cosmetics

MDPI

Communication

Comparing a Low-Fluence Picosecond 1064 nm Nd:YAG Laser with a 532 nm Nd:YAG Laser for the Treatment of Pigmented Lesions in Chinese Patients: A Retrospective Analysis

Po-Hsuan Lu [1,2], Xiao-Feng Yao [1], Yang-Chih Lin [1] and Pa-Fan Hsiao [1,2,3,*]

[1] Department of Dermatology, MacKay Memorial Hospital, Taipei 10449, Taiwan; pohsuanlu.4217@mmh.org.tw (P.-H.L.); maple0369@gmail.com (X.-F.Y.); lin1234@mmh.org.tw (Y.-C.L.)
[2] Department of Medicine, Mackay Medical College, New Taipei City 25245, Taiwan
[3] Mackay Junior College of Medicine, Nursing, and Management, Taipei 11260, Taiwan
* Correspondence: hpf01@ms1.hinet.net; Tel.: +886-2-2543-3535

Abstract: The use of low-fluence picosecond (LFPS) 1064 nm neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers, referred to as laser toning, is increasingly acknowledged as an effective treatment for pigmentation disorders in the Asian skin phenotype. This study aimed to conduct a comparative analysis on the effectiveness and safety of utilizing LFPS 1064 nm Nd:YAG lasers against picosecond 532 nm Nd:YAG lasers in treating pigmented lesions among Chinese patients. A retrospective photographic analysis and chart reviews were performed on 31 subjects exhibiting Fitzpatrick skin types III–VI who underwent LFPS 1064 nm Nd:YAG or picosecond 532 nm Nd:YAG treatments at a single tertiary center. Utilizing VISIA Complexion Analysis, comparative photographs were taken. Two independent physicians evaluated treatment efficacy using a visual analog scale (VAS) to assess the percentage of pigmentary clearance in standard photographs. Solar lentigines were the most prevalent pigmentary disorder, followed by post-inflammatory hyperpigmentation (PIH), nevus zygomaticus, melasma, freckles, and nevus of Ota. The clinical effectiveness of picosecond 532 nm and LFPS 1064 nm laser treatments proved comparable for lesions on the face, with mean VAS scores of 2.2 ± 1.1 and 1.8 ± 0.8, respectively. There were two cases of PIH in the picosecond 532 nm group, which resolved within one month. Overall, the LFPS 1064 nm laser demonstrates promise as a safe and efficient therapeutic modality for managing pigmented lesions in Chinese patients.

Keywords: picosecond; Nd:YAG laser; laser toning; pigmentary disorders

Citation: Lu, P.-H.; Yao, X.-F.; Lin, Y.-C.; Hsiao, P.-F. Comparing a Low-Fluence Picosecond 1064 nm Nd:YAG Laser with a 532 nm Nd:YAG Laser for the Treatment of Pigmented Lesions in Chinese Patients: A Retrospective Analysis. *Cosmetics* **2024**, *11*, 89. https://doi.org/10.3390/cosmetics11030089

Academic Editors: Steven Paul Nisticò and Harris Pratsinis

Received: 29 February 2024
Revised: 15 April 2024
Accepted: 21 May 2024
Published: 3 June 2024

1. Introduction

Q-switched (QS) lasers have been widely used for the treatment of pigmented lesions in Asians. However, they are associated with a considerable risk of post-inflammatory hyperpigmentation (PIH), with reported incidence rates of up to 28% [1]. To address this concern, a low-fluence 1064-nanometer (nm) QS neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, also known as laser toning, has been introduced and it is a modality that has shown promise in improving various benign pigmentary disorders, including melasma, nevus of Ota, and lentigines [2–5]. Laser toning has gained popularity in the management of benign pigmented lesions among Asians due to its ability to achieve successful outcomes while minimizing side effects commonly associated with conventional QS laser therapy [4–6]. In recent years, picosecond lasers operating at various wavelengths have emerged as effective tools for pigment removal [2]. Picosecond laser technology utilizes ultra-short pulse durations, typically measured in trillionths of a second (10^{-12}), in contrast to the pulse durations in the billionths of a second (10^{-9}) used in Q-switched lasers [7]. The shorter pulse duration of picosecond lasers allows for expedited power delivery, resulting in elevated target pressure within tissues while minimizing thermal dispersion. This characteristic makes picosecond lasers, particularly those operating at

1064 nm, promising alternatives for laser toning as they can swiftly eliminate both epidermal and dermal melanin pigments with reduced thermal effects compared to nanosecond pulse lasers.

Picosecond 532 nm lasers have demonstrated efficacy in treating pigmented lesions, especially those located in the epidermis [2]. The 532 nm wavelength is well-absorbed by melanin, making it ideal for targeting superficial pigmented lesions [8]. Studies have shown that Asians treated with picosecond 532 nm lasers experience low rates of PIH [3]. For instance, Chan and colleagues observed significant pigment clearance and enhanced melanin appearance in 20 Asian subjects treated with picosecond 532 nm lasers; however, they reported a PIH incidence rate of 10.2% [3].

