications and asking questionnaires at each follow-up visit

The questionnaires to be asked are about the followings:

1. Pain score ranging from 0 to 10

2. Duration (days) of erythema or swelling

3. Other unintended effects such as post inflammatory hyperpigmentation or hypopigmentation, burning sensation, and infection

## 3.12 Data Analysis

SPSS software will be used to record and document the medical records of the study participants as well as the findings.

3.12.1 Descriptive Statistics

1. General demographic data of subjects will be documented and calculated by descriptive statistical analysis.

2. Descriptive statistical analysis will also be used to examine the GAIS, the subjects' adverse consequences and patients' satisfactory score.

3. The data of a descriptive statistical study will be categorized into standard deviations, means, median, modes, ranges and percentages.

3.12.2 Inferential Statistics

1. Statistical significance will be achieved by comparing the mean values of the trans-epidermal water loss, viscoelasticity and wrinkle scores at each follow-up appointment and prior to treatment.

2. A paired t test will be used to compare the difference in the parameters before and after treatment in the same treatment group.

3. In comparisons between the groups, repeated measure ANOVA test will used for analysis.

4. Significance level: p-value $<0.05$ will be set.

## 3.13 Ethical Considerations

This study adheres rigorously to the Good Clinical Practice (GCP) guidelines, an internationally recognized ethical and scientific standard for planning, executing, documenting, and reporting trials involving human subjects, as outlined by the International Conference on Harmonization (ICH). The GCP guidelines encompass ensuring the protection of human rights for subjects in clinical trials, confirming the safety and efficacy of newly developed compounds, and establishing standards for the conduct of clinical trials.

1. The researchers elucidate the research details to the volunteers, furnishing them with a research information sheet that encompasses explanations of the study's objectives, methods, safety measures, symptoms, and possible risks.

2. There will be no financial involvement between the researchers and the subjects; this research is offered without charge.

3. Volunteers are required to voluntarily sign, based on the information provided in a research information sheet by the researchers. They face no consequences for withdrawing at any point.

4. To the extent possible, the researcher assumes responsibility for the well-being of the subjects. Participants are notified that, in the event of harm caused by the research, they will receive complimentary medical care from the research team and compensation for any lost wages due to medical treatment.

5. All data provided will be held in strict confidentiality. The researcher will replace the file names of the patients' pictures with serial numbers, ensuring that both the names and the numbers are identical.

# CHAPTER 4

# RESULT

## 4.1 Participant Demographics

**Table 4.1** Participant Demographics Characteristics: Descriptive Analysis

| Demographic Data | n=12 |
|---|---|
| Sex | |
| Male | 6 |
| Female | 6 |
| Age (years) | |
| Mean±SD | 30.75±3.28 |
| Underlying Disease | |
| No | 12 |
| Photosensitivity or drug induced photosensitivity | |
| No | 12 |
| Active Facial Skin Condition | |
| No | 12 |
| Previous facial Treatment | |
| No | 12 |

According to Table 4.1, half of the participants were males and half were females, with the average age of 30.75±3.28 years. They all did not have any underlying disease, photosensitivity or drug induced photosensitivity, active facial skin condition or previous facial treatment.

## 4.2 Outcome Assessment

4.2.1 Wrinkles Assessment by VISIA

**Table 4.2** Wrinkle Score measurement by statistical analysis compared between monotherapy and combination therapy (n=12)

| | **Monotherapy** | **Combination Therapy** | **Paired Difference** | **p-value(a)** |
|---|---|---|---|---|
| | **Mean±SD** | **Mean±SD** | | |
| Baseline | 45±21.46 | 52.25±21.27 | 7.25±0.20 | 0.04 |
| 4th week | 49.5±19.00 | 63.92±16.56 | 14.42±2.44 | <0.001 |
| 8th week | 58.17±17.54 | 74.08±13.24 | 15.92±4.30 | <0.001 |
| 12th week | 62±15.80 | 81.5±11.07 | 19.5±4.73 | <0.001 |
| p-value(b) | <0.001 | <0.001 | | |

Data were analyzed by Paired t-test (a), between groups and by Repeated ANOVA (b), within group. Statistical significance at $p<0.05$.

According to table 4.2, combination therapy produced significantly greater wrinkle improvement than monotherapy at all follow-ups: 4th week (63.92±16.56>49.5±19.00), 8th week (74.08±13.24>58.17±17.54) and 12th week (81.5±11.07>62±15.80). The difference between treatments increased over time, indicating a stronger cumulative effect.

**Table 4.3** Multiple comparison analysis (Post-hoc test) of Wrinkle Scores (n=12)

| **Compare to** | | **Monotherapy** | **Combination Therapy** |
|---|---|---|---|
| | | **p-value** | **p-value** |
| Baseline | 4th week | <0.001 | <0.001 |
| Baseline | 8th week | <0.001 | <0.001 |
| Baseline | 12th week | <0.001 | <0.001 |
| 4th week | 8th week | <0.001 | <0.001 |
| 4th week | 12th week | <0.001 | <0.001 |
| 8th week | 12th week | <0.001 | <0.001 |

**Note** Post-hoc comparisons performed following repeated measures analysis. Higher wrinkle scores indicate greater improvement.

According to the multiple comparison analysis, wrinkle scores in both monotherapy and combination therapy groups improved significantly from baseline to 4th, 8th, and 12th weeks ($p < 0.05$). However, combination therapy showed significantly greater improvement than monotherapy at all time points, with the largest difference observed at week 12.

