THE EFFICACY OF COMBINATION THERAPY OF FRACTIONAL PICOSECOND LASER AND 20% GLYCOLIC ACID PEELING FOR FACIAL REJUVENATION

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ABSTRACT
Human aging is characterized by skin laxity, wrinkles and depigmentation. Skin aging is a chronic process that is accelerated by UV radiation. Rejuvenation refers to the removal and regeneration of the skin, resulting in a more organized, "younger" dermal matrix and epidermal normalization. Picosecond lasers originally developed for tattoo removal and have proven effective in treating a variety of skin conditions. Glycolic Acid (GA) is a natural AHA with good skin penetration due to its hydrophilic properties and small size. To study the efficacy of a combination of fractional picosecond laser 1064 nm wavelengths and 20%glycolic acid peeling for facial rejuvenation. Twelve subjects, age 30-50 years with Fitzpatrick skin ranging from III to V who desire to undergo facial rejuvenation received 3 treatment sessions of 1064 fractional picosecond laser and glycolic acid combination with 2 weeks interval. Wrinkles, skin elasticity and trans epidermal water loss will be assessed at baseline and each 2nd, 4th, 8th and 12th week follow up visit accordingly. The combination of fractional picosecond laser 1964nm wavelengths and 20% glycolic acid peeling have better statistically significant results in wrinkles, skin elasticity and trans epidermal water loss. And the volunteers also gave satisfactory result after final treatment. This study pointed that the combination of fractional picosecond laser 1964nm wavelengths and 20% glycolic acid peeling method can get better outcomes than the mono therapies.
Keywords: Picosecond, Chemical Peels, Glycolic, Rejuvenation

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INTRODUCTION

Human aging is characterized by skin laxity, wrinkles and depigmentation. Skin aging is a chronic process that is accelerated by UV radiation. The cumulative UV radiation from the sun damages human skin and causes visible signs of photoaging consisting of changes in skin color, vascularity, texture and wrinkles (Wu et al., 2016).

Rejuvenation refers to the removal and regeneration of the skin, resulting in a more organized, "younger" dermal matrix and epidermal normalization (Ross et al., 2022). A lot of medical and surgical techniques have been developed to stop, slow down, or treat skin aging, and skin resurfacing has been a big concern in recent years. Over the past ten years, laser technology has significantly advanced both dermatology and cosmetic surgery. Lasers, both ablative and non-ablative, have been utilised to improve skin synthesis of collagen and rejuvenation. But these techniques also have disadvantages, like comparatively long downtime, post inflammatory pigment changes and persistent erythema (Nilforoushzadeh et al., 2020).

Lasers treat hyperpigmented melanocyte damage by removing excessive pigmentation without causing damage to surrounding normal tissue since they have precise wavelengths that are absorbed by the target. The pigmentation lightens or disappears when the laser radiation reaches the skin but are absorbed by more melanin. Melanosomes have a thermal relaxation time of between 10 and 100 nanoseconds. The nanosecond pulse lengths of Q-switched lasers that are now on the market have the potential to cause more harm than good since they can heat the nearby unaffected skin. Melanin is destroyed and melanin levels are decreased by the quick absorption of picosecond light energy, which also balances the skin tone and texture (Khetarpal et al., 2016).

Picosecond lasers are useful for treating a range of skin diseases; however, they were first created for the purpose of removing tattoos. Following skin analysis, neocollagenesis and neoelastinogenesis are observed. These responses could be the result of localised thermal effects of superheated plasma and/or photoacoustic stimulation of cellular signals that propagate deeper into the dermis than the depth of acute injury that is easily visible on immediate histology. Tissue remodelling may also result from a notably higher thermal temperature linked to fractionated picosecond laser irradiation than from unfractionated delivery (Wu et al., 2021).

Chemical peels are one of the most common methods used by dermatologists around the world to treat conditions such as melasma, acne, scars, and aging skin. Its mechanism of action is based on cell stimulation in the dermis and epidermis as well as keratolysis, which causes keratinocyte differentiation and new collagen synthesis. Because of their virtually immediate outcomes, short recovery period, and comparatively minimal risk of side effects, alpha-hydroxy acid (AHA) peels are popular and frequently used. Because of its small size and hydrophilic characteristics, glycolic acid (GA) is a naturally occurring AHA that has good skin penetration. By adjusting the concentration, pH, and application duration to meet the specific needs of each patient and achieve the desired outcomes, GA peels provide a great deal of flexibility (Rouvrais et al., 2018). However, chemical peeling alone needs to wait longer to get the better results, but when combined with the laser, it shows the rapid more favorable results than the mono therapy (Vachiramon et al., 2015). And when combined with the fractional picosecond laser, it may get the synergistic effect in reduction skin wrinkles and dryness, but skin elasticity can be improved with laser treatment.

The aim of this study is to determine the efficacy of a combination of fractional picosecond laser 1064 nm wavelengths and 20%glycolic acid peeling for facial rejuvenation. There is no previous research about this combination treatment for facial rejuvenation. We expect that this combination method can get better outcomes than the mono therapies.

LITERATURE REVIEWS

Pico laser and Uses

A pulse in billionths of a second (10^{-2}) is called a picosecond, whereas a pulse in billionths of a second (10^{-9}) is a nanosecond. Picosecond lasers have a faster energy delivery rate than nanosecond lasers, which results in a higher target pressure in irradiated tissue thermal diffusion, even though each of these two pulse lengths can achieve high target temperatures above steam formation (Saluja et al., 2020).

