A COMPARATIVE STUDY OF FRACTIONAL RADIOFREQUENCY MICRONEEDLE AND SUBLATIVE BIPOLAR RADIOFREQUENCY TREATMENT IN ACNE SCARS

CHANESD SRISUKHO

MASTER OF SCIENCE
IN
DERMATOLOGY

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I have learned not only knowledge. I find the way of how to develop myself for the rest of my life and how to apply skills and knowledge for the benefits of mankind.

Chanesd Srisukho

Thesis Title	A Comparative Study of Fractional Radiofrequency Microneedle and Sublative Bipolar Radiofrequency Treatment in Acne Scars
Author	Chanesd Srisukho
Degree	Master of Science (Dermatology)
Advisor	Lecturer Paisal Rummaneethorn

ABSTRACT

BACKGROUND: Fractional radiofrequency technology plays a major role for the treatment of acne scars today. It provides fractionated ablation with minimal disruption to skin and thus remodeling of collagen tissue. Since 2011, sublative bipolar radiofrequency (SBR) treatment has become popular for improving the appearance of facial skin, reducing scars, treating textural irregularities and wrinkles. Fractional radiofrequency microneedle (FRM) device is a new technology which claims to be more-selective for heating the dermis at accurate depth, through small needles at its tip.

OBJECTIVE: To compare the clinical efficacy and side effects of the fractional radiofrequency microneedle with those of the sublative bipolar radiofrequency device in treatment of acne scars.

MATERIALS AND METHODS: Seventeen volunteers with atrophic acne scars were enrolled. They received three split-face sessions of treatment every four weeks, one side with FRM, and the opposite side with SBR device. Clinical improvement of acne scars was evaluated at 1 and 3 months after the last treatment. Other parameters measured by cutometer and sebumeter had been recorded. Side effects were recorded after each treatment session. Satisfaction scores were surveyed after 4 month post-treatment.

RESULTS: Seventeen volunteers enrolled in the study without discontinuation. Acne grades at follow-ups were statistically reduced from the baseline. FRM's grades between before and after treatment at one and three months were statistically different with p=0.001 and <0.001, correspondingly. There were statistical significance on SBR's grades at one month (p<0.001) and three month (p=0.002). This study showed that the face using FRM had more passive behavior of the skin to force (firmness) than SBR's at 1-month follow-up (p=0.004). No statistically change in sebum production between baseline and follow-ups. All volunteers indicated more pain and all bleeding in FRM side; more burning sensation and all burning smell in SBR side. Their common immediate side effects were erythema and swelling; hyperpigmentation and acne occurrence at follow-ups. After four months, volunteers had most scores for improvement of acne scars as "satisfied" for FRM and "somewhat satisfied" for SBR with no statistic difference between them. Eight volunteers gave higher satisfaction scores for FRM side; three people gave higher scores for SBR side; and six people gave equal scores for both sides.

CONCLUSION: Both FRM and SBR treatment can be effective treatments for acne scars. Cutometer found more firmness of the skin in FRM side at 1 month follow-up. Sebumeter found no difference in sebum production. They had some common temporary side effects. Longer follow-ups for next studies should be done with comparative studies for different levels of RF energy in future.

The author has indicated no interest with commercial supporters.

Keywords: RF/Fractional Radiofrequency Microneedle/Sublative Bipolar Radiofrequency/Acne scars

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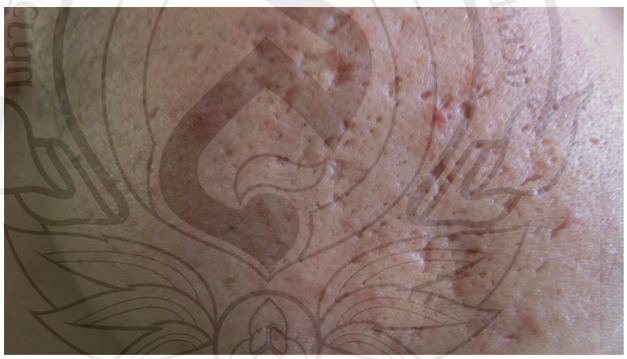
CHAPTER 1

INTRODUCTION

1.1 Background & Rationale

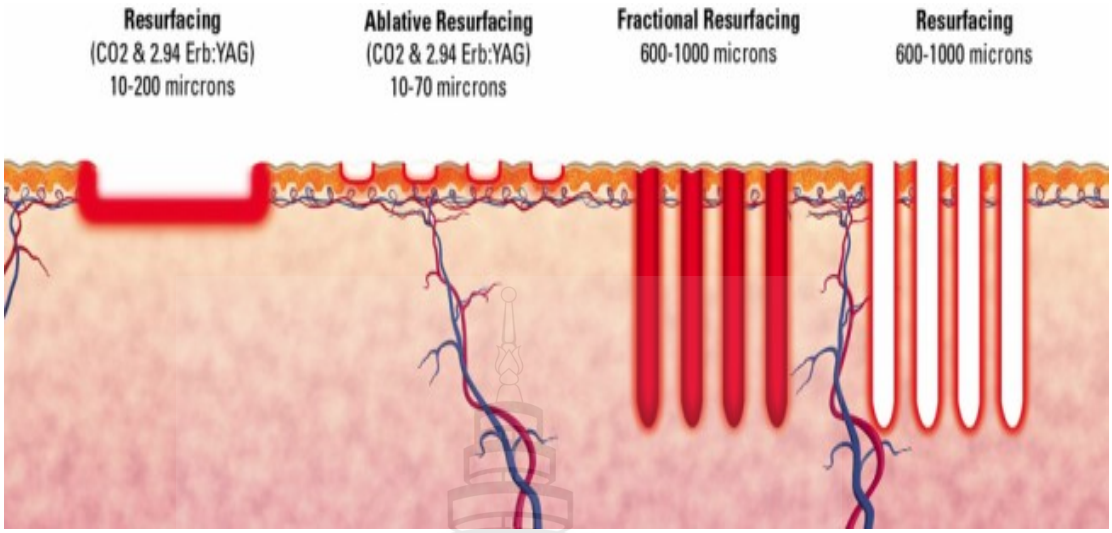
Simply acne is a common disease among Thai adolescents. Atrophic acne scars occur as one of results of damage to the skin during healing process of acne lesions. Many people suffer from this consequence of acne more than the original problem itself (Dunn, O'Neill, & Feldman, 2011). Facial acne scars affect the psychological aspect of people: they make people less self-confident about their looking. Previous studies have indicated variation of acne scars in severity, duration and age at onset (Capitanio et al., 2010; Ghodsi, Orawa, & Zouboulis, 2009; Williams & Layton, 2006).



Source Fabbrocini et al. (2010)

Figure 1.1 Acne scars

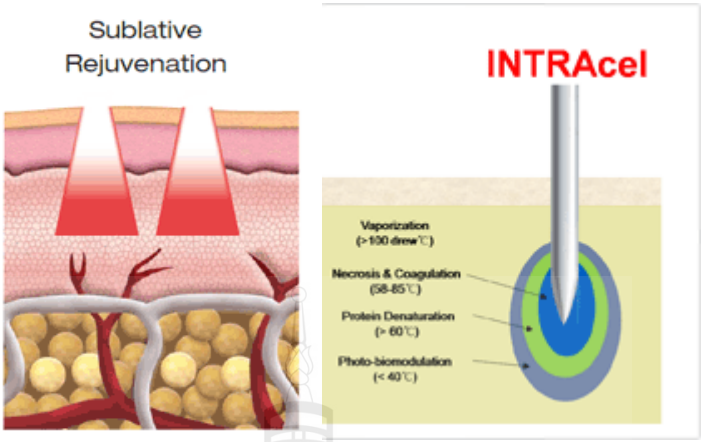
There are many treatments for acne scars, such as chemical peels, dermabrasion, needling/dermal rollers, subcision, punch excision, dermal grafting, hair transplantation, tissue augmentation/dermal fillers, stem cell therapy, and laser treatment (Fabbrocini et al., 2010; Goodman, 2000). Although this problem is difficult to be 100% cured, laser is one of the recently advanced treatments which plays a major role in the treatment of acne scars (Khatri, Mahoney, & McCartney, 2011). Laser treatment has its long own history. First of all, we will discuss about the ablative laser resurfacing. It was used since before 2000. A systematic review shows the improvement of facial acne scarring ranging from 25 to 81% for the ordinary ablative carbon dioxide (CO_2) laser, and from 50 to 70% for ablative erbium: yttrium-aluminum-garnet (Er:YAG) laser (Jordan, Cummins, & Burls, 2000). Because ablative laser treatments gave high chance of some unwanted side effects such as swelling, redness and dyspigmentation, this came into the invention of non-ablative laser treatments (Ang & Barlow, 2002). The use of non-ablative laser treatments is based on the concept of dermal tissue coagulation without epidermal vaporization. Undoubtedly, the side effects are less. But the efficacy of non-ablative laser treatments is less than ablative ones also. As the years passed, non-ablative laser resurfacing faded away. Fractional photothermolysis principle (FP) showed up after that in the history after with the idea of the generation arrays of microscopic thermal wounds at specific depths in the skin (Manstein, Herron, Sink, Tanner, & Anderson, 2004). These small wounds were called microscopic treatment zones (MTZs). The FP technology was applied with both ablative and non-ablative laser treatments and widespread used today. Based on a systematic review, the means of acne scar improvement after treatments with ablative fractional photothermolysis, fractional CO_2 laser and fractional Er:YAG 2940 nm laser, were 26-83% (Ong & Bashir, 2012).



Source SKINPECCABLE (2013)

Figure 1.2 Laser resurfacing

Nowadays, this is the era of radiofrequency (RF) and the FP technology was used with it either, so called fractional radiofrequency. The efficacy of fractional RF devices for the treatment of acne scars was studied and it was found that acne scars improved significantly (Gold & Biron, 2012; Peterson, Palm, Kiripolsky, Guiha, & Goldman, 2011; Ramesh, Gopal, Kumar, & Talwar, 2010; Taub & Garretson, 2011). This recent technology addresses some of limitations of both ablative and non-ablative laser treatment. There are types of RF device in the market, such as unipolar, monopolar, bipolar, tripolar, multi-polar RF. What we are interested in is fractional bipolar radiofrequency device, eMatrix^{TM} (Syneron Medical Inc., Irvine, CA). It has been widely used for treatment of acne scars recently, referred to as "sublative rejuvenation" (Brightman et al., 2009). Though it is successful in commercial aspect, it was questionable that sublative rejuvenation may find some disadvantages of inaccurate depth control and possible indirect damage to the epidermis.



Source Brightman et al. (2009); The Cosmetic Skin Clinic (2013)

Figure 1.3 Sublative rejuvenation versus fractional radiofrequency microneedle

So, the newest idea after sublative rejuvenation was introduced. It was minimally invasive fractional radiofrequency microneedle (FRM) device (Cho, S. I. et al., 2012). This concept goes beyond the ordinary RF device because the very fine microneedle is equipped at the applicator to deliver radiofrequency into accurate depths of the skin.

Because treatments for acne scars are now competitive and their costs are high, this study is aimed to compare the clinical efficacy and side effects of fractional radiofrequency microneedle and conventional sublative bipolar radiofrequency device for treatment of atrophic acne scars. It will then lead into the cost-benefit consideration for a majority of people who seek the treatment in future. Meanwhile, side effects of both treatments will be recorded.

1.2 Research Question

Could the fractional radiofrequency microneedle (FRM) be as effective as sublative bipolar radiofrequency device for treatment of atrophic facial acne scars?

1.3 Objectives

1.3.1 Primary Objective

To compare the clinical efficacy of the fractional radiofrequency microneedle with those of the sublative bipolar radiofrequency device in treatment of atrophic facial acne scars

1.3.2 Secondary Objectives

1.3.2.1 To study role of both devices for other possible benefits such as effects on sebum production and skin laxity

1.3.2.2 To study side effects of them

1.3.2.3 To survey volunteers' satisfaction for both treatments.

1.4 Research Hypothesis

The fractional radiofrequency microneedle is as effective as sublative bipolar radiofrequency device for the treatment of atrophic acne scars

1.5 Conceptual Framework

After occurring of inflamed acnes, damaged tissues are repaired in wound healing process. There is the new production of collagen by fibroblasts, called collagenesis. Inadequate response results in diminished deposition of collagen that cause the formation of atrophic scars while if excessive response, hypertrophic scars formation occur instead. RF-based technologies are capable of producing higher metric heating via tissue impedance with subsequent heat diffusion to deeper tissue compared to laser-based technologies. In general, applying thermal energy to the skin activates a cascade of physiological healing responses to promote re-epithelialization and remodeling of the extra-cellular matrix (ECM). Therefore, both fractional radiofrequency microneedle and sublative bipolar radiofrequency device stimulate collagenesis which can improve the atrophic acne scars.

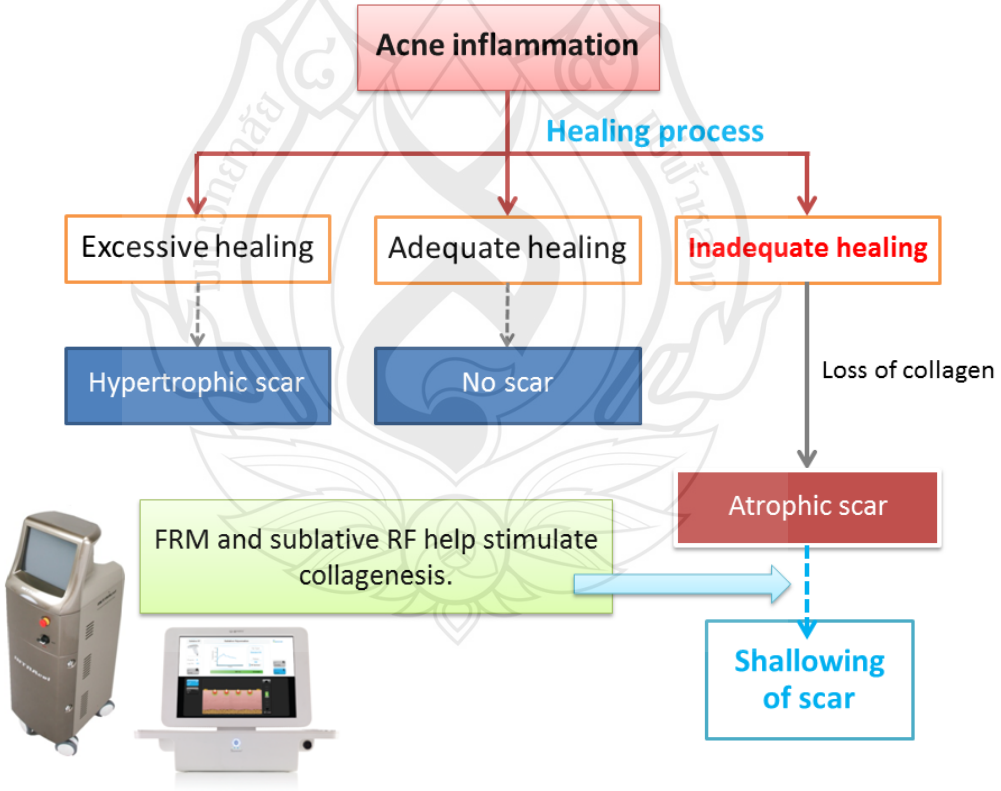


Figure 1.4 Conceptual framework

1.6 Assumption

Volunteers enrolled in this study had no difference from people who normally desire to treat their atrophic acne scars and come to see doctors.

1.7 The Scope of the Research

Seventeen volunteers, eight men and nine women with atrophic acne scars grading II o IV according the Goodman and Barron classification on both cheeks, ages 23-51, were randomly assigned to the treatment with the FRM and SBR on each half of the face. The treatments were performed every four weeks for three consecutive times at Mae Fah Luang University Hospital, Bangkok. During the study volunteers were allowed to use only facial products from the researcher, those were moisturizer, sunscreen, and cleansing agent. Photographic documentation using identical camera setting, subject positioning and environmental light by VISIA® Complexion Analysis System was performed before each treatment and at 1, 3 months after the last treatment. Other measurements of sebumeter and cutometer were done in the same occurrence. Clinical improvement of atrophic acne scars was independently evaluated by three masked dermatologist. Compared satisfaction scores for both treatments were surveyed at 4 months after the last treatment session.

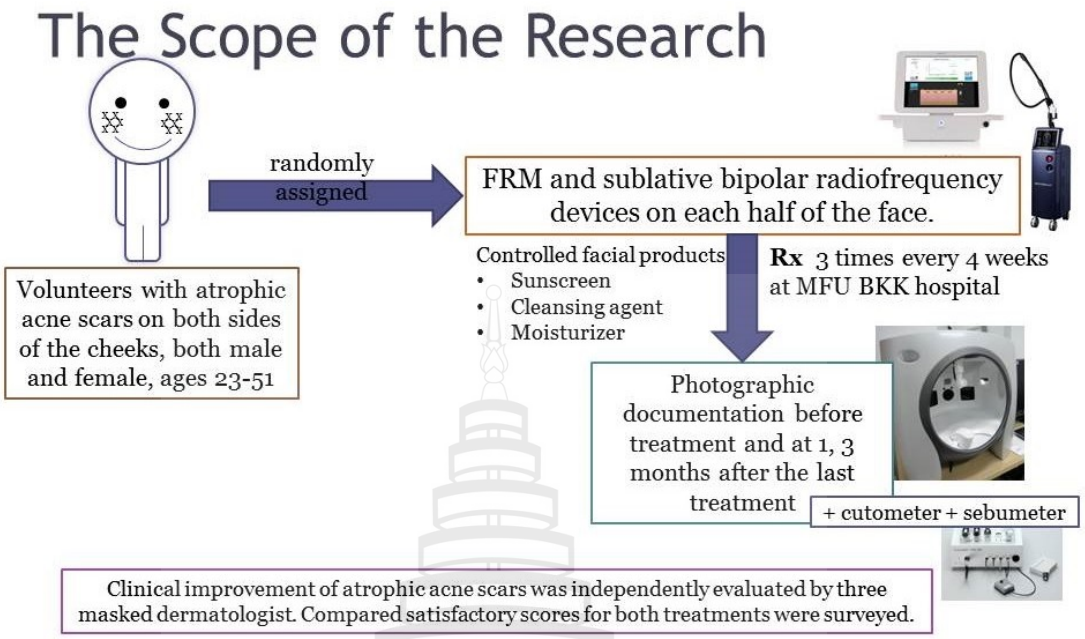


Figure 1.5 The scope of the research

1.8 Research Limitation

1.8.1 Lack of prior studies on the topic

There is a lack of prior research that compare clinical efficacy between these two treatments. This limitation serves as an important need for our research.

1.8.2 Longitudinal effects

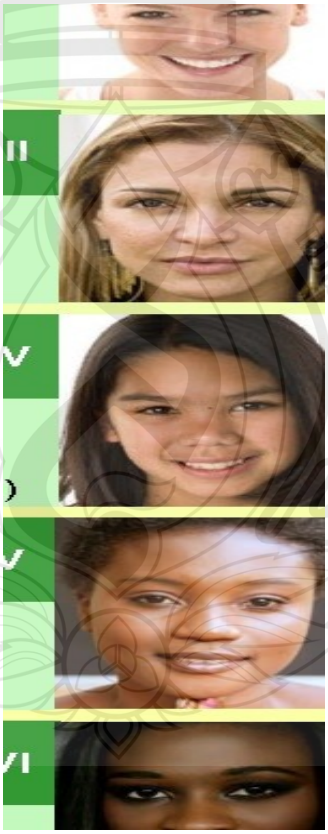
The time available to complete a research is about 12 months. The study plans to measure results of treatment at 1, 3 months after the last treatment session even the generation of collagen in human skin takes time about 4-6 months. We believe the improvement of subjects' face can be detected until 6 months after the last treatment session but this study was limited by the research time.

1.9 Operational Definition

1.9.1 Acne scars means atrophic acne scars on both cheeks. In this study, we use subjects with acne scars grading II to IV according to Goodman and Barron classification.

1.9.2 Cutometer means a device to measure viscoelasticity of the skin named Cutometer® MPA 580. It uses the photometry principle.

1.9.3 Fitzpatrick skin type is a numerical classification schema for the color of skin. It was developed in 1975 by Thomas B. Fitzpatrick, a Harvard dermatologist, as a way to classify the response of different types of skin to UV light. It remains a recognized tool for dermatologic research into the color of skin (Sachdeva, 2009).



Note. Current Perth UV = 0.0 (2013) About UV. Skin type downloaded from myuv.com.au/about-uv

Figure 1.6 Six Fitzpatrick's skin types

FRM means fractional radiofrequency microneedle device.

Global satisfaction means for the improvement of an appearance of acne scars and less side effects.

Month means 30-days period

Random Allocation Software means a computer program named Random Number Free.

RF means for radiofrequency.

SBR means sublative bipolar radiofrequency

SD means standard deviation

Sebumeter means a device for sebum measurement named Sebumeter® SM 815.

TEWL means transepidermal water loss

Visia is VISIA™ Complexion Analysis or VISIA®-CR.

CHAPTER 2

REVIEW OF RELATED LITERATURES

In this study, the researcher had reviewed research articles and involved studies as the following.

1. Acne Scars
    1) Pathogenesis of acne scars
    2) Classification of acne scars
    3) Grading of acne scars
    4) Treatment of atrophic acne scars
    5) Laser treatment and its history
        A. Ablative lasers
        B. Non-ablative lasers
        C. Fractional photothermolysis
2. RF technology and its role for the treatment of acne scars
    1) Sublative Bipolar Radiofrequency Treatment
    2) Fractional Radiofrequency Microneedle (FRM)

2.1 Acne Scars

2.1.1 Pathogenesis of acne scars

Acne vulgaris is the most common skin disorder seen in primary care offices today with significant associated morbidity. The pathogenesis of acne is complex and multifactorial. Recent advances in acne pathogenesis include theories regarding the sequence of events in acne formation, the functions of *Propionibacterium acnes*, Toll-like receptors (TLR) involvement, role of the sebaceous gland and factors influencing sebum production, such as androgen activity and follicular hyperkeratinization (Bellew, Thiboutot, & Del Rosso, 2011). These factors stimulate inflammatory processes in the follicles, resulting in perifollicular abscess formation (Kurokawa et al., 2009).

Acne vulgaris is characterized by areas of skin with seborrhea (scaly red skin), comedones (blackheads and whiteheads), papules (pinheads), pustules (pimples), nodules (large papules) and possibly scarring (Adityan, Kumari, & Thappa, 2009). Acne scars occur as a consequence of skin damage during the healing process of active acne. There is a significant correlation between the initial acne grade and the overall severity of acne scars (Layton, Henderson, & Cunliffe, 1994). Therefore, the volunteers should have received adequate treatment in the earlier stage of inflamed acne before they get more severe acne scars as a result.

2.1.2 Classification of acne scars

There are two major types of acne scars depending on whether there is overall gain of collagen (hypertrophic scars) or loss of collagen (atrophic acne scars) (Fabbrocini et al., 2010; Goodman, 2000). The majority of scars is the atrophic type and caused by inadequate collagen deposit in healing process.

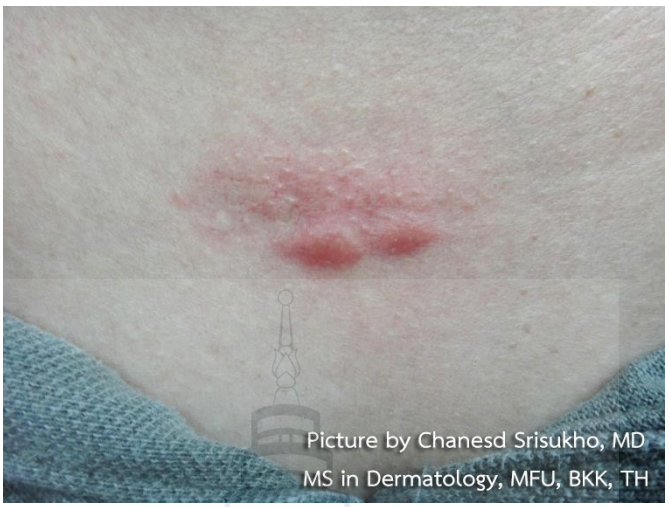


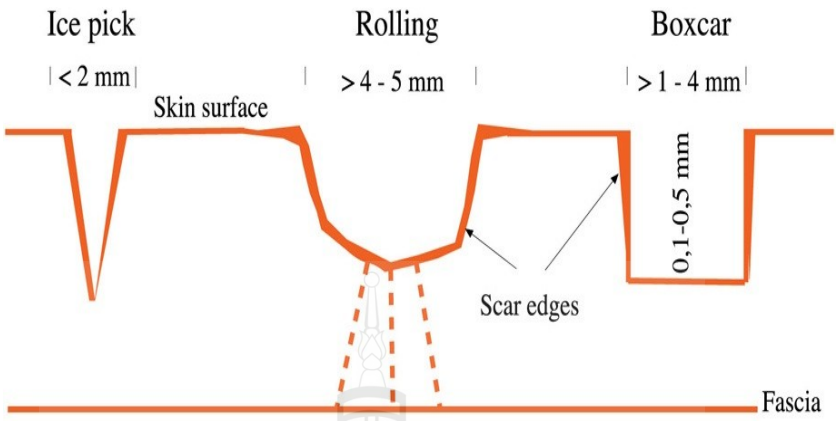
Figure 2.1 Hypertrophic scars

Physical acne scars are often referred to as “ice pick” scars because the scars tend to cause indentation in the skin's surface. Although quite rare, the medical condition atrophia maculosa varioliformis cutis also results in “acne-like” depressed scars on the face. Atrophic acne scars are classified into icepick, boxcar and rolling scars.

Ice pick scars are deep pits; those are the most common and a classic sign of acne scarring. They are v-shaped, 2mm punctiform scars.

Box car scars are circular to oval scars those usually occur on the temple and cheeks, and can be either superficial or deep. They are u-shaped, 1 to 4 mm in width and 0.1 to 0.5 mm in depth.

Rolling scars are scars those give the skin a wave-like appearance. They are m-shaped, 5mm or more in width. This type of scars usually has fibrotic tissue under the lesions.



Note. Modified from Fabbrocini et al. (2010)

Figure 2.2 Types of atrophic acne scar

Figure 2.3 Clinical pictures of atrophic acne scars

There are sub-types of atrophic scar, which are deep rolling scar, shallow rolling (saucer), box car, raised papule (bump), deep pit, shallow pit, and enlarged pore. However, we do not use this sub-classification in practice or in research. It is not so useful and it is difficult to differentiate them.

2.1.3 Grading of acne scars

Simple qualitative global acne scarring grading system is presented by Goodman & Baron (2006). There are 4 grades of acne scars. The description is in the picture below.

Grade	Description
1	Macular scarring or flat scarring that is characterized by flat areas of increased or decreased pigmentation visible from a distance of > 500 mm
2	Mild disease that is visible at distances of < 500 mm and can be covered by make-up. Examples include mild rolling acne scars
3	Moderate disease that is visible at ≥ 500 mm and is not easily covered with make-up or the normal shadow of a shaved beard. Stretching the skin can flatten the scar. Examples include more significant rolling scars, shallow boxcar scars and mild to moderate hypertrophic scars
4	Severe disease as in grade 3 but scarring is not flattened by stretching the skin. Examples include severe boxcar scars, deep divots, ice pick scars and hypertrophic keloid scarring (very raised/pigmented scars)

Source Goodman & Baron (2006)

Figure 2.4 Classification of acne severity

2.1.4 Treatment of atrophic acne scars

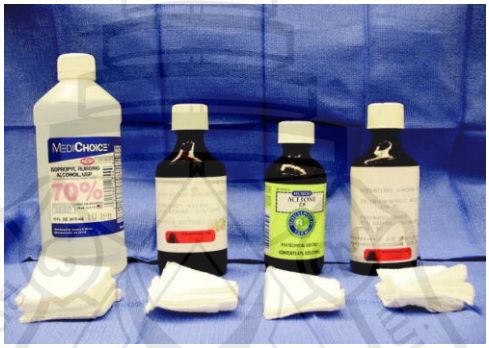
There is no gold standard treatment alone of atrophic acne scars. Because the problem is challenging, treatments are usually combined to get more satisfied result. One example is a study with triple therapy of dot peeling, subcision and fractional laser (Kang, Kim, Pyo, Park, & Kim, 2009).

2.1.4.1 Chemical Peeling

Chemical peeling is repeated light peels with variations of resorcinol, salicylic acid (Bae et al., 2013; Dainichi, Ueda, Imayama, & Furue, 2008), lactic acid (Sachdeva, 2010), trichloroacetic acid (Barikbin, Saadat, Akbari, Yousefi, & Toossi, 2012), or stronger glycolic acid peels. It was one of the oldest treatments of choice for early superficial scars.

Sometimes chemical peeling can use daily as home regimens, such as fruit acids and retinoic acids. Dermatologists use chemical peels for treatment of active acne also (Takenaka, Hayashi, Takeda, Ashikaga, & Kawashima, 2012). Some use them in combination with other acne scar treatments (Ayhan et al., 1998; Herbig et al., 2009). The process is after destroying the surface of the skin, the generation of new skin layers will be stimulated.

There have been great advances in peeling techniques. Long-term impressive improvement may occur (Jansen, 2000), but it is the least likely of the resurfacing techniques to improve the acne-scarred patient.



