Single Treatment Protocol With Microneedle Fractional Radiofrequency for Treatment of Body Skin Laxity and Fat Deposits

Macrene Alexiades, MD, PhD [1,2]* and Gilly S. Munavalli, MD, MHS, FACMS [3]
[1]*School of Medicine, Yale University, New Haven, Connecticut 06510*
[2]*Dermatology and Laser, Surgery Center, New York, New York 10028*
[3]*Dermatology, Laser & Vein Specialists of the Carolinas, Charlotte, North Carolina 28207*

Background and Objectives: Treatment modalities have been developed to address patient concerns with skin laxity and focal adipose excess. A previously published multicenter clinical trial reported improvement in cellulite severity after a single dermal and subcutaneous treatment on the upper thigh with a microneedle radiofrequency device. In the current study, this device was used to improve the esthetic appearance of body skin laxity and localized fat deposits above the knee, upper arms, and upper-mid back/axillary region ("bra-line").
Study Design/Materials and Methods: Subjects with cellulite, skin laxity, and/or subcutaneous adipose excess in the suprapatellar region of the anterior thigh, upper arms, and bra-line underwent a single dermal and/or subcutaneous treatment. Investigators and subjects assessed outcome at 1-, 3-, and 6-month follow-up, using 5-point Likert scales for global esthetic improvement, skin laxity improvement, and satisfaction.
Results: In total, 31 females (mean age 51 ± 9 years) with Fitzpatrick skin types I–IV received a single treatment on 62 treatment areas: 22 upper arms, 34 suprapatellar, and 6 bra-lines. Investigator assessments at 1, 3, and 6 months for global esthetic improvement and skin laxity for the upper arms and bra-line demonstrated improvements in 100% of subjects at all timepoints; for the suprapatellar region, these values were 69%, 92%, 65%, and 85%, 92%, 65%, respectively. Investigator satisfaction at each timepoint was satisfied or very satisfied in 80%, 100%, 90% for upper arms; 80%, 80%, 80% for bra-line; and 50%, 81%, 65% for suprapatellar region. Subject self-assessments at 1, 3, and 6 months for global esthetic improvement and skin laxity for the upper arms demonstrated improvements in 100% of subjects at all timepoints; for the bra-line, these values were 40%, 60%, 80%, and 60%, 60%, 80%, respectively; for the suprapatellar region, these values were 81%, 92%, 88%, and 69%, 85%, 88%, respectively. Subject satisfaction at each timepoint was satisfied or very satisfied in 80%, 100%, 100% for upper arms; 40%, 40%, 80% for bra-line; and 50%, 77%, 65% for suprapatellar. Treatments were well tolerated with subjects reporting transient erythema and edema associated with 69% and 46% of treatments, respectively. Mild bruising, resolving within 5 days, was reported after 32% of the treatments.
Conclusion: Microneedle fractional radiofrequency provides a single treatment protocol to improve the esthetic appearance of body skin laxity and localized adipose excess to the upper arms, bra-line, and suprapatellar regions. Further study is warranted to evaluate the degree of improvement and long-term effect beyond 6 months post-treatment. Lasers Surg. Med. © 2021 The Authors. *Lasers in Surgery and Medicine* published by Wiley Periodicals LLC

Key words: microneedling; radiofrequency; microneedle RF; skin laxity; fat deposits; body sculpting

INTRODUCTION

Treatment modalities have been developed to address patient concerns with skin laxity and focal adipose excess. A previously published multicenter clinical trial reported improvement in cellulite severity after a single dermal and subcutaneous treatment of the upper thigh with a microneedle fractional radiofrequency (RF) device [1]. In the current study, this device was used to improve the esthetic appearance of body skin laxity and localized adipose deposits above the patella to mid-thigh, upper arms, and upper axillary back (bra-line) (ClinicalTrials.gov ID: NCT03078647).

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: Drs. Alexiades and Munavalli received research grants and serve on the Candela Lasers medical advisory board.

