EVALUATION OF EFFICACY AND SIDE EFFECTS OF FRACTIONAL MODE Q-SWITCHED RUBY LASER 694 NM FOR FACIAL REJUVENATION IN ASIANS

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MASTER OF SCIENCE

PROGRAM IN DERMATOLOGY

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ABTRACT

Facial skin rejuvenation remains an extremely popular elective procedure for treatment of ageing skin. Ablative approach has potential complications and prolonged down time, therefore, non-ablative lasers were developed to avoid these problematic and uncomfortable sequelae. Fractional mode Q-switch Ruby Laser (QSRL) have high peak power and utilize also the fractional photothermolysis principle to achieve facial rejuvenation. Objectives: To evaluate the resurfacing capability of the fractional mode QSRL in Asian skin. Materials and Methods: 24 Thai volunteers with different grades of photo-damaged facial skin and post acne scarring, complete 3 sessions of non-ablative resurfacing of the whole face by 690 nm fractional QSRL at 4 weeks interval. Subjective evaluations include photographs, Patient Global Satisfactory score, and Global Improvement score. However, objective evaluation were also done by using Mexameter, MX18, and Visioscan® VC 98. Results: There is significant improvement in the dyschromia as measured by Mexameter, MX18 (*P* value .002). Patient Global Satisfactory score shows 80% have good to excellent response. No side effects like postinflammatory hyperpigmentation (PIH) were detected. Conclusions: Fractional mode QSRL have resurfacing capability that can targets major features of photodamaged facial skin in Asians, with little downtime, and adverse effects.

Keywords: Photo-damaged skin / Post-acne scarring / Skin resurfacing / Fractional laser / QSRL

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CHAPTER 1

INTRODUCTION

1.1 Background

The treatment of ageing skin remains a very hot topic, and facial skin rejuvenation remains an extremely popular elective procedure (Trelles, Mordon, & Calderhead, 2007), with a remarkable increase in the demand for facial rejuvenation in last decades. Fueled in part by reality television programming and the associated increase in public familiarity with, and acceptance of, the available procedures (Donath, 2010), which has driven up patient demand for the rejuvenation of photoaged skin, particularly of the face. Skin aging is a consequence of genetically programmed processes of intrinsic aging and extrinsic aging caused by ultraviolet light and other environmental insults (Jung, Kelly, & McCullough, 2006) like smoking, drugs, alcohol, poor diet, etc. These insults results in a change in the health of the collagen and the loss of the elastic properties of the skin which prematurely age the skin (Hoefflin, 2007). Aging skin exhibits progressive changes such as thinning, skin laxity, fragility, thus the skin loosens, wrinkles, and turns into a brownish-gray tone. Sun-exposed areas demonstrate other photoaging changes, including dyschromia, premature wrinkling, actinic elastosis and telangiectasiasthe (Pitanguy, Pamplona, & Radwanski, 2008; Ling, 2010). Histopathologically, photoaging is characterized by disorganized collagen fibrils, decreased normal collagen (Bernstein et al., 1996) with significantly elevated levels of cross-linked, partially degraded fragmented collagen, which inhibits healthy collagen biosynthesis (Orringer et al., 2005). Other histopathological changes in aging skin includes, an increased abnormal elastic fibers termed solar elastosis at the upper dermis, as well as flattening of the dermal–epidermal junction with elongated and collapsed fibroblasts (Bernstein et al., 1996). However, Asian skin differs from Caucasian skin in both structure and physiology, which make it exhibit alternate clinical manifestations of photoaging.

Asian skin have higher melanin content compared with white skin, which make Asian skins generally manifest the classic signs of photoaging later in life, typically beyond the fifth decade, and they are most susceptible to post-inflammatory hyperpigmentation as a direct consequence of cutaneous inflammation or injury (Ling, 2010).

Facial rejuvenation is the art and science of improving the aesthetics of the face, scalp, and neck areas to give a more youthful appearance (Shiffman, 2008). There are many methods of resurfacing and rejuvenating the facial skin including dermabrasion, chemical peels and surgical face lift. More recently, laser resurfacing with ablative carbon-dioxide (CO2) or erbium: yttrium aluminum- garnet (Er:YAG) lasers (Seoighe, Conroy, & Beausang, 2010; Orringer et al., 2005). The mechanism of facial rejuvenation of all these traditional methods of resurfacing based on removal of the epidermis, wounding of the dermis, which induce wound-healing process and subsequent production of collagen and remodeling of the dermal extracellular matrix. Although effective, these treatment methods are generally associated with a significant recovery period and associated with the potential for serious complications such as scarring, infection, and dyspigmentation (Orringer et al., 2005). In deed ablative lasers were first used for the treatment of rhytides and acne scars; however, investigators soon discovered that superficial sun damage changes, including lentigines, as well as actinic keratoses, fine lines, and other superficial imperfections also improved. Additionally, the deposition of heat was noted to cause a tissue-tightening effect, which softened deeper wrinkle (Kilmer & Semchyshyn, 2005). which make the laser resurfacing refined to allow precise, predictable and cosmetically acceptable results (Seoighe et al., 2010). Despite these advances, the prolonged postoperative erythema, a side effect experienced by virtually all patients treated with this modality, and other potential risks like delayed healing, postoperative pigmentary changes, and scarring (Goldberg & Whitworth, 1997) associated with ablative resurfacing has led to the development of nonablative lasers to improve solar skin damage, including rhytides, telangiectases, and pigmentation, and also improve the visual appearance of acne-scarred skin (Nikolaou, Stratigos, & Dover, 2005).

Nonablative technology evolved beginning with the use of early-pulsed dye lasers (Zelickson et al., 1999; Kilmer & Semchyshyn, 2005) when he noticed that laser treatment not only improved the port wine stain, but the scars as well (Kilmer & Semchyshyn, 2005). The mechanism of noninvasive or nonablative laser procedures involves the laser passing through the epidermis without any significant or damaging impact and inflicting thermal damage to the lower layers of dermis, thus encouraging the generation of collagen and resulting in tighter skin (Lee, 2003). Sparing of the epidermis, thus, minimize the laser surgical risks and essentially eliminating the period of post laser recovery (Orringer et al., 2005) and side effects.

Laser has progressed significantly over the last three decades (Seoighe et al., 2010). The cutting-edge technology of laser allows predictable and precise collagen enrichment with resultant skin rejuvenation to produce a fresh and youthful appearance. Newer wavelengths, pulsing techniques and delivery devices have confirmed the resurgence of this technology in aesthetic plastic surgery (Gupta & Jacob, 2007). Laser and laser-like assisted facial rejuvenation has become very popular during the last decade (Fernandes, 2003) and it's an optimal technique for treating severe photodamaged, premalignant lesions, and wrinkles. Laser resurfacing can also remove seborrheic keratosis, nevi, benign adnexal growths, and sebaceous hyperplasia (Goldman, 2006). A wide variety of lasers and non-laser light sources have been used for nonablative resurfacing therapy (Keyvan, Maria, Navid & Sahar, 2006) with wavelengths ranging from those in the visible spectrum to those in the infrared (Orringer et al., 2005). Noninvasive techniques for skin rejuvenation, also termed laser toning, are quickly becoming standard in the treatment of mild rhytids and overall skin toning (Lee, 2003) and to improve skin color (Schmults, Phelps, & Goldberg, 2004). We end now with few basic effective approaches in promoting facial rejuvenation by lasers, ranging from those that ablate the epidermis, to those which provide minimal thermal effects through non-ablative lasers and light sources (Alexiades-Armenakas, Dover, & Arndt, 2008). As would be expected, each has some advantages and disadvantages (Fernandes, 2003). Therefore, the search for an ideal and reproducible method to rejuvenate photoaged skin has been a long one (Trelles, 2003).

The newest technology to enter the laser arena is fractional resurfacing (Alexiades-Armenakas et al., 2008). The novel concept of non-ablative fractional photothermolysis (FP) was introduced to the market in 2003 as an answer to the need for effective, yet low risk, resurfacing techniques. Unlike conventional ablative and non-ablative lasers, fractional ablative and non-ablative photothermolysis treats only a fraction of the skin, leaving up to a maximum of 95% of the skin uninvolved. The undamaged surrounding tissue allows for a reservoir of viable tissue, permitting rapid epidermal repair (Manstein, Herron, Sink, Tanner, & Anderson, 2010). In fractional laser resurfacing technique the laser beam is ‘fraxelated’ and instead of a large single beam, a number of microscopic laser beams are produced causing microscopic thermal wounds to specific areas whilst sparing the surrounding tissues. This creates an adjustable 3D microscopic thermal burn. These areas are called microscopic treatment zones (MTZs) (Seoighe et al., 2010), which are barely detectable to the naked eye (Hedelund, Moreau, Beyer, Nymann, & Haedersdal, 2010; Manstein, Herron, Sink, Tanner, & Anderson, 2004). There is high irradiance in the MTZ, while, avoids heating of the adjacent skin. This is allowing collagen denaturation in the MTZ and subsequent skin tightening (Seoighe et al., 2010). The low level of side effects and a proven efficacy in cutaneous resurfacing has led to the emerging popularity of FP (Manstein et al., 2010; Seoighe et al., 2010).

Q- Switched Ruby Laser (QSRL) is one of the common lasers in dermatology (Seoighe et al., 2010). Q-switched lasers produce short pulse of light that has very high peak intensity, these pulses in the nanosecond range shorter than the approximately 1-ms thermal relaxation time of the melanosomes or the tattoo ink particles (Dierickx, 2005), the target chromophores of skin pigmented lesions and tattoos. Q-switched mode, lasers exhibit both minimal tissue destruction and postoperative erythema (Goldberg & Whitworth, 1997). To date, these lasers have been shown to treat both epidermal, dermal, and mixed epidermal and dermal pigmented lesions effectively in a safe, reproducible fashion (Dierickx, 2005). Both superficial pigmented lesions and general dyschromia are two major issues in facial skin aging (Goodman, 2007), which make them as one of the major indication for facial resurfacing. Both nanosecond (Q-switched), and millisecond (long-pulsed) Nd:YAG lasers are currently used for nonablative dermal remodeling (Schmults et al., 2004). They are thought to stimulate new collagen production by producing a thermal injury to the dermis that initiates a wound-healing response.

The whole face treatment with fractional QSRL 694nm has not been settled as an approach of facial rejuvenation targeting dyschromia, and other problem encountered in skin aging including wrinkles (rhytides), texture abnormalities, benign skin lesions like seborreic keratosis, as well as post acne scaring. This research is to evaluate the efficacy and safety of this approach in Asian skin.

Fractional mode Q- Switched Ruby Laser is a newly developed machine which utilize both the fractional photothermolysis principle and the high peak power of conventional Q-switch ruby laser, which can produce homogenous energy to produce less tissue injury, less downtime, and less adverse effects like postinflammatory hyperpigmentation (PIH), compared to other available ablative and non-ablative approaches for facial rejuvenation.

