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ORIGINAL ARTICLE

Efficacy and safety of long pulse Nd:YAG laser versus fractional erbium:YAG laser in the treatment of facial skin wrinkles

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Abstract

Fractional lasers such erbium:YAG (Er:YAG) are among popular options for facial rejuvenation. Lasers with infrared wavelength ranges such as long pulse Nd:YAG have been used in nonablative rejuvenation of skin with variable outcomes. In this study, we plan to compare safety and efficacy of fractional Er:YAG and long pulse Nd:YAG for facial rejuvenation applying objective and subjective measurements. Twenty-five patients with Glogau photo aging scale of II to IV were recruited in this randomized face-split double-blind controlled trial. Individuals received three monthly treatments on two sides of the face; one side was treated by fractional Er:YAG laser and the other side by long pulse Nd:YAG laser. Outcomes were evaluated by two blinded dermatologists, patient satisfaction reports and objective measurements of cutaneous resonance running time (CRRT). Both modalities significantly improved periorbital wrinkling, nasolabial folds, dyschromia and skin laxity, and sagging of jowls (p value < 0.05), with no noticeable difference between two lasers. Mean CRRT values decreased significantly after treatment with both lasers. The downtime was significantly lower for the Nd:YAG-treated side. Fractional Er:YAG laser and long pulse Nd:YAG has comparable effects in facial rejuvenation but little to no downtime of the latter makes it popular for many patients. ClinicalTrials.gov Identifier: IRCT2015120320468N3

Keywords Erbium:YAG laser · Face · Nd:YAG laser · Wrinkle · Rejuvenation

Introduction

The lasers commonly used for facial rejuvenation may be classified into ablative and non-ablative lasers, both of which may be fractionated [1]. Traditionally, ablative lasers such as carbon dioxide (CO2; 10,600 nm) or erbium:YAG (Er:YAG; 2490 nm) were considered more effective than non-ablative devices [2, 3]. These lasers have a prolonged recovery time and a greater chance of complications [4]. Therefore, fractionated lasers have been introduced to minimize these complications while achieving the comparable outcome [1]. Er:YAG lasers ablate tissue without producing significant lateral thermal heating [5]. Compared to fractional CO2, fractional Er:YAG laser exert similar efficacy in facial rejuvenation with a more satisfactory safety profile [6].

On the other hand, non-ablative devices have been used for facial rejuvenation [7–10]. Among several types of non-ablative laser, long pulsed 1064 nm Neodymium-doped yttrium aluminum garnet (Nd: YAG) laser can deliver energy to deep dermis where heat-induced damage results in collagen and elastin remodeling with little or no downtime and less patient discomfort [7]. In addition, long-pulse Nd:YAG lasers are weakly absorbed by melanin, allowing for safer laser treatment in patients of all skin types. [8]. However, to the best of our knowledge, no trial to date has compared the safety and efficacy of fractional Er: YAG laser and long pulse Nd: YAG laser in the facial rejuvenation. Therefore, we performed the current face-split randomized controlled trial to compare the safety and efficacy of these lasers for facial rejuvenation.

Material and methods

Study design

The current study was a randomized controlled double-blind split-face trial performed on 25 volunteers who desired facial rejuvenation for treatment of wrinkles and laxity. The subjects

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presented to our Dermatology outpatient clinic from May 2016 to June 2017. Enrolled individuals were females who aged 50 to 75 with baseline Glogau [9] photoaging classification II to IV. The study was conducted according to the Declaration of Helsinki and received approval by the Ethical Committee of Shahid Beheshti University of Medical Sciences. Subjects were provided with a full explanation of the laser procedures and study details and all signed a written informed consent. The protocol was approved by the Iranian Registry of Clinical Trials (IRCT2015120320468N3).

