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RESEARCH

Fractional Q-switched Nd: YAG 1064 nm laser treatment improves facial skin quality with zero downtime

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Abstract

This study aimed to conduct a dose-ranging assessment of the cavitation potential of a fractional Q-switched Nd: YAG laser system and then to assess its skin rejuvenating effect on photoaged facial skin. Abdominal skin samples were subjected to increasing doses of laser energy (300–2400 mJ/p). The optimal dose range was then applied in a trial in which 36 female subjects with Glogau scale type 1–3 facial skin wrinkles underwent four laser treatment sessions. The investigator assessed changes in fine lines, skin tone, tightness, and texture, and three blinded assessors rated changes in overall appearance 1 and 3 months after the last session. Subjects rated pain, downtime, and satisfaction with outcomes. Cavitation in the subepidermal layer was noted in all abdominal samples subjected to medium or high laser settings. Optimal-dose laser treatments resulted in improved (27.8%) or much improved (72.2%) facial wrinkles within 3 months of treatment. By 3 months post-treatment, the investigator noted ≥ 3-point improvements in skin tone, tightness and texture in all subjects. Subjects reported on a pain-free experience, zero downtime, and high satisfaction (94.4%). Fractional Q-switched 1064 nm Nd: YAG laser therapy can refine skin texture, tone, and overall appearance, with no pain or recovery time.

Keywords Fractional q-switched laser · Nd:YAG 1064 nm laser · Facial skin quality · Wrinkles

Introduction

Skin aging, both intrinsic and photoaging, results as dermal collagen degradation and epidermal thinning with resultant wrinkles and textural changes. Laser therapy has become an important component of non-surgical facial rejuvenation, providing an alternative to surgery. Among the modalities used, the neodymium-doped yttrium aluminum garnet (Nd: YAG) laser has particular advantages since it reaches deeply into the dermis without injuring the epidermis. Water absorption, hemoglobin, and melanin lead to selective thermal effects with fibroblast stimulation, collagen contraction, and dermis remodeling [1, 2, 3]. Q-switched lasers emit ultra-short pulses of high-peak-power that create photomechanical effects with minimal thermal build-up. Originally used for pigment targeting, they have yielded promising results for rejuvenation when they are used in fractional or low-fluence modalities. For example, in a split-face trial involving 20 patients, more improvement in post-acne scars was demonstrated with 1064 nm Q-switched Nd: YAG compared with fractional CO_2 (33.3% vs. 17.4% reduction in Sharquie scores) [4]. Comparable wrinkle improvement was achieved with Nd: YAG and Er: YAG lasers, with significantly less downtime in the former (< 1 day vs. ~ 6 days) [5]. Fractional technology is a significant advancement, delivering energy to microscopic treatment zones (MTZs) without uniformly heating the

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entire surface [6]. Fractionated Q-switched Nd: YAG creates accurate dermal microinjuries that are surrounded by uninjured tissue to allow quick recovery, reduce the likelihood of complications, and maximize comfort during therapy without the use of anesthesia [7, 8]. A pilot study employing a fractional non-ablative Q-switched Nd: YAG (Pixel QS, Alma Lasers) realized a diminishment of rhytids by 11.3% after ~ 2.6 sessions with no pain and transient erythema only [9]. According to this information, the present prospective, single-centre study examined a fractional Q-switched Nd: YAG laser device for facial wrinkle treatment in 36 women. The parameters of treatment were selected following *ex vivo* histological dose-ranging analysis of human abdominal tissue.

Patients and methods

Ex vivo dose-ranging and histological analysis

An *ex vivo* acute-response investigation was conducted using a human abdominal skin explant obtained from a consenting 46-year-old, healthy, non-smoking female (Fitzpatrick skin type III) undergoing abdominoplasty, as approved by the Ethics Committee of Shamir Medical Center (approval #0085-24-ASF). Immediately after surgery, specimens of the skin explant was treated with the Alma Harmony/ClearLift Pro 5 × 5 (Alma Lasers Ltd., Caesarea, Israel), set to "Low" (300 mJ/p), "Medium" (1500 mJ/p), or "High" (2400 mJ/p) ($n = 8$ per treatment), and to one of two accumulated energy settings of 500–800 J per 20 cm^2 grid ($n = 4$ samples per setting), delivered in stack mode. Following laser treatment, samples were trimmed, embedded in paraffin, sectioned, stained with hematoxylin and eosin (H&E), and viewed under a Nikon Eclipse E200 microscope (Nikon, Tokyo, Japan). Histology slides were examined under an Olympus light microscope BX43, ToupCam, XCAM4K8MPB, 4 K HDMI, Industrial digital camera with software ToupView.

