Thermo-Mechanical Fractional Injury Therapy for Facial Skin Rejuvenation in Skin Types II to V: A Retrospective Double-Center Chart Review

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Background and Objectives: Thermo-mechanical fractional injury (TMFI) therapy (Tixel®; Novoxel®, Netanya, Israel) is an innovative technology. Along with its drug delivery enhancement features, it is widely used for facial skin rejuvenation. Our study explores the beneficial effect of the Tixel® on the different features of facial skin rejuvenation along with patients′ satisfaction rate, aiming to suggest practical recommendations for an optimal aesthetic result.

Study Design/Materials and Methods: A retrospective chart review of 24 patients (20 women, 4 men, average age 56 years old) with skin types II–V who received 2 or 3 Tixel® treatments, 3–5 weeks apart in two medical centers (12 from Israel, 12 from the United Kingdom). Four experienced dermatologists compared standardized clinical photographs taken before each treatment and 3 months after the final treatment based on seven parameters that were set by 10 physicians and rated the difference on a scale of −1 to 4. Furthermore, epidemiology, treatment data, satisfaction, and safety were reviewed.

Results: Out of the seven parameters that were compared (blood vessels and erythema, skin complexion, periorbital wrinkles, pigmentation and toning, pore size, vitality, wrinkles, and laxity), all features demonstrated an overall improvement, with the greatest improvement demonstrated in skin complexion (2.1 ± 0.49) and periorbital wrinkling (2.09 ± 0.65) followed by vitality (1.7 ± 0.49). Side effects were transient, including erythema and hyperpigmentation, and the average downtime was 1.7 days.

Conclusion: TMFI is a safe and effective method for improving facial skin quality. Addressing patient′s expectations while maximizing the benefits of this novel technology will provide superior aesthetical results.

Key words: Tixel; TMFI; Skin Rejuvenation

INTRODUCTION

Skin rejuvenation is an evolving field, focusing on a great interest for patients and physicians alike [1]. Nonetheless, the term *skin rejuvenation* is amorphous and may contain an improvement of several components [2]: skin pigmentation, wrinkling, laxity, skin glow, redness, prominent blood vessels, scarring, texture, pore size, and other skin imperfections. While many topical treatments, either minimally invasive or invasive, improve skin quality [3–5], each modality might provide a different change. Our study evaluates the clinical skin changes observed following treatment with thermo-mechanical fractional injury (TMFI) technology using the Tixel® device to establish the utility of this modality in skin rejuvenation.

METHODS

A retrospective chart review of all consecutive patients seeking treatment for facial skin rejuvenation treated in two centers (Tel Aviv, Israel and London, UK) using the Tixel® between March 2018 to January 2020 was conducted. The study was approved by an ethics committee and followed the tenets of the declaration of Helsinki.

The analysis included adults with skin type ranging from Fitzpatrick II–V. The subjects were treated according to the Tixel® TMFI technology systems′ instructions for use. Inclusion criteria were as follows: healthy males or females aged 20–80 years, seeking skin rejuvenation, and were willing and able to provide informed consent. Exclusion criteria were as follows: women who are pregnant or lactating, having severe sun damage, excessive skin laxity on the lower face and neck, keloid scarring or open wounds in the treatment areas, severe or cystic facial

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acne, a history of cosmetic treatments in the area to be treated (skin tightening procedure within the past year; injectable filler or botox within the past month; ablative or nonablative resurfacing/rejuvenating laser treatment or light treatment within the past 6 months; dermabrasion or deep facial peels within the past 6 months), isotretinoin treatment within the past 6 months, and inability to understand the treatment protocol or to give informed consent.

