Clinical Evaluation of the Efficacy of Fractional Radiofrequency for the Treatment and Reduction of Stretch Marks: A Prospective Study

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Abstract

Background/Objectives: Skin resurfacing with fractional radiofrequency results in reepithelization, collagen shrinkage, fibroblast stimulation and neocollagenesis which may be beneficial for the improvement of various skin lesions. This clinical study was conducted to evaluate the safety and efficacy

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of fractional radiofrequency device (FRF) for the treatment of striae.

Methods: 17 subjects, totalling 67 treatment zones were evaluated. Subjects had 4 FRF treatment sessions to the striae areas, at 4-weeks interval. 3D standardized photographs of the treatment area with a 3D camera were used to evaluate striae volumetric improvement from baseline to follow up (FU) visits at 12 and 16 weeks post final treatment. A satisfaction questionnaire was completed by subjects at each of the follow up visits. Additionally, the mean scores of the live investigator assessments of Global Aesthetic Improvement Scale (GAIS), Subject Satisfaction Scale, Pain Visual Analog Scale and Tolerability Score were calculated.

Results: A total of 15 subjects completed the study (Fitzpatrick skin type I-III, average age 36.2 years) received 4 FRF treatments on multiple different body zones with multiple passes over stretch marks on the abdomen, inner arms, lower buttocks, inner thighs and/or flanks. Analysis of 3D photographs of the striae affected zones at 16-week FU revealed an average reduction in the striae volume of 19.1%, a reduction of redness of 14.3%, a reduction of pigmentation of 11.2%, and a reduction of striae colour of 8.82%. The GAIS improved by 1.7-points when compared to baseline. Treatments were well tolerated with subjects reporting a mean score of 3.8 out of 10 for pain and 3.1 out of 4 for tolerability (indicating the treatment was 'tolerable'), with no occurrences of serious adverse events. The average subject satisfaction at 16-week follow-up was 3.1, out of a total of 4, which signified subjects were "satisfied" with their treatment.

Conclusion: 3D Image analysis of the treated zones presented overall reductions in the colour and texture of striae after four treatments with FRF. A combination of ablation and coagulation introduced by FRF treatment resulted in improvement to the appearance of the treated striae.

1.0. Introduction

Striae distensae (frequently referred to as stretch marks or striae) are a common dermatologic skin lesion, observed in both women and men. Striae typically develop after accelerated weight gain or hypertrophy of muscle mass, but the vast majority of striae develop after pregnancy in women[1,2].

Anatomically, striae are commonly located on the abdomen, breasts, thighs and buttocks, as they most commonly endure volumetric change[3]. Immature striae first present as erythematous and violaceous appearing fuchsia stripes (called striae rubra) and ultimately fade into sunken wrinkled, hypo-pigmented, atrophic scar-like, white stripes within several months (called striae alba). The latter of these has been described as a permanent form of striae[4]. These lesions can fade minimally over time, however they rarely resolve without some level of treatment[5].

Although the pathogenesis remains unknown, key aetiological theories have been postulated, such as the inadequate development of the elastic fibers and collagen in the skin[6,7], combined with a mechanical stretching of the skin and endocrine imbalance[8,9]. During the first stages of striae formation, macrophages and mast cells accumulate around dermal elastic fibers, causing them to dissolve and lose their function. The next stage of striae formation is when the horizontal eosinophilic collagen become visible in the shallow layer of the dermis and the epidermal layers shrink, which leads to the disappearance of stripe edges[10,11]. Striae distensae promote fibroblast activity, leading to increased protein catabolism and thus alterations to collagen and elastic fibers[12]. In clinical practice, the pigmentation of striae affected areas is of great concern due to changes in the cutaneous chromophores found in the epidermis and dermis[13].

While striae will rarely cause any serious medical complications, it may have significant negative psychological effects. Treatment modalities such as topical retinoids, chemical peeling[14], or microdermabrasion, have been tested for treatment of striae, but the findings are discouraging and contradictory[15]. While some studies have demonstrated that fractional laser photothermolysis is successful in the treatment of straie[16–18], hyperpigmentation after laser therapy is a major obstacle, especially in subjects with darker skin[19,20]. Furthermore, these procedures are usually associated with prolonged recovery times[19,20]. To bypass these concerns, nonsurgical approaches that do not require significant downtime are becoming the favoured method of procedures subjects seeking cosmetic

improvements in striae.