Clinical study

This single-centre study was conducted in accordance with the current revision of the Declaration of Helsinki and was approved by the Albanian Ministry of Health and Social Protection Deputy Minister Ethics Committee. Signed informed consent was obtained from each subject prior to initiation of any study-related procedures. Participants underwent four Alma Harmony/ClearLift Pro 5 × 5 treatment sessions performed at 4-week intervals with standard laser safety precautions, and attended two follow-up visits, held 4 and 12 weeks after the last treatment session.

Subjects

Females between the ages of 35 and 55 years, with Glogau scale types 1–3 facial skin wrinkles, and in generally good health, were eligible to participate in the study. Subjects committed to avoid tanning and other facial procedures throughout the entire course of the treatment and follow-up periods. Exclusion criteria included women with any of the following: an active infection (including cellulitis), inflammatory skin condition, history of cancer, immunosuppression, collagen vascular disease, thrombocytopenia, peripheral vascular disease, melasma, keloid or hypertrophic scarring. Additional exclusion criteria were tanning within the past 30 days, prior treatment in the target area, use of oral retinoids within the past 6 months, prior surgical procedures or tattoos in the target area and current pregnancy or lactation.

Laser treatment

The investigational device was the Alma Harmony/ClearLift Pro (Alma Lasers, Caesarea, Israel), a Q-switched 1064-nm Nd: YAG module; treatments used the Multi-Depth Pixel 6 × 6-mm (5 × 5-pixel) fractional spot geometry (25 pixels/shot; fixed pattern). All treatments were delivered by the first author (A.A.) using the in-motion mode (continuous movement across the treatment field), with parameters selected by anatomic region. All necessary precautions were taken, and laser protection goggles were worn by the subject and personnel. The procedure was well tolerated, with no need for pre-treatment anesthetics. After evaluation of the facial skin and determination of the treatment goals, one of two treatment protocols, adjusted to best address collagen remodelling vs. pigmentation, was selected (Table 1).

Table 1 Treatment parameters

Skin type	Focal depth	Energy (mJ/*p*)	Total energy (J) per 20 cm^2 grid	Frequency (Hz)
I-VI	(-2), (-1), (0)	2200–2400	1000–1200	3–4
	(+1), (+2)	1600–2200	800–1000	3–4

Assessments

Clinical imaging was obtained at Screening/Baseline, 1-month follow-up, and 3-month follow-up. Digital images were captured using 2D (Canon Inc., Tokyo, Japan) and 3D (VISIA, Canfield Scientific Inc., Fairfield, NJ) cameras. Photos of the treated areas were collected at baseline and at the two follow-up visits.

2D photography was used for the primary effectiveness endpoint (GAIS at 3-month follow-up vs. baseline by three blinded assessors), and the VISIA 3D imaging system was used in standardized capture mode and was used for the PI's rating of improvement. After each of the four treatments, subjects were asked to rate treatment-related pain using the Numeric Pain Rating Scale (NPRS), with "0" indicating "no", "5" indicating "moderate" and "10" indicating "worst possible" pain. In addition, subjects were asked to report actual downtime, defined as the period of time following the procedure during which they felt uncomfortable, unwilling or unable to appear in public. At the month 1 and month 3 follow-up visits, the investigator evaluated and documented all adverse events and changes in medication intake since the previous visit. Before vs. after photos were compared and improvements in fine lines, wrinkles, skin tone/pigmentation, skin tightness, skin texture, and overall appearance were rated by three blinded assessors (one dermatologist and two plastic surgeons) using the GAIS scale with "1" indicating not at all improved, "2" indicating slightly improved, "3" indicating improved, "4" indicating much improved and "5" indicating very much improved. At the last follow-up visit, subjects were asked to rate their satisfaction with the treatment results, using a 5-point Likert scale questionnaire with "1" indicating very disappointed, "2" indicating disappointed, "3" indicating satisfied, "4" indicating very satisfied and "5" indicating very much satisfied.

Statistical analysis

A sample size of 30 evaluable participants was selected to estimate the primary endpoint. The primary endpoint was the proportion of participants classified as responders at 3-month follow-up relative to baseline, with responders defined as having a Global Aesthetic Improvement Scale (GAIS) rating ≥ 3 (i.e., 3 = Improved, 4 = Much improved, 5 = Very much improved). GAIS is an ordinal categorical scale (1 = Worse, 2 = No change, 3 = Improved, 4 = Much improved, 5 = Very much improved). The endpoint was assessed using standardized 2D photographs and evaluated by three independent blinded assessors. For analysis, the participant-level GAIS score was defined as the median of the three assessors' ratings, and the responder rate was calculated as the proportion with median GAIS ≥ 3. Exact 95% confidence intervals for responder proportions were calculated using the Clopper–Pearson method. Assuming an expected responder rate of ~75%, $n = 30$ provides an absolute precision of ~16% for the 95% CI; allowing for up to 20% attrition, 36 participants were recruited.