The Tixel® (Novoxel®, Israel) is a nonlaser, fractional, nonablative, thermomechanical skin rejuvenation system, which combines thermal energy with motion. The thermal energy is delivered to the tissue via a tip. The system consists of two types of tips, (i) a standard tip consisting of 81 (9×9) tiny titanium pyramids, and (ii) a small tip (also known as the periorbital tip) consisting of 24 (6×4) tiny pyramids. The tip base is heated to 400°C within a handpiece, which quickly moves toward the skin surface to achieve contact and coagulate tissue, creating microcraters by evaporation and desiccation. The amount of thermal energy delivered to the skin is determined by the pulse duration (PD; range: 5–18 milliseconds) and protrusion distance or depth (100–1000 μm). The protrusion is the distance the heated tip projects from the edge of the handpiece gauge per actuation. Hence a greater protrusion distance leading to a greater degree of skin contact between the titanium pyramids, fewer air gaps, and greater thermal transfer. Importantly, thermal transfer in TMFI technology does not involve any mechanical penetration of the epidermis.

Animal studies have shown that thermal lesions obtained at pulse duration ranging from 6 to 16 milliseconds and protrusion ranging from 400 to 800 μm exhibit nonablative results. For example, Tixel treatment settings (12 milliseconds and 600 μm) on a young porcine abdomen have shown a visualized and a localized dermoepidermal coagulation zone with an average depth of 237 ± 40 μm and width of 354 ± 67 μm. Tissue interactions presented with intra-epidermal vacuolization, subepidermal clefting, and intense eosin staining corresponding to the thermal treatment zone. The nonablative nature of the system's titanium tip and geometry of the thermal effect corresponds with mathematical analysis of skin temperature upon contact of the tip with the tissue. The analysis shows that a hemispherical heatwave is formed where the tip contacts the tissue. The tip is made of a gold-plated copper base rigidly connected to a thin-walled titanium shell. Analyzing the thermal behavior of the tip structure reveals that although the tip base is heated to 400°C, the titanium shell cools to below 150°C when making contact with the tissue for an extremely short duration (measured in milliseconds). For longer pulse durations (18 milliseconds and above), the titanium shell regains its high temperature and provides an ablative dermal treatment. The unique titanium tip and tissue thermal behavior are based on the dedicated tip's geometrical design combined with the thermal properties of the different material.

Treatment with Tixel® was delivered following the application of topical anesthetic cream. Patients received