One of these non-invasive treatments is fractional radiofrequency (FRF). FRF treatment has been established to be an innocuous, tolerable and effective choice to diminish striae and provide an overall enhancement in skin texture[21–23]. However, the most effective therapeutic strategy for improving the appearance of striae remains to be determined. In this study, we evaluated the efficacy and safety of FRF using 3D analysis and measurement, clinical assessments of improvement, patient satisfaction rating, pain rating, and adverse effects assessment.

2.0 Materials and Methods

2.1 Participants

This study was a prospective, clinical study conducted at one clinical center between June 2019 and February 2021. The study protocol complied with the CONSORT 2010 statement for reporting a randomized controlled trial (see Supplementary Material), and the trial was conducted according to the Declaration of Helsinki and all its revisions. It was registered to Clinical Trials (NCT05097573). All subjects provided written informed consent to participate in the trial.

Male and female subjects requesting FRF to treat stretch marks were included. Subjects 18 to 60 years old and of Fitzpatrick skin types (I-III) were eligible. Exclusion criteria included the presence of pacemaker or defibrillator, metal implants in treated anatomy, any past or current significant systemic illness, illness localized in area of treatment, therapies or medication that may have interfered with the treatment or healing process, recent surgery in treatment area, and acute or chronic infection in the area. Lastly, treatment would not be administered over any tattoo's, permanent makeup, or excessively tanned skin.

2.2 Description of treatment

Skin in the treatment area was cleansed and dried prior to treatment. Treatments were performed using the Venus VivaMD™ (Venus Concept Inc, Toronto, Canada). No topical anesthesia was required, except on one patient. The tip of the applicator was then held perpendicular to and in close contact with the skin surface when emitting pulses. Treatment consisted of 1, 2 or 3 passes over the designated area using a range of energies, the voltage ranged from 180 to 270 Volts and the pulse duration ranged from 5 to 30 milliseconds. Treatment parameters, such as voltage and pulse duration, were determined at the discretion of the primary investigator (M.A.) based on skin type and severity of disease. Nothing was applied to the treatment area immediately after the treatment. Subjects were also instructed to use a high factor of sunscreen (SPF ≥ 30) to protect the treated area from direct sunlight beginning the next day and for the entire period of the study.

2.3 Outcome measures

Two primary outcome measures were included. First, objective volumetric evaluation of striae was evaluated via ANTERA™ 3D Imaging System Analysis (Miravex Limited, Dublin, Ireland) at 12 and 16 weeks post-final treatment. ANTERA 3D® analyzes skin by imaging processing and feature extraction. At each treatment and follow-up visits, standardized photographs were taken at 0° and 45° angles from both sides of the subject. All photographs were taken with standardized settings including anatomical alignment, and illumination throughout the study. For analysis of skin colour variation, redness, pigmentation, texture, and volume (colour meaning the general colour aspect of the striae, and redness is the specific erythema index) ANTERA™ 3D® imaging was performed at treatment 1, treatment 3, 12-week follow-up and 16-week follow-up of each participant. 3D imaging uses multi-directional illumination and computer-aided reconstruction of the skin surface to reconstruct the surface in three dimensions; the field of view is 56x56mm with a lateral resolution of 0.1 mm and a vertical resolution of 0.01 mm. The measurement error of the camera is approximately 5%.

Miravex has used a statistical approach to define the interval of the scores. Images of the skin from different areas of the face, selected across representative age groups, skin phototypes and ethnicity and corresponding to different levels of damage for wrinkles, texture, pigmentation, and redness have been analysed. The distribution of the skin damage has been divided into 5 intervals: mild, moderate, advanced, severe, and very severe. Depending on which interval the values of a certain image fall, the Antera software will allocate it to the corresponding score interval. To validate our approach, a selected number of dermatologists was asked to score a set of images, and their clinical findings were compared to the scores calculated by the Antera algorithm. The results show a good correlation between the Antera scores and clinical results by doctors. Images were obtained under standard and cross-polarized lighting conditions. Improvement in colour variation was described as a reduction of the heterogenous colours appearance of the stretch mark, improvement in redness was described as the reduction of redness on the stretch mark, improvement in pigmentation was described as the reduction of pigment on the stretch mark and improvement in volume was the reduction of raised or lowered areas on the stretch mark.

The second primary outcome measure was improvement in striae at 12- and 16-weeks post-treatment compared to baseline as assessed by the investigator. The change from baseline was scored using the Global Aesthetic Improvement Scale (GAIS). GAIS is a 5-point scale rating global aesthetic improvement in appearance, compared to pre-treatment, as judged by the investigator. The GAIS rating categories were "worse," "no change," "improved," "much improved," and "very much improved." The primary investigator evaluated images to grade the change between the pre- and post-treatment images, using the GAIS measure.