In addition to picosecond 532 nm lasers, low-fluence picosecond (LFPS) 1064 nm Nd:YAG lasers have also shown promise in pigment removal. These lasers induce tissue reactions at relatively low-energy settings [9], making them suitable for treating pigmented lesions while minimizing adverse effects [7]. A recent meta-analysis evaluated the safety and efficacy of picosecond laser treatment for melasma, including wavelengths of 1064 nm, 755 nm, 595 nm, and 532 nm, in 437 patients. While the meta-analysis indicated clinical efficacy of 1064 nm picosecond laser treatment for melasma, data on other picosecond laser wavelengths were limited due to small sample sizes [10].

Despite the proven efficacy of laser toning in managing various skin lesions, there is limited research comparing the efficacy of picosecond laser toning with picosecond 532 nm lasers. Given the mechanical acoustic and minimal thermal effects associated with picosecond lasers, it is possible that the risk of inducing PIH with picosecond laser toning is lower than that with QS lasers [2].

The objective of this study is to compare the efficacy and safety of LFPS 1064 nm Nd:YAG and picosecond 532 nm Nd:YAG lasers for the treatment of benign pigmented lesions in Chinese patients.

2. Materials and Methods

2.1. Study Design

In this retrospective study conducted at a single tertiary center in Taiwan, our primary objective was to conduct a thorough evaluation of the efficacy and safety of two distinct laser treatments for pigmentary lesions in Chinese patients. We examined the medical records and accompanying photographs of all individuals who underwent either LFPS 1064 nm Nd:YAG laser or picosecond 532 nm Nd:YAG laser therapy over the period spanning January 2018 to December 2019.

Detailed demographic data, including age, skin phototype, and the specific type of pigmentary lesion, were systematically recorded for each patient. Utilizing the VISIA Complexion Analysis system, standardized photographs were taken at baseline and post-treatment, enabling a comparison by trained medical professionals.

Furthermore, adverse events associated with laser therapy, such as crusting, scaling, erythema, and pigmentation changes, were recorded. All patients were followed up until 6 months after the last laser session. This study was approved by the Ethics Committee of Mackay Memorial Hospital (Institutional Review Board code 18MMHIS109e).

2.2. Photograph Analysis

Digital photographs were captured and analyzed utilizing VISIA Complexion Analysis (Canfield Scientific, Inc., Voorhees, NJ, USA) to establish pre- and post-treatment skin pigment scores. To ensure consistency, the region of interest for each image was defined uniformly using predefined landmarks on the face. The VISIA software version 1 was employed to automatically identify and quantify features such as pigment scores. Detailed data for each skin feature were indexed, enabling comparisons within the same patients at different time points and across different patients.

Additionally, two dermatologists, board certified by the Taiwan Dermatologist Association, blinded to the treatment, independently evaluated the digital images for clinical assessment of the pigmented lesions. They employed a four-point grading scale: grade 1 (<25% improvement), grade 2 (25–49% improvement), grade 3 (50–74% improvement), and grade 4 (>75% improvement) [11].

2.3. Treatment Protocol

In this study, a picosecond-domain 532 and 1064 nm Nd:YAG laser system (PicoPlus; Lutronic Corp., Goyang, Republic of Korea) was utilized, featuring a pulse duration of 450 picoseconds. The pulse width remained constant across varying output fluences, thanks to the implementation of a master oscillator power amplifier configuration. Through the use of suitable optics, the laser energy was directed towards the target tissue in the form of a single flattop beam [9]. The clinical end point was the immediate lightening of the pigment or mild erythema without petechiae. The parameters of Pico toning were as follows: wavelength, 1064 nm; spot size, 7–10 mm; fluence, 0.6–1.4 J/cm^2; frequency, 5 or 10 Hz; and 2–4 passes under the 450 ps mode [12]. These patients received the Pico toning treatment at variable intervals between 1 and 3 months. The subjects received picosecond 532 nm laser treatment once, with the following parameters: wavelength, 532 nm; spot size, 2.3–4.3 mm; fluence, 0.3–0.4 J/cm^2; frequency, 2.0 (2.0–5.0) Hz; and one pass under the 450 ps mode [12].

2.4. Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, version 17.0. To compare the efficacy between the picosecond 532 nm laser (PS532) and low-fluence picosecond 1064 nm laser (LFPS1064) groups, independent *t*-tests were employed. All *p*-values were calculated as two-tailed, with a significance level set at 0.05. Moreover, Cronbach's alpha value was computed to assess inter-rater reliability, which measures the consistency of clearance assessment among different raters. Typically, values below 0.5 indicate poor reliability, those between 0.5 and 0.75 suggest moderate reliability, values ranging from 0.75 to 0.9 indicate good reliability, while values exceeding 0.90 signify excellent reliability.

3. Results

3.1. Patient Characteristics and Treatment Parameters

The clinical characteristics of the patients are summarized in Table 1. A total of 43 patients (2 males and 42 females) were enrolled in this study: 17 patients (1 male and 16 females) for picosecond 532 nm Nd:YAG treatments and 26 (1 male and 25 female) for LFPS 1064 nm Nd:YAG treatments, respectively. The mean age at the time of laser treatment was 49.2 (range, 20–82) years. There was no significant difference in age between the PS532 (50.8 years) and LFPS1064 (48.2 years) groups (p = 0.56). The most common Fitzpatrick skin type was type III in both PS532 (84.2%) and LFPS1064 (88.5%) groups, followed by type IV. There was no significant difference in the distribution of skin types between the two groups (p = 0.67).

