

Use of intense pulsed light and a retinyl-based cream as a potential treatment for cellulite: a pilot study

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Summary

Background There are few therapeutic treatments established for cellulite.

Objective We studied the response of intense pulsed light (IPL) treatment with or without a compounded prescription retinyl-based cream on a small group of patients who had visible cellulite present on the buttocks and thigh regions.

Patients and methods Twenty patients were selected to complete a 12-week course of IPL treatment either with or without a retinyl-based cream. Assessment was based on visual evaluation, photographs, skin ultrasounds, and patient satisfaction.

Results Fifteen (75%) completed the study, and nine (60%) had a self-improvement rating of $\geq 50\%$. Seven (78%) of nine patients used IPL/cream. Of the remaining six (40%) completing the study, four (27%) had self-improvement ratings of 25–50% and two (13%; IPL only) were considered treatment failures with a rating of 10–25%. Both IPL/cream and IPL-only groups exhibited an improvement in the smoothness of the affected area even following weight gain. Skin ultrasounds confirmed an increase in the deposition of collagen. During an 8-month phone follow-up, 8 (67%) of 12 responding reported the same or improved results.

Conclusion IPL treatment with or without a retinyl-based cream can improve the appearance of peau d'orange cellulite, though the cream may augment cosmetic improvement. This approach is well tolerated, has minimal side effects, and is accompanied by a high degree of patient satisfaction.

Keywords: cellulite, collagen, intense pulsed light, IPL, peau d'orange, retinyl palmitate

Introduction

Cellulite is a disorder that afflicts mainly women and tends to occur in areas of the buttocks and thighs. It may occur as early as adolescence and can be unrelated to the patient's weight. Large pathologic studies documenting the histopathology of this disorder are not apparent. Pop

culture and numerous commercial internet sites claim that cellulite is caused by a variety of conditions ranging from inflammation, edema, poor lymphatic drainage, and fibrous adhesions to unspecified "toxins".

In an article on cellulite etiology, Draelos & Marenus¹ claimed that cellulite is caused by projections of subcutaneous fat into the reticular and papillary dermas. They further postulated that gaps in the "dermal structure" may be the consequence of a subclinical inflammatory process which may result in the constant activation of collagenase and elastase. The theory that the inflammatory process is involved in the production of cellulite seems to

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stem from one article by Zalla *et al.*² which found macrophages in close proximity to fat lobules. The projection of fat into the dermis ("finger lakes of fat") was also appreciated using high resolution *in vivo* magnetic resonance imaging (MRI) of the posterolateral thigh.³ The projection of fat into the reticular dermis was also qualified by Rosenbaum *et al.*⁴ in wedge biopsies and *in vivo* sonograms of the thigh.

Intense pulsed light (IPL) therapy, which emits light in the visible spectrum, has been approved by the FDA as a safe and effective means to decrease pigmented and vascular lesions and remove excess hair. Studies have shown that the thermal energy of IPL is also a means of stimulating collagen.^{5–8} Goldberg⁵ verified that IPL has collagen-boosting potential.

In addition, two studies demonstrated the benefits of low pulse fluences on collagen production. Bjerring *et al.*⁶ used a 585-nm pulse dyed laser to enhance collagen production. Prieto *et al.*⁷ studied the effects of IPL (560-nm cutoff filter) and the 1064-nm neodymium:yttrium-aluminum-garnet (Nd:YAG) laser on sun-damaged skin. The researchers concluded that both the IPL and Nd:YAG laser treatment resulted in deposition of collagen in the papillary dermis without evident morphologic damage to the epidermis or dermis.

We theorized, therefore, that IPL therapy may reduce small peau d'orange cellulite depressions by stimulating the deposition of collagen and thereby decreasing the projections of fat through the dermis. In a series of patients studied from October through December 2004, we noted in unpublished data that IPL treatment caused a clinically observable improvement in visible peau d'orange cellulite in eight (89%) out of nine patients following 12 weekly IPL treatments.