The selective photothermolysis described by Anderson and Parish is the first step towards the foundation of laser science. Adjacent tissue is spared, limiting destruction to the target alone, if the target chromophore is exposed to radiation at a wavelength that is preferentially absorbed in an energy configuration capable of destroying the target, delivered in pulse durations shorter than the target's thermal relaxation times. By using this method, nonselective thermal damage is greatly reduced, and laser irradiation precision is increased to produce the desired effects (Saluja et al., 2020).

Fractional photothermolysis was developed by a novel concept in skin rejuvenation. Fractional photothermolysis was created using a cutting-edge skin rejuvenation concept. Rapid healing is achieved using fractional photothermolysis, which produces transitory amplifying cells that are viable in between minute thermal wounds. Skin that is still intact is frequently scattered among the epidermal tissue that remain between thermal zones. The wound healing response is different from that of fully ablative lasers because undamaged, untreated skin forms bridges between microscopic treatment zones (MTZs) that are capable of rapid re-epithelialization.

Non-ablative and fractional lasers are becoming more and more popular as a means of assisting in lowering recovery times. In particular, 1064 nm non-ablative lasers have been demonstrated to enhance rejuvenation of the skin and aging. Compared to earlier generations of nanosecond lasers, the picosecond alexandrite laser creates a higher tensile strength and induces photomechanical and photothermal effects in the tissue. The picosecond alexandrite laser has demonstrated efficacy not just in repairing tattoos but also in pigmented lesions, acne scars, and visible signs of photoaging on the décolletage (Wu et al., 2016).

It has been suggested that laser-induced optical breakdown is the mechanism of action in previous studies on fractional picosecond laser. It is likely that different wavelengths cause the dermis and epidermis to react in different patterns. According to the relative proportions of melanin's absorption coefficient compared to blood, 755 nm would result in the greatest specific pigmentary disorder and relative vascular sparing, whereas 1064 nm should cause a slightly greater vascular response and less pigmentary disorder. Because of the high selective absorption of HgB, the 532 nm wavelength—which is well absorbed by both pigments and blood—should be more superficially restricted and dispersed than its 755 and 1064 nm counterparts (Ross et al., 2022).

In contrast, due to the side effects of ablative laser most patients prefer non ablative laser treatment. Because the fractional picosecond laser is well tolerated and showed mild to moderate improvement in wrinkles and pigment by building new collagen and elastin. And Picoway modern technique has subsurface remodeling without breaking the stratum corneum and low downtime.

Pico laser and Safety

Numerous studies have discussed the safety of picosecond lasers as well as their side effects, such as swelling and erythema, which resolved without causing any long-term consequences. But there were reports of any bruising, scarring, hypo- or hyperpigmentation, and infections (Wu et al., 2016; Khetarpal et al., 2016; Habbema et al., 2013; Haimovic et al., 2016).

Yim et al. (2020) evaluated the safety of picosecond 1064 laser with for the treatment of wrinkles and pores in Asian skin. In this study, there is an increased in the rate of erythema. That indicates picosecond laser treatments are not suitable for the treatment of cutaneous

erythema and can even exacerbate erythema due to inflammation after laser treatment. These transient erythematous papules and macules have been reported in the treated facial area, indicating that localized erythema is a potential adverse event of which clinicians should be aware (Yim et al., 2020).

There're also a lot of research that studied the laser and peeling combination treatment for various diseases. Vasanop et al. studied the treatment of melasma in men with Q-switched Nd:YAG 1064 laser compared with combined laser and 30% glycolic acid peeling. In this study, there was just mild stinging and burning on both sides in some patients and all lasted less than 12 hours and no needed further treatment. But laser and peeling combined group can get the better and faster results than the laser therapy alone (Vachiramon et al., 2015).

Glycolic Acid

Glycolic acid is also known as hydroxyacetic acid, acetic acid, hydroxyethanoic acid, alpha-hydroxyacetic acid (AHA), acetoacetic acid and ethylethanoic acid (Distributor, n.d.). Numerous studies have shown that glycolic acid can be used as a medium-depth and superficial chemical peel for treating photoaged skin. Chemical peeling can change the histology of the epidermis by restoring a more typical pattern, with columnar cells displaying polarity again and melanocytes and melanin granules distributed more regularly (Kubiak et al., 2020).

Because of their virtually immediate outcomes, short recovery period, and comparatively minimal risk of side effects, alpha-hydroxy acid (AHA) peels are popular and frequently used. Because of its small size and hydrophilic characteristics, glycolic acid (GA) is a naturally occurring AHA that has good skin penetration. By adjusting the concentration, pH, and application duration to meet the specific needs of each patient and achieve the desired outcomes, GA peels provide a great deal of flexibility (Rouvrais et al., 2018).

FDA suggest that safety range concentration of glycolic acid as skin peeling agents presents from 3% to 67% (Distributor, n.d.). When administered to the skin at high doses, it has been observed to produce epidermolysis and keratinocyte exfoliation. It increases collagen formation and cell turnover after exfoliating the skin. Additionally, GA helps to enhance skin tone, unclog pores, reduce fine lines and wrinkles, lighten sun damage and dark spots, and moisturise skin to give it a more youthful appearance. Medical professionals and estheticians can both utilise glycolic acid as a less potent refreshing peel. After instantaneous exfoliation, morbidity is usually modest and consists of erythema or irritation (if present), which is easily covered up with makeup (Piacquadio et al., 1966).

In the last ten years, the number of products on the market containing AHA has practically increased. GA is also used in several topical products, such as keratolytic, antiaging, and moisturisers. AHA-containing cosmetics are frequently and persistently used on sun-exposed skin, and there have been anecdotal reports of increased sensitivity to sunlight. These factors have prompted numerous clinical studies investigating the effects of AHAs on UV sensitivity. Therefore, following glycolic acid treatment, patients should limit their exposure to the sun and wear sunscreen whenever they go outside (Kaidbey et al., 2003).

