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A randomized, single-blind, study evaluating a 755-nm picosecond pulsed Alexandrite laser vs. a non-ablative 1927-nm fractionated thulium laser for the treatment of facial photopigmentation and aging

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ABSTRACT

Background: Laser toning is one of the most popular strategies to treat facial photopigmentation and aging. Several laser modalities, including fractional non-ablative, Q-switched (QS) lasers and new generation picosecond lasers have been used for this indication. However, there is paucity of head to head comparisons of older generation of lasers with new ones.

Objective: To compare a 755 nm picosecond pulsed alexandrite laser with a non-ablative 1927 nm fractionated thulium laser for the treatment of facial photopigmentation and aging through a randomized, single-blind study.

Materials and methods: 20 subjects (skin types I–IV) were randomized to receive either four 755-nm picosecond alexandrite laser treatments, spaced 3 weeks apart, or two dual wavelength thulium fiber fractionated 1550/1927 nm laser treatments, spaced 6 weeks apart. Follow-up assessment visits occurred 4 and 12 weeks after the last study treatment.

Results: At the 4- and 12-week follow-up, both groups showed significant improvement of photoaging, pigmentation, skin quality according to the investigator and subjects assessments. When comparing the two groups, subjects in 755 nm group had statistically significant greater improvement in investigator assessments of photoaging/skin quality and subject satisfaction than those in the 1927 nm group.

Conclusion: Both the non-ablative 1927 and 755 nm picosecond laser can improve facial photopigmentation, but the latter can yield superior results with less pain and side effects according to patient and investigator assessments.

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Aging; photoaging; 755 nm picosecond laser; 1927 nm fractionated thulium laser

Introduction

Treatment of photopigmentation and aging is one of the strongest forces driving patients to the dermatologist and demand for safer, faster and more effective procedures is on the rise. Several modalities exist for this indication, from prescription topicals or cosmeceuticals, to chemical peels and energy-based devices, namely radiofrequency and lasers.

Laser toning performed by non-ablative lasers is commonly employed to eliminate dyschromias, fine lines, sun spots and textural irregularities. Unlike traditional laser skin resurfacing treatments that have harsh side effects and require prolonged downtime and recovery, laser toning using new generation non-ablative lasers has dramatically increased in popularity due to their safety, efficacy and minimal downtime required after treatment (1–3). These devices treat skin photoaging through selective photothermolysis and rely on thermal-induced tissue response for any tissue change. With the development of nanosecond and picosecond pulse durations, quality switched (QS) lasers, including the QS Nd:YAG, QS alexandrite and QS ruby lasers, have been regularly used in the treatment of these epidermal/dermal pigmented lesions. Intense-pulsed light (IPL) devices and fractional photothermolysis devices also provide nonablative skin treatment options for cutaneous photodamage and have been studied for the treatment of photoaging (4–6).

In this study, the 755 nm picosecond alexandrite laser (Picosure, Cynosure, MA) was compared to the 1927 nm wavelength of the dual wavelength thulium fiber fractionated 1550/1927 nm laser (Fraxel Dual; Solta, Hayward, CA) for the treatment of photopigmentation and aging. The 1927 nm laser is a nonablative fractional resurfacing device intended for epidermal and superficial dermal coagulation, while the 755 nm picosecond laser causes both photomechanical and photothermal effects on tissue, and has been shown to be efficacious in photoaging, tattoo removal, benign pigment, acne and wrinkles (7–12). In addition, utilizing a specialized diffractive lens array, focal increases in energy density can be delivered within a hexagonal grid of spots while maintaining overall fluence at a low level (13). Via this fractionation, clinical effect can be increased while still maintaining an excellent safety profile. The primary endpoints for the comparison included the degree of improvement in photodamage as rated by trained independent-evaluator using the Global

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Aesthetic Improvement Score (GAIS), live assessments by blinded-evaluator, side effects and subject self-assessments/satisfaction 4 and 12 weeks post the last treatment.