The included participants did not have any active skin disease within the treatment area (e.g., cancer, autoimmune disease, or active infection). The other exclusion criteria were pregnancy, pigmentary conditions such as melasma, history of isotretinoin use in the year before laser treatment, coagulation disorders or anticoagulant treatment, history of keloid scarring, known allergy to topical lidocaine anesthetic, history of photosensitizing medications, or any cosmetic procedure in areas of treatment in the last 12 months. Patients were not allowed to receive chemical peels, botulinum toxin injection, soft tissue augmentation, topical tretinoin treatment, or microdermabrasion during the study period. Home skin care regimens were assessed and standardized to remove possibly confounding factors.

Devices and techniques

Patients were assigned to receive three monthly treatments on each side of the face, one with fractional Er:YAG laser and the other with long pulse Nd:YAG laser. The right and left sides of the face of each patient were randomized to receive treatment with Er:YAG (2940 nm) or Nd:YAG (1064 nm), based on a randomization table provided by a statistician not otherwise involved in the study.

The device used for fractional resurfacing was Er:YAG, LOTUS II erbium device (LOTUS II; Laseroptek Co., Ltd., Sungnam, Gyenggido, Korea). We applied fluence of 1200 mJ/cm^2, with a pixel number of 30/cm^2, pixel size of 270 m via the short-pulse mode (350 μs), repetition rate of 3–5 Hz and spot size of 7 mm; two passes was performed on the treated area.

For treatment of the contralateral side of the face, we used long pulse Nd:YAG 1064 nm laser (Hyperion; Laseroptek Co., Ltd., Seongnam, Gyeonggi-do, South Korea) with parallel cooling by a spot size of 10 mm, pulse duration of 20 ms and fluence of 20–24 J/cm^2 to reach an obvious erythema following the laser procedure. Three passes were performed over the treated area.

With regard to both lasers, we used the optimal setting provided by the manufactures for treatment of facial rhytides. The setting used by Nd:YAG device was chosen according the optimal dose setting for skin tightening. These parameters were chosen for each laser to reach a mild and objective erythema on each side of the face following the laser treatment. Moreover, both lasers performed with a stamping application pattern as synchronized fractionated or long pulse non-fractionated beams to have an equivalent form of laser performance in this comparative study.

Treatment protocol

Before the initiation of the procedure, the face was cleansed with a gentle skin cleanser. The skin was covered with a thin layer of topical anesthesia (lidocaine 2.5% and prilocaine 2.5% cream) for 30 min before the procedure in all patients. During the laser therapy, eye protection goggles were applied to the patients. Treatment with each device was performed all over the face from hairline to chin.

After the procedure, the treatment area was covered with zinc oxide ointment and the patients were instructed about the post laser therapy care and sun protection.

The patients were allocated to receive three monthly treatment sessions on each side of the face, one with long pulse Nd: YAG laser and the other with fractional Er:YAG laser. Patients returned 1 week after each treatment session for evaluation and documentation of complications such as pain, erythema, edema, depigmentation, scar and atrophy. Moreover, the downtimes after the laser procedures were also recorded. The downtime shows the period of time that the possible erythema or edema of the face subsided after the laser treatment.

Photographs were obtained by a Canon digital camera (Power Shot S110 with 12.1 megapixels high-sensitivity CMOS sensor; Canon, Inc., Japan) at baseline, before each treatment session, and 3 months after the final treatment.

Outcome evaluation

Evaluation of the outcomes was performed by two board-certified dermatologists blinded to the type of treatment performed on each side of the face. The evaluators were asked to rate the percentage of improvement for periorbital wrinkling, nasolabial folds, dyschromia (lentigines, loss of translucency and a sallow color) and skin laxity and sagging of jowls. Additionally, Global Aesthetic Improvement Scale (GAIS), which is a 5-point scale from −1 (worse) to 3 (very much improved) was rated by evaluators [10]. Patients were also asked to report their subjective satisfaction by stating the percentage of their improvement in each visit.

