Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Fractional Co_2 Laser for Eyelid and Periorbital Wrinkles and Laxity: Short- and Long-term Clinical Results Using a Standardized Protocol

Justo M. Alcolea

jmalcolea@seme.org

Clínica Alcolea, L'Hospitalet de Llobregat

Irene Pizarro-Egea

IMC-Investiláser

Elena Bonafonte-Márquez

Clínica de Oftalmología Bonafonte

Estefanía Hernández-Torres

Instituto Médico Vilafortuny

Pilar Martín-Santiago

IMC-Investiláser

Pedro A. Martínez-Carpio

IMC-Investiláser

Mario A. Trelles

Instituto Médico Vilafortuny

Research Article

Keywords: Eyelid rejuvenation, Periorbital rejuvenation, Laxity, Wrinkles, Skin resurfacing, CO_2 laser, Fractional photothermolysis

Posted Date: May 6th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9332783/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Objective

Eyelid and periorbital rejuvenation is a common aesthetic concern. This study aimed to describe an original and detailed fractional CO_2 laser protocol and evaluate its efficacy and safety for skin tightening and wrinkle reduction in the upper and lower eyelids and periorbital region, with 12-month follow-up.

Materials and Methods

A single-arm, evaluator-blinded clinical trial was conducted in 27 patients presenting with eyelid and periorbital laxity and wrinkles. All patients underwent a single session of fractional CO_2 laser treatment. Clinical outcomes were assessed at 3, 6, and 12 months using two study-specific grading scales evaluated by two independent expert assessors, along with patient-reported outcomes.

Results

Significant reductions were observed in eyelid and periorbital laxity ($p < 0.0001$) and in fine lines and wrinkle depth ($p < 0.0001$). At 3 months, 74% of patients achieved good overall improvement (50–75% correction; $p < 0.0001$). Improvements were maintained over time with minor variations, including a peak effect at 6 months followed by a slight decline at 12 months. At 12 months, 70% of patients reported being satisfied or very satisfied. No unexpected adverse events or complications were observed.

Conclusion

The protocol described appears to be a safe and potentially effective approach for eyelid and periorbital rejuvenation, associated with improvements in skin tightening and wrinkle reduction, with high patient satisfaction and results generally maintained over at least a 12-month follow-up.

INTRODUCTION

Eyelid and periorbital aging, characterized by laxity, skin redundancy, fine lines, and wrinkles, is a common clinical concern with significant aesthetic impact. Management includes conventional surgical techniques, laser therapy, radiofrequency, plasma devices, chemical peels, recombinant human collagen, and hyaluronic acid fillers, frequently combined with botulinum toxin type A for lateral canthal lines. To provide context for this study, we conducted a comprehensive review of these techniques, with a particular focus on approaches using fractional ablative lasers.[1–35]

Fractional ablative lasers (CO_2, Er:YAG) achieve effective periorbital skin tightening with shorter recovery times and reduced anesthetic requirements compared with conventional surgery, demonstrating

moderate-to-high efficacy and patient satisfaction in mild-to-moderate dermatochalasis.[9] In contrast to early non-fractional ablative lasers, which were limited by prolonged downtime and higher complication rates[14,15], fractional CO_2 systems based on fractional photothermolysis[16] provide comparable rejuvenation outcomes with a more favorable safety profile.[17–19] Fractional CO_2 laser shows particularly superior results in the treatment of fine periorbital wrinkles[10–13] due to dermal tightening and texture improvement, histologically evidenced by increased collagen deposition.[19,20]

Despite widespread clinical use in private practice, published data on fractional CO_2 eyelid rejuvenation remain limited, with heterogeneous protocols hindering comparative analysis. This study describes a standardized fractional CO_2 laser protocol for upper and lower eyelid and periorbital area rejuvenation and evaluates its short- and long-term efficacy in skin tightening and wrinkle reduction.

MATERIAL AND METHODS

A single-arm, evaluator-blinded clinical trial was conducted between November 2022 and March 2025, involving 30 patients with varying degrees of eyelid laxity and wrinkles. The study was carried out at Clínica Alcolea (Barcelona, Spain) in accordance with the ethical principles of the Declaration of Helsinki and with the approval of the Ethics Committee of the Instituto Médico Vilafortuny (Cambrils, Tarragona, Spain). Patients were included if they presented with objective signs of eyelid and periorbital aging, provided written informed consent for participation, and had not undergone previous surgical blepharoplasty or any other medical or surgical procedure involving the eyelids (e.g., laser, radiofrequency, intense pulsed light, chemical peels). Patients signed informed consent regarding publishing their data and photographs.

The authors have no relevant financial or non-financial interests to disclose and have no conflicts of interest to declare that are relevant to the content of this article. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. The authors have no financial or proprietary interests in any material discussed in this article and have no conflicts of interest to declare that are relevant to the content of this article.

Exclusion criteria included severe dermatochalasis with eyelid folds less than 1 mm from the lash line, malar festoon, eyelid ptosis secondary to levator dysfunction, deep nasojugal groove, marked orbital fat prolapse, and complex periorbital defects related to advanced aging, as well as aesthetic concerns not amenable to this technique. Additional exclusions comprised connective tissue disorders, hypersensitivity to local anesthetics, and organic or psychiatric conditions that could compromise outcome evaluation. Written informed consent for the publication of clinical photographs was obtained from all participants.

Treatment protocol

All procedures were performed by the same physician, with extensive experience in the technique, who did not participate in outcome assessment. Topical anesthesia was applied using a compounded preparation containing lidocaine 7%, prilocaine 7%, and tetracaine 4%, ensuring broad coverage of the periorbital area in both eyes, with meticulous application over both eyelids. Prior to the procedure, two drops of topical ophthalmic anesthetic were instilled in each eye to facilitate placement of ocular protective shells (Cox II eye shields, Oculoplastik Inc., Montreal, Canada).

Treatment was performed using a CO_2 laser (10.600 nm) (CO_2RE, Syneron Candela Inc., Irvine, CA, USA). The device was set to fractional ablative mode for each energy-delivery pass, utilizing various emission patterns or shapes. Parameters and dosimetry were preselected from the system console without the need to change the handpiece. The degree of eyelid laxity and wrinkling in each patient was considered to optimize the energy delivered during each pass. Program settings, working spot sizes and shapes, coverage percentage, peripheral ring and central zone fluence, and fluence per pattern are summarized in Table I.