All statistical analyses were descriptive. Continuous variables were summarized by mean, standard deviation, minimum, and maximum, and categorical variables by count and percentage. Baseline was defined as the last valid value prior to treatment. No formal hypothesis testing was planned; therefore, no "significance level" statement is included.

Safety and tolerability were assessed throughout the study. Adverse events (AEs) were monitored during the treatment and follow-up periods. Before each treatment session, the treating investigator evaluated and documented any AEs reported since the previous session, and AE assessment was also performed at the follow-up visits. After each treatment session, subjects rated treatment-related pain on a 0–10 Numeric Pain Rating Scale (NPRS). Procedure-related downtime was collected after each session using a standardized definition: downtime was defined as the period following the procedure during which the subject felt uncomfortable, unwilling, or unable to go out in public; downtime (days) was recorded at subsequent study visits.

Results

Abdominal skin explant samples exhibited a dose-dependent response to fractional Q-switched Nd: YAG laser treatment. More specifically, histological analyses identified cavitations in the subepidermal layer, without evidence of epidermal injury, in all tissue sample subjected to medium or high fluence doses (Fig. 1). Across the *ex vivo* parameter screen, LIOB ("cavitation") and thermal injury were recorded per treated grid. In 5×5 mode, LIOB vacuoles were observed in 17/24 grids (70.8%), while thermal injury (ablation and/or coagulation) occurred in 3/24 grids (12.5%). These ex-vivo findings support that pixelated 5×5 delivery can induce dermal LIOB with generally minimal thermal injury within the tested range. Given observation of the desirable effects at the higher energy settings, the doses were later implemented in the clinical study described below.

