STUDY

Blinded, Randomized, Quantitative Grading Comparison of Minimally Invasive, Fractional Radiofrequency and Surgical Face-lift to Treat Skin Laxity

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Objectives: To quantify the improvements in laxity from the surgical face-lift and to perform a randomized, blinded comparison with the clinical effects of a novel, minimally invasive fractional radiofrequency (FRF) system.

Study Design: Randomized, blinded, comparative trial.

Patients: Fifteen sequential patients with facial skin laxity enrolled in the trial and completed FRF treatment and follow-up. Baseline and follow-up digital photographs of patients undergoing FRF were randomly mixed with 6 sets of baseline and follow-up images of patients undergoing surgical face-lift with equivalent baseline facial laxity grades.

Main Outcome Measures: Five independent blinded evaluators graded randomized baseline and 3- to 6-month follow-up photographs using a comprehensive quantitative 4-point laxity grading scale. Quantitative changes in laxity grades were calculated and compared statistically for FRF treatment vs surgical face-lifts. Patient satisfaction and adverse events were also evaluated.

Results: Blinded grading of unmarked, randomized baseline and follow-up photographs of patients undergoing FRF treatment randomized with baseline and follow-up photographs of patients undergoing surgical face-lift demonstrated statistically significant improvement in facial laxity, with a mean grade improvement of 1.20 for patients in the surgical face-lift group and of 0.44 for FRF-treated patients on a 4-point laxity grading scale ($P < .001$). The improvements relative to baseline were 16% for FRF treatment compared with 49% for the surgical face-lift. The mean laxity improvement from a single FRF treatment was 37% that of the surgical face-lift. Patient satisfaction was high (dissatisfied, 0%; neutral, 7%; satisfied, 60%; and very satisfied, 33%). All participants in the FRF treatment group experienced transient erythema, mild edema, and mild to moderate purpura that resolved in 5 to 10 days, and they returned to normal activities within 24 hours. There were no adverse events or complications in the FRF group. All patients in the surgical face-lift group experienced scarring at surgical margins, erythema, edema, and ecchymosis, and they returned to normal activities on suture removal at 7 to 10 days.

Conclusions: This randomized, blinded, quantitative assessment using a validated grading scale of skin laxity improvement from the gold standard treatment, the surgical face-lift, and comparative analysis to a novel, minimally invasive FRF treatment has demonstrated 49% improvement in skin laxity relative to baseline for the surgical face-lift, compared with 16% for FRF. The surgical face-lift resulted in a mean 1.20-grade improvement on the 4-point laxity grading scale. In comparison, a single, minimally invasive FRF treatment demonstrated a 0.44–laxity grade improvement, or 37% that of the surgical face-lift, without the adverse effects and complications of surgical procedures. This study provides a basis for quantifying cosmetic outcomes from novel treatments with comparative analysis to the gold standard. It also suggests that minimally invasive FRF treatment may provide an important nonsurgical option for the treatment of facial skin laxity.

Trial Registration: clinicaltrials.gov Identifier: NCT00791414

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SKIN AGING MAY BE CATEGORIZED as intrinsic aging, owing to genetic factors and characterized by laxity and deep rhytids, and photoaging, owing to ultraviolet damage and characterized by dyschromia, elastosis, fine rhytids, erythema, telangiectasia, textural changes, and keratoses.[1] Laser, light, and radiofrequency (RF) energy sources have succeeded in treating the second category of skin aging; however, the surgical face-lift remains the gold standard for the treatment of laxity associated with intrinsic aging. Nonsurgical devices have been used to treat rhytids and laxity because patients are willing to trade the greater cosmetic improvement obtained from surgical treatment for the minimal risk and rapid recovery associated with the former.[2] To date, however, the level and consistency of outcomes from laser and energy-based technologies have not been comparable to surgical face-lift results, nor,

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to our knowledge, has a valid comparative study to the gold standard of surgical face-lifts ever been conducted.

The Miratone minimally invasive bipolar fractional RF (FRF) system (Primaeva Medical, Inc, Pleasanton, California) heats the dermis from within using a microneedle electrode array.[3] The microneedle electrodes are arranged in pairs between which bipolar RF energy is delivered. Thermal lesions are fractionally generated directly within the reticular dermis. The volume of each lesion is defined by the geometry of the microneedle electrode pairs. Real-time feedback of lesion temperature from sensors in the tips of the microneedle electrodes allows energy delivery to be precisely modulated so that lesions are created at a specific preselected temperature and for defined time periods. The fractional pattern of injury, wound healing, and dermal remodeling processes induced following treatment were recently described histologically in skin to be excised in subsequent abdominoplasty or face-lift procedures.[3,4] Fractional thermal injury of deep dermal collagen induced a vigorous wound healing process leading to dermal remodeling and the generation of new collagen, elastin, and hyaluronic acid, suggesting the device could become an effective treatment option with predictable outcomes for the treatment of laxity and rhytids associated with intrinsic aging. To date, there remain no published reports quantifying the laxity improvements from the gold standard treatment, the surgical face-lift, or comparatively analyzing the clinical outcome of noninvasive or minimally invasive nonsurgical treatment of skin laxity with surgical face-lift outcomes. In prior studies evaluating outcomes from surgical face-lifts, descriptive impressions were used, including "poor, good, or excellent."[5-7] In contrast, the present study is the first to use quantitative, blinded evaluations with a tested laxity grading scale. In this investigational study, we evaluate the clinical effects of FRF for the treatment of facial laxity and compare the outcomes with surgical face-lift results through randomized, blinded assessment of digital baseline and follow-up clinical photography.

METHODS

The study protocol was approved by the Western Institutional Review Board. All participants provided verbal and written consent before enrollment. Patient consent for digital photography was also obtained before treatment. Randomized (not paired in sequence) digital baseline and 3- to 6-month follow-up images of 15 sequential patients completing FRF treatment and follow-up were intermixed with 6 sets of randomized baseline and 3- to 6-month follow-up images of surgical face-lift patients with equivalent baseline facial laxity, selected from a surgical face-lift pool by one of us, a plastic surgeon (D.R.). The FRF treatment and surgical face-lift photographs were equivalently cropped and randomly intermixed. Pretreatment and posttreatment photographs were not in sequence, but randomly assorted throughout the intermixed FRF and surgical photographs. Blinded grading was performed by 5 independent evaluators (J.D., K.A., and 3 others), including dermatologists and plastic surgeons, who were unaware of the nature or types of treatments being tested, using a quantitative 4-point grading scale assessing changes in skin laxity.[8-10] The blinded evaluators were unaware that surgical face-lift photographs were included in this study, nor were they privy to the type of nonsurgical treatment being tested.