Source Herbig et al. (2009)

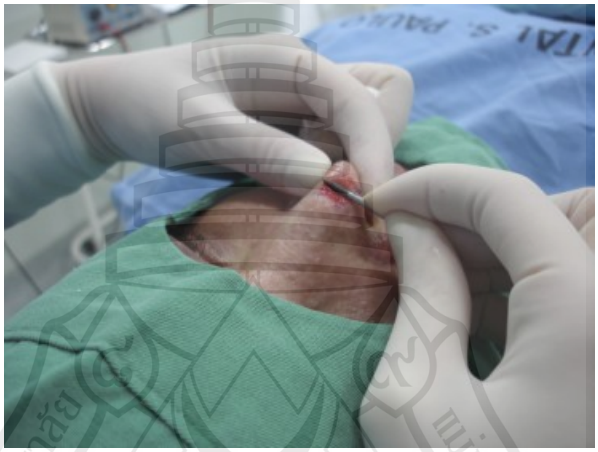
Figure 2.5 Shows solutions, from left to right, 70% ethyl alcohol, Jessner's solution, acetone, and trichloroacetic acid. Jessner's solution is one of the chemical peelings which contains salicylic acid, resorcinol, and lactic acid in 95% ethanol solution

2.1.4.2 Dermabrasion

Dermabrasion was the first advance in the treatment of acne scars (Blau & Rein, 1954; Johnson, 1957; Kligman & Strauss, 1956; Rattner & Rein, 1955). Dermabrasion is a good and safe technique to treat the scar of acne (Cai et al., 2005). It can be performed with a variety of devices. Both wet and dry sandpaper has been used (Pavlidis & Spyropoulou, 2012). Machine-driven techniques were introduced after. The procedure is taken into papillary dermis and reticular dermis. Dermabrasion may be performed on top of

CO_2 laser resurfacing and seems to speed healing in a similar fashion of erbium laser (Franz, 2001).

All dermabrasion techniques are at their best in the treatment of dishlike rather than ice pick scarring. They are best in fair skinned or very dark patients. Microdermabrasion utilizing small aluminum oxide crystals has been touted as being useful in the treatment of facial scarring. It is now used in many cosmetic clinics. The probable side effects are irregularity in skin color, post-inflammatory dyspigmentation.



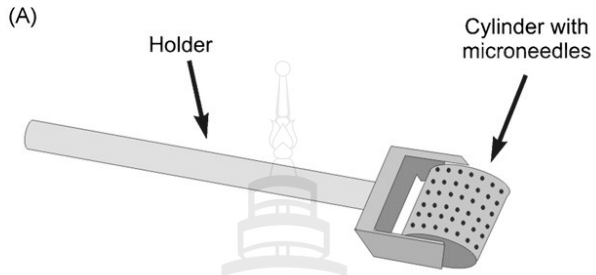
Source Bagatin, dos Santos Guadanhim, Yarak, Kamamoto, & de Almeida (2010)

Figure 2.6 Manual dermabrasion with diamond fraise in nasal area of 1 cm2 with depressed acne scars

2.1.4.3 Needling / Dermal Rollers

Needling is the method using a needle to make micronized injury to the skin (Fabbrocini, Fardella, Monfrecola, Proietti, & Innocenzi, 2009). Dermal rollers comprise of a series of fine, sharp needles to puncture the skin (Badran, Kuntsche, & Fahr, 2009; Doddaballapur, 2009; Schwarz & Laaff, 2011). It is a simple and relatively cheap modality that also can be used for transdermal drug delivery (Badran et al., 2009; Doddaballapur, 2009). The physician rolls this tool on the acne scar areas backward and forward with some pressure in various directions. The needles penetrate about 1.5 to 2 mm into the dermis. The skin develops multiple micronized bruises in the dermis which then initiate the complex

cascade of growth factors that eventually contribute to collagen production. Clinical results vary among patients. Skin needling can be safely performed on all skin colors and types due to lower risk of post-inflammatory hyperpigmentation.



Source Badran et al. (2009)

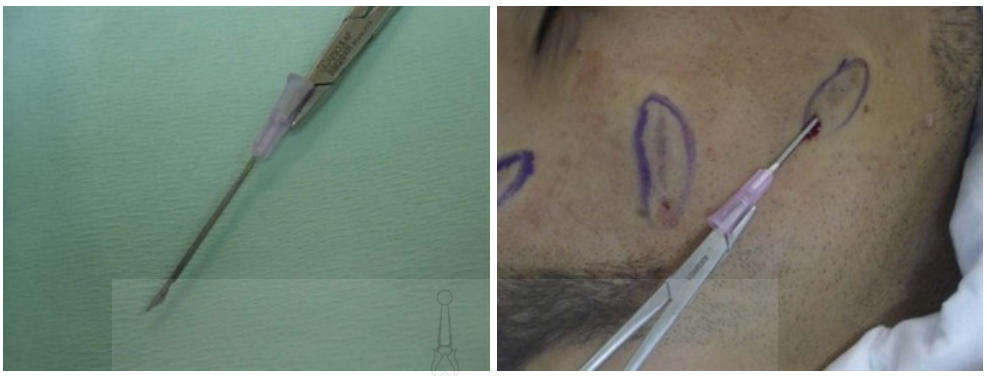
Figure 2.7 A Dermaroller®

2.1.4.4 Subcision

Subcision (Chandrashekar & Nandini, 2010) is an undermining of scars, breaking up the scar, detaching it, and releasing the surface from deeper attachments. This technique produces a pooling of blood under the defect and keeping the scar base from immediately reattaching to the surface layers. The subsequent organization of this blood clot induces longer term correction by the formation of connective tissue.

A probe, either a sharp hypodermic needle, Nokor needle (AlGhamdi, 2008), blade (Ayeni, Carey, & Muhn, 2011), or a blunt cannula, is inserted under the skin subdermal adjacent to the scar. An initial backward and forward motion much like tunneling is used. When the scar is almost freed from the surface, the direction is changed. Subcision may be combined with other treatment, such as subdermal implant (Balighi, Robati, Moslehi, & Robati, 2008).

The side effects are bruising and swelling present for 1-2 weeks. A range of responses ranging from partial to excessive is seen.



Source AlGhamdi (2008)

Figure 2.8 Nokor needle and the subcision procedure

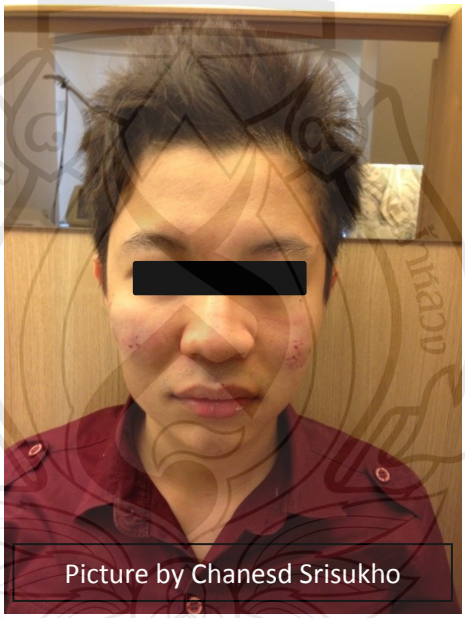
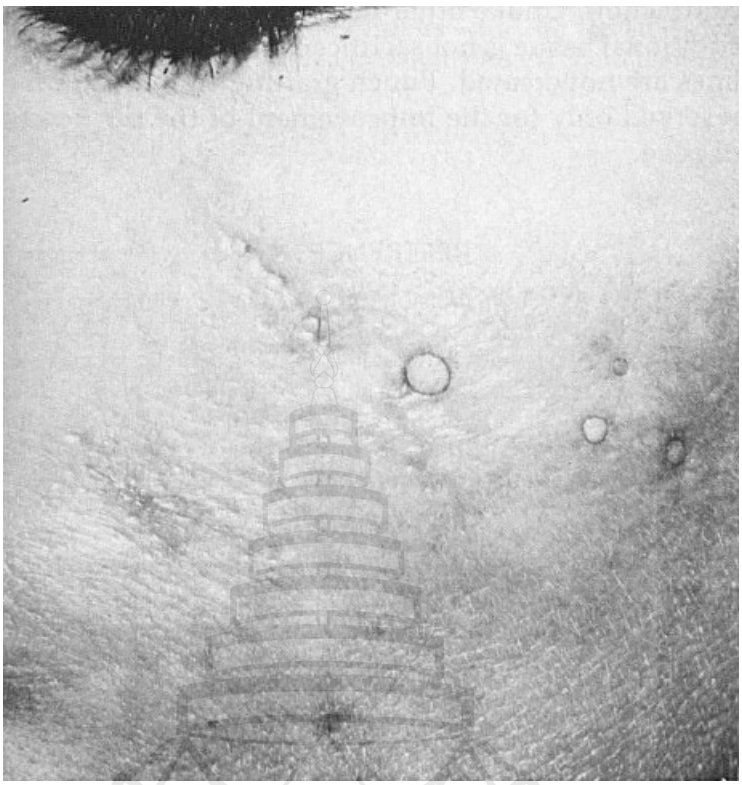


Figure 2.9 This picture shows immediate side effects in a patient after subcision with Nokor needle no.18

2.1.4.5 Punch Excision

Punch excision (Field, 2001) is a technique using a surgical knife or a special equipment to remove the scar tissue out of the skin. This may lead into the new scarring. So, it has been used for resistant scarring.



Source Dzubow (1985)

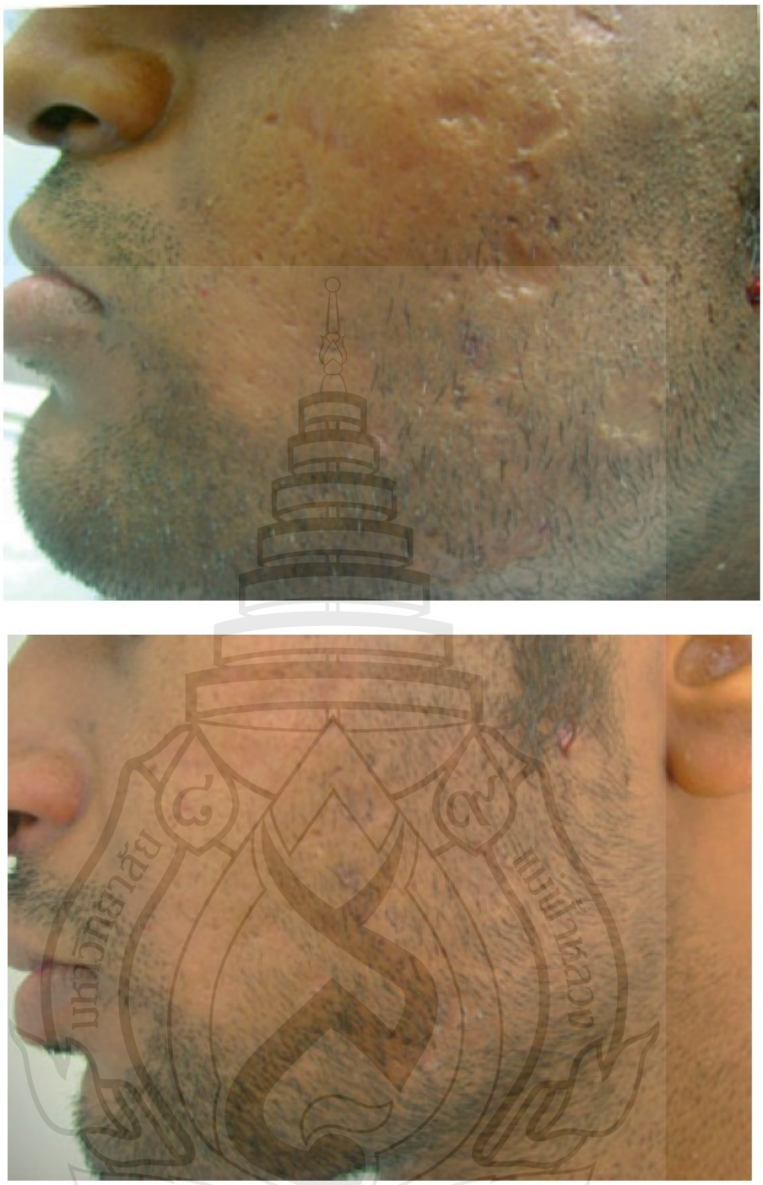
Figure 2.10 Scars after punch excision and punch grafting technique

2.1.4.6 Dermal Grafting

A dermal graft (Dzubow, 1985) is a strip or a section of dermis removed from one skin region and transplanted to replace lost dermis in another region. This permanent autologous collagen may be used to correct a linear or deep dermal scar. The common complication is cyst formation.

2.1.4.7 Hair transplantation

There is a new innovative study (Sarangal et al., 2012) describing a method of simply doing hair transplantation in acne scars and hence making them less visible and cosmetically well acceptable to the patient.



Source Sarangal et al. (2012)

Figure 2.11 Picture before and three months after hair transplantation in acne scars

2.1.4.8 Tissue Augmentation/Dermal Fillers

Tissue augmentation is the injection of a material into the skin. There have been many kinds of material used for scar augmentation, such as autologous fat tissue, dermalogen, bovine collagen, hyaluronic acid, and others. This technique is usually combined with other techniques to improve an appearance of acne scars. By the way, the result is varied. Some low molecular weight filler may be used (Hasson & Romero, 2010).

Source Hasson & Romero (2010)

Figure 2.12 A sample brand of dermal filler that was used for acne scar augmentation

2.1.4.9 Stem Cell Therapy

Most of the pioneering clinical work for this procedure is taking place in Japan. Stem cells are harvested from the connective tissue underneath the fat. They are incubated in the lab so that they multiply to numbers sufficient to inject underneath the skin. As stem cells, they would ordinarily travel through the bloodstream to their destination, building connections with surrounding cells to form fatty tissues. Japanese doctors are using the technique for treating not just acne scars but also for filling in frown lines and wrinkles and for breast augmentation.

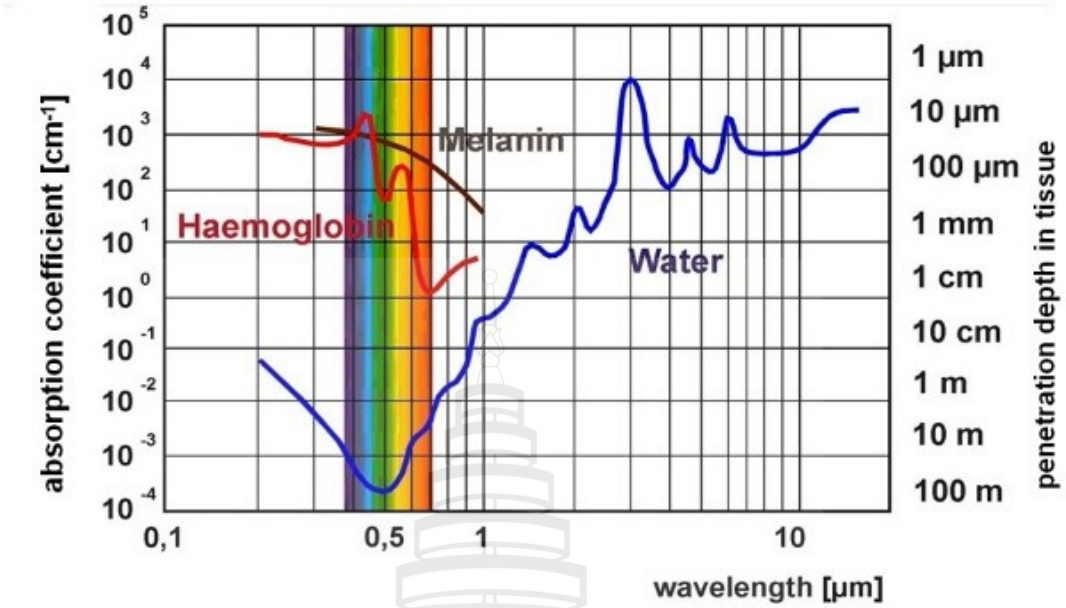
2.1.5 Laser treatment and its history

A laser device emits light through a process of optical amplification based on the stimulated emission of electromagnetic radiation. This term originated as an acronym for Light Amplification by Stimulated Emission of Radiation.

The theory of selective photothermolysis (Anderson & Parrish, 1983) lead in to the development of laser. It refers to the precise targeting of a structure or tissue, called chromophore, by using a specific wavelength of light with the purpose of absorbing light into that particular target area. The energy is directed into the target area, generating sufficient heat to damage the target while allowing the surrounding area to remain relatively unaffected (Zhang J. Z., Zhang, X. X., & Audette, 2011).

2.1.5.1 Ablative lasers

The first ablative laser for skin resurfacing was carbon dioxide (CO_2) laser (Garrett, Dufresne, Ratz, & Berlin, 1990). Carbon dioxide laser emits light at a wavelength of 10,600 nm. Another ablative laser resurfacing is erbium YAG laser (Er:YAG) (Teikemeier & Goldberg, 1997) with a wavelength of 2940 nm. Both of them have the same chromophore which is water in patient's cells. Energy is preferentially absorbed and creating rapid heating and vaporization of tissue. Due to the fact that the wavelength of the Er:YAG laser (2940 nm) is more closely approximates the absorption peak of water (3000 nm) than the CO_2 laser (10,600 nm), nearly all of the energy is absorbed in the epidermis and papillary dermis, yielding superficial ablation and less underlying thermal damage.



Note. Frontiers in Guided Wave Optics and Optoelectronics, Book edited by: Bishnu Pal, ISBN 978-953-7619-82-4, pp. 674, February 2010, INTECH, Croatia, downloaded from SCIYO.COM

Figure 2.13 Absorption and penetration depth in water and other biological tissue constituents for different wavelengths

Both ablative lasers produce improvement of scars by inducing new collagen formation beneath the scar and by reducing the shoulder of the scars. Improvements in the appearance of acne scarring after a single CO_2 laser resurfacing treatment were noted to be 69% at one month after the treatment. Prolonged clinical and histologic effects from CO_2 laser resurfacing of atrophic acne scars continued up to 18 months after the treatment, suggesting that dermal remodeling and new collagen formation occur long after laser resurfacing (Walia & Alster, 1999). A systematic review of the previous studies shows the improvement of facial acne scars ranging from 25% to 81% for ablative CO_2 laser and from 50 to 70% for ablative Er:YAG laser (Jordan et al., 2000).

Though ablative lasers have been considered as gold standards for skin resurfacing, adverse effects such as erythema, swelling, and even dyspigmentation, hyperpigmentation and hypopigmentation were reported, especially in patients with darker

skin. Some studies noted that the hyperpigmentation side effect occurred over 40% (Alster & Tanzi, 2003).

2.1.5.2 Non-ablative lasers

Because ablative laser treatments gave high chance of some unwanted side effects, this came into the invention of non-ablative laser treatments (Chan, Ho, Yeung, Shek, & Chan, 2010).

There are many types of non-ablative lasers used to treat atrophic acne scars. For instance, the 1320-nm (Bhatia, Dover, Arndt, Stewart, & Alam, 2006) or 1064-nm Nd: YAG lasers (Friedman et al., 2004; Keller, Belda Junior, Valente, & Rodrigues, 2007), 1450-nm diode lasers (Tanzi & Alster, 2004), and the 585-nm PDL (Lee, Choi, Min, Yoon, & Suh, 2009), can reduce acne scarring without significant downtime because non-ablative devices coagulate dermal tissue in the absence of epidermal vaporization. The exact mechanism through which these lasers induce new collagen production is still unclear. Previous studies have shown that Nd: YAG laser treatment induces expression of several heat-shock proteins and Type I procollagen by dermal dendritic cells, thereby suggesting that activation of these cells may be the underlying mechanism for collagen deposition (Prieto, Diwan, Shea, Zhang, & Sadick, 2005). However, non-ablative lasers provide lower efficacies, with only about 20%-30% improvement and multiple treatments are required and. So, the era of non-ablative lasers has finally ended.

2.1.5.3 Fractional photothermolysis

In practice, ablative devices such as CO_2 laser and Er:YAG laser have significant downtime and adverse effects on patients. And the use of non-ablative selective photothermolysis lasers has resulted in less clinical efficacy. Fractional photothermolysis (FP) principle came up and produces arrays of microscopic thermal wounds, called microscopic treatment zones (MTZs) at specific depths in the skin. The uninjured surrounding tissue serves as a reservoir of cells that accelerates and promotes rapid healing. This technique increases the efficacy with the patients' faster recovery and a lower risk of side effects compared with the ablative resurfacing systems (Hantash & Mahmood, 2007; Jih & Kimyai-Asadi, 2008).

The first medical laser utilizing fractional photothermolysis is known as the Fraxel® which was developed by Reliant Technologies, Inc. (Mountain View, CA). The device uses an erbium fiber laser to deliver a microarray pattern to a target tissue. The laser

operates at a wavelength of 1,550 nm and targets water as a chromophore. Fraxel® is now widely used today. Because of its popularity, many Thai cosmetic offices use this 'Fraxel' name instead of actual name of their fractional laser procedures.

2.2 RF technology and its role for the treatment of acne scars

RF is non-ionizing electromagnetic radiation with the frequency range between 3 kHz and 300GHz.

Fractional bipolar radiofrequency (RF) has recently been introduced to improve the efficacy and reduce the side effect of fractional photothermolysis lasers. It is safe (Lee et al., 2011).

Compared with fractional photothermolysis lasers, RF technology is claimed to have two advantages as follows: 1. In contrast to most fractional photothermolysis lasers, RF is chromophore-independent; thus, it does not require absorption by any specific chromophore. Although the main chromophore targeted for the fractional photothermolysis laser in acne scar treatment is the water in the keratinocyte of dermis, melanin pigment in epidermis can also absorb light within a large spectrum, resulting in heat generation which brings about a rise in melanocyte activity (Cole, Hatef, Kaufman, & Pozner, 2009). Consequently, RF is expected to have a better safety profile for all skin types. 2. While with the fractional photothermolysis lasers, the depth of absorption can be varied depending on inconstant chromophore absorption, fractional RF can determine a more precise treatment depth, an area of coverage and the ratio of ablation and thermal zone to suit each patient's condition, skin type, the desired outcome of the treatment and tolerance of downtime depending on the program selected.

2.2.1 Sublative Bipolar Radiofrequency Treatment

It was the first introduced fractional RF device. The fractional resurfacing utilizing this RF device has been termed "sublative rejuvenation", which means low epidermal disruption with high dermal remodeling. The RF current flows via the skin between the electrode-pin rows. It generates fractional deep dermal heating in the region of the electrode matrix to induce skin injury and then elicits a wound healing response, thereby stimulating the remodeling of dermal collagen (Hruza et al., 2009). Assessment for improvement in skin

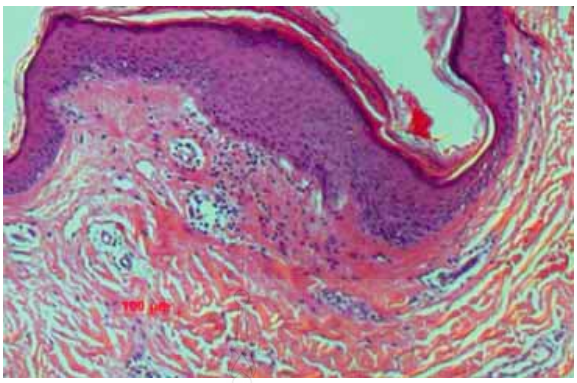
texture correlated with subjects' evaluation in Hruza's study was greater than 40% for approximately 50% of subjects. Active dermal remodeling process occur after exposure to fractional radiofrequency was driven by the collagen heat shock protein 47 (Hantash, Ubeid, Chang, Kafi, & Renton, 2009). The same study displayed an increase in reticular dermal volume, cellularity, hyaluronic acid, and elastin content within 10 weeks after the treatment. These findings meant for neoelastogenesis and neocollagenesis. A marked induction of tropoelastin, fibrillin, as well as procollagens 1 and 3 was also observed within 28 days after the treatment. It is safe (Man & Goldberg, 2012).

In a study (Gold & Biron, 2012), subjects with mild to moderate acne scars received three treatments every four weeks using single pass of RF energy ranging from 32 to 56 mJ/pin. The analysis showed a significant reduction in the median ECCA grades at 1 month and 3 month follow-ups compared to baseline ($p < 0.0001$).

Compared to the previous successful fractional Erbium: Glass 1550 nm device, a fractional bipolar RF had similar effectiveness for the treatment of atrophic acne scars (Rongsaard & Rummaneethorn, 2014).

Source Avecinia Wellness Center (2013)

Figure 2.14 Sublative rejuvenation device



Source Hruza et al. (2009)

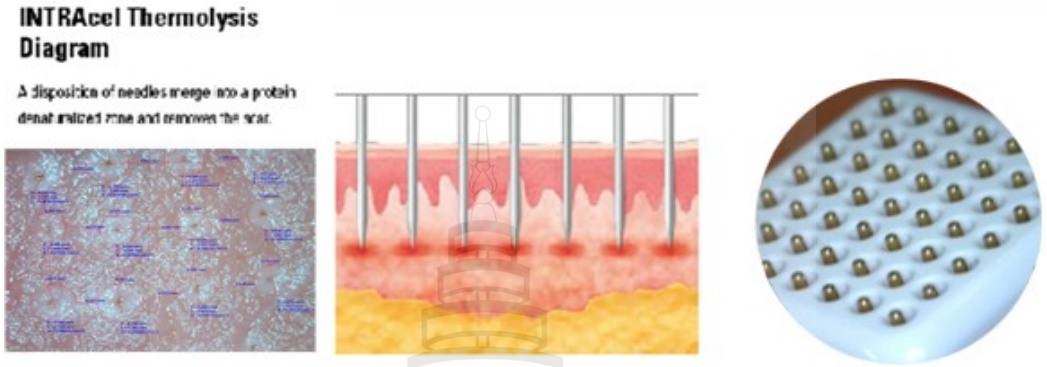
Figure 2.15 The picture demonstrates histologic finding of sublative rejuvenation device. Thirty six hours after treatment, note crust formation and deep dermal coagulation and remodeling

2.2.2 Fractional Radiofrequency Microneedle (FRM)

FRM is recently introduced (Hantash, Renton, Berkowitz, Stridde, & Newman, 2009) with the very fine microneedle equipped at the applicator to deliver radiofrequency into accurate depths of the skin. This kind of device was invented to overcome the weakness of sublative bipolar radiofrequency device. Although previous studies on fractional lasers have confirmed their clinical efficacy in acne scars and large facial pores, the efficacy of FRM treatment in such skin conditions has not been fully elucidated (Cho, Lee, Choi, Lee, & Oh, 2009).

Despite of a few studies, which are mostly from Asia, FRM is safe and effective (Kraimak, Rojanamatin, & Sayasonthi, 2012; Seo, Yoon, Kim, & Lee, 2012). There is a study comparing FRM and fractional CO_2 laser (Shin, Lee, Jung, & Lee, 2012). It indicated that FRM can be used for acne vulgaris patients and more convenient than fractional CO_2 laser resurfacing because of its short downtime. There are clinical studies suggest that FRM is a successful treatment for acne vulgaris (Lee et al., 2012), and large facial pores (Cho et al., 2012). Cho's study indicated that grade of acne scars and investigator global assessment of large pores improved in more than 70% of all patients. Combined treatment of FRM with human stem cells proved more effective than FRM alone (Seo, Kim, Lee, Yoon, &

Lee, 2013). Thus, this FRM can be used to transfer medication or cell therapy directly into the dermis.



Source Beijing Nubway S & T Development Co., Ltd. (2013)

Figure 2.16 The picture demonstrates histologic finding of sublative rejuvenation device. Thirty six hours after treatment, note crust formation and deep dermal coagulation and remodeling

2.2.3 Other benefits from RF and FRM devices

In practices, many physicians found RF technology useful not only for improvement of acne scars, large pores, but also effective for skin laxity or so-called rejuvenation (Alexiades-Armenakas, Rosenberg, Renton, Dover, & Arndt, 2010; Javate, Cruz, Khan, Trakos, & Gordon, 2011; SKINPECCABLE, 2013). RF devices have been known for nearly a decade for treatment of skin laxity (Alster & Tanzi, 2004). They were useful in treatment for midface and lower face laxity (Fritz, Counters, & Zelickson, 2004) which are common problems of aging; face and neck rhytids and laxity (Alexiades-Armenakas et al., 2013); thigh laxity (Kassim & Goldberg, 2013). Another study indicated FRM can use for the treatment of periorbital wrinkles (Kim, J. K. et al., 2013). There are many tradenames of RF devices in the market which claimed to be effective (Alexiades-Armenakas, Dover, & Arndt, 2008; Edwards, Massaki, Fabi, & Goldman, 2013; Royo de la Torre, Moreno-Moraga, Munoz, & Cornejo Navarro, 2011). They are differed in power source, tips, principles, but all has the same fractional radiofrequency principle. For skin

laxity treatment, patients immediately notice a microlifting retraction in the treated tissues according to the vectors mapped in the area (Rusciani, Curinga, Menichini, Alfano, & Rusciani, 2007). They also have less side effects, safe (Alexiades-Armenakas et al., 2008; Alexiades-Armenakas et al., 2013; Kassim & Goldberg, 2013), thereby substantiating the popularity of noninvasive rejuvenating procedures. One blinded, randomized study demonstrated 16% improvement in skin laxity relative to baseline for the FRM, compared with 49% for the surgical facelift (Alexiades-Armenakas et al., 2010).

What was about the effect on sebum reduction? Few studies about RF effect on sebum production were recorded. One prospective study from Korea demonstrated the sebosuppressive effect from a single FRM treatment (Lee, K. R., Lee, E. G., Lee, H. J. & Yoon, 2013). In that study, casual sebum level (CSL) and sebum excretion rate (SER) showed 30-60% and 70-80% reduction, respectively, at week 2 ($P < 0.01$), and remained below the baseline level until week 8. FRM in another study helped for apocrine function. It was effective for the treatment of primary axillary hyperhidrosis due to direct volumetric heating of the lower dermis (Kim, M., Shin, Lee, Kim, J. Y., & Oh, 2013).

One study found that fractional RF helped improving the skin quality in gene level (Rangarajan, Trivedi, Ubeid, & Hantash, 2013). It upregulated one of anti-senescence pathways, sirtuin gene family.

FRM could use to treat diseases: a study from Korea used it to treat recalcitrant sycosis barbae (Cho, Park, & Kim, 2013), a type of chronic infection at chin area.

CHAPTER 3

RESEARCH METHODLOGY

3.1 Study Design

Clinical randomized trail

3.2 Study Population and Sample Size

3.2.1 Study population

Volunteers, both male and female, age 18-55 years old, Fitzpatrick skin types III to IV, with acne scars

3.2.2 Sample size

Volunteers, ages 23-51 years old, Fitzpatrick skin types III to IV, with atrophic facial acne scars on both sides of cheeks, who desire to enroll in the study for treatments of their acne scars at Mae Fah Luang University Hospital, Bangkok

3.2.3 Sample Size Determination

The sample size was calculated from the formula of 2-mean dependence (Dattalo, 2008), using the results of measurement from the previous study of fractional bipolar radiofrequency device (Rongsaard & Rummaneethorn, 2014) at Mae Fah Luang University Hospital, Bangkok. Pre-test mean texture score in that study was 7.04 and post-test mean texture score was 4.34. The SD of difference was 1.92 and the *n* was 19.