Two studies of topical retinol as a treatment of cellulite further peaked our interest. In a study of 15 women, Pierard-Franchimont *et al.*⁹ observed that retinol appeared to improve the resting tensions inside the skin, resulting in a smoother skin surface. In studying vitamin A on natural aging skin, Varani *et al.*¹⁰ concluded that vitamin A treatment reduces matrix metalloproteinase expression and stimulates collagen synthesis in both naturally aged and photoaged skin.

In this pilot study, we hypothesized that a compounded prescription retinyl-based cream may enhance the effects of IPL treatment on cellulite.

Materials and methods

Based on past observation, we speculated that weekly IPL treatments, up to a period of 12 weeks, would be needed to stimulate the formation of collagen. All IPL treatments were performed at our office (Mount Kisco, NY) using the

Quadra Q4 Intense Pulsed Light System loaned to the study by DermaMedUSA, Inc. (Media, PA).

The Quadra Q4 IPL system was chosen because of its safety profile, ease of use, and particular spectral pattern, which ranges between 510 nm and 1200 nm, with the majority of light energy centrally peaked in the 585-nm spectrum.

The retinyl-based cream (330 U/cc) used was prepared by Cross River Compounding Pharmacy (Cross River, NY). We chose retinyl palmitate as the base because of its short half-life,¹¹ well-known ability to stimulate type I collagen,^{9,10} and its ability to resist air oxidation.¹² Retinyl palmitate is not a hydrating cream.

Standardized 35-mm photographs were taken before and after the series of treatments.¹³ All photos were taken 3 feet away from the subject using a Nikon F-3 camera with a 60 macro lens, at f/22 and a shutter speed of 1/60, with Kodachrome 25 film.

Selected skin ultrasounds, obtained before and after the study on the treated leg, were performed by USA-Photonics (Nyack, NY) using the Dermascan C ultrasound (Cortex Technology, Hadsund, Denmark). All ultrasounds were performed by the same operator and taken in the same position: mid-posterior thigh, at the point deemed to be midway between the gluteal fold and the top of the posterior margin of the knee.

With each patient, one leg was randomly chosen as the treatment site; the other leg was the patient's own control. Patients who used the cream first removed the stratum corneum with acetone, then applied the cream to the affected area 5 nights a week. The cream was not applied the day before IPL treatment nor the day of IPL treatment due to concerns of photosensitivity.¹² Patients were encouraged to continue their present lifestyle and to avoid making any changes in their diet or exercise routines during the course of this study.

Patient population

A total of 20 women aged 23–56 years were selected for this study (Table 1), which was conducted from 10 January through 25 April 2005. All patients in the study had cellulite that was visible while standing or lying down. Patient exclusion criteria included (1) any major preexisting condition that might interfere with the patient's ability to maintain a regular treatment schedule, (2) a history of prior skin cancer, diabetes, autoimmune diseases, active infection, morbid obesity, known sensitivity to IPL, keloid formation or severe medical problems, and (3) a history of active tanning.

In our patient population, one patient had a history of selective serotonin reuptake inhibitor (SSRI) usage. Three

Table 1 Clinical features of women treated with IPL therapy, with or without cream.

Patient No.	Age (y)	Area Treated/ Skin Type*	Treatments (No.)	Treatment Modality	Average Energy Level (J/cm ²)	Comments
1	37	LT/II	11	IPL and cream	12	–
2	56	LT/II	12	IPL only	11.9	<ul style="list-style-type: none"> • Former smoker (24y) • Taking doxycycline during study • Hx heavy sun tanning
3	23	LT/II	12	IPL only	10.8	• Positive response despite short course of OCs
4	32	LT/IV	12	IPL and cream	10.5	• Developed cellulite at age 31y
5	54	RT/IV	12	IPL and cream	12.7	–
6	49	LT/III	12	IPL and cream	12.4	–
7	34	RT/IV	11	IPL and cream	12.3	• Taking topiramate and nortriptyline during study
8	46	LT/IV	9	IPL and cream	12.1	–
9	50	LT/III	12	IPL and cream	11.7	• Uses large amounts of MVIs, flax seed, borage oil
10	45	RT/III	12	IPL and cream	12	<ul style="list-style-type: none"> • On OCs >10y • Cellulite since age 14y
11	37	LT/III	12	IPL only	11.8	• Smoker
12	44	RT/II	12	IPL and cream	11.6	<ul style="list-style-type: none"> • Hx of rosacea • Used OCs for 15y
13	52	LT/ III	12	IPL and cream	11.5	<ul style="list-style-type: none"> • A/E: minor hypopigmentation; resolved at end of study • Hx heavy sun tanning • Cellulite appeared after leg lift in 2004
14	35	LT/III	12	IPL only	11.8	<ul style="list-style-type: none"> • Former smoker • Taking cetirizine • Daily SSRI use
15	52	LT/III	12	IPL only	11.7	–
16	45	LT/IV	8	IPL only	11	–
17	45	RT/II	5	IPL only	11.6	–
18	25	RT/II	5	IPL and cream	11.5	• Liposuction in 2003
19	44	RT/III	1	IPL and cream	9.5	–
20	45	RT/II	5	IPL only	9.4	–