Laser application began on the upper eyelids, immediately below the eyebrow line, using “Fusion” and/or “Deep” patterns, with higher energy delivery in this area to induce greater tissue contraction. As treatment approached the free eyelid margin (pretarsal skin) and lash line (tarsal area), progressively lower energy levels were applied using more superficial patterns on both eyelid borders. The same sequence was applied to the lower eyelids but in reverse order. Energy delivery was reduced in the lateral third of the lower eyelid to avoid undesirable retraction of its outermost portion (Fig. 1). Finally, a gradual tapering of laser energy was applied to avoid external demarcation lines. The treated area ranged approximately from 95 to 105 cm², depending on each patient’s facial dimensions. This surface was estimated using an elliptical model to highlight a broader treatment area compared with other eyelid rejuvenation treatments.

Figure 1 illustrates the laser treatment approach following the described methodology. “Fusion” mode was used in areas immediately beneath the eyebrows—avoiding hair damage—and on the lower eyelid. “Deep” mode enabled fractional energy delivery to the deeper dermis, promoting tissue tightening, particularly in areas with pronounced wrinkles. “Mid” mode was applied to the free eyelid skin to improve laxity and wrinkles, while “Light” mode was used progressively closer to the lash line. Detailed dosimetric parameters are presented in Table I.

At the level of laser–tissue interaction, according to manufacturer technical specifications, the system organizes its parameters according to depth, delivery pattern, and energy density, adapted to the periorbital region being treated: the Deep mode uses a 9 × 9 mm spot and may reach depths of up to 800 µm through ablative columns delivering 41 mJ per microbeam and 283 J/cm² per pulse, and would be intended for thicker skin areas; the Fusion program combines Mid-type impacts with central Deep columns, potentially producing a simultaneous effect at different tissue levels; the Mid mode may reach up to 500 µm with a fractional pattern of 30% coverage over a 7.2 × 8.2 mm area, delivering 125 mJ per ring and 292 J/cm² per pulse, and would be applied to intermediate regions; and the Light programs

operate more superficially (250–350 μm) using circular fractional patterns on thinner skin. Overall, this framework is broadly consistent with descriptions in the literature on ablative fractional lasers such as CO_2 and Er:YAG systems, where parameters including energy per microcolumn, coverage density, and ablation/coagulation depth are adjusted according to the clinical objective; in this context, the different modes may be interpreted as integrated parameter configurations, whereas in other platforms these variables are typically presented more explicitly and require greater manual selection by the operator.

Standardized postoperative care instructions were provided to all patients, detailing the expected course of wound healing and the specific topical treatments to be applied at each stage of recovery. During the first postoperative week, and until crust detachment, patients applied a topical ophthalmic ointment containing chloramphenicol (10 mg/g) and dexamethasone (0.5 mg/g) (Oftalmolosa Cusí de Icol®) over the treated periorbital area. After re-epithelialization (approximately day 7), this regimen was discontinued. From that time point onward, patients initiated a non-retinoid, non-hydroquinone depigmenting agent (Brightalive®, ZO Skin Health, Irvine, CA, USA) in combination with continuous broad-spectrum photoprotection for 3 months. The use of corrective cosmetic products was allowed from the same time point to mask residual erythema.

Outcome Assessment

Standardized clinical digital photographs were taken in frontal view, with eyelids open and closed, before treatment and at 3, 6, and 12 months after completion of the procedure. Open-eye photographs were prioritized for clinical and aesthetic evaluation and are those typically presented in this type of research. However, for study purposes, closed-eye photographs were also obtained, as they allowed visualization of the treated upper eyelid skin and provided complementary information regarding wrinkle dynamics during assessment.

All photographs of each patient were reviewed and evaluated on a computer screen by two independent physician assessors, both experts in orbital rejuvenation who were not involved in the design or execution of the study. Scores were assigned jointly and by consensus, following meticulous observation and evaluation of every detail. Upper eyelid and periorbital laxity and wrinkle severity in both eyelids were assessed using a discrete 5-point qualitative ordinal periorbital aging scale (0–4), as follows: grade 0 (none), no detectable eyelid laxity and smooth periorbital skin without visible wrinkles; grade 1 (mild), minimal laxity with approximately 1 mm descent of the upper eyelid fold, accompanied by fine, superficial wrinkles without skin redundancy; grade 2 (moderate), definite laxity with approximately 2 mm descent of the upper eyelid fold and moderate wrinkles with early skin redundancy; grade 3 (severe), marked laxity with approximately 3 mm descent of the upper eyelid fold and deep, well-defined wrinkles with evident skin redundancy; and grade 4 (very severe), advanced laxity with the upper eyelid fold located ≤ 1 mm above or resting on the lash line, associated with extensive, deep wrinkles, pronounced skin redundancy, and tissue collapse. The periorbital aging scale used, although not previously validated, was selected by the evaluators as part of their routine clinical practice and is specifically suited to the assessment of the periorbital region, integrating eyelid laxity and periorbital wrinkles and textural

changes based on precise and objective anatomical references. Image evaluation was performed in a blinded fashion, with assessors unaware of whether photographs corresponded to pre-treatment, 3-month, 6-month, or 12-month follow-up.

Additionally, to assess the degree of Global Aesthetic Improvement of the periocular area—covering reduction of sagging, laxity, fine lines, wrinkles, as well as improvements in skin texture and visually perceived elasticity—at 3, 6, and 12 months, expert evaluators used a simple discrete ordinal 5-point scale (0–4), as follows: 0: No apparent improvement. 1: Slight improvement (< 25% correction). 2: Moderate improvement (25–50% correction). 3: Good improvement (50–75% correction). 4: Very good improvement (75–100% correction). For each follow-up timepoint, photographs were directly compared with baseline images in a non-blinded manner, to compare pre-treatment photographs with those obtained at each follow-up timepoint.

Adverse events and complications were recorded in the medical records of all patients through clinical examination and anamnesis during follow-up visits and photographic assessment visits. Participants completed three questionnaires administered 30 minutes after the intervention, at the 3-month follow-up, and at the end of the study. The questionnaires included different questions and 10-point Likert scales adapted to each evaluation time point. At 12 months, a final questionnaire was completed to evaluate clinical and aesthetic outcomes, both objective and subjective, consisting of 14 closed-ended (multiple-choice) questions and 2 open-ended questions to capture additional perceptions of interest, together with 3 Likert scales assessing overall experience. At the end of the questionnaire, participants were asked to categorize their level of satisfaction with the treatment using a qualitative ordinal scale with five categories: “Dissatisfied,” “Minimally Satisfied,” “Moderately Satisfied,” “Satisfied,” and “Very Satisfied.”