FRACTIONAL RF

Patient Selection

The FRF treatments were performed by the lead author (M.A.-A.) using a study protocol approved by an institutional review board. Inclusion criteria were being older than 18 years, in good health, and with mild to severe facial rhytids or laxity (minimum baseline laxity, grade 2). Exclusion criteria consisted of history of injection with silicone, fat, collagen, or a synthetic material in the intended treatment area, bleeding disorder, hypertrophic scar or keloid formation, isotretinoin treatment in the past 12 months, anaphylaxis, or lidocaine hypersensitivity. Other exclusion criteria included prior, current, or anticipated treatment with anticoagulants; thrombolytics; chemotherapeutics; systemic corticosteroids; or anabolic steroids. Patients with a compromised immune system, impaired wound healing (eg, patients with diabetes mellitus), collagen vascular disease, an implantable electronic device (eg, pacemaker), or active infection were also excluded. Participants were required to be available for posttreatment follow-up evaluation.

FRF Treatment Protocol

Patients undergoing FRF received fixed-temperature symmetrical treatment of the lateral mid and lower face with the Miratone system. The FRF energy was delivered through 5 microneedle electrode pairs deployed in the reticular dermis at an angle of 20° to the skin surface, with the exposed electrode length extending from 0.75 to 2 mm below the skin surface (**Figure 1**). The precise intradermal location of the electrode tips was determined by real-time impedance measurements, such that impedance measurements between 300 and 2000 Ω were used to define ideal intradermal placement.[3] Typical dermal impedance measurements were between 500 and 1500 Ω. Software built into the device precluded energy delivery if impedance between an electrode pair measured less than 300 or more than 3000 Ω, thereby restricting energy delivery to proper intradermally placed electrodes.[3] Software was also programmed to deliver energy until a preselected intradermal target temperature was attained and for a specified duration in seconds (**Figure 2**). Epidermal cooling was achieved by positioning a cooling device maintained at a temperature of 15°C directly on the skin above the exposed electrode length. The spacing of the bipolar needle pairs and the spacing during successive applications of the device were selected to give 15% to 35% fractional skin coverage by surface projection. Patients 1 through 5 received topical anesthesia (EMLA cream; APP Pharmaceuticals, LLC, Schaumburg, Illinois) only, applied for 45 to 60 minutes before treatment. Conservative treatment parameters of 62°C and 3 seconds were selected for these patients. Patients 6 through 15 received additional local infiltration with diluted lidocaine (0.25% with 1:400 000 epinephrine). A local anesthetic (mean quantity, 18 mL of 0.25% lidocaine) was used in both cheeks and in the submental and lateral neck regions. For these patients, more aggressive treatment parameters of 68°C to 78°C and 5 seconds were selected. A representative real-time temperature curve for a preselected target temperature of 70°C for 5 seconds is shown in Figure 2. Before treatment, the patient's skin was cleansed with Betadine (Purdue Pharma, Stamford, Connecticut), and treatments were delivered medial to lateral in rows following anatomical margins. Postoperatively, the patient's skin was cleansed with isotonic sodium chloride solution, and a thin coat of white petrolatum was applied. Patients were allowed to resume normal activities immediately and were instructed to wash the skin with mild cleansers, to avoid makeup for 24 hours, and to minimize sun exposure for 14 days. Patients were required to report any discomfort, ad-