From the formula

$$n = \frac{\sigma_d^2 (Z_{\alpha/2} + Z_\beta)^2}{d^2}$$

The SD of difference is 1.92, so $\sigma_d = 1.92$.

We assign $\alpha = 0.01$ (type I error) and $\beta = 0.005$ (type II error), so $\alpha/2 = 0.005$. Thus, from table of z score

$$Z_{\alpha/2} = Z_{0.005} = 2.576 \text{ and } Z_\beta = Z_{0.01} = 2.326$$

Pre-test mean texture score is 7.04 and post-test mean texture score is 4.34, so

$$d = |7.04 - 4.34| = 2.70$$

Thus,

$$n = \frac{(1.92)^2 (2.576 + 2.326)^2}{(2.70)^2}$$

$$n = 12.1513$$

However, n is a sample which needs to be a numeral. We make it round number as n = 13.

A drop-out rate of 20% was expected, so at least sixteen volunteers ($n = 16$) were needed.

3.3 Variable of the Study

3.3.1 Independent Variable

Fractional radiofrequency microneedle and sublative bipolar radiofrequency treatment

3.3.2 Dependent Variable

Improvement of the appearance of acne scar

3.3.3 Control Variable

Facial products those are moisturizer, sunscreen, and cleansing agent,

3.4 Research Equipment in the Study

3.4.1 Information sheet, as in appendix A (Thai and English)

3.4.2 Questionnaire, as RESEARCH PROFILE: (VOLUNTEER'S PART) in appendix B (Thai and English)

3.4.3 Informed Consent Form, as in appendix C

3.4.4 Study Record, as in appendix D and E (researcher's part and volunteer's part)

3.4.5 Side Effect Record, as in appendix D and E (researcher's part and volunteer's part)

3.4.6 Volunteer Satisfaction Survey for the Result of Treatment (two times at 1, 3 months after the last treatment session), as in appendix E

3.4.7 Fractional Radiofrequency Microneedle (INTRAcel^{TM})

The FRM device in this study was INTRAcel^{TM}; Jeisys, Seoul, Korea. It used bipolar radiofrequency technology to provoke plasma sparks, creating multiple partial thermal injury columns in the deep dermis.

3.4.8 Sublative Bipolar Radiofrequency Device (eMatrix^{TM})

The RF device in this study was eMatrix^{TM}; Syneron, Israel. It uses bipolar radiofrequency technology. Radiofrequency current flows between the positive and negative mini-electrodes. Control of this current allows varying degrees of tissue impact. In the space of no current flow a healing reservoir is obtained.

3.4.9 VISIA®-CR

Specifications of VISIA device are 12 megapixel resolution, automatic focus, automated white balance correction, facial positions: Left 37°, Center 0°, Right 37°, Multi-spectral Imaging (standard daylight fluorescent lighting, cross Polarized flash, and ultraviolet lighting)

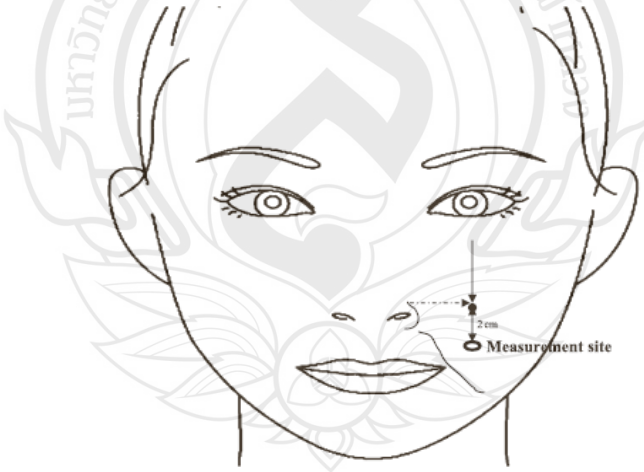
Figure 3.1 VISIA®-CR

3.4.10 Cutometer® MPA 580

Cutometer® MPA 580 is used to measure skin viscoelasticity. The device produces negative pressure, adjustable within the range of 20 to 500 mbar. During measurement, a selected point of the skin is drawn into the probe opening by negative pressure. The depth of skin penetration into the opening is immediately determined by a non-contact optical system, consisting of a light source and a receiver. These are two glass prisms, facing each other and leading the light from the transmitter to the receiver. The light beam intensity changes according to the depth of penetration in the skin. This device portrays the skin's ability to return to its original state, thus defining its elastic and plastic properties. Cutometer® MPA 580 allows four different methods of measurement according to the negative pressure applied. The most frequent method of measurement works with constant negative pressure. During measurement by this method, the skin is drawn into the probe by constant pressure. Subsequently, negative pressure is disconnected and the skin returns to its original shape.

To evaluate skin elasticity, measurements were taken using the Cutometer® MPA 580 (Courage + Khazaka Electronic GmbH, Ko¨ln, Germany) at the cheek (Ohshima et al., 2013) lateral to the nasolabial fold, in a room without direct sunlight (temperature, 20–22°C; relative humidity, 45–55%). All measurements were performed with subjects in a supine position.

Figure 3.2 Cutometer measure firmness and elasticity in this study



Source Ohshima et al. (2013)

Figure 3.3 An example picture shows site of the left cheek where the Cutometer® was applied for this study. We do the same in the right cheek.

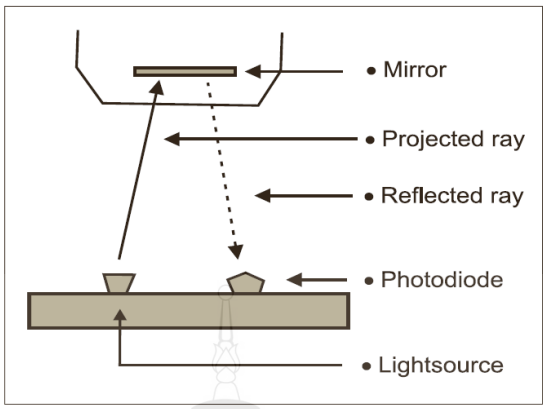
3.4.11 Sebumeter® SM 815

Sebumeter is a simple and quick method of sebum estimation (Pande & Misri, 2005). There are many useful applications of this device. In this study, sebumeter was used to measure sebum production which indicates sebaceous gland activity before and after treatment.

The Sebumeter affords direct photometric reading of the amount of lipids collected on a probe of opaque plastic strip after 30 seconds contact with the skin, and thus provides a measurement of the amount of lipids on the skin. This method of measuring sebaceous secretion, which has good repeatability and reproducibility, is based on the premise that lipids increase the transparency of opaque glass when in contact (Pierard, Pierard-Franchimont, Marks, Paye, & Rogiers, 2000; Segot-Chicq et al., 2007). The measuring head of the cassette with its special tape is placed on the skin. It is then inserted into a slot of the device, where the transparency is measured by a light source passing through the tape. A photocell measures the transparency. A microprocessor calculates the result, which is shown on the display in mg sebum/cm^2 of the skin.

The Sebumeter-cassette contains a matt synthetic tape, 0.1 mm thick. The measuring head of the cassette exposes a 64 mm^2 section of the tape, which is transported forward by a trigger at the side of the cassette for the next measurement. The measuring time of 30 seconds is controlled by a clock set in the device. Sebum is then determined as explained in the measurement principle above. The instrument has an accuracy of ± 5%. The reading of sebum also displayed as a number or as type of skin i.e. Dry; Dry/Normal; Normal; Normal/Oily; Oily.

In this study, the sebum measurement points for each half-face were (1) the point located 2 cm above the eyebrow in the lateral canthus line (2) the point located 1 cm above the midpoint of nose wing (alar). These points were applied from a previous study about sebum production (Kuldilokchai, 2012).



Source Pande & Misri (2005)

Figure 3.4 Mechanism of sebumeter

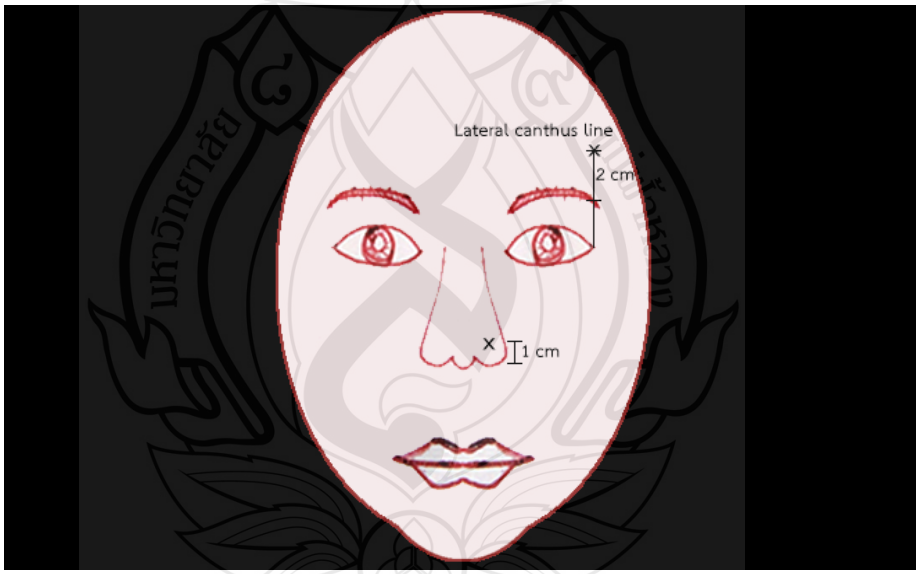


Figure 3.5 Sebum measurement points (x)

3.4.12 Facial products from the researcher

3.4.12.1 Moisturizer

We use Cetaphil® moisturizing cream.

3.4.12.2 Sunscreen

We use BR Derm® Facial Sunscreen.

3.4.12.3 Mild soap

We use VITARA® Facial Cleansing Foam Mousse.

Figure 3.6 Cetaphil® moisturizing cream, Galderma. One unit of this cream (15 g) was given to the volunteer after each session of treatment.

Figure 3.7 BR Derm® Facial Sunscreen with SPF 60 and PA++. Each volunteer received one unit of this sunscreen (15 g) after each session of treatment.

Figure 3.8 VITARA® Facial Cleansing Foam Mousse. This picture demonstrates total two bottles each volunteer received to use after sessions of treatment.

3.5 Selection Criteria

3.5.1 Inclusion Criteria

3.5.1.1 All subjects were required to sign an informed consent form of benefits, risks and possible complications of the treatment and publication of photographs.

3.5.1.2 Healthy volunteers with diagnosis of mild to severe atrophic acne scars on both sides of cheeks, according to Goodman and Barron classification

3.5.1.3 Both males and females, ages 18-45, Fitzpatrick skin types III to V

3.5.1.4 All subjects were able to participate in the treatment once every four weeks for three times and could be followed up at one and three months after the last treatment. Only volunteers who consented to longitudinal follow-up during the study period were enrolled.

3.5.1.5 All subjects were able to stop using own facial products during the study. They used the products given by the researcher only to prevent any bias that may occur.

3.5.1.6 All subjects did not receive any other treatment during the study.

3.5.1.7 All female of child-bearing potential had an acceptable form of birth control during the study.

3.5.1.8 Subject who has a present history of smoking and alcoholic drinking needs to stop smoking and drinking the study.

3.5.2 Exclusion Criteria

3.5.2.1 Subject has no required atrophic acne scars.

3.5.2.2 Subject has required scars but not on the cheeks.

3.5.2.3 Subject has an active inflammation, wound, pre-malignancy, malignancy, or other skin disease on top of the lesions. These conditions affect wound healing.

3.5.2.4 History of herpes simplex and herpes zoster on the face

3.5.2.5 Pregnancy and lactation

3.5.2.6 Serious concurrent medical illnesses such as heart disease, liver disease, kidney disease, hematologic disease, cancer, poorly controlled diabetic mellitus, severe hypertension, coagulopathy, photosensitivity, electrical implantation and immunocompromised state

3.5.2.7 History of microdermabrasion, chemical peeling, ablative and nonablative laser resurfacing, radiofrequency treatment or any treatment for acne scar within three months before the study

3.5.2.8 History of botulinum toxin or filler injection within six months before the study or permanent implant in the treatment area

3.5.2.9 History of poor wound healing, keloids and hypertrophic scars on the face

3.5.2.10 Use of systemic isotretinoin, vitamin E derivatives, hormones, herbs, prednisolone, antiplatelet and anticoagulant, and NSAIDS within one month before the study

3.5.2.11 Previous history of hypersensitivity to anesthetic creams

3.5.3 Discontinuation Criteria

3.5.3.1 Serious side effects occurring

3.5.3.2 The volunteer does not give the appropriate cooperation

3.5.3.3 Failure in follow-up appointment

3.5.3.4 The volunteer want to quit

3.5.3.5 Pregnancy, serious illness, and dying

3.6 Study Location

Mae Fah Luang University Hospital, Bangkok

3.7 Intervention

Half of the volunteer's face was treated with the fractional radiofrequency microneedle (INTRAcel™) and another half with the sublative bipolar radiofrequency device (eMatrix™). Both devices were approved by Thai FDA.

3.7.1 System Specifications of the Sublative Bipolar Radiofrequency Device (eMatrix™, Syneron)

Sublative RF Output Parameters

Total Radiofrequency energy:	up to 25 J/cm^3, up to 62 mJ/pin
Frequency	1 MHz
Programs' RF energy:	
Program A	10–30 mJ/pin, in 5mJ increments
Program B	32–48 mJ/pin, in 4mJ increments
Program C	50–62 mJ/pin, in 3mJ increments
Power range:	20–75 W (Impedance: 200–2,500 Ohms)
Max. Voltage output (applicator electrodes):	
	275 VRMS (without load)
Electrodes:	Two active and bi-polar applicator electrodes

Sublative iD Standard Treatment Tips	64 electrode pins
Disposable tip footprint:	12 x 12 mm
Distance between electrode pins	1.5 mm

Source Advanced Cosmetic Laser Center (2013)

Figure 3.9 Sublative Bipolar Radiofrequency Device (eMatrix™, Syneron) and its gun

3.7.2 System Specification of the Fractional Radiofrequency Microneedle Device (INTRAcel™; Jeisys000).

Applied Energy	RF 1 Mhz
Output Power	Mono-polar up to 700W and Bi-polar*: up to 700W

* In our study, we used the Bi-polar output to control the output power as the same type as in sublative bipolar radiofrequency device.

Spot Size (Treated Area)	1cm x 1cm / 0.2cm x 0.2cm
Disposable Tip Matrix	49 electrode needles, 4 electrode needles, and 7 electrode needles

Source Jeisys (2013)

Figure 3.10 Fractional Radiofrequency Microneedle Device (INTRAcel™; Jeisys, Seoul, Korea) and its tip

3.7.3 Parameter of the Treatment with Sublative Bipolar Radiofrequency Device (eMatrix™)

Treatment with Program C: Energy 62 mJ/pin x 2 passes at area of acne scars and 1 pass for area of normal skin

Estimated pulses for each volunteer were about 100 shots for the half side of the face per session. Overlapping area of each continuous shot was less than 20%. (The energy would be adjusted in mentioned range according to the severity of atrophic acne scar, reaction of the volunteers' skin, volunteer tolerance, and volunteers' skin types to make the best treatment for each volunteer and each session.)

3.7.4 Parameter of the Treatment with Fractional Radiofrequency Microneedle Device (INTRAcel™)

Its tip for this study has 49 microneedle electrodes in an area of 1 cm^2 and deployed into the deep dermis. The entire needle electrode is nonconductive expect the tip, beginning 0.3 mm from the distal end, to protect from radiofrequency heating at the insertion site.

Radiofrequency energy is emitted to the dermis 0.2 seconds after microneedle insertion. The radiofrequency energy delivery durations differ according to energy levels.

In this study, a 1.5-mm depth needle at a power of 500 W (maximum power 700 W) was used for treatment of all the face except forehead and scar area. The forehead area was treated with 0.8-mm depth needle because of its thin skin width. At the second pass for acne scar area, a 2.0-mm depth needle was used.

We used level 4 energy (the maximum level is 7), bipolar mode.

Estimated shots for each volunteer were about 200 shots for the half side of the face per session. Lesion was treated for 2 passes at area of acne scars and 1 pass for area of normal skin. Overlapping area of each continuous shot was less than 20%.

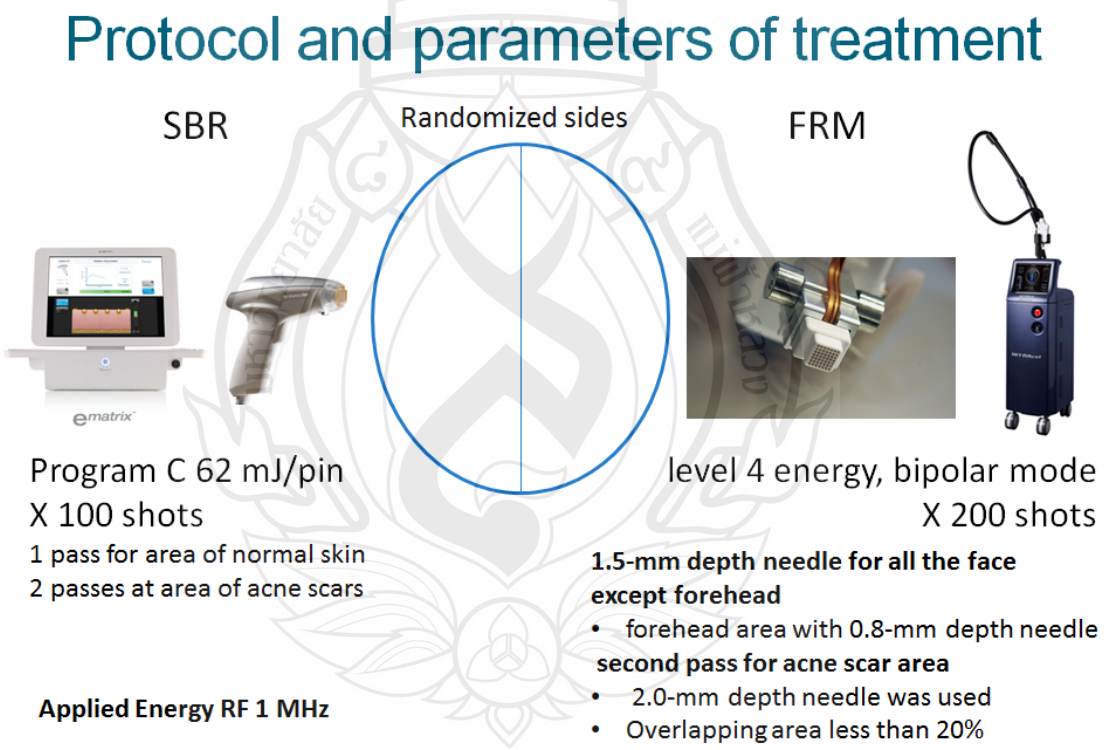


Figure 3.11 Protocol and parameters of treatments

3.8 Study Procedures

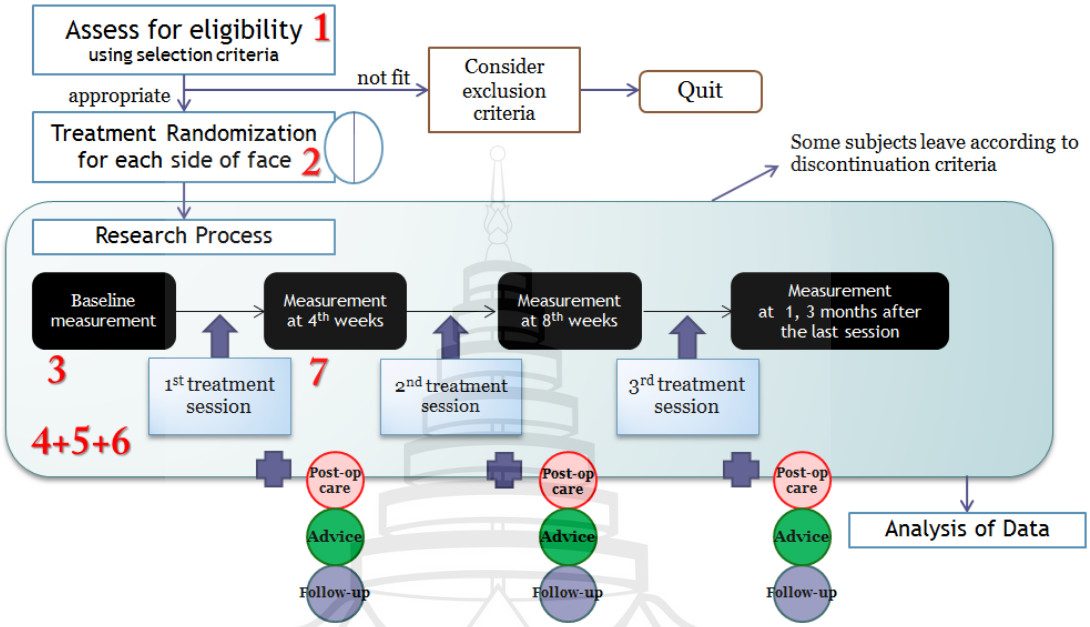


Figure 3.12 Research Design

3.8.1 Research subject selection

3.8.1.1 Advertisement for research application was performed via posts for patients in the hospital, and areas outside. Some volunteers were from private connection according to the researcher without any personal benefits.

3.8.1.2 Subjects were selected to enroll in the study according to the inclusion criteria

3.8.1.3 Exclude subjects according to the exclusion criteria

3.8.1.4 Considered volunteers were advised for research objectives, methodology, benefits, side effects which may occur, and other research information as in appendix I

3.8.1.5 All curious questions were discussed and answered completely by the researcher.

3.8.1.6 The volunteer needs to complete the research profile as in appendix II

3.8.1.7 Informed consent of the volunteer

3.8.1.8 The researcher recorded every performed task according to Checklist for the first visit in appendix IV. He needed to make acne scar examination and wrote it down in Classification of acne severity form, also in appendix IV.

3.8.2 Generate randomization sequence

3.8.2.1 A dermatologist who was not involved in the study generated block randomization sequence which randomly determined which side of the volunteer's face to be treated with the fractional radiofrequency microneedle and which side with the sublative radiofrequency device by using "Random Allocation Software" and conceals the sequence in opaque envelopes.

3.8.2.2 Because this study was split-face. We had twenty volunteers recruited. There were forty faces of them.

3.8.2.3 The dermatologist used Random Number Free program of GK soft to randomize numbers. It is a program which can be downloaded for free from the URL http://winapps.lisisoft.com/seller/gk-soft.html.

3.8.2.4 He randomized twenty Arabic numbers from minimal 1 to maximal 1000. Twenty of these randomized numbers were referred to twenty of our volunteers according to first-come, first-served order.

3.8.2.5 Twenty numbers would be interpreted individually as if it was in the first 1 to 500 or it was in the last 501-1000. If it was in the first 1 to 500, it meant that the left face of the volunteer should be treated with FRM and another side with sublative bipolar radiofrequency device. If it was in the last 501 to 1000, it meant that the left face of the volunteer should be treated with sublative bipolar radiofrequency device and another side with FRM.

3.8.2.6 This method of randomization gave 50/50 chance for which one of two treatments the volunteer get.

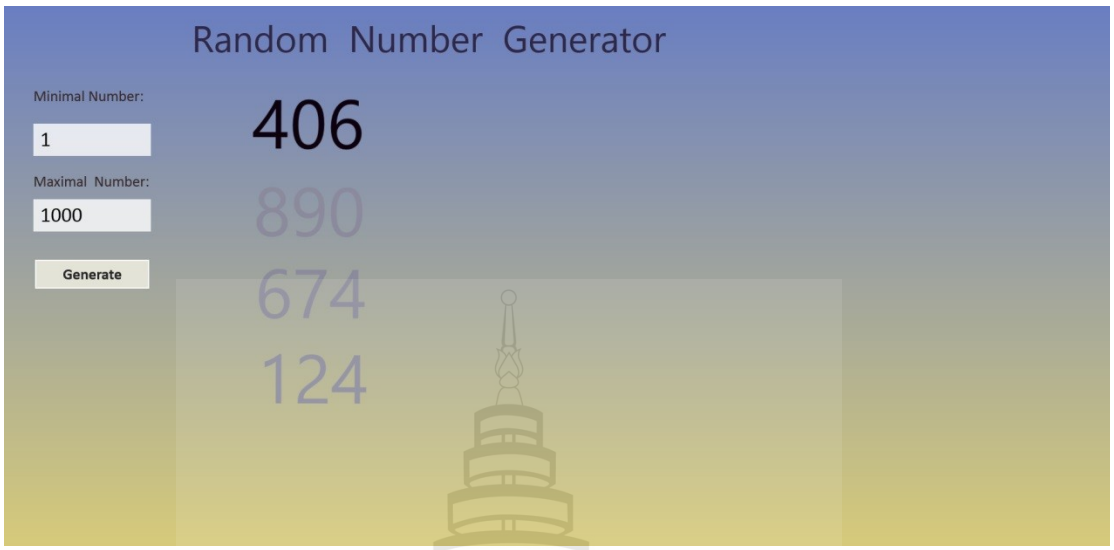


Figure 3.13 This is Random Number Free program.

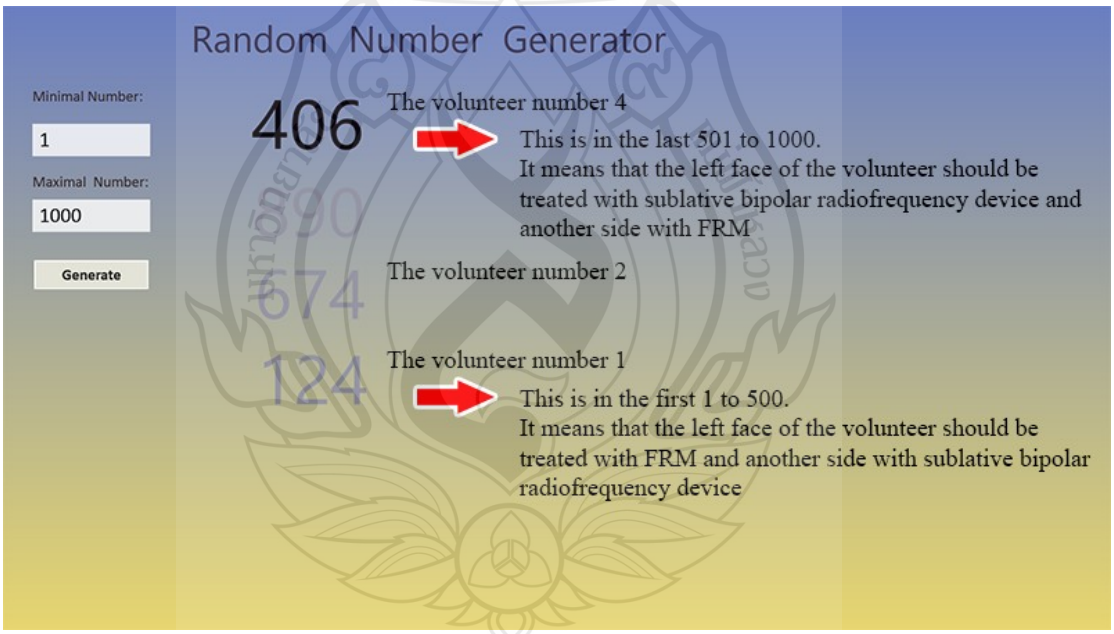


Figure 3.14 This is an example of randomization process.

3.8.3 Volunteer evaluation and scoring

Before each treatment,

3.8.3.1 The researcher took photographs of each volunteer using VISIA® Complexion Analysis System (Canfield, Fairfield, NJ) in three facial positions: Left 37°, Center 0°, and Right 37° positions. The volunteer needed to close his/her eyes during photographs were taking.

3.8.3.2 The researcher measured the viscoelasticity of both cheeks of the volunteer by using cutometer.

3.8.3.3 The researcher measured the sebum production by using sebumeter.

3.8.3.4 Two independent physicians made dermatological assessment for classification of acne severity (Goodman & Baron, 2006) as macular, mild, moderate, or severe acne scars. This is for the first time only and then at 1, 3 months after the last session of treatment.

3.8.3.5 The researcher recorded every performed task according to Checklist for the first visit in appendix IV.

3.8.4 Treatment process

3.8.4.1 Before the treatment procedure, volunteers' faces were cleansed with a mild soap.

3.8.4.2 Because our study is about dermal procedures. At least 2.5 grams of anesthetic cream (2.5% lidocaine/prilocain, EMLA, APP Pharmaceuticals) per 25 cm^2 was applied to the treatment area with occlusion for at least one hour (Friedman, Mafong, Friedman & Geronemus, 2001). Normally the facial skin has a surface area of about 630-850 cm^2. This topical application is along with the indications and usage of the drug. The multiple-layered technique was applied for the skin.

3.8.4.3 After that, the anesthetic cream was removed and the face was cleaned with 70% alcohol. The skin was then dried with a non-humid dryer for five to ten minutes, until the skin was completely dry.

3.8.4.4 The researcher did the intervention on each side of the volunteers' cheeks according to the prepared randomized sequence.

3.8.4.5 The treatment was performed as a session once a month for three months consecutively. The devices treating each side of the face were the same devices in three treatment sessions.

3.8.5 Immediate care after treatment

3.8.5.1 The researcher evaluated the volunteers immediate post-treatment period about their discomfort, tenderness, burning sensation, erythema, and other side effects.

3.8.5.2 The researcher applied cold compression to relieve the volunteers' burning sensation.

3.8.5.3 After the recovery period, the researcher gave the volunteer facial products.

3.8.6 Advice for volunteers

3.8.6.1 Avoid makeup for 24 hours. In the first 24 hours after each treatment, wash the face with pure sterile water.

3.8.6.2 After 24 hours, apply the moisturizer at least twice daily, apply sunscreen in the morning and wash their face with mild soap twice daily.