Statistical Analysis

Given the exploratory nature of the study, no formal a priori power calculation was performed, and no adjustment for multiple comparisons was applied. Sample size and study design were consistent with those commonly used in similar exploratory studies.

Statistical analyses were performed using SPSS software, version 22 (IBM Corp., Armonk, NY, USA). In addition, all inferential analyses were independently reproduced using the R programming language (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria) to verify the results and extend the analysis.

Descriptive statistics were calculated, including arithmetic mean (m) as the measure of central tendency, standard deviation (SD) as the measure of dispersion, and percentages (%) to represent relative frequencies. Differences between pre-treatment and follow-up scores for eyelid and periorbital laxity and wrinkles were analyzed using the Wilcoxon signed-rank test for paired samples. The same test was also used to assess differences between the different follow-up time points. Wilcoxon tests were recalculated in R using the wilcox.test function with the parameters paired = TRUE, exact = TRUE, and correct = FALSE,

thereby obtaining exact p-values based on the Wilcoxon distribution without normal approximation or continuity correction. Effect sizes (r) were calculated from the standardized test statistic (Z/√N) to estimate the magnitude of change. Confidence intervals (95% CI) were computed for mean paired differences. Statistical significance was set at $p < 0.05$.

RESULTS

Twenty-seven patients completed all study evaluations **(**Table II**)**, comprising 24 women and 3 men, with a mean age of 56.5 ± 5.2 years (SD) and Fitzpatrick skin phototypes II (n = 7; 26%), III (n = 15; 56%) and IV (n = 5; 18%). Of the 30 patients recruited, one patient withdrew from the study for reasons unrelated to treatment, and two patients had missing data at one or more follow-up points; these three cases were excluded from the analysis.

Table II details the sample characteristics and the consensus scores assigned by the two evaluators regarding eyelid and periorbital laxity and wrinkle severity at baseline and at 3, 6, and 12 months post-treatment. Statistically significant improvements were observed in both laxity and wrinkle severity at all follow-up time points compared with baseline. Statistically significant improvements were observed in all paired comparisons versus baseline ($p < 0.0001$ at 3, 6, and 12 months).

Regarding changes in laxity, the mean baseline severity score was 2.63 ± 0.5, which decreased to 1.04 ± 0.5 at three months, 0.81 ± 0.4 at six months, and 1.07 ± 0.6 at twelve months (all $p < 0.0001$). Pairwise comparison using the Wilcoxon signed-rank test showed a significant reduction at 3 months ($Z = -4.54$, $p < 0.00001$), with a very large effect size ($r = 0.87$). The mean reduction was − 1.59 (95% CI: −1.78 to − 1.40).

For wrinkle appearance, marked reductions were also documented. The mean baseline severity score was 2.56 ± 0.5, which decreased to 1.15 ± 0.5 at three months, 0.89 ± 0.4 at six months, and 1.15 ± 0.6 at twelve months (all $p < 0.0001$). Pairwise comparison confirmed significant improvement ($Z = -4.31$, $p < 0.0001$), with a large effect size ($r = 0.83$). The mean paired reduction was − 1.41 (95% CI: −1.58 to − 1.24).

At a markedly lower magnitude of change, a borderline result was observed in laxity scores between 6 and 12 months ($p = 0.052$), suggesting a possible trend toward partial regression, although it did not reach conventional statistical significance. On the other hand, wrinkle severity showed a small but statistically significant increase over the same interval ($p = 0.020$, $r = 0.38$), indicating a detectable change of limited magnitude.

Statistical–Clinical Results: The statistically significant result observed in the Wilcoxon signed-rank test ($p = 0.020$, $r = 0.38$) should be interpreted with caution given several inherent limitations. The relatively small sample size may increase variability, and the ordinal nature of the 0–4 scale may either amplify, or attenuate changes influenced by subjective assessment. In this context, the absence of a clear correlation with perceived clinical evolution, together with GAI scale data—which showed no statistically

significant differences between months 6 and 12 and only a trend— suggests that the apparent attenuation of effect at 12 months is likely of limited clinical relevance and should be interpreted as preliminary pending further confirmation. In contrast, sustained efficacy was consistently observed, with highly significant differences in both scales at 12 months compared with baseline ($p < 0.0001$), supporting adequate internal validity within the study design.

With respect to global aesthetic improvement in sagging, laxity, fine lines, wrinkles, skin texture, and visually perceived elasticity, 74% of patients achieved a score of 3 ("good improvement"), corresponding to an estimated overall aesthetic correction of 50% to 75%. Table III summarizes global aesthetic improvement scores at 3, 6, and 12 months. At all evaluated time points, changes relative to baseline remained highly statistically significant ($p < 0.0001$), indicating sustained improvement over time. Within this scale, no statistically significant differences were observed between 3 and 6 months or between 6 and 12 months, despite categorical trends suggesting some degree of regression.

Figure 2 shows Patient 5 (57 y, Fitzpatrick IV). Baseline: marked periorbital wrinkles and upper eyelid laxity, greater on the left. Image B: fine crusts, more adherent left side after higher fluence. At three months (C): upper folds elevated, left more separated from lash line; crow's feet resolved bilaterally. Right eye: complete elimination of lateral and infraorbital wrinkles with reduced laxity. Left eye: > 75% reduction of lateral wrinkles; only faint mixed infraorbital lines remained. Closed eyes (D): smooth, firm, normally colored surface without irregularities; residual wrinkles nearly disappeared with eyelid closure, confirming dynamic origin. Overall outcome: very good (> 75%).

Figure 3 shows Patient 9 (59 y, Fitzpatrick II). Baseline (A): pronounced upper eyelid laxity to lash line and deep bilateral infraorbital wrinkles. Three months (B): wrinkles markedly reduced, skin firm and uniform with only faint creases right and nearly imperceptible left, no sequelae. Results maintained at 6 and 12 months; slightly greater improvement at 12 months due to gaze variation. Upper eyelid laxity improved modestly. Overall outcome: good (50–75%).

Figure 4 shows three six-month results. Top: Patient 6 (64 y, Fitzpatrick III), baseline laxity and grade 3 wrinkles; post-treatment, visible reduction with canthal retraction. Outcome: moderate (25–50%). Middle: Patient 26 (59 y, Fitzpatrick II–III), baseline folds with lentigines and grade 3 wrinkles; post-treatment, improved texture, lentigines resolved, corrected laxity and pronounced wrinkle reduction. Outcome: good (50–75%). Bottom: Patient 25 (54 y, Fitzpatrick IV), baseline elastosis, bilateral laxity, deep infraorbital creases; post-treatment, wrinkles nearly disappeared with smoother contour. Outcome: very good (75–100%).