In Zhao et al study, the effect of 5% glycolic acid complex and 20% glycolic acid on mild to moderate facial acne vulgaris is evaluated. These showed that in the patients treated with 20% glycolic acid can get higher TWEL and lower score for pores compared with patients given 5% glycolic acid. And both groups showed similar effects in the improvement of wrinkles (Zhao et al., 2022).

In Marlena et al study, showed that Comparative study of 15% trichloroacetic acid peel combined with 70% glycolic acid and 35% trichloroacetic acid peel for the treatment of photodamaged facial skin in aging women. These evaluated that 70% GA plus 15% TCA peel shows no severe adverse effect, and this combination treatment did not cause dryness, edema or intensive lysis of the epidermis, and the frequency of peel-induced erythema did not increase with the addition of glycolic acid, but with higher concentration of the TCA solution. And

combined therapy is more comfortable and tolerated than 35% TCA peel alone (Kubiak et al., 2020).

In Vansanop et al study, evaluated that treatment of Melasma in Men with Low-Fluence Q-Switched Neodymium-Doped Yttrium-Aluminum-Garnet Laser Versus Combined Laser and Glycolic Acid Peeling. In this study, on the combined side 30% glycolic acid was applied for 2 minutes and then wash off with clean water (Vachiramon et al., 2015). The lag period before laser treatment was at least 10 minutes. There is greater reduction in relative lightness index in combined treatment than the laser treatment alone (Vachiramon et al., 2015).

From the literature review, the conceptual framework can be drawn as shown in Figure 1.

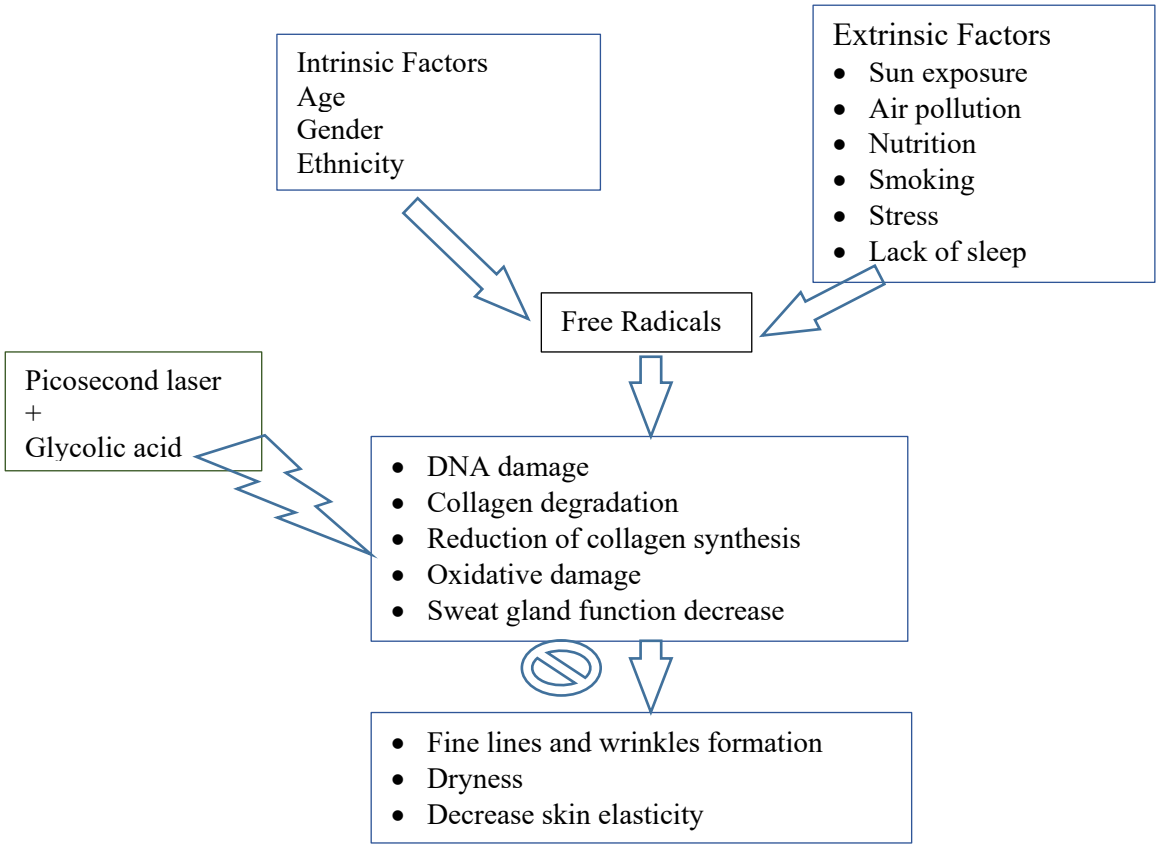


Figure 1 Conceptual framework

RESEARCH METHODOLOGY

The research is designed as an opened label quasi-experimental, clinical study involving twelve subjects, age 30-50 years with Fitzpatrick skin ranging from III to V with a duration of 12 weeks. The protocol and informed consent were reviewed and approved by the Ethics Committee of Mae Fah Luang University, Thailand on 15th May 2024 (Acceptance code: EC 23008-20). Prior to the study, participants were selected by fulfilled criteria. The researcher explained a purpose and step of procedures during the study including the benefit and possible adverse reaction after treatment. Participants signed an informed consent form for research participation. The information of the subjects was recorded. Standardized photographs will be taken before treatment at 0th, 2nd, 4th, 8th and 12th week using VISIA. Wrinkles, skin elasticity and trans epidermal water loss will be assessed at baseline and each 2nd, 4th, 8th and 12th week visit accordingly by using VISIA, Cutometer and tewameter respectively. The participants will be received total three treatment session of 1064 fractional picosecond laser and glycolic acid combination at 0th, 2nd and 4th week with 2 weekly intervals. After topical anesthesia, glycolic acid 20% peel will be applied over the face for 2 minutes and wash off with water. PicoWay laser treatment will perform over the entire face and external adhesive eye shields were worn