*Correspondence to: Macrene Alexiades, MD, PhD, School of Medicine, Yale University, New Haven 06510, CT. E-mail: dralexiades@nyderm.org

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STUDY DESIGN

Study was approved by an institutional review board (Advarra IRB, ClinicalTrials.gov ID: NCT03078647). Thirty-one healthy female subjects with clinically appreciable skin laxity or subcutaneous fat deposits in the upper arms, above the patella to mid-thigh, and upper and middle back were enrolled at two US clinics, to undergo a single RF microneedling treatment. Pregnancy, systemic disorders, or history of severe edema excluded subjects from eligibility.

Clinical photography under standardized conditions was performed at each study visit. Immediately after the treatment, subjects self-reported any discomfort with treatment, using a numerical scale response of 0 = no pain to 10 = worst possible pain. Investigators and subjects assessed outcome at 1-, 3-, and 6-month follow-ups, using 5-point Likert scales for global esthetic improvement, skin laxity improvement, and satisfaction.

TREATMENT

Subjects underwent a single bipolar RF microneedling treatment on their upper arms, bra-line, or suprapatellar areas. The Profound System (Candela, Wayland, MA) is a minimally invasive device that directly delivers bipolar, non-ablative RF energy to the dermal and subdermal layers beneath the surface of the skin through pairs of microelectrode needles. Within each pair of needles, a temperature sensor is located at the distal tip of the electrode to provide real-time feedback of target tissue temperature from within the area of thermal injury. The handpiece deploys the microneedles through the epidermis at a nominal angle of 25° (Dermal) or 75° (SubQ) to the skin's surface. With the Dermal (25°) cartridge, the five microneedle pairs produce fractionated thermal injuries at the depth of 1–2 mm from the skin surface, whereas the seven microneedle pairs of the SubQ (75°) cartridge target the superficial aspects of the subcutaneous layer at 2.9–5.8 mm below the epidermis. The electrode pairs are electrically isolated from each other and controlled independently by separated RF channels within the console. The energy is delivered directly within the target tissue in a volume largely defined by the geometry of the individual microneedle pair. The RF energy heats the dermal/subdermal tissue, thereby causing collagen contraction and denaturation. Clinical studies suggest this thermal denaturation of collagen induces a wound-healing process, resulting in skin remodeling and the production of collagen, elastin, and hyaluronic acid in the treated skin [1,2].

Thermal settings of 67°C and 4-second pulse durations were used for treatment, according to a previously published optimized treatment protocol [3]. The handpiece was selected on the basis of the body location, thickness of fat in the treatment area, and proximity to bone. According to the manufacturer's treatment guidelines and for patient comfort, approximately 15–40 minutes before treatment, local infiltration of tumescent solution (0.25% lidocaine with 1:400,000 epinephrine) was injected into the treatment area, using a multi-port syringe device.

RESULTS

In total, 31 female subjects (mean age, 51 ± 9 years; range, 31–62) with Fitzpatrick skin types I–IV were enrolled and treated on contralateral sides of the suprapatellar, upper arms, or bra-lines for a total of 62 treated areas. One subject moved out of state after the 1-week safety follow-up. Treatment assessments are available for 30 subjects at the 1-, 3-, and 6-month follow-ups.

One study investigator (M.A.) treated each contralateral side with the same treatment parameters (i.e., handpiece, number of pulses), whereas the other study investigator (G.M.) treated each side differently. Also, 17 subjects were treated on the suprapatellar areas ($n = 34$ treated areas; 55%), 11 subjects were treated on the upper arms ($n = 22$; 35%), and three subjects were treated on the bra-line areas ($n = 6$; 10%).

Pulses were applied to an approximately 15–20-mm square treatment area, using the Dermal cartridge (mean = 91 ± 46 pulses), SubQ cartridge (mean = 103 ± 29 pulses), or combined cartridges (first pass with SubQ, mean = 63 ± 17 pulses and second pass with Dermal, mean = 83 ± 40 pulses).

As shown in Figure 1, treatment on the upper arms was done primarily using the SubQ cartridge only (16/22 areas), whereas bra-line areas were treated mainly with the Dermal cartridge only (4/6 areas). The suprapatellar areas were treated with either SubQ only (16/34), Dermal only (13/34), or with a combination of both handpieces (5/34 areas).

Most treatments (98%) were associated with no pain to mild discomfort, with a mean of 2.9 ± 1.7 (range, 0–6). Similar discomfort levels were reported after SubQ and Dermal treatments ($P > 0.05$, Mann–Whitney U test). Moderate discomfort was reported by one subject for SubQ treatment on the right and left suprapatellar areas.

