DOI: https://doi.org/10.53350/pjmhs221610368

ORIGINAL ARTICLE

Efficacy of 2% Kojic Acid Containing Formulation vs Picosecond Laser for Treatment of Melasma

NASEEMULLAH[1], ABDUL QAYUM KHAN[2], FAROOQ AZAM KHAN[3], SHAHZAD RASHID AWAN[4], SARAH RIAZ KHAN[5]
[1]*Assistant Professor of Dermatology, Qazi Hussain Ahmad Medical Complex Nowshera*
[2]*Assistant Professor of Dermatology, Lady Reading Hospital Peshawar*
[3]*Head of the department, Naseer Ullah Khan Baber Memorial Hospital Peshawar*
[4]*Consultant Dermatologist, Alhidmat Hospital Peshawar*
[5]*Assistant Professor of Dermatology, Naseer Teaching Hospital Peshawar*
Corresponding author: Sarah Riaz Khan, Email: drsarahkhan.sk@gmail.com

ABSTRACT

Background: Melasma is a frequently observed dermatological condition. The conventional therapies for melasma improvement established to date are mainly categorized into chemical peeling, topical agents and laser therapy. A new technique to reduce discomfort and post-laser discoloration induced by heat effects is the picosecond laser system.

Objective: To find out efficacy of 2% kojic acid containing formulation vs picosecond laser for treatment of melasma

Methodology: This was comparative randomized controlled study carried out at the department of dermatology Qazi Hussain Ahmad Medical Complex Nowshera and alshifa clinic and skin aesthetic, Nowshera for duration of one year from July 2020 to July 2021. Totally, 300 patients were included in the study. Each picosecond laser and kojic acid group comprise of 150 patients. All the information was recorded at the baseline and each following visit. Severity Index (MASI) score was calculated and color photographs were taken of all patients.

Results: At baseline, the mean MASI scores for picosecond laser and kojic acid group was 10.5±3.5 and 11.2±4.1 respectively (p=0.31). In both the group significant improvement occur in the MASI scores at weeks 12 and week 20. In picosecond laser group, the most remarkable improvement rate (62%) was noted while in kojic acid containing formulation group the rate of improvement was 41.96%.

Conclusion: Our study concludes that picosecond Laser device is an efficient and well-tolerated therapeutic option for melasma as compared to kojic acid containing formulation.

Keywords: Efficacy; Kojic acid; Picosecond laser; Melasma

INTRODUCTION

Melasma is an important problem as it affects the face in a cosmetically conscious age group and has a significant impact on a person's psychological and social well-being, having contribution to low performance, social functioning, and personality [1, 2]. Melasma is a comparatively prevalent, attained symmetric hypermelanosis distinguished by inconsistent, light to grey brown macules and patches surrounding the sun exposed areas of the face and neck [3]. Oral contraceptives, cosmetics, sun exposure, Pregnancy, genetics, and race have all been suggested to have a role in the etiology and patho-physiology of melasma [4]. Melasma is divided into three categories regarding the distribution of face lesions, including mandibular, malar and Centro-facial patterns [5]. According to the results of the Wood's lamp test, it may be divided into epidermal, dermal, mixed, and ambiguous forms [6]. As a result of the awareness of the significance of treating the disease for both patients and doctors, a variety of contemporary therapies have been developed to fight the disease. Chemical peels, Hypopigmenting agents, dermabrasion, lasers, and a variety of cosmeceutical agents are some of the therapies available. Earlier studies have shown an increased rate of prevalence in Latino of up to 35%, mostly affecting women of the middle ages [7, 8]. Facial melasma management often involves recommendations to prevent UV radiation and other risk factors, such as specialized photosensitive treatment and exogenous hormone replacement treatment [9]. The usual first-line therapies for melasma are topical anti-melanogenesis drugs, such as hydroquinone, retinoic acid, alpha albutin, kojic acid and glycolic acid [10], which mainly act by inhibiting the enzyme tyrosinase. But, the results of topical therapy are frequently deceptive with little improvement in cosmetics, undesirable outcomes and high recurrence rates [11, 12].