Secondary outcome measures were the subjects' assessments of satisfaction with the treatment using a Subject Satisfaction Scale (SSS) at 12- and 16-weeks post-treatment. Subject satisfaction was evaluated with the following 5-point Likert scale: (4) very satisfied, (3) satisfied, (2) no opinion, (1) unsatisfied, (0) very unsatisfied. Additionally, immediately after each treatment, subject discomfort was

assessed using a 10 centimeter Visual Analog Scale (VAS) on a scale from 0 cm (no pain) and 10 cm (pain as bad as it can be), 0 to 0.4 cm: No pain, 0.5 to 4.5 cm: Mild pain, 4.6 to 7.5 cm: Moderate pain, 7.6 to 10 cm: Severe pain[24]. Subjects were not permitted to view their previous VAS or SSS treatment scores. All adverse events (AEs) were recorded up to the 16-week post-treatment follow-up visit.

2.4 Statistical analysis

Quantitative data are presented as mean, and/or range, while qualitative data are presented as percentage (%). Unless otherwise stated, standard error (SE) is shown. Two-sided Student's paired t-test was used to test for changes from baseline to follow up visits at 6 and 12 weeks after the last treatment. P values less than 0.05 were considered statistically significant.

3.0 Results

3.1 Patient demographics

Seventeen (17) subjects were enrolled and completed the study, 2 were lost to follow-up, therefore 15 subjects completed treatment in overall 67 different anatomical areas. The mean age and standard deviation at study consent was 36.2 years. Fourteen (14) subjects (82.4%) were female and 3 (17.6%) were male. One (1) subject had Fitzpatrick's skin type I (5.9%), 10 had type II (58.8%), and 6 had type III (35.3%). There were 6 areas of focus: 9 subjects had treatment on their abdomen, 3 subjects had treatment on the inner thigh, 2 subjects had treatment on their flanks, 1 subject had on their upper thigh, 1 subject had treatment on their upper arm interior, and 1 had treatment on their lower buttocks. All subjects had one primary area treated (i.e., abdomen, buttocks, etc.), and two to four sections of striae in that primary area (Table 1, Figure 1)

3.2 Primary outcomes: 3D Analysis and Global Aesthetic Improvement Scale

An average reduction of 19.1% of striae volume at 16 weeks post treatment, which was a statistically significant change when compared to baseline was measured using analysis of the 3D photographs. When stratified by body part, striae on the abdomen (volume reduced by 24.0%), flanks (volume reduced by 23.2%) and inner thighs (volume reduced by 22.7%) had the greatest reductions in volume. Additionally, redness on average was reduced in the striae by 14.3% which was statistically significant, when comparing baseline data to 16-week follow-up data, most prominently on their upper thigh (redness reduced by 18.2%) and the abdomen (15.6%). Pigmentation of striae was also statistically significantly reduced on average by 11.2%, striae on the abdomen saw the most reduction in pigmentation (17.4%). Finally, the colour variation was significantly reduced by 8.8% on all body parts, most notably on the upper thigh (18.2%) and lower buttocks (10.2%) (Table 2, Figure 2 and 3a,b).

The primary investigator assessed GAIS reported a significant improvement from baseline to an average of 1.7 (SE 0.4) at 16 weeks, which correlates to between "1=improved" to "2=much improved", respectively (baseline to 16-weeks, p=0.000). When stratified by specific body parts, the abdomen and flanks had statistically significant improvement at 16 weeks when compared to baseline, 2.4 (0.4) at 12 weeks and 2.0 (0.4) at 16 weeks, which correlate to between "3=very much improved" and "2=much improved" (baseline to 16-weeks, p=0.000 for the abdomen and p=0.003 for the flanks). The upper thigh and lower buttocks also had improvement when compared to baseline, 2.5 (0.4) and 1.0 (0.0) (Table 3).

3.3 Secondary outcomes: Subject satisfaction

Subjects were consistently satisfied with their treatment, with mean scores of 2.8 (0.3) at 12 weeks and 3.1 (0.3) at 16 weeks after the last treatment. At the 12-week follow-up, 68.8% reported being "satisfied" (37.5%) or "very satisfied" (31.3%), with 12.5% reporting they had "no opinion". By the 16-week follow-up visit, 82.4% of the subjects reported satisfaction due to their treatments, of which 41.2% reported being "very satisfied". "No opinion" was reported by 5.9% of subjects (Table 4).