The treatment was well tolerated. Intraoperative pain was notable but acceptable, with a mean Likert scale (0–10) score of 5.71 ± 1.26. Erythema, edema, and fine crusting were observed in all cases. Edema generally resolved within 5–6 days, with only one patient showing clinically significant persistence at two weeks. Fine crusts developed in the most affected areas on the day following treatment and typically detached between days 7 and 11. Erythema persisted for approximately three weeks, with considerable interindividual variability. Four patients (15%) developed post-inflammatory hyperpigmentation 3–5

weeks after treatment; all cases were mild to moderate, with no severe presentations, as discussed later, and occurred exclusively in Fitzpatrick phototype III individuals. No cases of hypopigmentation, infection, scarring, keloid formation, or other complications reported in comparable studies were observed.

The main patient-reported limitation was the strict recommendation to avoid crust manipulation and the use of makeup during the first week. Five patients (18%) required temporary work leave. The remaining patients resumed their usual daily activities using sunglasses, with temporary social downtime limited to essential interactions. By 7–9 days post-procedure, residual signs of treatment remained but could be effectively concealed with makeup, allowing patients to comfortably resume normal social activities.

At the end of the study, 5 patients (18%) reported being *Very Satisfied* with the outcome, 14 (52%) *Satisfied*, 5 (18%) *Moderately Satisfied*, 2 (7%) *Minimally Satisfied*, and 1 (4%) *Dissatisfied*. Notably, 80% of patients who reported being Moderately Satisfied expressed willingness to undergo an additional intervention for further improvement and stated that they would recommend the procedure to others. Of particular interest, 23 of 27 participants (85%) indicated that they would recommend the intervention to other individuals.

DISCUSSION

Few studies have comprehensively addressed the entire periorbital region, including all four eyelids, despite its relevance for achieving global aesthetic improvement. Most reports focus exclusively on either the upper[16,19,21–23] or lower eyelids[24–26], thereby limiting the assessment of full periorbital rejuvenation. Although some studies using combined approaches have reported favorable outcomes[4,27], only a very limited number of reports have employed protocols comparable to ours, and alternative technologies such as erbium-based combinations cannot be considered equivalent.[28] In this context, our study provides a standardized and reproducible protocol together with a comprehensive evaluation strategy, offering clinically relevant insights.

Treatment resulted in significant early improvements at three months that were sustained over a one-year follow-up period. A peak effect was observed at six months, followed by a slight attenuation at 12 months, although outcomes remained clearly improved compared with baseline. This trend warrants confirmation in larger cohorts using alternative methodologies. Overall, these findings provide meaningful long-term evidence and help address an important gap in the current literature.

Laser treatment of the periorbital region requires high precision due to the thin skin and proximity of critical ocular structures. Fractional CO_2 laser–induced thermal injury triggers an inflammatory cascade followed by tissue repair, associated with predictable adverse effects whose course varies with treatment area and intensity; however, these effects in the periorbital region are inconsistently and poorly reported.[16–19,30–34] In general, within 24–72 hours, progressive erythema, periorbital edema peaking at 48–72 hours, burning sensation, localized heat, skin tightness, and mild serous exudate occur. Microcrusting and superficial epidermal exfoliation begin within 48–72 hours, with shedding around

days 3–5, coinciding with pruritus and re-epithelialization (4–7 days). Edema resolves within 3–7 days (up to 10), whereas erythema may persist for 2–4 weeks. Extraocular complications include post-inflammatory hyperpigmentation, hypopigmentation, dyschromia, cutaneous infections, hypertrophic scarring, burns, ectropion, and palpebral synechiae, as well as rare severe entities such as necrotizing fasciitis or toxic shock syndrome. Ocular complications are less frequent but potentially serious, including conjunctival burns, keratitis, corneal injury, epithelial erosions, transient or permanent visual disturbances, and, rarely, globe perforation.[16–19,30–34]

The Materials and Methods section details the theoretical laser–tissue interaction of our procedure. Clinical experience and knowledge of orbital anatomy guide the use of higher fluences in severely affected regions, with a descending gradient required for safe application to delicate eyelid structures. Of particular interest, delivering energy in parallel bands across each eyelid—with higher fluence in the subciliary upper lid and gradual reduction toward the free margin—appears to optimize results, likely due to greater thermal deposition at the muscular and tendinous framework. However, special caution must be taken to preserve the lateral lower lid (lateral canthal trapezoid) to avoid complications such as scleral show or ectropion[29]. In this series, with the ocular protection employed and adherence to these precautions, the procedure demonstrated a favorable safety profile, with adverse effects consistent with the applied dosimetry, no ocular complications, and only mild extraocular events that resolved without sequelae. The absence of complications reported in other studies (e.g., hypopigmentation, infection, scarring, or keloid formation) represents a favorable finding and may support the safety profile of the protocol. Post-inflammatory hyperpigmentation (PIH) was the most notable complication.

A recent review on PIH following CO_2 laser treatments reports a highly variable incidence (0–100%), primarily attributed to the inflammatory response induced by thermal injury.[35] Notably, no consistent association between Fitzpatrick phototype and PIH risk was demonstrated, suggesting that the traditionally assumed higher risk in darker phototypes may be overestimated.[35] Preventive strategies focus on inflammation control: clobetasol propionate 0.05% significantly reduces incidence (39% vs 75% with emollients), fusidic acid outperforms erythromycin (53.3% vs 91.1%), and adjunctive platelet-rich plasma (PRP) may provide additional benefit.[35] In contrast, other agents have not demonstrated clearly significant efficacy. The authors acknowledge substantial methodological limitations, precluding firm recommendations. Once established, PIH typically requires prolonged treatment with agents such as hydroquinone, retinoids, or glycolic acid, with gradual resolution over several months.[35]