This prospective study aims to asses the efficacy and side effects of the use of fractional mode Q-switched Ruby laser in the facial rejuvenation in Asians.

1.2 Research Questions

1.2.1 Primary Question: will the fractional mode QSRL be an effective approach facial rejuvenation?

1.2.2 Secondary Question: will this approach be effective treatment for aldyschromia- a major issue- in facial rejuvenation?

1.3 Research Objective

To evaluate the resurfacing capability of the fractional mode QSRL in Asian skin.

1.4 Hypothesis

Fractional mode QSRL have resurfacing capability that can targets major features of photodamaged facial skin.

CHAPTER 2

LITERATURE REVIEW

2.1 Previous Related Studies

Michel, Hohenleutner, Bäumler and Landthaler (1997) reviewed many studies on Q-switched ruby laser (QSRL) with its wavelength of 694 nm and a pulse duration of around 40 nanosecond. They found that QSRL is an effective modality for the removal of tattoos and cutaneous pigmented lesions. These applications are based on the principle of selective photothermolysis, selective damage to cutaneous pigment or pigmented cells leading to the scar-free elimination of endogenous or exogenous pigment in the skin. They briefed main indications for the treatment with the QSRL including tattoos (amateur, professional, accidental, or cosmetic) and lentigines, beside lightening or even removing other pigmented lesions such as nevus spilus or café au lait macules. Even more, pigmented lesions of mucous membranes could also be removed easily. So, they concluded that QSRL is an excellent therapy for the removal of endogenous and exogenous pigment because of both the excellent treatment results and the lack of side effects, which were limited to transient hypo- and hyperpigmentation. As result, QSRL has occurred a wide range of applications within the field of dermatology.

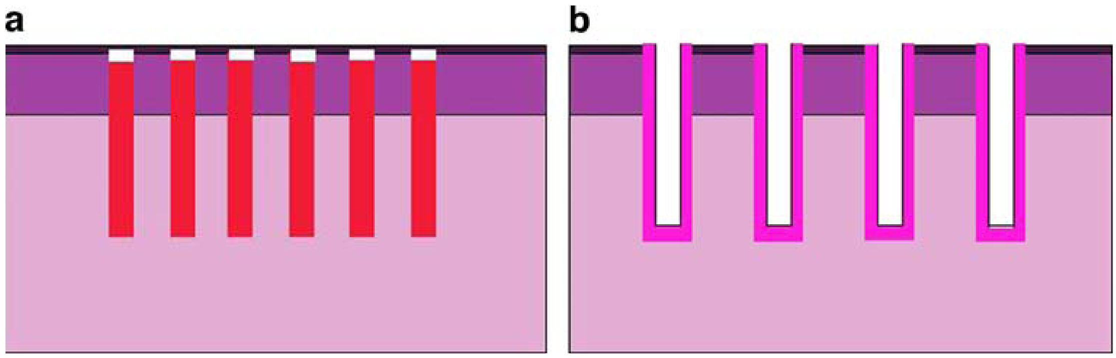
Stratigos, Dover, & Arndt (2000) considered treatment of cutaneous pigmentation as one of the most interesting areas of cutaneous laser surgery. They reviewed the 4 main short-pulsed, pigment-selective lasers in clinical use at that time, and Q-switched ruby laser (694 nm, 25-40 nanoseconds) was one of them which used successfully for decades in treatment of superficial pigmented lesions, such as ephelides, solar and labial lentigines, and flat seborrheic keratoses. Dermal and mixed epidermal/dermal pigmented lesions like melasma shows variable responses. However, the authors state that within four decades of the time that the first laser light was produced from a ruby laser in 1961, it is now possible to bring about extraordinary changes in pigmentary and other abnormalities on and within the skin.

Fernandes (2003) divided laser and laser-like assisted facial rejuvenation into four basic approaches, those that (i) ablate the epidermis, causing dermal wounding with a significant thermal effect like CO2 lasers; (ii) ablate the epidermis, causing dermal wounding, with minimal thermal effects like short pulsed Erbium:Ytrrium- Aluminum-Garnet [Er:YAG] lasers; (iii) ablate the epidermis, causing dermal wounding with variable thermal effects like combined CO2/Er:YAG lasers, and ablative radiofrequency devices; and (iv) do not ablate the epidermis,but causing dermal wounding, with minimal thermal effects referred as non-ablative lasers and light sources. Those modalities are effective in promoting facial rejuvenation, but each has some advantages and disadvantages. Occasional prolonged healing and erythema are seen after C02 laser resurfacing, although shown to be highly effective in the treatment of photodamaged skin, with tissue tightening' effect. The most significant advantage of Er:YAG resurfacing is the precise removal of skin, providing safety and reliability with minimal thermal damage which may account for the rapid healing and decreased adverse effects, but there is greatest limitation of Er:YAG resurfacing, that is the need for multiple passes to obtain improvement making the procedure potentially slower than C02 resurfacing. all deep rhytides and all deep acne scars responded better to a sequential CO2/Er:YAG laser treatment compared with C02 laser treatment alone. Healing times were on average 2-3 days faster with sequential treatment. Radiofrequency resurfacing have several benefits including complete hemostasis during the procedure, lack of a smoke plume, no need for eye protection required with laser procedures, and compact solid state technology. However, the author stated that further clinical studies looking at electrosurgical resurfacing and comparing electrosurgical resurfacing to other modalities are necessary. Non-ablative lasers and light sources represented the newest approach to improve photodamaged skin at the time when the author wrote this article, and he explained that the degree of collagen remodeling is not expected to be as great as that seen with other more destructive, ablative approaches, so it is more appropriate for the treatment of those individuals who wish to improve the quality of their sun-damaged skin but do not like to take time away from their daily activities. Even more, he concluded that this technique is not intended for those with extensive, solar-induced, epidermal pigmentary changes, and those individuals are best treated with either an ablative laser or a specific, pigmented lesion laser. At the end of this article, the author wish that in the future, lasers can cause the same degree of improvement as that seen with ablative systems without the potential complications and down time from such systems.

Goodman (2007), the author of Facial Rejuvenation: A Total Approach, talked about the Q-switched laser systems used for facial rejuvenation. Basically Q-switched lasers are able to deliver pulses of laser light with high peak powers within nanosecond duration, using wavelengths that are selectively absorbed by pigment granules (melanosomes), such lasers tend to break up pigment particles. Since the duration of the pulse is so short, heat damage to adjacent tissues is minimized. The Q-switched frequency-doubled Nd: YAG, the Q-switched ruby, and the Q-switched alexandrite lasers are probably equally effective in the treatment of pigmented lesions. The author stated that although Q-switched lasers are the accepted gold standard for dermal melanocytic lesions and tattoos, several of these lasers also being used for both the treatment of superficial pigmented lesions and general dyschromia – two major issues in facial rejuvenation. Frequency-doubled KTP:YAG (532 nm), long-pulsed-dye, and alexandrite (755 nm) lasers are among such lasers successfully utilized for photorejuvenation.

Alexiades-Armenakas, Dover and Arndt (2008) made a review of ablative, fractional , and nonablative laser resurfacing. They stated that although the carbon dioxide (CO2) and erbium: yttrium aluminium garnet (Er:YAG) lasers remain the gold standards for rejuvenating photodamaged skin, but their use is associated with significant risk of side effects including scarring, and a prolonged unpleasant postoperative recovery period. Therefore, nonablative, and recently fractional laser were developed to overcome these disadvantages. Nonablative resurfacing produces dermal thermal injury to improve rhytides and photodamage while preserving the epidermis leading to minimal efficacy in exchange for minimal risk, while fractional resurfacing is an intermediate approach increases efficacy as compared to nonablative resurfacing, but with faster recovery as compared to ablative resurfacing.

Manstein et al. (2010) studied fractional technologies and divided them into ablative and nonablative fractional photothermolysis based on the wavelength's affinity for water. Those devices with wavelengths that are highly absorbed by water are termed ablative like carbon dioxide (CO_2; 10,600 nm) laser. Those with wavelengths only moderately absorbed are 'non-ablative' (1,410 nm, 1,440 nm, 1,540 nm, 1,550 nm). The researcher studied the thermal damage induced by these ablative and nonablative in the epidermis and dermis histologically. With the non-ablative lasers, they observed a column-like denaturation of the epidermis and dermis (Figure 2.1a), a disruption of the dermo-epidermal junction, with subepidermal clefting within the Microscopic Thermal Zones (MTZ), and an intact stratum corneum. The surrounding tissue is unharmed. The thermally destroyed tissue replaced by keratinocytes that migrate from the surrounding healthy tissue within the first 24 hours. The button-shaped necrotic tissue, which is called Microscopic Epidermal Necrotic Debris (MEND), is eliminated transepidermally by the keratinocytes, and its migration upwards and through the stratum corneum is facilitated by the subepidermal clefting. This migration is called the MEND-shuttle, within each amount of MEND, elastic tissue, melanin and other dermal contents are found. The clinical outcome of this process is slight scaling and bronzing of the skin, which occurs roughly after 1 week. The replacement of the MTZs with new collagen occurs within 3–6 months. Ablative fractional technologies showed histologically ablated micro-columns, varying in thickness and depth depending on pulse width and wavelength used. A thin layer of eschar lines the cavity, which is consistent with ablative laser treatment. Around these cavities annular coagulation zones of varying thickness, which represent denatured collagen, have been observed, and the stratum corneum is mostly absent, contrary to the situation in non-ablative fractionated technology (Figure 2.1b). Reepithelialization of the coagulation zones occurs rapidly, within 48 hours



From Manstein, D., Herron, G. S., Sink, R. K., Tanner, H., & Anderson, R. R. (2010). Fractional photothermolysis-an update. **Lasers Med Sci, 25**(9), 137-144.

Figure 2.1 (a) Schematic histology of non-ablative and ablative FP. Column-like denaturation of the epidermis and dermis, with a disruption of the dermo-epidermal junction, clefting within the MTZ, and an intact stratum corneum. The surrounding tissue is unharmed. (b) Schematic histology of ablative FP. Ablated micro-columns, lined by a thin layer of eschar and with annular coagulation zones.

2.2 Facial Rejuvenation

2.2.1 Definition

Facial rejuvenation is the art and science of improving the aesthetics of the face, scalp, and neck areas to give a more youthful appearance (Shiffman, 2008). Facial rejuvenation includes varieties of major permanent and long-term plastic surgery, less invasive mid-range surgical procedures, and non-invasive temporary skin treatments (Peter et al., 2005).