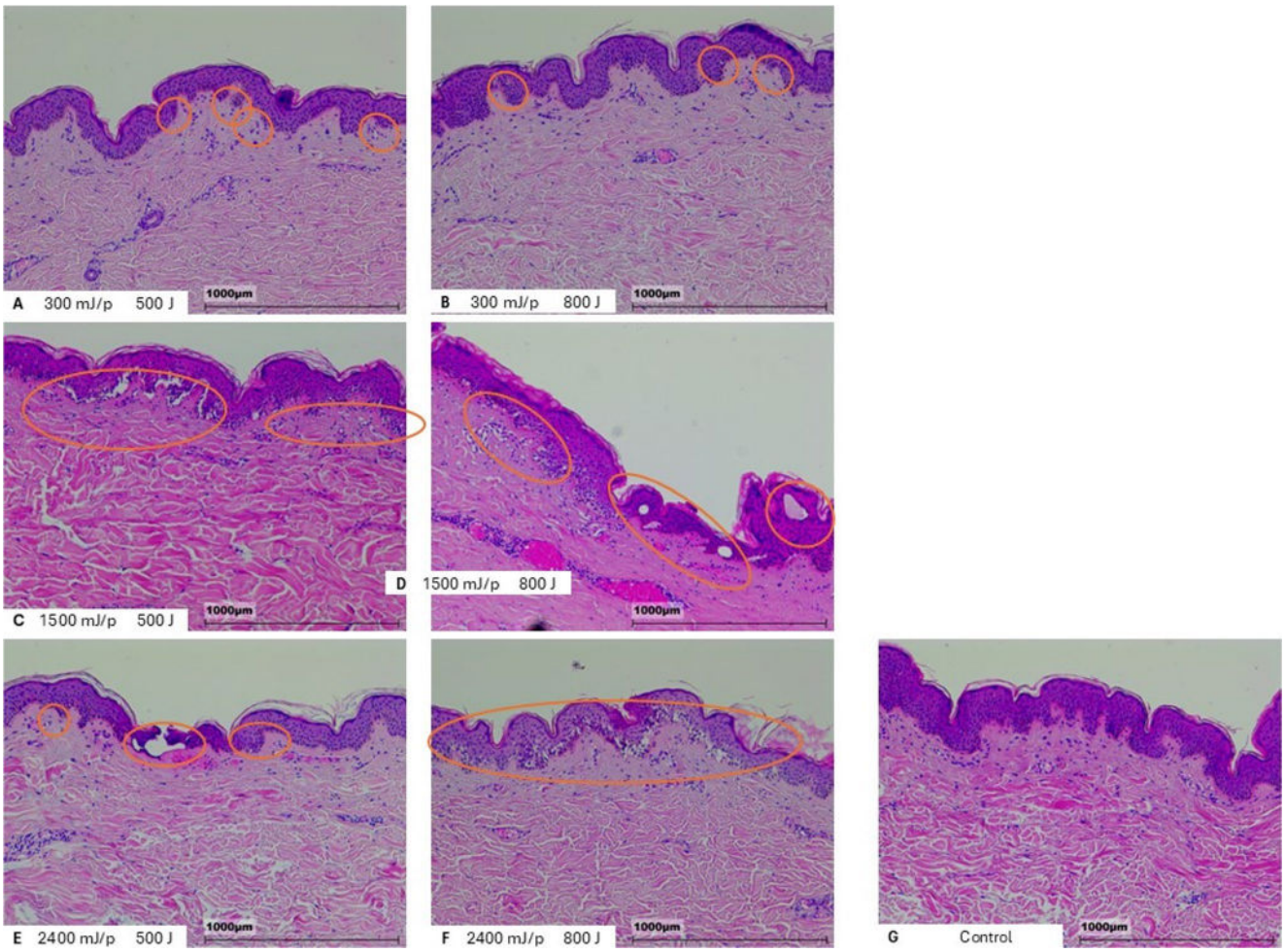

Fig. 1 Histologic analysis of an abdominal skin sample treated with a Q-switched Nd: YAG laser. The samples were subjected to Low **A**, **B**, Medium **C**, **D**, or High **E**, **F**, settings. Circles indicate treatment-induced cavitationslocations. Untreated sample **G** served as control

All 36 enrolled participants successfully completed the entire treatment regimen. The mean age of the participants was 44.2 ± 6.0 years and most subjects had Fitzpatrick skin type III (69.5%) or IV (19.4%) and had never previously attempted to treat their skin wrinkles (88.9%) (Table 2).

At baseline, the majority of subjects presented with Glogau grade 2 (58.3%), while the remaining subjects had grade 1 (19.4%) or grade 3 (22.2%) wrinkles. Treated areas included forehead, cheeks, perioral, mandibular, submandibular, and infraorbital areas. The laser parameters were set to 1200 J/20 cm^2, at a frequency of 3 Hz and focal depths of -2 to + 2 mm for all areas, apart from infraorbital areas, where the total energy delivered was in the range of 1100 and 1200 J/20 cm^2. At session 1, 33 subjects reported feeling no pain, while 3 subjects rated their pain as mild. At the remaining three sessions, all subjects reported a pain-free experience. Additionally, all subjects felt comfortable and willing to go out in public immediately after each session. No adverse reactions were reported throughout the study period.

Median GAIS scores provided by the blinded assessors at the month 3 follow-up indicated improved (27.8%) or much improved (72.2%; 95% CI [54.8%; 85.8%]) facial skin appearance for all subjects (Table 3). At the same time point, the investigator rated fine lines/wrinkles as improved (33.3%), much improved (44.4%) or very much improved (13.9%), with ratings generally similar to those documented 1 month after the last treatment session (Table 3).

Three subjects (8.3%) achieved only a slight improvement in fine lines/wrinkles. At 3 months post-treatment, all subjects showed ≥ 3-point improvements in skin tone, tightness and texture, which were classified as either improved (11.1%, 2.8%, 16.7%, respectively), much improved (41.7%, 58.3%, 50%, respectively) or very much improved (47.2%, 38.9%, 33.3%, respectively) (Table 4).

Table 2 Patient demographics and baseline characteristics

Characteristics	
Age	44.2 (6.0)
Gender (F)	36 (100)
BMI (kg/m^2)	25.2 (3.7)
Skin type	
II	4 (11.1)
III	25 (69.5)
IV	7 (19.4)
Wrinkles Severity (Glogau Scale)	
1	7 (19.4)
2	21 (58.3)
3	8 (22.2)
Medical history	
Tympanus	1 (2.8)
Bisoprolol	1 (2.8)
Hashimoto	2 (5.6)
Hysterectomy	1 (2.8)
Seasonal allergy	1 (2.8)
Previous procedures	
Laser	1 (2.8)
Botox	2 (5.6)
Microneedling	1 (2.8)

Categorical variables are presented as *n* (%) and numeric variables as mean (SD)

Overall appearance was much improved for 63.9% of the subjects, while 22.2% showed an improved and 13.9% a very much improved overall appearance. The vast majority of subjects were very (61.1%) or very much satisfied (33.3%) with treatment outcomes. Representative 3-month-follow-up vs. baseline images are provided in Figs. 2, 3, and 4 below:

Pain scores were minimal across all sessions. At Treatment 1, 33/36 subjects reported NPRS 0, 2/36 reported NPRS 1, and 1/36 reported NPRS 3 (mean 0.14); at Treatments 2–4, all subjects reported NPRS 0 (mean 0 for each session). No procedure-related downtime was recorded (downtime = 0 for all subjects) at the 1- and 3-month follow-up visits, based on the protocol downtime definition above. No adverse events were recorded during the study, and no subjects discontinued due to an adverse event.