The most common pigmentary disorder treated was solar lentigines (72.1%), followed by PIH (7%), nevus zygomaticus (7%) and melasma (7%), freckles (2.3%), and nevus of Ota (2.3%). The mean fluence and spot size applied were 0.35 (0.3–0.4) J/cm^2 and 3.3 (2.3–4.3) mm in the PS532 group and 0.82 (0.7–1.0) J/cm^2 and 8.2 (7–10) mm in the LFPS1064 group, respectively.

Table 1. Patient characteristics and treatment parameters.

	PS532	**LFPS1064**	***p*-Value**
Number of subjects (%)	17	26	
Male Female	1 (5.9) 16 (94.1)	1 (3.8) 25 (96.2)	1
Age (mean (SD))	50.8 (12.7)	48.2 (14.2)	0.56
Fitzpatrick skin type (%)			
III IV	14 (84.2) 3 (15.8)	23 (88.5) 3 (11.5)	0.67
Lesion type			
Lentigines	15	16	0.09
Post-inflammatory hyperpigmentation	0	3	0.27
Nevus zygomaticus	1	2	1
Melasma	0	3	0.27
Freckles	1	0	0.35
Nevus of Ota	0	1	1
Treatment parameters	Mean (min–max)		
Fluence (j/cm^2)	0.35 (0.3–0.4)	0.82 (0.6–1.4)	
Spot size (mm)	3.3 (2.3–4.3)	8.2 (7–10)	
Repetition rate (Hz)	2.0 (2–5)	5.0 (2–10)	
Interval between treatments (weeks)	0	4 (0–11)	
Treatment sessions	1	1–3	

PS532, picosecond 532 nm laser; LFPS1064, low-fluence picosecond 1064 nm laser.

3.2. Efficacy

The clinical efficacy of picosecond 532 nm and LFPS 1064 nm laser treatments were comparable for lesions treated on the face. A total of 17 patients underwent picosecond 532 nm laser treatment with a mean visual analog scale (VAS) score of 2.2 ± 1.1, corresponding to approximately 50% pigmentary clearance (Figure 1). In the 26 patients who received LFPS 1064 nm laser treatments, the mean VAS score was 1.8 ± 0.8 (p = 0.35) (Figures 1 and 2). There was no between-group significant difference in the VISIA pigment score after treatment (Figure 3). The percentage of reduction of the VISIA pigment score, which was analyzed before and after the treatment, showed no significant difference in the PS532 (0.9%) and LFPS1064 (1.6%) groups (p = 0.95). In the PS532 group, the kappa value was 0.92, whereas it was 0.61 in the LFPS1064 group, which corresponded to excellent and moderate reliability among both raters, respectively.

3.3. Safety and Adverse Effects

According to the medical records, the overall adverse effects were 18.6% (Figure 4). Of the 17 patients in the PS532 group, 3 (17.6%) developed PIH, and 4 (23.5%) developed erythema after the treatment, but all subsided during follow-up. Only 1 patient (4%) in the LFPS1064 group presented erythema, and none reported PIH, according to the medical record. The adverse effects were lower in patients who received LFPS 1064 nm laser treatments although without statistical significance.

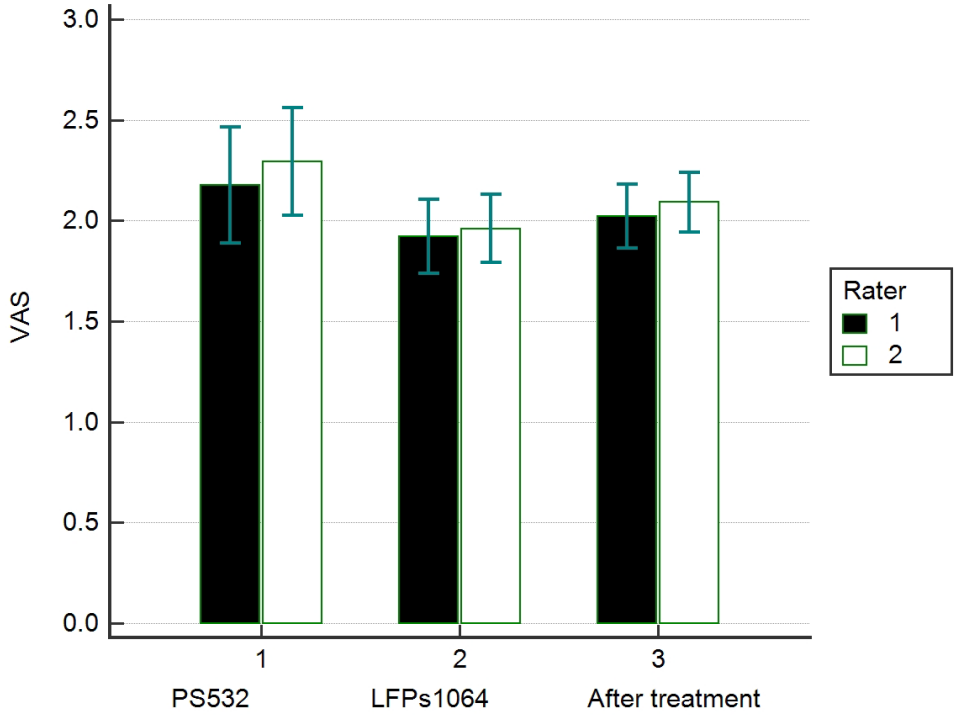

Figure 1. Visual analog scale (VAS) scores. Clearance data for two independent investigators. PS532, picosecond 532 nm laser; LFPS1064, low-fluence picosecond 1064 nm laser.