*Skin type noted is based on Fitzpatrick scale.

Note: LT indicates left thigh; Rx, treatment; Hx, history; OCs, oral contraceptives; RT, right thigh; MVIs, multivitamins; A/E, adverse effects; and SSRI, selective serotonin reuptake inhibitor.

patients had a history of smoking, although only 1 patient smoked during the study time frame. Patient skin type varied from Fitzpatrick type II through IV. Individual weight among the participants varied widely.

This study met the criteria of our central Institutional Review Board (Liberty IRB, Deland, FL.). All patients signed written informed consent prior to participating in the study.

Treatment protocol

The treatment area was determined by visually inspecting the cellulite while the patient was standing as well as lying in the prone position. Before proceeding with IPL therapy, a test site was prepared. The stratum corneum was removed using acetone, and the skin was cooled with ice.

After waiting 2 min to be certain there was no significant erythema response to a given level of energy, fluence levels between approximately 8 and 14 J/cm² were applied, depending on skin type and patient tolerability. All patients received three 14 ms repetitive pulses, with 7 ms delay between the pulses, for a total treatment interval of approximately 56 ms.

All patients were encouraged to receive a total of 12 once-weekly IPL treatments. Patients were excluded from the study if they missed more than two consecutive weeks of treatment. Because some patients missed a few isolated treatments, total treatments ranged from 9 to 12 sessions.

IPL was applied in a step-by-step circumferential pattern. A repeat application was then performed depending on the patient's pain threshold and skin response. No anaesthetic cream was used. The average treatment time varied from 20 to 30 min, depending on the size of the

patient, the area of the leg being treated, and the length of time it took to cool the skin prior to therapy.

After administration of IPL therapy, the skin was again cooled with ice, and commercially available 99% pure aloe vera gel was applied to the treated area. Patients were instructed to use aloe vera at home, if needed. Patients were advised that IPL and retinyl palmitate may cause photosensitivity, and they were instructed to use adequate sunscreen and avoid direct sunlight at all times.

Eight (40%) patients were treated only with IPL and did not receive the cream. These patients either had a history of smoking and/or had questionable compliance.

Clinical evaluation

Clinical evaluation was completed both before and after the treatment period. Response to treatment was defined as patient evaluation of a 25% improvement in the appearance of cellulite by visual inspection. Before and after photographs of patient nos. 1 and 9 are shown in Figs 1 and 2, respectively. Both patients were treated with IPL and cream.

The primary objective of the study, to evaluate the effectiveness of IPL therapy in conjunction with retinyl-based cream, was met. Nine (60%) of 15 patients who completed the study reported a self-assessment of $\geq 50\%$, and 7 (78%) of these patients were treated with both IPL therapy and cream. However, our population base was not large enough to draw a definitive conclusion or provide adequate statistical analysis.

Results

Patient characteristics are summarized in Table 1. Fifteen (75%) of 20 patients completed the study, and 5 (25%) left the study for various reasons. Five (33%) of the patients completing the study were treated only with IPL therapy, while the remaining 10 (67%) patients were treated with both IPL therapy and cream. Nine (60%) patients who completed the study had a self-improvement assessment of $\geq 50\%$; 7 (78%) of these patients used both IPL and cream (Table 2). Patient #16 did not complete the study; however, she reported a 10–25% improvement prior to leaving the study.