Materials and methods

Patients

A total of 20 subjects were enrolled in this trial. All subjects provided written informed consent prior to receiving any study-related procedures. Eligible subjects were healthy male or female 30 years or older age, Fitzpatrick photo skin types I–IV that classified as number 2 or 3 on the Global Photoaging Scale. Subjects had to agree not to have any procedures affecting facial wrinkles (e.g. filler, botulinum toxin, radiofrequency, laser, IPL, ultrasound) or skin quality (microdermabrasion, peels, acne treatments, etc.) for the duration of the study. Subjects had to agree with all requirements of the study including being photographed, following post treatment care and attending all treatment and follow-up visits. Negative urine pregnancy test results were required for women with childbearing potential before enrollment. Exclusion criteria included pregnancy, breastfeeding, prior treatment with Accutane, parenteral gold therapy, hypersensitive to light exposure, keloids, presence of active or localized systemic infections, coagulation disorder, compromised wound healing or any other condition which, in the investigator's opinion, would make it unsafe for the subject to participate in this research study. Subjects with excessive facial hair (e.g. beards, sideburns, moustaches, etc.), moderate or severe rhinophyma, dense telangiectases (score 3, severe), or plaque-like facial edema were also excluded from the study. Subjects could not participate if they had laser therapy (for telangiectasia or other conditions), electrodessication and phototherapy to the facial area within 180 days prior to study entry, botulinum toxin in the treatment area in the past 12 months or any kind of facial dermabrasion, chemical peel, laser, or IPL treatment including superficial treatments for esthetic reasons in the past 6 months or for the duration of the study.

Study design

This was a randomized, single-blind single-center study conducted in accordance with the principles of the Declaration of Helsinki, current GCP guidelines, and IRB approval. Subjects were randomized and received either: (755 nm group) four 755 nm picosecond alexandrite laser treatments, spaced 3 weeks apart or (1927 nm group) two dual wavelength thulium fiber fractionated 1550/1927 nm laser treatments, spaced 6 weeks apart. All subjects were asked to use a topical sunscreen (La Roche Posay® Anthelios 60) daily starting 1 week prior to baseline therapy and continue using it throughout the entire study. Assessments were performed at baseline, 4 and 12 weeks after the last visit.

Laser treatments

For the 1927 nm group, application of topical lidocaine and eye protection took place prior to each treatment. Laser treatments were performed according to manufacturer's instructions using a pulse energy of 10 mJ and a treatment level 5, corresponding to surface area coverage of 40%, with 4–6 passes. The total energy delivered ranged from 0.81 to 2.29 kJ. The treatment area covered the entire face and neck. Forced air cooling was used with a SmartCool brand cooler set on fan speed of moderate to high. For the 755 nm group, topical lidocaine and eye protection was also used, and laser treatments were performed using the settings according to manufacturer's instructions shown in Table 1. The treatment area covered the entire face and neck. Forced air cooling was used with a SmartCool brand cooler set on fan speed of moderate to high. For discrete pigmented lesions, the flat (zoom) optic (3–4 mm spot size) was used and lesions were treated to endpoint of frosting/whitening. The optic was then switched to the Focus and treatments were continued to treat the full face for revitalization using the 6 mm spot with 5000–8000 pulses.

Photography

Standardized photographs were taken at baseline, follow-up 1 and follow-up 2 study visits at 0°, 45° and 315° angles using the Visia® CR system (Canfield Imaging Systems, Fairfield, NJ). For each angle, a set of four different photographs were taken including non-polarized, cross-polarized and parallel-polarized white light as well as UV light images. The OMNIA® Imaging System (Canfield Imaging Systems, Fairfield) was also used. For each angle, a set of four different photographs were taken, and these photographs were used as an assessment tool for looking at improvement (independent evaluation).

Evaluations

The efficacy assessments were performed on the treatment area for each subject by the same blinded evaluating investigator in real time throughout the course of the study. The effectiveness parameters were 9-point Fitzpatrick Wrinkle Scale for the assessment of wrinkle severity, a 10-point scale for the assessment of skin quality and the modified melasma area and severity index (mMASI) was used to score the degree of photodamage on the face. mMASI was calculated based on the percentage of involved area, darkness of pigment, and homogeneity or density of hyperpigmentation (14). Photographs were rated using the GAIS and Global Photoaging Scale by an independent trained evaluator who was blinded to all time points and treatments. Subject assessments included questionnaires in regard to satisfaction with results, pain levels during and after treatment, skin satisfaction, impact on daily activities and self-assessments of symptoms. All patients reported self-assessments were performed prior to any other effectiveness assessments throughout the course of the study.