Treatments were well tolerated with transient erythema (69% of treatments) and edema (46%) that resolved on average after 2.3 ± 1.9 and 1.2 ± 1.8 days, respectively. Tingling sensation was reported after 12% of the treatments and resolved on average after 0.5 ± 1.5 days. Pin-point bleeding at the insertion sites was observed after four treatments (10%) and resolved on the treatment day. Mild bruising or ecchymosis was reported after 32% of treatments and resolved on average after

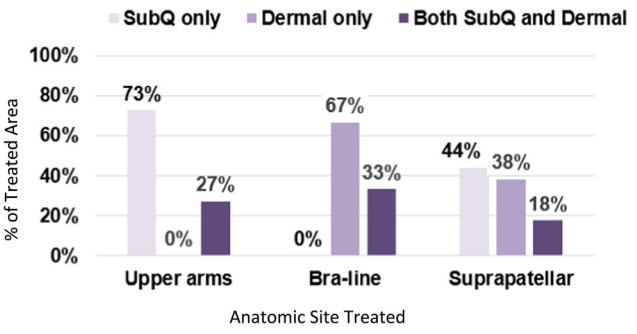

Fig. 1. Percentage of treatments performed with the different handpieces.

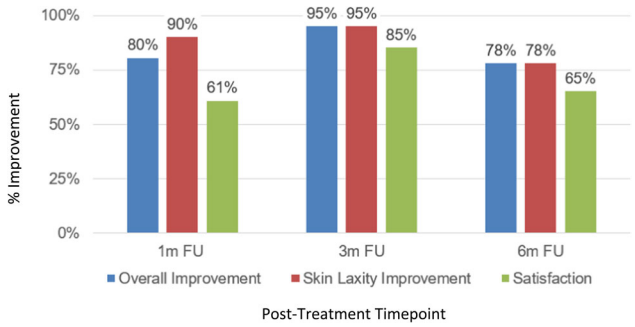

Fig. 2. Investigator assessments at study follow-up visits.

1.3 ± 2.1 days. Blistering, scarring, and pigmentary changes were not observed.

INVESTIGATOR ASSESSMENTS

Investigators assessed overall improvement in the appearance of undulations, crepiness of the skin, and localized fat deposits, as well as skin laxity improvement and satisfaction with treatment outcome at the 1-, 3-, and 6-month follow-ups. A single assessment was reported for both left and right sides of the body that were treated with the same parameters. Contralateral sides treated with different parameters were assessed separately, for a total of 41 assessments (26 suprapatellar areas, 10 upper arms, and 5 bra-line areas). Overall Global Esthetic Improvement (GAI) was 80% at the 1-month follow-up, increasing to 95% at the 3-month follow-up (Fig. 2). Skin laxity improvement increased from 90% at the 1-month follow-up to 95% at the 3-month follow-up (Fig. 2). Some level of overall improvement was maintained till the 6-month follow-up, with 68% of the treated areas showing at least 25% improvement. Twenty-seven percent (27%, 11/41) of treated areas showed 75%–100% overall improvement and very visible skin laxity improvement. Investigator satisfaction was 61%, 85%, and 73% at the 1-, 3-, and 6-month follow-ups, respectively. Results of treatment on upper arms and suprapatellar areas are shown in Figures 3 and 4.

Assessment of GAI by body area showed that there was some degree of improvement for 69% (18/26) of the suprapatellar areas and for all (100%, 10/10) upper arms and 100% (5/5) bra-line areas at the 1-month follow-up. At the 6-month follow-up, greater than 25% improvement was observed in 58% (15/26), 90% (9/10), and 80% (4/5) of the various treated areas, respectively. Investigator assessment of skin laxity showed that there was slightly visible to very visible improvement (score of 1–3) for 85% (22/26) of the suprapatellar areas and for all (100%, 10/10) upper arms and 100% (5/5) bra-line areas at the 1-month follow-up. At the 6-month follow-up, 58% (15/26), 80% (8/10), and 80% (4/5) of the various treated areas, respectively, showed visible (score of 2) to very visible (score of 3) improvement. Investigator satisfaction was 50%, 81%, and 65% for suprapatellar areas; 80%, 100%, and 90% for upper arms; and 80%, 80%, and 80% for bra-line at the 1-, 3-, and 6-month follow-ups, respectively. Investigator Assessments of GAI and skin laxity at the 6-month follow-up showed significantly greater improvement ($P < 0.05$) with SubQ treatments as compared with Dermal treatments.