the entire time. The parameter set as: 1064 nm wavelength, frequency 5 Hz, spot size 6mm, fluency 1.1-1.3 mJ/μbeam, repeat 3 passes/treatment and duration of the whole treatment is about 15 minutes. All post treatment complications such as pain, swelling, burn, numbness and other side effects were assessed. Global Aesthetic Improvement Scale and Participant's Satisfaction Score were assessed to see the improvement. The medical record data of the participants and the results of this study trial conducted at Mae Fah Luang University Dermatology Clinic, were analyzed using SPSS 18 and Microsoft Excel 2021 software. Statistical significance is obtained by comparing the mean values of wrinkle, viscoelastic, and transdermal water loss scores at each follow-up visit and before treatment using repeated measures ANOVA. Physician Global Aesthetic Improvement Scale Outcomes and Participant Satisfaction Scores are ordinal (nonparametric) time elements (each follow-up) with repeated measures and differences are tested using with McNemar's test and Adverse events by Cochran's Q test.

RESEARCH RESULTS

Demographic data of the participants

Table 1 Descriptive statistic of demographic data

Demographic data	**n=12**
Gender, n(%)	
Male	3
Female	9
Age (years), mean±SD	33.25±1.91
Occupation, n(%)	
Student	8
Employee	4
Underlying disease, n(%)	
No	12
Personal Medication, n(%)	
No	12
History of allergy, n(%)	
No	12

According to Table 1, showing the demographic data of the 12 participants, 9 were female and 3 were male. The mean age was 33.25±1.91 years. 8 were students and 4 were employees. All research participants had no underlying disease, history of medication, or allergies.

Clinical Evaluation

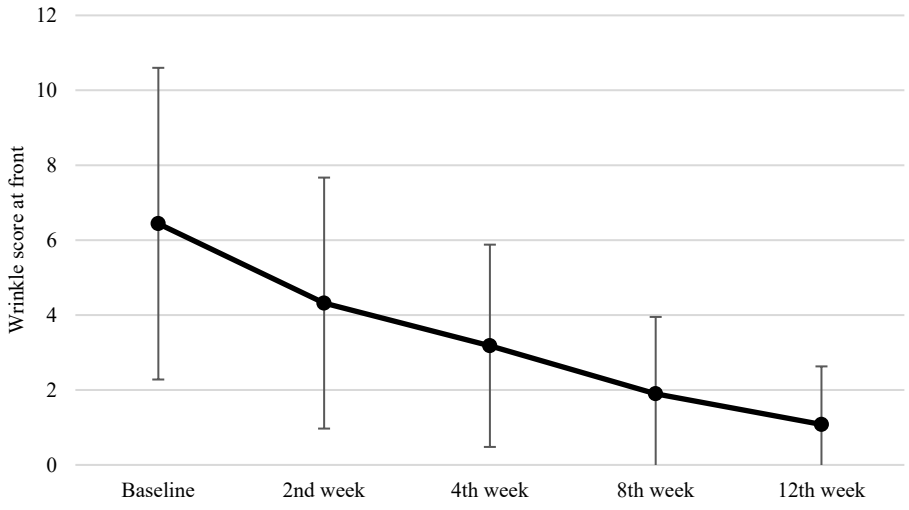
Wrinkle score by VISIA

Table 2 Statistical analysis of wrinkle score at front and whole face (right and left side) on baseline, follow-up 2nd, 4th, 8th, and 12th week (n=12)

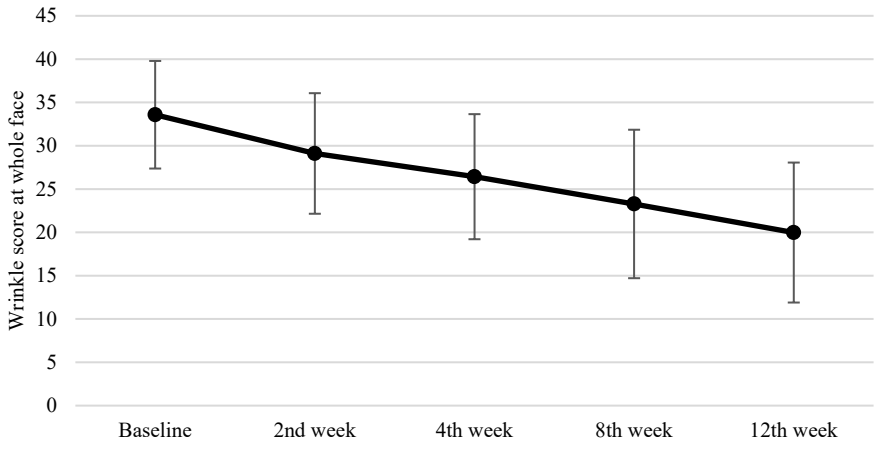
Follow-up	**Front (mean±SD)**	**Whole face (mean±SD)**
Baseline	6.44±4.16	33.58±6.21
2nd week	4.32±3.35	29.11±6.96
4th week	3.18±2.70	26.43±7.22
8th week	1.90±2.05	23.28±8.57
12th week	1.08±1.55	19.98±8.08
P-value	<0.001*	<0.001*
Partial η^2	0.755	0.950

Data were analyzed with Repeated measure ANOVA

* Statistically significant at the 0.05 level



(a)



(b)