Table 1. Treatment parameters for the 755 nm laser group.

For lesions such as ephelides and solar and senile lentigines using zoom/fixed hand pieces				
Skin type	Spot size		Rep. rate	
I–III	3–3.5 mm		1–5 Hz	
IV	4–6 mm		1–5 Hz	
V–VI	6–1 mm		1–5 Hz	
Treatment guidelines, diffuse pigmentation focus array				
Skin type	Fixed spot size HP	Passes	Txs intervals	Number of txs
I–IV	6 or 8 mm	3–6	2–4 weeks	2–4

Statistical analysis

A paired *t*-test was used to compare values at the end of follow-up from baseline between the two groups. A *p* value of less than 0.05 was considered statistically significant. For ratio scaled variables normal distribution was verified by Kolmogorov–Smirnoff test and then analyzed using Student-*t* test for paired variables or Wilcoxon test. Analyses were carried out using SAS version 9.4 statistical software (Cary, NC).

Results

Population

20 female subjects total with an average age of 55 (±7.5) years were enrolled into this study. Three subjects (two from the 755 nm group and one from the 1927 nm group) were lost to follow-up prior to the completion of the study and were not included in the statistical analysis of the results. A total of 70% of patients were skin type II ($n = 12$), 25% skin type III ($n = 4$) and 5% were skin type IV ($n = 1$).

Investigator assessments

At baseline, there were no differences in the global photoaging scale scores between the two groups (2.7 ± 0.8 and 2.8 ± 0.7 for 1927 nm group and 755 nm group, respectively), as rated by a blinded to the treatment independent investigator. At the 4 and 12-week follow-up, both groups showed a statistically significant improvement in global photoaging scores compared to baseline. However, the improvement was greater in the 755 nm group compared to the 1927 nm group at both the 4 weeks (1.7 ± 0.6, 755 nm group vs 1.8 ± 0.4, 1927 nm group; $p = 0.08$) and 12-week follow-up (1.1 ± 0.03, 755 nm group vs 1.4 ± 0.32, 1927 nm group; $p = 0.04$).

At the 4-week follow-up, the average GAIS score for both groups was 1.0 ± 0.7 (mild improvement) for both treatment groups. At the 12-week follow-up, however, the GAIS score for the 755 nm group was 2 ± 0.8 (moderate improvement), while the 1927 nm group GAIS score remained unchanged. This difference in GAIS score between the two groups was statistically significant ($p = 0.03$) (Figure 1).

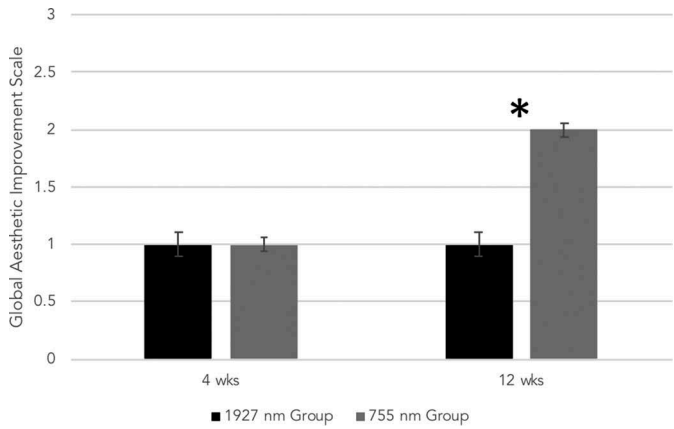


Figure 1. Average Global Aesthetic Improvement Scale Assessment (GAIS) from baseline to 4- and 12-week follow-up in the 1927 and 755 nm group. Asterisk indicates statistical significance ($p < 0.05$).

Table 2. Average Fitzpatrick Wrinkle Scale score at baseline, 4- and 12-week follow-up for the 1927 and 755 nm groups.