3.8.6.3 Use of physical sun barriers, such as umbrella and hat, and totally avoid sun exposure for at least 1-2 weeks after the treatment.

3.8.6.4 The volunteers were given a "side effect record" sheet to record the side effects of the treatment. If the volunteers experienced any severe side effects, they had to go to see the researcher before the next treatment session. The researcher would treat the side effects.

3.8.7 Follow up

3.8.7.1 One and three month after the last treatment session, the researcher took a photograph of each volunteer by using VISIA® Complexion Analysis System.

3.8.7.2 The researcher used cutometer to measure viscoelasticity of both volunteer's cheeks at each follow-up time.

3.8.7.3 The researcher used sebumeter to measure sebum production of both volunteer's face at each follow-up time.

3.8.7.4 The researcher and the volunteer completed their forms, as in appendixes. Volunteers' satisfaction was evaluated twice at one and three months after the last treatment.

3.9 Outcome Measurement and Data Collection

3.9.1 Subjective measurement of improvement of acne scars

Three physicians assessed the subjects at different times for their improvement of acne scar. Clinical improvement scores were then used to calculated acne grades at baseline and follow-ups. Comparisons between two sides of face at the same time were evaluated at 1, 3 months after the last treatment. Also comparison in the same side of face was compared before and after the treatment.

3.9.2 Objective measurement of improvement of other aspects

Objective assessment for this study was focused because of its reliability. Cutometer could give us score of skin viscoelasticity. Sebumeter could give us score of sebum production. So, with VISIA complexion analysis system and other measurements we can portray the improvement of acne scar and effects on other aspects such as skin laxity and sebum production.

3.9.3 Volunteer assessment of improvement of acne scars

Volunteers were asked to help evaluate the improvement of acne scars and effects on other aspects such as skin laxity and sebum production by using survey questionnaire. The survey occurred twice times at one and three months after the last treatment session.

3.9.4 Measurement of Side Effects

Physicians evaluated for immediate side effects. Volunteers also helped us by telling side effects they experienced at home.

3.10 Data Analysis

The researcher did the following at significance levels of p-value < 0.05,

3.10.1 Volunteers' research profile data

Made descriptive statistical analysis to provide descriptive information, such as percentages, means, modes, medians, ranges, standard deviations

3.10.2 Improvement scoring and comparative scoring for acne scar appearance at times

Because these two are subjective measurement, the reliability is low. We use student tests or R-by-C crosstabs statistical analysis

3.10.3 Comparing acne grades in one side of face before and after 3 sessions of treatment

3.10.3.1 In case there is normal distribution of data, we could use paired t-test statistics

3.10.3.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.4 Comparing acne grades between both sides of face at a single time

3.10.4.1 In case there is normal distribution of data, we could use student t-test statistics

3.10.4.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.5 Comparing scores from cutometer in one side of face before and after 3 sessions of treatment

3.10.5.1 In case there is normal distribution of data, we could use paired t-test statistics

3.10.5.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.6 Comparing scores from cutometer between both sides of face at a single time

3.10.6.1 In case there is normal distribution of data, we could use student t-test statistics

3.10.6.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.7 Comparing scores from sebumeter in one side of face before and after 3 sessions of treatment

3.10.7.1 In case there is normal distribution of data, we could use paired t-test statistics

3.10.7.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.8 Comparing scores from sebumeter between both sides of face at a single time

3.10.8.1 In case there is normal distribution of data, we could use student t-test statistics

3.10.8.2 In case data is not along with normal distribution of data, Wilcoxon Match Pair sign rank test would be used.

3.10.9 Side effects

Use descriptive statistical analysis

3.10.10 Volunteer's Satisfaction

Use descriptive statistical analysis

3.11 Ethical Considerations

This study was strictly followed Good Clinical Practice (GCP) guidelines. Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. It is provided by International Conference on Harmonisation (ICH).

Good Clinical Practice guidelines include protection of human rights as a subject in clinical trial. It also provides assurance of the safety and efficacy of the newly developed compounds.

Good Clinical Practice Guidelines include standards on how clinical trials should be conducted; define the roles and responsibilities of clinical trial sponsors, clinical research investigators, and monitors.

For general understanding, considerations were as followed.

1. Because RF treatments for acne scars are now competitive and their costs are high, this study aims to compare the clinical efficacy of fractional radiofrequency microneedle and sublative bipolar radiofrequency device. It is useful and lead into the people's cost-benefit consideration. Meanwhile, side effects of both treatments will be recorded.

2. The study needs to conduct in human to see clinical efficacy. Reviewed articles indicate success of these treatments, but the comparative study has been rarely performed yet.

3. FRM and sublative bipolar radiofrequency device are USFDA and Thai FDA-approved for treatment on the facial skin. They are both very safe and able to use for treatment of acne scars. There might be some side effects after the treatment, such as pain, discoloration, swelling, etc. However, these side effects are not lifelong or life-threatening.

After subjects enroll in the study due to the selection criteria and are excluded by exclusion criteria, their faces will be divided into two groups. One group will be treated with FRM, another with sublative radiofrequency microneedle.

4. Volunteers may face different appearance of both facial sides after each session of treatment. The researcher will inform them for this complication and reassure they exist for short amount of time.

5. Subjects completely understand research objectives, methodology, and probable side effects.

6. Subjects write informed consent before entering into the study. They can leave anytime without any disadvantage.

7. There is no interest between the researcher and subjects.

8. Subjects' number is according to the size calculation. We use a small sample size just for the need of the study. Safety is controlled more easily in the small size than large size.

9. The researcher cannot guarantee results. The purpose of acne scar treatment is subjects' own desire. In any case problem occurs; the researcher will help and pay responsibility with subjects as much as possible.

3.12 Obstacles and Strategies to Solve the Problems

This study could not use double-blind method. The perception of volunteers in both FRM and sublative bipolar radiofrequency treatment were totally different. We prevented this co-intervention bias by using independent masked assessors and multiple outcome measurements which helped improving accuracy.

CHAPTER 4

RESULTS

4.1 Demographic Information

Seventeen volunteers, 8 men and 9 women, with atrophic acne scars on both sides of cheeks were enrolled in the study. No one was discontinued from the study. Mean age was 29.9 years and standard deviation was 7.85. Most of volunteers had Fitzpatrick skin type IV and the grading of acne scars were mostly III and IV. The details are as in followed table 4.1.

Table 4.1 Demographic Data: age, skin type and grading of acne scars

	Number of volunteers
Age (years)	
21 – 35	14
36 – 50	2
More than 51	1
Fitzpatrick's skin type (Sachdeva, 2009)	
III	6
IV	8
V	3
Grading of acne scars (Goodman & Baron, 2006)	
Grade II	2
Grade III	8
Grade IV	7

4.2 Outcome measurement

4.2.1 Subjective measurement of improvement of acne scars

In each volunteer and in each side of face, we brought his photos at baseline to compare with 1-month follow-up and baseline to compare with 3-month follow-up. So, one had two pairs of pictures for each side of face. Evaluators, three masked dermatologists, could not identify which comparison belongs to which treatment. And it was not in a principle that one side of every volunteer is treated with the same type of treatment. Actually, each device was randomized selected for each side of face before the beginning of treatments. They did neither know whenever pictures were taken. Evaluators saw these pictures of comparison. They were asked to pay attention to accuracy and details. Thus, they made an evaluation thoroughly in different points of time, totally separate from each other. Raw evaluation was about improvement of acne scars ranged from -3 to +3, and other side effects such as redness, hyperpigmentation, hypopigmentation, and more acne occurrence were recorded. +1, +2, +3 meant 20%, 40%, 60% increases, in order, for improvement or occurrence for side effects. -1, -2, -3 meant for 20%, 40%, 60% decreases, of clinical result, or disappearance for side effects. Median results from three evaluators were used to calculate as post-treatment grades. +1, +2, +3 clinical improvement score were converted to +0.5, +1, +1.5 grade improvement in order. Side effects from this process will be discussed later along with volunteer's side effect records.

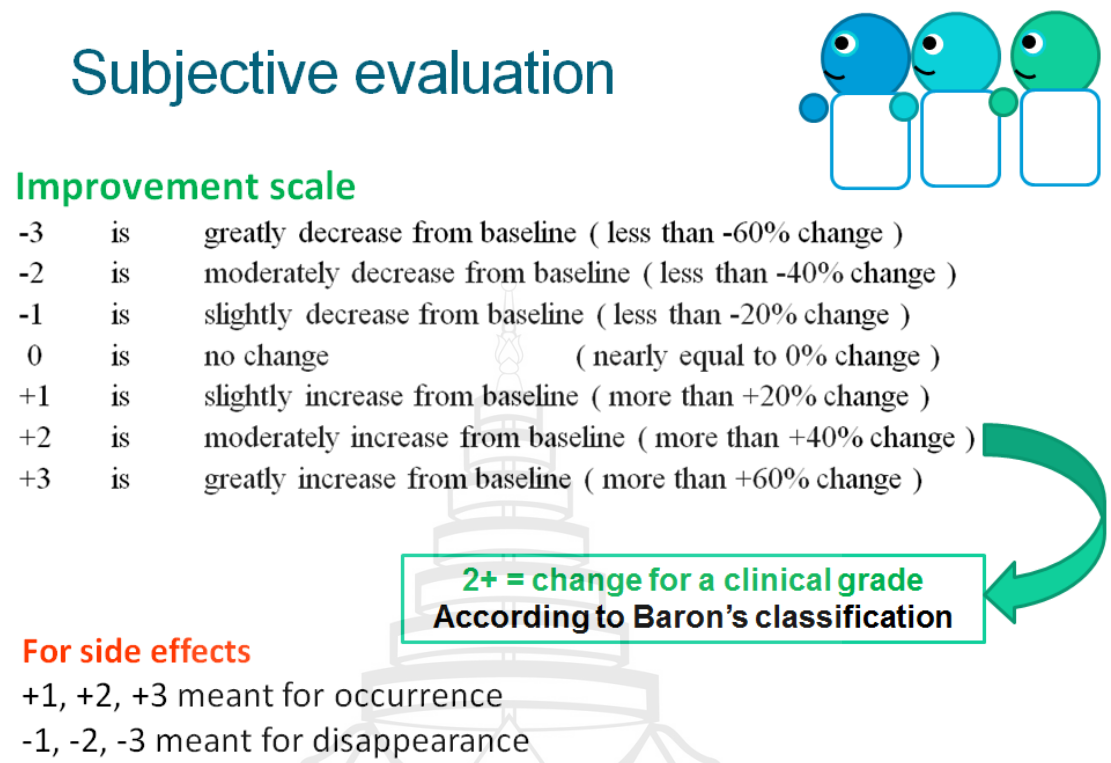


Figure 4.1 How was the process of the subjective measurement for improvement of acne scars?

Figure 4.2 showed how pictures were paired and rearranged. Evaluators looked for improvement of acne scars, and other side effects such as redness, hyperpigmentation, hypopigmentation, and more acne occurrence. It took time for thirty to ninety minutes for each evaluator to complete the evaluation. Median clinical scores were used to calculated mean clinical improvement. For side effects, median scores were used.

Table 4.2 Median results for improvement of acne scars from three evaluators

Volunteer Number	FRM		Sublative Bipolar Radiofrequency	
	f/u 1 month	f/u 3 month	f/u 1 month	f/u 3 month
1	+2	+2	+3	+2
2	+2	+1	+1	+2
3	+3	+2	+2	+2
4	+1	+1	+1	+1
5	+2	+3	+2	+2
6	+1	+2	+1	+2
7	+1	+2	+2	+2
8	0	+1	0	+1
9	0	+1	+2	+2
10	+2	+2	+1	+1
11	+1	+1	+1	+1
12	0	0	0	+1
13	+1	+1	+1	0
14	+1	+1	+2	0
15	+1	+1	+2	0
16	0	0	+1	0
17	+2	+2	+2	0
Mean	+1.1765	+1.3529	+1.4118	+1.1176
SD	0.8828	0.7859	0.7952	0.8575

Mean clinical improvement scores of FRM were +1.1765 (SD = 0.8828) at 1 month follow-up and +1.3529 (SD = 0.7859) at 3 month follow-up. And mean clinical improvement scores of sublative bipolar radiofrequency were +1.4118 (SD = 0.7952) at 1 month follow-up and +1.1176 (SD = 0.8575) at 3 month follow-up. These clinical improvement scores were not in normal distribution.

When clinical improvement scores of both treatments were compared in the same points of time at 1-month follow-up and 3-month follow-up, there was no statistically difference. Wilcoxon Matched-Pairs Signed-Ranks tests were used.

Table 4.3 Clinical improvement scores with Wilcoxon Matched-Pairs Signed-Ranks test to compare between scores at baseline and follow-ups

Mean clinical improvement scores		Z	p-value (2-tailed)
FRM and SBR	1 month f/u to baseline	-1.155[n]	0.248
	3 month f/u to baseline	-1.155[p]	0.248

Note. n. Based on negative ranks.
p. Based on positive ranks.

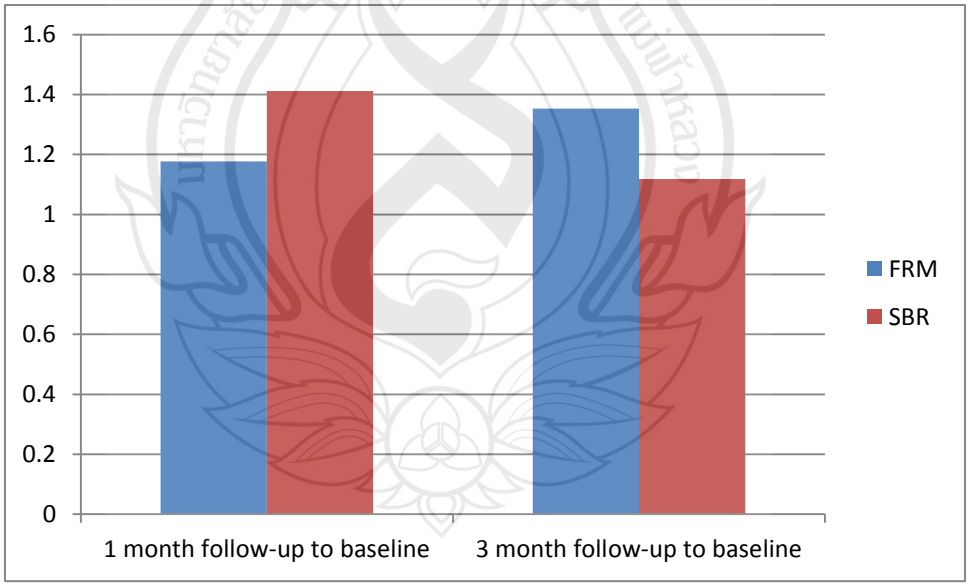


Figure 4.2 Clinical improvement scores of acne scars compared at 1 month follow-up to baseline; at 3 month follow-up to baseline

From clinical improvements scores we had got, we tested them by independent-samples Kruskal-Wallis test to investigate the relationship between severity of acne scars and improvement score after treatment. They were not related for FRM and SBR at 1 month and 3 month-follow ups (p-value = .481, .346, .736 and .789 in order)

We then use these improvement scores to calculate as post-treatment grades. The results were as followed.

Table 4.4 Acne grading from physician's assessment

Number	Acne grading from physician's assessment					
	FRM			SBR		
	Baseline	1-month f/u	3-month f/u	Baseline	1-month f/u	3-month f/u
1	3	2	1.5	3	2	2
2	3	2	2.5	3	2.5	2
3	4	2.5	3	4	3	3
4	4	3.5	3.5	4	3.5	3.5
5	3	2	2	3	1.5	2
6	4	3.5	3.5	4	3	3
7	2	1.5	1	2	1	1
8	3	3	3	3	2.5	2.5
9	4	4	3	4	3.5	3
10	3	2	2.5	3	2	2.5
11	3	2.5	2.5	3	2.5	2.5
12	3	3	3	3	3	2.5
13	4	3.5	3.5	4	3.5	4
14	4	3.5	3	4	3.5	4
15	3	2.5	2	3	2.5	3
16	2	2	1.5	2	2	2
17	4	3	3	4	3	4
Max	4	4	3.5	4	3.5	4
Min	2	1.5	1	2	1	1
Mean	3.29	2.71	2.59	3.29	2.62	2.74
SD	0.69	0.73	0.75	0.69	0.74	0.83

In details, we saw improvement in 88.2% of all patients (15/17) for FRM side and improvement in 94.1% of all patients (16/17) for SBR side. Mean grading of FRM at baseline, 1-month and 3-month follow-ups were 3.29 (SD=0.69), 2.71 (0.73) and 2.59

(SD=0.75). And mean grading of SBR at baseline, 1-month and 3-month follow-ups were 3.29 (SD=0.69), 2.62 (0.74) and 2.74 (SD=0.83).

From these grades, statistics showed there was significant difference between baseline and follow-ups in both treatments.

FRM's grades between before and after treatment at one and three months were statistically different with p=0.001 and <0.001, correspondingly. There were statistical significance on SBR's grades at one month (p<0.001) and three month (p=0.002).

Compared at points of time at 1-month and 3-month follow-ups, we found no differences (p=0.257 at 1-month f/u and p=0.222 at 3-month f/u).

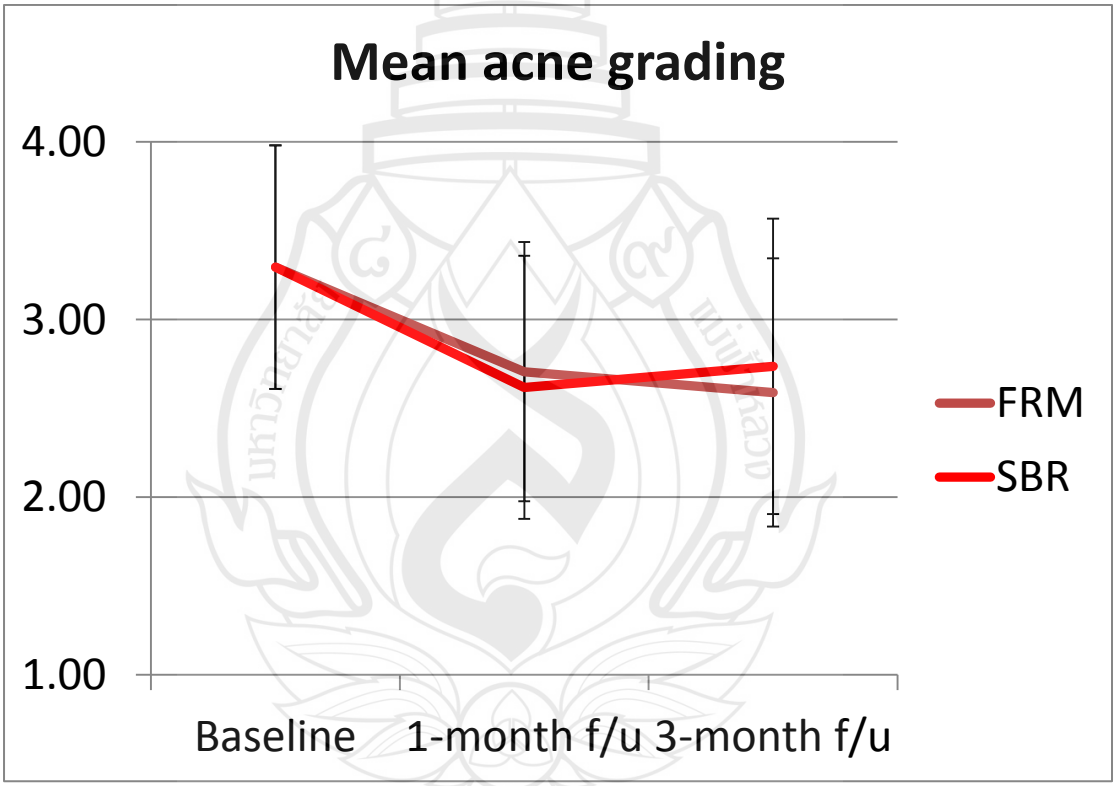


Figure 4.3 Mean acne grading at baseline and follow-ups

Evaluators also evaluated for side effects and found no statistic difference between two devices (p-value>0.05).

Details were mean acne occurrence of FRM at 1 month and 3 month follow-ups were -0.29 (SD = 0.69) and -0.06 (SD = 0.75); SBR's at 1 month and 3 month follow-ups

were -.024 (SD = 0.90) and 0.12 (SD 1.05). Mean redness of FRM were +0.41 (SD = 0.94) at 1 month follow-up and +0.47 (SD = 1.07) at 3 month follow-up; mean redness of SBR were +0.18 (SD = 0.88) at 1 month follow-up and +0.18 (SD = 1.13) at 3 month follow-up. Hyperpigmentation's mean scores in FRM side were +0.47 (SD = 0.62) at 1 month follow-up and +0.41 (SD = 0.62) at 3 month follow-up; +0.53 (SD = 0.51) at 1 month and +0.65 (SD = 0.70) at 3 month follow-ups for SBR side. Mean scores of hypopigmentation were +0.18 (SD = 0.39) at 1 month and +0.29 (SD = 0.47) at 3 month follow-ups for FRM side; +0.29 (SD = 0.47) 1 month and +0.18 (SD = 0.53) at 3 month follow-ups for SBR side.

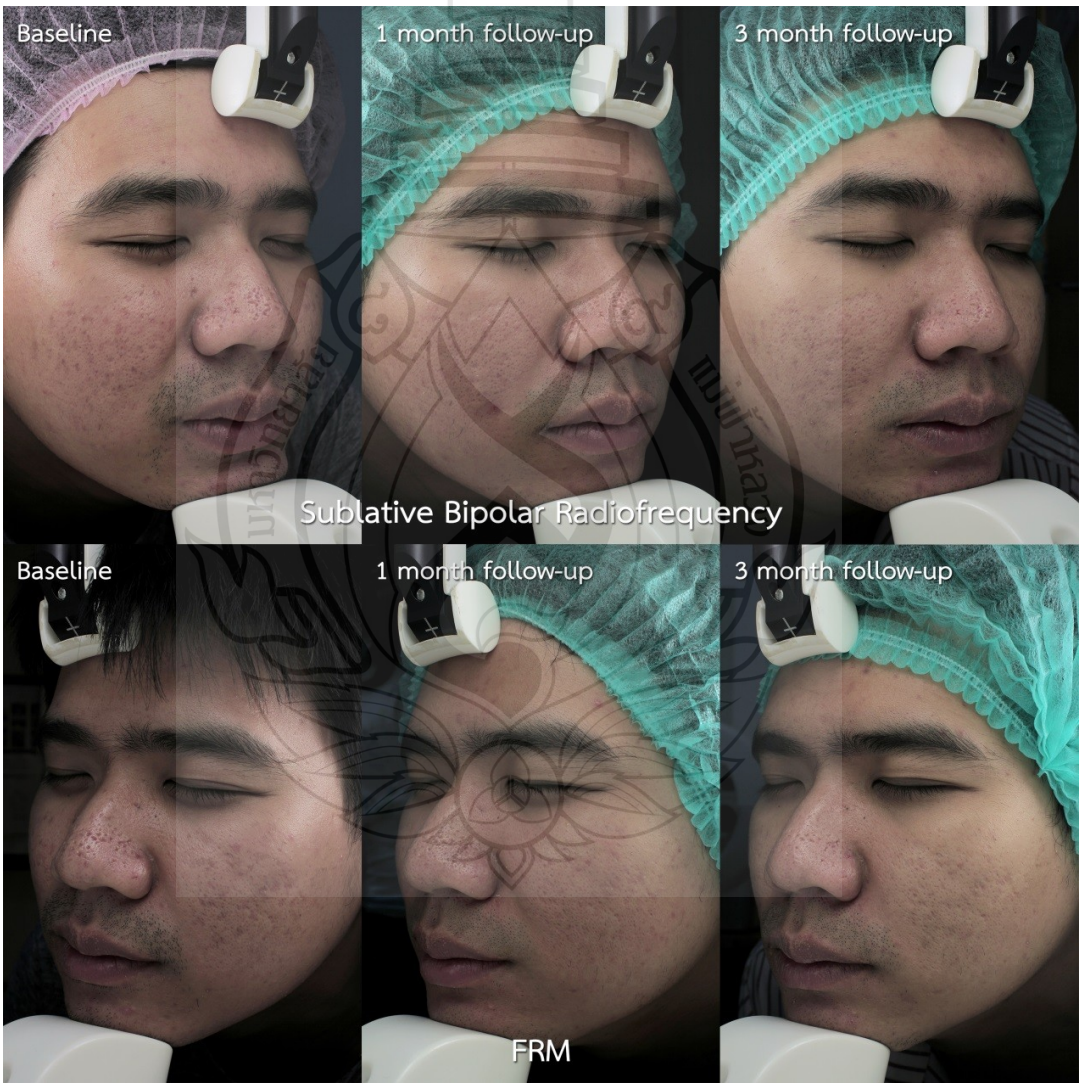


Figure 4.4 The volunteer number 3 was a 27-year-old Thai man with skin type V and class 4 acne scars

Figure 4.4 showed a 27-year-old Thai man with skin type V and class 4 acne scars. His median clinical improvement scores of acne scars for both sides of face were +3 for FRM side and +2 for sublative bipolar radiofrequency side at 1 month follow-up; +2 for both sides at 3 month follow-up. He was one of two volunteers who had got highest median clinical improvement scores in our study. Note that atrophic acne scars on his nose and cheeks were improved signally.

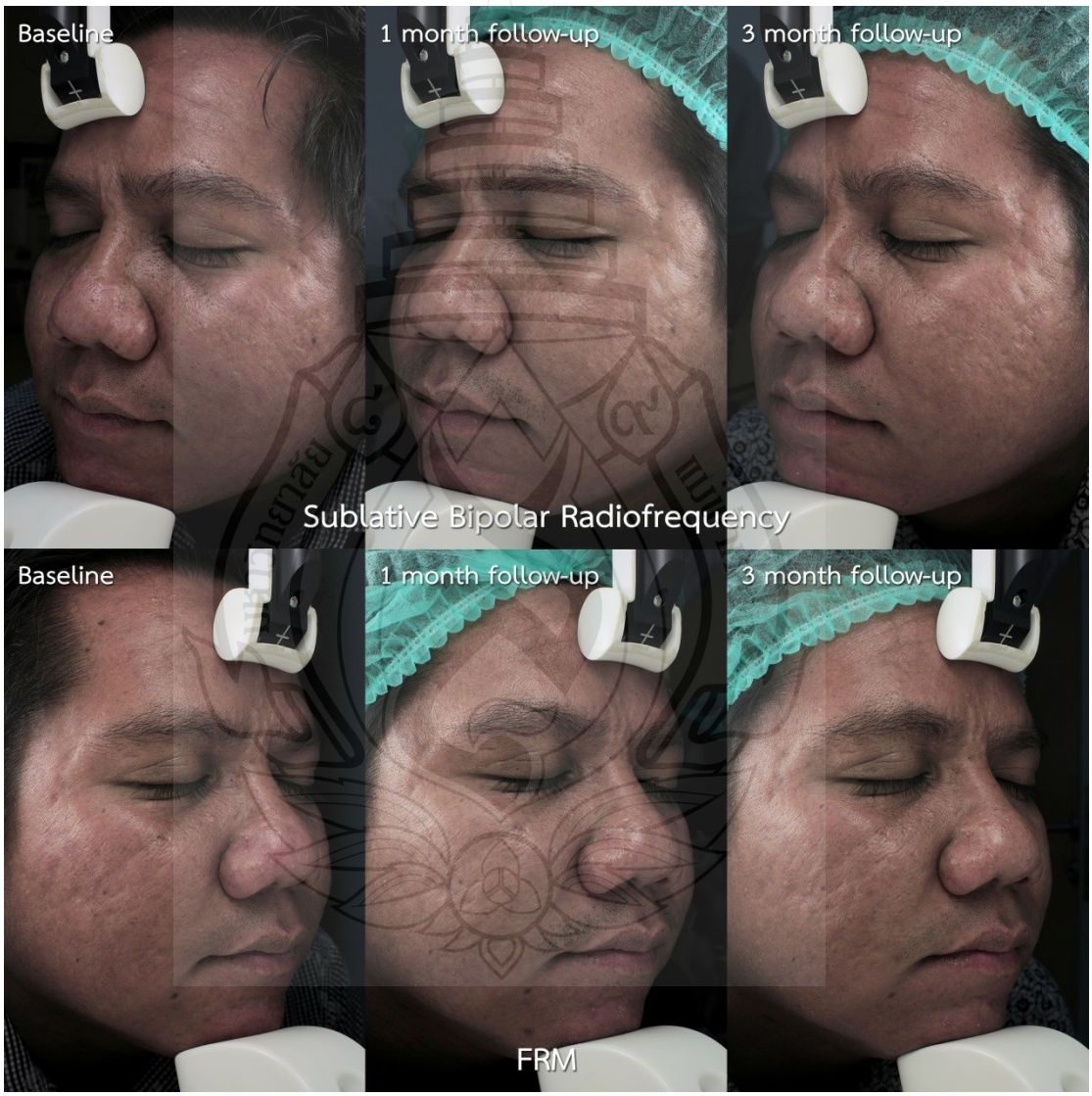


Figure 4.5 The volunteer number 9 was a 28-year-old Thai man with skin type V and grade 4 acne scars. He had mainly rolling scars

Figure 4.5 showed a 28-year-old Thai man with skin type V and grade 4 acne scars. He had mainly rolling scars. His median clinical improvement scores of acne scars for both sides of face were 0 for FRM side and +2 for SBR side at 1 month follow-up; +1 for FRM side and +2 for SBR side at 3 month follow-up. Although he had got less clinical improvement score for FRM side, he gave satisfaction score of FRM as "satisfied" which was more than SBR's "somewhat dissatisfied". It was because we did not tell any volunteer the clinical improvement scores.