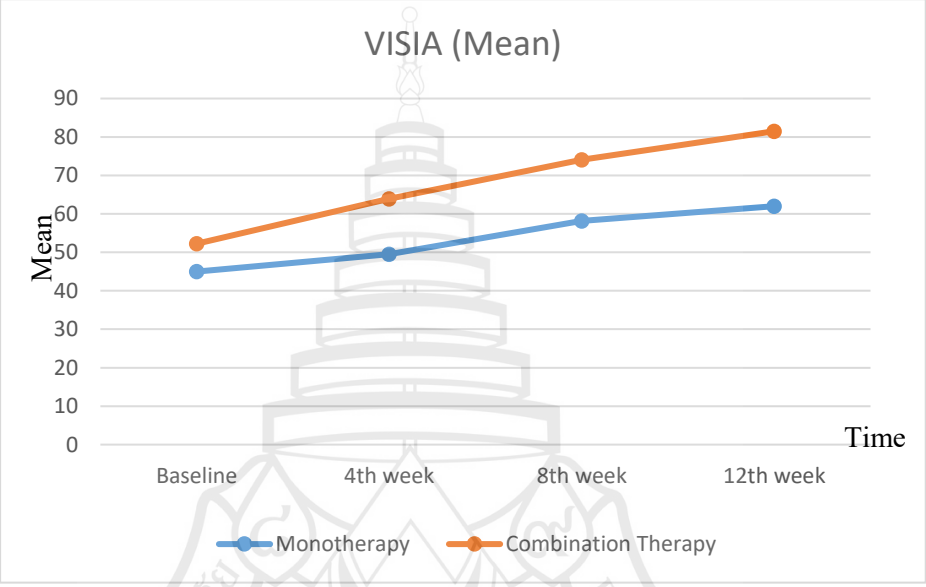



**Figure 4.1** Mean Value of VISIA Over Time Between Monotherapy and Combination Therapy

4.2.2 Viscoelasticity Assessment by Cutometer

**Table 4.4** Viscoelasticity Score measurement by statistical analysis compared between monotherpy and combination therapy (n=12)

| | **Monotherapy** | **Combination Therapy** | **Paired Difference** | **p-value(a)** |
|---|---|---|---|---|
| | **Mean±SD** | **Mean±SD** | | |
| Baseline | 60.11±10.86 | 58.00±7.62 | -2.10±3.24 | 0.19 |
| 4th week | 59.23±7.56 | 67.06±8.92 | 7.83±1.37 | <0.001 |
| 8th week | 64.35±7.13 | 77.32±6.65 | 12.98±0.48 | <0.001 |
| 12th week | 69.03±8.13 | 84.61±6.88 | 15.56±1.25 | <0.001 |
| p-value(b) | <0.001 | <0.001 | | |

Data were analyzed by Paired t-test (a), between groups and by Repeated ANOVA (b), within group. Statistical significance at $p<0.05$.

Table 4.4 showed that combination therapy produced significantly greater viscoelasticity score than monotherapy at each follow-up visits: 4th week (67.06±8.92>59.23±7.56), 8th week (77.32±6.65>64.35±7.13) and 12th week (84.61±6.88>69.03±8.13). Over time, the difference between therapies increased, demonstrating a more potent effect.

**Table 4.5** Multiple comparison analysis (Post-hoc test) of Viscoelasticity Scores (n=12)

| Compare to | | Monotherapy | Combination Therapy |
|---|---|---|---|
| | | p-value | p-value |
| Baseline | 4th week | >0.05 | <0.001 |
| Baseline | 8th week | <0.001 | <0.001 |
| Baseline | 12th week | <0.001 | <0.001 |
| 4th week | 8th week | <0.001 | <0.001 |
| 4th week | 12th week | <0.001 | <0.001 |
| 8th week | 12th week | <0.001 | <0.001 |

**Note** Post-hoc comparisons conducted after repeated measures analysis.
Higher viscoelasticity scores indicate improved skin elasticity.

Multiple comparison analysis showed that viscoelasticity scores in the combination therapy group improved significantly at all follow-up visits compared with baseline ($p < 0.05$). In the monotherapy group, significant improvement was observed from the 8th week onward, while the change at the 4th week was not statistically significant. Between-group comparison revealed no significant difference at baseline ($p = 0.19$). However, combination therapy demonstrated significantly greater improvement than monotherapy at the 4th, 8th, and 12th weeks, with the largest difference observed at week 12.