Discussion

This pilot clinical trial tested fractional Q-switched Nd: YAG laser treatment for facial wrinkles and associated measures of texture, tone, and tightness in women with Fitzpatrick skin type III–IV. The endpoint was wrinkle severity reduction measured by blinded raters, supplemented by ratings by the treating dermatologist. Clinically significant reduction of fine lines and rhytids was accompanied by enhancement of skin quality and appearance.

Table 3 Treatment outcomes

Test	*n* (%)	
GAIS – blinded assessors, median	Month 3	
1 – Worse	0 (0)	
2- No change	0 (0)	
3- Improved	10 (27.8)	
4- Much improved	26 (72.2)	
5- Very much improved	0 (0)	
GAIS – physician		
Fine lines/wrinkles	Month 1	Month 3
1 – Not at all	0 (0)	0 (0)
2- Slightly	5 (13.9)	3 (8.3)
3- Improved	13 (36.1)	12 (33.3)
4- Much improved	15 (41.7)	16 (44.4)
5- Very much improved	3 (8.3)	5 (13.9)
Skin tone	Month 1	Month 3
1 – Not at all	0 (0)	0 (0)
2- Slightly	1 (2.8)	0 (0)
3- Improved	4 (11.1)	4 (11.1)
4- Much improved	16 (44.4)	15 (44.4)
5- Very much improved	15 (41.7)	17 (47.2)
Skin tightening	Month 1	Month 3
1 – Not at all	0 (0)	0 (0)
2- Slightly	0 (0)	0 (0)
3- Improved	2 (5.6)	1 (2.8)
4- Much improved	20 (55.6)	21 (58.3)
5- Very much improved	14 (38.9)	14 (38.9)
Skin texture	Month 1	Month 3
1 – Not at all	0 (0)	0 (0)
2- Slightly	0 (0)	0 (0)
3- Improved	4 (11.1)	6 (16.7)
4- Much improved	22 (61.1)	18 (50.0)
5- Very much improved	10 (27.8)	12 (33.3)
Overall improvement	Month 1	Month 3
1 – Not at all	0 (0)	0 (0)
2- Slightly	0 (0)	0 (0)
3- Improved	8 (22.2)	8 (22.2)
4- Much improved	24 (66.7)	23 (63.9)
5- Very much improved	4 (11.1)	5 (13.9)

Table 4 Patient satisfaction scores

Test	*n* (%)
Satisfaction with improvement	
1 – Not improved	0 (0)
2- Slightly improved	0 (0)
3- Somewhat improved	6 (16.7)
4- Very improved	24 (66.7)
5- Very much improved	6 (16.7)
Satisfaction from treatment	
1 – Very disappointed	0 (0)
2- Disappointed	0 (0)
3- Satisfied	2 (5.6)
4- Very satisfied	22 (61.1)
5- Very much satisfied	12 (33.3)
Will recommend treatment	
1 – Definitely not	0 (0)
2- Perhaps	0 (0)
3- Likely	0 (0)
4- Very likely	6 (16.7)
5- Extremely likely	30 (83.3)