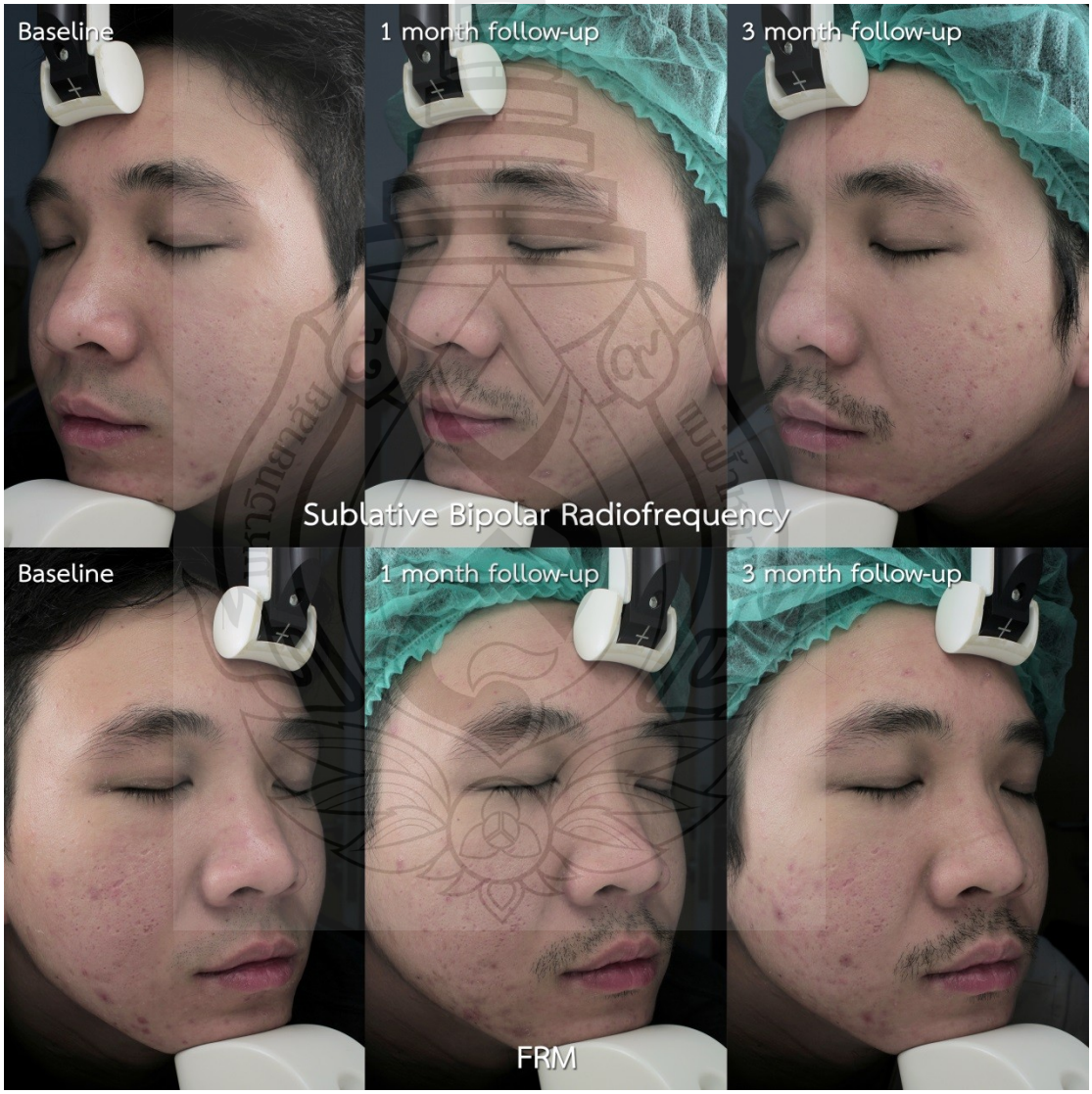


Figure 4.6 The volunteer number 12 was a 27-year-old Thai man with skin type III and class 3 acne scars

Figure 4.6 showed a 27-year-old Thai man with skin type III and class 3 acne scars. His median clinical improvement scores of acne scars for both sides of face were 0 at 1 month follow-up; 0 for FRM side and +1 for sublative bipolar radiofrequency side at 3 month follow-up. They were the lowest scores in this study which made him one of two volunteers with little improvement of acne scars. He also said he had acne occurrence after every treatment session. Note that he had atrophic acne scars mainly in boxcar and ice pick types and he had acne vulgaris and multiple focal lesions of post-inflammatory hyperpigmentation for both sides of face in 1 and 3 month follow-ups.

4.2.2 Objective measurement of improvement of other aspects

4.2.2.1 Cutometer scores

Cutometer® MPA 580 could give researchers many types of "R" ratio parameters: R0 to R9. We chose R0 and R2 parameters to use in this research. This R0 parameter represents the passive behavior of the skin to force (firmness) and R2 parameter represents resistance versus ability of returning (gross elasticity). When R0 is near to "0" value, it means more firmness. When R2 is near to "1", it means more gross elasticity. Table 4.5 and table 4.6 showed raw results from the cutometer.

Table 4.5 "R0" ratio scores from the cutometer

Volunteer No.	Parameter R_0 from Cutometer® MPA 580					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
1	0.24	0.285	0.249	0.257	0.286	0.263
2	0.272	0.228	0.277	0.244	0.214	0.226
3	0.279	0.275	0.3218	0.344	0.298	0.245
4	0.231	0.232	0.276	0.191	0.23	0.241
5	0.338	0.309	0.28	0.298	0.321	0.281
6	0.341	0.241	0.284	0.334	0.299	0.299
7	0.36	0.355	0.309	0.333	0.367	0.346
8	0.312	0.218	0.225	0.285	0.266	0.232

Table 4.5 (continued)

Volunteer No.	Parameter R_0 from Cutometer® MPA 580					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
9	0.212	0.216	0.243	0.176	0.234	0.229
10	0.305	0.292	0.251	0.31	0.314	0.247
11	0.256	0.247	0.257	0.301	0.263	0.223
12	0.238	0.206	0.186	0.245	0.254	0.217
13	0.192	0.241	0.271	0.224	0.268	0.257
14	0.283	0.234	0.248	0.244	0.228	0.23
15	0.412	0.291	0.316	0.415	0.415	0.323
16	0.325	0.252	0.243	0.306	0.265	0.276
17	0.29	0.209	0.193	0.32	0.281	0.258
Mean	0.287412	0.254765	0.260576	0.283941	0.282529	0.258412
SD	0.0573	0.040659	0.03801	0.060191	0.051509	0.036517

Table 4.6 "R2" ratio scores from the cutometer

Volunteer No.	Parameter R_2 from Cutometer® MPA 580					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
1	0.65	0.7719	0.7309	0.93	0.8217	0.8897
2	0.8934	0.557	0.5199	0.8852	0.528	0.5133
3	0.8602	0.9564	0.8037	0.8227	0.698	0.5878
4	0.6883	0.8966	0.5942	0.8586	0.8435	0.7095
5	0.855	0.754	0.7714	0.8456	0.8131	0.7224
6	0.6452	0.6515	0.662	0.7246	0.7592	0.6054
7	0.7917	0.8056	0.767	0.8859	0.812	0.7948

Table 4.6 (continued)

Volunteer No.	Parameter R_2 from Cutometer® MPA 580					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
8	0.7436	0.6789	0.5733	0.786	0.6579	0.6293
9	0.934	0.6389	0.6749	0.9602	0.6752	0.7031
10	0.7672	0.8904	0.7211	0.7871	0.8376	0.7449
11	0.7266	0.8623	0.7082	0.8472	0.8365	0.6816
12	0.5294	0.6068	0.586	0.551	0.6299	0.6267
13	0.8021	0.9295	0.7712	0.7411	0.8843	0.7354
14	0.7032	0.7393	0.629	0.6598	0.6272	0.6217
15	0.8301	0.7526	0.8354	0.9133	0.9253	0.7864
16	0.8554	0.6706	0.642	0.8137	0.7283	0.837
17	0.9517	0.7177	0.9016	0.85	0.7936	0.9457
Mean	0.778065	0.757647	0.699518	0.815412	0.757135	0.713806
SD	0.112747	0.118204	0.102776	0.102506	0.106885	0.113314

Raw results were all in normal distribution ($p>0.05$), and then paired t-tests were used.

Table 4.7 R0 and R2 scores tested with Kolmogorov-Smirnov test for normality

	Kolmogorov-Smirnov		
	Statistic	**df**	**p-value**
FRM_R0_baseline	0.090	17	0.200*
FRM_R2_baseline	0.105	17	0.200*
SBR_R0_baseline	0.122	17	0.200*
SBR_R2_baseline	0.152	17	0.200*
FRM_R0_1mo_after	0.174	17	0.180
FRM_R2_1mo_after	0.106	17	0.200*
SBR_R0_1mo_after	0.140	17	0.200*
SBR_R2_1mo_after	0.167	17	0.200*
FRM_R0_3mo_after	0.145	17	0.200*
FRM_R2_3mo_after	0.097	17	0.200*
SBR_R0_3mo_after	0.156	17	0.200*
SBR_R2_3mo_after	0.125	17	0.200*

Table 4.8 R0 and R2 scores with paired t-tests

Pair	**Paired differences**		**t**	**df**	**p-value (2-tailed)**
	Mean	**SD**			
FRM's R0 at baseline - 1 month f/u	0.033	0.049	2.755	16	0.014
FRM's R0 at baseline - 3 month f/u	0.027	0.055	2.022	16	0.06
FRM's R2 at baseline - 1 month f/u	0.020	0.163	0.515	16	0.614
FRM's R2 at baseline - 1 month f/u	0.079	0.117	2.778	16	0.013
SBR's R0 at baseline - 1 month f/u	0.001	0.034	0.169	16	0.868
SBR's R0 at baseline - 3 month f/u	0.026	0.046	2.276	16	0.037
SBR's R2 at baseline - 1 month f/u	0.058	0.123	1.947	16	0.069
SBR's R2 at baseline - 3 month f/u	0.102	0.121	3.476	16	0.003
FRM's R0 at baseline - SBR's R0 at baseline	0.003	0.033	0.439	16	0.667
FRM's R2 at baseline - SBR's R2 at baseline	-	0.095	-1.63	16	0.123
FRM's R0 at 1 month f/u - SBR's R0 at 1 month	-	0.034	-3.37	16	0.004
FRM's R2 at 1 month f/u - SBR's R2 at 1 month	0.001	0.096	0.022	16	0.983
FRM's R0 at 3 month f/u - SBR's R0 at 3 month	0.002	0.035	0.254	16	0.802
FRM's R2 at 3 month f/u - SBR's R2 at 3 month	-	0.093	-0.63	16	0.536

When R0 and R2 scores were compared at baseline and follow-ups at 95% confidence interval of the difference. We saw statistically difference in four pairs: FRM's

R0 at baseline and 1 month follow-up; FRM's R2 at baseline and 3 month follow-up; Sublative Bipolar Radiofrequency's R0 at baseline and 3 month follow-up; Sublative Bipolar Radiofrequency's R2 baseline and 3 month follow-up.

When both sides of face were compared in the same point of time, just R0 scores between FRM and Sublative Bipolar Radiofrequency at 1 month follow-up were different (p-value=0.04).

4.2.2.2 Sebumeter scores

We used Sebumeter® SM 815 to measure the sebum production capacity at forehead and nose area. More value indicated more sebum production capacity. Raw results are as followed.

Table 4.9 Scores from sebumeter for forehead area

Volunteer No.	Measured forehead area with Sebumeter® SM 815					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
1	84	147	75	62	185	67
2	77	58	52	75	92	83
3	56	103	56	76	227	34
4	91	96	44	96	107	80
5	92	81	64	88	71	72
6	65	94	58	49	80	39
7	100	53	68	102	64	93
8	72	90	70	95	73	51
9	188	195	197	168	157	114
10	72	143	136	50	136	131
11	63	81	142	53	57	68
12	37	69	38	31	71	55
13	92	124	90	59	119	69

Table 4.9 (continued)

Volunteer No.	Measured forehead area with Sebumeter® SM 815					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
14	66	43	70	40	17	68
15	45	61	37	45	53	32
16	92	69	55	66	53	52
17	65	93	34	67	57	58
Mean	79.82353	94.11765	75.64706	71.88235	95.23529	68.58824
SD	32.93409	39.26494	43.70775	32.2488	54.25579	26.45529

Table 4.10 Scores from sebumeter for nose area

Volunteer No.	Measured nose area with Sebumeter® SM 815					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
1	254	183	296	216	249	263
2	187	77	138	221	138	148
3	277	244	188	260	188	234
4	119	188	164	74	199	197
5	173	230	77	157	209	73
6	187	195	190	149	143	156
7	195	95	114	185	124	188
8	128	133	175	138	124	220
9	221	305	202	246	275	227
10	194	204	237	237	228	216

Table 4.10 (continued)

Volunteer No.	Measured nose area with Sebumeter® SM 815					
	FRM			Sublative Bipolar Radiofrequency		
	Baseline	1 month after	3 month after	Baseline	1 month after	3 month after
11	88	117	103	62	61	73
12	109	206	52	85	225	71
13	84	168	197	42	157	244
14	202	147	63	214	85	75
15	166	60	70	199	53	99
16	140	126	154	96	119	202
17	147	211	225	171	123	234
Mean	168.8824	169.9412	155.5882	161.8824	158.8235	171.7647
SD	54.51362	64.01804	68.6131	69.1754	65.18074	68.72548

Tests of normality found these values from Sebumeter® SM 815 were not all in normal distribution. When values before and 1-month follow-up, before and 3-month follow-up were compared in FRM side and so did sublative bipolar radiofrequency side, there were no statistically difference. The Wilcoxon Matched-Pairs Signed-Ranks test was used.

Table 4.11 Scores from the sebumeter tested with Kolmogorov-Smirnov test for normality

	Kolmogorov-Smirnov[a]		
	Statistic	df	p-value
FRM_sebu_forehead_baseline	0.238	17	0.011
FRM_sebu_nose_baseline	0.101	17	0.200*
SBR_sebu_forehead_baseline	0.155	17	0.200*
SBR_sebu_nose_baseline	0.127	17	0.200*

Table 4.11 (continued)

	Kolmogorov-Smirnov[a]		
	Statistic	**df**	**p-value**
FRM_sebu_forehead_1mo_after	0.187	17	0.118
FRM_sebu_nose_1mo_after	0.110	17	0.200*
SBR_sebu_forehead_1mo_after	0.199	17	0.073
SBR_sebu_nose_1mo_after	0.125	17	0.200*
FRM_sebu_forehead_3mo_after	0.271	17	0.002
FRM_sebu_nose_3mo_after	0.109	17	0.200*
SBR_sebu_forehead_3mo_after	0.155	17	0.200*
SBR_sebu_nose_3mo_after	0.182	17	0.139

Note. *. This is a lower bound of the true significance.

Table 4.12 Scores from the sebumeter tested with Wilcoxon Matched-Pairs Signed-Ranks test to compare between scores at baseline and follow-ups

Sebumeter scores			**Z**	**p-value (2-tailed)**
FRM	Forehead	1 month f/u and baseline	-1.658[n]	0.097
		3 month f/u and baseline	-1.267[p]	0.205
	Nose	1 month f/u and baseline	-0.024[n]	0.981
		3 month f/u and baseline	-0.829[p]	0.407
SBR	Forehead	1 month f/u and baseline	-1.160[n]	0.246
		3 month f/u and baseline	-0.805[p]	0.421
	Nose	1 month f/u and baseline	-0.308[p]	0.758
		3 month f/u and baseline	-0.166[n]	0.868

Note. n. Based on negative ranks.

p. Based on positive ranks.

4.2.3 Volunteer assessment of improvement of acne scars and measurement of side effects

In February 2014, approximately four months after the last treatment session, seventeen volunteers were asked for satisfaction of improvement of acne scars for each side of face. Overall global satisfaction score were “not satisfied at all”, “not very satisfied”, “somewhat dissatisfied”, “neutral”, “somewhat satisfied”, “satisfied” and “very satisfied”. They equals to the scale from 1 to 7 points. They were told to focus on improvement of acne scar appearances. Results were as followed.

Table 4.13 Satisfaction score of both treatments, asked at four months after the last treatment session

Volunteer number	Satisfaction score	
	FRM	SBR
1	5	6
2	6	5
3	5	5
4	6	5
5	6	6
6	5	5
7	6	6
8	5	6
9	5	4
10	7	6
11	6	5
12	4	5
13	6	6
14	6	5

Table 4.13 (continued)

Volunteer number	Satisfaction score	
	FRM	**SBR**
15	6	5
16	6	4
17	5	5
Mean	5.59	5.24
Median	6	5
SD	0.71	0.66

For FRM's satisfaction, there were one of "neutral", six of "somewhat satisfied", nine of "satisfied" and one of "very satisfied". For SBR's satisfaction, there were two of "neutral", nine of "somewhat satisfied" and six of "satisfied". Mean satisfaction score of FRM was 5.59 (SD = 0.71) and it was 5.24 (SD = 0.66) for sublative bipolar radiofrequency treatment. Median satisfaction score of FRM was 6 which mean "satisfied" and median satisfaction score of sublative bipolar radiofrequency was 5 which mean "somewhat satisfied". We saw six volunteers who gave equal scores for both treatments, eight volunteers who gave higher score for FRM and three volunteers who gave higher score for SBR. However, satisfaction scores of both treatments showed by no mean difference statistically.

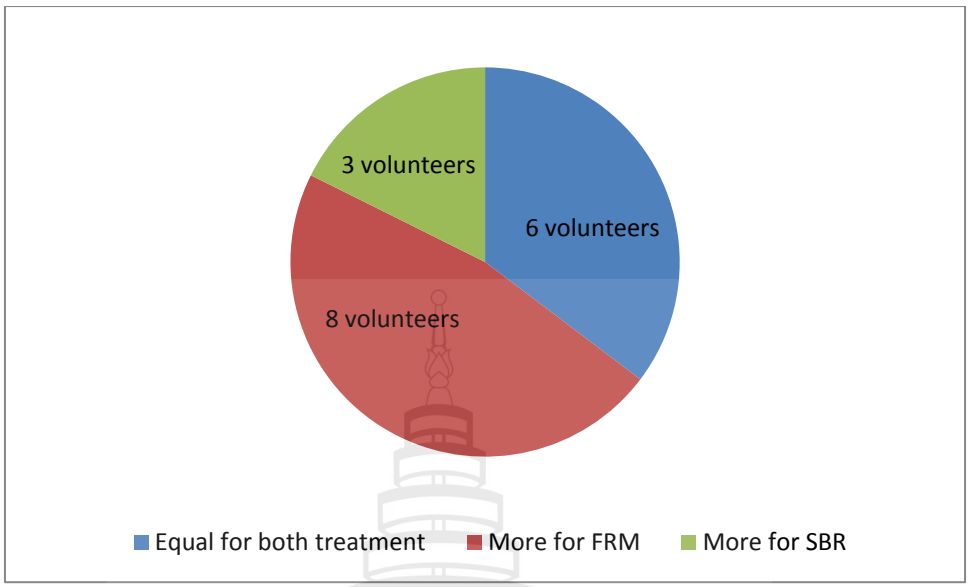


Figure 4.7 What did volunteers like more? Six volunteers gave equal scores for both treatments. Eight volunteers gave higher score for FRM and three volunteers gave higher score for SBR.

Before that time, we surveyed side immediate side effects of both treatments for three times after every treatment session. And we also surveyed side effects at follow-ups for three times at four weeks after each treatment session. We used physician's assessment along with questionnaire for immediate side effects such as erythema, bleeding, swelling, burning smell. Volunteers were asked for pain score and burning sensation score for each side of face in the scale 0 to 10. At follow-ups, we used questionnaires for side effects such as redness, hyperpigmentation, whitening effect and acne occurrence. Raw answers were used to find median nominal data. And data we have got were as followed.

Table 4.14 Descriptive side effects of both treatments

Immediate side effects		**FRM**	**Sublative Bipolar Radiofrequency**
Erythema (redness)	None	-	-
	Mild	4 volunteers	7 volunteers
	Moderate	11 volunteers	8 volunteers
	Severe	2 volunteers	2 volunteers
Bleeding	Yes	17 volunteer	-
	No	-	17 volunteers
Swelling	No swelling	1 volunteer	1 volunteer
	Mild	11 volunteers	9 volunteers
	Moderate	5 volunteers	7 volunteers
	Severe	-	-
Burning smell	Yes	-	17 volunteers
	No	17 volunteers	-
Itching		-	-
Numbness		-	-
Vesicle and signs of burn		-	-
Others		-	-
Reported side effects at follow-ups		FRM	Sublative Bipolar Radiofrequency
Hyperpigmentation		1 volunteer	1 volunteer
Acne occurrence		4 volunteers	1 volunteer
Redness (Post-inflammatory erythema)		-	-
Prolonged swelling		-	-
Whitening effect (Post-inflammatory hypopigmentation)		-	-

Table 4.14 (continued)

Immediate side effects	FRM	Sublative Bipolar Radiofrequency
Dyspigmentation	-	-
Abnormal sensation	-	-
Numbness	-	-
Burning	-	-
Telangiectasia	-	-
Others	-	-

Table 4.15 Raw results of pain scores and burning sensation scores

Volunteer Number	Pain score		Burning sensation	
	FRM	SBR	FRM	SBR
1	5	3	2	2
2	7	4	2	6
3	7	4	2	7
4	7	4	3	5
5	5	3	3	5
6	6	4	4	5
7	6	5	4	5
8	6	4	6	7
9	6	3	2	4
10	7	4	3	6
11	5	7	4	7
12	6	6	3	5
13	5	3	2	4
14	4	4	3	4
15	5	4	1	3

Table 4.15 (continued)

Volunteer Number	Pain score		Burning sensation	
	FRM	SBR	FRM	SBR
16	5	5	3	5
17	4	3	2	2
Mean	5.65	4.12	2.88	4.82
SD	1.00	1.11	1.17	1.55

The study found side effects such as erythema, bleeding, swelling, hyperpigmentation and acne occurrence in the FRM side; erythema, swelling, burning smell, hyperpigmentation and acne occurrence in sublative bipolar radiofrequency side. It has been noted that there were bleeding in all volunteers in the side of FRM and burning smell in all volunteers in the side of sublative bipolar radiofrequency. Most side effects were temporary. Volunteers who indicated acne occurrence were treated with topical clindamycin application twice a day and 2.5% benzyl peroxide application for 20 minutes before face washing twice a day.

Mean pain score from FRM was 5.65 with SD of 1; and sublative bipolar radiofrequency's was 4.12 with SD of 1.11. Mean burning sensation score of FRM was 2.88 with SD of 1.17; and sublative bipolar radiofrequency's was 4.82 with SD of 1.55. Pain scores between FRM and SBR were statistically different ($p=0.003$). Burning sensation scores between them were also statistically different ($p=0.001$).

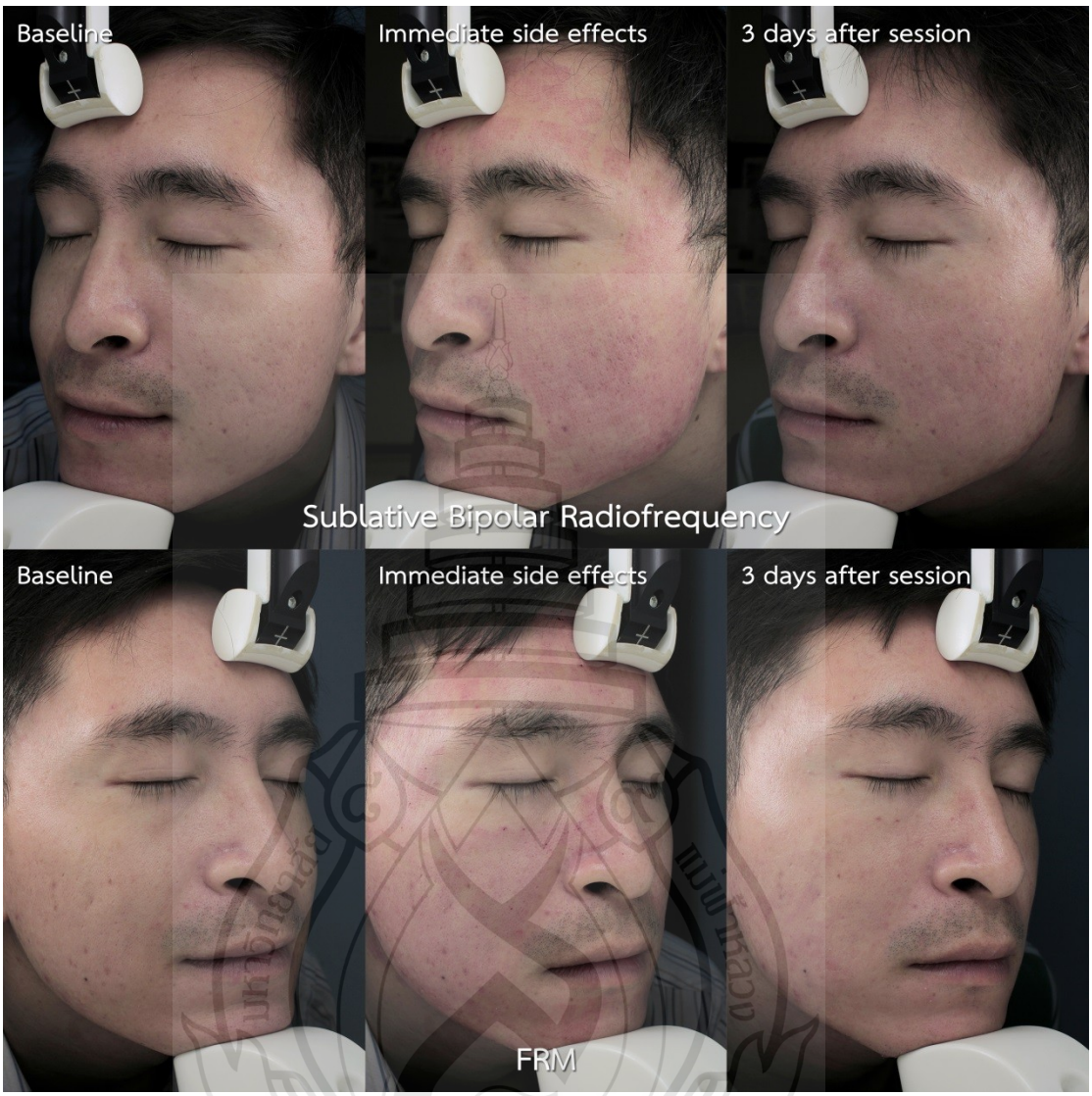


Figure 4.8 A 27-year-old Chinese man (volunteer number 1) with his photographs from VISIA®-CR

Figure 4.8 showed a 27-year-old Chinese man with his photographs from VISIA®-CR. He had a skin type III and class 3 acne scars. Photos show immediate side effects from both treatments. These side effects such as redness of the skin, bleeding and swelling were temporary. Note the resolution of side effects at 3 days after the treatment session which was much better than the immediate appearance.

There was one volunteer who indicated hyperpigmentation in both sides of face during treatment sessions which was more prominent in sublative bipolar radiofrequency side. She was treated with whitening agent named TM4 cream of Mae Fah Luang University hospital, Bangkok. Its active ingredients were PT40 0.2%, Arbutin 7%, Tyrostat 3.5%, Vit.B3, Vit.B5, Aloe 40%, Allantoin 1%, Butylene Glycol, Nexbase. The physician adviced her to use it to apply at face twice a day.

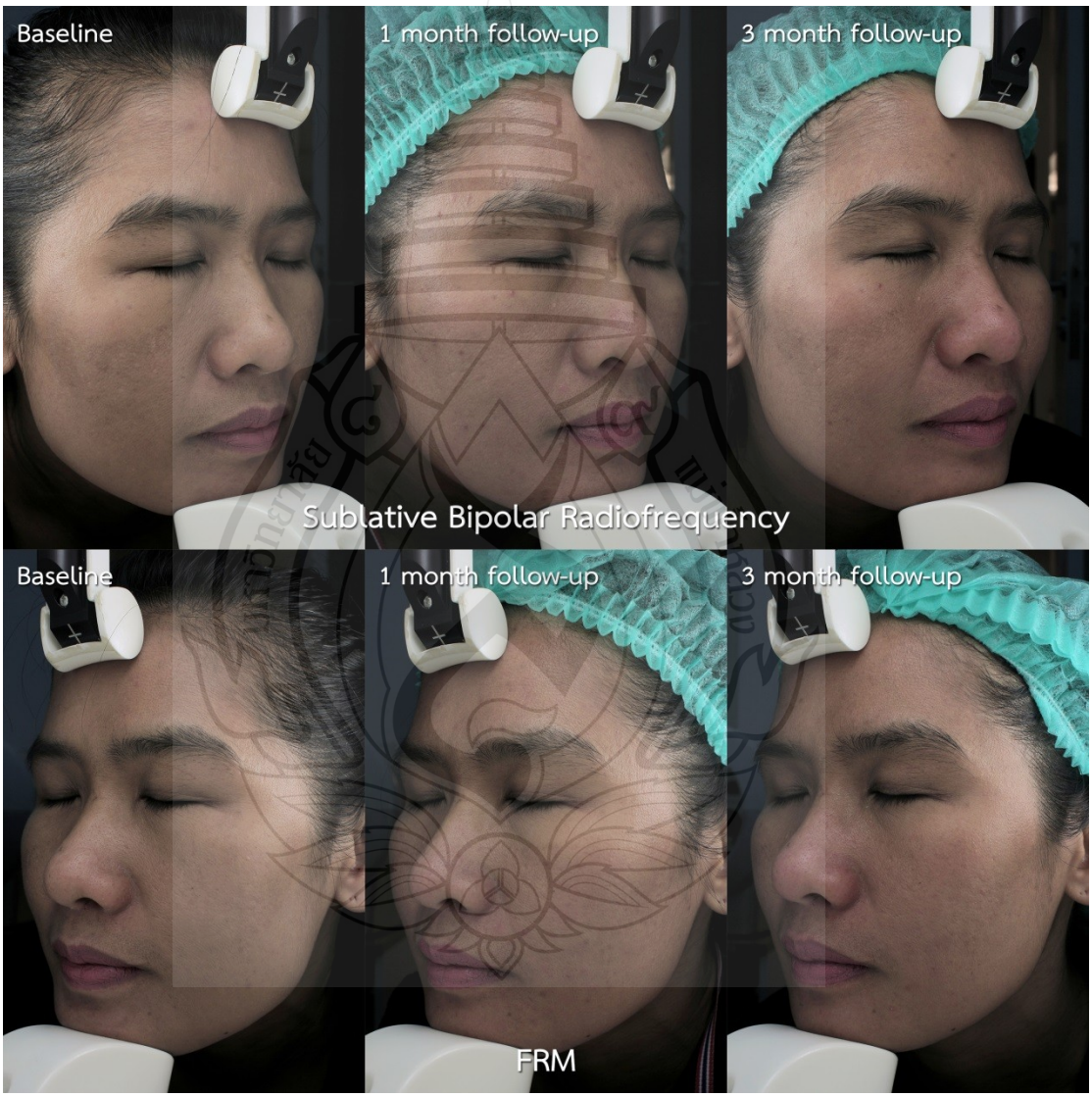


Figure 4.9 A 48-year-old Thai woman (volunteer number 11) with hyperpigmentation which she noticed darkening of her skin after 2nd treatment session

Figure 4.9 showed a 48-year-old Thai woman with hyperpigmentation which she noticed darkening of her skin after 2nd treatment session. She had a skin type IV and acne scars class 3. These pictures show both sides of face with identification of devices used with them. Note that there was increased redness of skin which seems to be 1st degree burning. Grossly more redness and more hyperpigmentation were seen in SBR side perhaps because of her previous melasma lesion. However, she had got a degree of clinical improvement. Her median clinical improvement scores of acne scars were +1 for FRM side and +1 for SBR side at 1 month follow-up; +1 for FRM side and +1 for SBR side at 3 month follow-up. She also gave "satisfied" score for FRM and "somewhat satisfied" score for SBR.