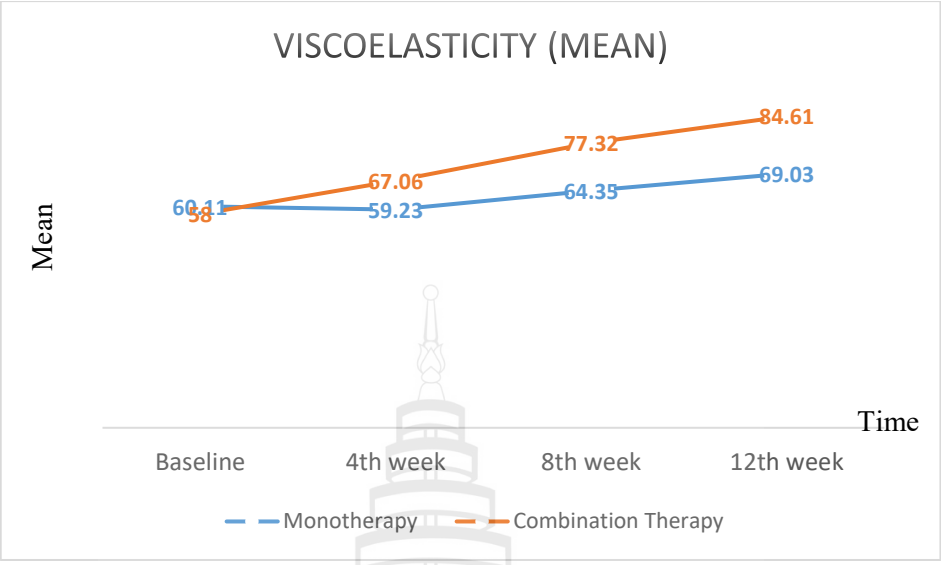



**Figure 4.2** Mean Value of Viscoelasticity Over Time Between Monotherapy and Combination Therapy

4.2.3 Trans-epidermal Water Loss (TEWL) Assessment by Tewameter

**Table 4.6** Trans-epidermal Water Loss measurement by statistical analysis compared between monotherpy and combination therapy (n=12)

| | **Monotherapy** | **Combination Therapy** | **Paired Difference** | **p-value(a)** |
|---|---|---|---|---|
| | **Mean±SD** | **Mean±SD** | | |
| Baseline | 21.93±1.82 | 22.14±1.90 | 0.21±0.08 | 0.19 |
| 4th week | 20.15±1.48 | 17.93±1.26 | -2.23±0.22 | <0.001 |
| 8th week | 18.53±0.83 | 15.76±1.00 | -2.77±0.17 | <0.001 |
| 12th week | 17.22±0.98 | 14.6±0.97 | -2.62±0.01 | <0.001 |
| p-value(b) | <0.001 | <0.001 | | |

**Note** Paired t-test (a) was used to determine the data between groups, and Repeated ANOVA (b) was used to analyze the data within groups. Statistical significance at $p<0.05$.

This table 4.6 indicates that combination therapy produced significantly lesser Trans-epidermal water loss score than monotherapy at each follow-up: 4th week (17.93±1.26<20.15±1.48), 8th week (15.76±1.00<18.53±0.83) and 12th week (14.6±0.97<17.22±0.98). Over time, both monotherapy and combination therapy mean

values decreased. Furthermore, combination therapy's mean values are lower than those of monotherapy (mean =17.61±3.32<19.46±2.04).

**Table 4.7** Multiple comparison analysis (Post-hoc test) of Trans-epidermal Water Loss Scores (n=12)

| Compare to | | Monotherapy | Combination Therapy |
|---|---|---|---|
| | | p-value | p-value |
| Baseline | 4th week | <0.001 | <0.001 |
| Baseline | 8th week | <0.001 | <0.001 |
| Baseline | 12th week | <0.001 | <0.001 |
| 4th week | 8th week | <0.001 | <0.001 |
| 4th week | 12th week | <0.001 | <0.001 |
| 8th week | 12th week | <0.001 | <0.001 |

**Note** Post-hoc comparisons conducted following repeated measures analysis. Lower TEWL values indicate improved skin barrier function.

Multiple comparison analysis demonstrated that TEWL significantly decreased from baseline at all follow-up visits in both groups ($p < 0.05$), indicating progressive improvement in skin barrier function.

Between-group comparison showed no significant difference at baseline ($p = 0.19$). However, combination therapy produced significantly greater reductions in TEWL at the 4th, 8th, and 12th weeks compared with monotherapy.

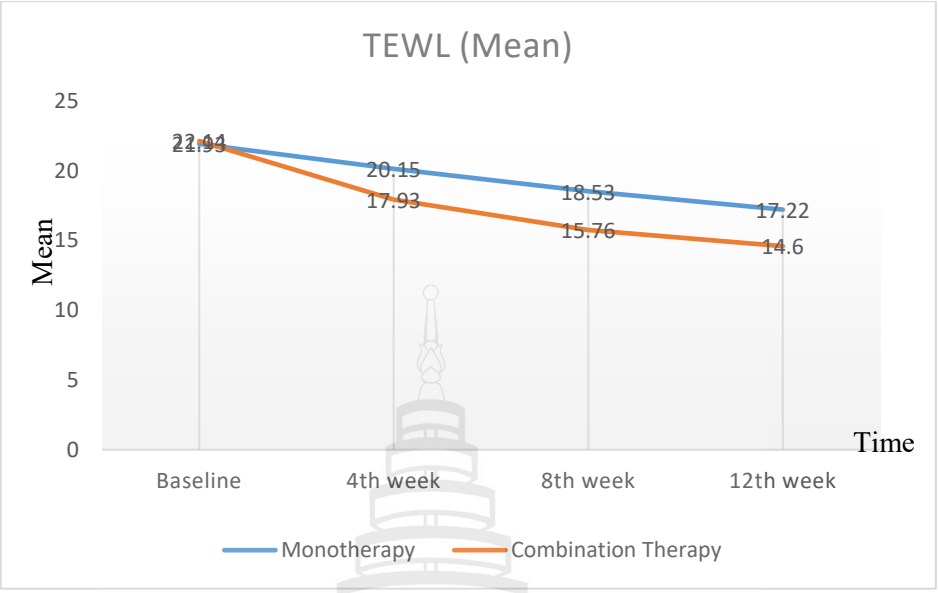



**Figure 4.3** Trans-epidermal Water Loss Over Time Between Monotherapy and Combination Therapy

4.2.4 Global Aesthetics Improvement Scale (GAIS)

**Table 4.8** GAIS between Monotherapy and Combination Therapy at week 12 (n=12)

| | **Monotherapy (n=12)** | **Combination Therapy (n=12)** |
|---|---|---|
| 1.Very much improved | 0 | 6 |
| 2. Much improved | 5 | 6 |
| 3. Improved | 7 | 0 |
| 4. No change | 0 | 0 |
| 5. Worse | 0 | 0 |

According to above table 4.8, GAIS in monotherapy shows 41.67% of “Much Improved” and 58.33% of “Improved” whereas indicates 50% in “Very Much Improved” and another 50% in “Much Improved” in combination therapy.