Skin biomechanical properties

Multi-Probe Adaptor System (MPA 9; Courage & Khazaka Electronic GmbH, Köln, Germany) is a device that can assess skin biomechanical properties with its several headpieces. In the current study, we applied the Reviscometer® RVM 600 handpiece, which measures the cutaneous resonance running

time (CRRT). Reviscometer® is an instrument that aims at evaluating the mechanical behavior of the skin and the direction of collagen and elastin fibers using the acoustic wave propagation time of a shear wave between two probes placed on the skin surface [11]. It is influenced by the collagen fibers in the papillary dermis, and inversely correlates with skin stiffness [12]. In order to measure CRRT, the patients were positioned supine. The mean CRRT over the four axes (0°, 180°, 90°, and 270°) was measured for the cheeks. These measurements were conducted at room temperature, 24–26 °C, with a relative humidity of 50 ± 3%. These measurements were documented for each patient at baseline, before each treatment session, and 3 months after the final treatment.

Data analysis

Quantitative data are presented as the mean ± the standard deviation (SD) and quantitative data as a percentile. In order to compensate for the effect of the correlation between the two sides of the face in each patient, the generalized linear mixed model was used. Inter-observer reliability was evaluated by measuring intraclass correlation coefficient; p value < 0.05 was defined as statistically significant.

Results

Baseline characteristics

All of our patients were female with the mean age of 59.91 ± 7.08 years. Among 30 volunteers who initially enrolled, 25 participants completed the entire study. Three patients were excluded due to their poor adherence to the study protocol and two did not come for the last follow-up visit. The baseline Glogau photoaging classification was type I in 1 (4%) participant, type II in 5 (20%), type III in 16 (64%) and type IV in 3 (12%) of the participants. Most of the participants in our study had Fitzpatrick skin type III (76%) and the rest had skin type II (24%).

Intraclass correlation coefficient

The intraclass correlation coefficient (ICC) between the two evaluators was excellent for GAIS, periorbital wrinkling, nasolabial folds, skin laxity and sagging of jowls, and dyschromia, at 0.87, 0.87, 0.89, 0.87, and 0.80, respectively.

Global esthetic improvement score

The mean clinical improvement and the Global esthetic improvement score (GIAS) rated by our evaluators are demonstrated in Table 1. Although less obvious in the first sessions of treatment by both lasers, the Global esthetic improvement was achieved in all of our patients at the three-month follow-up visit after the last treatment.

Objective assessment of various regions

As depicted in Table 2, both lasers led to significant improvement of periorbital wrinkling, nasolabial folds, dyschromia and skin laxity and sagging of jowls compared to the baseline without significant difference in their efficacy (Figs. 1, 2 and 3).

Patient satisfaction

The patient satisfaction rate is demonstrated in Fig. 4. One month after the first treatment the mean percentages of patient satisfaction following Er:YAG and Nd:YAG lasers were 32.92% ± 13.9 and 30.83% ± 14.72, respectively (p value = 0.510). One month after the second treatment, patients' satisfaction for Er:YAG laser treated area was 36.25% ± 13.4 vs. 34.80% ± 14.47 (p value = 0.666) for Nd:YAG treated area. The patient satisfaction scores were not statistically significantly different between the two lasers at any follow-up visit.

Cutaneous resonance running time (CRRT)

Alteration in CRRT is shown in Fig. 5. The mean CRRT of the side that underwent Er:YAG laser treatment reduced from 944.04 AU ± 200.83 at baseline to 856.80 AU ± 176.30 at

Table 1 GAIS score following treatment

	1 month number of participants (percentage)		1 months after second treatment number of participants (percentage)		3 months after third treatment number of participants (percentage)	
	Erbium	NdYAG	Erbium	NdYAG	Erbium	NdYAG
Worse	–	–	–	–	–	–
No response	5 (20%)	5 (20.8%)	–	–	–	–
Improved	18 (72%)	18 (75%)	15 (60%)	16 (64%)	9 (36%)	9 (36%)
Much improved	2 (8%)	1 (4.2%)	10 (40%)	9 (36%)	13 (52%)	14 (56%)
Very much improved	–	–	–	–	3 (12%)	2 (8%)