Two patients (#14 and #15) were recorded as treatment failures because their self-improvement ranking was $< 25\%$. It should be noted that patient #15 was on daily SSRI use.

Patients with a distant history of heavy tanning (using reflectors and baby oil), smoking, or prolonged oral contraceptive use (patients #10–13) tended to rate their improvement as 25–50%. Patient #14, a former smoker, rated her improvement as 10–25%. This is consistent with our clinical experience. Only patient #2, a former smoker, noted cellulite improvement as $\geq 75\%$ (Fig. 3).

The known adverse effects of IPL therapy are blister formation, hypopigmentation, and skin burn. None of the patients developed blisters. Patient #13 developed minor hypopigmentation, which was resolved at the end of the study. Patient #20 developed a minor burn, which resolved before she left the study. Both events were

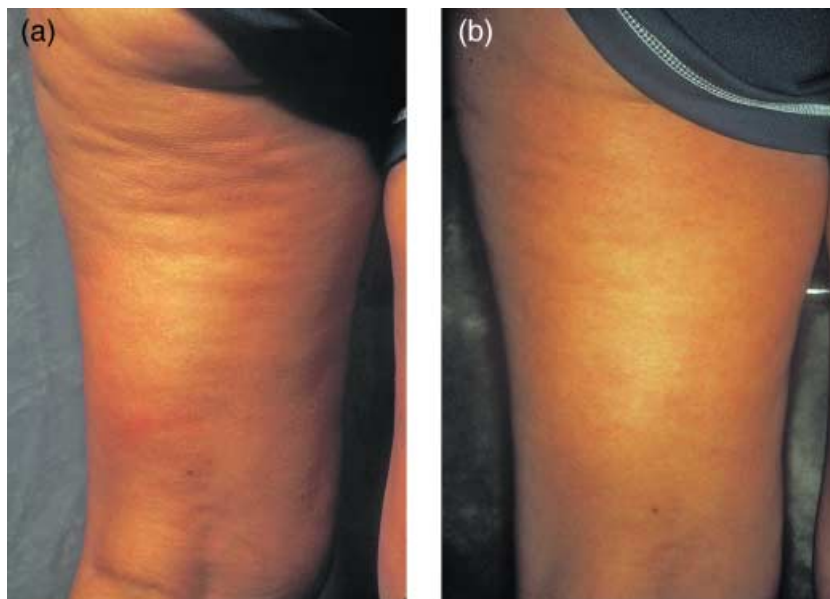


Figure 1 Patient #1. Treated with IPL and cream. (a) before treatment and (b) after 11 treatments at an average of 12 J/cm^2 . Self-assessment improvement rate, $\geq 75\%$. See Figure 4 for related ultrasound pictures.



Figure 2 Patient #9. Treated with IPL and cream. (a) before treatment and (b) after 12 treatments at an average of 11.7 J/cm². Self-assessment improvement rate, 50–75%.

reported as adverse effects (A/E), although they are not atypical of IPL therapy. There were no side effects noted from use of the cream. Two patients incurred unrelated orthopedic injuries, and both patients continued in the protocol.

Ultrasounds were completed on selected patients. Figure 3 compares the before and after ultrasound of patient #2, who received only IPL treatment. Figure 4 compares the before and after ultrasound of patient #4, who was treated with both IPL therapy and retinyl-based cream. The ultrasounds show an increased deposition of collagen in the cellulitic areas. This was accompanied by an increased density of the epidermis and dermis. There is a suggestion in the study that the increase in dermal density correlated with the improvement in the appearance of cellulite, though the study's design was not intended to prove or disprove this notion.

Half of the patients gained weight during the study and the other half did not. There was no correlation between changes in weight and perceived changes in cellulite.

Subjective patient evaluation

Of the 13 patients who showed a variable degree of improvement, there was agreement on the following statements:

- They would now have more confidence being seen in shorts.
- They want the untreated leg treated.
- They would recommend this treatment to a friend.
- IPL was not painful.