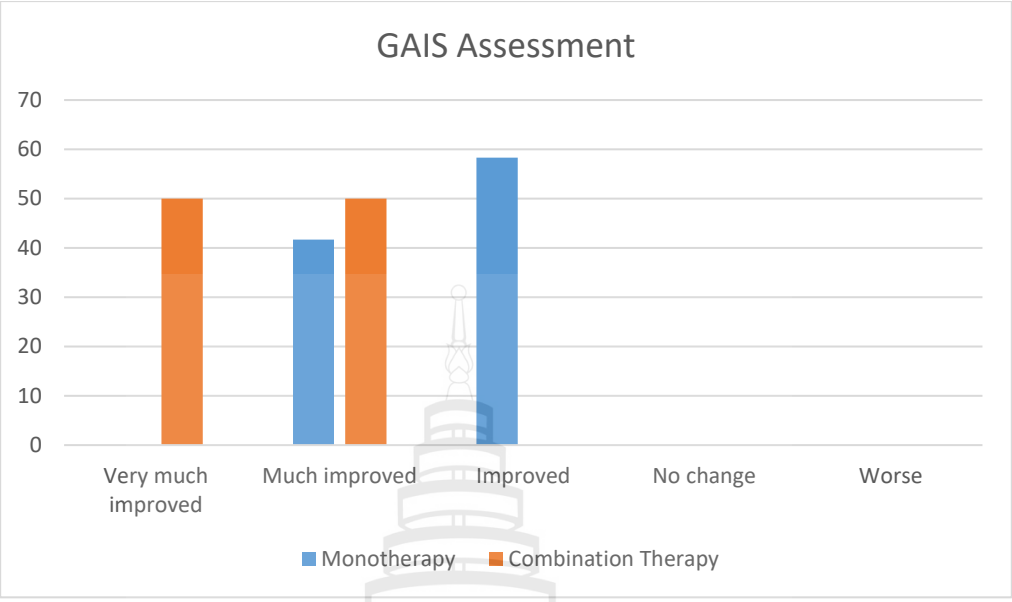



**Figure 4.4** GAIS Assessment with Bar Chart at week 12

Bar chart reveals the GAIS assessment between monotherapy and combination therapy at week 12.

**Table 4.9** Statistical Analysis of GAIS at 12th week (n=12)

| | **Monotherapy (n=12)** | **Combination Therapy (n=12)** | **p-value** |
|---|---|---|---|
| | **Median (IQR)** | **Median (IQR)** | |
| $12^{th}$ week | 3 (2-3) | 1.5 (1-2) | 0.002 |

**Note** Data was presented by Wilcoxon Signed Ranks Test. Significant p-value<0.05.

4.2.5 Participants' Satisfactory Score

**Table 4.10** Frequency of Participants' Satisfactory Score at 12th week (n=12)

| **Participants' Satisfactory Score** | **Monotherapy (n=12)** | **Combination Therapy (n=12)** |
|---|---|---|
| Score 0= not satisfy | 0 | 0 |
| Score 1= mildly satisfy | 0 | 0 |
| Score 2= moderately satisfy | 6 | 3 |
| Score 3= greatly satisfy | 6 | 9 |

Table 4.10 represents the frequency distribution of participants' satisfactory scores in which 3 of them reported "moderately satisfy" and 9 of them reported "greatly satisfy" in combination therapy group whereas each half of the participants reported "moderately satisfy" and "greatly satisfy" in monotherapy group.

4.2.6 Adverse Events

**Table 4.11** Pain Score

| | **Monotherapy (n=12)** | **Combination Therapy (n=12)** |
|---|---|---|
| Pain score 0-3 | 9 | 9 |
| Pain score 4-6 | 3 | 3 |
| Pain score 7-10 | 0 | 0 |

Pain scores were rated equally by participants between monotherapy and combination therapy. 75% of participants rated pain score 0-3 and 25% of them rated pain score 4-6.