Timepoint	1927 nm group	755 nm group	*p*-Value
Baseline	2	2	1.3
4-Week follow-up	1.62	1.5	0.2
12-Week follow-up	1.75	1.05	0.04

The average Fitzpatrick Wrinkle Scale score at baseline did not differ significantly between the two groups at baseline or the 4-week follow-up, but there was a statistically significant improvement in wrinkle score at the 12-week follow-up in the 755 nm group compared to the 1927 nm group ($p = 0.04$), Table 2.

There were no differences in the baseline radiance, smoothness, pigmentation, erythema, and pore size scores between the two groups ($p = 0.9$, 0.8, 0.6, 0.7 and 0.5). Statistically significant improvements in radiance and smoothness were observed in both groups at the 4- and 12-week follow-up compared to baseline, but the difference was comparable between the two groups ($p = 0.3$). Pigmentation and erythema scores also improved statistically significant in both groups at the 4- and 12-week follow-up compared to baseline, and improvement was statistically significantly greater in the 755 nm group compared to the 1927 nm group ($p = 0.03$ and $p = 0.04$ for pigmentation and erythema, respectively). Pore size was reduced from baseline in both groups at the 4- and 12-week follow-up but the reduction was not significant (Table 3).

A significant decrease in mean MASI score from baseline was observed in both treatment groups at the 4- and 12-week follow-up. The mean MASI score was statistically significantly reduced in the 755 nm group compared to the 1927 nm group at both time points ($p = 0.04$ for the 4 weeks and $p = 0.03$ for the 12-week follow-up). Figures 2 and 3 show a representative subject at baseline and 12-week follow-up from the 1927 and 755 nm group.

Subject assessments

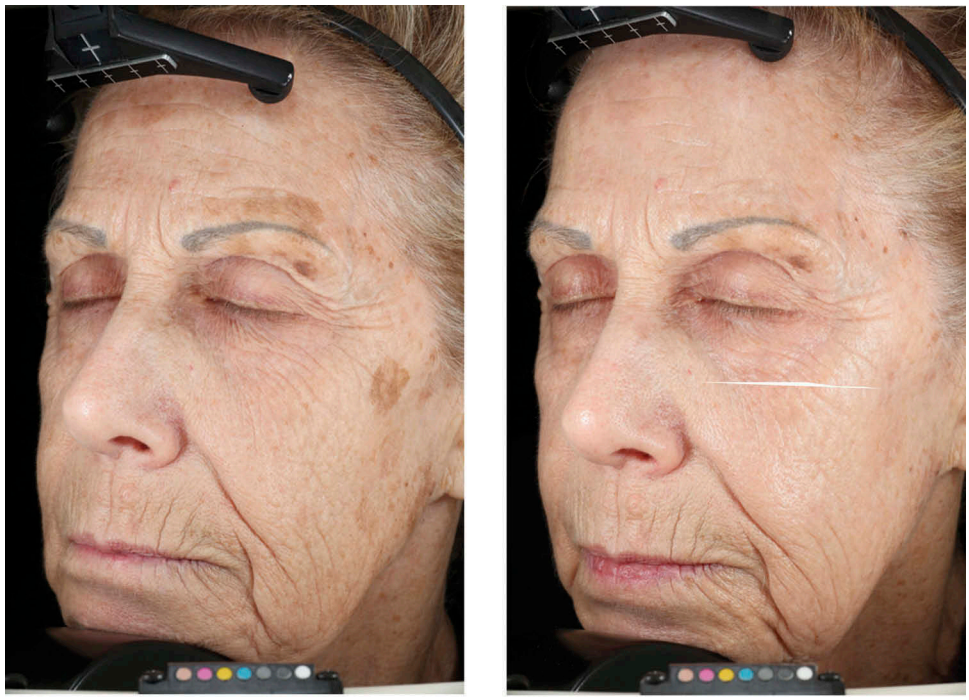
Subject satisfaction at the 4- and 12-week follow-up was significantly increased from baseline in both the 1927 nm ($p = 0.04$) and the 755 nm group ($p = 0.03$). More than half of the subjects in the 755 nm were satisfied/very satisfied by the treatment at the 4- and 12-week follow-up (57% and 65%, respectively), while only 40% of subjects in the 1927 nm were satisfied/very satisfied at both follow-up visits. The increased level of satisfaction in the 755 nm group compared to the 1927 nm group was statistically significant ($p = 0.03$).