3.4 Safety outcomes: Visual Analog Scale, tolerability, and adverse events

The treatments were well tolerated at all treatment sessions. The average tolerability level of all four treatments was 3.1 out of a possible total of 4.0, correlating to "very tolerable", there was no significant difference of tolerability between treatments (p=0.48). The average VAS of all four treatments was 3.8 cm out of 10.0 cm, which correlates to "mild pain". There was no difference in the discomfort or pain VAS scores between the four treatment visits (p=0.18), however pain did on average decrease by 0.9 from the first to the second treatment (Table 5). There were two reports of mild adverse events (mild hyperpigmentation which was resolved within days) but no unanticipated side effects during the duration of the study.

4.0 Discussion

This was a prospective, study of FRF for the treatment and reduction of striae in 17 subjects. Using 3D images along with other quantitative measures, the results of this study showed a significant reduction in four major categories of striae concern (volume, colour, pigmentation, and redness) after four treatments with FRF, as well as an overall positive aesthetic change. When stratified by area, the abdomen and flanks had the most significant changes. Subjects were consistently satisfied with their striae improvement results and rated the treatments as very tolerable. Pain also decreased over time and tolerability increased over time, presumably because subjects know what to expect over subsequent treatments. Pain was mild and only two minor instances of transient hyperpigmentation were seen.

The mechanism of action of fractional radiofrequency is it stimulates thermally ablated and coagulated columns of dermal tissue into the skin surface in spaced matrices, which in turn leads to novel collagen creation. This is all done while keeping sections of the tissue intact and resulting in an increased production in the treated region. FRF also fosters an increase in local inflammation as the energy

promotes a surge response in the expression of TGF-beta-1 (transforming factor beta-1 growth) and promotes HSP 47, this causes the fibroblasts to respond by boosting collagen production[25,26]. FRF also elicits an antioxidant response, which alleviates mast cell activity and contributes to the restructuring of the extracellular matrix that was previously damaged in the formation of striae[27,28]. This is anticipated, as the increase in local circulation and the release of cell growth factors would trigger the fibroblast response and reorganize the tissue structure[3,15,29–31].

The 3D analysis reported a statistically significant average reduction in volume (-19.1%), redness (-14.3%), pigmentation (-11.2%) and colour (-8.8%) for all anatomical areas, except in texture which very slightly increased (0.7%). FRF produces collagen, so the increased texture should not be seen as a negative outcome. There are three stages of development of striae; the acute stage is exemplified by red and slightly raised[17], next the striae rubra develop into striae alba (white, flat, and sometimes depressed in appearance)[11,32]. This study did not collect the severity of striae before treatment, as most striae included were flat striae alba or not raised striae rubra, and therefore the texture score (height and roughness) would not an important area of striae cosmetic improvement for this cohort of patients. Additionally, the increase of texture is proof of collagen production, and therefore the average increase of texture is beneficial to the improvement of striae. The flanks and abdomen showed a lot of reduction in overall volume of striae (-23.2% and -24%). Both areas are common areas of concern for stretch marks in women post pregnancy, meaning FRF could be a particularly effective mode of treating post-partum stretch marks.

There are many methods used to evaluate striae, direct evaluation includes the clinical score and related instruments (such as surface photometry) whereas indirect evaluation includes skin 3D replication technology and computer software analysis. Ordinary flash photography does not provide consistent visualization of important but subtle cutaneous characteristics[33]. There are clearly limitations of 2D clinical photographs for evaluating stretch marks. Using 3D digital analysis or moldings, therefore, should

be considered as a minimum standard for further studies.

Conclusions

In conclusion, our results suggest that FRF treatments showed prolonged improvements in the volume, colour, pigmentation, and redness of striae and is a safe option of striae removal.

using 3D analysis and measurement, clinical assessments of improvement, patient satisfaction rating, pain rating, and adverse effects assessment.

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Table 5. Average pain assessed using the Visual Analog Score (VAS) and average tolerability assessed by the tolerability rating.

Figure 1. Study overview. A flow chart representing patient enrollment.

Figure 2. Change over time in (A) colour, (B) redness, (C) pigmentation, and (D) volume variation of striae.

Figure 3a. ANTERA™ 3D analysis of (1) colour, (2) pigmentation, and (3) redness; (A) treatment 1(B) treatment 2 (C) 12-week follow-up (D) 16-week follow-up.