Cutaneous pigmented laser was suggested as an alternate and an added therapy for some skin disorders, especially melasma [13, 14]. The laser's primary function is to deliver high-pitch photothermal energy to the skin, particularly aimed at the melanin pigment leading to "selective photo-thermolysis" [15]. Melanin is broken down to little particles by the heat effects of the laser that are subsequently absorbed and eliminated by macrophages. A new technique to reduce discomfort and post-laser discoloration induced by heat effects is the picosecond laser system [16, 17]. The picosecond laser is a laser system that only lasts 300–500 picoseconds with numerous extremely short duration of pulse. Due to the short duration of pulse, more pulse energy may be supplied than earlier laser technologies, yet with a less thermal impact. The photoacoustic stress produced by picosecond laser leads to larger energy and a stronger fragmentation of melanin than the thermal pressure of nanosecond lasers [18]. Similarly, therapy with shorter duration of pulse enables for acceptable outcomes with lower fluencies to be obtained, reducing the danger of cavity-like skin structures being damaged by thermal burn [19, 20]. Presently accessible picosecond laser wavelengths include 1064 nm, 532 and 755 [21, 22]. With this background, this study had been undertaken to determine the efficacy of 2% kojic acid containing formulation vs picosecond laser for treatment of melasma.

MATERIALS AND METHODS

This study was comparative randomized controlled study carried out at the department of dermatology Qazi Hussain Ahmad Medical Complex Nowshera and alshifa clinic and skin aesthetic, Nowshera. The duration for this research study was one year from July 2020 to July 2021. Research and ethical committee of the hospital give approval to our study. From all the patients included in this study, a written consent form was signed. Expert dermatologist physically examined all the included patients in our study. The inclusion criteria for our study were all the patients of both the gender having age 18-60 with melasma confirmed by Wood's lamp test. All the included patients must be willing to take part in our study and ready to give informed consent in written form while the exclusion criteria was pregnant and lactating female, patients having more activities outside and more exposed to UV light, patients having allergy to UV, prior laser therapy within the preceding 3 months, treatment with supplementation of neutraceuticals or topical treatment with kojic acid within the previous 4 weeks, diabetic patients, patients with thyroid dysfunction, liver problem, kidney disease and photosensitive dermatosis, and patients having inability to comply with the protocol of the study. Totally, 300 patients were included in the study. They were categorized into two groups. 150 patients were included in picosecond laser group while 150 patients were

enrolled in 2 % kojic acid containing formulation group. The patients in the evening primrose oil group were treated picosecond laser group while patients in control group were treated with 2% kojic acid containing formulation. The Melasma Area and Severity Index (MASI) score was calculated and color photographs were taken from all patients under standard conditions in natural light. Patients were followed up every month for 3 months. During treatment period, patients were advised to avoid any oral or topical medications (e.g. oral contraceptive pills, cosmetics), which were known to influence the outcome of the study. Patients were also desired to use same brand of soap throughout the study period and avoid soaps containing hydroquinone, glycolic acid, vitamin E, benzoyl peroxide were avoided. During follow-up, patients with melasma were assessed with the help of MASI score for their monthly improvement for three months. Color photographs were taken before treatment and every month for 3 months during the follow-up period. Patients were advised to report immediately to OPD in case of any untoward effects during the course of treatment. Melasma Area and Severity Index (MASI) were calculated as developed by Kimbrough-Green et al.[23]. Data collected were imported into Microsoft Excel 2013 and analyzed using IBM SPSS 23.0. Chi square test was used for statistical analysis of the two treatment group. A p value of less than 0.05 was considered as significance.

RESULTS

In this study female patients were dominant in both the group. There were 125 (83.33%) female and 25 (16.67%) male in picosecond laser group while there were 130 (86.67%) female and 20 (19.33%) male in kojic acid containing formulation group. (Figure 1) According to the age wise distribution, number of patients in picosecond laser group of ≤40 years were 90 (60%), 41-54 were 45(30%) and ≥55 were 15 (10%) while in kojic acid containing formulation group they were 85 (56.67%), 50 (33.33%) and 15 (10%) respectively. (Figure 2) The mean age in kojic acid containing formulation group was 32.3±4.5 years while in picosecond laser group it was 33.1±2.3. (Figure 3) Before treatment, the mean MASI scores for picosecond laser group and kojic acid containing formulation group was 10.5±3.5 and 11.2±4.1 respectively. (Figure 4) No statistical significant difference was observed in the mean baseline MASI scores (p=0.31) between the two groups. In both the group significant improvement occur in the MASI scores at weeks 12 and week 20. The MASI score in picosecond laser group at week 12 was 6.1±3.2 while in kojic acid containing formulation group it was 8.3±3.9. The improvement in both the group was significant statistically (p =<0.05). The MASI score in picosecond laser group at week 20 was 3.8±2.1 while in kojic acid containing formulation group it was 6.5±2.9. (Table 1) In picosecond laser group, the most remarkable improvement rate (62%) was noted while in kojic acid containing formulation group the rate of improvement was 41.96%. (Table 2)