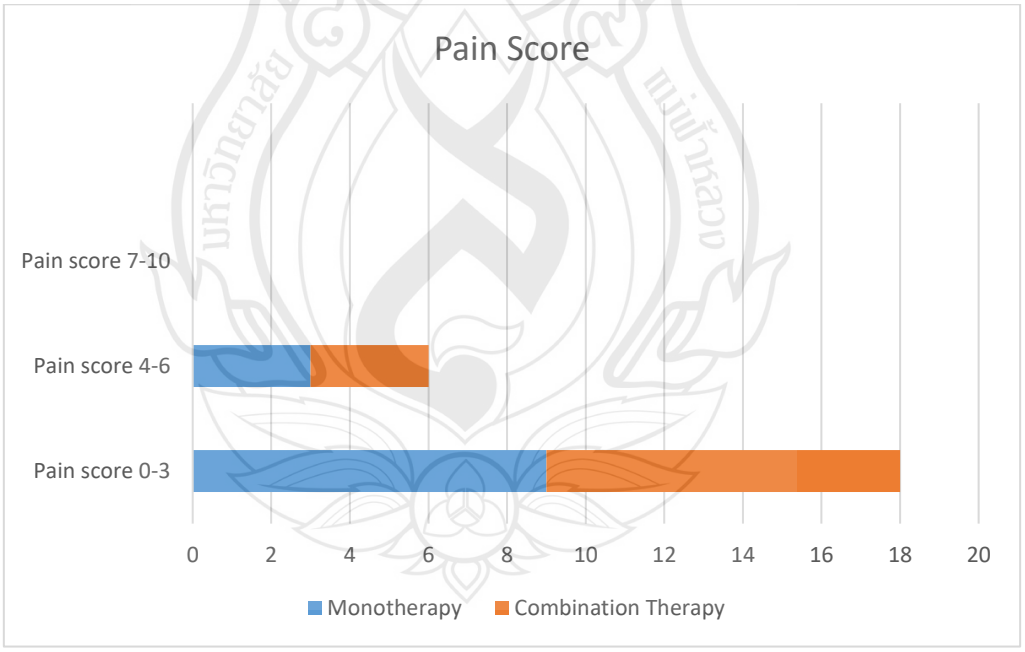



**Figure 4.5** Pain Score bar chat between monotherapy and combination therapy

**Table 4.12** Erythema or Swelling

| | **Monotherapy (n=12)** | **Combination Therapy (n=12)** |
|---|---|---|
| Slight Erythema or Swelling | 5 | 7 |

Those erythema or swelling were transient and relieved after 4-5 hours of procedure. No serious adverse events were seen in both therapies.

# CHAPTER 5

# DISCUSSION AND CONCLUSION

## 5.1 Discussion

Skin aging is a complex process influenced by both intrinsic and extrinsic factors. Intrinsic factors, driven by genetic factors and the passage of time, leads to a gradual decline in the skin's structural proteins like collagen and elastin. Extrinsic factors, such as sun exposure, pollution, and lifestyle choices, contribute to premature aging by accelerating the formation of fine lines, wrinkles, and age spots (6). Over time, the skin's ability to repair and regenerate diminishes, resulting in a loss of firmness and elasticity.

This study evaluated the effectiveness and safety of platelet rich plasma (monotherapy) alone and platelet rich plasma combined with intense pulsed light (combination therapy) for facial rejuvenation. Twelve healthy male and female participants, aged 25-45 years, with wrinkles grade 2 or 3 according to wrinkle severity rating scale (WSRS) or participants who want to undergo facial rejuvenation participated in this study. All participants were done 3 treatment sessions of monotherapy and combination therapy on each side of face. The parameters named wrinkle score, skin elasticity score, trans-epidermal water loss score, Global Aesthetic Improvement Scale (GAIS), participant's satisfactory score and adverse events were used to assess the effectiveness and safety of this study.

Facial wrinkle assessment was done by VISIA® and wrinkle score for both sides of treatment was analyzed. Both monotherapy and combination therapy showed significant improvement. However, combination therapy showed more improvement statistically than monotherapy with each follow-up visit. Monotherapy showed mean value increased in 49.5±19.00 in $4^{th}$ week from 45±21.46 in baseline while combination therapy showed significant increased from 52.25±21.27 to 63.92±16.56 in $4^{th}$ week, indicating that the combination therapy showed more noticable and favourable outcome in the acute period compared to monotherapy. In $12^{th}$ week period, monotherapy has

increased mean value of 62±15.80 from 45±21.46, while in combination therapy, the mean value has increased from 52.25±21.27 to 81.5±11.07 indicating more upward trend graph; which showed that combination therapy proved to be superior in longer term. The progressive improvement from weeks 4 to 12 observed in this study mirrors longitudinal findings from previous clinical trials, where wrinkle reduction becomes more pronounced over time due to ongoing collagen remodeling and extracellular matrix reorganization (10)

Skin elasticity score was measured by Cutometer® MPA 580. The values for combination therapy and monotherapy increased over time which meant improving dermal structure and firmness. Additionally, combination therapy has higher effectiveness than monotherapy at 4th (67.06±8.92>59.23±7.56), 8th (77.32±6.65> 64.35±7.13) and 12th week visits (84.61±6.88>69.03±8.13). Progressive increase in viscoelasticity from week 4 onward ($p < 0.001$). Sustained improvement through weeks 8 and 12, suggesting cumulative therapeutic effects. The progressive improvement seen in this study supported the concept of time-dependent dermal remodeling, which typically requires several weeks for collagen deposition and extracellular matrix reorganization. The observed increase in viscoelasticity with combination therapy aligns with prior dermatologic and cosmetic research showing that multimodal treatments improve skin elasticity more effectively than single modalities (14) (5). Previous studies have reported:

1. Combination approaches (e.g., topical agents + procedural treatments) enhance collagen synthesis and elastic fiber organization (36, 37)

2. Synergistic effects accelerate dermal remodeling, leading to measurable improvements in biomechanical properties (10)

TEWL was indicated by Tewameter® TM 300. The values of monotherapy and combination therapy from baseline (21.93±1.82, 22.14±1.90), 4th week (20.15±1.48, 17.93±1.26), 8th week (18.53±0.83, 15.76±1.00), to 12th week (17.22±0.98, 14.6±0.97) decreased significantally ($p<0.001$), which represented the increased stronger skin barrier function, skin hydration, lowering risk of irritation and dryness. Furthermore, combination therapy's values are lower than those of monotherapy statistically. The significant TEWL reduction in the combination group is consistent

with previous research demonstrating that therapies targeting both hydration and barrier repair improve epidermal integrity (30, 31). Earlier studies have shown:

1. Barrier-enhancing treatments reduce TEWL by restoring lipid lamellae and corneocyte cohesion (36)

2. Combination regimens are more effective because they address multiple barrier components simultaneously (lipids, natural moisturizing factors, and epidermal turnover) (37, 39)

GAIS were evaluated by 3 dermatologists using photographs taken by VISIA® Complexion Analysis System only at week 12. The results showed improvement in both therapies but very much improvement in combination therapy.