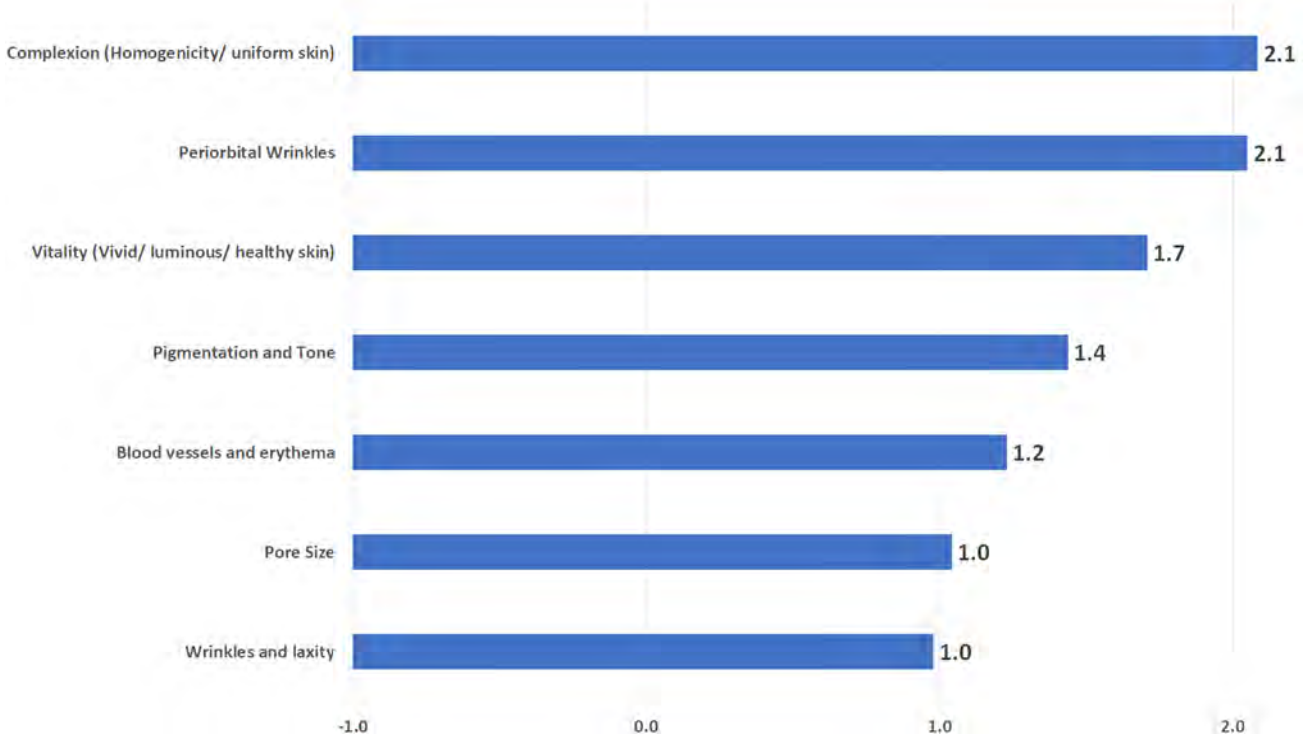

Fig. 1. The average weighted scores of the four dermatologists.

two or three treatments, and each treatment was 3–5 weeks apart. During each session, subjects received treatment with different PDs and different protrusion depths. The periorbital area (excluding the upper eyelids) was treated with a smaller (periorbital) tip while the rest of the face was treated with the standard tip in one to two passes with up to 0%–30% overlap. Adverse events and downtime (return to social activities) were assessed after each visit. As a standard of care, all patients were photographed preprocedure (before), at each visit, and 3 months postfinal treatment (after) by the "Visia" skin analysis imaging system (Canfield®, Parsippany, NJ, USA).

To define the changes observed following several Tixel® treatments, ten representatives before and after photographs were chosen and presented to 10 different non-involved physicians who were asked to offer 3 parameters, which were most improved. Changes that were mentioned more than twice by two different evaluators for at least two different sets of pictures were determined and included the following: blood vessels and erythema, skin complexion, periorbital wrinkles, pigmentation and toning, pore size, vitality, wrinkles, and laxity.

Then all left and right before and after photographs were randomly presented for evaluation. The above mentioned seven parameters as well as an extra general change parameter were scored by four experienced dermatologists on a 6-point scale according to the degree of improvement: -1 = worse result; 0 = no change; 1 = 1%–25% improvement; 2 = 26%–50% improvement; 3 = 51%–75% improvement; 4 = 76%–100% overall improvement. Finally, patient satisfaction with the results, treatment experience, and fulfillment of expectations were obtained on a 5-point scale (1–5).

Analyses were mainly descriptive in nature, summarized by count and percentage for categorical variables and mean, median, minimum, and maximum percentiles with standard error for continuous variables. Baseline and posttreatment outcomes were analyzed using Fisher′s test for categorical variables. All statistical analyses were performed by SPSS version 25.0 (IBM Corporation, Armonk, NY).

RESULTS

Twenty-four patients (12 from Israel, 12 from the United Kingdom; 20 women, 4 men) were included in this chart review. The age of the participants ranged from 39 to 69 years (average 56 years). Seven of them had Fitzpatrick skin type II, 11 had type III, 3 had type IV, and 3 type V. Patient demographics, medical history, and treatment characteristics are elaborated in Table 1. 87.5% ($n = 21$) and 12.5% ($n = 3$) of patients completed three and two treatments, respectively, every 3–5 weeks.