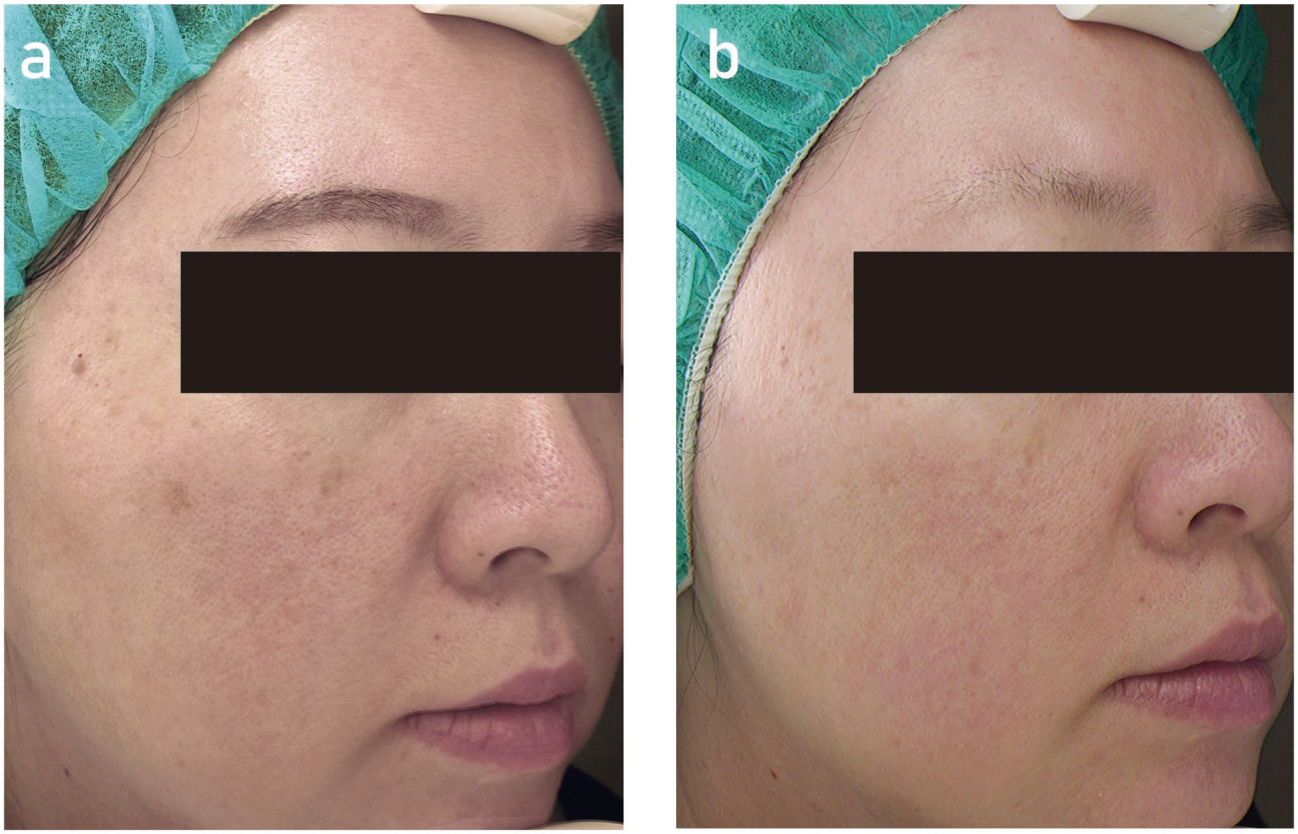

Figure 2. (**a**) Baseline. (**b**) After treatment with LFPS 1064.

