REVIEW ARTICLE

Nonablative Radiofrequency for Skin Rejuvenation

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There is growing interest in a wide range of nonablative interventions that, predictably, are claimed to rejuvenate skin and subcutaneous tissue "safely and effectively." Although for many years surgery in its many forms has been the criterion standard treatment in aesthetic aspect of aging, nonsurgical methods have always been an attractive choice because of their low invasiveness and shorter recovery time. Nevertheless, most nonsurgical modalities have centered around those that destroy the epidermis and cause a dermal wound, with resultant dermal collagen remodeling and secondary skin tightening and rhytid improvement. Radiofrequency (RF) tissue tightening was developed to create thermal effects in the dermis without external cutaneous wounding. The current review aims at summarizing the nonablative RF currently in use for skin rejuvenation.

History

Redundant facial, neck, or body laxity is a major feature of aging and, until recently, surgery was the sole option for its correction. As newer methods developed, RF was introduced at the beginning of the 21st century as a nonlaser technology for cosmetic dermatology, although it has been in use for much longer as a therapeutic option in medicine and surgery. Tissue tightening was one of the first dermatologic uses of RF, where it was used as an alternative or complement to nonablative laser technologies. RF-based systems have been used successfully for nonablative skin rejuvenation, atrophic scar revision, treatment of hypertrophic scars and keloids,[1] treatment of unwanted hair, rosacea,[2] vascular lesions, and inflammatory acne.[3,4]

RF Technology

How it Works: Biophysics of Thermal Collagen Remodeling

Thermal collagen contraction can be applied to the skin for use in aesthetic rejuvenation, restoring skin laxity and aging symptoms. Collagen fibers consist of triple helix strands of protein containing strong hydrogen bonds that deteriorate over the course of several years. The application of thermal energy over a period of time contracts, compresses, and thickens the collagen fibers. An ideal heat of 57°C to 61°C is adjusted for collagen shrinkage, with a time depending on type and area of skin applied. The dermal collagen fibers are detected at a depth of 1 to 2 mm for treatment of skin laxity.

Nonablative Skin Remodeling

Photomodulation, a nonablative laser treatment, allows matrix metalloproteinase reduction to produce an increase in the cellular response of dermal collagen. There are two hypotheses to explain this treatment method: (1) water and collagen absorb the light energy, producing a thermal effect on the dermis, and (2) cellular mediators and growth factors

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cause a wound healing effect due to the light energy absorbed by hemoglobin and melanin. Furthermore, laser energy applied to dermis microvasculature can cause cytokine-mediated responses that produce collagen. Nonablative laser treatment is believed to spark the production of type 1 procollagen messenger RNA associated with the restoration of the dermal matrix.

According to Ohm's law, which refers to the heat created by the natural resistance of the transport of electrons within tissue on an RF field, can be expressed using the following equation: $J = I^2 \times R \times T$, where I is current, R is tissue impedance, and T is time of application. The ideal energy and time of RF applied can be determined using Ohm's law.

RF is a nonablative method that produces resistance within the various layers of the skin. The tissue's resistance causes an electrical current, which transforms into thermal energy. Factors such as the size and depth of tissue and its various layers (dermis, muscle, fat, and fibrous tissue) must be considered, as they impose different degrees of impedance to the RF energy. In addition, because RF energy produces an electrical current instead of a light source, it does not damage tissue or epidermal melanin. Therefore, patients of all skin types can be treated with extensive RFs, allowing deeper penetration within tissue layers to allow for contraction and production of new collagen.

RF performs two collaborate functions: initial collagen contraction and a wound healing response, which tightens skin tissues over a period of time. Tightening of the dermis occurs in the $x-y$ dimension, and if ideal conditions apply, a z dimension tightening can occur without damaging fat. The process occurs when a target segment of the skin is treated with RF, denaturing the collagen and tightening the skin, allowing healthy tissue to heal the wound. RF works by allowing an electrical current to pass from an RF energy base into a monopolar electrode, traveling through the patient and to the grounding pad. Moreover, several trials at lower energy levels provide more substantial tissue contraction than one trial at a higher energy level.

The applied resistance to RF flow is greater on fat than on the surrounding fibrous septa. Hence, a greater amount of RF flow is critical for transfer energy through fat. The RF flow travels along the fibrous septa as the pathway of least resistance, causing the fibrous septa to absorb 1.4 to 3.0 times as much heat as fat.

The two major electrode configurations available in current RF devices are monopolar and bipolar. The energy field that these electrode configurations create differs, but the interaction between the emitted energy and the targeted tissue is similar.

Emergence of RF in Dermatology

Rhytides, wrinkles, and other signs of photoaging are becoming more prevalent because of greater sun exposure, phototoxic drugs, and demographic changes. Cosmeceutical products, lasers, and surgery have all been used to reverse signs of aging but have suffered from limited efficacy or a high incidence of side effects. These, together with the need for noninvasive procedures with shorter downtimes for patients in today's times with busy schedules, have led to exploration of nonablative modalities.

RF energy can be applied to tissue between two points on the tip of a probe (bipolar—second-generation RF technology) or between a single electrode tip and a grounding plate (monopolar—first-generation RF technology). Less current is required with a bipolar device than with a monopolar device to achieve the same effect, because the current passes through a much smaller volume of tissue. With a monopolar RF device, the penetration depth can be estimated to be half the electrode size, whereas for a bipolar RF device, the penetration depth of electrical current can be estimated to be half the distance between the electrodes.