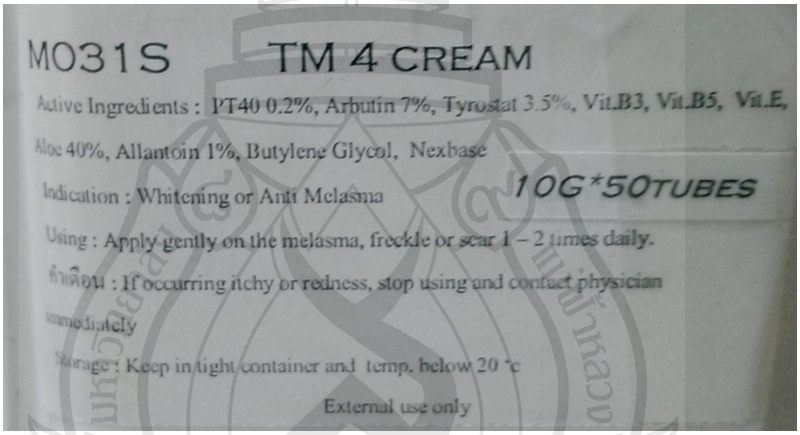


Figure 4.10 Ingredients of TM 4 Cream

There were reported acne occurrence in four volunteers of FRM side and one volunteer of sublative bipolar radiofrequency side.

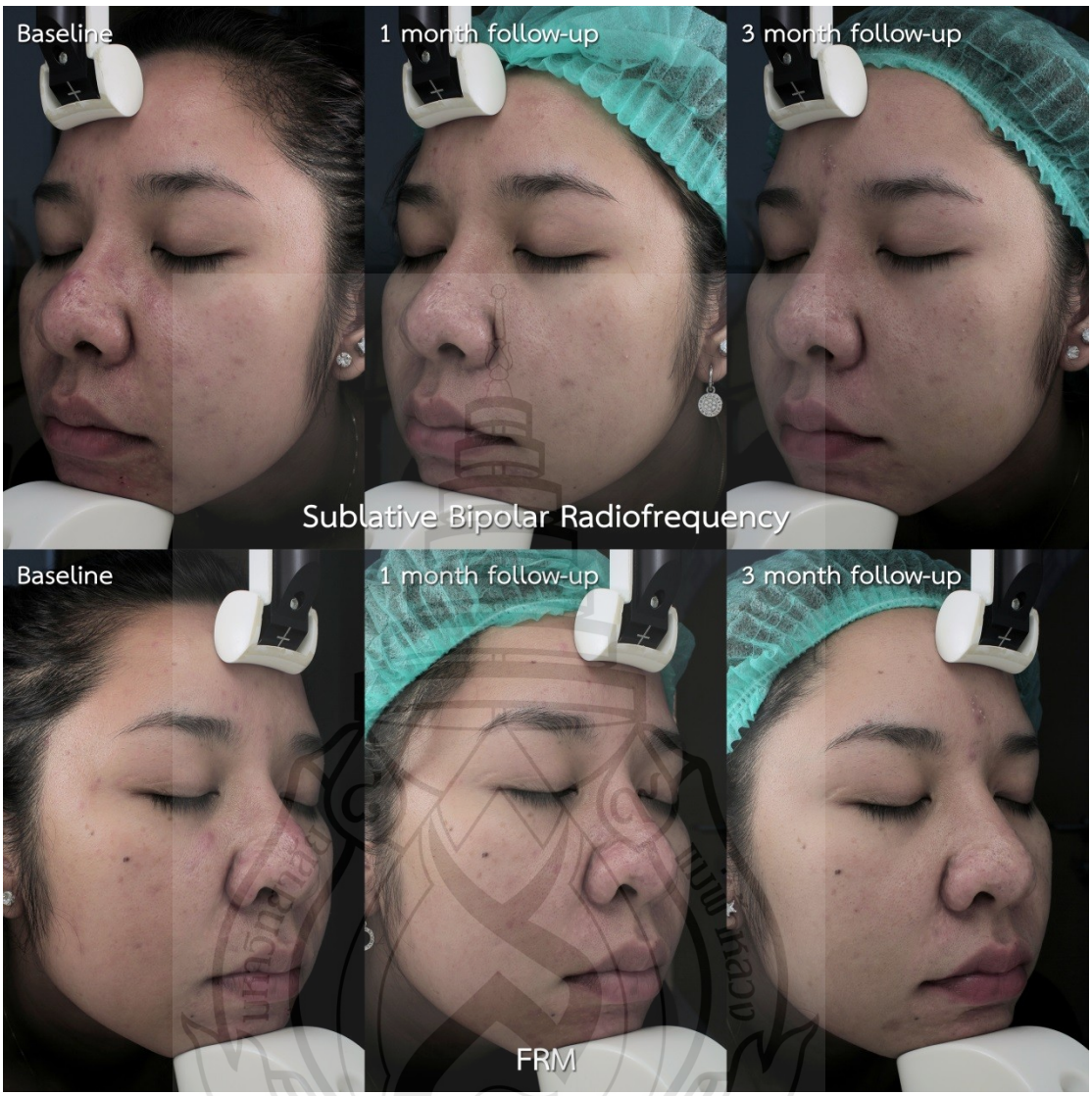


Figure 4.11 A 27-year-old Thai woman (volunteer number 7), skin type IV with class 2 acne scars , who had got less acne occurrence and whitening effects of both treatments

Figure 4.11 showed a 27-year-old Thai woman, skin type IV with class 2 acne scars , who had got less acne occurrence and whitening effects of both treatments. Our three masked evaluators gave -2, -1, -2, 0 scores for acne occurrence in order of FRM at 1 month and 3 month follow-ups and SBR at 1 month and 3 month follow-ups. They gave +1, +1, +1 and +1 of the same kind for scores of hypopigmentation or whitening effects. She was "somewhat satisfied" for both treatments.

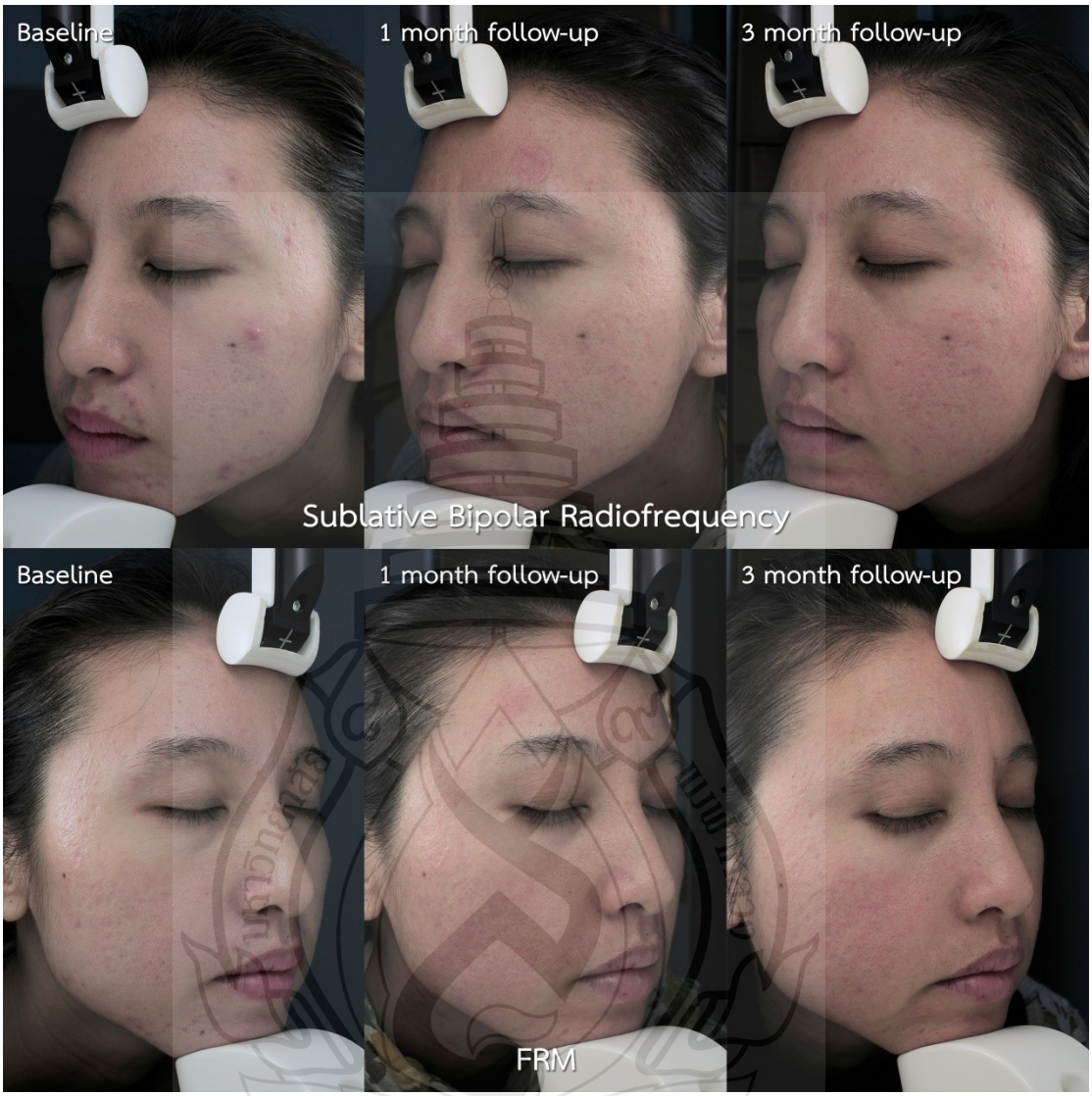


Figure 4.12 A 36-year-old Thai woman (volunteer number 4), skin type III with class 4 acne scars

Figure 4.12 showed a 36-year-old Thai woman, skin type III with class 4 acne scars. Clinical evaluation showed she had less acne occurrence but more redness of the skin. She indicated no care after treatments and she got some sunburns. Her median clinical scores of acne occurrence were -1, -1, -1 and -1. Her scores of redness were +2, +3, +1 and +2 at FRM's 1 month and 3 month follow-ups and SBR's 1 month and 3 month follow-ups, in order. Her scores of hyperpigmentation were +1, +1, +1 and +2.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Discussion

Sublative Bipolar Radiofrequency (SBR) came first as a successful radiofrequency device for treatment of acne scars. It generates fractional deep dermal heating to induce skin injury and then elicits a wound healing response, thereby stimulating the remodeling of dermal collagen (Hruza, et al., 2009). And assessment for improvement in skin texture correlated with subjects' evaluation in that study was greater than 40% for approximately 50% of subjects. Compared to the successful prior fractional laser, fractional Erbium: Glass 1550 nm device, it had similar effectiveness (Rongsaard & Rummaneethorn, 2014). Interesting note that Rongsaard found more post-inflammatory hyperpigmentaion in the side of fractional Erbium: Glass. In the present study, SBR showed clinical improvement in 94.1% of all patients (16/17).

The previous study for Fractional Radiofrequency Microneedle (FRM) indicated that grade of acne scars and investigator global assessment of large pores improved in more than 70% of all patients (Cho, S. I. et al., 2012). Skin surface roughness, dermal density, and microscopic and composite images also improved, whereas TEWL and sebum measurement did not change. Our study saw clinical improvement in 88.2% of all FRM patients (15/17).

According to the study, at first month follow up, SBR gave clinical improvement more than third month. In contrast with FRM that gave less clinical improvement at first month, but gradually increased until third month. It is possible that SBR created thermal effect onto the superficial skin, so rejuvenating effect came faster. Owing to using of microneedle transfer heat into deeper dermis, FRM may help for collagen remodeling better than SBR. Moreover, improvement of grading between SBR and FRM sides at 1st and 3rd month's follow-ups was no statistically different.

When analyzing the relationship between severity of acne scars and improvement score after treatment, there was no correlation. These were found on both FRM and SBR sides; contradicted to the prior study of Rongsaard (Rongsaard & Rummaneethorn, 2014) that mild and moderate classes were more improved after treatments, especially.

Concerning the benefit for skin laxity, this study showed that the face using FRM were firmer than SBR's at 1-month follow-up. A possible explanation for this effect was FRM can transfer energy to deeper dermis result in abundant collagen production. The depth of energy transfer of FRM was moret than 2000 μm due to microneedle length, while SBR was 750 μm, a half of the distance between electrodes (Rongsaard & Rummaneethorn, 2014). However, more firmness in FRM side was detected only at 1-month follow-ups. There was no difference between cutometer scores at baseline of two sides and at 3-month follow-ups. This meant that the effect for firmness was in a short period of time, a month.

For an aspect of sebum production, we used sebumeter to measure volunteers' faces at baseline and follow-ups. Previous study found after a single FRM treatment casual sebum level (CSL) and sebum excretion rate (SER) showed 30-60% and 70-80% reduction, respectively, at week 2, and remained below the baseline level until week 8. (K. R. Lee, Lee, Lee, & Yoon, 2013). Our study showed no change in sebum production for both SBR and FRM. The sebosuppressive effect may last for a short period, so this study could not detect it at 1 and 3-month follow-ups.

Immediate side effects for both treatments were temporary. All volunteers indicated more pain and all bleeding in FRM side; more burning sensation and all burning smell in SBR side. Their common immediate side effects were erythema and swelling. Long-term side effects of both treatments such as hyperpigmentation and acne occurrence were alike.

After four months, volunteers had most satisfaction scores for improvement of acne scars as "satisfied" for FRM and "somewhat satisfied" for SBR with no statistic difference between them. We saw six volunteers who gave equal scores for both treatments, eight volunteers who gave higher score for FRM and three volunteers who gave higher score for SBR. We could infer from these numbers that people thought differently for results and satisfaction did not always go in the same way with the result

With comparison between FRM and SBR, rejuvenation effects were seen in both treatments. Objective measurement such as melanin index should be measured in next studies. The process of whitening effect in some volunteers was still elucidative.

5.2 Conclusion

Both FRM and SBR treatment can be effective treatments for atrophic acne scars. Cutometer found more firmness of the skin in FRM side at 1 month follow-up. Sebumeter found no difference in sebum production. They had no different common side effects such as erythema, swelling, hyperpigmentation and acne occurrence. More pain with all bleeding in FRM side and more burning sensation with all burning smell in SBR side were seen. Longer follow-ups for next studies should be done with comparative studies for different levels of RF energy in future.

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APPENDICES

APPENDIX A

เอกสารคำอธิบาย/คำชี้แจง โครงการวิจัยแก่ผู้เข้าร่วมโครงการ

(INFORMATION SHEET)

1. โครงการวิจัย (Name of the research project)

การศึกษาเปรียบเทียบเครื่องแฟรกชันนอลเรดิโอฟรีเควนซีไมโครนีดเดิล กับ เครื่องซับเบลทีฟไบโพลาร์เรดิโอฟรีเควนซี ในการรักษาแผลเป็นหลุมสิว

A COMPARATIVE STUDY OF FRACTIONAL RADIOFREQUENCY MICRONEEDLE AND SUBLATIVE BIPOLAR RADIOFREQUENCY TREATMENT IN ACNE SCARS.

เครื่องมือ RF สองประเภท ที่ใช้ในการวิจัยนี้ มีชื่อการค้าคือ eMatrix™ และ INTRAcel™ ก่อนที่ท่านจะตกลงเข้าร่วมการศึกษาดังกล่าว ขอเรียนให้ท่านทราบถึงข้อมูล ที่มา และ รายละเอียดของการวิจัย ดังนี้

You were invited for participation in the clinical study. This study is the comparative study between two devices. Their trade names are eMatrix™ and INTRAcel™. We would like to inform you for background, rationale, and details of this study.

ผู้รับผิดชอบโครงการวิจัย Research Respondents

1. นายแพทย์ ชเนษฎ์ ศรีสุโข Chanesd Srisrukho, MD
2. อาจารย์นายแพทย์ไพศาล รัมณีย์ธร Lecturer Paisal Rummaneethorn, MD

2. วัตถุประสงค์และวิธีการวิจัย

วัตถุประสงค์การวิจัย Objectives of the Research

จุดประสงค์หลัก

เพื่อศึกษาเปรียบเทียบประสิทธิผลของการใช้เครื่องมือทั้งสองชนิด ในการรักษาแผลเป็นหลุมสิว

จุดประสงค์รอง

1. เพื่อศึกษาประโยชน์ของเครื่องมือทั้งสองชนิด ที่พึงได้รับอื่นๆ อาทิ การลดภาวะความมันบนใบหน้า และ ผลต่อภาวะผิวหนังหย่อนคล้อย

2. เพื่อศึกษาผลข้างเคียงที่อาจเกิดขึ้น สำหรับการรักษาจากเครื่องมือทั้งสองชนิด

3. เพื่อสำรวจความพึงพอใจของอาสาสมัคร สำหรับการรักษาจากเครื่องมือทั้งสองชนิด

Primary Objective

To compare the clinical efficacy of the fractional radiofrequency microneedle with those of the sublative bipolar radiofrequency device in treatment of atrophic facial acne scars

Secondary Objectives

1. To study role of both devices for other possible benefits such as effects on sebum production and skin laxity

2. To study side effects of them

3. To survey volunteers' satisfaction for both treatments.

วิธีการวิจัย

แบ่งใบหน้าอาสาสมัคร เป็นสองข้าง และสุ่มเลือกชนิดการรักษาสำหรับใบหน้าข้างนั้นๆ ระหว่าง เครื่อง eMatrix™ และ INTRAcel™ รักษาทุก 1 เดือน จนครบทั้งหมด 3 ครั้ง และนัดติดตามผลหลังจากนั้น ที่ระยะเวลา 1 และ 3 เดือน หลังการรักษาครั้งสุดท้าย

Research Method

Clinical study

Each volunteer's face would be divided in 2 sides for treatments. The randomization was occurred to select each device for each side of the face. Volunteers were treated once every month for 3 consecutive months. They had follow-up appointments at 1, 3 months after the last treatment.

3. ความเป็นมาของโครงการ ที่ทำให้ต้องศึกษาเรื่องนี้

หลุมสิว เป็นปัญหาที่ผู้คนแสวงหาวิธีการรักษามาเป็นระยะเวลานาน หลุมสิวเกิดจากการมีสิวอักเสบ และการรักษาตัวของผิวหนังผิดปรกติไป ทำให้เกิดการสลายคอลลาเจน และเกิดพังผืดขึ้นใต้ผิวหนัง

การรักษาหลุมสิว ในปัจจุบัน มีหลากหลาย ตั้งแต่ การใช้เข็มจิ้มผิวหน้า, การใช้เข็มพิเศษตัดพังผืดใต้หลุมสิว, การใช้สารเคมีลอกผิว, การกรอผิว, ตลอดจนเรื่องเลเซอร์

เลเซอร์มีบทบาทสำคัญในการรักษาหลุมสิวมาก ปัจจุบันเทคโนโลยีที่เรียกว่า RF (Fractional radiofrequency) ทำให้เกิดเครื่องมือที่ไว้ใช้รักษาหลุมสิว โดยการส่งคลื่นความถี่ไฟฟ้าลงเข้าไปในชั้นผิวหนัง ทำให้เกิดความร้อน และกระตุ้นการสร้างคอลลาเจน หลุมสิวจะตื้นขึ้นได้

การศึกษาของเราเป็นการเปรียบเทียบเครื่องมือ RF สองชนิด ตัวแรกใช้เทคโนโลยี Sublative bipolar radiofrequency และอีกตัวใช้เทคโนโลยี FRM (Fractional radiofrequency microneedle)

การรักษาโดยเครื่องเลเซอร์ต่างๆในปัจจุบันมีราคาสูง การศึกษานี้จะทำให้เราทราบถึงประสิทธิภาพ และความคุ้มค่าของเครื่องมือทั้งสองชนิดดังกล่าว หากท่านมีข้อสงสัยเกี่ยวกับวิธีการศึกษาวิจัย ท่านสามารถสอบถามแพทย์ได้ แพทย์ยินดีตอบคำถามและแจ้งให้ท่านทราบโดยละเอียด

Background

Acne scar is a difficult problem that people have sought absolute treatment for a long time. Acne scar generally occur following inflamed acne. After the inflammation process, abnormal recovery of the skin leads to degradation of collagen tissue and fibrous formation. Recent treatments for acne scars are needling, subcision, chemical peels, dermabrasion, and laser.

Laser plays a major role for acne scar treatment. Nowadays, RF technology (fractional radiofrequency) is widespread. Many devices have come after this technology by sending radiofrequency into the deep dermis and turn into heat. Heating makes tissue remodeling and new generation of collagen. Our study compares between fractional radiofrequency microneedle and sublative bipolar radiofrequency devices.

Because laser services for acne scar treatment now have high costs. This study will compare the efficacy between these two devices and lead into the cost-benefit study result. If you have any question or curiosity, please feel free to ask the researcher. The researcher is happy to answer them in details.

4. สถานที่และระยะเวลาที่ต้องทำการวิจัยกับอาสาสมัคร (Study location and Timing)

โรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพฯ

Mae Fah Luang University Hospital, Bangkok

อาสาสมัครได้รับการรักษาทุก 1 เดือน จนครบทั้งหมด 3 ครั้ง และนัดติดตามผลหลังจากนั้น ที่ระยะเวลา 1 และ 3 เดือน หลังการรักษาครั้งสุดท้าย

Volunteers were treated once every month for 3 consecutive months. They had follow-up appointments at 1, 3 months after the last treatment.

5. รายละเอียดที่จะปฏิบัติต่ออาสาสมัคร

ทางโครงการวิจัยมีข้อมูลแจ้งให้ท่านทราบดังต่อไปนี้ ก่อนที่ท่านจะตกลงเข้าร่วมการศึกษาวิจัยนี้

1. การรักษาโดย eMatrix™ และ INTRAcel™ เป็นการรักษาที่ใช้สำหรับหลุมสิว โดยปรกติ จะมีค่าใช้จ่ายสูง ทั้งคอร์ส ไม่ต่ำกว่า 60000 – 80000 บาท อ้างอิงตามราคาคลินิกความงามในปัจจุบัน

เครื่องมือ ทั้งสองชนิดนี้ มีหลักการ คือใช้คลื่นความถี่ไฟฟ้า ทำให้เกิดความร้อนจำเพาะในอุณหภมิที่เหมาะสม ประมาณ 60 องศาเซลเซียส ใต้ผิวหนัง เพื่อกระตุ้นให้มีการสร้างเนื้อเยื่อและคอลลาเจนใหม่ ภายในระยะเวลา 3-6 เดือนหลังการรักษา ส่งผลให้หลุมสิวดีขึ้น

เครื่องมือสองชนิดมีแหล่งพลังงานที่เหมือนกัน เป็นคลื่นความถี่ไฟฟ้าจากแหล่งกำเนิดพลังงานแบบสองขั้ว (bipolar radiofrequency) ความแตกต่างกัน คือ eMatrix™ ไม่มีเข็ม จะเป็นการใช้แผ่นทองคำนำกระแสคลื่นไฟฟ้า ส่วน INTRAcel™ จะติดเข็มไว้ที่ปลาย ปรับความยาวเข็มได้ในระดับ 0.5 ถึง 2.0 มิลลิเมตร เพื่อให้คลื่นความถี่ไฟฟ้าลงไปในความลึกที่แพทย์ต้องการ

2. ในการศึกษาวิจัยนี้ ผู้วิจัยไม่ได้รับประโยชน์เชิงพาณิชย์ กล่าวคือ ไม่ได้รับค่าแรงเงินเดือน หรือการสนับสนุนเงินทุนจากบริษัท/ห้าง/ร้าน รวมทั้งการตอบแทนในเชิงวัตถุ สิ่งของใดใด

3. เมื่อท่านได้รับการประเมินจากแพทย์แล้วเหมาะสมแก่การเข้าร่วมการวิจัย ท่านจะได้รับการรักษา โดยเครื่องมือทั้งสองตัว คือ eMatrix™ และ INTRAcel™ เป็นการรักษาโดยแบ่งครึ่งหน้าทำการสุ่มเลือกข้างในการรักษา เครื่องมือทั้งสองตัวต่างมีประสิทธิภาพในการรักษาหลุมสิว และผ่านการรับรองจากองค์กรอาหารและยาแล้วว่าเป็นเครื่องมือที่ปลอดภัย

4. ท่านจะหยุดการรักษาหลุมสิวด้วยวิธีอื่นตลอดการวิจัย และใช้สบู่ ครีมบำรุง รวมทั้งกันแดด ที่ผู้วิจัยได้จัดหามาให้ โดยที่ท่านไม่ต้องเสียค่าใช้จ่ายแต่อย่างไร

5. ท่านสามารถมารับการรักษาและตรวจติดตาม ตามที่แพทย์นัดได้ทุกครั้ง ขั้นต่ำคือ 5 ครั้ง แบ่งเป็น การประเมินสภาพผิวหน้าร่วมกับการรักษา 3 ครั้งแรก และ การติดตามผลการรักษา 2 ครั้งหลัง

6. คำแนะนำสำหรับอาสาสมัคร

6.1. หลังจากการรักษาแต่ละครั้ง ใน 24 ชั่วโมงแรก ขอให้ท่านล้างหน้าด้วยน้ำสะอาดเพียงอย่างเดียว และ ห้ามแต่งหน้า เพราะผิวท่านจะระคายเคืองง่าย เกิดผื่นแพ้ได้

6.2. หลัง 24 ชั่วโมง ท่านสามารถใช้ผลิตภัณฑ์ดูแลผิวหน้า ที่ผู้วิจัยมอบให้ ได้แก่ ผลิตภัณฑ์บำรุงผิวหน้า ให้ใช้ทาสองครั้ง เช้า และ ก่อนนอน, ใช้ผลิตภัณฑ์กันแดดทุกเช้า, และ ใช้ผลิตภัณฑ์ทำความสะอาดผิวหน้า เช้า และ เย็น

6.3. ใช้ร่มกันแดดเสมอ และงดให้ผิวหน้าถูกแดด ในช่วง 1-2 สัปดาห์ หลังการรักษาแต่ละครั้ง

7. ท่านจะได้รับบันทึกผลข้างเคียงทั้ง สำหรับใบหน้าซ้าย และใบหน้าขวา ระหว่างการศึกษาวิจัยหากเกิดผลข้างเคียงอันเป็นเหตุจากการรักษา ให้รีบติดต่อผู้วิจัยทันที เมื่อผู้วิจัยประเมินแล้วว่าเป็นผลข้างเคียงในระดับที่ควรได้รับการรักษาเพิ่มเติม ท่านจะได้รับการรักษาโดยไม่เสียค่าใช้จ่ายใดๆ

8. การประเมินผลบางส่วน แพทย์จะให้ท่านเป็นผู้กรอกข้อมูล

9. ข้อมูลต่างๆของท่านจะถูกเก็บเป็นความลับ และจะเปิดเผยเฉพาะข้อมูลที่ได้สรุปผลหลังเสร็จสิ้นโครงวิจัยเท่านั้น โดยข้อมูลที่เปิดเผยเป็นผลการวิจัยที่ไม่ได้ระบุชื่อและข้อมูลส่วนตัวของท่านแต่อย่างใด

10. การเข้าร่วมโครงการวิจัยนี้เป็นไปโดยสมัครใจ ท่านอาจจะปฏิเสธที่จะเข้าร่วมหรือถอนตัวจากการศึกษานี้ได้ตลอดเวลา โดยไม่กระทบต่อการดูแลรักษาที่ท่านจะได้รับจากแพทย์

ประการสำคัญที่ท่านควรทราบ ผลการศึกษานี้ ใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น ข้อมูลส่วนบุคคลต่างๆจะถูกเก็บรักษาไว้เป็นอย่างดี และไม่มีการเผยแพร่เพื่อจุดประสงค์อื่นใด

ขอขอบคุณในความร่วมมือของท่านมา ณ ที่นี้

Take Home Message

Information and methodology

We have to inform you that,

1. eMatrix™ and INTRAcel™ , are treatments for acne scars, large pores, skin laxity. They are expensive.

These two devices have the same principle using radiofrequency to cause around 60 degree Celsius temperature in the skin. This principle subsequently leads into new collagen production and tissue remodeling in 3 to 6 months after the treatment. Thus, acne scar appearance is improved. These devices have the similarity in the source of energy that produces bipolar radiofrequency.

The major difference between two devices is eMatrix™ has the gold plate to conduct the RF on the volunteer's skin, without any sharp needle. In contrary, INTRAcel™ device uses adjustable needles to penetrate skin at specific depths (0.5, 0.8, 1.5, 2 mm) and release the RF into the skin.