SUBJECTS ASSESSMENTS

Subject assessments were similar to investigator assessments with an overall improvement rate of 80% at the 1-month follow-up, increasing to 90% for both the 3- and 6-month follow-ups (Fig. 5). Similarly, self-reported skin tightening improvement was 76%, 85%, and 90% at the 1-, 3-, and 6-month follow-ups. There was high patient satisfaction and willingness to recommend the treatment to others (Fig. 5). Nearly half of the subjects (14/30) reported that they had received positive comments from others (i.e., spouse, personal trainer) during the study.

DISCUSSION

The rising demand for skin tightening and body sculpting has given rise to multitudes of treatments annually performed in both the surgical (abdominoplasty, thigh lifts, and brachioplasty) and non-surgical realms (non-invasive skin laxity treatments, body contouring, and fat reduction). Surveys done by the American Society of Esthetic Plastic Surgery and the American Society of Dermatologic Surgery demonstrate that increasing trends are evident, especially in the last 5 years [4,5]. Skin laxity is principally due to the loss of dermal extracellular matrix constituents, collagen, and elastin. In non-facial skin, this is a multifactorial process, arising from anatomic considerations (lack of retaining ligamentous support), excessive unprotected UV exposure in the extrinsic aging process, and mechanical forces (chronic expansion and collapse from underlying changes in adipose volume).

There has been no shortage of device-driven technology solutions introduced as treatment options in efforts to avoid more invasive approaches such as liposuction or the formation of cosmetically unappealing scars secondary to cold steel excisional solutions. Non-ablative and ablative fractional lasers, as well as infrared lasers/light sources, have been previously considered [6,7]. However, non-surgical skin tightening has been a historically difficult procedure to promote in the past with many treatments not achieving significant clinical results and, therefore, resulting in low patient satisfaction. Perhaps the most studied devices in recent years have been microfocused ultrasound (MFU) with visualization and radiofrequency-based devices in both facial [8,9] and non-facial skin [10,11].

MFU can be focused on a subcutaneous tissue, where the temperature briefly reaches greater than 60°C, producing small ($1\ mm^3$) thermal coagulation points to a depth of up to 5 mm within the mid-to-deep reticular layer of the dermis and subdermis. Layering different depths of coagulation points has been studied as an optimal method for simultaneously contracting the deeper fascial layers at depths of 3 (7-mHz transducer) and 4.5 mm (4-mHz transducer), while stimulating dermal collagen at more superficial depths of 1.5 and