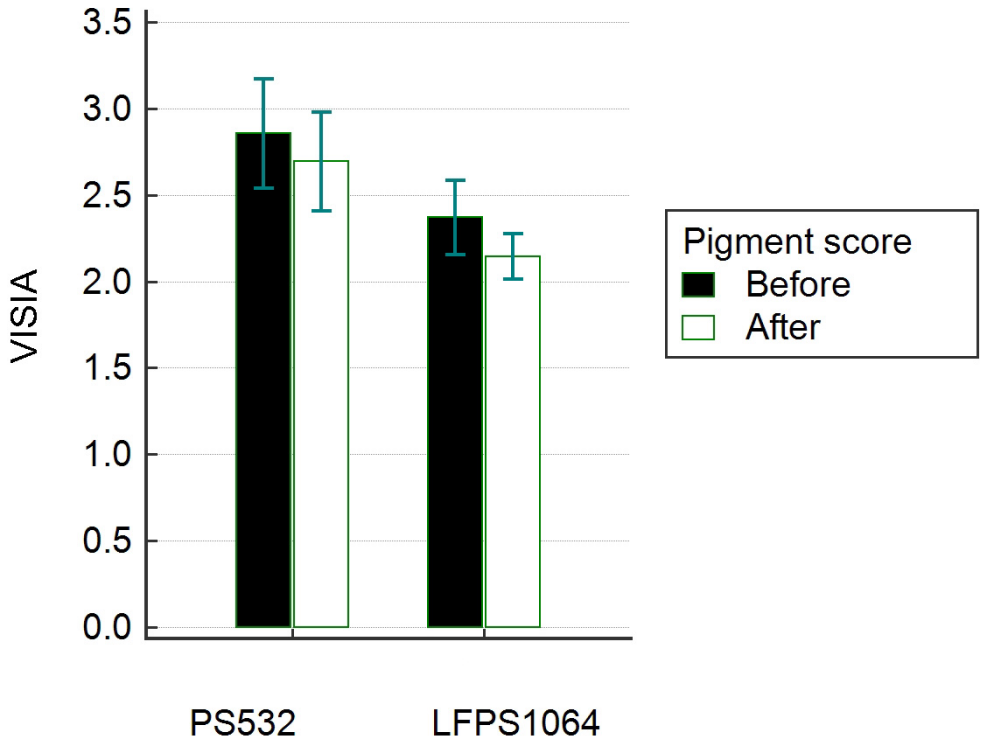

Figure 3. VISIA pigment scores.

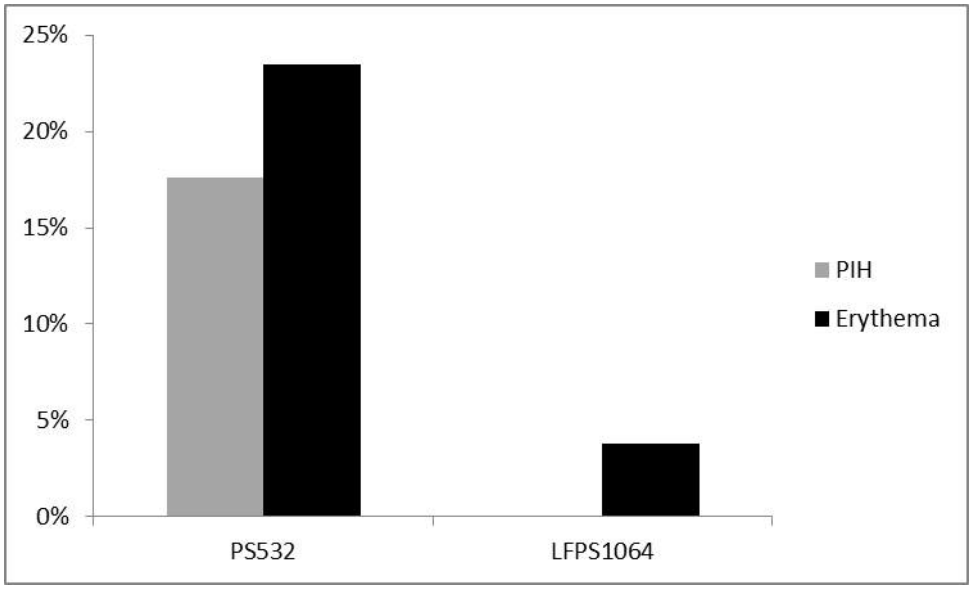

Figure 4. Adverse effects. % of cases in treatment group. PS532, picosecond 532 nm laser; LFPS1064, low-fluence picosecond 1064 nm laser.

4. Discussion

A picosecond laser has pulse widths in the picosecond range (10^{-12}). It started to become clinically available in the 1990s and was approved by the US Food and Drug Administration for the treatment of unwanted tattoos and pigmented lesions in 2012 [13]. Compared with the traditional nanosecond (10^{-9}) laser, it can produce higher peak powers with a shorter pulse duration, reducing the photothermal effect while increasing the photomechanical effect [9]. High-energy photons absorbed by pigments generate acoustic waves within the particles leading to their break up [14].

On the other hand, the photothermal effects, which include desiccation and immediate to delayed thermal injuries, could also be reduced with picosecond lasers by reducing the laser exposure time to the tissue [15]. Currently, the picosecond 532 nm laser is considered an effective treatment to remove epidermal and dermal pigments [2]. Friedmann reported that the 532 nm picosecond laser resulted in significant pigmentation eradication (96% clearance) and melanin reduction (78.4% lesion decrease) with mild PIH (3.4%) [8]. In our study, seventeen patients received picosecond 532 nm laser therapy, achieving an around 50% pigment clearance. The extent of pigmentation clearance in this study was similar compared with other studies using the same wavelength and similar treatment parameters in Asians [16,17], but lower than in Caucasian subjects with Fitzpatrick skin Type I–III [8]. Hypopigmentation following picosecond 532 nm laser treatment for lentigines in Asians has been reported in 3.6–4.65% [17,18]. In our study, there were only transient PIH and erythema.