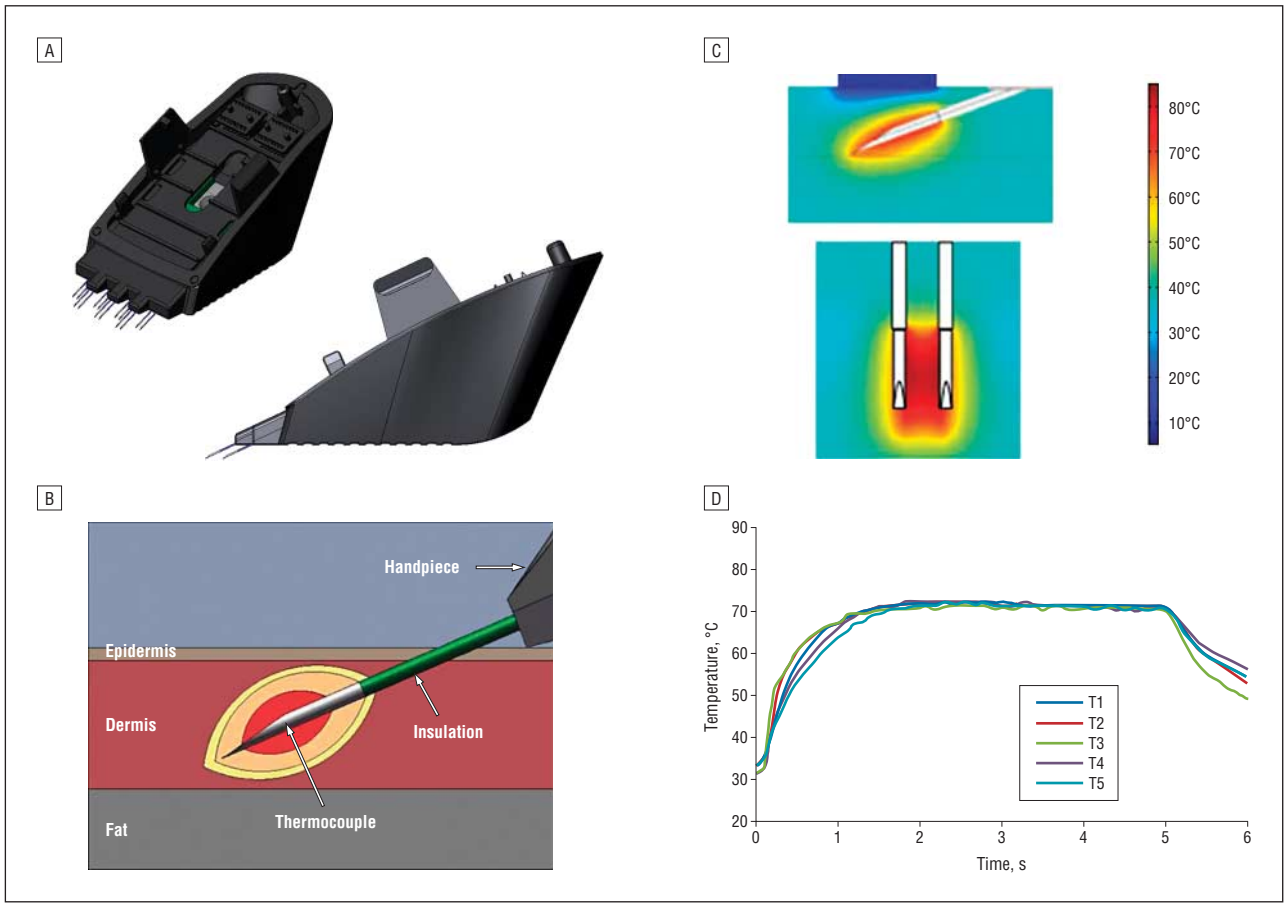

Figure 1. Schematic of the fractional radiofrequency (FRF) handpiece, energy delivery, real-time temperature feedback, and time-at-temperature control. The FRF handpiece consists of 5 paired electrodes that are insulated, except for the distal tips extending from 0.75 to 2 mm beneath the skin surface, thereby assuring dermal energy delivery and protection of the superficial dermis and epidermis (A). The 32-gauge electrode tips are inserted into the dermis at a 20° angle (B). Temperature sensors are built into each electrode pair (C), thereby providing accurate real-time temperature readings, as opposed to mathematical modeling, as in prior modalities. Software is programmed to emit energy until preselected target temperatures (eg, 70°C) are attained and to maintain temperature for a desired duration (eg, 5 seconds); parameters are selected for optimal collagen denaturation (D).

verse effects, and complications during or following treatment and completed questionnaires at each follow-up visit. Patients were followed up at 1, 3, and 6 months following treatment. During 3- and 6-month follow-up visits, patients were asked to rate their overall satisfaction and their impression of wrinkles and laxity improvement using a 5-point scale.

SURGICAL FACE-LIFT PROCEDURE

Surgical face-lifts were performed by one of us (D.R.). Each patient received general endotracheal and local anesthesia. The procedure consisted of submentoplasty, suction and excisional lipectomy, and deep-plane plication. The incision and dissection extended from the malar eminence and mandibular angle into the neck in the preplatysmal plane to the midline and submental incision. The deep-plane dissection extended deep to the jowl fat and inferiorly to 2 cm below the mandibular angle and continued anteriorly within the fibroadipose tissues of the melolabial fold and deep to the superficial muscular aponeurotic system of the jowl. The melolabial fold was approached by undermining the fibroadipose layer of the cheek overlying the zygomatic muscles and anteroinferiorly to the nose and lip. The superficial muscular aponeurotic system of the jowl was undermined from the parotid gland to the masseter. The dissection continued anteriorly over the masseter muscle border and inferiorly over the lower border of the mandible, extending anteriorly to where the facial artery crosses. The cheek flap was closed by suturing the superficial muscular aponeurotic system flap to the preauricular tissue and anchoring the flap posteriorly, just anterior to the tragus. The platysmal flap, beginning at the mandibular angle, was sutured to the mastoid periosteum. Redundant preauricular tissue was excised. Excision and closure of the skin flap commenced at the apex of the postauricular incision, followed by skin excision and closure anteriorly and posteriorly. The postauricular, hair-bearing region and temporal incision were closed superficially with staples and sutures. A compression head dressing was placed and secured with burn netting. Patients received treatment overnight by a registered nurse, were instructed about wound care, and had sutures removed 7 to 10 days posttreatment.

QUANTITATIVE LAXITY GRADING, ASSESSMENTS, AND STATISTICAL ANALYSIS

Standardized photographs were taken for the FRF patient group at baseline on the day of treatment and during each follow-up visit. Standardized photographs were taken for the surgical face-lift pool during their preoperative office visit and during routine 3- to 6-month follow-up visits. Six sets of baseline and follow-up surgical face-lift images with baseline facial laxity spanning mild (n=1), moderate (n=3), and advanced (n=2) categories were selected by one of us (D.R.) as representative surgical face-lift patients. Photographs were taken