There were no differences in the baseline subject assessments of skin quality (photodamage, fine lines, wrinkles, roughness) between the two groups ($p = 0.5$, 0.9, 0.9 and 0.7). Although improvements in all subject measurements of skin quality were shown in both groups at the 4- and 12-week follow-up compared to baseline, statistically significant greater improvement in the 755 nm compared to the 1927 nm group was shown for photodamage at 12 weeks, and fine lines/wrinkles at both the 4- and 12-week follow-up (Table 4).

Analysis of the facial skin questionnaires revealed a statistically significant improvement in the 755 nm group compared to the 1927 nm in the subject's perception of their facial

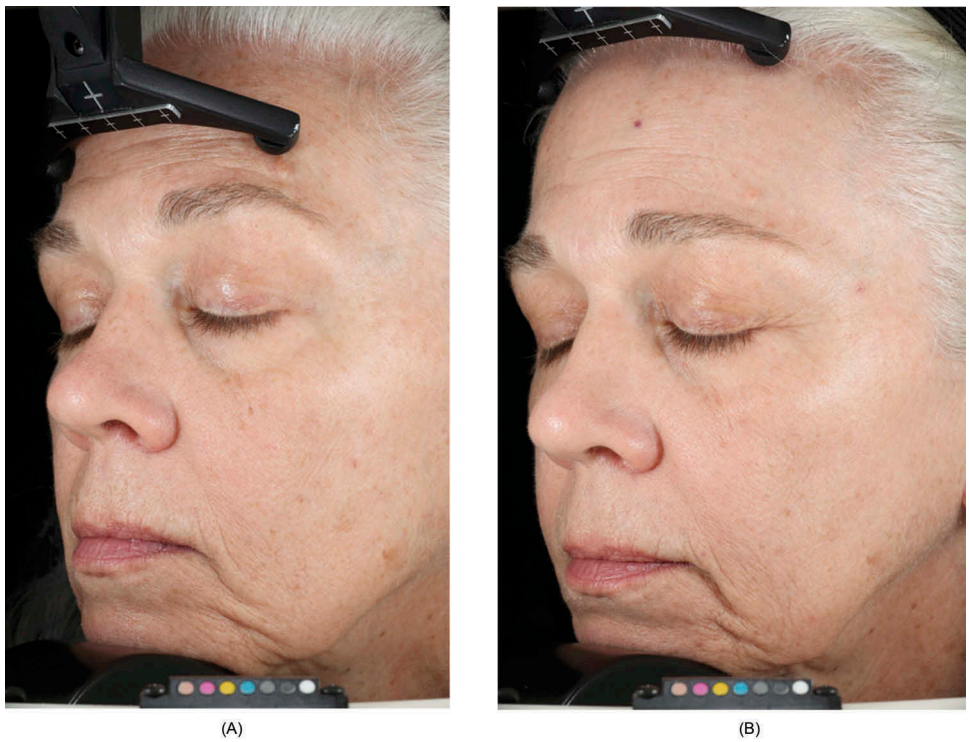
Table 3. Investigator skin quality ratings for radiance, smoothness, pigmentation, erythema and pore size at baseline, 4 and 12 weeks after the final treatment for the 1927 nm and 755 nm group. Asterisk indicates statistical significance from baseline ($p < 0.05$). Gray shadings indicate statistically significant difference between the 755 nm group and 1927 group for pigmentation ($p = 0.03$) and erythema ($p = 0.04$).

	Radiance		Smoothness		Pigmentation		Erythema		Pore size	
	1927 nm	755 nm	1927 nm	755 nm	1927 nm	755 nm	1927 nm	755 nm	1927 nm	755 nm
Baseline	4	3.9	4.6	4.3	3	3.5	6.1	5.8	6.5	7
4 Weeks	5*	6*	5.6*	6*	5*	5*	5.6	6	5.6	5.7
12 Weeks	5.5*	6.1*	6*	6.3*	5.2*	6.7*	5.5	7*	6.1	6



(A) (B)

Figure 2. (A) 58-year-old woman at baseline and (B) 12 weeks post last treatment with 755 nm laser.