Table 2 Mean clinical improvement in each segments of the face following laser rejuvenation

	1 month			1 month after second treatment			3 months after third treatment		
	Erbium	Nd:YAG	*p* value	Erbium	Nd:YAG	*p* value	Erbium	Nd:YAG	*P* value
Periorbital (%)	16.60 ± 6.5	16.25 ± 5.5	0.493	21.20 ± 7.2	21.20 ± 6.1	0.987	25.80 ± 7.9	26.80 ± 8.4	0.395
Nasolabial (%)	16.40 ± 6.2	17.71 ± 6.7	0.033	21.40 ± 7.1	23.20 ± 7.0	0.059	25.60 ± 5.6	28.00 ± 8.9	0.069
Dyschromia (%)	19.40 ± 7.5	20.00 ± 7.6	0.328	25.20 ± 8.1	26.00 ± 7.0	0.294	31.00 ± 8.9	31.20 ± 7.5	0.802
Skin laxity and sagging of jowls (%)	17.60 ± 6.6	19.58 ± 7.3	0.009	24.00 ± 5.4	25.20 ± 6.2	0.136	29.40 ± 5.8	30.40 ± 6.7	0.327

Data are presented as mean standard ± deviation

p value analyzed by linear mixed model

1 month; however, the difference was not statistically significant (p value = 0.146). Further, reduction was observed at 1 month after the second treatment (696.96 AU ± 157.81) and 3 months after the final treatment (535.28 AU ± 205.26) (p value < 0.001).

On the Nd:YAG treated side, after 1 month, the mean CRRT reduced from 958.68 AU ± 262.59 at baseline to 813.25 AU ± 244.25 (p value < 0.001). Further, reduction was observed 1 month after the second treatment (663.84 AU ± 256.66, p value < 0.001) and 3 months after the final treatment (582.12 AU ± 236.45, p value = 0.109). Linear mixed model analysis of the difference of each laser during the follow-up demonstrated that Er:YAG laser had led to a lower value of CRRT compared to Nd:YAG laser (mean difference = −101.42 ± 43.88, CI 95% = −188.19, −14.65; p value = 0.022).

Side effects

Overall, both lasers were relatively safe since no serious or persistent complications, such as prolonged erythema, pain, dyspigmentation, or scarring, developed in the participants. The mean downtime for the side that was treated with fractional Er:YAG was 6.52 ± 2.25 days after the first treatment, 6.52 ± 1.65 days after the second treatment and 6.39 ± 1.78 after the third treatment, with erythema and edema being the most frequently reported side effects.

The mean downtime for long pulse Nd:YAG-treated area was less than a day after each treatment. Mild pain and transient erythema were the two main discomforts associated with this treatment. Hence, downtime was significantly lower on the side that was treated with long pulse Nd:YAG (p value < 0.0001).