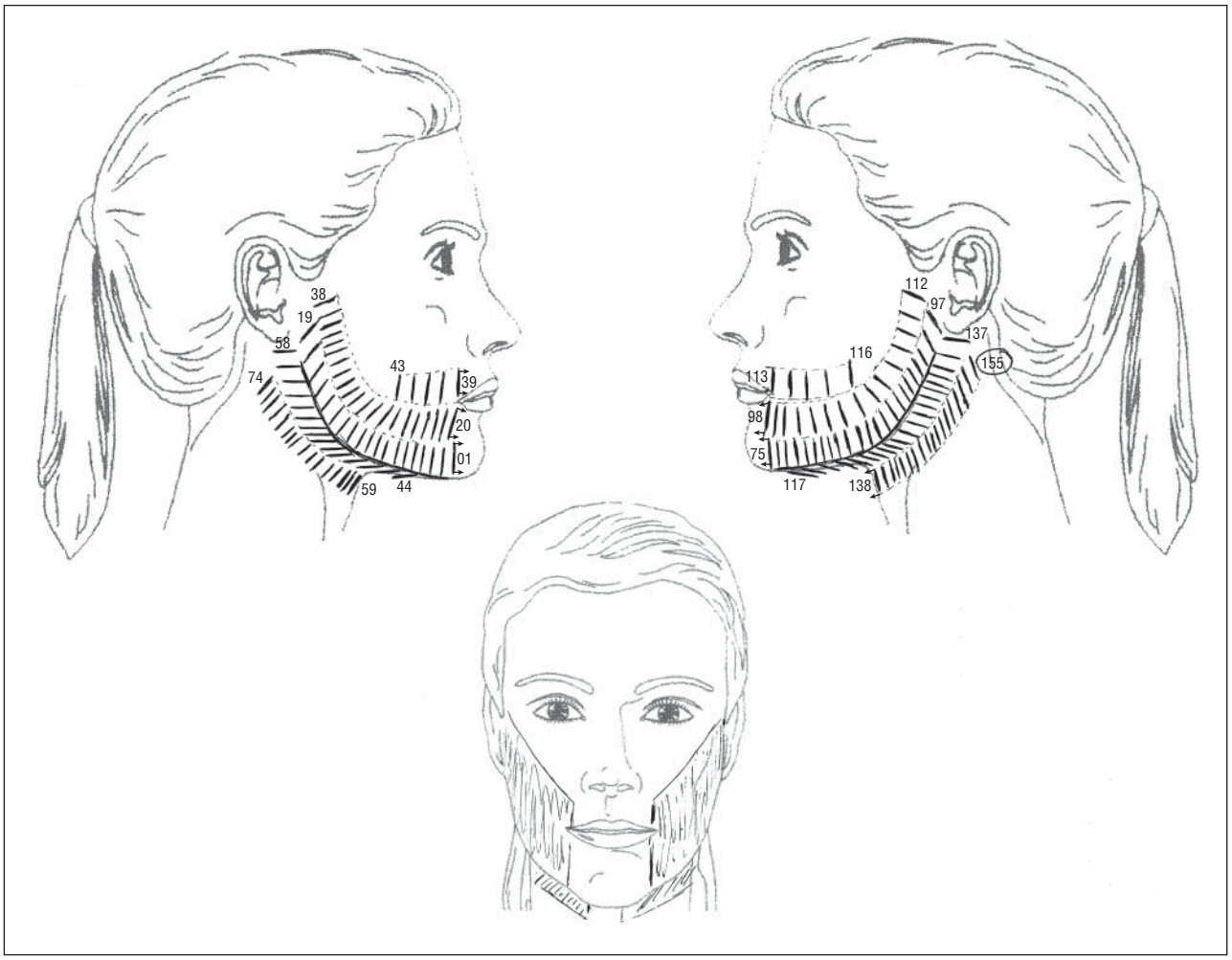

Figure 2. Schematic representation of the insertion sites and distribution of the electrode tips of the handpiece. The paired electrode tips were inserted at an interval of 3 to 5 mm apart in the distribution shown. A total of 155 insertions were administered to this patient. The insertion sites typically involved the melolabial folds medially on the lower part of the face extending to the preauricular regions, as shown. In the submental and submandibular regions, insertions were typically delivered from the midline submental region medially extending to the infra-auricular regions laterally and the lateral aspects of the upper part of the neck inferiorly.

using a digital single-lens reflex camera (model E-500; Olympus America, Central Valley, Pennsylvania) fitted with an external shoe-mounted electronic flash (model FL-50, Olympus America) and a fixed focal length 50-mm 1:2 macro lens (Olympus ED), using standardized settings (F9.0, 1/125, ISO400) from a 1-m distance and in a photography room with set lighting for every patient. The FRF treatment and surgical face-lift photographs were equivalently cropped and randomized. Five independent blinded evaluators graded the unidentified images using a Quantitative Comprehensive Grading Scale for facial and neck laxity[8-10] (**Table 1**). The grading system is binary, and blinded evaluators determine the patient's laxity grade category based on the presence or absence of a given finding (eg, melolabial folds). Two of the blinded evaluators (J.D. and K.A.) have used this grading scale in a prior study.[12] The evaluators were not informed of the randomized comparison to the surgical face-lift or of the nature of the intervention. Upon unblinding, the results were tabulated, grouped, and analyzed. Mean baseline and follow-up grades with standard deviations were calculated for each patient. The reliability of the grade assignment agreement of independent evaluators was assessed by calculating a Fleiss κ statistic using each one-half point grade assignment from 0 to 4 of the laxity scale as categorical ratings. The improvement for each patient was calculated as the difference between the mean baseline and mean follow-up grades, and a paired *t* test was used to assess statistical significance. The mean baseline and follow-up grades for each treatment modality group were then averaged and compared using a paired *t* test. The percentage FRF to surgical face-lift result and the percentage improvement over baseline for each patient pool were calculated.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

Fifteen sequential patients completing treatment and follow-up were included in the FRF group. All patients were women, and the mean (SD) age was 59.7 (8.9) years. Two patients (13%) were Fitzpatrick skin type I, 8 (53%) were type II, 4 (27%) were type III, and 1 (7%) was type IV. In the surgical face-lift group (6 patients), all patients were women, and the mean (SD) age was 54.0 (9.2) years. Three patients (50%) were Fitzpatrick skin type I and 3 (50%) were type II. The baseline mean laxity grades were similar: 2.76 for

Table 1. Quantitative Comprehensive Grading Scale[a] of Rhytids, Laxity, and Photoaging[8-10]

Grading Scale	Descriptive Parameter	Skin Aging and Photodamage						
		Rhytids	Laxity	Elastosis	Dyschromia	E-T	Keratoses	Texture
0	None	None	None	None	None	None	None	None
1	Mild	Wrinkles in motion: few, superficial	Localized, NL folds	Early, minimal yellow hue	Few (1-3) discrete, small (<5 mm) lentigines	Pink E or few T, localized to a single site	Few	Subtle irregularity
1.5	Mild	Wrinkles in motion: multiple, superficial	Localized, NL and early ML folds	Yellow hue or early, localized PO EB	Several (3-6) discrete, small lentigines	Pink E or several T, localized 2 sites	Several	Mild irregularity in a few areas
2	Moderate	Wrinkles at rest: few, localized, superficial	Localized, NL/ML folds, early jowls, early submental/SM	Yellow hue, localized PO EB	Multiple (7-10) small lentigines	Red E or multiple T, localized to 2 sites	Multiple, small	Rough in a few localized sites
2.5	Moderate	Wrinkles at rest: multiple, localized, superficial	Localized, prominent NL/ML folds, jowls and SM	Yellow hue, PO and malar EB	Multiple small and few large lentigines	Red E or multiple T, localized to 3 sites	Multiple, large	Rough in several localized areas
3	Advanced	Wrinkles at rest: multiple forehead, periorbital, and perioral sites, superficial	Prominent NL/ML folds, jowls and SM, early neck strands	Yellow hue, EB involving PO, malar and other sites	Many (10-20) small and large lentigines	Violaceous E or many T; multiple sites	Many	Rough in multiple, localized sites
3.5	Advanced	Wrinkles at rest: multiple generalized, superficial; a few deep	Deep NL/ML folds, prominent jowls and SM neck strands	Deep yellow hue, extensive EB with little uninvolved skin	Numerous (>20) or multiple large lentigines with little uninvolved skin	Violaceous E and numerous T; little uninvolved skin	Little uninvolved skin	Mostly rough with little uninvolved skin
4	Severe	Wrinkles throughout: numerous, extensively distributed, deep	Marked NL/ML folds, jowls and SM, neck redundancy and strands	Deep yellow hue, EB throughout, comedones	Numerous, extensive lentigines; no uninvolved skin	Deep, violaceous E and numerous T throughout	No uninvolved skin	Rough throughout

Abbreviations: EB, elastotic beads; E-T, erythema-telangiectasia; FRF, fractional radiofrequency; ML, melolabial; NL, nasolabial; PO, perio-orbital; SM, submental/submandibular.

[a]This 4-point grading scale has been extensively tested and used for evaluating laser and energy-based cosmetic treatments.[9,11-13] The laxity category was used by blinded evaluators to assess the baseline and follow-up laxity grades following surgical face-lift and FRF treatment in the present study.

the FRF group and 2.47 for the surgical face-lift group (**Table 2**).