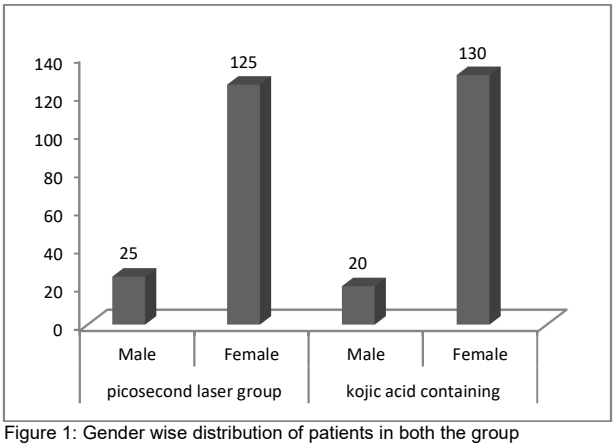


Figure 1: Gender wise distribution of patients in both the group

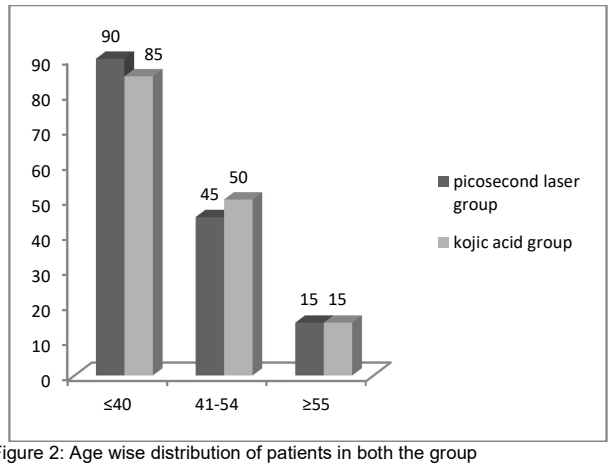


Figure 2: Age wise distribution of patients in both the group

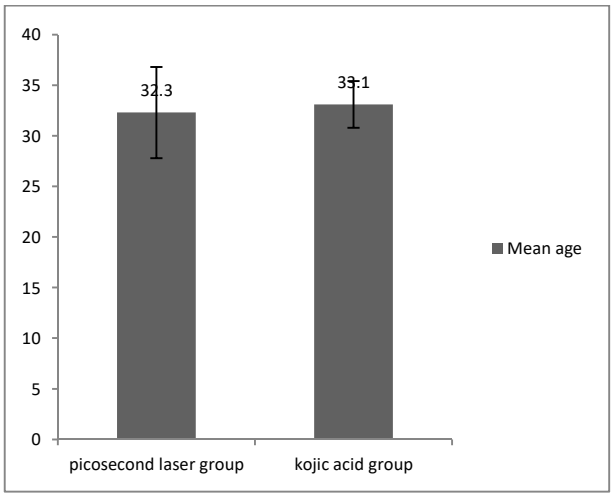


Figure 3: Mean age of patients in both the group

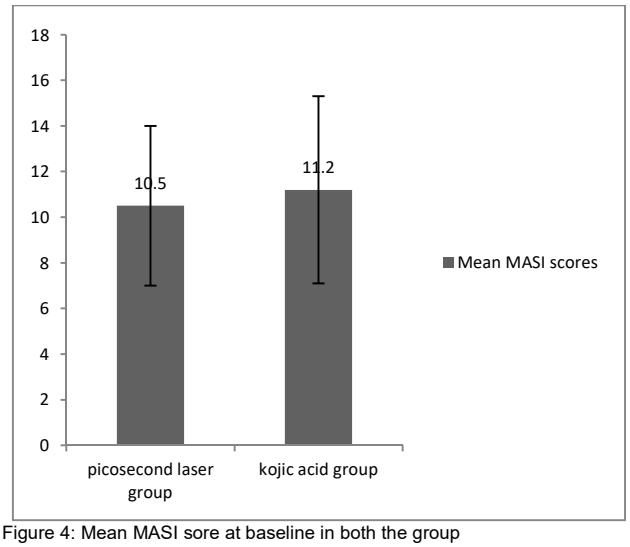


Figure 4: Mean MASI sore at baseline in both the group

Table 1: Mean MASI sore at baseline and differ follow up

Mean MASI scores (Stand deviation)	picosecond laser group	kojic acid group	P value
Baseline	10.5±3.5	11.2±4.1	0.31
Week 12	6.1±3.2	8.3±3.9	0.01
Week 20	3.8±2.1	6.5±2.9	0.01