Compared with the nanosecond laser, in which the PIH rate is 25% for darker skin types [19], PIH is reported with lower incidence, ranging from 0.8% to 10.4% [3,18,20] in Asians with Fitzpatrick skin types III and IV treated by picosecond laser. Besides PIH, erythema has been reported in patients receiving picosecond 532 nm Nd:YAG laser [2]. The incidence of PIH in our study was slightly higher than in previous reports in picosecond 532 nm Nd:YAG laser for the treatment of solar lentigines in Asians, which may be related to different treatment settings and varied lesion types [3]. PIH is the most common complication after laser treatment and more common in darker skin types [21], and is caused by the lysis of cells containing melanosomes due to heating from the high fluence of the laser [21,22]. Due to the high incidence, recent studies in Asia are mostly focused on the safety of reducing PIH and usually include laser toning, especially with QS lasers. In our study, we also used the technique of laser toning. Laser toning is known as a low-fluence and multi-passed laser with a large spot size [23]. In one study evaluating the structural modifications of melanocytes and melanosomes, laser toning was found to alter the ultrastructure of the melanosome and decrease the number of melanocytic dendrites [23]. Such a mechanism is called "subcellular selective photothermolysis" [22,24]. By destroying the melanosomes and melanin granules but keeping the cell membrane and nucleus intact, laser toning is considered to prevent the risk of PIH after laser treatment. However, mottled and rebound hyperpigmentation has been reported to be related to laser toning [25–27]. The rate of mottled hypopigmentation or rebound hyperpigmentation was 14.1% after laser toning using a 1064 nm QS Nd:YAG laser for the treatment of melasma [28]. Theoretically, both complications could be reduced under the picosecond laser treatment. A histological investigation was conducted to assess the effects of picosecond laser-toning therapy on photoaging, and a 1064 nm Nd:YAG picosecond pulse laser for 750 psec, known as picosecond laser-toning therapy, led to the rejuvenation of the entire dermis with reconstitution [29]. Whitening effects are clinically noted, which may contribute to improved pigmented lesions, but it is important to avoid complications like vitiligo [29]. The 750 psec pulse width falls between the thermal relaxation time (50 nm) of melanosomes and the stress relaxation time (200–400 psec) of melanin granules, suggesting minimal damage to melanocytes unless applied frequently at high output causing bleeding [29]. In the treatment of melasma in Asian skin, a picosecond 1064 nm Nd:YAG laser toning demonstrates comparable effectiveness and safety to a traditional Q-switched 1064 nm Nd:YAG laser toning [30]. Another study conducted microscopic analysis to examine the patterns of tissue reaction after picosecond 532 and 1064 nm laser treatments and found both generated great vacuolization in the epidermal and dermal cells [9]. Because the laser-induced tissue reaction could be found in both the high- and low-energy settings of the picosecond laser, we tried to apply the picosecond pulse duration as an effective treatment for melasma while minimizing the side effects of the higher-energy setting of picosecond 532 nm. Combining the benefits of lower thermal effects and subcellular selective photothermolysis, which then prevent PIH conceptually, picosecond laser with

toning is used to provide an alternative laser treatment for patients with darker skin types with pigmentary disorders.

In the present study, we analyzed the efficacy and safety of picosecond 532 nm and LFPS 1064 nm lasers with toning for pigmentary disorders in patients with Fitzpatrick skin types III and IV. Picosecond laser toning has the same treatment principle as nanosecond lasers. For the largest spot (7–10 mm, available on the system), a lower fluence will be chosen depending on the spot size of the laser [12,24]. We applied a spot size of 7–10 mm, and the fluence range was between 0.6 and 1.4 J/cm^2 [12]. Our results showed comparable efficacy to that of the picosecond 532 nm laser, but no PIH was noted, and only one patient presented with erythema, which subsided within one month. The incidence of PIH and erythema after LFPS 1064 nm laser with toning in our study was lower than that in the PS532 group. Lower fluence may have reduced the incidence of erythema occurring in the PS532 group [2]. Q-switched (Qs) laser toning for melasma treatment among Asians poses significant concerns regarding adverse effects, such as mottled hypopigmentation and post-inflammatory hyperpigmentation. The hypothesis suggests that potential harm to perilesional normal tissue, melanocytes, and surrounding oxyhemoglobin triggers inflammatory responses and melanogenesis [30]. However, no mottled or rebound hyperpigmentation was noted in our study compared with the previously published studies of laser toning using a 1064 nm QS Nd:YAG laser [25–27]. It is possible that the picosecond laser may offer superior peak power compared to its QS counterpart, enabling treatment of pigmentary lesions at lower energy levels and with significantly shorter pulse durations than the melanosome's thermal relaxation time. Consequently, laser energy can be more precisely targeted at the chromophore, thereby reducing the occurrence of adverse effects [30]. A retrospective study in a single center with small sample size is our limitation. Although our study has a small sample size, the LFPS 1064 nm laser with toning could still be considered a safe treatment for Asians.

5. Conclusions

Our study proved the efficacy and safety of LFPS 1064 nm Nd:YAG lasers for the treatment of benign pigmented lesions in Chinese patients. This is a retrospective review and has a small sample size from our hospital. Further studies are required to determine the fluence and treatment interval of picosecond laser toning.