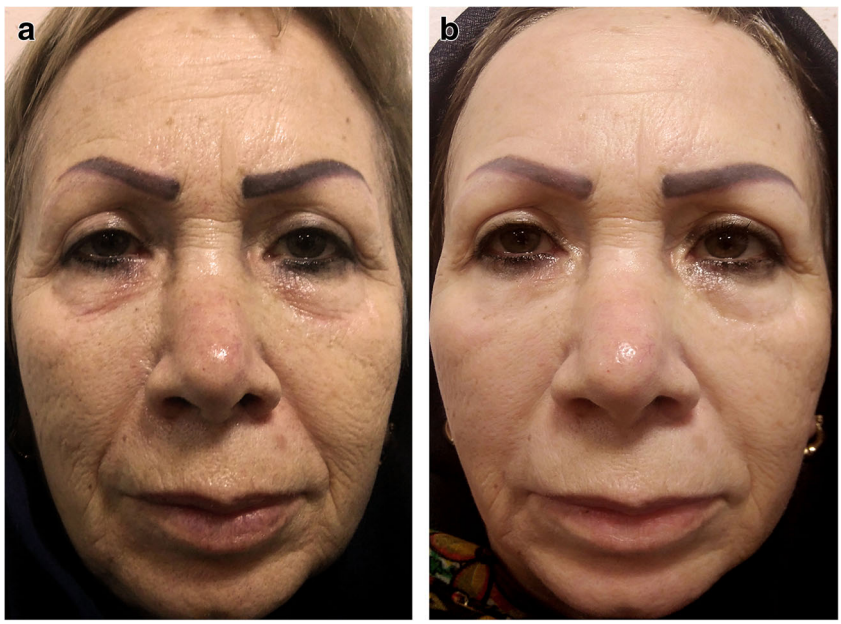

Fig. 1 Improvement of GAIS after laser treatment in a 62-year-old woman, left side (long pulse Nd: YAG), right side (fractional erbium:YAG laser). **a** Before treatment; **b** 3 months after final treatment

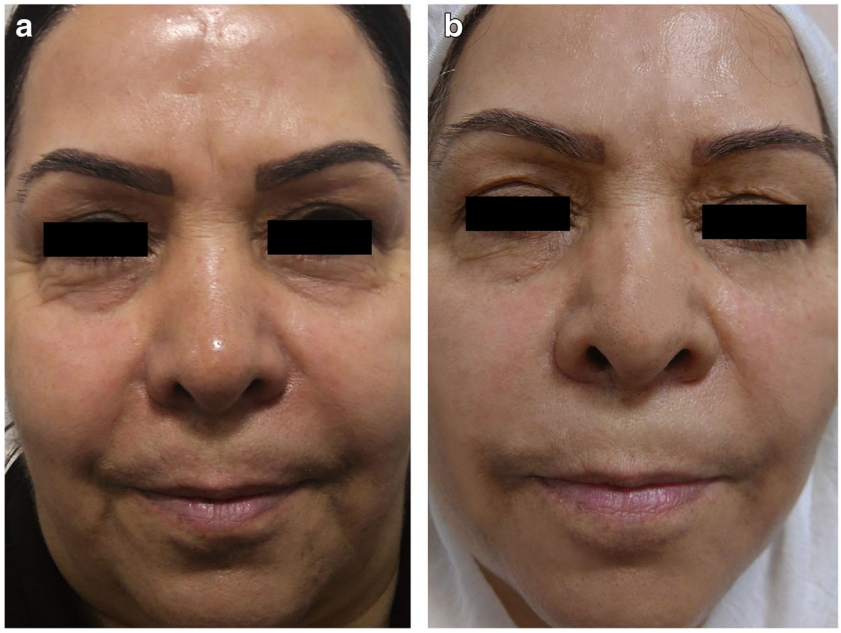

Fig. 2 Improvement of dyschromia, nasolabial fold, periorbital wrinkles, and lower face sagging after laser treatment in a 61-year-old woman, right side (long pulse Nd: YAG), left side (fractional erbium:YAG laser). **a** Before treatment; **b** 3 months after final treatment

Discussion

Laser resurfacing is a mainstay in facial rejuvenation that may be ablative, non-ablative, or fractional [13]. The fractional photothermolysis devices such as Er:YAG were developed to reduce the side effects caused by ablative lasers [14]. Non-ablative laser resurfacing with Nd:YAG has been shown to produce favorable but moderate improvement with minimal downtime and complications [15]. In a recent study, we compared the efficacy of these lasers on hand wrinkles and we found mild to moderate improvement of hand wrinkles with no significant difference or considerable side-effects between these laser systems [16]. The current study confirms the efficacy of fractional Er:YAG and long pulse Nd:YAG lasers in the improvement of Global Esthetic Improvement Score (GIAS), periorbital wrinkling, nasolabial folds, dyschromia and skin laxity and sagging of jowls rejuvenation with no considerable difference.