During each session, subjects received treatment with PD between 8 and 14 milliseconds and protrusion depths between 500 and 1000 μm. The face was treated with the standard tip and an average of 503 + 174 pulses were delivered per treatment. At each treatment, the periorbital skin was also treated with the periorbital tip and an average of 115 + 82 pulses were given per treatment. Treatment was delivered in one to two passes with 0%–30% overlap.

TABLE 1. Demographics and Treatment Characteristics

Age	Mean (SD)	56.2 (8.7)
	Median [IQR]	57.0 [48.5–64.5]
	Min–max	39.0-69.0
Sex	Female	20 (83.3%)
	Male	4 (16.7%)
Medical History	Anxiety	1 (4.2%)
	Cardiac arrhythmia	1 (4.2%)
	Cold sores	1 (4.2%)
	Depression	1 (4.2%)
	Herpes	1 (4.2%)
	Hip-joint pain	1 (4.2%)
	S/P Ca of breast	1 (4.2%)
	NA	17 (70.8%)
Fitzpatrick′s skin type	2	7 (29.2%)
	3	11 (45.8%)
	4	3 (12.5%)
	5	3 (12.5%)
Number of treatments	2	3 (12.5%)
	3	21 (87.5%)
Interval between treatments (weeks)	3	4 (16.7%)
	4	18 (75.0%)
	5	2 (8.3%)

IQR, interquartile range.

While processing four dermatologist′s assessments, all features demonstrated an overall improvement, and the greatest improvement was demonstrated in skin complexion (2.1 ± 0.49), and periorbital wrinkling (2.1 ± 0.65) followed by vitality (1.7 ± 0.49). The average weighted scores of the four dermatologists are shown in Figure 1. Figure 2 elaborates on the score distribution of every parameter. Skin complexion was improved in all patients, with a more than 50% improvement in 74% of cases. While addressing features with lower scores of improvement (wrinkles, laxity, and pore size), the κ coefficient of agreement between raters was 0.192 and 0.194, respectively, suggesting a disagreement between raters′ assessment, hence explaining the unfavorable result. The average patient′s satisfaction score (1–5) with skin improvement measured 3.6 (SD + 1.2), with treatment experience at 3.9 (SD + 1.3) and with the fulfillment of expectations at 3.4 (SD + 1.5). Patient satisfaction with improvement, treatment experience, and fulfillment of expectations correlated with treatment protrusion settings but not with pulse duration settings.

Posttreatment side effects included transient erythema lasting between 3 and 6 days in 3 out of 24 (12.5%) patients and hyperpigmentation in one patient with skin type III (healthy individual, F, 45, smoker). Notably, hyperpigmentation is not a common side effect of