Discussion

The basic premise of our research is that cellulite is caused largely by a disruption of collagen. Collagen turnover in connective tissue is thought to be controlled in part by the balance between the levels of interstitial collagenase and tissue inhibitors of metalloproteinases (TIMPs).¹⁰

In an earlier series of patients we observed that IPL can lead to both a subjective and objective improvement in peau d'orange cellulite, mainly through the stimulation of collagen. Although we have not obtained biochemical evidence of collagen formation, we believe that the dermal ultrasounds (Figs 3 and 4) serve as an acceptable means by which the new deposition of collagen can be demonstrated.

Topical retinol has been previously evaluated as a treatment for cellulite.^{9,10} Collagen is a major component of the extracellular matrix,¹⁴ and derivatives of vitamin A target matrix metalloproteinase-1 (MMP-1) or collagenase.¹⁵ Indeed, 1% vitamin A cream applied topically can stimulate fibroblast growth and collagen synthesis after just 7 days and at the same time can reduce the levels of matrix-degrading metalloproteinases.¹⁵

Oral contraceptives may decrease levels of type I and type III procollagen. This is especially noted in formulas with an ethinyl estradiol concentration > 20 µg.^{16,17} Patient #10, who had been on oral contraceptives for > 10 years, reported only a 25–50% improvement despite the use of IPL and cream. Patient #3, who was on oral contraceptives transiently during the study due

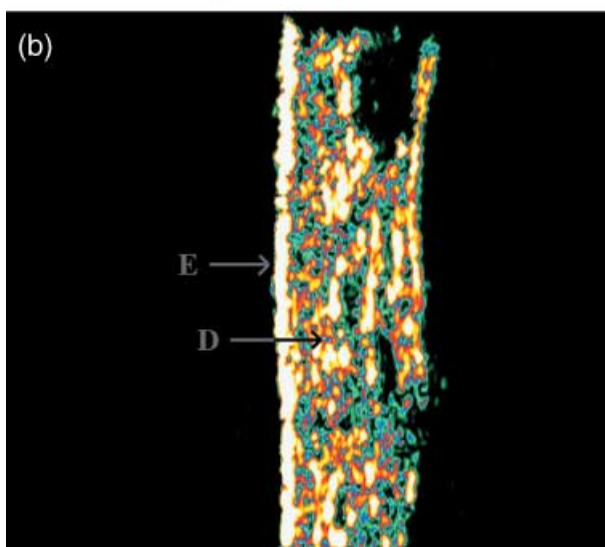
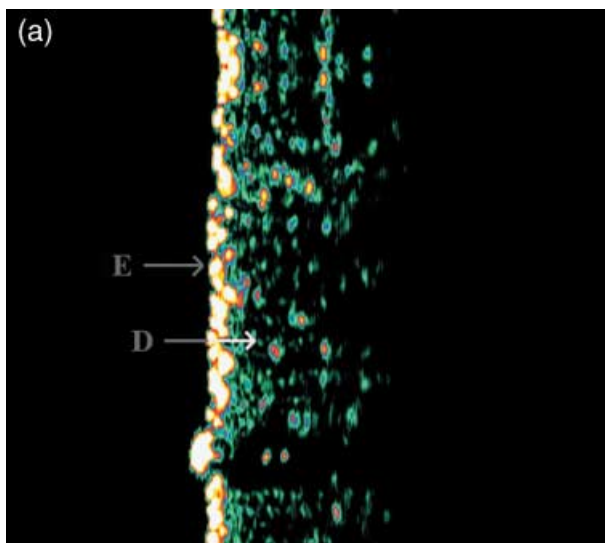


Figure 3 Patient #2. Treated with IPL only. Skin ultrasound. (a) before treatment and (b) after 12 treatments at an average of 11.9 J/cm^2 . Self-assessment improvement rate, $\geq 75\%$. Arrow E points to the epidermis, which is shown in white. Arrow D points to the dermis, which is shown as mainly green. The different colors represent different densities of tissue. The white areas represent the densest tissue, while the green areas represent tissue of a middle-density range. Note the denser appearance of the dermis after IPL treatment. Patient claimed cellulite was improved by treatment 4.

to dysfunctional uterine bleeding, reported a $\geq 75\%$ improvement.