Participants' satisfactory scores were significantly high after all treatment sessions, 9 participants scored "greatly satisfy" and 3 participants scored "moderately satisfy" in combination therapy group while half of participants reported "moderately satisfy" and another half reported "greatly satisfy" in monotherapy group.

Furthermore, as adverse events, pain scores were rated equally by participants between monotherapy and combination therapy. 75% of participants rated pain score 0-3 and 25% of them rated pain score 4-6. Some of the them encountered slight erythema or swelling, which were transient and relieved after 4-5 hours of procedure. No serious adverse events were seen in both therapies.

This study demonstrated that IPL was effective for addressing periorbital skin aging, with over half of the patients experiencing moderate to significant improvement. Using ablative fractional laser (AFL) treatment along with IPL significantly reduced wrinkles and pore size while improving skin texture and elasticity in Chinese individuals with photoaged skin (24). Importantly, it didn't harm the skin barrier and there were no severe side effects although post inflammatory hyperpigmentation (PIH) occurred after AFL treatment.

In the study by (15), patients reported greater improvement in wrinkles, texture, and elasticity when CO2 laser was combined with PRP, as opposed to PRP alone. (41) found substantial improvement on both sides of the face when combining fractional CO2 laser treatment with PRP for treating atrophic acne scars. (42) demonstrated that combining PRP with erbium laser yielded superior efficacy compared to 12 sessions of single plasma-rich therapy within the same timeframe.

Likewise, according to above data, the combination of intense pulsed light (IPL) therapy and platelet-rich plasma (PRP) showed to be a powerful, tolerable and synergistic approach for comprehensive facial rejuvenation by means of growth factors released from PRP, enhancing extracellular matrix production and thermal stimulation from IPL; known to activate fibroblasts and promote neocollagenesis (30) Furthermore, IPL therapy accelerates epidermal turnover and improve skin texture by removing damaged keratinocytes, promoting uniform pigmentation and enhancing light reflection, reducing wrinkle visibility (14). Therfore, combination therapy targets multiple layers of the skin simultaneously:

1. Epidermal renewal
2. Dermal collagen remodeling
3. Barrier repair and hydration (5, 42)

## 5.2 Conclusion

In this study, both monotherapy and combination therapy reduced facial wrinkles and trans-epidermal water loss, increased skin elasticity at each follow-up visit. However, combiantion therapy far more outweigh than monotherapy statistically without any severe side effects during and after treatment and with great satisfication. The main conclusion that can be drawn is that this research provides a safe and effective alternative combined treatment for facial rejuvenation intense pulsed light (IPL) therapy and platelet-rich plasma (PRP).

## 5.3 Limitations

This study has some limitations. The relatively small sample size may limit the generalizability of the findings. The follow-up period was short, preventing assessment of the long-term durability of treatment outcomes. In addition, performing a tissue biopsy is not feasible due to concerns related to volunteers' cosmetic considerations and privacy. Even though the author told the volunteers to limit their sun exposure and abstain from alcohol and tobacco, they were unable to control certain aspects that

contribute to wrinkles, like their eating and sleeping habits. However, this study showed efficacy of combonation therapy is greater than monotherapy.

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# APPENDIX A

# INFORMED CONSENT FORM

Research Project: The project is about the Efficacy of The Combination of Intense Pulsed Light Therapy and Platelet-Rich Plasma With Platelet-Rich Plasma Alone For Facial Rejuvenation in the volunteers with the age between 25-45 years old, who have exhibiting wrinkles, diminished elasticity and those who want to undergo facial rejuvenation at Mae Fah Luang University Hospital, Bangkok. This project is the randomized split-face study.

**I, Mr./ Mrs./ Miss ……**

**Address: ……..**

I have thoroughly reviewed the material provided here as well as every detail from the forms that the study project's volunteers must sign to receive the information.

**Issue date: ……**

In order to participate in the research project, I have signed and dated a copy of the informed consent letter and the research information sheet that I have received. Before I signed the consent form, I received a complete and full explanation from the researcher outlining the goals of the study, any potential risks or discomfort, the anticipated benefits, and alternate possibilities. I've had adequate time and chance to ask questions regarding everything associated with the research project, and the answers I've received have satisfied me. I understand that because the results are dependent on the individual skin of each participant, the researcher cannot guarantee a definitively meaningful outcome. I am also aware that after undergoing treatment, there is a possibility of experiencing side effects such erythema, post-inflammatory hyperpigmentation or hypopigmentation, burning, bleeding, and infection. I have received confirmation from the researcher that I will be treated medically as specified in the Research Information Sheet in the event that any adverse effects or dangers result from the research. Furthermore, I have the right to discontinue the research endeavour at any point. My right to medical treatment and other rights will not be impacted by this withdrawal. The researcher attests to the confidentiality of my personal data. My personal information will only be shared for academic purposes with certain departments involved in the study project. I've read the material above and can understand it all. I willingly agree to take part in this study as a participant.

**Signature of participant: ……**

**Written name of participant: …….**

**Date: …….**

As the researcher and principal investigator, I, Dr. Yamin Eaint, have correctly read the Research Information Sheet to the prospective participant and provided a detailed explanation. I've made sure that the subject is aware of the goals, the research's methodology, any pain or possible hazards, the study's anticipated benefits, and their other options. I certify that the participant was given the chance to ask questions concerning the study, and that I have accurately and fully addressed each question to the best of my abilities. I certify that the consent was freely and voluntarily provided by the individual and that they were not forced to give it.