2. The researcher does not get any commercial benefits from any drug company.

3. After you are evaluated by physician and fitted for enrollment to the study, you will be treated by two RF devices. One device for each side of face. Both devices use for acne scar treatment and approved by Thai Food and Drug Administration office (FDA). What determine the treatment for each side of the face came from randomization process.

4. You will be absent from other acne scar treatments during the study. You will use facial products from the researcher.

5. You are able to make follow-up treatments and evaluations. At least 5-6 times of appointments will occur.

6. Advice for volunteers

6.1 Avoid makeup for 24 hours. In the first 24 hours after each treatment, wash the face with pure sterile water.

6.2 For given facial products, we need to give you information how to use them. After 24 hours, apply the moisturizer at least twice daily; apply sunscreen in the morning; and wash your face with mild soap twice daily.

6.3 Use of physical sun barrier such as umbrella, hat, and totally avoid sun exposure for at least 1-2 weeks after the treatment.

7. You were given a “side effect record” sheet to record the side effects of the treatment. If any serious side effect occurs, please contact the researcher immediately. The researcher will evaluate it and help for correct it.

8. You may need to give the researcher data. You will tell the truth only.

9. All of your data will be kept confidentially. No personal identity will be published.

10. Participation to this study is voluntary. You may leave anytime for necessary reasons.

Any further publication is for educational purpose only.

Thank you for your attention.

เกณฑ์ในการคัดเลือกผู้เข้าร่วมวิจัย (INCLUSION CRITERIA)

1. ผู้เข้าร่วมวิจัย ยินดีเข้าร่วมโครงการวิจัยด้วยความสมัครใจ ยินยอมให้ใช้ข้อมูลภาพถ่าย เพื่อจุดประสงค์ทางด้านวิชาการ ได้เขียนหนังสือยินยอมเข้าร่วมโครงการวิจัย เรียบร้อยแล้ว และเข้าใจในเนื้อหาของเอกสารทุกฉบับเป็นอย่างดี

2. เป็นชาวไทย ที่สุขภาพแข็งแรง ได้รับการวินิจฉัยจากแพทย์ว่าเป็นโรคหลุมสิว บริเวณแก้มทั้งสองข้าง ในระดับ ที่ 1-4 ตาม Baron and Goodman classification

3. เป็นเพศชายและหญิง อายุระหว่าง 18-45 ปี ลักษณะสีผิวประเภท 3 ถึง 4

4. ผู้เข้าร่วมวิจัยสามารถมาพบแพทย์ได้ตามที่แพทย์นัด โดยเป็นการนัดรักษาและเก็บข้อมูล 3 ครั้งแรก และ 2 ครั้งหลัง เป็นการเก็บข้อมูลติดตามผล หลังการรักษา 1, 3 เดือนตามลำดับ

5. ระหว่างการศึกษา ผู้เข้าร่วมวิจัย จะใช้ผลิตภัณฑ์ดูแลผิวหน้าเฉพาะตามที่แพทย์ระบุเท่านั้น

6. ผู้เข้าร่วมวิจัยไม่รับการรักษาหลุมสิวด้วยวิธีอื่นตลอดการวิจัยนี้

7. หากเป็นเพศหญิง สามารถคุมกำเนิดได้ตลอดการวิจัย

8. อาสาสมัครที่สูบบุหรี่และดื่มสุรา สามารถงดพฤติกรรมดังกล่าวได้ตลอดการวิจัย

Selection Criteria

Inclusion Criteria

1. All subjects were required to sign an informed consent form of benefits, risks and possible complications of the treatment and publication of photographs.

2. Healthy Thai volunteers with diagnosis of mild to severe atrophic acne scars on both sides of cheeks, according to Goodman and Barron classification

3. Both males and females, ages 18-45, Fitzpatrick skin types III to V

4. All subjects were able to participate in the treatment once a month for the duration of three months and could be followed up at one, three and six months after the last treatment. Only volunteers who consented to longitudinal follow-up during the study period were enrolled.

5. All subjects were able to stop using own facial products during the study. They used the products given by the researcher only to prevent any bias that may occur.

6. All subjects did not receive any other treatment during the study.

7. All female of child-bearing potential had a birth control during the study.

8. Subject who has a present history of smoking and alcoholic drinking needs to stop smoking and drinking the study.

เกณฑ์ในการคัดออกจากโครงการวิจัย

1. ผู้เข้าร่วมวิจัยไม่มีลักษณะหลุมสิวที่ต้องการ

2. ผู้เข้าร่วมวิจัยมีลักษณะหลุมสิวที่ต้องการ แต่ไม่มีที่บริเวณแก้ม

3. ผู้เข้าร่วมวิจัยมีลักษณะสิวอักเสบ แผล โรคมะเร็ง โรคผิวหนังอื่นๆ เกิดขึ้นบริเวณหลุมสิว

4. ผู้เข้าร่วมวิจัยมีประวัติโรคเริมบริเวณใบหน้า

5. ผู้เข้าร่วมวิจัยตั้งครรภ์ หรืออยู่ระหว่างในนมบุตร

6. ผู้เข้าร่วมวิจัยมีความเจ็บป่วยร้ายแรง อาทิเช่น โรคหัวใจ, ตับ, ไต, โรคมะเร็ง, โรคเบาหวานรุนแรงที่ไม่สามารถควบคุมระดับน้ำตาลในเลือดได้, ความดันโลหิตสูงรุนแรง, โรคเลือดออกหยุดยาก, แพ้แสง, การฝังอุปกรณ์ไฟฟ้าไว้ในร่างกาย, และภาวะภูมิคุ้มกันบกพร่อง

7. ผู้เข้าร่วมวิจัยมีประวัติได้รับการรักษาหลุมสิว ด้วย การกรอผิว, การใช้สารเคมี, เลเซอร์, RF หรือการรักษาหลุมสิวด้วยวิธีอื่นใด ภายใน 3 เดือนก่อนการวิจัยนี้

8. ผู้เข้าร่วมวิจัยมีประวัติได้รับการฉีดสารโบทูลินัม, สารเติมเต็ม, หรือการฝังสิ่งแปลกปลอมในบริเวณที่รักษา มาภายใน 6 เดือนก่อนการวิจัย

9. ผู้เข้าร่วมวิจัยมีประวัติ การฟื้นฟูบาดแผลไม่ค่อยดี หรือ โรคคีลอยด์ และการเกิดแผลเป็นง่ายบริเวณใบหน้า

10. มีประวัติใช้ยา ดังต่อไปนี้ ในระยะเวลา 1 เดือน ก่อนเข้าร่วมโครงการวิจัย ได้แก่ วิตามินเอ, วิตามิน อี, ฮอร์โมน, สมุนไพร, ยาเสตียรอยด์, ยาต้านการแข็งตัวของเลือด, ยาต้านลิ่มเลือด และ ยาต้านอักเสบ แบบ NSAIDS

11. มีประวัติการแพ้ยาชาประเภททามาก่อน

Exclusion Criteria

1. Subject has no required atrophic acne scars.
2. Subject has required scars but not on the cheeks.
3. Subject has an active inflammation, wound, pre-malignancy, malignancy, or other skin disease on top of the lesions. These conditions affect wound healing.
4. History of herpes simplex and herpes zoster on the face
5. Pregnancy and lactation
6. Serious concurrent medical illnesses such as heart disease, liver disease, kidney disease, hematologic disease, cancer, poorly controlled diabetic mellitus, severe hypertension, coagulopathy, photosensitivity, electrical implantation and immunocompromised state
7. History of microdermabrasion, chemical peeling, laser resurfacing, radiofrequency treatment or any treatment for acne scar within three months before the study
8. History of botulinum toxin or filler injection within six months before the study or permanent implant in the treatment area
9. History of poor wound healing, keloids and hypertrophic scars on the face
10. Use of systemic isotretinoin, vitamin E derivatives, hormones, herbs, prednisolone, antiplatelet, anticoagulant, and NSAIDS within one month before the study
11. Previous history of hypersensitivity to anesthetic creams

เกณฑ์การให้ออกจากการศึกษาในขณะที่ดำเนินโครงการวิจัยอยู่

1. เกิดผลข้างเคียงที่เป็นอันตรายร้ายแรง
2. ผู้เข้าร่วมวิจัยไม่ให้ความร่วมมือที่ดี
3. ผู้เข้าร่วมวิจัยไม่มาตามแพทย์นัด
4. ผู้เข้าร่วมวิจัยต้องการออกจากการวิจัย ด้วยเหตุผล .....
5. ตั้งครรภ์ เจ็บป่วยร้ายแรง หรือเสียชีวิต ในช่วงอยู่ระหว่างการดำเนินการวิจัย

Discontinuation Criteria

1. Serious side effects occurring
2. The volunteer does not give the appropriate cooperation
3. Failure in follow-up appointment
4. The volunteer want to quit
5. Pregnancy, serious illness, and dying

รายละเอียดของเครื่องมือที่ใช้ในการรักษาอาสาสมัคร และ รายละเอียดในการยิงเลเซอร์รักษาของผู้วิจัย มีดังนี้

Intervention

Half of the volunteer's face was treated with the fractional radiofrequency microneedle (INTRAcel^{TM}) and another half with the sublative bipolar radiofrequency device (eMatrix^{TM}). Both devices were approved by Thai FDA.

System Specifications of the Sublative Bipolar Radiofrequency Device (eMatrix^{TM}, Syneron)

Sublative RF Output Parameters	
Total Radiofrequency energy:	up to 25J/cm3, up to 62 mJ/pin
Programs' RF energy:	
Program A	10 – 30 mJ/pin, in 5mJ increments
Program B	32 – 48 mJ/pin, in 4mJ increments
Program C	50 – 62 mJ/pin, in 3mJ increments
Power range:	20 – 75 W (Impedance: 200 – 2,500 Ohtms)

Max. Voltage output (applicator electrodes):	275 VRMS (without load)
Electrodes:	Two active and bi-polar applicator electrodes
Sublative iD Standard Treatment Tips	64 electrode pins
Disposable tip footprint:	12 x 12 mm
Distance between electrode pins	1.5 mm

Source eMatrix (2013)

Figure A1 Sublative Bipolar Radiofrequency Device (eMatrix™, Syneron) and its gun

System Specification of the Fractional Radiofrequency Microneedle Device (INTRAcel™; Jeisys000).

Applied Energy	RF 1 Mhz
Output Power	Mono-polar up to 700W and Bi-polar*: up to 700W

*In our study, we used the Bi-polar output to control the output power as the same type as in sublative bipolar radiofrequency device.

Spot Size (Treated Area)	1cm x 1cm / 0.2cm x 0.2cm
Disposable Tip Matrix	49 electrode needles, 4 electrode needles, and 7 electrode needles

Source INTRAcel (2013)

Figure A2 Fractional Radiofrequency Microneedle Device (INTRAcel^{TM}; Jeisys, Seoul, Korea) and its tip

Parameter of the Treatment with Sublative Bipolar Radiofrequency Device (eMatrix^{TM})

Treatment with Program C: Energy 62 mJ/pin x 2 passes at area of acne scars and 1 pass for area of normal skin

Estimated pulses for each volunteer were about 100 shots for the half side of the face per session. Overlapping area of each continuous shot was less than 20%.
(The energy would be adjusted in mentioned range according to the severity of atrophic acne scar, reaction of the volunteers' skin, volunteer tolerance, and volunteers' skin types to make the best treatment for each volunteer and each session.)

Parameter of the Treatment with Fractional Radiofrequency Microneedle Device (INTRAcel^{TM})

Its tip for this study has 49 microneedle electrodes in an area of 1 cm^2 and deployed into the deep dermis. The entire needle electrode is nonconductive expect the tip, beginning 0.3 mm from the distal end, to protect from radiofrequency heating at the insertion site. Radiofrequency energy is emitted to the dermis 0.2 seconds after

microneedle insertion. The radiofrequency energy delivery durations differ according to energy levels.

In this study, a 1.5-mm depth needle at a power of 500 W (maximum power 700 W) was used for treatment of all the face except forehead and scar area. The forehead area was treated with 0.8-mm depth needle because of its thin skin width. At the second pass for acne scar area, a 2.0-mm depth needle was used.

We used level 4 energy (the maximum level is 7), bipolar mode.

Estimated shots for each volunteer were about 200 shots for the half side of the face per session. Lesion was treated for 2 passes at area of acne scars and 1 pass for area of normal skin. Overlapping area of each continuous shot was less than 20%.

6. ประโยชน์ที่ได้รับจากการวิจัย

1. ผลโดยตรง คือ อาสาสมัครมีหลุมสิวที่ดูตื้นขึ้น รวมทั้งผลประโยชน์ด้านอื่นที่ได้อาจได้รับ อาทิ ผลกระทบเกี่ยวกับภาวะหน้ามัน และ ภาวะผิวหนังหย่อนคล้อย

2. การศึกษานี้ ทำให้เราบอกได้ว่า ในระยะยาว เครื่องมือใดมีประสิทธิผลในการรักษาหลุมสิว ที่ดีและคุ้มค่า คุ้มราคา ผลข้างเคียงน้อย

3. ผลการศึกษาเป็นแรงบันดาลใจสำหรับการศึกษาที่น่าสนใจถัดถัดไป

Expected Benefits & Application

1. The direct impact is subjects get better in appearance of atrophic acne scars. Improvement of other aspects such as sebum production and skin laxity will be recorded also.

2. In long term, this study leads further into the question which acne scar treatment is more appropriate in the aspect of cost, benefits, and side effects.

3. The result will then inspire Thai researchers for a new interesting study.

7. ความเสี่ยงหรือผลข้างเคียงที่จะเกิดขึ้นต่ออาสาสมัคร พร้อมทั้งระบุมาตรการหรือวิธีแก้ไขที่ผู้วิจัยเตรียมไว้

หลังการรักษา จะเกิดผลข้างเคียงที่เกิดขึ้นทันที คือ ใบหน้า แดง, บวม, มีเลือดซึม, ช้ำ ซึ่งโดยทั่วไปจะหายเองภายในระยะเวลา 3-7 วัน และอาจมีสะเก็ดหลุดลอกได้ แพทย์จะใช้ผ้าสำลีชุบน้ำเกลือประคบหลังการรักษาทันที และ แนะนำให้อาสาสมัครใช้ครีมบำรุงที่แพทย์มอบให้ ขณะอยู่

ที่บ้าน ทำให้ผิวหนังชุ่มชื้น ฟื้นตัวได้ดีขึ้น และช่วยลดผลข้างเคียงดังกล่าว พร้อมกันนี้ ให้ท่านปฏิบัติตามคำแนะนำในการปฏิบัติตัวอย่างเคร่งครัด

หากเกิดผลข้างเคียงที่รุนแรง เช่น ผิวหนังไหม้จากความร้อน แพทย์จะดูแล ทำแผลท่านจนบาดแผลดีขึ้น และแสวงหาการรักษาเพิ่มเติม เช่น ศัลยกรรมตกแต่งปลูกถ่ายผิวหนัง เพื่อให้สภาพผิวหนังกลับคืนสู่สภาพดีเท่าที่เป็นได้ พร้อมทั้งให้ค่าชดเชยตามสมควร พิจารณาจากรายได้และการงานที่สูญเสียไปของอาสาสมัครต่อวัน หากเกิดรอยคล้ำจากการรักษา แพทย์จะมอบครีมที่ลดการทำงานของเม็ดสีผิว (whitening product) ตัวอย่างเช่น ครีมที่มีสาร transexamic acid, kojic acid, azelic acid, หรือสารอื่นๆ ผสม แก่ท่านเพื่อช่วยลดรอยคล้ำ โดยทั่วไปรอยคล้ำเหล่านี้จะจางลงใน 2-3 เดือน

8. ขอบเขตการดูแลรักษาความลับของข้อมูลต่างๆ ของอาสาสมัคร

ข้อมูลต่าง ๆ ของอาสาสมัคร จะถูกจดบันทึกไว้ในแฟ้มและจัดเข้าเก็บในลิ้นชักที่ต้องใช้กุญแจไข หัวหน้าโครงการวิจัย เป็นผู้เดียวที่มีกุญแจลิ้นชักเก็บไว้ และจะใช้ข้อมูลนี้เพื่อจุดประสงค์ทางด้านวิชาการเท่านั้น ไม่เปิดเผยชื่อหรือข้อมูลที่ระบุอัตลักษณ์แก่ผู้อื่น

ในส่วนข้อมูลภาพ และข้อมูลอิเล็กทรอนิกส์ จากเครื่องมือที่ใช้ในการวิจัยต่างๆ จะถูกเก็บไว้ในแผ่นเก็บข้อมูล (Harddisk) ส่วนตัวของผู้วิจัย ไม่มีการเผยแพร่หรือทำซ้ำนอกเหนือจากเพื่อการวิจัยนี้ และจุดประสงค์ทางด้านวิชาการเท่านั้น

9. การดูแลรักษาที่ผู้วิจัยจัดให้

ผู้วิจัย จะดูแลรักษาอาสาสมัคร ทั้งระหว่างการรักษา คือ หลังยิงเลเซอร์เสร็จบนใบหน้าทั้งสองข้าง จะมีการใช้ผ้าสำลีสะอาดชุบน้ำเกลือสะอาดประคบแผลหลังทำเลเซอร์ รวมทั้งให้ชุดสำลีนี้ให้อาสาสมัครกลับบ้านประคบลดความแสบร้อน นอกจากนี้ผู้วิจัยจะทำการประเมินผลข้างเคียงที่เกิดขึ้น บนใบหน้าของอาสาสมัครหลังการรักษาทันที และประเมินก่อนให้กลับบ้าน อย่างละเอียดเสมอ มีการจดบันทึก ความรู้สึกชา, ความคัน, ความบวม, ภาวะช้ำ, บาดแผล, ความแดง, รอยไหม้ต่างๆ ที่เกิดขึ้นบนใบหน้า และให้อาสาสมัครประเมินระดับความเจ็บปวด และความแสบร้อนเปรียบเทียบกัน ระหว่างใบหน้าทั้งสองข้าง

หลังการรักษาผู้วิจัย ให้คำแนะนำในการปฏิบัติตัว และให้ผลิตภัณฑ์ดูแลรักษาผิวหน้า อันได้แก่ยากันแดด, ครีมบำรุง, และน้ำยาทำความสะอาดผิวหน้า

คำแนะนำสำหรับอาสาสมัคร มีดังนี้

9.1 หลังจากการรักษาแต่ละครั้ง ใน 24 ชั่วโมงแรก ขอให้ท่านล้างหน้าด้วยน้ำสะอาดเพียงอย่างเดียว และ ห้ามแต่งหน้า เพราะผิวท่านจะระคายเคืองง่าย เกิดผื่นแพ้ได้

9.2 หลัง 24 ชั่วโมง ท่านสามารถใช้ผลิตภัณฑ์ดูแลผิวหน้า ที่ผู้วิจัยมอบให้ ได้แก่ ผลิตภัณฑ์บำรุงผิวหน้า ให้ใช้ทาสองครั้ง เช้า และ ก่อนนอน, ใช้ผลิตภัณฑ์กันแดดทุกเช้า, และ ใช้ผลิตภัณฑ์ทำความสะอาดผิวหน้า เช้า และ เย็น

9.3 ใช้ร่มกันแดดเสมอ และงดให้ผิวหน้าถูกแดด ในช่วง 1-2 สัปดาห์ หลังการรักษาแต่ละครั้ง

10. ค่าตอบแทนอาสาสมัคร และค่ารักษาพยาบาล ค่าชดเชย กรณีเกิดอันตรายหรือผลที่ไม่พึงประสงค์จากการวิจัยแก่อาสาสมัคร

การตอบแทนอาสาสมัคร คือการให้ผลิตภัณฑ์ดูแลรักษาผิวหน้า อันได้แก่ ยากันแดด, ครีมบำรุง , และน้ำยาทำความสะอาดผิวหน้า โดยที่อาสาสมัครไม่เสียค่าใช้จ่ายใดใด

กรณีเกิดอันตรายหรือผลไม่พึงประสงค์ ผู้วิจัยรับผิดชอบค่ารักษาพยาบาลในเบื้องต้นทั้งหมด และหากมีผลข้างเคียงระยะยาว อาทิเช่น ใบหน้าไหม้ ผู้วิจัยจะรับผิดชอบดูแล และแสวงหาการรักษาให้อาสาสมัครมีอาการดีขึ้นมากที่สุดเท่าที่เป็นไปได้ และให้ค่าชดเชย โดย พิจารณาจากการสูญเสียความสามารถในการทำงาน และรายได้ที่อาสาสมัครสูญเสียไปจากอาชีพการงานเป็นรายวัน

11. สิทธิของอาสาสมัครที่สามารถถอนตัวจากโครงการวิจัยได้ทุกเมื่อ โดยไม่กระทบต่อการดูแลรักษาที่พึงได้รับตามปกติ

อาสาสมัครมีสิทธิถอนตัวได้ทุกเมื่อ โดยไม่มีผลกระทบต่อการดูแลรักษาใดใดที่พึงได้รับตามปกติ

12. ข้อพิจารณาด้านจริยธรรม

โดยทั่วไป การรักษาหลุมสิวโดยเครื่องเลเซอร์ เมื่อยิงครบคอร์ส (จำนวนครั้งที่ควรกระทำในการวิจัยนี้ คือ ยิงทุก 1 เดือน เป็นจำนวน 3 ครั้ง) จะได้ผลให้หลุมสิวดีขึ้นได้ประมาณ 10-20% จากของเดิม จากผลการศึกษาในหลายการศึกษาในอดีต และจากประสบการณ์ของแพทย์ที่ใช้เครื่องมือเหล่านี้ในผู้ป่วยจำนวนหลายร้อยคน ก็ยืนยันไปในทางเดียวกัน

ซึ่งหมายความว่า ผู้วิจัยคาดหมายว่าหลังการรักษาจนครบตามกำหนด อาสาสมัครจะมีลักษณะใบหน้าทั้งสองข้างไม่แตกต่างกันมากนัก

แต่หากหลังการศึกษา ผลการรักษาบนใบหน้าอาสาสมัครมีความแตกต่างกันมาก อาทิเช่น ใบหน้าข้างหนึ่งมีหลุมสิวตื้นขึ้นมากในขณะที่ใบหน้าอีกข้างหนึ่ง มีสภาพหลุมสิวลึกลงไปกว่าเดิม จนดูสูญเสียสมดุลบนใบหน้า และเกิดความเสียโฉม ผู้วิจัยจะรับผิดชอบโดยใช้เครื่องเลเซอร์ที่ได้ผลดีกว่า มาทำการยิงหน้าข้างที่หลุมสิวลึกลงไปกว่าเดิม รวมทั้งแสวงหาการรักษาอื่นๆแนะนำให้อาสาสมัคร โดยไม่คิดค่าใช้จ่าย อาทิเช่น วิธีการรักษาโดยใช้เข็มกลิ้งบนใบหน้า (Dermaroller) หรือ การใช้เข็มตัดพังผืดใต้หน้า (Subcision) ฯลฯ จนอาสาสมัครมีอาการดีขึ้นและ ใบหน้าดูมีสมดุลของความเป็นหลุมสิวทั้งสองข้าง มากขึ้นภายใต้วิจารณญาณของแพทย์ผู้ดูแล และความเหมาะสมของบริบทที่เกิดขึ้น

13. ชื่อ ที่อยู่ เบอร์โทรศัพท์ ของหัวหน้าโครงการวิจัย หรือแพทย์ที่ผู้วิจัยกำหนด โดยสามารถติดต่อได้ทุกเวลา กรณีมีเหตุจำเป็นหรือฉุกเฉิน

นพ.ชเนษฎ์ ศรีสุโข
โรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพมหานคร
38/11-13 อาคารอโศกเพลส ถนนอโศก สุขุมวิท 21 แขวงคลองเตยเหนือ
เขตวัฒนา กทม. 10110
เบอร์โทรศัพท์เคลื่อนที่ 08-9669-4875

APPENDIX B

ข้อมูลการวิจัย: ส่วนของอาสาสมัคร

RESEARCH PROFILE: (VOLUNTEER'S PART)

A COMPARATIVE STUDY OF FRACTIONAL RADIOFREQUENCY MICRONEEDLE AND SUBLATIVE BIPOLAR RADIOFREQUENCY TREATMENT IN ACNE SCARS

(ALL DATA WILL BE KEPT CONFIDIDENTIALLY)

ขอให้ท่านอาสาสมัคร กรอกข้อมูลตามจริง ข้อมูลจะถูกเก็บไว้เป็นความลับ

วัน/เดือน/ปี ที่เริ่มเก็บข้อมูล (Date) ...../...../.....

ส่วนที่ 1: ข้อมูลทั่วไป **(Part I: General demographic data)**

ลำดับที่ (Number)..... HN .....

ชื่อ-นามสกุล (Name and Surname) .....

เพศ (Sex) ..... อายุ (Age) .....ปี

ที่อยู่ (Address) .....

.....

.....

เบอร์โทรศัพท์ติดต่อ (Mobile phone) .....

จดหมายอิเล็กทรอนิกส์ (E-mail) .....

อาชีพ (Occupation) .....

1. ข้าราชการ (government officer)
2. ลูกจ้าง / พนักงานบริษัท (office worker)
3. ธุรกิจส่วนตัว (business owner)
4. แม่บ้าน (housekeeper)
5. นักเรียน/นักศึกษา (student)
6. อื่นๆ.....

โรคประจำตัว (Medical illness)

1. .....
2. .....
3. .....
4. .....

ยาหรืออาหารเสริมที่ใช้เป็นประจำ ทั้งรูปแบบรับประทาน และยาทา

(Personal medication, supplement and drugs)

1. .....
2. .....
3. .....
4. .....

ประวัติแพ้ยา แพ้อาหาร (History of food or drug allergy)

1. .....
2. .....
3. .....
4. .....

ส่วนที่ 2: ข้อมูลตามเกณฑ์คัดเลือกในการวิจัย (Part II: data for selection criteria)

คุณมีหลุมสิวบนใบหน้า ใช่หรือไม่ (Do you have atrophic acne scars?)

O No (ไม่) O Yes (มี)

เป็นหลุมสิว บริเวณแก้มทั้งสองข้าง ใช่หรือไม่ O No (ไม่ใช่) O Yes (ใช่)

เป็นมาระยะเวลานาน กี่ปี กี่เดือน (Duration) .....

คิดว่าสาเหตุเกิดจากอะไร (What is the cause of them?)

O เป็นสิวอักเสบมาก่อน (Inflamed acne) O อุบัติเหตุ/การกระทบกระแทก (Trauma)

O ไม่ทราบสาเหตุ เกิดขึ้นเอง (Idiopathic and spontaneous)

อื่นๆ (others) .....

มีประวัติคนในครอบครัวเป็นหลุมสิว/พันธุกรรม (Do you think if it is a genetic inheritance?) O No (ไม่มี) O Yes (มี)

รายละเอียด (Detail) .....

หากเป็นเพศหญิง ท่านกำลังตั้งครรภ์ หรือให้นมบุตร ใช่หรือไม่
(In case you are female. Are you pregnant or in lactation?)

O No (ไม่) O Yes (ใช่ ฉันกำลังตั้งครรภ์ หรือ ให้นมบุตร อยู่)

O I am not female (ฉันไม่ใช่ผู้หญิง)

หากเป็นเพศหญิงและไม่ได้กำลังตั้งครรภ์อยู่ ท่านสามารถคุมกำเนิดตลอดการศึกษาวิจัยได้หรือไม่
(In case you are female and not pregnant. Do you have an appropriate plan for contraception?)

O I have a good plan for contraception. I promise I will not get pregnant during the study. (ได้)

O I cannot promise that (ไม่ได้)

O I am not female (ฉันไม่ใช่ผู้หญิง)

ประวัติการสูบบุหรี่และใช้แอลกอฮอล์ (history of smoking and drinking)

O No (ไม่สูบบุหรี่ ไม่ใช้แอลกฮอล์)

O Yes, I like smoking (ฉัน สูบบุหรี่/ซิการ์/ยาสูบ/บาราคุ)

O Yes, I like drinking (ฉัน ดื่มเครื่องดื่มแอลกอฮอล์)

O Yes, I like both of them (ฉัน ทั้ง สูบ และ ดื่มเครื่องดื่มแอลกอฮอล์)

หากท่านสูบบุหรี่หรือดื่มเครื่องดื่มแอลกอฮอล์ ท่านจะสามารถหยุดพฤติกรรมดังกล่าว ตลอดการศึกษาวิจัยได้หรือไม่?

O No (ไม่ได้) O Yes (ได้) O I am not sure (ฉันไม่แน่ใจ)

ท่านมีประวัติโรคเริมบนใบหน้าหรือไม่ (Do you have a history of herpes infection on face?) O Never (ไม่เคยมี) O Yes (เคยมี)

, รายละเอียด (give the details) .....

ท่านมีประวัติโรคแผลเป็นนูน บริเวณใบหน้า หรือไม่ (history of keloid and hypertrophic scar) O Never (ไม่เคยมี) O Yes (เคยมี)

, รายละเอียด (give the details) .....

ท่านมีประวัติแผลหายช้าหรือไม่ (history of poor wound healing)

O Never (ไม่เคยมี) O Yes (เคยมี) , รายละเอียด (give the details) .....

ท่านมีประวัติแพ้ยาชา ทั้งแบบฉีด หรือ แบบทา หรือไม่

(Do you have an allergy to anesthetic cream or injection?)

O Never (ไม่เคยมี) O Yes (เคยมี) , โดยมีอาการ (give the details) .....

ท่านมีการฝังโลหะ หรืออุปกรณ์ไฟฟ้าในร่างกาย หรือไม่ (Do you have metal or electrical implants?) O Never (ไม่มี) O Yes (มี)

, รายละเอียด (give the details) .....

ท่านมีประวัติ แพ้โลหะ หรือไม่ (Do you have an allergy to metals before?)

O Never (ไม่เคยมี) O Yes (เคยมี) , โดยมีอาการ (give the details) .....

ประวัติการผ่าตัดบริเวณใบหน้า (history of surgical procedure on the face)

O Never (ไม่เคยมี) O Yes (เคยมี)

, รายละเอียด (give the details) .....