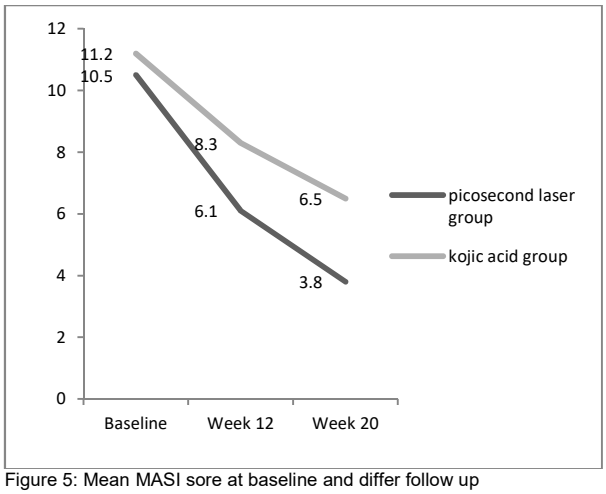


Figure 5: Mean MASI sore at baseline and differ follow up

Table 2: Difference in Mean MASI sore from baseline at differ follow up and improvement

Mean MASI scores Difference from baseline	Picosecond laser group (Improvement)	kojic acid group (Improvement)
Week 12	4.4±0.3 (41.90%)	2.9±0.2 (25.89%)
Week 20	6.7±1.4 (62%)	4.7±1.2 (41.96%)

DISCUSSION

Melasma is a frequently observed dermatological condition having prevalence of 8.8% in United States; however, their prevalence is up to 40% among Asian women [24]. The conventional therapies for melasma improvement established to date are mainly categorized into chemical peeling, topical agents and laser therapy [25]. The usual first-line therapies for melasma are topical anti-melanogenesis drugs, such as hydroquinone, retinoic acid, alpha albutin, kojic acid and glycolic acid [10], which mainly act by inhibiting the enzyme tyrosinase. But, the results of topical therapy are frequently deceptive with little improvement in cosmetics, undesirable outcomes and high recurrence rates [11, 12]. A new technique to reduce discomfort and post-laser discoloration induced by heat effects is the picosecond laser system [16, 17]. Picosecond laser devices have pulse durations in the sub-nanosecond region, which makes them ideal for use in medical applications. Picoseconds pulses impact coetaneous pigmentation via selective photothermolysis, which is achieved with a low energy. Furthermore, the energy supplied is restricted to the target and produces significant photomechanical effects while only a small amount of heat is transferred to the surrounding structure. It has been shown in different investigations that successful therapy can be accomplished with lower fluencies of energy, reduced epidermal damage, and a lower risk of dyspigmentation. This study was therefore conducted to determine the efficacy of 2% kojic acid containing formulation vs picosecond laser for treatment of melasma. In this study female patients were dominant in both the group with melasma. Previous studies reported similar high melasma prevalence to our study in female as compared to male [26, 27]. The reason for this is that when the skin is exposed to sunlight, Melasma stimulates melanocytes through the female sex hormones oestrogen and progesterone, resulting in increased production of melanin pigments [28-30]. In both the group significantly improvement occur in the MASI scores at weeks 12 and week 20. The MASI score in picosecond laser group at week 12 was 6.1±3.2 while in kojic acid containing formulation group it was 8.3±3.9. The improvement in both the group was significant statistically (p =<0.05). The MASI score in picosecond laser group at week 20 was 3.8±2.1 while in kojic acid containing formulation group it was 6.5±2.9. Similar findings were shown by a previous study who reported that improvement in melasma occurs at week 12 and 20 compared to baseline but they were not statistically significant [31]. Another study also reported better improvement of melasma with picosecond laser as compared to topical therapy [32]. In picosecond laser group, the most remarkable improvement rate (62%) was noted while in kojic acid containing formulation group the rate of improvement was 41.96%. An earlier study reported comparable results to our finding [26]. The limited sample size of this research is the most significant drawback of this research work. Additionally, once recruited in the research study, some individuals may adopt a significantly stricter sun protection regimen. As a consequence, neither hypo-pigmentation nor hyper-pigmentation was found in our research, contrary to what has previously been described. In order to determine the optimum impact of laser therapy, a comparison approach such as split-face evaluation and a larger sample size should be considered. The combined effects of laser therapy and other therapeutic approaches will also be a future area of study in the treatment of melasma.