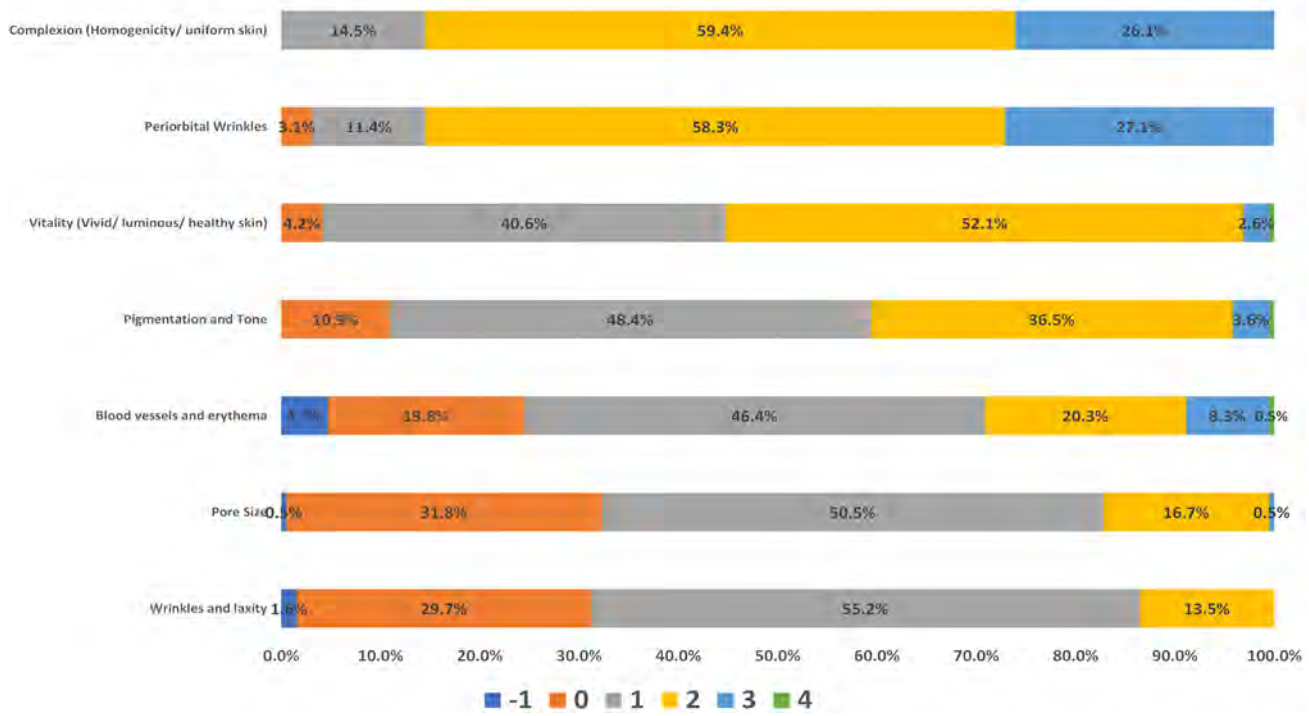

Fig. 2. The score distribution of every parameter.

TMFI; however, since this patient was treated with more aggressive settings (PD: 14 milliseconds; protrusion depth: 800 μm) for a higher-than-average number of pulses (669 and 162 pulses with the standard and small tip respectively), hyperpigmentation seems reasonable. The hyperpigmentation resolved after 9 months with bleaching agents. Average downtime (return to social activities) was 1.7 days (ranging 0–5 days) following medium settings.

DISCUSSION

The demand for skin rejuvenation modalities has greatly increased over the last few decades. *Skin rejuvenation* is a broad and amorphous term and includes many positive skin changes observed following various interventions. Different modalities are associated with different levels of improvement of the specific aspects of skin rejuvenation. The fractional CO_2 laser is considered to be the gold standard for skin resurfacing treatments [6]. However, its high cost, pain during treatment, and potential for complications are major disadvantages. Skin pigmentation is best treated with erbium laser [7], but IPL is considered to be an efficient alternative [8] with a shorter downtime [9]. Skin wrinkling [4] can be improved with the injection of hyaluronic acid-based fillers [10], peels [11], or ablative lasers [12], and skin laxity [13] can be improved by radiofrequency, ultrasound, or surgery. No well-defined guidelines exist for employing the correct modality to the suitable clinical scenario, thus turning facial skin rejuvenation, a fine art, into an exciting science.

The Tixel′s thermomechanical capabilities affect the dermal structure, implying a beneficial influence over skin appearance. Previous studies [14] demonstrated the unique characteristics of the epidermal microcraters and the beneficial effect of Tixel® on fibroblast proliferation and collagen production. Depending on the device settings, TMFI with the Tixel® creates a lesion 160-517μm in diameter and 170–350 μm in depth. The unique geometrical properties of the thermal lesion affect both the epidermis and superficial dermis with extensive coverage within a single treatment. In contrast to the effects of an ablative laser, the Tixel® craters are devoid of necrotic tissue without charring; thus, treatment is associated with accelerated recovery [15]. Posttreatment, the thermal effect spreads along the epidermis and superficial dermis. The temperature rapidly drops from 400°C at skin surface, to 50°C at 100 μm depth. Histological models [14] have demonstrated epidermal regeneration with a surface crust and a dermoepidermal cleft filled with new fibroblasts and macrophage cells 7 days posttreatment surrounded with new collagen formation. As shown in our study, the main improvements observed following several Tixel® treatments include changes in skin complexion (Fig. 3), periorbital wrinkling (Fig. 4), and vitality. These potential changes should be discussed with the patient prior to the initiation of the treatment course to meet expectations.