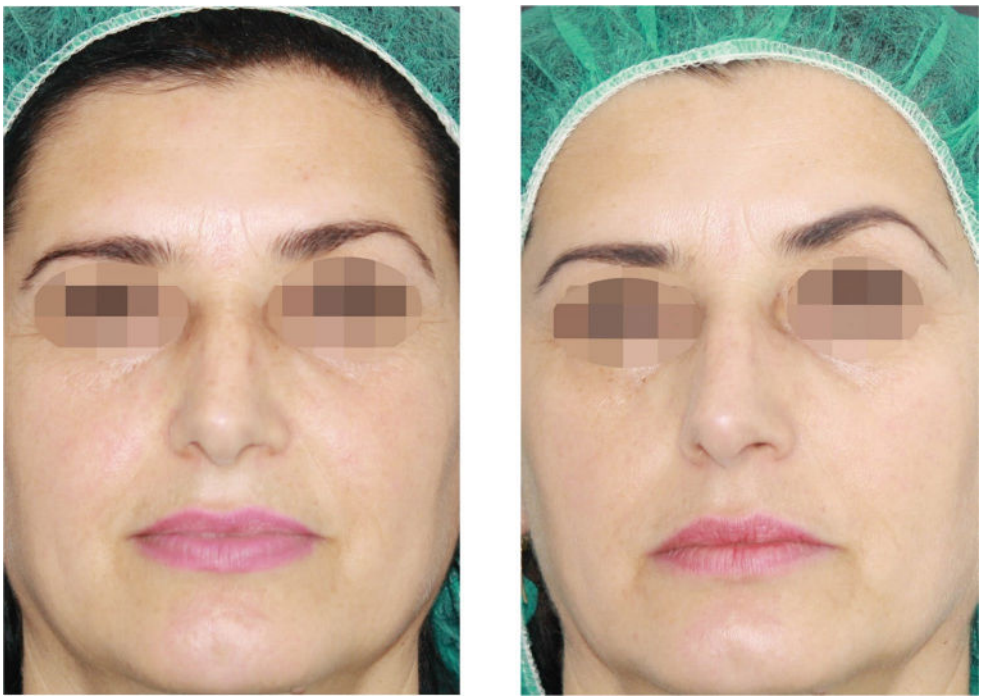

Fig. 2 Digital images of a 47-year-old subject with skin type III before (left) and 3 months after treatment (right), demonstrating reduction in periorbital wrinkles as well as an overall improvement in skin texture

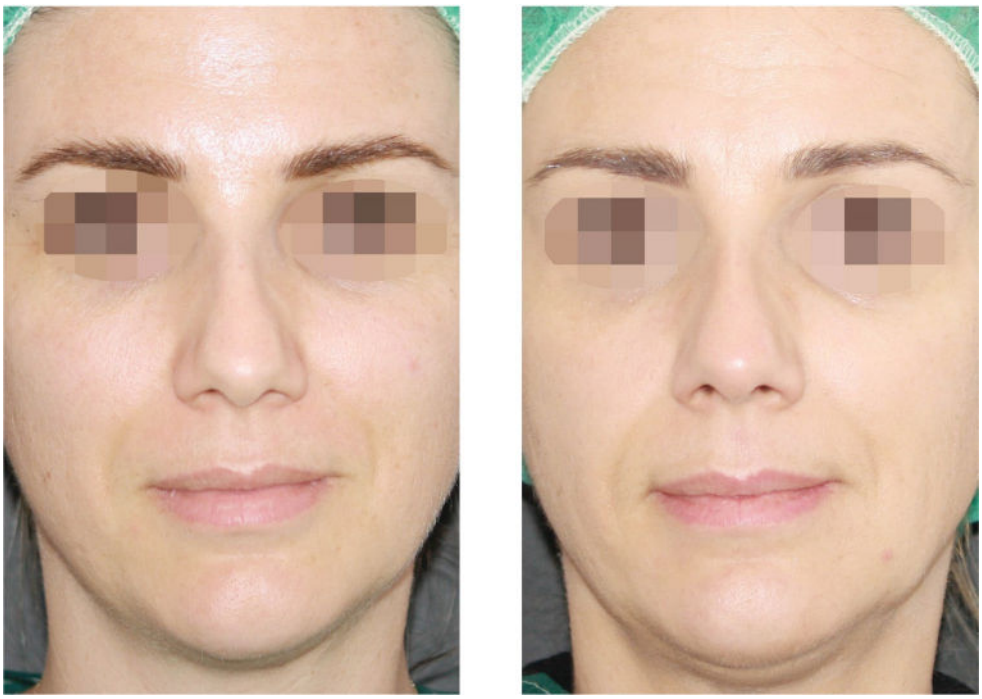

Fig. 3 Digital images of a 37-year-old subject with skin type II before (left) and 3 months after treatment (right), demonstrating reduction in periorbital wrinkles together with an improvement in skin texture

Notably, these improvements were manifested in the high levels of patient satisfaction, with 94.4% of the patients indicating a favourable outcome. While the numerical gains were small, their clinical utility is the discernible aesthetic improvement and patient-reported benefit, especially in groups frequently under-treated by energy-based devices. This study adds to the body of literature by providing data in darker skin phototypes (III–IV), where practitioners are generally cautious in employing lasers due to heightened risk of post-inflammatory hyperpigmentation or scarring. This precaution merely means that these patients have fewer rejuvenation options compared to lighter phototypes. The findings presented are that fractional Q-switched Nd: YAG laser can cause dramatic aesthetic improvement in this group of patients with minimal downtime and pigmentary complications, thereby adding