Author Contributions: Conceptualization, P.-H.L. and P.-F.H.; methodology, P.-H.L. and P.-F.H.; software, P.-H.L.; validation, Y.-C.L. and P.-F.H.; formal analysis, P.-H.L.; investigation, P.-H.L., Y.-C.L. and P.-F.H.; resources, P.-F.H.; data curation, P.-F.H.; writing—original draft preparation, P.-H.L. and X.-F.Y.; writing—review and editing, P.-H.L.; visualization, P.-H.L.; supervision, P.-F.H.; project administration, P.-F.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Mackay Memorial Hospital (Institutional Review Board code 18MMHIS109e).

Informed Consent Statement: Patient consent was waived because this is a non-interventional retrospective study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available because this is a retrospective chat review study.

Acknowledgments: We thank all our colleagues in MacKay Memorial Hospital, Taipei, Taiwan, for helping with this study.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Chan, J.C.; Shek, S.Y.; Kono, T.; Yeung, C.K.; Chan, H.H. A retrospective analysis on the management of pigmented lesions using a picosecond 755-nm alexandrite laser in Asians. *Lasers Surg. Med.* **2016**, *48*, 23–29. [CrossRef] [PubMed]
2. Torbeck, R.L.; Schilling, L.; Khorasani, H.; Dover, J.S.; Arndt, K.A.; Saedi, N. Evolution of the Picosecond Laser: A Review of Literature. *Dermatol. Surg.* **2019**, *45*, 183–194. [CrossRef] [PubMed]
3. Chan, M.W.M.; Shek, S.Y.; Yeung, C.K.; Chan, H.H. A Prospective Study in the Treatment of Lentigines in Asian Skin Using 532 nm Picosecond Nd:YAG Laser. *Lasers Surg. Med.* **2019**, *51*, 767–773. [CrossRef] [PubMed]
4. Choi, J.E.; Lee, D.W.; Seo, S.H.; Ahn, H.H.; Kye, Y.C. Low-fluence Q-switched Nd:YAG laser for the treatment of melasma in Asian patients. *J. Cosmet. Dermatol.* **2018**, *17*, 1053–1058. [CrossRef] [PubMed]
5. Wattanakrai, P.; Mornchan, R.; Eimpunth, S. Low-fluence Q-switched neodymium-doped yttrium aluminum garnet (1064 nm) laser for the treatment of facial melasma in Asians. *Dermatol. Surg.* **2010**, *36*, 76–87. [CrossRef] [PubMed]
6. Omi, T.; Yamashita, R.; Kawana, S.; Sato, S.; Naito, Z. Low Fluence Q-Switched Nd: YAG Laser Toning and Q-Switched Ruby Laser in the Treatment of Melasma: A Comparative Split-Face Ultrastructural Study. *Laser Ther.* **2012**, *21*, 15–21. [CrossRef] [PubMed]
7. Saluja, R.; Gentile, R.D. Picosecond Laser: Tattoos and Skin Rejuvenation. *Facial Plast. Surg. Clin. N. Am.* **2020**, *28*, 87–100. [CrossRef] [PubMed]
8. Friedmann, D.P.; Timmerman, A.; Cahana, Z. Prospective Study of 532-nm Picosecond Laser for the Treatment of Pigmented Lesions of the Face and Dorsal Hands. *Dermatol. Surg.* **2022**, *48*, 1215–1219. [CrossRef] [PubMed]
9. Lee, H.C.; Childs, J.; Chung, H.J.; Park, J.; Hong, J.; Cho, S.B. Pattern analysis of 532- and 1064-nm picosecond-domain laser-induced immediate tissue reactions in ex vivo pigmented micropig skin. *Sci. Rep.* **2019**, *9*, 4186. [CrossRef]
10. Feng, J.; Shen, S.; Song, X.; Xiang, W. Efficacy and safety of picosecond laser for the treatment of melasma: A systematic review and meta-analysis. *Lasers Med. Sci.* **2023**, *38*, 84. [CrossRef]
11. Ungaksornpairote, C.; Manuskiatti, W.; Junsuwan, N.; Wanitphakdeedecha, R. A Prospective, Split-Face, Randomized Study Comparing Picosecond to Q-Switched Nd: YAG Laser for Treatment of Epidermal and Dermal Pigmented Lesions in Asians. *Dermatol. Surg.* **2020**, *46*, 1671–1675. [CrossRef] [PubMed]
12. Choi, Y.J.; Nam, J.H.; Kim, J.Y.; Min, J.H.; Park, K.Y.; Ko, E.J.; Kim, B.J.; Kim, W.S. Efficacy and safety of a novel picosecond laser using combination of 1 064 and 595 nm on patients with melasma: A prospective, randomized, multicenter, split-face, 2% hydroquinone cream-controlled clinical trial. *Lasers Surg. Med.* **2017**, *49*, 899–907. [CrossRef] [PubMed]
13. Jakus, J.; Kailas, A. Picosecond Lasers. *J. Clin. Aesthet. Dermatol.* **2017**, *10*, 14–15. [PubMed]
14. Ross, E.V.; Naseef, G.; Lin, C.; Kelly, M.; Michaud, N.; Flotte, T.J.; Raythen, J.; Anderson, R.R. Comparison of Responses of Tattoos to Picosecond and Nanosecond Q-Switched Neodymium:YAG Lasers. *Arch. Dermatol.* **1998**, *134*, 167–171. [CrossRef] [PubMed]
15. Jacques, S.L. Laser-Tissue Interactions: Photochemical, Photothermal, and Photomechanical. *Surg. Clin. N. Am.* **1992**, *72*, 531–558. [CrossRef] [PubMed]
16. Kung, K.Y.; Shek, S.Y.; Yeung, C.K.; Chan, H.H. Evaluation of the safety and efficacy of the dual wavelength picosecond laser for the treatment of benign pigmented lesions in Asians. *Lasers Surg. Med.* **2019**, *51*, 14–22. [CrossRef]
17. Vachiramon, V.; Iamsumang, W.; Triyangkulsri, K. Q-switched double frequency Nd:YAG 532-nm nanosecond laser vs. double frequency Nd:YAG 532-nm picosecond laser for the treatment of solar lentigines in Asians. *Lasers Med. Sci.* **2018**, *33*, 1941–1947. [CrossRef] [PubMed]
18. Negishi, K.; Akita, H.; Matsunaga, Y. Prospective study of removing solar lentigines in Asians using a novel dual-wavelength and dual-pulse width picosecond laser. *Lasers Surg. Med.* **2018**, *50*, 851–858. [CrossRef]
19. Wang, C.-C.; Sue, Y.-M.; Yang, C.-H.; Chen, C.-K. A comparison of Q-switched alexandrite laser and intense pulsed light for the treatment of freckles and lentigines in Asian persons: A randomized, physician-blinded, split-face comparative trial. *J. Am. Acad. Dermatol.* **2006**, *54*, 804–810. [CrossRef]
20. Guss, L.; Goldman, M.P.; Wu, D.C. Picosecond 532 nm Neodymium-Doped Yttrium Aluminium Garnet Laser for the Treatment of Solar Lentigines in Darker Skin Types: Safety and Efficacy. *Dermatol. Surg.* **2017**, *43*, 456–459. [CrossRef]
21. Davis, E.C.; Callender, V.D. Postinflammatory Hyperpigmentation. *J. Clin. Aesthet. Dermatol.* **2010**, *3*, 20–31. [PubMed]
22. Mun, J.Y.; Jeong, S.Y.; Kim, J.H.; Han, S.S.; Kim, I.H. A low fluence Q-switched Nd:YAG laser modifies the 3D structure of melanocyte and ultrastructure of melanosome by subcellular-selective photothermolysis. *J. Electron. Microsc.* **2011**, *60*, 11–18. [CrossRef]
23. Shah, S.D.; Aurangabadkar, S.J. Laser Toning in Melasma. *J. Cutan Aesthet. Surg.* **2019**, *12*, 76–84. [CrossRef] [PubMed]
24. Kim, J.H.; Kim, H.; Park, H.C.; Kim, I.H. Subcellular selective photothermolysis of melanosomes in adult zebrafish skin following 1064-nm Q-switched Nd:YAG laser irradiation. *J. Investig. Dermatol.* **2010**, *130*, 2333–2335. [CrossRef] [PubMed]
25. Chan, N.P.; Ho, S.G.; Shek, S.Y.; Yeung, C.K.; Chan, H.H. A case series of facial depigmentation associated with low fluence Q-switched 1,064 nm Nd:YAG laser for skin rejuvenation and melasma. *Lasers Surg. Med.* **2010**, *42*, 712–719. [CrossRef]
26. Kim, H.S.; Jung, H.D.; Kim, H.O.; Lee, J.Y.; Park, Y.M. Punctate leucoderma after low-fluence 1,064-nm quality-switched neodymium-doped yttrium aluminum garnet laser therapy successfully managed using a 308-nm excimer laser. *Dermatol. Surg.* **2012**, *38*, 821–823. [CrossRef] [PubMed]