Methods of resurfacing and rejuvenating the face include dermabrasion, chemical peels and surgical face lift. More recently, the CO2 laser has been refined to allow precise, predictable and cosmetically acceptable results (Seoighe et al., 2010) all methods were designed to leave a layer of damage in the dermal tissue, associated with acceleration of the wound healing process in order to bring about the restoration of youthful characteristics to the treated skin, in particular collagen deposition and subsequent remodeling with tightening and shrinkage which would be transferred to the overlying epidermis (Ross et al., 2000; Trelles, 2003). However, all three types of resurfacing techniques were associated with scarring and other side-effects, and the results were at best inconsistent (Trelles, 2003). On other hand, most patients want cosmetic and rejuvenative procedures with minimal or no downtime and visible results. This has led to the popularity of nonablative lasers, light sources, and radiofrequency skin tightening (Holloman & Baker, 2008).

2.2.2 Indications for Facial Resurfacing

Laser facial resurfacing treat extensive cutaneous changes duo to solar damage, and other skin lesions including (Goodman, 2007; Kilmer & Semchyshyn, 2005):

2.2.2.1 Irregular pigmentation and Dyschromia**:** Many epidermal pigmented lesions that are due to photoaging, such as ephelides, lentignes, seborrheic keratoses, dermatosis papulosa.

2.2.2.2 Vascular lesions: Like telangiectasia, angiomas with venous lakes, standing erythema, and flushing disorders. Many patients who seek facial rejuvenation present with a vascular component.

2.2.2.3 Oily and acne prone skin: Oil production and tendency toward acne and sebaceous hyperplasia is a major concern and one that recently has become a potential target for many different wavelengths, including several diode lasers, and light technologies.

2.2.2.4 Problems with skin texture: Defined as a mixture of problems including roughness and dryness, with dilated pores. Many of the available nonablative lasers and light sources may improve skin texture.

2.2.2.5 Sallow and uneven color**:** It is probably the reflectance off sun-damaged dermal collagen that is responsible for the sallow appearance of sun-damaged skin. Collagen improvement can be improved with both ablative and nonablative technologies.

2.2.2.6 Post acne scarring: Postacne scarring may be atrophic or hypertrophic. Sometimes there is not true scarring, but simply pigmentary changes. Macular pigmentary changes can be brown, red, or white. Various lasers and light sources have been used treat these pigmentary changes. Atrophic scars have been dealt with by a variety of ablative, fractionated and nonablative technologies.

2.2.2.7 Pre malignant changes: Actinic keratoses, and similar lesions, may be treated by lasers, and light sources.

2.2.2.8 Wrinkles: Fine wrinkling may occur both with chronologic and or ultraviolet-induced aging, it can be treated with ablative laser systems, but increasingly targeted by nonablative technologies. Medium wrinkling is more commonly seen as a manifestation of photoaging. It is best treated with ablative lasers.

2.2.2.9 Lumps and bumps**:** Like benign intradermal nevi, syringomas, xanthelasma, fibrous papules, and seborrheic keratoses. These are conditions make patients seek facial rejuvenation, and may be well dealt with the different lights and lasers.

Nonablative resurfacing is best for patients with fine lines, and, if the appropriate device is used, erythema, telangiectasia, or pigmentary changes (Kilmer & Semchyshyn, 2005) also best treated by this technique.

2.2.3 Contraindications to Nonablative Technologies

Because of the possible varied side effects and complications after cutaneous laser surgery, it is essential that each patient receive consultation before treatment to asses the risk factors of adverse sequelae and contraindications (Tanzi, & Alster, 2008; Goodman, 2007; Kilmer & Semchyshyn, 2005) which include:

2.2.3.1 Concurrent isotretinoin remains a controversial issue.

2.2.3.2 Current or recent tan or intention to expose to high-dosage ultraviolet radiation. This is of much greater concern in patients who seek visible laser or light source treatment.

2.2.3.3 Medical conditions such as epilepsy, claustrophobia, photosensitizing medications, pregnancy, or in patients psychologically unable to cope with therapy (Goodman, 2007).

2.2.3.4 Unrealistic expectations.

2.2.3.5 Active herpes simplex or other infections or lesions of concern in the treatment field should be avoided (Kilmer & Semchyshyn, 2005).

2.2.4 Complication of Facial Skin Resurfacing

Any laser resurfacing treatment to face have the following complication (Woraphong Manuskiatti, Daranporn Triwongwaranat, Supenya Varothai, Sasima Eimpunth, & Rungsima Wanitphakdeedecha, 2009) including:

2.2.4.1 Post-inflammatory hyperpigmentation (PIH): is defined as the acquired presence of darker macules and patches of skin occurring at sites of previous cutaneous inflammatory conditions, or therapeutic interventions like laser therapies (Soriano & Grimes, 2006).

2.2.4.2 Acneiform eruptions

2.2.4.3 Allergic contact dermatitis

2.2.4.4 Herpes simplex virus infection

2.2.4.5 For non-ablative laser resurfacing, the degree of wrinkle reduction is not as significant as that seen with the ablative devices and thus, patient dissatisfaction can be an issue (Kilmer & Semchyshyn, 2005).

2.2.5 Assessment of Photo Rejuvenation

It is measured by improvement in the parameters of photorejuvenation including; wrinkling, skin texture, pigmentary changes, and telangiectasias (Gold, 2005)

2.3 Post Acne Scarring

Acne is one of the most common skin diseases (Koo, Yoon, Ahn, & Park, 2001). Acne scars affect approximately 14% of patients who have had acne (Hedelund et al., 2010), and appear as multiple depressive scars all over the face, causing problems cosmetically. They have been classified into four patterns including; (i) rolling depressed scars, (ii) ice-pick scars or prominent craters, (iii) conglomerated depressed scars, and (iv) a combined pattern (Koo et al., 2001). Many methods have been used for treatment of Acne Scar such as dermabrasion, chemical peeling, and punch grafting. These techniques cause complications as hypertrophic scars, contour change of the skin, and depigmentation (Koo et al., 2001; Raskin, 2010). Other methods including Ablative skin resurfacing with CO2 or erbium lasers which is considered the gold standard for laser treatment of atrophic acne scars (Hedelund et al. 2010). Typically acne scars require more than one treatment modality, such as lasers and lipofilling injections (Raskin, 2010).

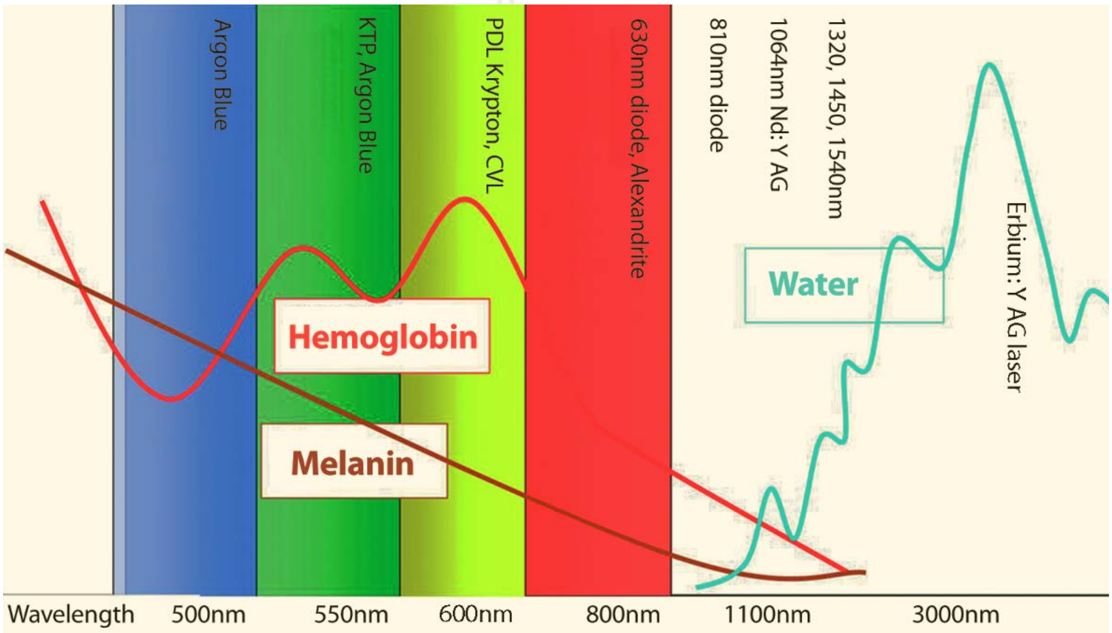
Sculpting of scars with the laser yields a more uniform skin texture and stimulates new collagen formation within the dermal defects. Patients can expect a mean improvement of 50-80% in moderate atrophic scars, with continued collagen remodeling and scar effacement for 12-18 months postoperatively. Patients with scars previously treated with dermabrasion or deep chemical peels may have additional fibrosis (Alster & Doshi, 2005). Ablative skin resurfacing are effective in recontouring the skin and improving scar texture, but they are limited by significant down-time, prolonged erythema and unwanted adverse effects such as postinflammatory hyperpigmentation, hypopigmentation and scarring.

Nonablative lasers and light sources in the visible, and the near- and mid-infrared parts of the electromagnetic spectrum have, therefore, been introduced; these include the potassium-titanyl-phosphate laser (532 nm), pulsed dye lasers (585 and 595 nm), diode lasers (810 and 1,450 nm), Nd:YAG lasers (1,064 and 1,320 nm), the erbium:glass laser (1,540 nm) and intense pulsed light systems (500-1,200 nm). These nonablative devices induce neocollagenesis and remodelling of scar texture without affecting the epidermis, thus reducing the risk of adverse effects. Nevertheless, compared to ablative lasers, the efficacy of nonablative dermal remodelling is limited (Hedelund et al., 2010). Fractional nonablative photothermolysis is a relatively new skin resurfacing technology that uses microzones of thermal injury to stimulate a wound-healing response which induce neocollagenesis and remodelling of scar texture (Manstein et al., 2010; Hedelund et al., 2010)

2.4 Laser

Light amplification by stimulated emission of radiation (lasers) are currently employed by a number of medical and surgical specialties and used to treat a wide range of conditions (Seoighe et al., 2010). A laser requires a number of fundamental components, namely an energy source, a laser medium, a resonator and focusing equipment (Goodman, 2007; Seoighe et al., 2010).

Characteristics of lasers including, monochromacity of laser that lends itself to a variety of uses in the medical field (Goodman, 2007; Yana, Tuchin, & Yaroslavsky, 2009). Monochromacity means that light energy has a specific wavelength thus allowing selection of a specific target tissue. Other characteristic of laser is coherence which enable the light energy to accurately select the target tissue with immense precision (Seoighe et al., 2010). The target substance (or chromophore) will absorb the laser energy preferentially depending on the wavelength of the laser beam. The three primary natural chromophores in the skin are haemoglobin, melanin and water as shown in (figure 2.2) (Goodman, 2007). Other typical chromophores include tattoo pigments. Common lasers in dermatology includes, Alexandrite 755, CO_2 10,600, PDL 585, Q-switched Nd:YAG 532, 1,064, Q-switched ruby 694 (Seoighe et al., 2010).