(A) (B)

Figure 3. (A) 56-year-old woman at baseline and (B) 12 weeks post last treatment with 1927 nm laser.

Table 4. Subject skin quality ratings for photodamage, fine lines, wrinkles, and roughness at baseline, 4 and 12 weeks after the final treatment for the 1927 nm and 755 nm group. Asterisk indicates statistical significance from baseline ($p < 0.05$). Gray shadings indicate statistically significant difference between the 755 nm group and 1927 group for photodamage ($p = 0.02$), fine lines ($p = 0.04$), and wrinkles ($p = 0.03$).

	Photodamage		Fine lines		Wrinkles		Roughness	
	1927 nm	755 nm	1927 nm	755 nm	1927 nm	755 nm	1927 nm	755 nm
Baseline	2.8	2.7	2.7	2.6	2	2.1	1.5	1.6
4 Weeks	1.7*	1.7*	2.3	1.6*	2.1	1.5*	1.1	0.8*
12 Weeks	2.3	1.1*	2.4	1.2*	1.8	1*	1*	0.8*

skin (Table 5). In terms of the effect of the treatment on the patient's daily lives, the 755 nm group experienced significantly less impact on their routine than that experienced by the 1927 nm group. Specifically, the 1927 nm group had erythema ($p = 0.03$), could not apply makeup ($p = 0.02$), felt uncomfortable ($p = 0.02$) and delayed resuming normal activities ($p = 0.03$) for more days than the 755 nm group (Figure 4).

Adverse events and tolerability

Eight subjects in the 755 nm group and nine in the 1927 nm group completed the study, and no adverse effects were reported. Physicians local tolerability assessments showed that although there was no significant difference between the two groups for dryness, peeling and roughness, the level of erythema was statistically significantly increased in the 1927 nm group at the 4-week follow-up compared to the 755 nm group ($p = 0.02$) (Figure 5). At the 12-week follow-up there were no significant differences in any of the tolerability assessments between the two groups. No significant differences were observed at any time point between the two groups when analyzing subject's local tolerability assessments post treatment (dryness, burning, stinging and skin sensitivity). The subjects in the 755 nm group experienced significantly less pain during treatment compared to the subjects in the 1927 nm group (average score 3 vs 6, $p = 0.01$, scale 1–10, 1: no pain, 10: severe pain).

Table 5. Percent change from baseline in subject scores in facial skin questionnaire at the 12-week follow-up in the 1927 and 755 nm group. Asterisk indicates statistically significant compared to the 1927 nm group.

Facial skin questionnaire	1927 nm	755 nm
Happier with appearance of facial skin	20%	31%*, $p = 0.04$
Less bothered by the appearance of facial skin	22%	35%*, $p = 0.04$
Less self-conscious about appearance of facial skin	10%	30%*, $p = 0.03$
Less embarrassed about appearance of facial skin	20%	25%
How much less old look because of the photodamage	15%	40%*, $p = 0.02$

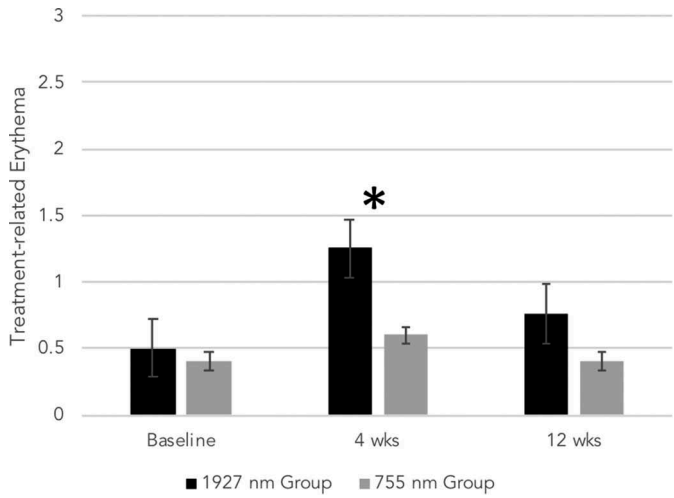


Figure 5. Average impact of laser treatments on daily activities. Asterisk indicates statistical significance ($p < 0.05$).