Previous studies have indicated the considerable efficacy of fractional Er:YAG laser in skin resurfacing [17, 18]. In our previous study, we demonstrated the comparable efficacy of fractional Er:YAG and fractional CO2 lasers in the treatment of facial wrinkles [6].

In an early study, 1064-nm Nd:YAG laser led to the subtle and gradual improvement of coarse wrinkles, skin laxity and overall improvement after 5 treatments [8]. The study by Goldberg et al. compared intense pulse light device and the 1064 nm Nd:YAG laser, demonstrating comparable improvement in rhytid reduction, while the 1064-nm Nd:YAG laser was associated with fewer complications and better patient tolerance [19]. Taylor and Prokopenko also observed a more favorable result after a one-session treatment with long pulse

Fig. 3 Improvement of lower face sagging and swallow color of the aged face after Nd:YAG laser treatment in a 68-year-old woman. **a** Before treatment; **b** 3 months after final treatment. **c**, **d** The other side of the face of the patient that shows Improvement of skin wrinkle and appearance after treatment with Er:YAG. **c** before treatment; **b** 3 months after final treatment

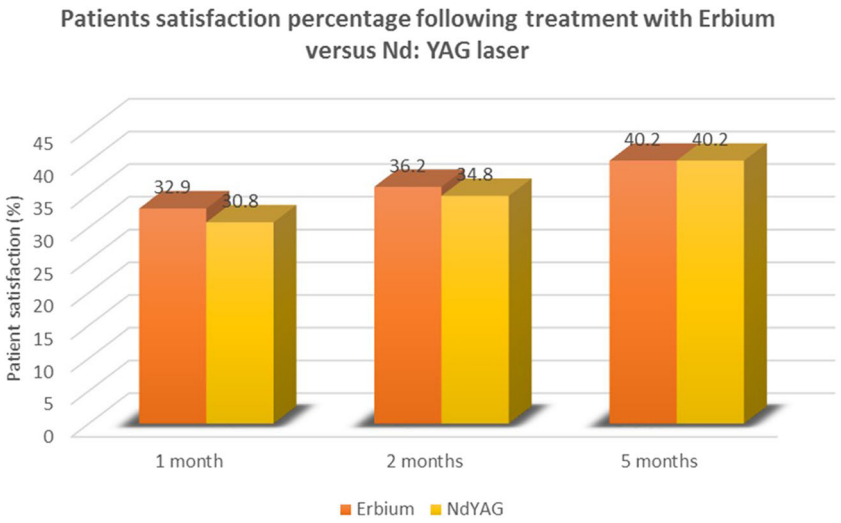

Fig. 4 Patients satisfaction (%) following treatment of erbium vs NdYAG laser

Nd:YAG [20]. Our study showed significant improvement of GIAS, periorbital wrinkling, nasolabial folds, dyschromia and skin laxity and sagging of jowls after 3 sessions of treatment with long pulse Nd:YAG. The efficacy of long pulse Nd:YAG was initially higher than that of fractional Er:YAG laser in the improvement of nasolabial folds and skin laxity and sagging of jowls; however, this result was not maintained until the last visit. Moreover, no persistent adverse effects were observed with these lasers, but we found significantly lower downtime period with long pulse Nd:YAG laser.

There have been comparative studies to investigate the safety and efficacy of non-ablative laser versus fractional Er:YAG for purposes other than rejuvenation [21, 22]. Recently, the combination of ablative and non-ablative laser resurfacing has been proposed as an attractive option for facial rejuvenation. The study by Cohen et al. demonstrated that facial rejuvenation using a combination treatment of fractional ablative 2940 and nonablative 1440 lasers provide an improvement in wrinkles and dyspigmentations similar to that achieved in purely ablative approaches [23].

It should be noted that the evaluator in our study evaluated pigmentary changes of aging rather than lentigines simply. These changes include lentigines, loss of translucency, and a sallow color [24]. Therefore, the improvement of dyschromia in our study may mainly include the improvement in translucency and yellow-gray color of skin.