From Goodman, J. G. (2007). Lasers and lights. In D. J. Goldberg (Ed.), **Facial rejuvenation: A total approach** (1st ed., pp.19, 35-38). Berlin: Springer Berlin Heidelberg.

Figure 2.2 lasers in dermatology: Absorption curve of major skin pigments and the lasers and lights that take advantage of this absorption. *KTP* Potassium tritanyl phosphate, *PDL* pulsed-dye laser, *CVL* copper vapor laser, *Nd* Neodymium-doped, *YAG* yttrium-aluminum-garnet.

CHAPTER 3

METHODOLOGY

3.1 Research Design

Prospective single-center open clinical trial, with longitudinal follow up

3.2 Materials

Materials used in the research include:

3.2.1 Q-Switched Ruby Laser-Fractional mode

This research has utilized Q-Switched Ruby Laser -Fractional mode- 694 nm from (Tattoo Star®, Asclepion Laser Technologies GmbH, Germany). Specification of this laser is shown in table (3.1).

A ruby laser is a solid-state laser that uses a synthetic ruby crystal as its gain medium. The first working laser was a ruby laser made by Theodore H. "Ted" Maiman at Hughes Research Laboratories on May 16, 1960 (Maiman, 1960). The cutaneous application of laser technology was launched in 1959 with the development of the 694-nm ruby laser by Maiman (Maiman, 1960; Alster & Doshi, 2005), which become one of the common lasers in dermatology (Seoighe et al., 2010). Q-switched lasers produce short pulse of light that has very high peak intensity (Seoighe et., 2010), these pulses in the nanosecond range with a pulse width shorter than the approximately 1-ms thermal relaxation time of the melanosomes or the tattoo ink particles (Dierickx, 2005), the target chromophores of pigmented lesions is the melanosome and that of tattoos. The absorbance of light by melanin occurs across a broad band of the electromag- netic spectrum (351-1,064 nm) allowing such lesions to be routinely treated with Q-switched ruby (694 nm) and Nd:YAG (532/1,064 nm) lasers providing cosmetically acceptable, scar-free results (Duke, Byers, Sober, Anderson, & Grevelink, 1999; Seoighe et al., 2010). Various Q-switched lasers (532-nm frequency- doubled Q-switched Nd:YAG, 694-nm ruby, 755-nm alexandrite, 1064-nm Nd:YAG) are therefore used for the treatment of various epidermal, dermal, and mixed epidermal and dermal pigmented lesions and tattoos (Michel et al., 1997; Dierickx, 2005).

Table 3.1 Specifications of Q-Switched Ruby Laser-Fractional mode

Item	Specification	
Type	Q-Switched Ruby Laser	
Mode	Fractional	
Wave length	694 nm	
Pulse duration	40 ns	
Energy& Fluences		
Max Energy	1,13 J	⟶ 8,2 J/cm2
Min Energy	0,31 J	⟶ 2,2 J/cm2
Speed	2.0- 1.5 Hz/second	
Spot size total	7,1 x 7,1 mm	
Number of Spots	14 x 14	
MicroSpot Ø	300 µm	
Gap	200 µm	
Coverrate	27,7 %	
Brand	Tattoo Star®, Asclepion Laser Technologies GmbH, Germany	

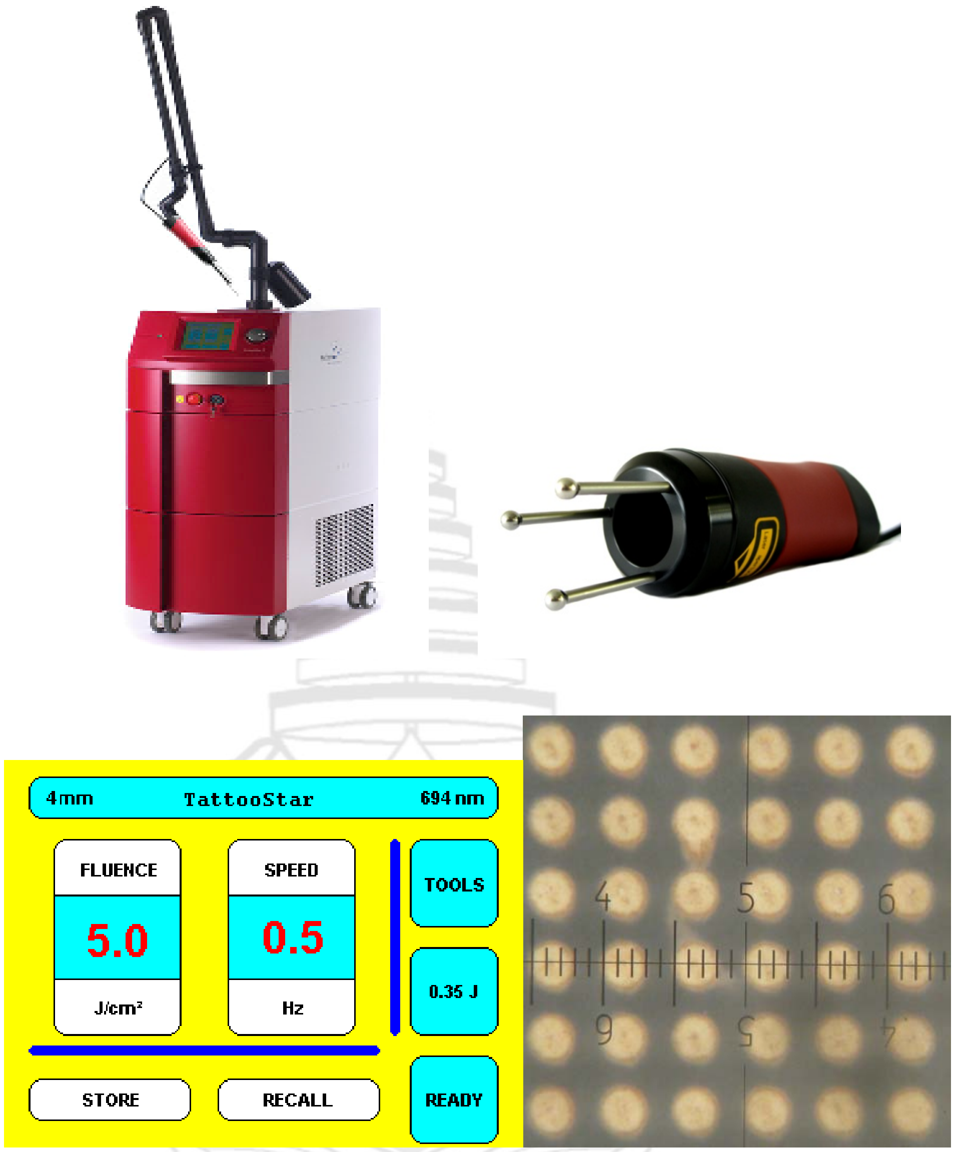


Figure 3.1 Q-Switched Ruby Laser with Fractional Mode with Handpiece, and operational screen (Asclepion Laser Technologies).

3.2.2 Visioscan® VC 98

It is a special UV-A light video camera with high resolution has been developed especially to study the skin surface directly. The images show the structure of the skin and the level of dryness very impressively, and also can be used to study degree of wrinkling.

In contrary to the conventional color video cameras, the Visioscan® VC 98 is shown in figure (3.2), consists of a special b/w video sensor chip with very high resolution, an objective and an UVA-light source in a small, easy to handle, plastic casing (Khazaka, 2005a). Two special halogenide lights, arranged on opposite sides, illuminate the skin uniformly. The spectrum of the light, its intensity and the way it is arranged is chosen so that only the stratum corneum without reflections from deeper layers is monitored. This special light excludes almost all undesired light reflections on the skin, thus bringing out a very sharp, non glossy image of the skin and hair. The measuring area is 6*8 mm. the image of the skin is taken by a build in CCD-camera. The connection of the Visioscan® VC 98 to the PC is done via an image digitalization unit which configures the image in 256 gray levels pixel by pixel, where 0 is black and 255 is white. The special Surface Evaluation of Living Skin (SELS)-program offers a lot of possibilities and calculations of surface parameters which has been utilized by many previous researches on aging skin (Béguin, 2005)

In this project, we utilize few measurements of the skin surface that can be calculated by Visioscan® VC 98, and related to the objectives of this study. In this project, we utilize few measurements of the skin surface that can be calculated by Visioscan® VC 98, and related to the objectives of this study. These measurements include: SELS parameters**, t**he SELS calculations (Surface Evaluation of Living Skin) consist of following parameters: Roughness "SEr" calculates the portion of dark pixels. The smaller this value, the less rough the skin, Smoothness "SEsm" is proportional to width and form of the wrinkles. A treatment with moisturizing or anti-aging products should let SEsm go up, and lastly Wrinkles, "SEw" is proportional to number and width of the wrinkles. The more wrinkles, the higher this value.

3.2.3 Mexameter® MX 18

This device meet the requirements for a precise determination of the skin color which is based on few features. Mexameter® MX 18 specifically measures the content of melanin (pigmentation) and only hemoglobin (erythema) in the skin. These two component are largely responsible for the skin color. Mexameter® MX 18 probe is shown in figure (3.2)

The measurement is based on the absorption principle. The special probe of the Mexameter® MX 18 emits light of three defined wavelengths. A receiver measures the light reflected by the skin. The positions of the emitter and receiver guarantee that only diffuse and scattered light is measured. The achieved results are shown on as indices on the screen on a scale from 0-999 (Khazaka, 2005b).

3.2.4 Glogan's Categories of Photodamage

Glogan's Categories of Photodamage (Goodman, 2007) is shown in the following table (3.2)

Table 3.2 Glogau's categories of photodamage

Glogau's category of photodamage	Photodamage skin type description
1	No keratoses, little wrinkling, no scarring, little or no requirement for make up
2	Early actinic keratoses, slight yellow skin discoloration, early wrinkling, parallel smile lines, mild scarring, small amount of make up required
3	Actinic keratoses, obvious yellow skin discoloration with telangiectasia, wrinkling present at rest, moderate acne scarring, always requires make up
4	Solar keratose and skin cancers have occurred. Wrinkling, and cutis laxa of actinic, gravitational, and dynamic origin

From Khazaka, G. (2005a). **Information and operating instruction for the visioscan VC 98 and the software SELS (Surface Evaluation of the Living Skin)**. Cologne, Germany: CK Electronic.**;** Khazaka, G. (2005b). **Information and operating instructions for the multi probe adapter MPA and its probes**. Cologne, Germany: CK Electronic.

Figure 3.2 Visioscan® VC 98 (upper), and Mexameter® MX 18 (lower).

3.2.5 Volunteers

Volunteers who met the research inclusion criteria have been enrolled in this study at the outpatient clinic in Mae Fah Luang University Hospital-Bangkok, School of Anti-Aging and Regenerative Medicine.