EFFICACY

Photographic examples of typical patient outcomes from surgical face-lift and FRF treatment are shown in **Figures 3**, **4**, **5**, **6**, and **7**. The results of the blinded grading evaluation and statistical analysis for the FRF treatment and surgical face-lift patient groups are shown in Table 2. These results are summarized and compared in **Table 3**. There was good agreement between the laxity grades assigned by all independent evaluators (Fleiss $\kappa=0.45$), with standard errors less than or equal to the laxity scale resolution. The mean (SD) laxity grade improvement for the FRF treatment and surgical face-lift patient pools were 0.44 (0.20) ($P<.001$) and 1.20 (0.44) ($P<.001$), respectively. The percentage improvements relative to mean baseline for the FRF treatment and surgical face-lift patient pools were 16% and 49%, respectively. The mean percentage improvement for FRF treatment was 37% that of the surgical face-lift.

Patient self-assessments of clinical improvements from FRF yielded a mean rating of moderate for rhytids and moderate to significant for laxity. Patient satisfaction with FRF treatment was high: 0% were dissatisfied; 7%, neutral; 60%, satisfied; and 33%, very satisfied.

ADVERSE EVENTS

There were no adverse events or complications in the FRF treatment group. All participants experienced transient erythema, swelling, and ecchymoses, which resolved in 5 to 10 days. On a scale of minimal, mild, moderate, advanced, and severe, the erythema was mild to moderate and resolved within 24 hours in the vast majority of patients. The edema varied from minimal to moderate among the patients and resolved gradually in 5 to 10 days. Ecchymoses varied from minimal to advanced and resolved in the vast majority of patients within 5 to 10 days, with the exception of 1 patient who had residual yellow-brown discoloration that resolved 2 to 3 weeks postoperatively. Topical anesthesia minimized discomfort associated with microneedle deployment. However, topical anesthesia alone proved marginal to inadequate for managing discomfort associated with dermal heating during FRF energy delivery. In contrast, patients receiving diluted local anesthesia with or without prior topical anesthesia tolerated all aspects of treatment with minimal discomfort. All patients returned to normal activities within 24 hours.

All surgical face-lift patients had sutures in place for 7 days and experienced scarring, which varied from mild to hypertrophic, at surgical margins. In 4 of the 6 surgical patients, hypertrophic scars developed in the pre- and

Table 2. Blinded Grading Data of 15 FRF and 6 Surgical Face-lift Patients[a]

Patient No.	Grade (SD)			*P* Value
	Baseline Laxity	Follow-up Laxity	Laxity Change	
FRF Treatment Group				
M01	2.7 (0.3)	2.1 (0.4)	0.6	.004
M02	3.0 (0.0)	2.4 (0.2)	0.6	.004
M03	2.4 (0.2)	1.9 (0.2)	0.5	<.001
M04	2.3 (0.4)	1.7 (0.3)	0.6	.004
M05	3.0 (0.5)	2.6 (0.5)	0.4	.02
M06	3.3 (0.3)	3.1 (0.5)	0.2	.18
M07	3.4 (0.4)	3.0 (0.4)	0.4	.10
M08	2.3 (0.3)	1.7 (0.3)	0.6	.004
M09	2.4 (0.4)	2.0 (0.4)	0.4	.10
M10	2.0 (0.0)	1.5 (0.0)	0.5	<.001
M11	2.2 (0.3)	1.5 (0.0)	0.7	.005
M12	3.8 (0.3)	3.3 (0.3)	0.5	<.001
M13	3.5 (0.0)	3.5 (0.0)	0.0	NA
M14	2.5 (0.5)	2.4 (0.2)	0.1	.70
M15	2.4 (0.4)	1.9 (0.4)	0.5	<.001
Mean	2.75	2.31	0.44	<.001
Surgical Face-lift Group				
P1	2.8 (0.4)	1.3 (0.4)	1.5	<.001
P2	3.4 (0.4)	1.8 (0.4)	1.6	<.001
P3	2.0 (0.4)	1.4 (0.2)	0.6	.03
P4	3.2 (0.3)	1.7 (0.3)	1.5	.001
P5	2.0 (0.4)	1.3 (0.3)	0.7	.005
P6	1.4 (0.2)	0.1 (0.2)	1.3	<.001
Mean	2.47	1.27	1.20	<.001

Abbreviations: FRF, fractional radiofrequency; NA, not applicable.
[a]Each randomized digital baseline and follow-up image was evaluated by 5 blinded evaluators using the quantitative 4-point laxity grading scale. Upon unblinding, the mean baseline and follow-up laxity grades were calculated for each FRF and surgical face-lift patient, and the mean change in laxity grade was calculated. In both groups, the mean laxity grade change was statistically significant ($P<.001$).

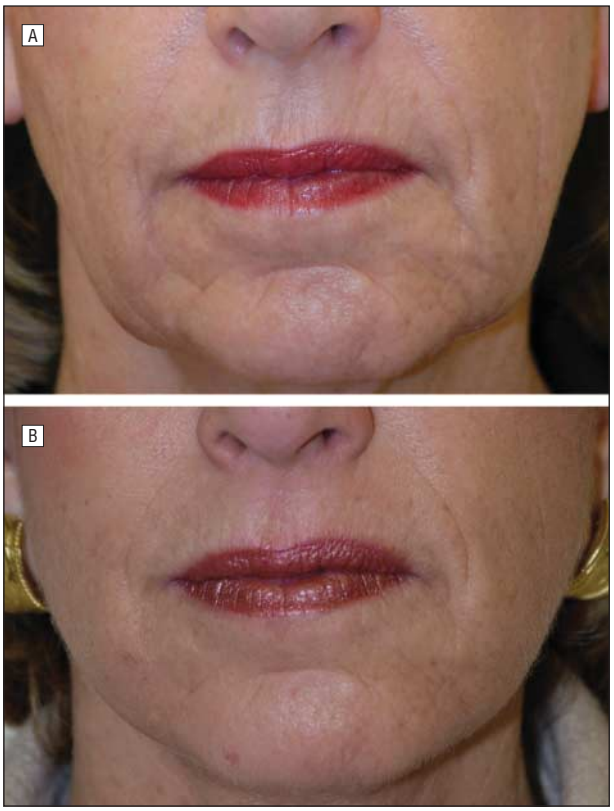

Figure 3. Surgical face-lift patient (P2) at baseline (A) and at the 6-month follow-up visit (B). Blinded grading by 5 independent physicians resulted in a mean improvement in skin laxity of 1.60 grades on the 4-point grading scale. Blinded evaluators were unaware of the types of treatments being evaluated (fractional radiofrequency or surgical face-lift) and were also blinded to pretreatment and posttreatment photographs.

posterior-auricular regions. These were treated postoperatively with intralesional triamcinolone acetonide and pulsed dye laser localized to the scar margins. Ecchymoses and edema were present in all patients postoperatively for 2 to 4 weeks. The ecchymoses were mild to advanced and resolved by the 4-week follow-up visit. The edema varied from mild to advanced and resolved within 2 to 4 weeks. Among the 6 patients selected, no patients experienced hematoma formation, flap necrosis, or infection. Patients returned to normal activities within 7 to 10 days.