Sun-induced molecular effects are primarily located in the dermis the dermoepidermal junction [25]. Nd:YAG laser induces dermal changes and, therefore, has a beneficial role in dermal changes of photoaging. Hence, it is rational to believe that dermal changes as the result of laser treatment were responsible for the improvement in dyschromia scores.

As we demonstrated in our previous studies, measurement of cutaneous resonance running time (CRRT) is a non-invasive method to evaluate skin biophysical property [6, 12, 16]. CRRT associates inversely with skin stiffness and varies with age, body regions, and gender [11]. We used CRRT assessment as an additive measure to objectively evaluate the laser efficacy. In our study, mean CRRT values

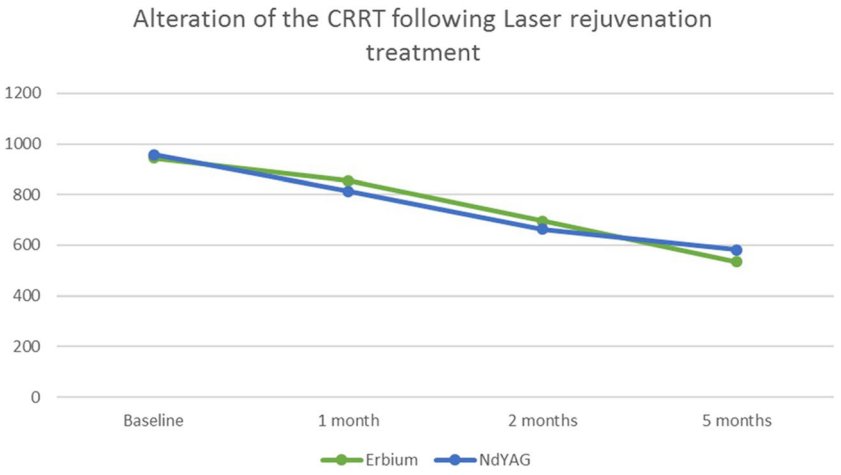

Fig. 5 The alterations of the CRRT following laser rejuvenation treatment in Er:YAG and NdYAG laser treated area

declined significantly after treatment in both laser groups but the reduction was greater for the side that was treated with Er:YAG.

As with any study, there were some limitations in ours. Most significantly, none of our participants volunteered to undergo a facial skin biopsy in order to accurately investigate and compare the efficacy of these modalities by assessing the laser-induced neocollagenesis. Moreover, it was only possible for us to enter a limited number of participants and could not use these lasers in combination due to some restrictions in the facilities and the duration of the study. Further studies with larger sample size, a combination of both lasers and histopathology evaluation of neocollagenesis after laser treatment would be more advantageous to shed light on the optimal laser modality for facial rejuvenation either used alone or in combination.

All in all, our study seems to have several novelties since it is a distinctive prospective, randomized clinical trial using skin biomechanical evaluation along with a meticulous clinical assessment of various regions of the face to compare the efficacy and safety of long pulse Nd:YAG and fractional Er:YAG laser in the facial rejuvenation. Additionally, in spite of the earlier concept that considered fractional ablative laser to be superior to non-ablative lasers, our study demonstrated similar safety and efficacy in these two modalities by subjective and objective measurements. Both laser systems seem to be safe and effective options for facial rejuvenation. However, non-ablative lasers such as long pulse Nd: YAG has minimal to no downtime and they can be more favorable choices for facial rejuvenation in today's busy societies.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval This study was approved by the Ethical Committee of Shahid Beheshti University of Medical Sciences with number of Ir.sbmu.ram.rec.1394.418. This project was performed according to the principles of the Declaration of Helsinki. The protocol was approved by the Iranian Registry of Clinical Trials (IRCT2015120320468N3).

Informed consent All of the subjects signed a written informed consent after explanation of the procedure.

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