Post-inflammatory hyperpigmentation (PIH) occurred in four patients in our series, all presenting with mild-to-moderate pigmentation. Resolution was achieved within 3 months in three cases, whereas one patient exhibited a markedly prolonged course lasting nearly one year. This delayed resolution was associated with substantial sun exposure, repeated seawater contact, cosmetic camouflage use, and lack of photoprotection or depigmenting therapy, underscoring the critical role of treatment adherence in clinical outcomes. Following appropriate counseling and initiation of 4% hydroquinone combined with adjunctive depigmenting agents and close monthly follow-up, progressive improvement was observed,

with near-complete resolution by 8 months and complete resolution at the final follow-up. All affected patients were Fitzpatrick phototype III, consistent with the predominant phototype in our cohort, thereby precluding meaningful assessment of phototype as an independent risk factor for PIH. Our findings are in line with those reported by Kotlus et al., who described in a prospective cohort (n = 15) re-epithelialization within 4–7 days (mean, 5.2 days) and erythema persisting for 13–40 days, reflecting transient inflammatory responses that may promote melanogenesis.[17] In their study, PIH occurred in 13.3% of patients and resolved within 3 months with topical hydroquinone and strict photoprotection.[17] Collectively, these and other observations support the notion that PIH represents a relatively common and expected complication, particularly in anatomically sensitive areas prone to inflammation and edema, and highlight the importance of early intervention and strict adherence to photoprotective measures to reduce its duration and severity. In our protocol, prevention includes topical dexamethasone (0.5 mg/g) during the first postoperative week followed by a 3-month regimen with a cosmetic, non-pharmacological depigmenting agent. Once PIH developed, all cases responded favorably to 4% hydroquinone combined with adjunctive therapy, highlighting the importance of strict photoprotection and adherence to treatment in limiting persistence.

At 12 months, improvements in eyelid laxity and wrinkle severity remained largely preserved, supporting a sustained clinical effect consistent with collagen remodeling described after fractional CO_2 resurfacing. The applied protocol resulted in clinical improvement in all patients, with the degree of response variability consistent with prior clinical experience. Variability in outcomes despite a standardized protocol may be explained by baseline anatomical and biological differences among patients. In our experience, greater baseline severity may be associated with larger absolute improvements, as patients with more advanced wrinkles or laxity have a wider margin for measurable change; however, these cases often show less complete correction and greater variability in outcomes. In contrast, patients with mild-to-moderate aging typically achieve more uniform, predictable, and aesthetically balanced results, despite smaller absolute changes. It is well known that factors such as dermal thickness, baseline collagen content, degree of elastosis, and individual regenerative capacity influence both the magnitude and durability of improvement, while variability in inflammatory response and fibroblast activity may further modulate collagen remodeling dynamics. As with other energy-based treatments, individual biological variability and intrinsic patient factors remain important determinants of final outcomes.

The overall findings suggest a potentially durable aesthetic benefit. Further long-term studies are warranted to better characterize the longevity of these effects and to define evidence-based intervals for potential retreatment. However, it is important to acknowledge the limitations of this study: its single-center design and the absence of a control group, which may affect the generalizability of the findings. Another limitation lies in the variability of laser dosimetry across different platforms, which may influence reproducibility in other settings. In addition, the assessment scales were specifically designed for this study to better capture the nuances of periorbital rejuvenation, an area not fully addressed by existing standardized tools. While this approach allowed for a tailored evaluation of clinically relevant

changes, it also limits comparability with other reports. Nevertheless, the use of a standardized protocol and consistent evaluation methods provides high internal consistency and strengthens the reliability of the reported outcomes.

In conclusion, fractional CO_2 laser resurfacing of the eyelids and periorbital skin, using the protocol described, is associated with sustained and clinically meaningful improvements in skin laxity, wrinkles, and overall appearance for at least one year. High patient acceptance supports its potential role as a valuable alternative for well-selected candidates seeking correction while avoiding surgery. Future multicenter studies using diverse devices are needed to confirm these long-term observations, refine treatment parameters, and establish consensus guidelines for the optimal use of fractional CO_2 laser in the periorbital area.

Declarations

Funding:

None

Author Contribution

J.M.A. and P.A.M. wrote the main manuscript text.J.M.A. and I.P.E. prepared figures 1-4 and tables I-III.E.B. and M.A.T. evaluated and scored the photographs.P.M.C. and P.M.S. conducted the statistical analysis.All authors reviewed the manuscript.

Acknowledgement

We thank María Alejandra Svensson, Executive Director of Clínica Alcolea, for her key role in patient management and in promoting integration and cooperation among participating centers and authors. We are also grateful to Lucas Trelles-Cohen, BSc (Barts and The London School of Medicine and Dentistry), for his careful assistance with the linguistic revision of this manuscript.

References

1. Rossi Santos Silva K, Cardoso Rossi D, Petroianu A (2021) A new classification of the lateral dermatochalasis of upper eyelids. Plast Reconstr Surg Glob Open 9:e3711. 10.1097/GOX.0000000000003711
2. Barbee PH (2024) Periorbital rejuvenation. Atlas Oral Maxillofac Surg Clin North Am 32:49–55. 10.1016/j.cxom.2023.09.002Epub 2023 Oct 29
3. Russel SM, Clark JM (2023) Periorbital rejuvenation in the clinic: A state-of-the-art review. World J Otorhinolaryngol Head Neck Surg 9:242–248. 10.1002/wjo2.124