3.2.5.1 Inclusion criteria

Both sex (male and female) are eligible, aged 21-70 with photodamaged facial skin, wrinkles, and/or post-acne scarring. Fitzpatrick skin photo-type II-V (Klause, & Richard 2005; Goldman, 2008) and sign the consent form to participate in the study.

3.2.5.2 Exclusion criteria

Those who are mentally incompetent, pregnant, under 21 or over 70 years old, or immunocompromised or those who have an active infection or a photosensitivity disorder (Woraphong Manuskiatti et al., 2009). Those who have facial resurfacing by any approach in last 6 months are also excluded.

3.3 Methods

This is a prospective single-center open clinical study, which has been performed in accordance with Good Clinical Practice. The treatment protocol have been reviewed with each eligible volunteer and signed the informed consent. This research has taken place at Mae Fah Luang University Hospital, Bangkok / Outpatient clinic.

3.3.1 Treatment Protocol

This study have been performed in accordance with Good Clinical Practice. The treatment protocol were reviewed with each eligible volunteer and then signed the informed consent. At the study entry, each eligible volunteer have undergone clinical assessment and diagnosis of photo damaged facial skin by a dermatologist at the outpatient clinic, and Glogau's classifications of photodamage (Goodman, 2007) were followed in determining the severity of photo damaged facial skin. Each eligible individual then signed the informed consent. There were 3 sessions of laser treatment at 4 wk intervals (wk 0, 4, 8), with another follow up visit on week 12 for final assessment. On each session, the treatment areas were cleansed of debris, including dirt, makeup, and powder, using a mild cleanser. Lidocaine, 2.5%, and prilocaine, 2.5%, cream (a eutectic mixture of local anesthetic) have been applied under occlusion to the entire face. After an hour of application, the anesthetic cream were gently removed and then, to obtain a completely dry skin surface, normal saline were used to degrease the skin. Eyes were protected with opaque goggles specific for the laser wavelength.

The whole face were treated through a single-pass treatment with some pulse overlapping using a fractional mode 694 nm QSRL (RubyStar, Asclepion Laser Technologies GmbH, Germany), with Spot size total (7,1 x 7,1 mm) used at a flounce of 2.5-4 J/cm2 and pulse duration of 25 nanoseconds, and speed of (1.5-2 Hz). On subsequent sessions, parameters were adjusted accordingly. Immediately after the procedure, a layer of a antibiotic cream were applied to the treated surface. Postoperatively, the subjects are instructed to cleanse the treated sites gently with tap water, and a moisturizing cream to be applied 4 times daily for 1 wk, and continue twice daily application of the antibiotic cream for 3-5 days. All the subjects were instructed to wear a broad-spectrum sunscreen with a sun protection factor of 50, avoiding sun exposure (Shieh, & Chan Henry, 2010), and avoiding the use of any topical preparations on the face for the period of the study. History of herpes labialis has been taken, but oral antiviral prophylaxis were prescribed only for subjects with documented history due to minimal risk of herpes simplex reactivation (Fernandes, 2007).

In deed, the volunteers has been divided into two groups, first group are those who received the same treatment parameters over the all three sessions of laser treatment, and the other one that received progressive increasing treatment parameters on subsequent visits. 7 volunteers out of the 24 who completed the tree sessions of laser treatment were receiving the nonablative facial resurfacing at the same parameters using fractional mode 694 nm QSRL (RubyStar, Asclepion Laser Technologies GmbH, Germany), at flounce of 2.5 J/cm2, speed of 2.0 Hz, and pulse duration of 25 nanoseconds. On other hand, 14 volunteers have received laser treatment starting with flounce of 2.5 J/cm2 on the first session at speed of 2.0 Hz, pulse duration of 25 nanoseconds by fractional mode 694 nm QSRL (RubyStar, Asclepion Laser Technologies GmbH, Germany). Then, on next second and third sessions, there were gradual increase in flounce to (3.0, 3.5, or 4.0 J/cm2) according to the patient skin color, improvement, and patient satisfaction.

3.3.2 Evaluation Criteria

Before and after each treatment and in last visit, photograph was taken using a digital camera (Canon, Power Shot A3100 IS, 12.1 Mega pixels). Objective assessment of skin included skin- color measurement by skin color- measuring device (Mexameter, MX18, Courage & Khazaka, Electronic GmbH, Cologne, Germany) and measuring degree of roughness, smoothness, and wrinkling by Visioscan® VC 98 (Courage & Khazaka, Electronic GmbH, Cologne, Germany). There are also subjective evaluation including assessment for photographs, and in last visit, all patients need to complete a self assessment sheet by rating the degree of improvement for each facial skin problem separately (Pigmented lesions, Uneven color-Dyschromia-, problems with skin texture like roughness, dryness, and dilated pores, Fine and Medium wrinkles ,and post acne scarring) using the following numeric responses: 0%, less than 25%, 25% to 50%, 51% to 75%, and 76% to 100%. Beside that, each volunteers need to complete the patient satisfaction questionnaire using a 4-point grading system: 0= poor (dissatisfied), 1=fair (slightly satisfied), 2=good (satisfied), 3=excellent (very satisfied)

Table 3.3 Global Improvement Score

Score	Rate of improvement	Appreciation
4	76% to 100%	Excellent
3	51% to 75%	Good
2	25% to 50%	Fair
1	less than 25%	Slightly better
0	0%	No improvement

Table 3.4 Patient Global Satisfactory

Score	Degree of satisfaction
1	Poor (dissatisfied)
2	Fair (slightly satisfied)
3	Good (satisfied)
4	Excellent (very satisfied)

3.3.3 Post laser Symptoms and Side Effects

After each laser treatment, there are assessment for pain level, degree of redness (erythema), and edema using specific scales. Adverse effects and recovery times have been recorded at each treatment session and follow-up visits.

Table 3.5 Scores of Pain level

Score	Pain level
1	Painless
2	Mild pain
3	Moderate pain
4	Significant pain
5	Very painful

Table 3.6 Scores of the degree of Erythema (redness)

Score	Degree of redness
0	No redness
1	Faint redness
2	Moderate redness
3	Strong redness

Table 3.7 Scores of the degree of Edema

Score	Degree of edema
0	No edema
1	Mild edema
2	Moderate edema
3	Markedly edema

3.3.4 Statistical Analysis

Data have been collected, descriptive statistics used to analyze demographic characteristics of the sample. Paired t-test (student t test), have been used to analyze data collected from Mexameter® MX 18 and Visioscan® VC 98, and (*P* value < 0.05) considered statistically significant. Degree of global patient satisfaction, and Grade of Improvement are also analyzed statistically by using SPSS (Statistical Package for Social Sciences) version (11.5).

CHAPTER 4

RESULTS

31 volunteers has been recruited in this study. 24 of them completed 3 sessions of the non-ablative laser resurfacing of whole face. 2 volunteers have only one session of the laser treatment, while 5 of them completed 2 sessions. For those who complete the 3 sessions of non-ablative facial resurfacing of the whole face, age mean is 37.5 ± 10 yr (min 26 yr, max 67 yr old), 83% of them are female (20 volunteers), and 17% are male (4 volunteers). All of them are Asian, one of them (4%) only is non-Thai nationality (Korean), other volunteers (96%) are Thai. Fitzptrick's Skin Phototypes Classification has been followed (Klause & Richard, 2005), volunteers with skin phototypes II-V have been recruited, 50% of them have skin type III, 14 volunteers (58%) have mild to moderate photodamage according to Glogau's category of photodamage. Summery of demographic characteristics of study sample are shown in table (4.1).

4.1 Objective Evaluation Results

4.1.1 Mexameter® MX 18 evaluation:

Statistical analysis by Paired T-test (Student T- test) of the Melanin Index at the baseline visit, and at one month follow-up visit (week 12) after third session of treatment, shows significant improvement in dyschromia as reduction in melanin pigmentation intensity (*P* value = .002) (table 4.2).

However, half of the volunteers have 3 reading by Melanin Index at week (0, 8, 12), which means these measurements done at (baseline, after second session, and third session) of laser treatment respectively. There are progressive reduction in Melanin Index after second, and third sessions, however, these reductions were statistically non significant, and it shown in figure (4.1).

Table 4.1 Demographic characteristics of study sample (24 volunteers)

Variable	Mean (SD)	Freq. (%)
Age (year)	37.5 (±10)	
21-30		3 (12.5%)
31-40		15 (62.5%)
41-50		3 (12.5%)
51-60		2 (8%)
61-70		1 (4%)
Gender		
Male		4 (17%)
Female		20 (83%)
Ethnic		
Asian (Thai)		23 (96%)
Asian (other)		1 (4%)
Skin phototypes		
II		4 (17%)
III		12 (50%)
IV		6 (25%)
V		2 (8%)
Glogau's category of photodamage		
1		4 (17%)
2		10 (42%)
3		8 (33%)
4		2 (8%)

Note. SD= Standard Deviation; Freq.= Frequency; %= Percent

Table 4.2 Mexameter® MX 18 Evaluation

	Mean	Std. Deviation	Sig.
Mexameter			
Baseline (MEX1)	224	±49.5	
Week 12 (MEX2)	205	±38	
MEX1-MEX2	19	±23	0.002

Note. Std. deviation = Standard Deviation; Sig.= significant

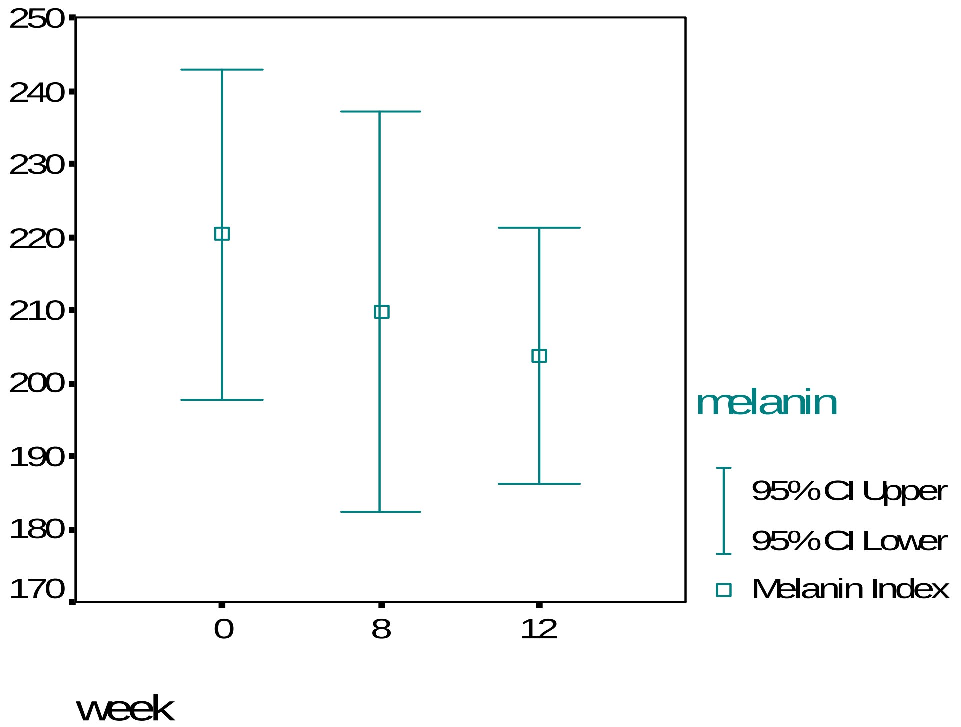


Figure 4.1 Melanin Index at week (0,8,12). CI; Confidence Interval.