COMMENT

In evidence-based medicine, it is generally agreed that the validity of a novel treatment is best tested by comparative trial to the gold standard. Until now, such a comparative trial had not been performed for nonsurgical treatments of skin laxity, owing to the absence of a quantitative measure for the outcome of the surgical face-lift. In this study, a quantitative blinded graded value in laxity improvement has been assigned to the gold standard surgical face-lift, allowing for comparison with a minimally invasive nonsurgical FRF treatment. When assessed by 5 blinded evaluators of randomized photographs, the mean laxity grade improvement from the surgical face-lift in this cohort of patients was 1.20 on a 4-point laxity grading scale, with FRF treatment achieving a 0.44-grade improvement (Table 3). The improvement in skin laxity relative to baseline from a surgical face-lift was calculated as 49%, and FRF treatment resulted in a 16% improvement over baseline, or 37% of a surgical face-lift result from a single minimally invasive treatment. A 16% laxity improvement above the baseline from a single nonsurgical intervention is a significant improvement, considering that the gold standard treatment with its associated risks and complications yielded a 49% improvement.

The laxity improvements quantified here for the surgical face-lift and this novel RF device provide needed evidence-based outcome measurements for what has been a largely descriptive field and will assist in managing patient expectations. The mean improvement in laxity grade of 1.20 for the surgical face-lift indicates that this gold standard procedure can provide a reduction in a patient's laxity grade from severe to advanced, advanced to moderate, or moderate to mild, but will not, on average, improve laxity from severe to moderate, advanced to mild, or moderate to none. By placing patients in a specific laxity grade category, it is now possible to show them on the grading table what outcome to expect from a single grade

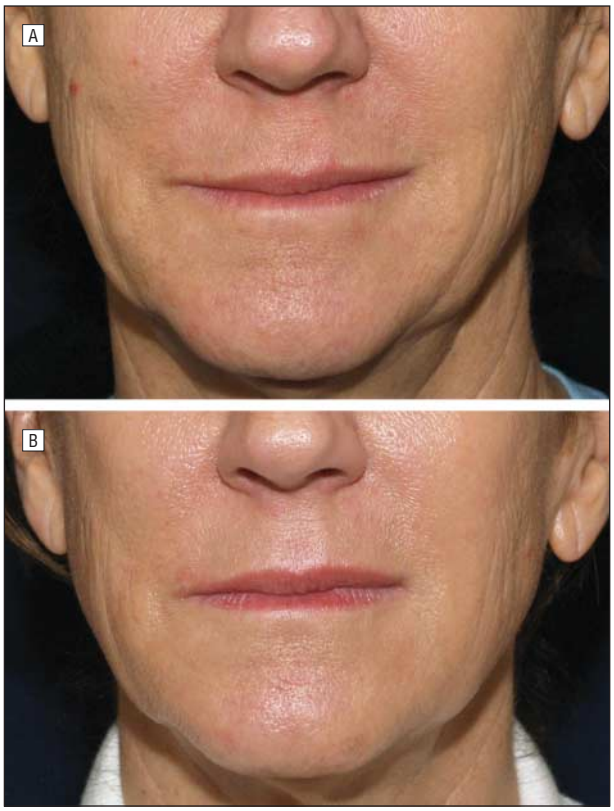

Figure 4. Fractional radiofrequency (FRF) treatment patient (M09) at baseline (A) and at the 6-month follow-up visit (B). Blinded grading by 5 independent physicians of randomized baseline and 6-month follow-up photographs, which had been randomized with surgical face-lift photographs, demonstrated a mean improvement in skin laxity of 0.40 grade on the 4-point grading scale after a single FRF treatment. The 2 erythematous papules on the right cheek in the pretreatment photograph are acne lesions, which are no longer present in the posttreatment photograph.

Figure 5. Surgical face-lift patient (P3) at baseline (A) and at the 6-month follow-up visit (B). Blinded grading by 5 independent physicians resulted in a mean improvement in skin laxity of 0.60 grade on the 4-point grading scale. Blinded evaluators were unaware of the types of treatments being evaluated and were also blinded to pretreatment and posttreatment photographs, which were randomized with fractional radiofrequency (FRF) images.

reduction following a surgical face-lift, thereby tempering expectations in specific terms. Of equal importance, the quantitative measure of relative outcome of nonsurgical alternatives enables patients to make more informed choices from among different treatment modalities based on their baseline condition and treatment expectations. The findings and methods presented herein provide a basis for future studies to test the validity of novel therapies and to quantitatively assess and compare changes in skin laxity from surgical and nonsurgical treatments alike to the gold standard treatment.

Two important aspects of the methods used in the present study were the rigor of randomization and blinded evaluation and the use of a quantitative grading scale. Baseline and follow-up photographs from patients undergoing both surgical face-lift and FRF were randomly assorted, then sent to 5 independent evaluators who were blinded to which image was baseline or follow-up and to the types of treatments being compared. The evaluators were unaware that photographs of 2 different treatment modalities were randomly intermixed or that surgical face-lift photographs were included in the study. The use of 5 evaluators, including dermatologists and plastic surgeons, allowed for greater statistical accuracy of laxity grades.

Given the rigor of blinding and the inclusion of dermatologist and plastic surgeon graders, the benefits of grading to a quantitative scale was demonstrated by the strong agreement between laxity grades assigned by all independent evaluators. The grading system resulted in narrow standards of error and a Fleiss κ statistic of 0.45, consistent with strong agreement given the nine ½-grade categories and 5 graders. The baseline mean laxity grades in the 2 groups were similar, with a slightly higher baseline grade for the FRF group (2.76 vs 2.47 for surgical face-lift), therefore eliminating bias toward more advanced cases in the surgical face-lift group. The extent of change in laxity from surgical treatment is greater than that from FRF; therefore, fewer surgical than FRF participants were required to achieve statistical significance. Statistical significance was achieved in both patient pools, suggesting that the number of patients in each pool was appropriate for the degree of improvement achieved.