In comparison with ablative lasers, Tixel® treatment is associated with minimal procedural pain, short downtime, few side effects, and fast wound healing [15], allowing for a more frequent treatment regimen and a

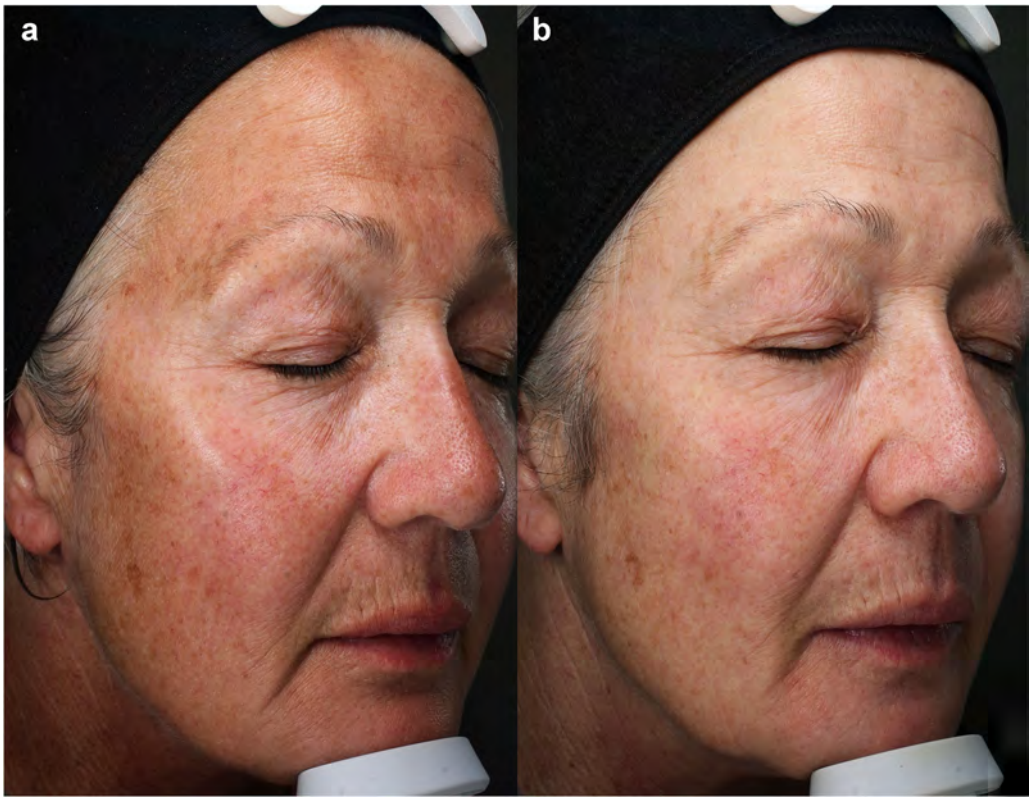

Fig. 3. A representative patient before (**a**) and after (**b**) several treatments. Please note the change in skin complexion.

shorter period to achieve the final result. In addition, Tixel® revolutionized the field of fractionated devices in dark skin types, as no chromophores are targeted. However, although less frequent than lasers, high settings and multiple passes of TMFI in dark skin patients might result in hyperpigmentation.