Figure 2 Displays line graph showing the wrinkle score at the front [(a)] and the whole face [(b)] from baseline to the follow-up 12th week

According to Table 2, which shows the statistical analysis of the wrinkle score at the front and the whole face, the mean wrinkle score at the front on baseline, follow-up 2nd, 4th, 8th and 12th week were 6.44±4.16, 4.32±3.35, 3.18±2.70, 1.90±2.05, and 1.08±1.55, respectively. The mean wrinkle score at the front of each visit decreased statistically significantly at the level of 0.05 (partial $\eta^2 0.755$, $p<0.001$). In other words, the treatment effect of the fractional picosecond laser and glycolic acid combination on the wrinkle score at the front was 75.5%.
The mean wrinkle score at whole face on baseline, follow-up 2nd, 4th, 8th ,and 12th week were 33.58±6.21, 29.11±6.96, 26.43±7.22, 23.28±8.57, and 19.98±8.08, respectively. The mean wrinkle score on the whole face in each visit decreased statistically significantly at the level of 0.05 (partial $\eta^2 0.950$, $p<0.001$). In other words, the treatment effect of the fractional picosecond laser and glycolic acid combination on the wrinkle score at the whole face was 95.0%.

Table 3 Multiple comparison (Post-hoc) of wrinkle score at front and whole face (n=12)

Pairewise	Front		Whole face	
	Mean difference	**P-value**	**Mean difference**	**P-value**
Baseline-2nd week	-2.120	0.012*	-4.471	0.002*
Baseline-4th week	-3.269	0.008*	-7.148	<0.001*
Baseline-8th week	-4.547	0.003*	-10.300	<0.001*
Baseline-12th week	-5.361	0.002*	-13.599	<0.001*
2nd week-4th week	-1.149	0.071	-2.677	0.002*
2nd week-8th week	-2.427	0.008*	-5.829	0.002*
2nd week-12th week	-3.241	0.005*	-9.128	<0.001*
4th week-8th week	-1.278	0.063	-3.152	0.008*
4th week-12th week	-2.092	0.006*	-6.451	<0.001*
8th week-12th week	-0.814	0.023*	-3.299	0.006*

Data were analysis with Bonferroni method

* The mean difference is statistically significant at the 0.05 level

According to Table 3, which displays the multiple comparison result, the wrinkle score at the front on the 2nd, 4th, 8th, and 12th week was lower than at baseline. Additionally, on the 8th and 12th week, it was lower than the 2nd week. Moreover, the 12th week was lower than the 4th and 8th week, which was statistically significant at the level of 0.05 ($p<0.05$). The decrease in the wrinkle score at the front from baseline to the follow-up 12th week was 5.361.

The wrinkle score at whole face on the 2nd, 4th, 8th, and 12th week was lower than at baseline. Additionally, on the 4th, 8th, and 12th week, it was lower than the 2nd week. Moreover, the 8th and 12th week were lower than the 4th week, and the 12th was lower than the 8th week, which was statistically significant at the level of 0.05 ($p<0.05$). The decrease in the wrinkle score on the whole face from baseline to the follow-up 12th week was 13.599.

Cutometer score

Table 4 Statistical analysis of cutometer score at whole face (right and left side) on baseline, follow-up 2nd, 4th, 8th, and 12th week (n=12)

Follow-up	mean±SD
Baseline	0.8333±0.0370
2nd week	0.8733±0.0261
4th week	0.8975±0.0216
8th week	0.9242±0.0201
12th week	0.9495±0.0117
P-value	<0.001*
Partial η^2	0.880

Data were analyzed with Repeated measure ANOVA

* Statistically significant at the 0.05 level

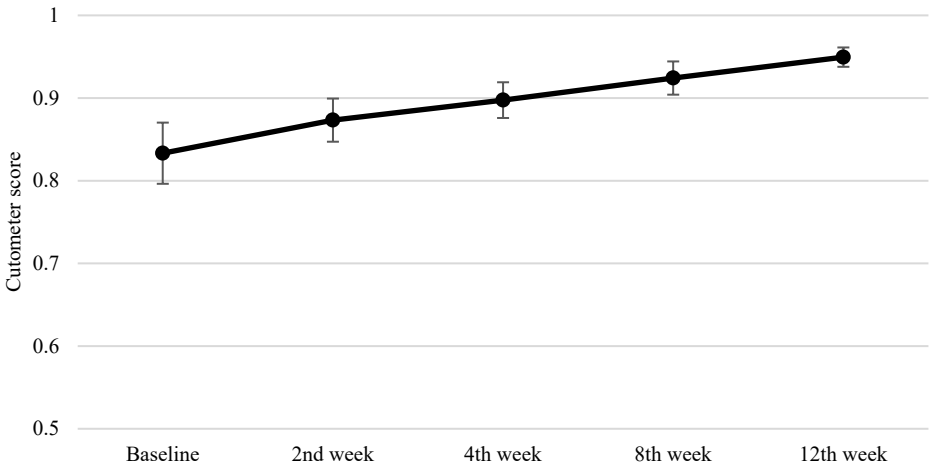


Figure 3 Displays line graph showing the cutometer score at the whole face from baseline to the follow-up 12th week

According to Table 4, which shows the statistical analysis of the cutometer score at whole face, the mean of the cutometer score on baseline, follow-up 2nd, 4th, 8th and 12th week were 0.8333±0.0370, 0.8733±0.0261, 0.8975±0.0216, 0.9242±0.0201, and 0.9495±0.0117, respectively. The mean cutometer score at whole face in each visit increased statistically significantly at the level of 0.05 (partial $\eta^2$0.880, p<0.001). In other words, the treatment effect of the fractional picosecond laser and glycolic acid combination on the cutometer score at the whole face was 88.0%.