This study is the first to use a reproducible, quantitative grading scale for the evaluation of skin laxity by blinded evaluators to assess the clinical outcome from the surgical face-lift and to compare it with an alternative, nonsurgical therapy. Nonsurgical skin tightening

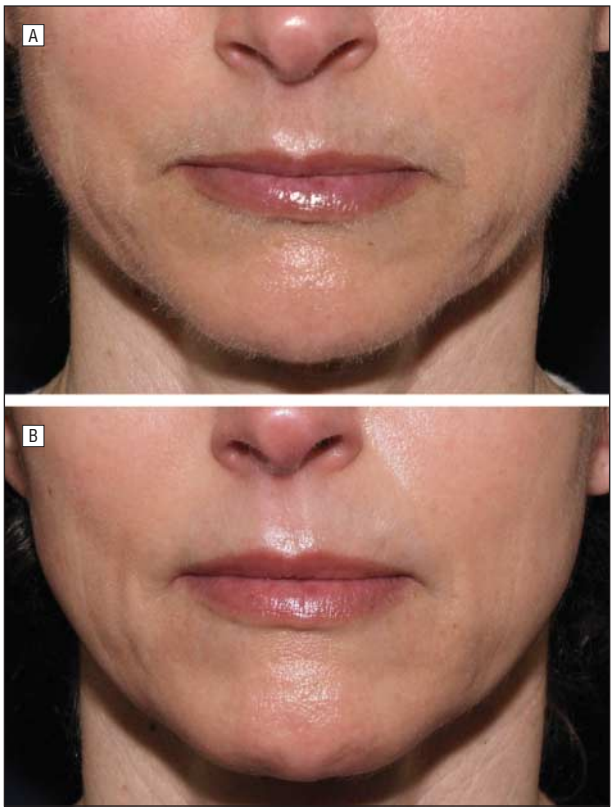

Figure 6. Fractional radiofrequency (FRF) treatment patient (M10) at baseline (A) and at the 6-month follow-up visit (B). Blinded grading by 5 independent physicians of randomized baseline and 6-month follow-up photographs, which had been randomized with surgical face-lift photographs, demonstrated a mean improvement in skin laxity of 0.50 grade on the 4-point grading scale following a single FRF treatment.

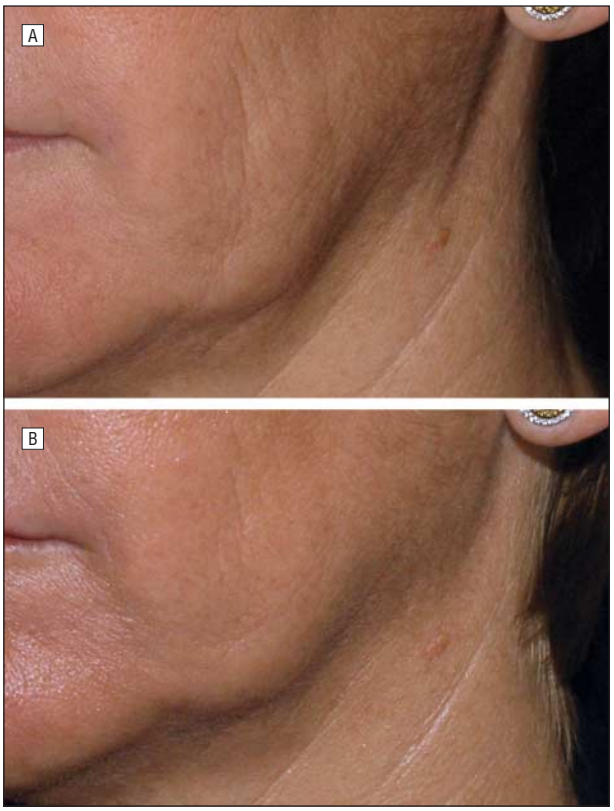

Figure 7. Three-quarter–angle view of fractional radiofrequency (FRF) treatment patient (M02) at baseline (A) and at the 6-month follow-up visit (B). Blinded grading by 5 independent physicians of randomized baseline and 6-month follow-up photographs, which had been randomly intermixed with surgical face-lift photographs, demonstrated a mean skin laxity improvement of 0.60 grade on the 4-point grading scale from a single FRF treatment.

techniques have previously been quantitatively assessed using this grading scale; however, the current device demonstrated much higher efficacy in treating skin laxity. These prior device studies reported 0.075 to 0.236 mean laxity grade improvement per treatment.[9,11-13] All of these previously tested techniques were skin-surface applied RF or infrared laser or light devices. The current device demonstrated a mean grade improvement of 0.44, significantly higher than all prior studies following a single treatment. Prior skin-surface RF devices have been observed to yield lower efficacy in reducing laxity in fat faces; in contrast, the FRF treatment demonstrated similar laxity grade reductions among the thin vs fat faces in the present study, although the numbers were too small for statistical comparison.

To date, there has been no prior report of surgical face-lifting evaluated with quantitative grading scales by blinded evaluators. Prior studies evaluating the improvements from surgical face-lifts have used subjective, descriptive grades of "poor," "good," or "excellent" in an unblended manner.[5-7] In addition, it is important to note that the surgical face-lift entails treating the subcutaneous and deeper tissues, including lipectomy and platysmal flaps, in contrast to FRF, which only targets the dermis (see the "FRF Treatment Protocol" sub-subsection of the "Methods" section). Thus, the results of the quantitative, blinded, and randomized study design presented here provide the first quantitative measure of laxity improvements from the surgical face-lift and a basis for comparison of this novel FRF technology with prior skin-tightening technologies. The findings presented here also now make possible further research into translation of clinical laxity grade reductions from these "turn-back-the clock" treatments into age-specific reductions. The rationale for such an analysis is that the current laxity grading scale with its small margins of error among 5

Table 3. Comparison of FRF Treatment and Surgical Face-lift Blinded Grading Results[a]

	Mean[b]			Improvement, %	
Treatment	Baseline Laxity Grade	Follow-up Laxity Grade	Laxity Improvement	vs Face-lift[c]	vs Baseline[d]
FRF	2.75	2.31	0.44	37	16
Surgical face-lift	2.47	1.27	1.20	NA	49

Abbreviations: FRF, fractional radiofrequency; NA, not applicable.
[a] The mean baseline, follow-up, and improvements in laxity grades as assessed by 5 independent blinded evaluators of randomized digital images are shown. The percentage improvement was then calculated for FRF relative to the surgical face-lift group and for each treatment relative to baseline.
[b] $P < .001$ for all comparisons.
[c] FRF treatment resulted in 37% of the level of improvement of the surgical face-lift result, ie, $(0.44/1.20) \times 100$.
[d] Comparison of each percentage improvement in laxity compared with baseline for each treatment group.