The patients in our study did not need to wear an occlusive dressing. In a study by Rao and Goldman,¹⁸ patients used a “novel topical agent” with an occlusive garment. Their study reported a 65% improvement in the appearance of cellulite.¹⁸

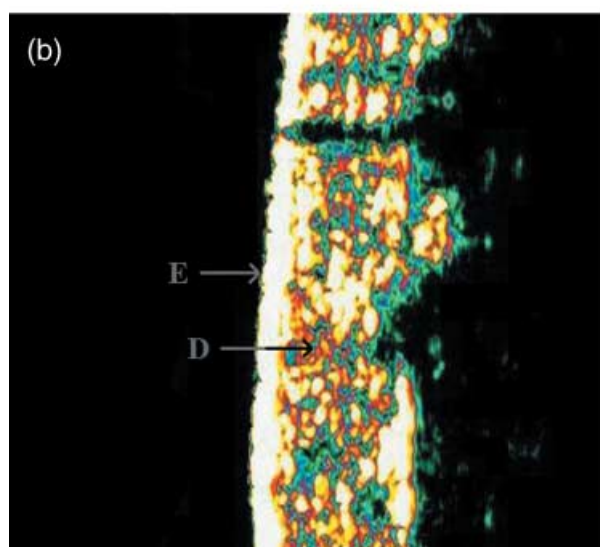
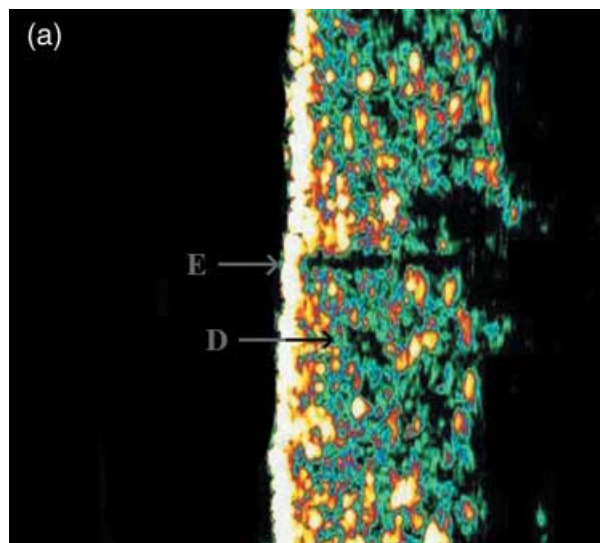


Figure 4 Patient #1. Treated with IPL and cream. Skin ultrasound. (a) before treatment and (b) after 11 treatments at an average of 12 J/cm^2 . Self-assessment improvement rate, $\geq 75\%$. Arrow E points to the epidermis, which is shown in white. Arrow D points to the dermis, which is shown as mainly green. The different colors represent different densities of tissue. The white areas represent the densest tissue, while the green areas represent tissue of a middle-density range. Note the denser appearance of the dermis after IPL treatment. See Figure 1 for patient leg photographs.

Cigarette smoke is known to decrease the formation of collagen.¹⁹ The active smoker in our study (patient #11) reported improvement, though less than other responders.

Patient #2, a former smoker, had an excellent response to IPL therapy, both from the perspective of ultrasound improvement (Fig. 3) and cosmetic correction (self-

Table 2 Self-assessment response at end of study and at 8-month follow-up.