Table 5 Multiple comparison (Post-hoc) of cutometer score at whole face (n=12)

Pairewise	**Mean difference**	**P-value**
Baseline-2nd week	0.040	0.005*
Baseline-4th week	0.064	<0.001*
Baseline-8th week	0.091	<0.001*
Baseline-12th week	0.116	<0.001*
2nd week-4th week	0.024	0.001*
2nd week-8th week	0.051	<0.001*
2nd week-12th week	0.076	<0.001*
4th week-8th week	0.027	0.001*
4th week-12th week	0.052	<0.001*
8th week-12th week	0.025	0.010*

Data were analysis with Bonferroni method
* The mean difference is statistically significant at the 0.05 level

According to Table 5, which displays the multiple comparison result, the cutometer score at whole face on the 2nd, 4th, 8th, and 12th week was higher than at baseline. Additionally, on the 4th, 8th, and 12th week, it was higher than the 2nd week. Moreover, the 8th and 12th week were higher than 4th week, and the 12th was higher than the 8th week, which was statistically significant at the level of 0.05 (p<0.05). The increase in the cutometer score on the whole face from baseline to the follow-up 12th week was 0.116.

Tewameter score

Table 6 Statistical analysis of tewameter score at whole face (right and left side) on baseline, follow-up 2nd, 4th, 8th, and 12th week (n=12)

Follow-up	mean±SD
Baseline	20.42±4.00
2nd week	17.45±3.77
4th week	15.52±3.24
8th week	13.20±2.95
12th week	11.19±3.23
P-value	<0.001*
Partial η^2	0.841

Data were analyzed with Repeated measure ANOVA
* Statistically significant at the 0.05 level

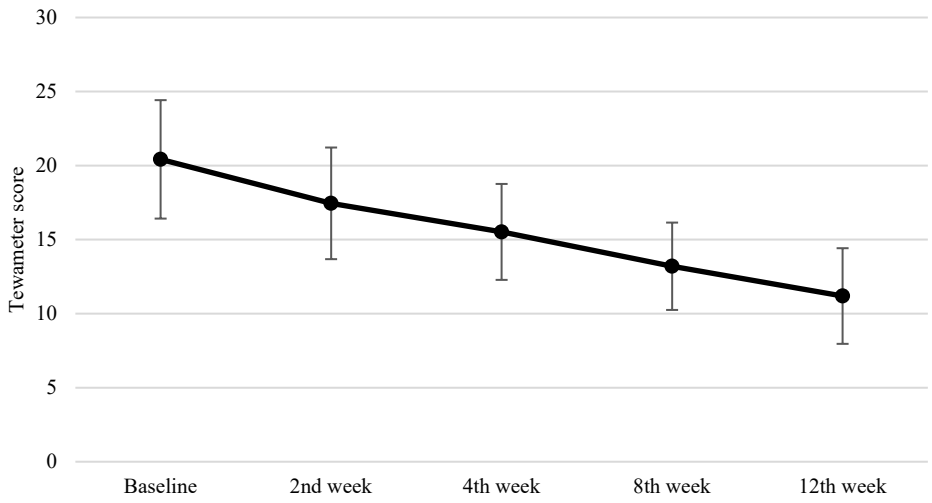


Figure 4 Displays line graph showing the tewameter score at the whole face from baseline to the follow-up 12th week

According to Table 6, which shows the statistical analysis of the tewameter score at whole face, the mean of the tewameter score on baseline, follow-up 2nd, 4th, 8th, and 12th week were 20.42±4.00, 17.45±3.77, 15.52±3.24, 13.20±2.95, and 11.19±3.23, respectively. The mean tewameter score at whole face in each visit decreased statistically significantly at the level of 0.05 (partial $\eta^2$0.841, p<0.001). In other words, the treatment effect of the fractional picosecond laser and glycolic acid combination on the tewameter score at the whole face was 84.1%.

Table 7 Multiple comparison (Post-hoc) of tewameter score at whole face (n=12)

Pairewise	Mean difference	P-value
Baseline-2nd week	-2.962	0.006*
Baseline-4th week	-4.896	<0.001*
Baseline-8th week	-7.212	<0.001*
Baseline-12th week	-9.225	<0.001*
2nd week-4th week	-1.933	0.003*
2nd week-8th week	-4.250	<0.001*
2nd week-12th week	-6.262	<0.001*

Pairewise	Mean difference	P-value
4th week-8th week	-2.317	<0.001*
4th week-12th week	-4.329	<0.001*
8th week-12th week	-2.013	0.001*

Data were analysis with Bonferroni method
* The mean difference is statistically significant at the 0.05 level

According to Table 7, which displays the multiple comparison result, the tewameter score at whole face on the 2nd, 4th, 8th, and 12th week was lower than at baseline. Additionally, on the 4th, 8th, and 12th week, it was lower than the 2nd week. Moreover, the 8th and 12th week were lower than the 4th week, and the 12th was lower than the 8th week, which was statistically significant at the level of 0.05 ($p<0.05$). The decrease in the tewameter score on the whole face from baseline to the follow-up 12th week was 9.225.