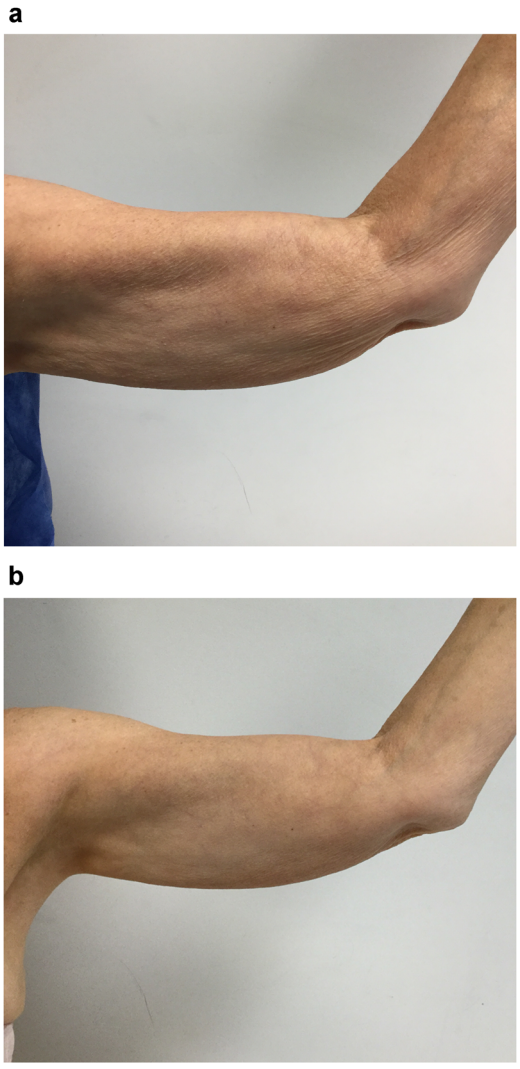

Fig. 3. Representative improvement in upper arm skin laxity, rhytids, and fat deposits after a single treatment with microneedle fractional radiofrequency (RF). (**a**) Upper arm of a 60-year-old female with Fitzpatrick skin type III before treatment; (**b**) 3-month follow-up showing improvement in skin laxity and crepiness after a subcutaneous microneedling treatment with 160 RF pulses.

2 mm [12]. Comparison studies have shown no difference in efficacy with regards to MFU and monopolar radiofrequency in the improvement in facial/neck skin laxity [13]. However, even with layering techniques, MVU-targeted, thermally coagulated tissue does not reach the same volume of the treated tissue as microneedle fractional RF, as previously mentioned in this article. Presumably, the more volume targeted tissue appropriately treated, the more amplified is the clinical response.

More recently, RF (bipolar, fractionated microneedle) has been studied for the treatment of facial and non-facial skin laxity, alone and in combination. As noted, areas such as the back/fat axillary rolls and pre-patellar skin are especially challenging in patients with poor skin elasticity who do not

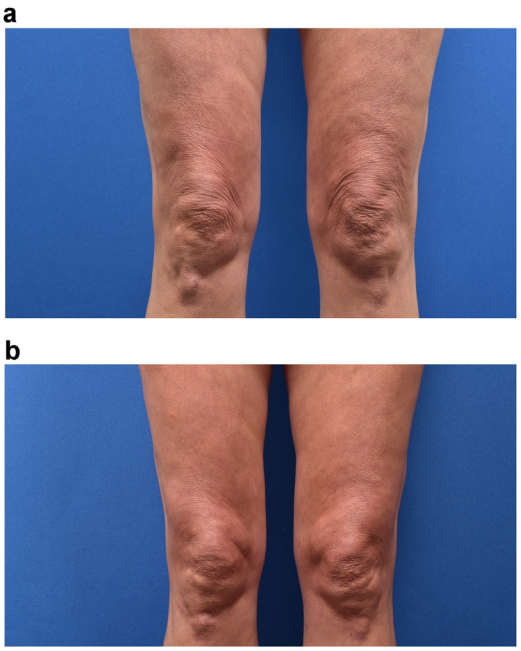

Fig. 4. Representative improvement in anterior thigh laxity, rhytids, and fat deposits after a single microneedle fractional radiofrequency (RF) treatment. (**a**) Suprapatellar areas of a 51-year-old female with Fitzpatrick skin type III before treatment; (**b**) 6-month follow-up showing 75%–100% overall improvement on the Global Esthetic Improvement scale and very visible skin laxity improvement after a dermal microneedling treatment with 87 RF pulses on each side.

desire skin excision but also would not retract with traditional liposuction techniques [14]. As the authors have demonstrated, temperature-controlled bipolar RF microneedling offers a single treatment session option for clinically improving laxity in these challenging anatomic areas. By reproducibly attaining optimal dermal/subdermal target temperature for the appropriate amount of time, maximal collagen and elastin stimulation is achieved, resulting in skin tightening and subdermal adipose remodeling. It is possibly a combination of neoelastogenesis and neocollagenesis induced by temperature-controlled bipolar RF microneedling [15] and fat destruction that improves the esthetic appearance of fat deposits. In support of this, the Investigator Assessments of GAI and skin laxity at the 6-month follow-up were significantly better ($P < 0.05$) with SubQ treatments as compared with Dermal treatments. The depth of penetration and increased volume of heating with the seven microneedle pairs likely contribute to this effect. Histological evaluation is warranted to confirm a mechanism of action for fat destruction.