ประวัติการรักษาหลุมสิวที่เคยได้รับ (past history of acne scar treatment)

1. ชื่อ (Name of treatment) .....
   ระยะเวลาที่ใช้ (How long is it for the duration?) ..... ปี (years) .....เดือน (months)
   - O ยังรักษาอยู่ (Currently in the treatment)
   - O หยุดรักษาแล้ว เป็นเวลา (Stopped the treatment already for)
     ..... ปี (years) …… เดือน (months)
2. ชื่อ (Name of treatment) .....
   ระยะเวลาที่ใช้ (How long is it for the duration?) ..... ปี (years) .....เดือน (months)
   - O ยังรักษาอยู่ (Currently in the treatment)
   - O หยุดรักษาแล้ว เป็นเวลา (Stopped the treatment already for)
     ..... ปี (years) …… เดือน (months)
3. ชื่อ (Name of treatment) .....
   ระยะเวลาที่ใช้ (How long is it for the duration?) ..... ปี (years) .....เดือน (months)
   - O ยังรักษาอยู่ (Currently in the treatment)
   - O หยุดรักษาแล้ว เป็นเวลา (Stopped the treatment already for)
     ..... ปี (years) …… เดือน (months)

เครื่องสำอางหรือครีมบำรุงผิวบริเวณใบหน้าที่ใช้อยู่ปัจจุบัน (Recent products for facial use)

โปรดใส่ชื่อผลิตภัณฑ์ ที่ใช้ทั้งหมด ในปัจจุบัน Please name all of them

1. .....
2. .....
3. .....
4. .....

ท่านได้ทำหัตถการเสริมความงาม ประเภทสารโบทูลินัม, สารเติมเต็ม หรือหัตถการต่างๆ ในรอบ 6 เดือนนี้หรือไม่ (Did you get botulinum toxin, filler injection or any aesthetic procedure in this 6 months?)

O No (ไม่) O Yes (ใช่) , รายละเอียด (give the details) .....

ส่วนที่ 3: ความตั้งใจในการเข้าร่วมการวิจัย (Part III: self-determination)

ท่านมีความตั้งใจจะเข้าร่วมการวิจัยจริง (Do you have an intention to enroll in the study?)

O No (ไม่ใช่) O Yes (ใช่)

ท่านมีความตั้งใจจะพบแพทย์ตามนัด อย่างสม่ำเสมอ ไม่บิดพลิ้ว
(Do you have an intention to make all follow-up visits?)

O No (ไม่ใช่) O Yes (ใช่)

ท่านมีความรู้ความเข้าใจเกี่ยวกับการรักษาหลุมสิว ตลอดจนการดูแลผิวหน้าหลังการรักษา ในการวิจัยนี้เป็นอย่างดี (Do you have a good understanding for this study?)

O No (ไม่ใช่) O Yes (ใช่)

ท่านสามารถปฏิบัติตามสิ่งที่คณะผู้วิจัยแนะนำ และเอกสารการวิจัยอย่างเคร่งครัด
(Do you have an intention to cooperate with the researcher and all advise?)

O No (ไม่ใช่) O Yes (ใช่)

ข้าพเจ้าขอรับรองว่าข้าพเจ้าให้ความจริงทุกประการ I certify that I tell the truth only.

.....

ลายมือชื่ออาสาสมัคร Volunteer's Signature

อาภรณ์ คูสุวรรณ

ลายมือชื่อพยาน (พญ.อาภรณ์ คูสุวรรณ): Witness A' Signature

.....

ลายมือชื่อพยาน (.....): Witness B' Signature

ชเนษฎ์ ศรีสุข

ลายมือชื่อผู้วิจัย The researcher's Signature

APPENDIX C

INFORMED CONSENT FORM

REH_3

Mae Fah Luang University Hospital
38/11-13 Asoke Place Building, Asoke road, Sukhumvit 21, Klong Toey Nua,
Wattana, Bangkok 10110, Thailand

หนังสือยินยอมเข้าร่วมโครงการวิจัย

(INFORMED CONSENT)

วันที่.....เดือน.....พศ..... (Date: D/M/Y)

ข้าพเจ้า (นาย/นาง/นางสาว) ..... (Name)

อายุ.....ปี (Age) อาศัย อยู่ บ้าน/หมู่บ้าน/คอนโด ชื่อ..... (Address)

เลขที่..... (House No.) หมู่ที่..... (Village No.) ซอย..... (Lane/alley)

ถนน..... (Road) แขวง/ตำบล..... (Sub-district/sub-area)

เขต/อำเภอ..... (District/Area) จังหวัด..... (Province) รหัสไปรษณีย์..... (Postal code)

เบอร์โทรศัพท์..... (Mobile phone)

ขอทำหนังสือแสดงความยินยอมเข้าร่วมโครงการวิจัยเพื่อเป็นหลักฐานแสดงว่า
I would like to make this informed consent form. The purpose is to show that,

1. ข้าพเจ้ามีสติสัมปัชชัญญะที่สมบูรณ์ และต้องการเข้าร่วมโครงการวิจัยของ นายแพทย์ชเนษฎ์ ศรีสุโข และ อาจารย์นายแพทย์ ไพศาล รัมณีย์ธร เรื่อง การศึกษาเปรียบเทียบเครื่องแฟรกชันนอลเรดิโอฟรีเควนซีไมโครนีดเดิล กับ เครื่องซับเบลทีฟไบโพลาร์เรดิโอฟรีเควนซี ในการรักษาแผลเป็นหลุมสิว

I am fully conscious and would like to participate in A COMPARATIVE STUDY OF FRACTIONAL RADIOFREQUENCY MICRONEEDLE AND SUBLATIVE BIPOLAR RADIOFREQUENCY TREATMENT IN ACNE SCARS of Chanesd Srisukho, MD and Lecturer Paisal Rummaneethorn

2. ข้าพเจ้าต้องการรับการรักษาหลุมสิว ที่โรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพฯ เป็นโรงพยาบาลที่ได้รับการรับรองอย่างถูกต้องโดยกระทรวงสาธารณสุข ตรวจรักษาโรคทั่วไป โรคผิวหนัง ความงาม และ การชะลอวัย รวมทั้งด้านอื่นๆ ทั้งนี้โรงพยาบาลแห่งนี้ ยังมีการเรียนการสอนปริญญาโททางด้านผิวหนังให้แก่แพทย์อีกด้วย

I am in Mae Fah Luang University Hospital, Bangkok seeking treatment for acne scars. I understand that Mae Fah Luang University Hospital has been accredited by the public health ministry of Thailand. Its purpose is for treatments of general diseases, dermatologic conditions, aesthetic procedures, anti-aging and other aspects. Otherwise, this hospital is a place for MS in dermatology studying and training.

3. ข้าพเจ้ารับทราบว่านายแพทย์ชเนษฎ์ และ อาจารย์นายแพทย์ไพศาล เป็นแพทย์แผนปัจจุบัน ที่ได้รับการรับรองโดยแพทยสภา ถูกต้องตามกฎหมาย

I understand that Dr.Chanesd and Lecturer Dr.Paisal are legal physicians certified by Thai medical council.

4. ข้าพเจ้าเข้าใจว่าข้าพเจ้าจะต้องเปิดเผยข้อมูลตามความเป็นจริงเพื่อการรักษา รวมทั้งให้ข้อมูลที่จำเป็นต่างๆ อาทิเช่น ประวัติโรคประจำตัว, การใช้ยาต่างๆ, การแพ้ยา, ฯลฯ

I understand that I must disclose all of the medical information to doctors and notify of any chandes that may occur during the course of treatment. It is important to list all of the medication I take, or state any known allergies.

5. ข้าพเจ้าได้อ่าน เอกสารชี้แจง: ข้อมูลสำหรับผู้ร่วมการวิจัย และได้รับการอธิบาย ถามตอบข้อสงสัยจากผู้วิจัยอย่างละเอียด ครบถ้วนแล้ว เกี่ยวกับวัตถุประสงค์การวิจัย , วิธีการวิจัย , ความปลอดภัย , ประโยชน์ที่จะได้รับจากการวิจัย, ข้อดี, รวมทั้งผลเสียที่อาจเกิดขึ้น

I have read all the documents and the clarification letter: data for the volunteer. I have questioned the researcher for all what I am curious. He answered me thoroughly. I understand objectives, methodology, safety, expected benefits, advantages, and possible disadvantages.

6. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ การเปิดเผยใดใดที่เกิดขึ้น เป็นการใช้ข้อมูลและผลการศึกษาเพื่อจุดประสงค์ทางวิชาการเท่านั้น จะไม่มีการระบุ ชื่อ-นามสกุล รวมทั้งข้อมูลส่วนตัวอื่นที่จะระบุตัวตนของผู้เข้าร่วมวิจัยได้ นอกเหนือจากจุดประสงค์ทางวิชาการแล้วจะไม่มีการเปิดเผยข้อมูลใดใด แก่บุคคลภายนอกโครง การวิจัย ยกเว้นได้รับคำสั่งศาล เท่านั้น

I receive the guarantee that all of my data will be kept confidentially. Any disclosure of it will occur as an educational purpose only and there will be no name or anything indicating my identity published.

7. ข้าพเจ้าทราบว่า หากเกิดอันตรายใดๆจากการวิจัย แพทย์ผู้วิจัยจะร่วมรับผิดชอบการรักษาพยาบาลที่เป็นผลสืบเนื่องจากการวิจัยนี้

I understand that if any serious complication occurs, the researcher will help for treatment of it.

8. ข้าพเจ้าได้รับทราบว่า หากเกิดอันตรายหรือเหตุจำเป็น ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากการวิจัย

I understand I can leave the study if any serious complication occurs.

9. เมื่อเข้าร่วมโครงการวิจัยแล้ว ข้าพเจ้ามีความมุ่งหมายว่า จะมาตามนัดการรักษา – การติดตามผล จำนวน 5 ครั้ง ได้ทุกครั้ง ข้าพเจ้าจะให้ความร่วมมือกับผู้วิจัยด้วยดี และรับทราบว่า หากข้าพเจ้าไม่สามารถทำตามนั้นได้ ข้าพเจ้าไม่ควรจะเข้าร่วมในงานวิจัยนี้ตั้งแต่แรก

I guarantee that I will give full cooperation to the researcher. I consent to longitudinal follow-up during the study period.

10.ข้าพเจ้าสามารถหยุดใช้ผลิตภัณฑ์ดูแลรักษาผิวหน้าอื่น ระหว่างการศึกษาวิจัย และจะใช้ผลิตภัณฑ์ที่คณะผู้วิจัยมอบให้ ซึ่งเป็นการดูแลรักษาผิวหน้าหลังการทำหัตถการ

I can stop other treatments for acne scars and other facial products during the study. I will use only products what the researcher give me.

ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้ทั้งหมดแล้ว จึงได้ลงลายมือชื่อไว้เป็นสำคัญ พร้อมกับหัวหน้าโครงการวิจัยและพยาน

I read every paragraph carefully and understood it well.

ลงชื่อ .....

(.....)

ผู้ยินยอมเข้าร่วมการวิจัย Volunteer's signature and name

ลงชื่อ .....

(Chanesd Srisukho, MD)

หัวหน้าโครงการวิจัย นายแพทย์ ชเนษฎ์ ศรีสุโข

ลงชื่อ .....

(.....)

พยานคนที่ 1 Witness A

ลงชื่อ .....

(.....)

พยานคนที่ 2 Witness B

APPENDIX D

บันทึกการวิจัย: ส่วนของคณะผู้วิจัย

RESEARCH RECORD: (RESEARCHERS' PART)

A COMPARATIVE STUDY OF FRACTIONAL RADIOFREQUENCY MICRONEEDLE AND SUBLATIVE BIPOLAR RADIOFREQUENCY TREATMENT IN ACNE SCARS

Name of the volunteer..... HN.....
Tasks at the first visit

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

Please use ✓ symbol

Checklist for the first visit		
Process	**Already done?**	
	Yes	**No**
The volunteer has his/her face cleansed for at least 30 minutes		
Physical examination of acne scars indicates they are fit to the selection criteria		
The volunteer has completed the RESEARCH PROFILE: (VOLUNTEER'S PART)		
All of the profile data is fit to selection criteria		
Assure that the volunteer can understand information in appendix I and how to care his/her face after treatment		
The volunteer has written the informed consent form		
The researcher asked the volunteer for any curiosity		
The researcher answered the volunteer's questions		
VISIA was performed		
Cutometer was performed		
Sebumeter was performed		

After these tasks, there is the form for evaluate the volunteer in the next page.

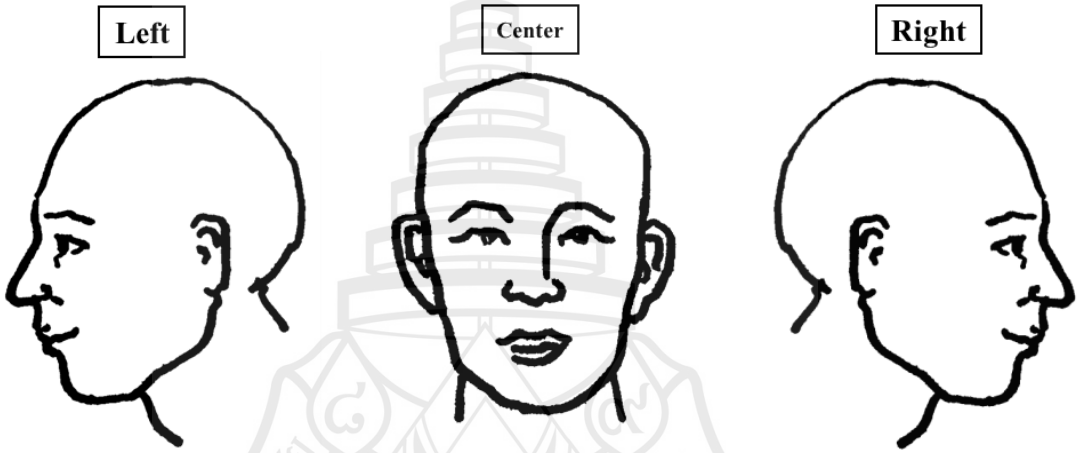
Classification of acne severity (Goodman & Baron, 2006)

Before treatment		
	Left	**Right**
Classification		

1st Physician's name ……..

Before treatment		
	Left	**Right**
Classification		

2nd Physician's name ……..



Grade	Description
1	Macular scarring or flat scarring that is characterized by flat areas of increased or decreased pigmentation visible from a distance of > 500 mm
2	Mild disease that is visible at distances of < 500 mm and can be covered by make-up. Examples include mild rolling acne scars
3	Moderate disease that is visible at ≥ 500 mm and is not easily covered with make-up or the normal shadow of a shaved beard. Stretching the skin can flatten the scar. Examples include more significant rolling scars, shallow boxcar scars and mild to moderate hypertrophic scars
4	Severe disease as in grade 3 but scarring is not flattened by stretching the skin. Examples include severe boxcar scars, deep divots, ice pick scars and hypertrophic keloid scarring (very raised/pigmented scars)

1. Photographs of each volunteer using VISIA®-CR

Please record the data every time after taking photographs and use ✓ symbol when finished processing

Checklist for VISIA®-CR photography						
Date	**Time**	**Treatment**	**Left**	**Center**	**Right**	Recorder's signature
		1st				
		2nd				
		3rd				
		1 months after				
		3 months after				

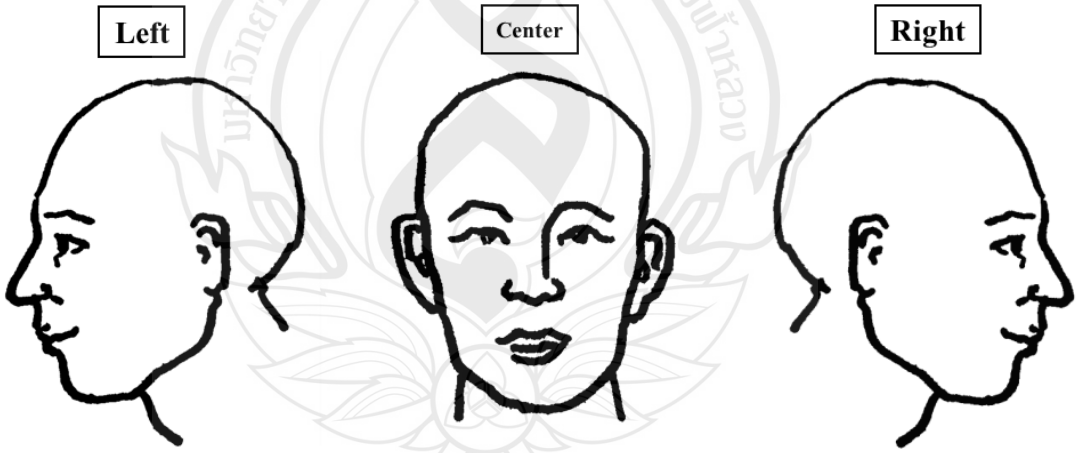
Classification of acne severity at 1 month after the last treatment

At 1 month after the last treatment		
Date …../……./…..	**Left**	**Right**
Classification		

1st Physician's name ……..

At 1 month after the last treatment		
Date …../……./…..	**Left**	**Right**
Classification		

2nd Physician's name ……..



Grade	Description
1	Macular scarring or flat scarring that is characterized by flat areas of increased or decreased pigmentation visible from a distance of > 500 mm
2	Mild disease that is visible at distances of < 500 mm and can be covered by make-up. Examples include mild rolling acne scars
3	Moderate disease that is visible at ≥ 500 mm and is not easily covered with make-up or the normal shadow of a shaved beard. Stretching the skin can flatten the scar. Examples include more significant rolling scars, shallow boxcar scars and mild to moderate hypertrophic scars
4	Severe disease as in grade 3 but scarring is not flattened by stretching the skin. Examples include severe boxcar scars, deep divots, ice pick scars and hypertrophic keloid scarring (very raised/pigmented scars)

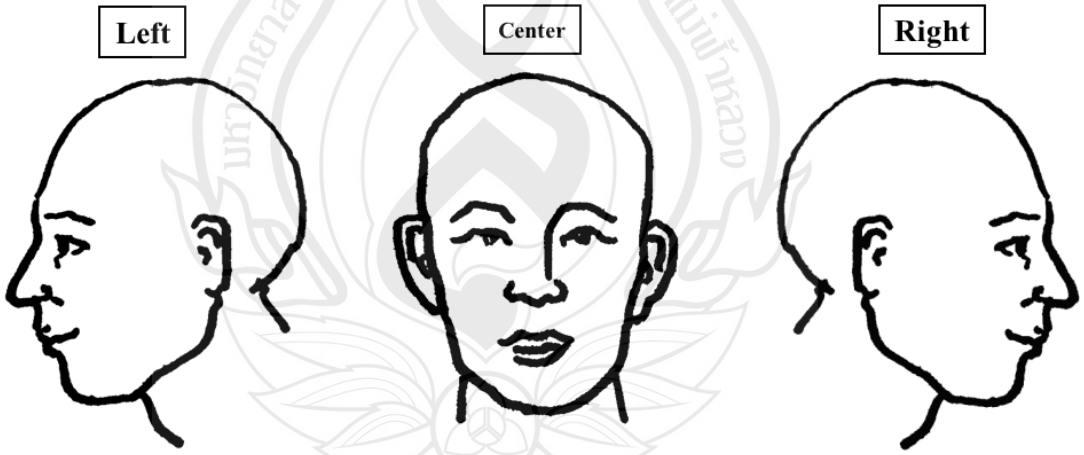
Classification of acne severity at 3 months after the last treatment

At 3 month after the last treatment		
Date …../……./…..	**Left**	**Right**
Classification		

1st Physician's name ……..

At 3 month after the last treatment		
Date …../……./…..	**Left**	**Right**
Classification		

2nd Physician's name ……..



Grade	Description
1	Macular scarring or flat scarring that is characterized by flat areas of increased or decreased pigmentation visible from a distance of > 500 mm
2	Mild disease that is visible at distances of < 500 mm and can be covered by make-up. Examples include mild rolling acne scars
3	Moderate disease that is visible at ≥ 500 mm and is not easily covered with make-up or the normal shadow of a shaved beard. Stretching the skin can flatten the scar. Examples include more significant rolling scars, shallow boxcar scars and mild to moderate hypertrophic scars
4	Severe disease as in grade 3 but scarring is not flattened by stretching the skin. Examples include severe boxcar scars, deep divots, ice pick scars and hypertrophic keloid scarring (very raised/pigmented scars)

2. VISIA®-CR scores

Baseline VISIA®-CR scores **Date** ...../...../..... **Name**..... **HN**.....		
Scores	**Left**	**Right**
Major Texture (skin smoothness) Enlarged pores		
Others Fine lines and wrinkles Hyperpigmentation		
.....		

	VISIA®-CR scores					
	Date ...../...../....		**Date** ...../...../....		**Date** ...../...../....	
Scores	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
Texture (skin smoothness)						
Enlarged pores						
Fine lines and wrinkles						
Hyperpigmentation						
.....						

	VISIA®-CR scores					
	Date ...../...../....		Date ...../...../....		Date ...../...../....	
Scores	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
Texture (skin smoothness)						
Enlarged pores						
Fine lines and wrinkles						
Hyperpigmentation						
.....						

3. Cutometer

Baseline Cutometer scores **Date** ...../...../..... **Name**..... **HN**.....		
Parameters	**Left**	**Right**
R_0		
R_2		
Parameter		
Parameter		
Parameter		
Parameter		

	Cutometer scores					
	Date ...../...../....		Date ...../...../....		Date ...../...../....	
Parameters	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
R_0						
R_2						
Parameter						
Parameter						
Parameter						
Parameter						

	Cutometer scores					
	Date ...../...../....		Date ...../...../....		Date ...../...../....	
Parameters	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
R_0						
R_2						
Parameter						
Parameter						
Parameter						
Parameter						

4. Sebumeter

Baseline Sebumeter scores **Date** ...../...../..... **Name**..... **HN**.....		
Parameters	**Left**	**Right**
Forehead		
Nose		
Parameter		
Parameter		
Parameter		
Parameter		

	Sebumeter scores					
	Date ...../...../....		Date ...../...../....		Date ...../...../....	
Parameters	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
Forehead						
Nose						
Parameter						
Parameter						
Parameter						
Parameter						

	Sebumeter scores					
	Date ...../...../....		**Date** ...../...../....		**Date** ...../...../....	
Parameters	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
Forehead Nose Parameter ..... Parameter ..... Parameter ..... Parameter						

5. Treatment and Side Effect Record (for the researcher's evaluation)
Please use ✓ symbol and record every detail during treatment

Treatment Record			
Tasks	First Rx Date...../...../.... Time:	Second Rx Date...../...../.... Time:	Third Rx Date...../...../... . Time: .....
Cleansing with a mild soap			
Topical anesthetic application for at least 1 hour			
Remove of anesthetics and cleansing with 70% alcohol			
Skin drying			
Intervention			
Immediate care after treatment			
Give facial products and suggest him/her how to use them			
Physician's signature			

Please use ✓ symbol and give details

Immediate side effects by physical examination						
Signs	First Rx Date..../...../....		Second Rx Date...../...../....		Third Rx Date...../...../....	
	Left	Right	Left	Right	Left	Right
Erythema						
Minimal bleeding						
Swelling						
Itching						
Pain						
Numbness						
Burning sensation						
Vesicle and signs of burn						
Other.....						
Other.....						

6. Improvement scoring for acne scar appearance at times

Notice: this table is for two dermatologists who are not involved in the study. They need to individually evaluate the improvement of acne scar appearance between before and after photographs from VISIA. The score are as followed.

-3 is greatly decrease from baseline (less than -60% change)
-2 is moderately decrease from baseline (less than -40% change)
-1 is slightly decrease from baseline (less than -20% change)
0 is no change (nearly equal to 0% change)
+1 is slightly increase from baseline (more than +20% change)
+2 is moderately increase from baseline (more than +40% change)
+3 is greatly increase from baseline (more than +60% change)

Left side	**Time after the last treatment**		
	At 1 month Date ..../...../....	At 3 months Date ..../...../....	Comment
Improvement score (-3 to +3 compared to baseline)			
1st Physician .....signature			

Right side	**Time after the last treatment**		
	At 1 month Date ..../...../....	At 3 months Date ..../...../....	Comment
Improvement score (-3 to +3 compared to baseline)			
1st Physician .....signature			

Left side	**Time after the last treatment**		
	At 1 month Date ..../...../....	At 3 months Date ..../...../....	Comment
Improvement score (-3 to +3 compared to baseline)			
2nd Physician .....signature			

Right side	**Time after the last treatment**		
	At 1 month Date ..../...../....	At 3 months Date ..../...../....	Comment
Improvement score (-3 to +3 compared to baseline)			
2nd Physician .....signature			

7. Comparative scoring for acne scar appearance

Notice: this table is for two dermatologists who are not involved in the study. They need to individually compare the improvement of acne scar appearance between left and right photographs from VISIA. They need to pick which side that is improved better than another side and give the score, which are as followed.

+1 is slightly improved comparing to another side (more than +20% better)
+2 is moderately improved comparing to another side (more than +40% better)
+3 is greatly improved comparing to another side (more than +60% better)

The example is

Side	Score
Left	2+

This means an evaluator suggests that an appearance of acne scars after the treatment in the left photograph showed better improvement than the right photograph for 40%.

If an evaluator think the left and right photographs showed improvement in the same level, so-called nearly equal, please write "Left = Right" in the 'Side' cell and give '0' score.

Which side is improved more than another side?	**Time after the last treatment**				
	At 1 month Date ..../...../....		At 3 months Date ..../...../....		Comment
	Side	score	Side	score	
Comparative score (Left versus right)					
1st Physician's signature					

APPENDIX E

บันทึกการวิจัย: ส่วนของอาสาสมัคร

RESEARCH RECORD: (VOLUNTEER'S PART)

หลังเข้ารับการรักษา ท่านพบอาการเหล่านี้หรือไม่ โปรดใช้เครื่องหมายถูก และกรอกรายละเอียด
After the treatment, do you experience these side effects? Please use ✓ symbol and give us details

Side Effect Record of left side บันทึกผลข้างเคียงในใบหน้าซ้าย				
อาการ Signs	I experience this		เป็นเวลา (วัน/สัปดาห์) Duration (days/weeks)	หายแล้ว Recovered?
	พบ Yes	ไม่พบ No		
ลักษณะอาการแดงเป็นระยะเวลานาน Post-inflammatory erythema				
อาการบวมเป็นระยะเวลานาน Prolonged swelling				
ลักษณะผิวเปลี่ยนสี เข้มขึ้น Post-inflammatory hyperpigmentation				
ลักษณะผิวเปลี่ยนสี ขาวขึ้น Post-inflammatory hypopigmentation				
ลักษณะสีผิวไม่สม่ำเสมอ Dyspigmentation				
ความรู้สึกแปลกๆบริเวณที่รักษา Abnormal sensation				
อาการชาบริเวณที่รักษา Numbness				
เกิดรอยไหม้บริเวณที่รักษา Burning				
เส้นเลือดแดงฝอยขึ้น Telangiectasia				
อาการอื่นๆ โปรดระบุ Others.....				

Side Effect Record of right side บันทึกผลข้างเคียงในใบหน้าขวา				
อาการ Signs	I experience this		เป็นเวลา (วัน/สัปดาห์) Duration (days/weeks)	หายแล้ว Recovered?
	พบ Yes	ไม่พบ No		
ลักษณะอาการแดงเป็นระยะเวลานาน Post-inflammatory erythema				
อาการบวมเป็นระยะเวลานาน Prolonged swelling				
ลักษณะผิวเปลี่ยนสี เข้มขึ้น Post-inflammatory hyperpigmentation				
ลักษณะผิวเปลี่ยนสี ขาวขึ้น Post-inflammatory hypopigmentation				
ลักษณะสีผิวไม่สม่ำเสมอ Dyspigmentation				
ความรู้สึกแปลกๆบริเวณที่รักษา Abnormal sensation				
อาการชาบริเวณที่รักษา Numbness				
เกิดรอยไหม้บริเวณที่รักษา Burning				
เส้นเลือดแดงฝอยขึ้น Telangiectasia				
อาการอื่นๆ โปรดระบุ Others.....				

ความพึงพอใจ หลังสิ้นสุดการรักษา

Volunteer's satisfaction after the last treatment

โปรดใส่เครื่องหมายถูก ให้คะแนนความพึงพอใจ ในด้านต่างๆ Please use ✓ symbol

ที่ 1 เดือนหลังการรักษาครั้งสุดท้าย At 1 month after the last treatment session						
	ประเด็น for	น้อยมาก very poor	น้อย poor	ปานกลาง average	มาก good	มากมาก excellent
ด้านซ้าย Left side	หลุมสิว (acne scar)					
	ความมันบนใบหน้าลดลง (decrease in sebum production)					
	ความหย่อนคล้อย (skin laxity)					
ผลข้างเคียงและความไม่สะดวกสบายของการรักษาด้านซ้าย Side effects and uncomfortable feeling for left side						
ด้านขวา Right side	หลุมสิว (acne scar)					
	ความมันบนใบหน้าลดลง (decrease in sebum production)					
	ความหย่อนคล้อย (skin laxity)					
ผลข้างเคียงและความไม่สะดวกสบายของการรักษาด้านขวา Side effects and uncomfortable feeling for right side						

ที่ 3 เดือนหลังการรักษาครั้งสุดท้าย At 3 months after the last treatment session						
	ประเด็น for	น้อยมาก very poor	น้อย poor	ปานกลาง average	มาก good	มากมาก excellent
ด้านซ้าย Left side	หลุมสิว (acne scar)					
	ความมันบนใบหน้าลดลง (decrease in sebum production)					
	ความหย่อนคล้อย (skin laxity)					
ผลข้างเคียงและความไม่สะดวกสบายของการรักษาด้านซ้าย Side effects and uncomfortable feeling for left side						
ด้านขวา Right side	หลุมสิว (acne scar)					
	ความมันบนใบหน้าลดลง (decrease in sebum production)					
	ความหย่อนคล้อย (skin laxity)					
ผลข้างเคียงและความไม่สะดวกสบายของการรักษาด้านขวา Side effects and uncomfortable feeling for right side						

CURRICULUM VITAE

CURRICULUM VITAE

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