4.1.2 Visioscan® VC 98 evaluation

Statistical analysis by Paired T-test (Student T- test) shows no significant improvement in different parameters of Visioscan® VC 98 evaluation of the facial skin before and at one month follow-up visit (week 12) after third session of treatment, including Roughness Index, Smoothness Index, and Wrinkle Index (table 4.3).

Table 4.3 Visioscan® VC 98 Evaluation

Parameter	Mean	Std. Deviation	Sig.
SELS:			
ROUGHNESS "SEr"			
Baseline (SEr1)	1.4	±1.3	
Week12 (SEr2)	0.9	±0.6	
SEr1-SEr2	0.52	±1.3	0.092
SMOOTHNESS "SEsm"			
Baseline (SEsm1)	26	±4	
Week12 (SEsm2)	26.2	±4.3	
SEsm1-SEsm2	-0.39	±4.4	0.708
WRINKLES "SEw"			
Baseline (SEw1)	37.3	±4.2	
Week12 (SEw2)	36.3	±4.1	
SEw1-SEw2	1	±5	0.402

Note. Std. deviation = Standard Deviation; SELS =Surface Evaluation of Living Skin; Sig.= significant

4.2 Subjective Evaluation Results

Statistical analysis of Degree of global satisfaction shows that 33% of the patients noticed an excellent response, and another 46% were really satisfied, while only 21% were slightly satisfied, and nobody were dissatisfied with the nonablative facial resurfacing by Q-Switched Ruby Laser -Fractional mode. This means that 80% (n=19) detected a good to excellent response to QSRL resurfacing. Patient rating Grade of Improvement are shown in (table 4.4). subjective evaluation of photographs at baseline and one month after third laser session of QSRL, shows slight differences except for pigmented lesions which shows much improvement.

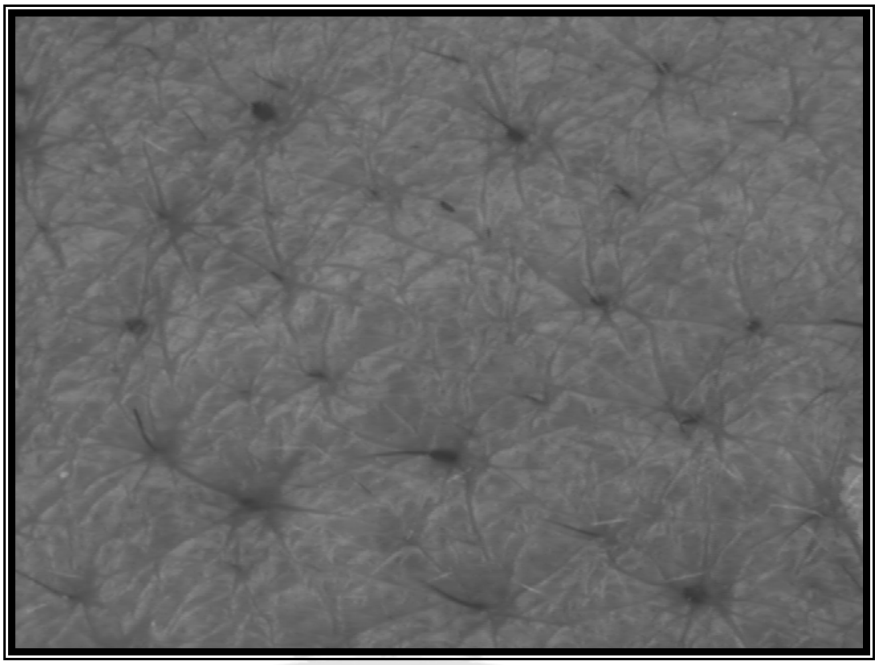
Table 4.4 Patient rating Grade of Improvement (n=24)

	Grade of Improvement				
	0%	**<25%**	**25-50%**	**51-75%**	**76-100%**
	Freq. (%)	**Freq. (%)**	**Freq. (%)**	**Freq. (%)**	**Freq. (%)**
Skin texture		3 (12.5%)	8 (33%)	9 (37.5%)	4 (17%)
Wrinkles		3 (12.5%)	13 (54%)	5 (21%)	3 (12.5%)
Pigmented lesions	1(4%)	1 (4%)	7 (29%)	12 (50%)	3 (12.5%)
Dyschromia		1 (4%)	8 (33%)	12 (50%)	3 (12.5%)
Scarring			4 (44.4%)	4 (44.4%)	1 (11%)

Note. Freq.= Frequency; %= Percent

Figure 4.2 A patient with post acne scarring and solar lentignes, before (right) and after (left) 3 laser resurfacing sessions with fractional QSRL 694nm.

Figure 4.3 A patient with skin laxity, problems of skin texture and wide pores, and mild wrinkles before (up) and after (down) 3 laser resurfacing sessions with fractional QSRL 694nm.



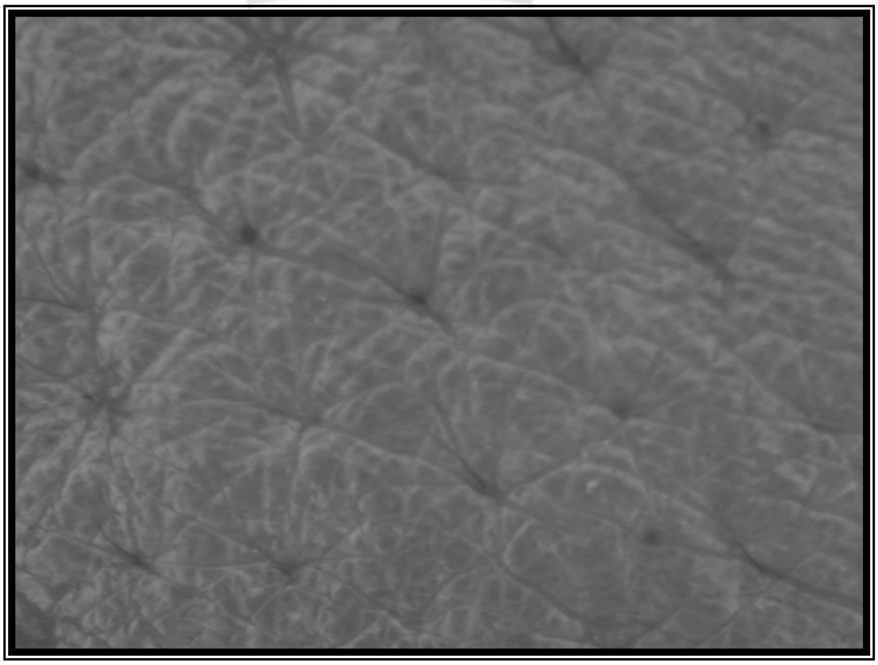


Figure 4.4 Visioscan® VC 98 pictures. A patient with problems of skin texture and wide pores as shown in Visioscan® VC 98 before (up) and after (down) 3 laser resurfacing sessions with fractional QSRL 694nm.

4.3 Post Laser Symptoms

Most of the subjects did not feel any pain at (fluence of 2.5 J/cm2), and mild pain detected by few patients at increasing fluences (3-3.5 J/cm2). Only 2 subjects feel mild pain with burning sensation at fluences of (4 J/cm2). Erythema was mild after first session of treatment at (fluence of 2.5 J/cm2), while moderate erythema has been detected with higher fluences (3-4 J/cm2). The redness last up to 3 hours, and then completely fade of. Edema was undetected at low fluences, and only mild edema noticed in some volunteers at higher flounces, which fade within hours.

4.4 Side Effects

No side effects has been detected in this project which can result from any laser resurfacing treatment to face. like Post inflammatory hyper pigmentation (PIH). Acneiform eruption, or herpes simplex reactivation although 1 subject receive acyclovir prophylaxis. However, only there were only 2 cases of allergic contact dermatitis to (antibiotic, moisturizer). On other hand, some acne patients notice slight improvement in their acne, while others feels no change.

Figure 4.5 Post laser erythema at fluence (3 J/cm2) of laser resurfacing with fractional QSRL 694nm.

CHAPTER 5

DISCUSSION, CONCLUSION AND SUGGESTIONS

5.1 Discussion

Q-switched Ruby laser is one of the common lasers in dermatology. The target chromophores are melanosomes and tattoo ink particles, which absorb the very high peak intensity light within short pulse duration produced by Q-switched lasers. Thus, QSRL (694nm) has been used for decades in the treatment of dermal and epidermal pigmented skin lesion, and tattoos in a safe and effective manner with scar-free results. In this study photorejuvenation capability of QSRL in three sessions of treatment for photodamaged facial skin, and post acne scarring has been assessed by objective and subjective evaluation systems. Different parameters of photorejuvenation including, pigmented lesions, uneven color -dyschromia-, problems with skin texture like roughness, dryness, and dilated pores, fine and medium wrinkles ,and post acne scarring, have been evaluated to asses the clinical improvement in these problems and overall facial skin rejuvenation. Mexameter® MX 18 system has been used to measure the Melanin Index at baseline (week 0), and (week 12) follow up visit. The mean Melanin Index are (224 ± 49.5) and (205 ± 38) at week 0 and 12, respectively, with mean difference (19 ± 23), which indicates statistical significant reduction in the melanin intensity after three sessions of treatment (*P* value = .002). These results are supported by a profound clinical improvement, as more than 60% of the patients detected a good to excellent improvement in their pigmented lesions and generalized facial dyschromia, with brighter, lighter, and more even facial skin color. There were progressive reduction in Melanin Index over subsequent sessions. Mexameter® MX 18 measurement of melanin at week (0, 8, 12) of 12 volunteers, are (220 ± 49.7), (209.6 ± 43.1), and (203 ± 37.4), respectively. This indicates progressive reduction in melanin intensity with more sessions of laser treatment.