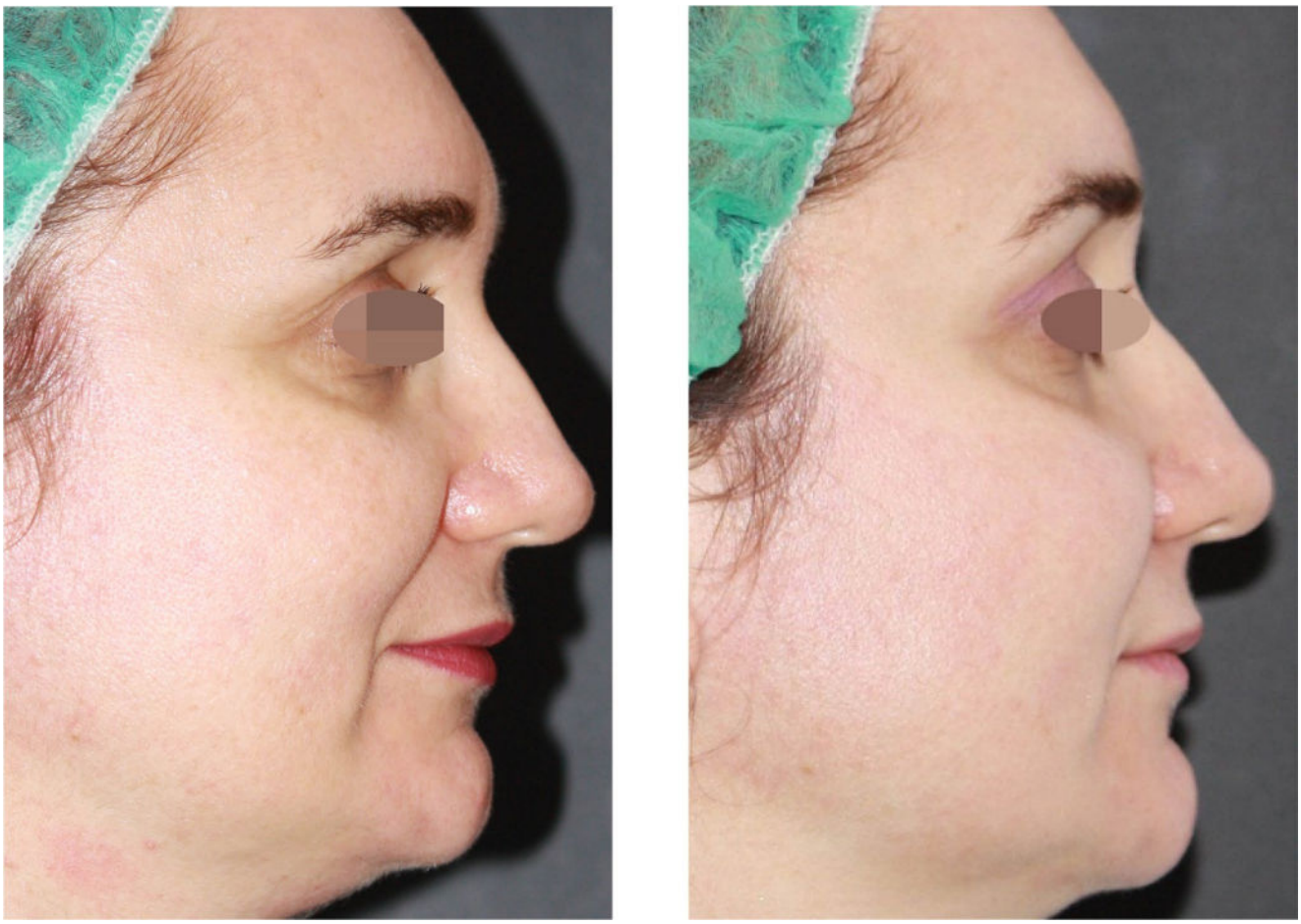

Fig. 4 Digital images of a 42-year-old subject with skin type III before (left) and 3 months after treatment (right), demonstrating reduction in wrinkles, especially in the periorbital and perioral areas

to safe treatment options. It is worthy to mention that Nd: YAG treatments, especially in these skin phototypes, are ideally performed by highly skilled practitioners because severe side effects ensue when inadequately administered treatments. The outcomes agree with earlier studies demonstrating the rejuvenating properties of Q-switched Nd: YAG lasers in various phototypes. Moderate-to-significant improvement of pigmentation, texture, and skin tone was observed in over 90% of Indian patients with skin types III–VI by Agarwal et al. [10]. Reduction of wrinkles, coarseness, pigmentation, and pore size with good tolerance on the part of patients has been observed in other prospective as well as open-label studies [11, 12, 13]. Significantly, the current research reproduces these results in a prospective cohort, as well as further confirms the mechanism of action through histological evidence. The addition of the histological marker presented here strengthens the clinical findings by correlating observed wrinkle reduction with underlying tissue remodelling. The *ex vivo* study was designed to map acute histologic thresholds (LIOB presence and absence of coagulation/ablation) across a broader parameter space (mode, depth, spacer, fluence, accumulated energy) than would be used clinically. Clinically, subjects were treated using the ClearLift Pro 5 × 5 applicator with focal depths − 2 to + 2, frequency 3 Hz, and energy per pulse 2000–2400 mJ/p, with total delivered energy 1100–1200 J per 20 cm² depending on facial region. These clinical choices align with the *ex vivo* observation that the 5 × 5 mode generally produced LIOB with minimal thermal injury.