**Signature of researcher: …….**

**Written name of researcher: ……..**

**Date: …….**

# APPENDIX B

# RESEARCH PROFILE (CONFIDENTIAL)

**Volunteer No.: ……...**

**Date: ……....**

**General Information**

1) D.O.B: ……
2) Telephone: ……
3) Gender
   - ☐ Male
   - ☐ Female
4) Occupation
   - ☐ Government officer:
   - ☐ Employer
   - ☐ Housewife
   - ☐ Student
   - ☐ Employee
   - ☐ Other (specify) ……
5) Underlying disease: ……
6) Photosensitivity or drug induced photosensitivity: ……
7) History of food or drugs allergy: ……
8) Facial skin conditions
   - ☐ Scar or ulcers: ……
   - ☐ Active dermatological condition: ……
   - ☐ Others (specify): ……
9) Medical history
   - ☐ Active skin disease: ……
   - ☐ Anaemia:…….
   - ☐ History of malignant or pre-malignant lesions: ……
10) Other (specify): ……
11) History of following treatment before the study
    - ☐ Chemical peeling
    - ☐ Dermabrasion

- ☐ Any device or laser treatment
- ☐ Neurotoxin treatment
- ☐ Collagen/fat injection
- ☐ Oral or topical retinoid
- ☐ Platelet Rich Plasma Injection
- ☐ Other (specify): …….

12) Gynecology history (if female)

- ☐ Pregnancy
- ☐ Breastfeeding
- ☐ Willing to get pregnancy during the program

13) Personal History

- ☐ Alcohol
- ☐ Smoking
- ☐ Drug abuse

14) Average sun exposure (from 10 am to 4 pm): …… minutes/ hours

15) Current skin care products use: ……

# APPENDIX C

# DOCTOR'S RECORD FORM

**Volunteer no.: ……**

The efficacy of the combination of intense pulsed light therapy and platelet-rich plasma with platelet-rich plasma alone for facial rejuvenation

Table 1: Wrinkle Score

| **Timeline** | **Wrinkle Score** | | | |
|---|---|---|---|---|
| | **Cheek** | | **Forehead** | |
| | **Monotherapy** | **Combination Therapy** | **Monotherapy** | **Combination Therapy** |
| Baseline | | | | |
| 4th week | | | | |
| 8th week | | | | |
| 12th week | | | | |
| **Mean** | | | | |

Table 2: Skin Elasticity Score

| **Timeline** | **Skin Elasticity Score** | | | |
|---|---|---|---|---|
| | **Cheek** | | **Forehead** | |
| | **Monotherapy** | **Combination Therapy** | **Monotherapy** | **Combination Therapy** |
| Baseline | | | | |
| 4th week | | | | |
| 8th week | | | | |
| 12th week | | | | |
| **Mean** | | | | |

Table 3: Trans-epidermal Water Loss Score

| Timeline | Trans-epidermal Water Loss Score | | | |
|---|---|---|---|---|
| | Cheek | | Forehead | |
| | Monotherapy | Combination Therapy | Monotherapy | Combination Therapy |
| Baseline | | | | |
| 4th week | | | | |
| 8th week | | | | |
| 12th week | | | | |
| **Mean** | | | | |

Table 4: Global Aesthetic Improvement Scale (GAIS) at 12th week

| | Rating | Description |
|---|---|---|
| 1 | Very much improved (>75%) | Optimal cosmetic result in this subject |
| 2 | Much Improved (>50%-75%) | Marked improvement in appearance form the initial condition, but not completely optimal for this subject |
| 3 | Improved (>25%-50%) | Obvious improvement in appearance from initial condition, but a re-treatment is indicated |
| 4 | No change | The appearance is essentially the same as the original condition |
| 5 | Worse | The appearance is worse than the original condition |

| | Monotherapy | Combination Therapy |
|---|---|---|
| GAIS at 12th week | | |

Table 5: Adverse Events at 4th week, 8th week and 12th week

| **Questionnaires** | **4th week** | | |
|---|---|---|---|
| | **Monotherapy** | **Combination Therapy** | **Remark** |
| Pain score 0-10 | | | |
| Days of Erythema or Swelling | | | |
| Burning Sensation | | | |
| Infection | | | |
| Post Inflammatory Hyperpigmentation or Hypopigmentation | | | |
| Others | | | |

| **Questionnaires** | **8th week** | | |
|---|---|---|---|
| | **Monotherapy** | **Combination Therapy** | **Remark** |
| Pain score 0-10 | | | |
| Days of Erythema or Swelling | | | |
| Burning Sensation | | | |
| Infection | | | |
| Post Inflammatory Hyperpigmentation or Hypopigmentation | | | |
| Others | | | |

| **Questionnaires** | **12th week** | | |
|---|---|---|---|
| | **Monotherapy** | **Combination Therapy** | **Remark** |
| Pain score 0-10 | | | |
| Days of Erythema or Swelling | | | |
| Burning Sensation | | | |
| Infection | | | |
| Post Inflammatory Hyperpigmentation or Hypopigmentation | | | |
| Others | | | |

# Participants' Satisfaction Record Form

**Volunteer No.: ……...**

1. Please score the satisfactory scale according to your desire and satisfaction after 3 sessions of the combination treatment of platelet-rich plasma and intense pulsed light therapy for your facial rejuvenation.
   (Please choose one of the following options)
   - ☐ Score 0 = Not satisfy
   - ☐ Score 1 = Mildly satisfy
   - ☐ Score 2 = Moderately satisfy
   - ☐ Score 3 = Greatly satisfy