Non ablative systems are known to improve overall skin texture, tone and elasticity (Alster & Doshi, 2005; Gold, 2005). In this study, Visioscan® VC 98 system has been used to measure Roughness Index, and Smoothness Index of skin texture at baseline (week 0), and (week 12) follow up visit. There are reduction in the skin roughness at week 12 compared to the baseline as shown in the results. So, Roughness index mean at baseline and week 12 follow up visit are (1.4 ±1.3), and (0.9 ± 0.6) respectively, with (mean difference = 0.52 ± 1.3), which indicates less scaly and more even skin texture. However, this was statistically non significant (*P* value = 0.092). The improvement in skin roughness are associated with enhancement in skin smoothness. Skin Smoothness Index are (26 ± 4), and (26.2 ± 4.3) at baseline and week 12 follow up visit respectively. This indicates mild enhancement of skin smoothness (mean difference = - 0.39 ± 4.4), which is statistically non significant (P value = 0.708). These objective evaluations of skin texture indicate some improvement which agree with the good patient satisfaction, as more than 50% of subjects noticed a good to excellent improvement in overall skin texture. However, all the patients noticed reduction in pore size, more even and smooth texture. Lee (2003) evaluated a combination technique using a long-pulsed, 532-nm potassium titanyl phosphate (KTP) laser and a long-pulsed 1064-nm Nd:YAG laser, separately and combined, for noninvasive photorejuvenation and skin toning with collagen enhancement. There were significant improvement in skin tone/tightening in all patients, however KTP and Nd:YAG in combination yielded greater results than either used alone, and KTP alone was superior to Nd:YAG alone. In other study, Schmults et al. (2004) evaluated nonablative facial remodeling by using a 300-Microsecond 1064-nm Nd:YAG laser. The face was treated in 4 sections, and punch biopsy specimens from the infra-auricular sun-exposed area were obtained at baseline and at 1 and 3 months after final treatment. There were improving skin texture, with significant decrease in collagen fiber diameter seen by EM analysis at 3 months after treatment and production of new collagen. They suggested that this new collagen production may be responsible for the improvement in skin quality seen after nonablative treatments.

Visioscan® VC 98 Evaluation of the wrinkles at baseline and at 12 week follow up visit shows mean Wrinkle Index of (37.3 ± 4.2) and (36.3 ± 4.1), respectively with mean difference of (1 ± 5). These results may indicate mild clinical improvement in the Wrinkle Index, although it is statically non significant (*P* value = .402). However, more than half of the patients noticed fair

(25-50%) clinical improvement in their wrinkles, and another 7 volunteers (34%), achieved 50% or more improvement with nonablative resurfacing using 694nm QSRL - Fractional mode. Goldberg and Whitworth (1997) did one of the first studies of nonablative laser skin resurfacing for treatment of wrinkles using Q-switched Nd: YAG Laser. They evaluated the rhytid resurfacing capability of the Q –switched neodymium: yttrium-alumimim- garden (QS Nd:YAG) laser at 1064 nm as compared with char-free carbon dioxide lasers at 10,600 nm. It is a split face study and 11 patients with perioral and periorbital rhytids were included. In 3 of them the QS Nd:YAG laser produced results clinically indistinguishable from that of the char-free pulsed carbon dioxide. 6 of the patients showed clinical improvement with QS Nd:YAG, but this improvement was not as marked as that with carbon dioxide lasers. Two patients have no improvement with the QS Nd:YAG, whereas clinical improvement in skin treated with carbon dioxide lasers was observed. In a review article by Grema, Greve and Raulin (2003) about the use nonablative resurfacing for facial rhytides. They stated that Diode laser (980/1450 nm) have been used for treatment of periorbital, and perioral rhytides and showed only mild clinical improvement, with some side effects like edematous papules (lasting 1-7 days) and transient hyperpigmentation. While, Dye laser (pulsed, 585/595 nm) were successfully achieved 50% or more improvement for mild to moderate wrinkling. However, pulsed dye laser is not suitable in severe wrinkles due to poor clinical improvement. Other nonablative laser used for facial rhytides were Er:Glass laser (1540 nm), and Nd:YAG laser (Q-switched, long-pulsed, 1064/532 nm) which resulted in poor clinical improvement with serious side effects like scarring for Er:Glass laser. Common side effects were also noted with (1064/532 nm) Nd:YAG including, pinpoint bleeding and petechiae, transient erythema, and postinflammatory hyperpigmentation. Nd:YAG laser (long-pulsed, 1320 nm) was the first commercially available system designed exclusively for non-ablative facial rejuvenation. However, there was only some improvement in facial rhytides treated by (1320 nm) Nd:YAG, and with postoperative transitive edema and erythema.

Orringer et al. (2005) used 585-nm pulsed dye laser and 1320-nm neodymium: yttrium-aluminum- garnet laser for nonablative resurfacing of forearm skin. Because the results of nonablative resurfacing for wrinkles, atrophic scars are generally modest, objective evaluation of these results has been difficult to achieve, Orringer et al. (2005) tried to examine and quantify biochemical events that occur in response to exposure to nonablative laser energy. They found statistically significant increases in type I procollagen messenger RNA expression occurred after exposure of photodamaged skin to each laser above baseline levels 1 week after laser therapy among those treated with the pulsed dye and neodymium:yttrium-aluminum-garnet lasers. Substantial induction of type III procollagen, various matrix metalloproteinases, and primary cytokines was also demonstrated. These results indicate that nonablative laser therapy induce quantifiable alterations in molecules with remodeling of the dermal matrix.

On other hand, more than 50% of the volunteers with scarring, have a good to excellent improvement, while the others noticed only mild improvement with more even scar texture. This clinical improvement is either due to the fact that sometimes these are not true scarring, but simply pigmentary changes (Goodman, 2007). These macular pigmentary changes can be brown, red, or white. Or may be the noticed improvement is due to neocollagenesis and remodeling of scar texture induced by nonablative devices (Hedelund et al., 2010). Fractional nonablative photothermolysis is a relatively new skin resurfacing technology that uses microzones of thermal injury to stimulate a wound-healing response, and so induce neocollagenesis. Hedelund et al. (2010) tried the fractional nonablative 1,540-nm laser resurfacing of atrophic acne scars in a randomized controlled trial with blinded response evaluation. The scar texture appeared more even and smooth on treated side than on the untreated control sides up to 12 weeks after the final treatment by blinded clinical evaluations. However, the clinical improvements were hard to be documented photographically, which explained by the lack of perception of small changes in depth by two-dimensional (photographic) methods.

There are several hypothesized molecular mechanisms to explain whereby nonablative lasers work to bring skin rejuvenation. Researches on photoaging have shown that photoaged human skin contains significantly elevated levels of cross-linked, partially degraded collagen, and that fragmented collagen inhibits collagen biosynthesis (Varani et al., 2001). Nonablative resurfacing will induce biochemical changes through induction of the MMPs activity which cause proteolytic clearance of these collagen fragments. This MMP activity will result in new collagen biosynthesis and enhanced new collagen production. The increased activity of MMPs is due to skin fibroblasts activation by laser. Furthermore, that clearance of fragmented collagen might result in up-regulation of type I and type III procollagen biosynthesis, resulting in net deposition of new collagen (Orringer et al., 2005). Other researchers suggests that nonablative laser produces mild subclinical epidermal injury that leads to enhanced skin texture and new papillary collagen synthesis by stimulation of cytokines and other inflammatory mediators (Tanzi & Alster, 2008). Another researchers found that lasers with wavelength at the visible light, generates a cascade of photochemical reactions, leading to increased Adenosine Triphosphate (ATP) production and elevated calcium ion (Ca2+) levels. This leads to enhanced cell metabolism with either cellular proliferation or elevated action mechanisms (Trelles et al., 2007). It is also known that fibroblasts, respond much better to red light like Ruby laser than infrared light (Trelles et al., 2007).

The treatments with QSRL associated with mild post laser symptoms including level of pain, erythema and edema. Erythema and edema will last only for hours and then completely fad out, and this is one of the advantages of nonablative laser resurfacing. Previous researches also found that treatments with nonablative lasers are variably painful and mostly associated with mild pain. Mild erythema and edema do occur following each treatment, but these sequelae remit within minutes to a few hours or may be concealed with cosmetics (Dover, 2008). Because nonablative remodeling involves creation of a dermal wound without epidermal injury (Lee, 2003), no complications were detected with fractional mode QSRL resurfacing even for Post-inflammatory hyperpigmentation (PIH) which is a common post laser complication in Asian skin (Ling, 2010). Therefore, dark-skinned patients or those with a tendency to develop hyperpigmentation after skin injury can safely undergo nonablative therapy with fractional QSRL. Other researcher stated that infrared lasers are also less susceptible to pigmentary complications, and patient skin color is less important when using these lasers (Dover, 2008). These advantages of the minimal postoperative recovery downtime and side effects, make nonablative skin remodeling an attractive procedure to patients and physicians (Tanzi & Alster, 2008). However, many users of these techniques suggested that the results are not descriptive and pale in their clinical improvement if compared with more aggressive ablative laser and nonlaser approaches. But, here in this research we can find improvement in major targets of facial rejuvenation including dyschromia and pigmented lesions as measured by objective methods using Mexameter® MX 18, beside the improvement felt by the subjects.

Clinical improvement and findings are difficult to represent in photographs when there is nonablative facial rejuventation (Dover, 2008), but this indicates the inherent limitations of both photographic and clinical evaluation of improvement (Goldberg, 2002) after what is more accurately called a nonablative dermal remodeling or dermal toning technique, rather than poor clinical improvement of these techniques. Even more, evidence of new collagen has been seen using blinded observer analysis of electron microscopic changes (Schmults et al., 2004) following nonablative dermal remodeling.

Patient selection is very important in non-ablative facial resurfacing, we completely agree with previous researches, which stated that good candidates for nonablative resurfacing tend to be relatively young, usually 25–65 years of age, and have minimal sagging of the face (Dover, 2008), with mild to moderate facial photodamage (Tanzi & Alster, 2008). These candidates should know and understand what they want and have realistic expectation, so that it can be determined if nonablative therapy is likely to provide these results (Dover, 2008). Unrealistic expectations is considered a main contraindication (Kilmer & Semchyshyn, 2005). Clinical aesthetic improvement from nonablative resurfacing are similar in type, but less in magnitude than the results of ablative resurfacing, and the changes occur gradually, typically after three to six or more treatments. Therefore, those receiving nonablative treatments should not expect dramatic results immediately (Dover, 2008). The age range in this research was (26-67) and 15 subjects (62 %) lying in age group between 30s and 40s years old, with mild-to moderate facial photodamage. This is completely agree with previous research finding, and this also can explain the high level of satisfaction among the volunteers.

5.2 Conclusion

Nonablative facial rejuvenation is an attractive procedure for both patients and physicians, because of the minimal post laser recovery time and associated side effects. Nowadays, nonablative resurfacing become the standard method for the treatment of mild rhytides and overall skin toning, and these procedures are expanding as the patient's demand "no downtime" wrinkle treatments. This approach are supported by the accumulated evidences of new collagen synthesis following nonablative resurfacing.