4. Wu HH, Chen MQ, Liu JH, Song LL, Luo DQ, Lu JF et al (2024) Combination of fractional carbon dioxide laser with recombinant human collagen in periocular skin rejuvenation. J Cosmet Dermatol 23:124–133. 10.1111/jocd.15942
5. Alghoul M, Blepharoplasty (2019) Anatomy, planning, techniques, and safety. Aesthet Surg J 39:10–28. 10.1093/asj/sjy034
6. Leclère FM, Alcolea J, Mordon S, Servell P, Kolb F, Unglaub F et al (2013) Long-term outcomes of laser assisted blepharoplasty for ptosis: About 104 procedures in 52 patients. J Cosmet Laser Ther 15:193–199. 10.3109/14764172.2012.758385
7. Bonan P, Fusco I, Bruscino N, Madeddu F, Troiano M, Verdelli A et al (2023) Laser-assisted blepharoplasty: An innovative safe and effective technique. Skin Res Technol 29:e13351. 10.1111/srt.13351
8. Brychta P, Francu M, Koupil J, Ludikovský K (2000) Our experience with transconjunctival, laser-assisted lower blepharoplasty. Acta Chir Plast 42:118–123
9. Bae-Harboe YS, Geronemus RG (2014) Eyelid tightening by CO_2 fractional laser: Alternative to blepharoplasty. Dermatol Surg 40(Suppl 12):S137–S141. 10.1097/DSS.0000000000000165
10. Alster TS, Lupton JR (2001) Erbium:YAG cutaneous laser resurfacing. Dermatol Clin 19:453–466. 10.1016/s0733-8635(05)70286-2
11. Alster TS (1999) Cutaneous resurfacing with CO_2 and erbium:YAG lasers: Preoperative, intraoperative, and postoperative considerations. Plast Reconstr Surg 103:619–632. 10.1097/00006534-199902000-00040
12. Ross EV, Miller C, Meehan K, McKinlay J, Sajben P, Trafeli JP et al (2001) One-pass CO_2 versus multiple-pass Er:YAG laser resurfacing in the treatment of rhytides: A side-by-side comparison study. Dermatol Surg 27:709–715. 10.1046/j.1524-4725.2001.01015.x
13. Kang DH, Choi JH, Koo SH, Park SH (2002) Laser blepharoplasty in Asians. Ann Plast Surg 48:246–251. 10.1097/00000637-200203000-00003
14. Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR (2004) Fractional photothermolysis: A new concept for cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med 34:426–438. 10.1002/lsm.20048
15. Ross RB, Spencer J (2008) Scarring and persistent erythema after fractionated ablative CO_2 laser resurfacing. J Drugs Dermatol 7:1072–1073
16. Balzani A, Chilgar RM, Nicoli M, Sapountzis S, Lazzeri D, Cervelli V et al (2013) Novel approach with fractional ultrapulse CO_2 laser for the treatment of upper eyelid dermatochalasis and periorbital rejuvenation. Lasers Med Sci 28:1483–1487. 10.1007/s10103-012-1255-4
17. Kotlus BS (2010) Dual-depth fractional carbon dioxide laser resurfacing for periocular rhytidosis. Dermatol Surg 36:623–628. 10.1111/j.1524-4725.2010.01516.x
18. Watson AH, Van Brummen A, Somogyi MB, Homer N, Nakra T (2022) Potent periorbital fractionated CO_2 laser resurfacing. Dermatol Surg 48:1089–1091. 10.1097/DSS.0000000000003533

19. De Filippi Sartori J, Osaki TH, Osaki MH, de Souza RB, Allemann N (2022) Split-face evaluation of collagen changes induced by periorbital fractional CO_2 laser resurfacing. Aesthet Surg J 42:239–248. 10.1093/asj/sjab357
20. Weniger FG, Weidman AA, Barrero Castedo CE (2020) Full-field Erbium:YAG laser resurfacing: Complications and suggested safety parameters. Aesthet Surg J 40:NP374–NP385. 10.1093/asj/sjz319
21. Alster TS, Bellew SG (2004) Improvement of dermatochalasis and periorbital rhytides with a high-energy pulsed CO_2 laser: A retrospective study. Dermatol Surg 30:483–487. 10.1111/j.1524-4725.2004.30160.x
22. Fitzpatrick RE, Rostan EF, Marchell N (2000) Collagen tightening induced by carbon dioxide laser versus erbium:YAG laser. Lasers Surg Med 27:395–403. 10.1002/1096-9101(2000)27:5%3C395::AID-LSM1000%3E3.0.CO;2-4
23. Rohrich RJ, Coberly DM, Fagien S, Stuzin JM (2004) Current concepts in aesthetic upper blepharoplasty. Plast Reconstr Surg 113:32e–42e. 10.1097/01.prs.0000105684.06281.32
24. Garcia CP, Badin AZD (2019) Treating excess lower eyelid skin without incisions. Aesthetic Plast Surg 43:1320–1325. 10.1007/s00266-019-01427-0
25. Guida S, Nisticò SP, Farnetani F, Del Duca E, De Carvalho N, Persechino F et al (2018) Resurfacing with ablation of periorbital skin technique: Indications, efficacy, safety, and 3D assessment from a pilot study. Photomed Laser Surg 36:541–547. 10.1089/pho.2018.4479
26. Mezzana P, Scarinci F, Costantino A, Marabottini N, Valeriani M (2010) Lower eyelid ablative fractional resurfacing: A new technique to treat skin laxity and photoaging. Acta Chir Plast 52:35–38
27. Bonan P, Campolmi P, Cannarozzo G, Bruscino N, Bassi A, Betti S et al (2012) Eyelid skin tightening: A novel niche for fractional CO_2 rejuvenation. J Eur Acad Dermatol Venereol 26:186–193. 10.1111/j.1468-3083.2011.04034.x
28. Trelles MA (2004) Laser resurfacing today and the cook book approach: A recipe for disaster? J Cosmet Dermatol 3:237–241. 10.1111/j.1473-2130.2004.00090.x
29. Trelles MA, Pardo L, Benedetto AV, García-Solana L, Torrens J (2000) The significance of orbital anatomy and periocular wrinkling when performing laser skin resurfacing. Dermatol Surg 26:279–286. 10.1046/j.1524-4725.2000.09313.x
30. Kotlus BS (2010) Dual-depth fractional carbon dioxide laser resurfacing for periocular rhytidosis. Dermatol Surg 36(5):623–628. 10.1111/j.1524-4725.2010.01516.xEpub 2010 Apr 2. PMID: 20384754
31. Blanco G, Clavero A, Soparkar CN, Patrinely JR (2007) Periocular laser complications. Semin Plast Surg 21(1):74–79. 10.1055/s-2007-967752PMID: 20567661; PMCID: PMC2884823
32. Tsur Shenhav L, Shehade W, Muravnik G, Horovitz T, Artzi O (2023) The Safety and Efficacy of a Dual CO 2 and 1570-nm Hybrid Laser for Periorbital Rejuvenation. Dermatol Surg 49(5):479–482. 10.1097/DSS.0000000000003750Epub 2023 Mar 6. PMID: 36877122; PMCID: PMC10194056

33. Lee KWA, Chan LKW, Lee AWK, Lee CH, Wan J, Yi KH (2024) Ocular Complication in Facial Aesthetic Laser and Light Treatments: A Comprehensive Review. Diagnostics (Basel) 14(18):2006. 10.3390/diagnostics14182006PMID: 39335685; PMCID: PMC11431483
34. Ancona D, Katz BE (2010) A prospective study of the improvement in periorbital wrinkles and eyebrow elevation with a novel fractional CO2 laser–the fractional eyelift. J Drugs Dermatol 9(1):16–21 PMID: 20120420
35. Miotti G, Zeppieri M, Pederzani G, Salati C, Parodi PC (2023) Modern blepharoplasty: From bench to bedside. World J Clin Cases 11(8):1719–1729. 10.12998/wjcc.v11.i8.1719PMID: 36969996; PMCID: PMC10037276
36. Bin Dakhil A, Shadid A, Altalhab S (2023) Post-inflammatory hyperpigmentation after carbon dioxide laser: review of prevention and risk factors. Dermatol Rep 15(4):9703. 10.4081/dr.2023.9703PMID: 38205425; PMCID: PMC10777097

Tables

Table I. Dosimetric parameters used in the different fractional CO_2 laser treatment modes: Values correspond to the CO_2RE system configuration. "—" indicates not applicable.