ex vivo dose-ranging analysis demonstrated laser-induced optical breakdown (LIOBs) and dermal cavitation at clinically meaningful fluences [14]. These microinjuries have been found to trigger collagen denaturation, fibroblast activation, and dose-dependent neocollagenesis. Additional histologic and immunohistochemical examination has proven cavitation, collagen fiber reorganization, and dermal thickening [2, 3, 15, 16, 17]. These changes are accompanied by improved indices of elasticity and supported by molecular evidence of TGF-β/Smad and

MAPK pathway activation, metalloproteinase regulation, and enhancement of principal extracellular matrix proteins [18, 19, 20, 21, 22]. All these processes together explain the clinically relevant wrinkle decrease in our cohort. All patients tolerated treatment and reported the treatment to be painless with no downtime. This was compared with noted discomfort and transient side effects of edema and petechiae with non-fractional treatments [11, 13]. Fractional photothermolysis used here to microscopic treatment zones (MTZs) likely maximized tolerability by sparing intervening skin and reducing nociceptive summation. Noteworthy, aside from CO_2 or thermal ablative lasers, Q-switched Nd: YAG lasers demonstrate a favorable safety record in darker-skinned patients again indicating their utility in this population.

This study has several limitations. The single-arm design without a control or split-face comparator precludes causal attribution of observed changes to treatment alone and does not account for temporal or placebo effects. Follow-up was limited to 3 months, so durability beyond this interval cannot be inferred. Generalizability is further limited by the small, all-female cohort and the predominance of Glogau type II ("wrinkles in motion"), in which the magnitude of achievable change is inherently constrained. The primary endpoint relied on blinded GAIS scoring from paired 2D photographs; although VISIA 3D images were acquired in standardized capture mode for the PI's assessments, standardized VISIA outputs were not used for blinded rating, and residual visit-to-visit variability in 2D capture conditions (e.g., lighting, reflections, and camera angle) may have influenced apparent rhytid severity and GAIS results. Additionally, "downtime" was defined as patient-reported social downtime, which may not capture brief transient post-treatment erythema/edema/petechiae that did not limit social activity, and objective quantitative measures of wrinkle depth/texture were not included. Finally, the *ex vivo* histology was performed on a single abdominal donor sample and reflects acute effects that may not fully generalize to facial skin or long-term remodeling. Larger controlled studies with longer follow-up, broader demographics/phototypes, and objective endpoints are warranted.

In conclusion, in this prospective, single-centre, single-arm study of 36 women, fractional Q-switched 1064-nm Nd: YAG treatment (ClearLift Pro 5 × 5) was associated with short-term improvement in facial rhytides at 3 months. Based on blinded assessment of paired 2D photographs, 72.2% of participants met the prespecified GAIS responder definition (median GAIS ≥ 3). Treatment was well tolerated in this cohort, with minimal patient-reported pain and no patient-reported social downtime as defined; no adverse events were recorded during the study period. These findings are preliminary and should be interpreted in the context of the uncontrolled design and photo-based ordinal outcome; controlled trials incorporating longer follow-up and objective measures are needed to confirm efficacy and durability and to better define safety across a broader range of skin phototypes. Because pigmentary complications such as post-inflammatory hyperpigmentation are more common in darker phototypes, particularly Fitzpatrick IV–VI, careful device/parameter selection remains important when extending energy-based rejuvenation approaches to higher phototypes.

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Author contributions A.A. wrote the main manuscript text and prepared the figures.S.M , Y.N., and A.O. reviewed the manuscript.

Data availability The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations

Ethics approval The study was approved by the Albanian Ministry of Health and Social Protection's Deputy Minister Ethics Committee, approval No. 633/33, and was conducted in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical principles.

Informed consent Informed consent was obtained from all individual participants included in the study. The authors affirm that human research participants provided informed consent for publication of the images in Figs. 2 and 3, and 4.

Financial interests Dr Avdulaj has received research support from Alma Lasers Ltd. All other authors have no relevant financial or non-financial interests to disclose.

Competing interests The authors declare no competing interests.

Clinical trial registration The study was registered in ClinicalTrials.gov, ID NCT06349096, on March 31, 2024.

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