Many lasers have been used for nonablative dermal remolding from visible light to infrared wavelength range. QSRL 694nm - Fractional Mode- have resurfacing capability that can target major features of photodamaged facial skin in Asians, with little down time and side effects. Like other nonablatives lasers, few sessions of treatment at 4 weeks intervals is needed to ensure clinical improvement. However, patient selection for nonablative resurfacing by fractional QSRL is a vital step to ensure promising results and a good patient satisfaction with the treatment.

5.3 Suggestions

There is a need for clear guidelines about specific nonablative lasers for each indication of facial rejuvenation, which can be achieved by reviewing related literature.

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APPENDIXES

APENDIX A

INFORMED CONCENT FORM

หนังสือยินยอมเข้าร่วมโครงการวิจัย (Informed Consent Form)

วันที่.........เดือน............พ.ศ ....

ข้าพเจ้า (นาย/นาง/นางสาว)...

อยู่บ้านเลขที่ ....หมู่ที่ .... ถนน ....ตำบล....................อำเภอ ....

จังหวัด ....รหัสไปรษณีย์ ....

ขอทำหนังสือแสดงความยินยอมเข้าร่วมโครงการวิจัยเพื่อเป็นหลักฐานแสดงว่าข้าพเจ้ายินยอม

1. ข้าพเจ้ายินยอมเข้าร่วมโครงการวิจัยของ (หัวหน้าโครงการ)...

เรื่อง...

ด้วยความสมัครใจ โดยมิได้มีการบังคับ หลอกลวงแต่ประการใด และพร้อมจะให้ความร่วมมือในการวิจัย

2. ข้าพเจ้าได้รับการอธิบายและตอบข้อสงสัยจากผู้วิจัยเกี่ยวกับวัตถุประสงค์การวิจัย วิธีการวิจัย ความปลอดภัย อาการ หรืออันตรายที่อาจเกิดขึ้น รวมทั้งประโยชน์ที่จะได้รับจากการวิจัย โดยละเอียดแล้วตามเอกสารชี้แจงผู้เข้าร่วมการวิจัยแนบท้าย

3. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ จะเปิดเผยได้เฉพาะในรูปแบบของการสรุปผลการวิจัยเท่านั้น

4. ข้าพเจ้าได้รับทราบจากผู้วิจัยแล้วว่า หากเกิดอันตรายใดๆ จากการวิจัย ผู้วิจัยจะรับผิดชอบค่ารักษาพยาบาลที่เป็นผลสืบเนื่องจากการวิจัยนี้

5. ข้าพเจ้าได้รับทราบว่า ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากการวิจัยครั้งนี้เมื่อใดก็ได้ โดยไม่มีผลกระทบใด ๆ ต่อการรักษาพยาบาลตามสิทธิ์ที่ข้าพเจ้าควรได้รับ

ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้แล้ว จึงได้ลงลายมือชื่อไว้เป็นสำคัญ พร้อมกับหัวหน้าโครงการวิจัยและพยาน

ลงชื่อ ....ผู้ยินยอม/ผู้ปกครอง

(...)

ลงชื่อ ....หัวหน้าโครงการ

(...)

ลงชื่อ ....พยาน

(...)

ลงชื่อ ....พยาน

(...)

Research Title:

Evaluation of Efficacy and Side Effects of Fractional Mode Q-Switched Ruby Laser for Facial Rejuvenation in Asians

I agree to participate in this research and receive 3 sessions of treatment with fractional mode ruby laser for facial rejuvenation with follow up for 3 months.

APPENDIX B

PATIENT INFORMATION FORM

Patient Information Form

Name:……………………………………………………………………………………...

Dateof birth:………………………………………………………..Age:……………

Sex: ☐ male☐ female

Job: ……………………………………………………………………………………

Address: ………………………………………………………………………………

H/P:

Chief complaint: ………………………………………………………………………

Duration:……………………………………………………………………………….

Previous history:

- **Facial skin resurfacing treatments: …………………………………**

  ……………………………………………………………………………...

- **Chronic illness: ………………………………………………………..**
- **Malignancy:……………………………………………………………**
- **Photosensitivity disorder ……………………………………………..**

Drughistory: …………………………………………………………………………..

For female patients: please tick

Are you pregnant: ☐ yes ☐ no

<u>Physical examination:</u>

Generalexamination: …………………………………………………………………

……………………………………………………………………………………….

………………………………………………………………………………………..

Specific examination:

- **Fitzpatrick skin type:**

- **Glogau's category of photodamage:**
- **Photograph:**

Session	**Done**	**Note**
Pre- Rx		
Post- Rx1		
Post- Rx2		
Post- Rx3		
Post- 3months		

- **Measurements:**

Treatment session	**Mexameter**	**cutometer**	**Visioscan** ---------- ------------ ---------- -------- ---------
Pre- Rx			
Post- Rx1			
Post- Rx1			
Post- Rx1			
Post- 3 m.			

- **Treatment parameters:**

Treatment session	**Treatment setting (fractional mode QSRL)**
1	
2	
3	

Post- Treatment assessment:

- **Treatment:**
- **Redness, pain, & edema:**

score	Degree of redness	Pain level	edema
0	No redness		No edema
1	Faint redness	painless	Mild edema
2	Moderate redness	Mild pain	Moderate edema
3	Strong redness	Moderate pain	Markedly edema
4		Significant pain	
5		Very painful	
Brief Session 1			
Brief Session 2			
Brief Session 3			
Brief			

Complication & Management:

APPENDIX C

PATIENT SATISFACTION

คะแนนความพึงพอใจของผู้ป่วย

Patient Satisfaction Score

Name :

H N :

Date :

หลังจากที่คุณได้รับการรักษาด้วยเลเซอร์เป็นจำนวน 3 รอบ

After you have been treated with three sessions of Laser therapy ,

การตอบสนองของคุณต่อการรักษาด้วยเลเซอร์ได้ผลดีหรือไม่ อย่างไร,

How do you find your response to the laser treatment ?

กรุณาเลือกผลการตอบสนองหลังการรักษาผิวหนังของคุณด้วยเลเซอร์ ดังตัวเลือกที่กำหนดให้ต่อไปนี้

Please appreciate your lesion response to the laser treatment by choosing the appropriate choice that meets your response :

การตอบสนองไม่ดี หรือ ไม่มีการเปลี่ยนแปลงในแผลของฉันหลังการรักษด้วยเลเซอร์ ☐ **Poor response (Nochange in my lesions after laser therapy) .**

☐ **ผม/ดิฉัน พอใจเล็กน้อย ในการตอบสนองของแผลหลังการรักษาด้วยเลเซอร์**

I am slightly satisfied about the response of my lesions to laser therapy

----

☐ **ผม/ดิฉัน พอใจค่อนข้างมาก ในการตอบสนองของแผลหลังการรักษาด้วยเลเซอร์**

I am really satisfied about the response of my lesions to laser therapy

การตอบสนองดีเยี่ยม ผม/ดิฉัน ---

พอใจอย่างมาก พบว่ามีการตอบสนองที่ดีเยี่ยม หลังการรักษาแผลด้วยเลเซอร์

☐ **Excellent response (I found an excellent response in my lesions to laser therapy)**

Signature ____________________

Name ________________________

GLOBAL IMPROVEMENT SCORE

❖ **Pigmented lesions (บริเวณที่สีผิวเข้มเช่น ฝ้าหรือกระ มีการเปลี่ยนแปลงดีขึ้นอย่างไร)**

	Score	Rate of improvement
	4	76% to 100% = excellent ดีขึ้นมากที่สุด
	3	51% to 75% = good ดีขึ้นมาก
	2	25% to 50% = fair ดีขึ้นปานกลาง
	1	less than 25% = slightly better ดีขึ้นเล็กน้อย
	0	0% = no improvement ไม่มีการเปลี่ยนแปลง

❖ **Uneven color , Dyschromia (สีผิวที่ไม่สม่ำเสมอ มีการเปลี่ยนแปลง)**

	Score	Rate of improvement
	4	76% to 100% = excellent ดีขึ้นมากที่สุด
	3	51% to 75% = good ดีขึ้นมาก
	2	25% to 50% = fair ดีขึ้นปานกลาง
	1	less than 25% = slightly better ดีขึ้นเล็กน้อย
	0	0% = no improvement ไม่มีการเปลี่ยนแปลง

❖ **<u>Problems with skin texture</u>: roughness, dryness, and dilated pores (ความเนียนเรียบของผิวมี การเปลี่ยนแปลงดี ขึ้นอย่างไร)**

	Score	Rate of improvement
	4	76% to 100% = excellent ดีขึ้นมากที่สุด
	3	51% to 75% = good ดีขึ้นมาก
	2	25% to 50% = fair ดีขึ้นปานกลาง
	1	less than 25% = slightly better ดีขึ้นเล็กน้อย
	0	0% = no improvement ไม่มีการเปลี่ยนแปลง

❖ **<u>Wrinkles</u> : Fine, Medium (ริ้วรอยเล็กๆ มีการเปลี่ยนแปลงดีขึ้นอย่างไร)**

	Score	Rate of improvement
	4	76% to 100% = excellent ดีขึ้นมากที่สุด
	3	51% to 75% = good ดีขึ้นมาก
	2	25% to 50% = fair ดีขึ้นปานกลาง
	1	less than 25% = slightly better ดีขึ้นเล็กน้อย
	0	0% = no improvement ไม่มีการเปลี่ยนแปลง

❖ **<u>Post acne scarring</u> (หลุมสิว มีการเปลี่ยนแปลงดีขึ้นอย่างไร)**

	Score	Rate of improvement
	4	76% to 100% = excellent ดีขึ้นมากที่สุด
	3	51% to 75% = good ดีขึ้นมาก
	2	25% to 50% = fair ดีขึ้นปานกลาง
	1	less than 25% = slightly better ดีขึ้นเล็กน้อย
	0	0% = no improvement ไม่มีการเปลี่ยนแปลง

CURRICULUM VITAE

CURRICULUM VITAE

NAME Thana'a Mohammed Ibrahim

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EDUCATIONAL BACKGROUND

1994-2000	M.B. Ch.B. in Medicine and Surgery College of Medicine, Mosul University (Iraq)
2008-2009	MSc. in Transfusion & Transplantation Science Uiversiti Sains Malaysia (USM) Advanced Medical & Dental Institute (IPPT)

WORK EXPERIENCE

2000-2002	Rotator Doctor in different medical & surgical departments. Ministry of Health, Iraq
2002-2003	G.P. Doctor Private Hospitals (Iraq)
2003-2006	Residence Doctor Rural areas (Iraq)
2006-2007	Permanent Doctor (Medical Officer) Dermatological Department (Iraq)
2008-2009	Lecturer Factuality of Health & Life Sciences, Management and Science University (MSU) KL, Malaysia