27. Kim, H.S.; Kim, E.K.; Jung, K.E.; Park, Y.M.; Kim, H.O.; Lee, J.Y. A split-face comparison of low-fluence Q-switched Nd: YAG laser plus 1550 nm fractional photothermolysis vs. Q-switched Nd: YAG monotherapy for facial melasma in Asian skin. *J. Cosmet. Laser Ther. Off. Publ. Eur. Soc. Laser Dermatol.* **2013**, *15*, 143–149. [CrossRef] [PubMed]
28. Choi, C.P.; Yim, S.M.; Seo, S.H.; Ahn, H.H.; Kye, Y.C.; Choi, J.E. Retrospective analysis of melasma treatment using a dual mode of low-fluence Q-switched and long-pulse Nd:YAG laser vs. low-fluence Q-switched Nd:YAG laser monotherapy. *J. Cosmet. Laser Ther. Off. Publ. Eur. Soc. Laser Dermatol.* **2015**, *17*, 2–8. [CrossRef] [PubMed]
29. Nakano, S. Histological investigation of picosecond laser-toning and fractional laser therapy. *Laser Ther.* **2020**, *29*, 53–60. [CrossRef]
30. Hong, J.K.; Shin, S.H.; Park, S.J.; Seo, S.J.; Park, K.Y. A prospective, split-face study comparing 1,064-nm picosecond Nd:YAG laser toning with 1,064-nm Q-switched Nd:YAG laser toning in the treatment of melasma. *J. Dermatol. Treat.* **2022**, *33*, 2547–2553. [CrossRef]