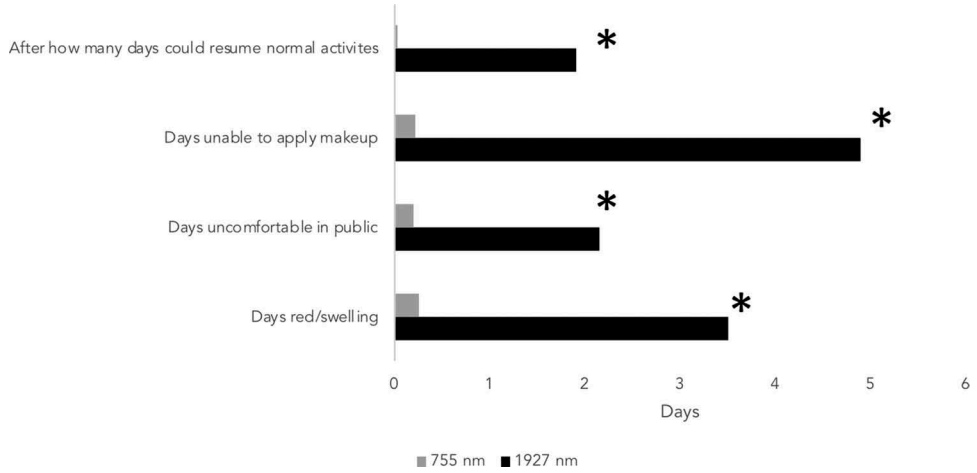


Figure 4. Treatment related erythema at baseline, 4 and 12 weeks follow-up in the 1927 and 755 nm group. Asterisk indicates statistical significance ($p < 0.05$).

Discussion

Fractional non-ablative lasers have been considered until the gold standard in treatment global photopigmentation and aging in a range of skin types (15). Compared to the older generation of ablative fractional lasers, fractional lasers such as the 1927 nm, have proven effective, safe and with a favorable safety profile {Cohen, 2009 #28}. Development of newer generation lasers, emitting picosecond pulses in a range of wavelengths, from 532 nm to 1064 nm, have been increasingly utilized in a variety of dermatologic indications, from aging to scars and pigmentation disorders (16). However, there has never been a head-to-head comparison of these lasers with traditionally used fractional non-ablative ones.

This is the first randomized, single-blind study comparing a 755 nm picosecond laser with a 1927 nm laser for the treatment of photopigmentation and aging. Using standardized scales and questionnaires, the 755 nm lasers was shown, according to investigators evaluations, to result in greater improvement of global photoaging, pigmentation and skin quality compared to the 1927 nm laser at the study follow-ups. Moreover, the tolerability profile was more favorable in the 755 nm laser treatment group. Similar results were noted in the analysis of the subject's self-assessments. Global satisfaction with the treatment results, and scores for stratified measures of skin and facial aging, were significantly greater in the 755 nm group compared to the 1927 nm group. The 755 nm group also experienced less pain, side effects and overall impact of the treatment in their daily life.

While the number of subjects was limited, and the 755 nm group received double the amount of treatments compared to the 1927 nm group, the data indicate that the new generation picosecond lasers can effectively target and treat photopigmentation and signs of aging, with minimal downtime. As picosecond laser energy results in a combined photothermal/photoacoustic effect to the tissue, the overall thermal damage to the tissue is reduced, accounting for less side effects. At the same time the energy absorption is great enough to stimulate pigment degradation and stimulation of neocollagenesis, which leads to its clinical effects (17).

In an era where the pace of life is dizzying, appearances matter and downtime is not an option, the mounting clinical evidence and promising results of picosecond lasers for aging, photodamage and other indications, may represent a technological advance such that warrants them to become the new gold standard of treatment (16).

Funding

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