Several pearls can be elaborated to augment results:

(1) Higher protrusion depths reduce the air gaps between the tip and the skin, and better results are observed while applying the treatment over bony prominences (forehead, cheekbones) than over fatty tissue, empowering the importance of thermal matching. The physician should consider changing the protrusion while treating different areas. Bony areas deserve low protrusion, while fatty soft areas require higher protrusion. Hence, using a designated intraoral spatula might improve the therapeutical effect in the perioral areas.
(2) Multiple passes in a prior animal study conducted by Novoxel assessed the thermal damage created by the Tixel®. A single pass of mild (6 milliseconds/400 μm), moderate (12milliseconds/600 μm), and aggressive (16 milliseconds/800 μm) settings will provide treatment densities of 6.7%, 8%, and 15.5%, respectively. While it is difficult to calculate the exact coverage on multiple passes because some of the microthermal zones might overlap, the authors estimate the coverage to be around 15% if double passes of moderate settings are performed. More passes will increase the coverage, elongate downtime, and potentially be associated with more adverse effects.
(3) Surface debridement in between passes: The majority of heat transferred from Tixel® is absorbed by the epidermis. Much of the epidermis can be sloughed following three passes of Tixel® and wet gauze abrasion. This exposes the dermis, which can be treated directly. When Tixel® is used over the exposed dermis, augmented results can be achieved.
(4) TMFI-assisted drug delivery: Tixel, known to improve drug delivery [16], has already been utilized in the treatment of several medical conditions, including hypertrophic scars [17], acne [18], and rosacea [19]. Therefore, combining the esthetic thermomechanical effect with different cosmeceutical or drug delivery might augment the results. However, this fascinating combination still needs to be fully explored and validated.

The main limitation of this study is its retrospective nature. This is a noncontrolled retrospective study, not comparing Tixel® clinical performances and patients' satisfaction with other modalities and technologies. Therefore, more prospective research studies are required to reveal the full benefits of this novel technology.

In conclusion, Tixel® is a minimally invasive modality in facial skin rejuvenation, having a clear benefit in improving

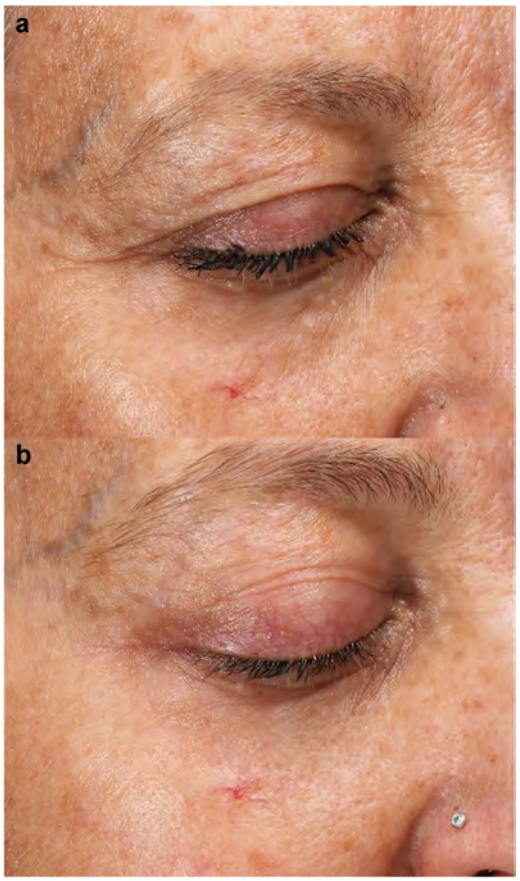

Fig. 4. A representative patient before (**a**) and after (**b**) several Tixel®treatments. Please note the change in periorbital wrinkles.

skin complexion, vitality, and periorbital wrinkling with a low incidence of side effects in a wide range of skin types. Although the objective physicians′ assessments indicate only mild-to-moderate improvements, patient′s satisfaction shows higher results. A baseline accurate clinical evaluation, an understanding of patients′ expectations, and full disclosure of the technology capabilities might allow the physician to optimize esthetic results.

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