Patient No.	Self-Assessed Improvement Rate (%)		Weight Before/ After Rx (kg)	Comments
	End of Study	8-Month Follow-up		
1	75	50–75	67.2/+3.3	• Improvement by Rx 5
2	75	75	60/–1.1	• Improvement by Rx 4
3	75	NA	64/+0.5	–
4	75	NA	67.3/–0.5	• Improvement by Rx 7
5	50–75	> 50–75	82.7/+1.3	• Improvement after Rx 7 • Gained 4.5–6.8 kg by 8-mo follow-up
6	50–75	50–75	69.5/+0	• Improvement by Rx 8
7	50–75	50–75	64/+0.5	• Improvement by Rx 8
8	50–75	50–75	64.1/–2.3	• Significant improvement by Rx 8
9	50–75	50–75	52.7/+0	• Improvement by Rx 5
10	25–50	10–25	55.9/+0.	–
11	25–50	25–50	62.7/–1.8	–
12	25–50	NA	63.6/–2.7	–
13	25–50	NA	62.3/+0.5	• Improvement by Rx 6
14	10–25	0	55.5/+0.9	–
15	10–25	25–50	52.3/+1.4	–
16	10–25	NA	67.7/NA	• Left study; no follow-up
17	NA	NA	70.4/NA	• Left study; no follow-up • Noticed difference after Rx 4
18	NA	NA	64.1/NA	• Left study; noncompliant • Improvement by Rx 3
19	NA	NA	86.4/NA	• Left study; no follow-up
20	NA	NA	59.1/NA	• Left study; no follow-up • A/E: small burn; resolved • Improvement by Rx 4

Note: Rx indicates treatment; NA, not available.

assessment improvement rate $\geq 75\%$). For unrelated reasons, this patient was taking doxycycline, a known inhibitor of collagenase,²⁰ and did not display any photosensitivity to IPL. Further evaluation of her case is warranted and may point the way to future research.

Patient #15, who was taking an SSRI for depression, did not exhibit an initial response to IPL therapy. This may be purely coincidental, though SSRIs have been shown to decrease collagen-induced platelet aggregation.²¹ In our experience, we have consistently seen decreased responses to IPL treatment in patients on SSRIs. It is unclear if this is due to an interaction between SSRIs and collagen or to a direct action of this class of drugs on the platelets. If the former is true, further studies are warranted to determine if SSRIs inhibit collagen formation or degradation.

We found it interesting that cellulite had responded in women of various weights up to 86.4 kg. There is a general consensus in both the medical and nonmedical

communities that cellulite can be improved by weight loss. However, it is the common experience of many physicians and patients that cellulite is not improved by localized changes of fat distribution (for example, following liposuction). In our study, cellulite did improve in individuals of varied weight, none of whom were consistently on diets nor followed any type of regimented diet or exercise program. This lends further support to the concept that the appearance or improvement of cellulite is not necessarily a function of fat, *per se*, as it is a disruption in collagen.

Mirrashed *et al.*³ found a correlation between the extrusion of underlying dermis and the grading of cellulite. These researchers also found that other tissue perimeters, such as the percentile of adipose vs. connective tissue in a given volume of hypodermis, correlate with the cellulite grade. This theory would further support our hypothesis that cellulite is caused by both fat herniation³ and the loss of collagen integrity.⁴ Ultrasounds taken after the IPL-only or IPL and cream treatments depict a denser dermis

(Figs 3 and 4). We speculate that the denser dermis made fat less likely to herniate, thereby improving the appearance of cellulite.

Overall, 60% (9) of our patients had a $\geq 50\%$ improvement in cellulite at 3 months; at 8 months, 47% (7) reported the same improvement; 13% (2) were lost to follow-up. Of the five patients treated only with IPL, two (40%) had a self-assessment rating of $\geq 75\%$. Of the ten patients who were treated with IPL and cream, two (20%) reported a self-assessment rating of $\geq 75\%$, and five (50%) patients reported a 50–75% improvement. In theory, the retinyl-based cream should have longer lasting benefits compared to other creams on the market because retinyl-based cream results in architectural changes.¹⁰

Our study had several limitations. Using a limited sample size of 15 patients, this pilot study was designed not to determine efficacy but rather to show a potential trend, stimulate interest in this as a possible treatment, and provide an impetus for further study. As a small study with several variables, including the number of treatments given, energy levels used, and self-assessment ranges, we were unable to run an accurate statistical analysis. In addition, we had limited access to an ultrasound machine. A larger study, including further evaluation of IPL therapy with retinyl creams and possibly pathological studies, would be welcomed.

Conclusion

We believe that IPL therapy using the Quadra Q4 system is an effective and painless means of treating peau d'orange cellulite in women of all ages including postmenopausal women. The use of retinyl-based cream may augment the cosmetic results obtained.

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