Physician Global Aesthetic Improvement Scale (GAIS)

Table 8 Statistical analysis of GAIS by 3 physicians on follow-up 4th, 8th, and 12th week (n=12)

Follow-up	GAIS					Median (IQR)
	No change (0)	Fair improvement (1)	Moderate improvement (2)	Good improvement (3)	Excellent improvement (4)	
4th week	-	-	8	4	-	2 (2, 3)
8th week	-	-	-	11	1	3 (3, 3)
12th week	-	-	-	6	6	3.5 (3, 4)
P-value						<0.001*

Data were analyzed with Friedman test
* Statistically significant at the 0.05 level

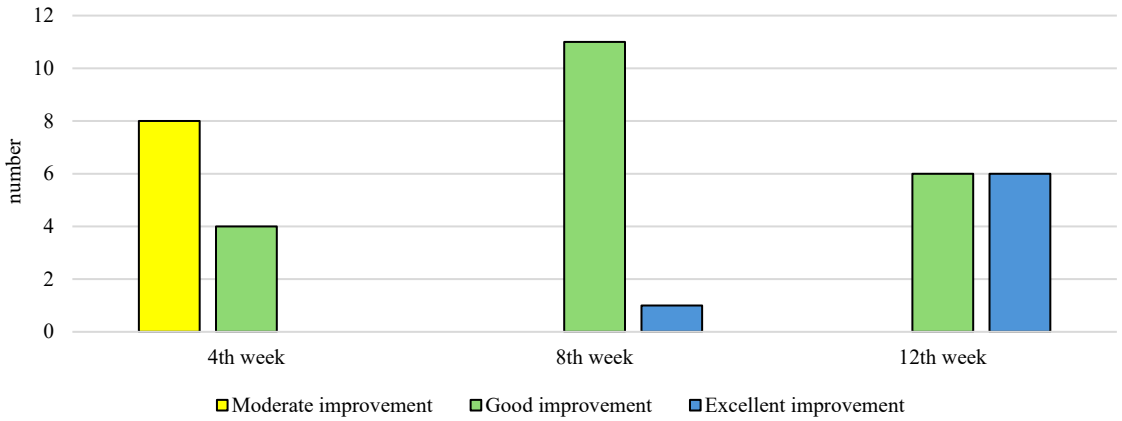


Figure 5 Displays a bar graph showing the GAIS from the follow-up 4th to 12th week

According to Table 8, which shows the statistical analysis of the GAIS, the GAIS level during the follow-up 4th week showed moderate improvement for 8 subjects and good improvement for 4 subjects, with a median value of 2 (IQR 2, 3). During the follow-up 8th week, 11 subjects showed good improvement and 1 subject showed excellent improvement, with a median value of 3 (IQR 3, 3). In the follow-up 12th week, 6 subjects showed good improvement and 6 subjects showed excellent improvement, with a median score of 3.5 (IQR 3, 4). The median GAIS in each visit increased statistically significantly at the level of 0.05 ($p<0.001$).

Table 9 Multiple comparison (Post-hoc) of GAIS (n=12)

Pairewise	P-value
4^{th} week-8^{th} week	0.032*
4^{th} week-12^{th} week	<0.001*
8^{th} week-12^{th} week	0.554

Data were analysis with Bonferroni method
* The mean difference is statistically significant at the 0.05 level

According to Table 9, which displays the multiple comparison result, the GAIS on the 8^{th}, and 12^{th} week was higher than 4^{th} week. Additionally, on the 12^{th} week, it was higher than the 8^{th} week, which was statistically significant at the level of 0.05 ($p<0.05$).

Patients' Satisfactory Score

Table 10 Frequency of patients' satisfactory score

Patients' satisfactory score	n
No satisfaction (0)	-
Little satisfaction (1)	-
Moderate satisfaction (2)	-
More satisfaction (3)	5
Most satisfaction (4)	7

According to Table 10, which displays the frequency of patients' satisfactory scores, 7 subjects rated their satisfaction as 'most satisfied,' while 5 subjects rated their satisfaction as 'more satisfied'.

DISCUSSION & CONCLUSION

Rejuvenation refers to the removal and regeneration of the skin, resulting in a more organized, "younger" dermal matrix and epidermal normalization. This was the study of the efficacy of a combination of fractional picosecond laser 1064 nm wavelengths and 20%glycolic acid peeling for facial rejuvenation. In this study, twelve subjects, age 30-50 years with Fitzpatrick skin ranging from III to V who desire to undergo facial rejuvenation were recruited. All participants can come regularly for the treatment and follow up sessions.

The participants received 3 treatment sessions of 1064 fractional picosecond laser and glycolic acid combination. Wrinkles, skin elasticity and trans epidermal water loss will be assessed at baseline and each 2^{nd}, 4^{th}, 8^{th} and 12^{th} week follow up visit accordingly by using VISIA, Cutometer and tewameter respectively. GAIS and patient's satisfactory were used to evaluate the effectiveness and adverse events. Wrinkle scores were measured at each visit and the mean wrinkle score at front and whole face decreased statistically significantly. Skin elasticity was measured at each visit and the mean cutometer score at whole face increased statistically significantly. GAIS score evaluated by 3 dermatologists using photographs from VISIA® Complexion Analysis System at each visit was increased statistically significantly. Patient's satisfactory score showed most of the patients were most satisfied with the results. Regarding side effects, there was no serious adverse effects apart from erythema.

Previous 1064nm fractional picosecond laser study, elevated by Edward et al, showed that 79% of patient had mild to moderate improvement by GAIS score after final treatment (Ross et al., 2022) and in their study, improvement in wrinkles is modest. In YIM et al. (2020) study, this is split face comparison of 1064nm Nd:YAG laser between pico-arm and Quasi-arm and there was moderate improvement in pico-arm than Quasi-arm (Yim et al., 2020). In this research study of combination treatment of 1064nm fractional picosecond laser and glycolic acid, all patients showed good to excellent improvement assessed by GAIS score after final treatment

and there was significant wrinkle reduction that is wrinkle score 75.5% improvement at front and 95.0% improvement at the whole face.

In Chung et al study, Fractional 1064nm picosecond laser with diffractive optic element was used for winkles and Acne scars and the skin elasticity improved by 10.96% (Lee et al., 2021). In this combination treatment study, the overall skin elasticity of the whole face was improved by 88.0%.