Clinical improvements extending beyond the treatment area have been reported after esthetic therapeutic interventions, including, but not limited to, radiofrequency and laser resurfacing treatments. In the current study, the treated areas included the upper arms (inclusive of the elbow and antecubital regions), supra-patella to mid-thigh, and upper and middle back. During the follow-up period, clinical improvements in skin rhytids, crepiness,

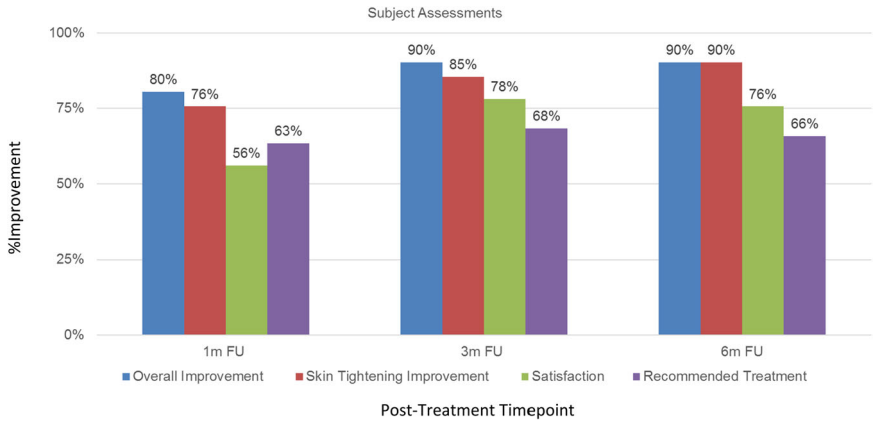

Fig. 5. Subject assessments at study follow-up visits.

laxity, and localized fat were observed in areas adjacent to the treatment zones, such as the lower arm, knees, and superior upper thighs (Figs. 3 and 4, Supplemental Video 1). Rhytid and laxity improvements of the face and neck extending beyond the treatment zone were previously observed in the multicenter study with the same device [1]. Clinical outcomes extending beyond the treated area may be explained by the induction, migration, and diffusion of the wound healing response, and/or the mechanical effects of cutaneous remodeling in lifting adjacent skin. Fractional microneedle radiofrequency and carbon dioxide (CO_2) laser resurfacing induce tissue mediators and granulation tissue that have been shown to diffuse and/or extend beyond the treated zones and to result in cutaneous remodeling of neighboring skin. Diffusion of heat shock proteins throughout the epidermis and dermis of flanking skin has been reported after fractional CO_2 laser resurfacing: "Hsp72 expression remained elevated throughout the epidermis and areas adjacent to the microlesion…In particular, expression of hsp47 became diffuse in the dermis at 3 months post-treatment, indicating that activation of fibroblasts was occurring in both treated and untreated tissue" [16]. Heat shock protein upregulation was demonstrated to induce an abundant spindle cell population—including dermal fibroblasts—and neocollagenesis around and beyond the treatment zones throughout the 3-month post-treatment follow-up interval [16]. Induction of heat shock gene expression, fibroplasia, and dermal remodeling extending beyond the treatment area has been demonstrated for the current microneedle fractional radiofrequency device [15]. Hantash et al. [15] showed: "at day 28 and 10 weeks post-FRF treatment, HSP47 staining became diffuse throughout the dermis and was not restricted only to the peri-RFTZ regions. The inflammatory response was not limited to the plane of dermal injury as the investigators found evidence of extension several millimeters beyond the RFTZ." The investigators reported "that a sufficiently high concentration of cytokine mediators is released in response to the initial FRF treatment. This response essentially establishes a passive diffusion gradient centered on the RFTZ, but capable of traversing through the fluid extracellular matrix to expand throughout the untreated and viable dermal tissue" [15]. Thus, the clinical improvements observed in areas flanking the treatment zones after microneedle fractional radiofrequency treatment correlate with demonstrated molecular and histologic remodeling diffusely in regions surrounding the treatment area. In addition, skin tightening and laxity reduction effect on the treated area may also result in a secondary lifting effect on flanking tissues. In sum, a generalization of the wound healing response after treatment with a fractional CO_2 or microneedle radiofrequency has been demonstrated to expand to surrounding untreated tissue, resulting in an extension of the clinical improvements circumambient to the treated area; however, mechanical lifting may also result in secondary visible improvements in flanking untreated areas.