Figure 3b. ANTERA™ 3D analysis of one patient (skin type: II, area treated: inside thigh, 36-year-old female) volume variation over time; (A) treatment 1, (B) treatment 2, (C) 12-week follow-up, (D) 16-week follow-up.

Supplementary Material: CONSORT 2010 statement.

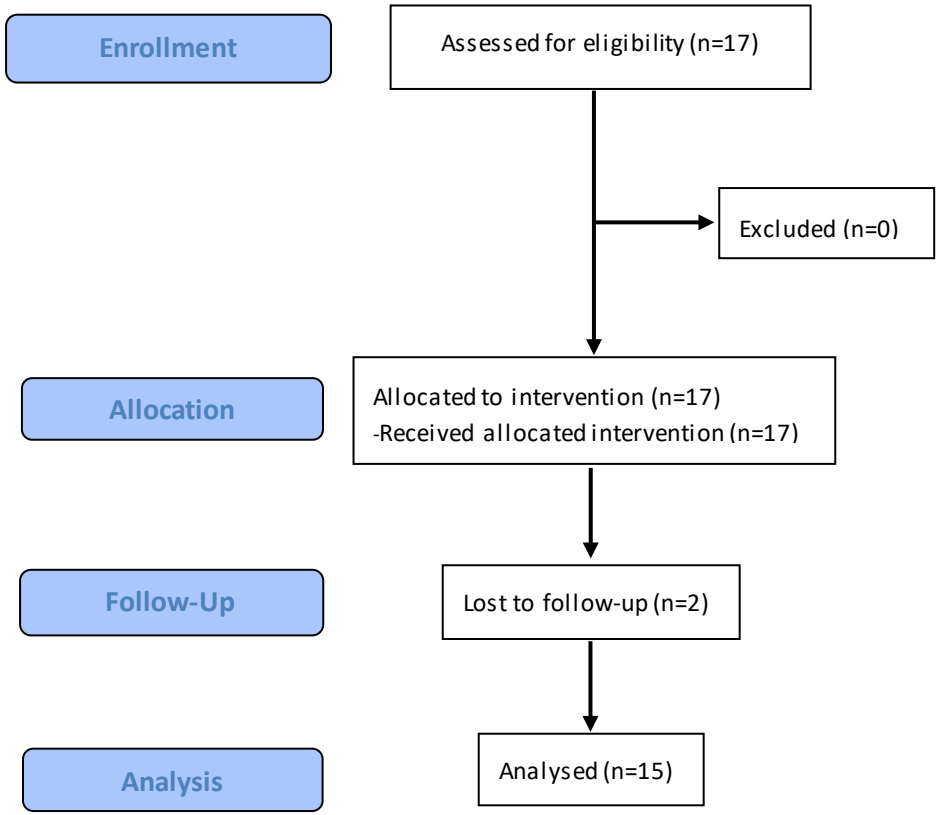

Figure 1. Study overview. A flow chart representing patient enrollment and analysis.