CONCLUSION

Our study concludes that picosecond Laser device is an efficient and well-tolerated therapeutic option for melasma. There were no signs of hypo or hyperpigmentation. Further research on a larger scale and with better control may be explored in order to maximize the impact in the long follow up. Combining topical lightening therapy with an inhibitor of melanin formation should be explored in order to improve clearance and maintain the impact of the treatment.

REFERENCES

1. Pawaskar, M D, Parikh, P, Markowski, T, Mcmichael, A J, Feldman, S R, and Balkrishnan, R, Melasma and its impact on health-related quality of life in Hispanic women. Journal of dermatological treatment, 2007. 18(1): p. 5-9
2. Anderson, R T and Rajagopalan, R, Development and validation of a quality of life instrument for cutaneous diseases. Journal of the American Academy of Dermatology, 1997. 37(1): p. 41-50
3. Deo, K S, Dash, K N, Sharma, Y K, Virmani, N C, and Oberai, C, Kojic acid vis-a-vis its combinations with hydroquinone and betamethasone valerate in melasma: a randomized, single blind, comparative study of efficacy and safety. Indian journal of dermatology, 2013. 58(4): p. 281
4. Dwari, B C, Palaian, S, Poudel, A, and Prabhu, S, Clinical profile and management pattern of melasma patients in Western Nepal: A Hospital Based Study. Internet Journal of Dermatology, 2009. 7(1)
5. Sanchez, N P, Pathak, M A, Sato, S, Fitzpatrick, T B, Sanchez, J L, and Mihm Jr, M C, Melasma: a clinical, light microscopic, ultrastructural, and immunofluorescence study. Journal of the American Academy of Dermatology, 1981. 4(6): p. 698-710
6. Asawanonda, P and Taylor, C R, Wood's light in dermatology. International journal of dermatology, 1999. 38(11): p. 801-807
7. Pichardo, R, Vallejos, Q, Feldman, S R, Schulz, M R, Verma, A, Quandt, S A, et al., The prevalence of melasma and its association with quality of life in adult male Latino migrant workers. International journal of dermatology, 2009. 48(1): p. 22-26
8. Dominguez, A R, Balkrishnan, R, Ellzey, A R, and Pandya, A G, Melasma in Latina patients: cross-cultural adaptation and validation of a quality-of-life questionnaire in Spanish language. Journal of the American Academy of Dermatology, 2006. 55(1): p. 59-66
9. Ak, G and Gover, M, Nouri k, et al. The treatment of melasma: A review of clinical trials. J Am Acad Dermatal, 2006. 55: p. 1048-65
10. Lynde, C, Kraft, J, and Lynde, C, Topical treatments for melasma and postinflammatory hyperpigmentation. Skin Therapy Lett, 2006. 11(9): p. 1-6
11. Kang, H. Mélasma et anomalies pigmentaires chez les asiatiques. in Annales de Dermatologie et de Vénéréologie. 2012. Elsevier
12. Taylor, S C, Torok, H, Jones, T, Lowe, N, Rich, P, Tschen, E, et al., Efficacy and safety of a new triple-combination agent for the treatment of facial melasma. CUTIS-NEW YORK-, 2003. 72(1): p. 67-73
13. Sheth, V M and Pandya, A G, Melasma: a comprehensive update: part II. J Am Acad Dermatol, 2011. 65(4): p. 699-714'10.1016/j.jaad.2011.06.001 10.1016/j.jaad.2011.06.001.
14. Anderson, R R, Margolis, R J, Watenabe, S, Flotte, T, Hruza, G J, and Dover, J S, Selective photothermolysis of cutaneous pigmentation by q-switched Nd: YAG laser pulses at 1064, 532. and 355 nm. Journal of investigative dermatology, 1989. 93(1): p. 28-32