There were several limitations to this study including the lack of a validated scale to assess treatment outcome and blinded evaluation of clinical photography to minimize bias of study assessments by the treating investigators. Despite this, the study findings revealed that there was a clinically appreciable improvement with SubQ treatments that was significant as compared with Dermal treatments, and this was observed by both the investigators and the subjects.

In conclusion, the current findings demonstrate that microneedle fractional radiofrequency provides a single treatment protocol for overall improvement in the appearance of body skin laxity and localized fat deposits, with minimal side effects, and with treatment outcomes maintained till at least six months after the procedure. Further study is warranted to evaluate the degree of improvement and long-term effect beyond 6 months post-treatment.

REFERENCES

1. Alexiades M, Munavalli G, Goldberg D, Berube D. Prospective multicenter clinical trial of a temperature-controlled subcutaneous microneedle fractional bipolar radiofrequency system for the treatment of cellulite. Dermatol Surg 2018;44(10):1262–1271.

2. Willey A, Kilmer S, Newman J, et al. Elastometry and clinical results after bipolar radiofrequency treatment of skin. Dermatol Surg 2010;36:877–884.
3. Alexiades M, Berube D. Randomized, blinded, 3-arm clinical trial assessing optimal temperature and duration for treatment with minimally invasive fractional radiofrequency. Dermatol Surg 2015;41(5):623–632.
4. The Aesthetic Society. Aesthetic Plastic Surgery National Databank. 2019. https://www.surgery.org/sites/default/files/Aesthetic-Society_Stats2019Book_FINAL.pdf. Accessed July 6, 2020.
5. American Society for Dermatologic Surgery. ASDS Consumer Survey on Cosmetic Dermatologic Procedures. 2019. https://www.asds.net/medical-professionals/practice-resources/asds-consumer-survey-on-cosmetic-dermatologic-procedures. Accessed July 6, 2020.
6. Blyumin-Karasikyumin-Karasik M, Rouhani P, Avashia N, et al. Skin tightening of aging upper arms using an infrared light device. Dermatol Surg 2011;37(4):441–449.
7. Juhász M, Korta D, Mesinkovska NA. A review of the use of ultrasound for skin tightening, body contouring, and cellulite reduction in dermatology. Dermatol Surg 2018;44(7):949–963.
8. Oni G, Hoxworth R, Teotia S, Brown S, Kenkel JM. Evaluation of a microfocused ultrasound system for improving skin laxity and tightening in the lower face. Aesthet Surg J. 2014;34(7):1099–1110.
9. Suh DH, Shin MK, Lee SJ, Rho JH, Lee MH, Kim NI, Song KY. Intense focused ultrasound tightening in Asian skin: Clinical and pathologic result. Dermatol Surg 2011;37(11):1595–1602.
10. Alster TS, Tanzi EL. Noninvasive lifting of arm, thigh, and knee skin with transcutaneous intense focused ultrasound. Dermatol Surg 2012;38(5):754–759.
11. Rokhsar C, Schnebelen W, West A, Hornfeldt C. Safety and efficacy of microfocused ultrasound in tightening of lax elbow skin. Dermatol Surg 2015;41(7):821–826.
12. Choi SY, No YA, Kim SY, Kim BJ, Kim MN. Tightening effects of high-intensity focused ultrasound on body skin and subdermal tissue: A pilot study. J Eur Acad Dermatol Venereol 2016;30(9):1599–1602.
13. Alhaddadlhaddad M, Wu DC, Bolton J, et al. A randomized, split-face, evaluator-blind clinical trial comparing monopolar radiofrequency versus microfocused ultrasound with visualization for lifting and tightening of the face and upper neck. Dermatol Surg 2019;45(1):131–139.
14. Dayan E, Chia C, Burns AJ, Theodorou S. Adjustable depth fractional radiofrequency combined with bipolar radiofrequency: a minimally invasive combination treatment for skin laxity. Aesthet Surg J. 2019;39(Suppl_3):S112–S119.
15. Hantash BM, Ubeid AA, Chang H, Kafi R, Renton B. Bipolar fractional radiofrequency treatment induces neoelastogenesis and neocollagenesis. Lasers Surg Med 2009;41:1–9.
16. Hantash BM, Bedi VP, Kapadia B, et al. In vivo histological evaluation of a novel ablative fractional resurfacing device. Lasers Surg Med 2007;39:96–107.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.