According to the study and results, combination of fractional picosecond laser 1064 nm wavelengths and 20%glycolic acid peeling was effective in treatment of facial rejuvenation with no serious side effects and have the better outcomes than the monotherapies. Therefore, it can be concluded that picosecond laser can be used safely and effectively for facial rejuvenation.

Moreover, it can be used as a reference paper for the treatment of facial rejuvenation in the future.

REFERENCES

Distributor, M. (n.d.). *Safety Data Sheet Glycolic Acid 70% Section 1-Product and Company Identification 1.1 Product identifier Product name: Glycolic Acid 70% Synonym(s): Hydroxyacetic Acid; 2-Hydroxyacetic Acid; Hydroxyethanoic Acid 1.2 Relevant identified uses of the substance or mixture and uses advised against*. Retrieved from www.silverfernchemical.com.

Habbema, L., Verhagen, R., Van Hal, R., Liu, Y., & Varghese, B. (2013). Efficacy of minimally invasive nonthermal laser-induced optical breakdown technology for skin rejuvenation. *Lasers in medical science, 28*, 935-940.

Haimovic, A., Brauer, J. A., Bae, Y. S. C., & Geronemus, R. G. (2016). Safety of a picosecond laser with diffractive lens array (DLA) in the treatment of Fitzpatrick skin types IV to VI: a retrospective review. *Journal of the American Academy of Dermatology, 74*(5), 931-936.

Kaidbey, K., Sutherland, B., Bennett, P., Wamer, W. G., Barton, C., Dennis, D., & Kornhauser, A. (2003). Topical glycolic acid enhances photodamage by ultraviolet light. *Photodermatology, photoimmunology & photomedicine, 19*(1), 21-27.

Khetarpal, S., Desai, S., Kruter, L., Prather, H., Petrell, K., Depina, J., ... & Dover, J. S. (2016). Picosecond laser with specialized optic for facial rejuvenation using a compressed treatment interval. *Lasers in Surgery and Medicine, 48*(8), 723-726.

Kubiak, M., Mucha, P., & Rotsztejn, H. (2020). Comparative study of 15% trichloroacetic acid peel combined with 70% glycolic acid and 35% trichloroacetic acid peel for the treatment of photodamaged facial skin in aging women. *Journal of Cosmetic Dermatology, 19*(1), 137-146.

Lee, C. H., Jin, E. M., Seo, H. S., Ryu, T. U., & Hong, S. P. (2021). Efficacy and safety of treatment with fractional 1,064-nm picosecond laser with diffractive optic element for wrinkles and acne scars: a clinical study. *Annals of Dermatology, 33*(3), 254.

Nilforoushzadeh, M. A., Alavi, S., Heidari-Kharaji, M., Hanifnia, A. R., Mahmoudbeyk, M., Karimi, Z., & Kahe, F. (2020). Biometric changes of skin parameters in using of microneedling fractional radiofrequency for skin tightening and rejuvenation facial. *Skin Research and Technology, 26*(6), 859-866.

Piacquadio, D., Dobry, M., Hunt, S., Andree, C., Grove, G., & Hollenbach, K. A. (1996). Short Contact 70% Glycolic Acid Peels as a Treatment for Photodamaged Skin A Pilot Study. *Dermatologic surgery, 22*(5), 449-452.

Ross, E. V., Tidwell, W. J., Guss, L., & Sutton, A. V. (2022). Study of a 532/1064 fractional picosecond laser for facial rejuvenation. *Dermatologic Surgery, 48*(1), 109-113.

Rouvrais, C., Baspeyras, M., Mengeaud, V., & Rossi, A. B. (2018). Antiaging efficacy of a retinaldehyde-based cream compared with glycolic acid peel sessions: A randomized controlled study. *Journal of cosmetic dermatology, 17*(6), 1136-1143.

Rouvrais, C., Baspeyras, M., Mengeaud, V., & Rossi, A. B. (2018). Antiaging efficacy of a retinaldehyde-based cream compared with glycolic acid peel sessions: A randomized controlled study. *Journal of Cosmetic Dermatology, 17*(6), 1136-1143.

Saluja, R., & Gentile, R. D. (2020). Picosecond laser: tattoos and skin rejuvenation. *Facial Plastic Surgery Clinics, 28*(1), 87-100.

Vachiramon, V., Sahawatwong, S., & Sirithanabadeekul, P. (2015). Treatment of melasma in men with low-fluence Q-switched neodymium-doped yttrium–aluminum–garnet laser versus combined laser and glycolic acid peeling. *Dermatologic Surgery, 41*(4), 457-465.

Wu, D. C., Fletcher, L., Guiha, I., & Goldman, M. P. (2016). Evaluation of the safety and efficacy of the picosecond alexandrite laser with specialized lens array for treatment of the photoaging décolletage. *Lasers in Surgery and Medicine, 48*(2), 188-192.

Wu, D. C., Goldman, M. P., Wat, H., & Chan, H. H. (2021). A systematic review of picosecond laser in dermatology: evidence and recommendations. *Lasers in Surgery and Medicine, 53*(1), 9-49.

Yim, S., Lee, Y. H., Choi, Y. J., & Kim, W. S. (2020). Split-face comparison of the picosecond 1064-nm Nd: YAG laser using a microlens array and the quasi-long-pulsed 1064-nm Nd: YAG laser for treatment of photoaging facial wrinkles and pores in Asians. *Lasers in Medical Science, 35*, 949-956.

Zhao, J., Zhou, B., Hou, Y., Li, L., & Zhuo, F. (2022). Effect of 5% glycolic acid complex and 20% glycolic acid on mild-to-moderate facial acne vulgaris. *Chinese Medical Journal, 135*(21), 2614-2616.

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