independent blinded evaluators, both dermatologists and plastic surgeons, provides a basis for analyzing the average laxity grade for each age. As stated in the introduction, skin aging may be categorized as intrinsic and extrinsic; laxity is a feature primarily of the former and is the result of many factors. In spite of the multifactorial nature of progressive skin laxity with age, it is possible to calculate the mean laxity grade per age group if one includes large numbers of patients of different skin types in the general population. These large numbers should control for additional variables such as body mass, sun exposure, or genetic variability. By calculating the mean laxity grades for age groups across the general population, it will now be possible to translate a laxity grade reduction into a correlate mean laxity age reduction in years. For example, a 1.20–laxity grade reduction from a surgical face-lift may translate into making a 55-year-old look 45, but not 35 if one examines the average laxity grade per age group and calculates a 1.20-grade reduction. The same type of calculation will now also be possible for nonsurgical alternatives; for example, a 0.44–laxity grade reduction from FRF may be translated in a several year reduction in laxity age, on average. The assignment of laxity age reductions to laxity grade reductions is another important application of the findings presented here that will further the ability to accurately inform patients of predicted outcomes of surgical and nonsurgical alternatives so that they may make better informed decisions. The underlying mechanism for improvement in laxity following thermal injury to the dermis is believed to derive from dermal remodeling and neocollagenesis following treatment.

Prior studies using various laser- and light-based devices have repeatedly demonstrated that dermal temperatures in excess of 55°C are required to induce collagen denaturation, and that this denaturation is followed by neocollagenesis during a 6- to-12-month period.[8] The disadvantage of prior modalities is that temperature attainment in the dermis is theoretical based on Monte-Carlo simulations and relies on skin surface infrared temperature measurements. The current FRF device has the technological advantage of real-time temperature feedback, allowing a specific target temperature of 62°C to 78°C to be preselected and attained in the dermis.[3,4] In addition, precise times-at-temperature have been implemented for the first time using this real-time feedback system, unique to the current device. The time-at-temperature is a second critical element to inducing adequate thermal denaturation. Once dermal thermal injury has been caused, this is followed by progressive neocollagenesis, which has been shown to correlate with progressive clinical tissue tightening.[8]

This FRF is the first light- or energy-based modality to be shown to induce elastogenesis.[4] This finding has been clinically correlated with increased skin elasticity as measured by elastometry.[14] It is possible that the induction of collagen and elastin in part contributes to the superior laxity reductions quantified here. Thus, the rational device-design approach put forth here resulted in significant clinical findings from a single treatment, which correlate with histological changes, and are supported by a legitimate comparison to the gold standard treatment, the surgical face-lift, using most rigorous standards. The direct insertion of paired electrodes into the dermis, precise delivery of the energy into the target dermis, real-time attainment of target tissue temperature, and specified time-at-temperature appear to correlate with more efficient skin tightening and laxity reductions following a single treatment as compared with prior skin-surface technologies. The goal in the nonsurgical field has been to reach this point, wherein a single treatment, as opposed to a series of treatments, can attain significant clinical results that can be compared with the gold standard and that can be designed rationally to target specific biological end points.

In conclusion, the gold standard treatment, the surgical face-lift, has been quantified in its degree of improvement in skin laxity and compared with a novel, minimally invasive FRF treatment using randomized, blinded grading with a previously tested laxity grading scale. This randomized, blinded, quantitative comparative study provides a basis for quantifying cosmetic outcomes from novel treatments with valid comparative analysis to the gold standard. It also suggests that minimally invasive FRF treatment may provide an important nonsurgical option for the treatment of facial skin laxity.

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REFERENCES

1. Rabe JH, Mamelak AJ, McElgunn PJS, Morison WL, Sauder DN. Photoaging: mechanisms and repair. *J Am Acad Dermatol*. 2006;55(1):1-19.
2. Alexiades-Armenakas M. Laser skin tightening: non-surgical alternative to the face-lift. *J Drugs Dermatol*. 2006;5(3):295-296.
3. Hantash BM, Renton B, Berkowitz RL, Stridde BC, Newman J. Pilot clinical study of a novel minimally invasive bipolar micro-needle radiofrequency device. *Lasers Surg Med*. 2009;41(2):87-95.
4. Hantash BM, Ubeid AA, Chang H, Kafi R, Renton B. Bipolar fractional radiofrequency treatment induces neoelastogenesis and neocollagenesis. *Lasers Surg Med*. 2009;41(1):1-9.
5. Berry MG, Davies D. Platysma-SMAS plication face-lift [published online ahead of print March 26, 2009]. *J Plast Reconstr Aesthet Surg*. 2009. doi:10.1016/j.bjps.2009.02.067.
6. Becker FF, Bassichis BA. Deep-plane face-lift vs superficial musculoaponeurotic system plication face-lift: a comparative study. *Arch Facial Plast Surg*. 2004;6(1):8-13.
7. Ivy EJ, Lorenc ZP, Aston SJ. Is there a difference? a prospective study comparing lateral and standard SMAS face-lifts with extended SMAS and composite rhytidectomies. *Plast Reconstr Surg*. 1996;98(7):1135-1147.
8. Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: non-ablative, fractional and ablative laser resurfacing. *J Am Acad Dermatol*. 2008;58(5):719-740.
9. Alexiades-Armenakas MR. Rhytides, laxity and photoaging treated with a combination of radiofrequency, diode laser, and pulsed light and assessed with a comprehensive grading scale. *J Drugs Dermatol*. 2006;5(8):609-616.
10. Alexiades-Armenakas M. A quantitative and comprehensive grading scale for rhytides, laxity and photoaging. *J Drugs Dermatol*. 2006;5(8):808-809.
11. Alexiades-Armenakas M. Non-ablative skin tightening with a variable depth heating 1310 nm–wavelength laser in combination with surface cooling. *J Drugs Dermatol*. 2007;6(11):1096-1103.
12. Alexiades-Armenakas M, Dover JS, Arndt KA. Unipolar versus bipolar radiofrequency treatment of rhytides and laxity using a mobile painless delivery method. *Lasers Surg Med*. 2008;40(7):446-453.
13. Alexiades-Armenakas M. Assessment of the mobile delivery of infrared light (1100-1800 nm) for the treatment of facial and neck skin laxity. *J Drugs Dermatol*. 2009;8(3):221-226.
14. Willey A, Newman J, Renton B, Berube D, Krishna S, Kilmer S. Minimally-invasive fractional bipolar radiofrequency for the treatment of facial laxity and rhytides. Poster presented at: 29th Annual Conference of the American Society for Laser Medicine and Surgery; April 1-5, 2009; National Harbor, MD.