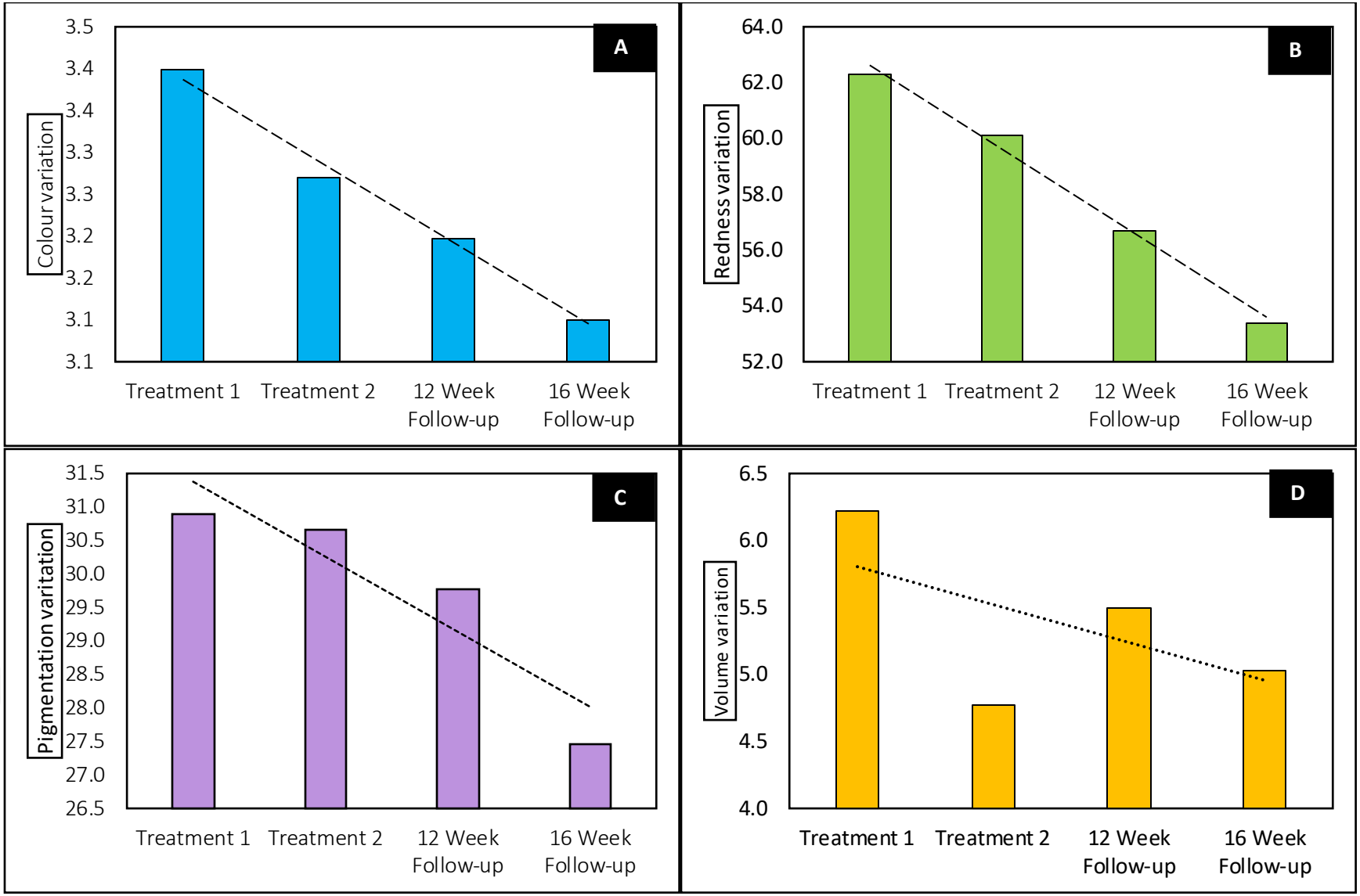

Figure 2. Change over time in (A) colour, (B) redness, (C) pigmentation, and (D) volume variation of striae.