15. Ho, C, Nguyen, Q, Lowe, N J, Griffin, M E, and Lask, G, Laser resurfacing in pigmented skin. Dermatologic surgery, 1995. 21(12): p. 1035-1037
16. Jones, C E and Nouri, K, Laser treatment for pigmented lesions: a review. Journal of cosmetic dermatology, 2006. 5(1): p. 9-13
17. Saedi, N, Metelitsa, A, Petrell, K, Arndt, K A, and Dover, J S, Treatment of tattoos with a picosecond alexandrite laser: a prospective trial. Archives of dermatology, 2012. 148(12): p. 1360-1363
18. Peyman, G A, Naguib, K S, and Gaasterland, D, Transscleral application of a semiconductor diode laser. Lasers in surgery and medicine, 1990. 10(6): p. 569-575
19. Alabdulrazzaq, H, Brauer, J A, Bae, Y S, and Geronemus, R G, Clearance of yellow tattoo ink with a novel 532-nm picosecond laser. Lasers in surgery and medicine, 2015. 47(4): p. 285-288
20. Brauer, J A, Kazlouskaya, V, Alabdulrazzaq, H, Bae, Y S, Bernstein, L J, Anolik, R, et al., Use of a picosecond pulse duration laser with specialized optic for treatment of facial acne scarring. JAMA dermatology, 2015. 151(3): p. 278-284
21. Jutley, G S, Rajaratnam, R, Halpern, J, Salim, A, and Emmett, C, Systematic review of randomized controlled trials on interventions for melasma: an abridged Cochrane review. Journal of the American Academy of Dermatology, 2014. 70(2): p. 369-373
22. Weiss, R A, McDaniel, D H, Weiss, M A, Mahoney, A M, Beasley, K L, and Halvorson, C R, Safety and efficacy of a novel diffractive lens array using a picosecond 755 nm alexandrite laser for treatment of wrinkles. Lasers in surgery and medicine, 2017. 49(1): p. 40-44
23. Kimbrough-Green, C K, Griffiths, C E, Finkel, L J, Hamilton, T A, Bulengo-Ransby, S M, Ellis, C N, et al., Topical retinoic acid (tretinoin) for melasma in black patients: a vehicle-controlled clinical trial. Archives of dermatology, 1994. 130(6): p. 727-733
24. Werlinger, K D, Guevara, I L, González, C M, Rincón, E T, Caetano, R, Haley, R W, et al., Prevalence of self-diagnosed melasma among premenopausal Latino women in Dallas and Fort Worth, Tex. Archives of dermatology, 2007. 143(3): p. 423-431
25. Molinar, V E, Taylor, S C, and Pandya, A G, What's new in objective assessment and treatment of facial hyperpigmentation? Dermatologic clinics, 2014. 32(2): p. 123-135
26. Wang, Y J, Lin, E T, Chen, Y T, Chiu, P C, Lin, B S, Chiang, H M, et al., Prospective randomized controlled trial comparing treatment efficacy and tolerance of picosecond alexandrite laser with a diffractive lens array and triple combination cream in female asian patients with melasma. Journal of the European Academy of Dermatology and Venereology, 2020. 34(3): p. 624-632
27. Hu, S, Yang, C-S, Chang, S-L, Huang, Y-L, Lin, Y-F, and Lee, M-C, Efficacy and safety of the picosecond 755-nm alexandrite laser for treatment of dermal pigmentation in Asians—a retrospective study. Lasers in medical science, 2020: p. 1-7
28. Basit, H, Godse, K V, and Al Aboud, A M, Melasma. StatPearls [Internet], 2021
29. Zubair, R, Lyons, A B, Vellaichamy, G, Peacock, A, and Hamzavi, I, What's new in pigmentary disorders. Dermatologic clinics, 2019. 37(2): p. 175-181
30. Passeron, T, Genedy, R, Salah, L, Fusade, T, Kositratna, G, Laubach, H J, et al., Laser treatment of hyperpigmented lesions: position statement of the European Society of Laser in Dermatology. Journal of the European Academy of Dermatology and Venereology, 2019. 33(6): p. 987-1005
31. Chalermchai, T and Rummaneethorn, P, Effects of a fractional picosecond 1,064 nm laser for the treatment of dermal and mixed type melasma. Journal of Cosmetic and Laser Therapy, 2018. 20(3): p. 134-139
32. Wong, C S M, Chan, M W M, Shek, S Y N, Yeung, C K, and Chan, H H L, Fractional 1064 nm picosecond laser in treatment of melasma and skin rejuvenation in Asians, a prospective study. Lasers in Surgery and Medicine, 2021