2. Will you undergo the same treatment in the future?
   - ☐ Yes
   - ☐ No

# APPENDIX D

# CLINICAL EVALUATION DATA

**Table D1** Wrinkle score of Monotherapy from VISIA® Complexion Analysis System at baseline, 4th week, 8th week, and 12th week

| | Cheek | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D2** Wrinkle score of Monotherapy from VISIA® Complexion Analysis System at baseline, 4th week, 8th week, and 12th week

| | Forehead | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |

**Table D2** (continued)

| Forehead | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D3** Wrinkle score of Combination Therapy from VISIA® Complexion Analysis System at baseline, 4th week, 8th week, and 12th week

| Cheek | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D4** Wrinkle score of Combination Therapy from VISIA® Complexion Analysis System at baseline, 4th week, 8th week, and 12th week

| Forehead | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |

**Table D4** (continued)

| Forehead | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D5** Skin elasticity score of Monotherapy from Cutometer® MPA 580 at baseline, 4th week, 8th week, and 12th week

| Cheek | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D6** Skin elasticity score of Monotherapy from Cutometer® MPA 580 at baseline, 4th week, 8th week, and 12th week

| Forehead | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D7** Skin elasticity score of Combination Therapy from Cutometer® MPA 580 at baseline, 4th week, 8th week, and 12th week

| Cheek | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D8** Skin elasticity score of Combination Therapy from Cutometer® MPA 580 at baseline, 4th week, 8th week, and 12th week

| Forehead | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D9** Trans-epidermal water loss score of Monotherapy from Tewameter® TM 300 at baseline, 4th week, 8th week, and 12th week

| Cheek | | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D10** Trans-epidermal water loss score of Monotherapy from Tewameter® TM 300 at baseline, 4th week, 8th week, and 12th week

| | Forehead | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D11** Trans-epidermal water loss score of Combination Therapy from Tewameter® TM 300 at baseline, 4th week, 8th week, and 12th week

| | Cheek | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D12** Trans-epidermal water loss score of Combination Therapy from Tewameter® TM 300 at baseline, 4th week, 8th week, and 12th week

| | Forehead | | | |
|---|---|---|---|---|
| **Volunteer No.** | **Baseline** | **4th week** | **8th week** | **12th week** |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |
| 11 | | | | |
| 12 | | | | |

**Table D13** The Global Aesthetic Improvement Scale (GAIS) at 12th week

| **Volunteer No.** | **Monotherapy** | **Combination Therapy** |
|---|---|---|
| 1 | | |
| 2 | | |
| 3 | | |
| 4 | | |
| 5 | | |
| 6 | | |
| 7 | | |
| 8 | | |
| 9 | | |
| 10 | | |
| 11 | | |
| 12 | | |

Score 1= Very much improved (>75%)

Score 2= Much improved (>50%-75%)

Score 3= Improved (>25%-50%)

Score 4= No change

Score 5= Worse

**Table D14** Participants Satisfaction Score at 12th week

| Volunteer No. | Satisfaction Score | |
|---|---|---|
| | Monotherapy | Combination Therapy |
| 1 | | |
| 2 | | |
| 3 | | |
| 4 | | |
| 5 | | |
| 6 | | |
| 7 | | |
| 8 | | |
| 9 | | |
| 10 | | |
| 11 | | |
| 12 | | |

**Table D15** Adverse events questionnaires record form of Monotherapy at 4th week, 8th week, and 12th week

| Volunteer No. | Follow up (week) | Pain Score | Days of Erythema or Swelling | Burning Sensation | Infection | Post Inflammatory Hyperpigmentation or Hypopigmentation | Others |
|---|---|---|---|---|---|---|---|
| 1 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 2 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 3 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 4 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 5 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |

**Table D15** (continued)

| Volunteer No. | Follow up (week) | Pain Score | Days of Erythema or Swelling | Burning Sensation | Infection | Post Inflammatory Hyperpigmentation or Hypopigmentation | Others |
|---|---|---|---|---|---|---|---|
| 6 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 7 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 8 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 9 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 10 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 11 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 12 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |

**Table D16** Adverse events questionnaires record form of Combination Therapy at 4th week, 8th week, and 12th week

| Volunteer No. | Follow up (week) | Pain Score | Days of Erythema or Swelling | Burning Sensation | Infection | Post Inflammatory Hyperpigmentation or Hypopigmentation | Others |
|---|---|---|---|---|---|---|---|
| 1 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 2 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |

**Table D16** (continued)

| Volunteer No. | Follow up (week) | Pain Score | Days of Erythema or Swelling | Burning Sensation | Infection | Post Inflammatory Hyperpigmentation or Hypopigmentation | Others |
|---|---|---|---|---|---|---|---|
| 3 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 4 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 5 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 6 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 7 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 8 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 9 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 10 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 11 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |
| 12 | 4th | | | | | | |
| | 8th | | | | | | |
| | 12th | | | | | | |

# CURRICULUM VITAE

| | |
|---|---|
| **NAME** | Yamin Eaint |
| **EDUCATIONAL BACKGROUND** | |
| 2020 | Bachelor of Medicine, Bachelor of Surgery (M.B., B.S)<br>University of Medicine, Mandalay, Myanmar |
| **WORK EXPERIENCE** | |
| 2022 | COVID 19 vaccination Campaign |
| 2021-2022 | Medical officer<br>Mandalar Hospital |
| 2020-2021 | Medical officer<br>Mingalar Hospital |
| 2019-2020 | House officer<br>Mandalay General Hospital and 300 bedded Children's Hospital |