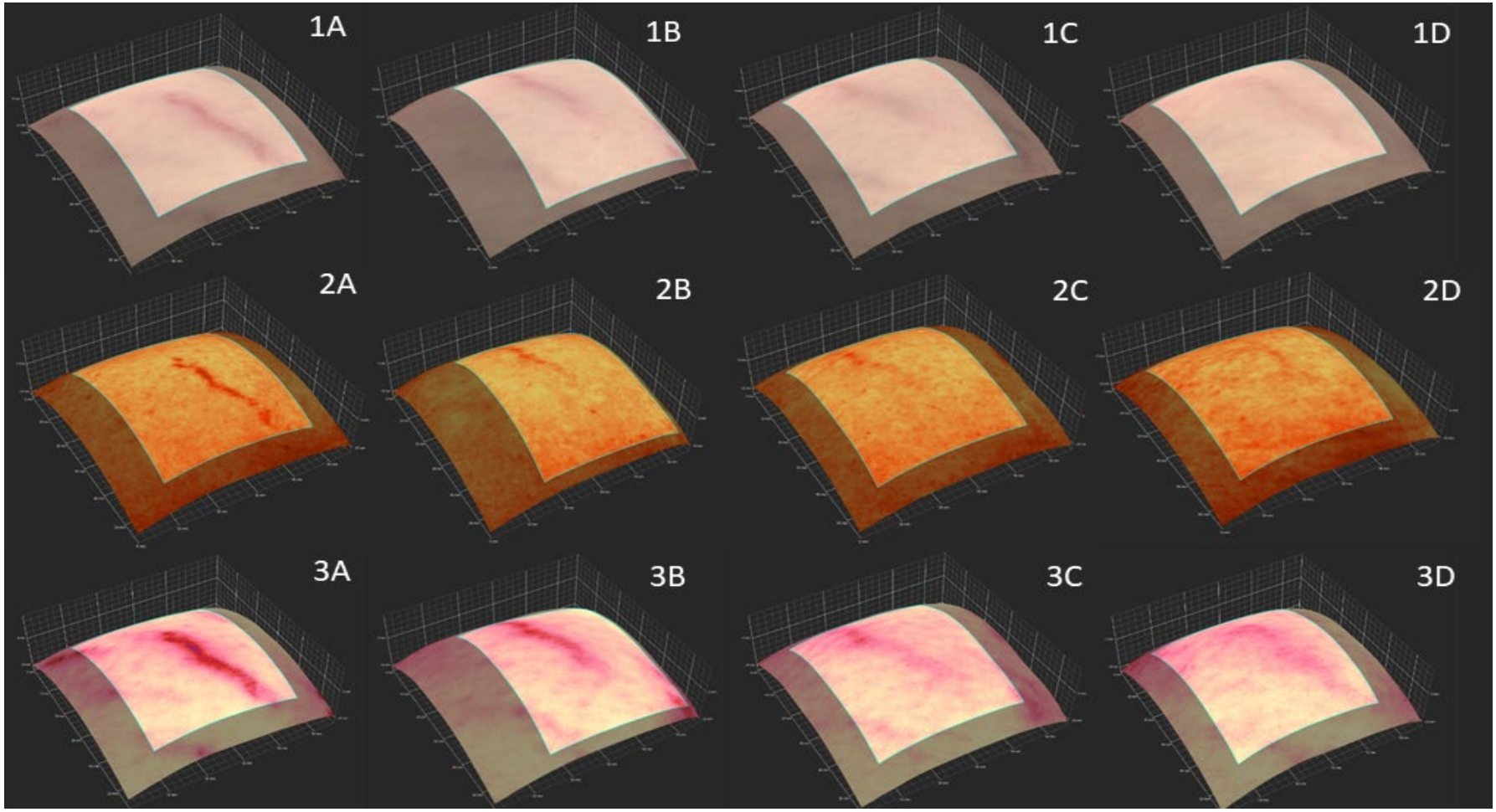

Figure 3a. ANTERA™ 3D analysis of one patient (skin type: II, area treated: abdomen, 35-year-old female), (1) colour, (2) pigmentation, and (3) redness; (A) treatment 1, (B) treatment 2, (C) 12-week follow-up, (D) 16-week follow-up.

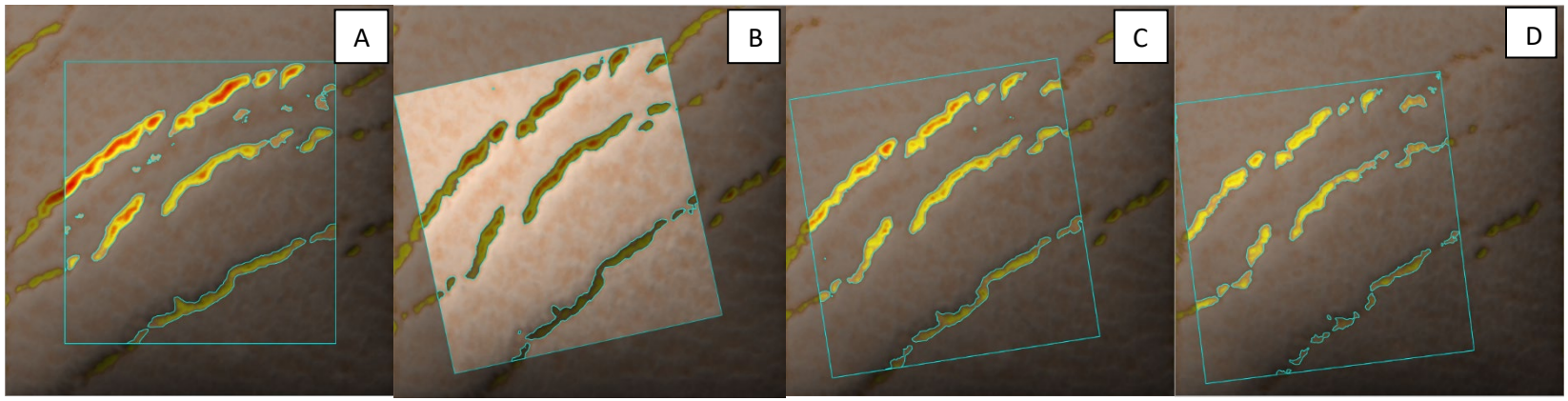

Figure 3b. ANTERA™ 3D analysis of one patient (skin type: II, area treated: inside thigh, 36-year-old female), volume variation over time; (A) treatment 1, (B) treatment 2, (C) 12-week follow-up, (D) 16-week follow-up.