Program	Pattern size (mm)	Fractional coverage (%)	Ring (mJ)	Core (mJ)	Fluence (J/cm²)	Pulse – Ring (J)	Pulse – Core (J)
Deep	D = 9	4	—	41	283	—	1.85
Fusion	D = 9	30	82.6	54	306	3.0	2.0
Mid	7.2 × 8.2	30	125	—	292	5.5	—
Light+	9.0 × 10.0	40	44.8	—	185	1.7	—
Light -	7.1 × 8.1	40	22.4	—	159	0.8	—

Table II. Patient characteristics and mean scores for eyelid laxity and wrinkle severity before and after treatment (3,6 and 12 months). Evaluation performed by two independent physicians under blinded conditions. m: mean; SD: standard deviation. Laxity and wrinkle severity scales range from 0 (none) to 4 (very severe).

No.	Sex	Age (years)	Laxity (Baseline)	3 m	6 m	12 m	Wrinkles (Baseline)	3 m	6 m	12 m
1	F	51	3	1	1	1	2	1	1	1
2	F	54	3	1	1	1	3	1	0	0
3	M	49	2	1	0	1	2	0	1	1
4	F	55	3	2	1	1	3	2	1	1
5	F	57	3	1	1	1	3	1	1	1
6	F	64	3	2	1	1	3	2	1	2
7	F	56	2	0	1	1	2	1	1	1
8	F	49	2	1	0	1	2	1	1	1
9	F	59	3	1	1	1	3	1	1	1
10	M	61	3	2	1	2	3	2	1	2
11	F	63	3	1	1	1	3	1	1	1
12	F	50	2	1	0	0	2	1	0	1
13	F	48	2	1	1	0	2	1	1	0
14	F	61	3	1	1	2	3	2	1	2
15	F	63	3	1	1	2	3	1	1	2
16	M	64	3	2	1	1	3	2	1	1
17	F	52	2	0	0	1	2	1	1	1
18	F	60	3	1	1	2	3	1	1	1
19	F	53	3	1	1	1	3	1	1	1
20	F	62	3	1	1	2	3	1	1	2
21	F	61	3	1	1	2	3	1	1	2
22	F	52	2	1	1	1	2	1	1	1
23	F	51	2	1	1	0	2	1	0	0
24	F	63	3	1	1	1	3	1	2	2
25	F	54	2	0	1	0	2	1	1	1
26	F	59	3	1	1	1	3	1	0	1
27	F	55	2	1	0	1	2	1	1	1

No.	Sex	Age (years)	Laxity (Baseline)	3 m	6 m	12 m	Wrinkles (Baseline)	3 m	6 m	12 m
Mean (m)		56.52	2.63	1.04	0.81	1.07	2.56	1.15	0.89	1.15
SD		5.2	0.5	0.5	0.4	0.6	0.5	0.5	0.4	0.6

Table III. Distribution of patients according to the Global Aesthetic Improvement (GAI) grade at 3, 6 and 12 months. Comparisons performed against baseline values. Photographs assessed without blinding for this measure.

GAI grade	Definition	3 months n (%)	6 months n (%)	12 months n (%)
0	No improvement	0 (0%)	0 (0%)	0 (0%)
1	Slight (< 25%)	0 (0%)	0 (0%)	0 (0%)
2	Moderate (25–50%)	4 (15%)	2 (7%)	6 (22%)
3	Good (50–75%)	20 (74%)	21 (78%)	19 (71%)
4	Very good (75–100%)	3 (11%)	4 (15%)	2 (7%)
p	–	< 0.0001	< 0.0001	< 0.0001