Table 1. Demographic data of participants.

Demographic data	Results (N=17)
Age, mean (SD) (years)	36.2 (9.1)
Age, range (years)	25-58
Gender, *n* (%)	
Female	14 (82.4%)
Male	3 (17.6%)
Fitzpatrick skin type, *n* (%)	
I	1 (5.9%)
II	10 (58.8%)
III	6 (35.3%)
Adverse events	
Hyperpigmentation	2 events
Location of striae, *n* (%)	
Abdomen	9 (52.9%)
Inner thigh	3 (17.6%)
Flank	2 (11.8%)
Upper thigh	1 (5.9%)
Upper arm interior	1 (5.9%)
Lower buttocks	1 (5.9%)

Table 2. Mean percent difference in striae volume, redness, pigmentation, colour, and texture from treatment 1 compared to 16-week follow-up as evaluated using the ANTERA 3D software.

Area	Combined (N=65)	Upper thigh (N=8)	Flank (N=8)	Stomach (N=37)	Lower buttock (N = 4)	Inner thigh (N = 8)
Volume	-19.1%*	5.7%	-23.2%	-24.0%	-5.0%	-22.7%
Redness	-14.3%*	-18.1%	-8.6%	-15.6%	-3.2%	-9.2%
Pigmentation	-11.2%*	-7.8%	-6.6%	-17.4%	19.1%	-3.0%
Colour	-8.8%*	-18.2%	-3.1%	-9.9%	-10.2%	2.8%
Texture	0.7%	0.0%	-8.2%	0.7%	105.3%	-2.1%

*Statistically significant between first treatment to 16-week follow-up.

Table 3. Average striae aesthetic improvement in photographs from baseline via 12 weeks and to the 16-week as determined by the primary investigator using photographs and measured using the Global Aesthetic Improvement Scale (GAIS).

Treated Body Area	Mean GAIS (SE) 12 Weeks	P-Value (baseline versus 12 week GAIS)	Correlated rating	Mean GAIS (SE) 16 Weeks	P-Value (baseline versus 16 week GAIS)	Correlated rating
Combined (N=17)	1.9 (0.2)	0.000000008	Improved to much improved	1.7 (0.4)	0.0001	Improved to much improved
Upper thigh (N=3)	2.5 (0.4)	*ns*	Much improved to Very much improved	2.5 (0.4)	*ns*	Much improved to Very much improved
Abdomen (N=9)	2.2 (0.1)	0.000006	Much improved to Very much improved	2.4 (0.1)	0.00002	Much improved to Very much improved
Flank (N=2)	2.0 (0.2)	0.003	Much improved	2.0 (0.1)	0.003	Much improved
Lower Buttocks (N=1)	0.0 (0.0)	*ns*	Improved	1.0 (0.0)	*ns*	Improved
Upper Arm Interior (N=1)	0.0 (0.6)	*ns*	No change	0.0 (0.0)	*ns*	No change

ns: not significant

GAIS: (3) Very much improved, (2) Much improved, (1) Improved, (0) No change, (-1) Worse, (-2) Much worse, and (-3) Very much worse.

Table 4. Average satisfaction with treatment results at follow-up using the Subject Satisfaction Scale (SSS).

SSS	Week 12	Week 16	Mean difference	Correlated Rating	P-value
Mean (SE)	2.8 (0.3)	3.1 (0.3)	+0.3	Satisfied	0.17

SE: standard error

SSS: (4) very satisfied, (3) satisfied, (2) no opinion, (1) unsatisfied, (0) very unsatisfied.

Table 5. Average pain assessed using the Visual Analog Score (VAS) and average tolerability assessed using the tolerability rating.

Mean (SE)	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Average of all visits	Correlated rating	ANOVA P-value
VAS (cm)	4.6 (0.5)	3.7 (0.5)	3.3 (0.4)	3.7 (0.4)	3.8 (0.2)	Mild pain	0.18
Tolerability	2.9 (0.2)	3.3 (0.2)	3.1 (0.2)	3.1 (0.2)	3.1 (0.1)	Tolerable	0.48

SE: standard error

VAS = 0 to 0.4 cm: No pain, 0.5 to 4.5 cm: Mild pain, 4.6 to 7.5 cm: Moderate pain, 7.6 to 10 cm: Severe pain[24].

Tolerability rating = 4: Very tolerable, 3: Tolerable, 2: Having no opinion, 1: Intolerable, 0: Very intolerable.