Figures

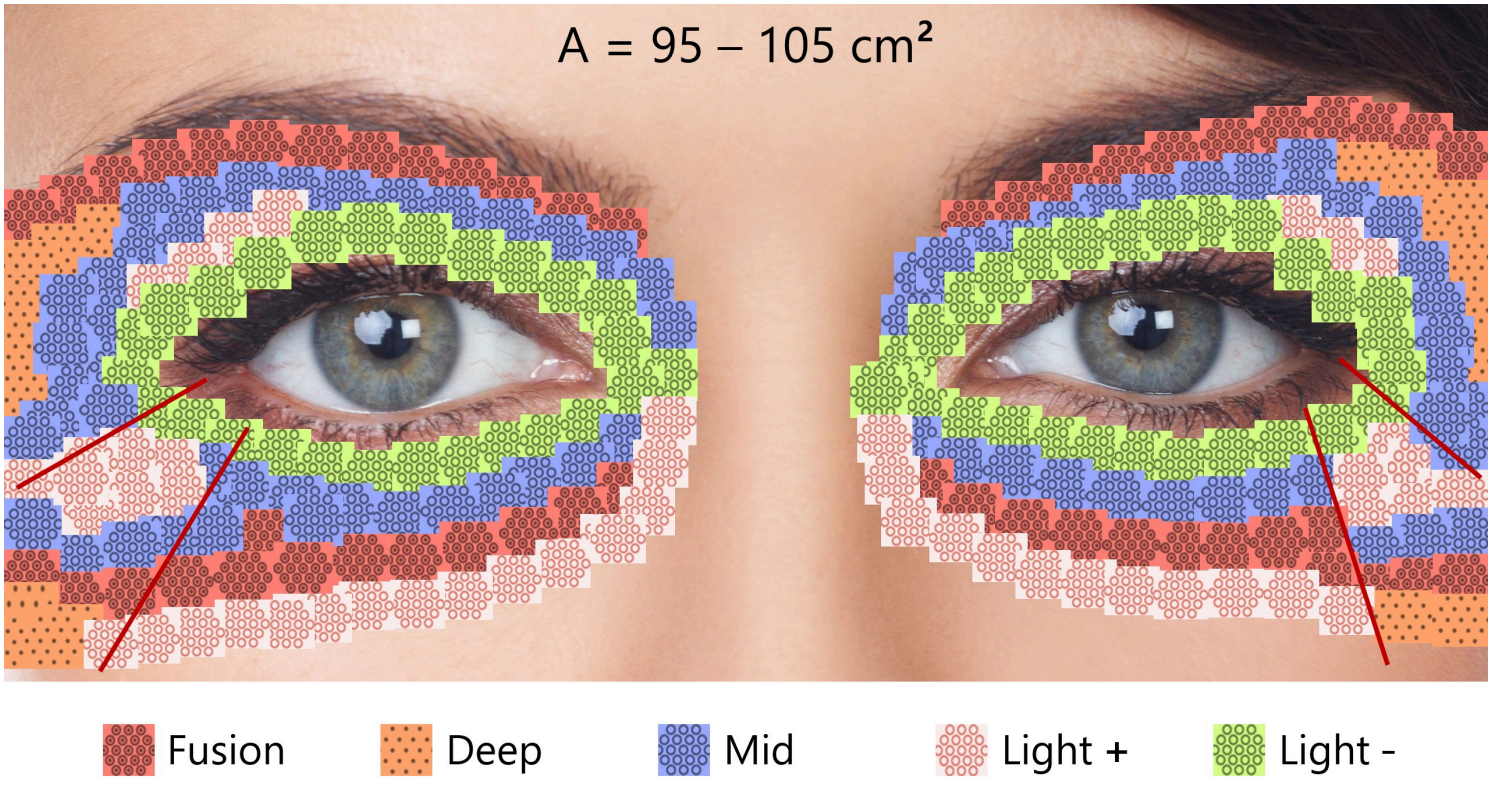


Figure 1

Laser treatment approach according to the anatomy and functionality of the eyelids and periorbital tissues. On the lower outer margins of both eyes, the canthal trapezoids are represented as areas of special caution.



Figure 2

Patient No.5. Postoperative and short-term results. (A) Before treatment; (B) 6 days after treatment; (C) 3 months after treatment, eyes open; (D) 3 months after treatment, eyes closed.

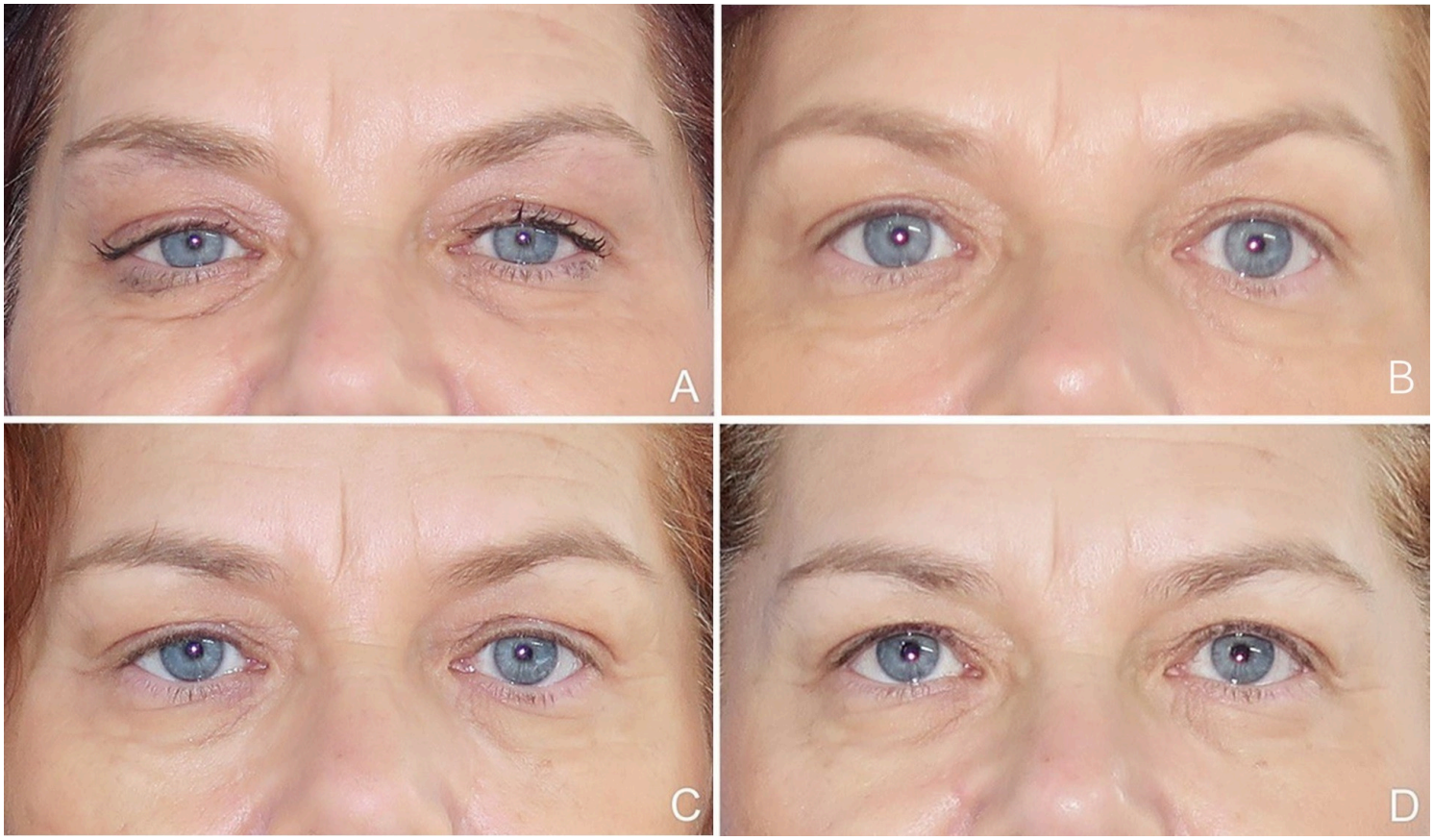


Figure 3

Patient No.9. Short-, mid-, and long-term results. (A) Before treatment; (B) 3 months after treatment; (C) 6 months after treatment; (D) 12 months after treatment.



Figure 4

Six-month improvement results in three different examples, with varying ratings on the Global Aesthetic Improvement Scale. The upper section (patient No.6) shows “Moderate improvement” (2 points), the middle section (patient No.26) “Good improvement” (3 points), and the lower section (patient No.25) “Very good improvement” (4 points). (A) Before treatment; (B) 6 months after treatment.