Monopolar RF

In a monopolar setting, one electrode emits the RF energy, and the other serves as a grounding pad. The ThermaCool (Solta Medical Inc., Hayward, CA) tissue contraction monopolar RF device has four important components and works on the principle of Ohm's law (as discussed above):

- a monopolar RF generator producing 6 MHz of alternating current RF signal
- a handpiece for directing the RF energy to the skin
- a disposable electrode treatment tip for transferring RF energy to the skin
- a cooling module that feeds cryogen through a controlled valve on the handpiece to the tip's contact cooling membrane.

The generator is regulated using a Pentium chip–based internal computer (Intel, Berkeley, CA) that processes feedback, including temperature of the tip interface with the skin, application force, amount of tissue surface area contact, and real-time impedance of the skin. A microprocessor in the handpiece gathers this information and relays it to the generator through a high-speed fiberoptic link. Using a unique capacitive coupling membrane, RF is dispersed uniformly across the thin (1/1,000 of an inch) dielectric material on the treatment tip. The RF generator changes the polarity of the electric field in the tissue 6×10^6 times per second, causing charged molecules to move with the electric field at the same frequency. The dermal tissue's natural resistance to electron movement generates heat. The friction from electron movement creates volumetrically distributed deep dermal heating. Before, during, and after delivery of RF energy, a cryogen spray delivered onto the inner surface of the treatment tip membrane provides cooling to protect the dermis from overheating and subsequent damage. Additionally, the treatment tip continually monitors heat transmission from the skin through thermistors mounted on the inside of the dielectric membranes. The cryogen spray also cools the upper dermis, which creates a reverse thermal gradient through the dermis and results in volumetric heating and tightening of deep dermal and subdermal tissues. This depth of heating depends on the treatment tip geometry and sizes (currently available in 0.25, 1, 1.5, and 3 cm) and duration of cooling.

Each treatment cycle consists of three phases: precooling, intratreatment cooling, and postcooling.

To prevent epidermal burning, the handpiece microprocessor stops the delivery of energy when all four tip corners are not in complete contact with the skin.

Fitzpatrick and colleagues[5] performed the largest multicenter clinical trial believed by the Food and Drug Administration (FDA) to demonstrate the clinical efficacy of the RF (monofrequency) device (Thermage ThermaCool System, Thermage, Inc., Hayward, CA). Eighty-six patients received a single treatment on the forehead and the temple area using the Thermatip. At the conclusion of the study, 83.2% of treated periorbital areas showed at least a 1-point improvement in Fitzpatrick wrinkle score, 14.3% showed no change, and 2.5% worsened. Photographic analysis revealed an eyebrow lift of 0.5 mm in 61.5% of patients at the end of the study period. Approximately 50% of the patients expressed satisfaction with the outcome. Erythema (36% immediately) and edema (14% immediately) were the only observed side effects, of which the latter cleared in a month's time, and the former lingered in 4% cases for a longer time. A 0.4% burn risk was noted. The investigators concluded that ThermaCool TC reduced periorbital wrinkles, produced lasting brow elevation, and improved eyelid aesthetics. Considering the fact that the physicians using the device had no previous experience with it, the safety profile was rated as impressive. The FDA approved Thermage for the noninvasive treatment of periorbital rhytides and wrinkles in 2002 and for full face treatment in 2004.[6]

In another study done in the same year, by Hsu and Kaminer,[7] who treated 16 patients, it was found that higher fluences generally led to more improved or consistent results. Also, the larger the surface area treated, the better were the results, and younger age was seen to be a predictor of increased efficacy of Thermage procedure. The FDA approved monopolar RF for the noninvasive treatment of periorbital rhytides and wrinkles in 2002 and for full-face treatment in 2004.

As shown in multiple studies, monopolar RF tissue heating creates a dual effect on collagen.[8,9] Primarily, heat disrupts hydrogen bonds, altering the molecular structure of the triple-helix collagen molecule, resulting in collagen contraction. Secondarily, a more gradual contraction due to wound healing is predicted to take place as collagen regenerates. This takes 2 to 6 months to develop and leads to a thicker remodeled dermis. Histologically, this is seen as epidermal and papillary dermal thickening and shrinkage of sebaceous glands.

Bipolar RF

Bipolar devices pass electrical current between two positioned electrodes applied to the skin. No grounding pads are necessary with these systems because no current flows throughout the rest of the body. The main advantage of a bipolar system is the controlled distribution of RF current inside the tissue, which is limited by the volume between the two electrodes. The effect achieved is similar to that of monopolar RF, which is conformational change in the structure and length of collagen and may also induce a fibroblast response for long-term collagen remodeling.

Bipolar RF devices are frequently combined with other light-based technologies, making it difficult to assess the exact role of bipolar RF in treatment outcomes.

Functional aspiration controlled electrothermal stimulation (FACES) is an innovative combination of bipolar RF and vacuum.[10] By using vacuum to fold the skin, variable predetermined depths of the dermis are placed in close alignment with the RF energy, unlike the constant and larger gap between the dermis and the RF energy when monopolar or conventional bipolar electrodes are placed on top of the skin surface. Furthermore, by limiting the volume of treated tissue to that located between the two electrodes in the specially designed tip, the required energy density can reach and affect the chosen skin layers, whether superficial or deep, using lower energy levels. This should lead to highly effective treatments with fewer safety concerns and less pain, even without topical anesthesia.

A FACES device (Aluma-System, Lumenis Inc., Santa Clara, CA) uses a handpiece that uses a vacuum to fold the skin. This ensures contact and positions the dermis in direct alignment with the path of RF. The positioning of the vacuum along with the use of a topical conductive coupling medium concentrates heat deep in the dermis. The results are predictable, effective, and virtually painless.[11,12]

Combined RF and Optical Energy

A new technology that integrates bipolar RF and optical energies, electro-optical synergy (Syneron Medical Ltd, Yokneam, Israel), is based on the premise of a synergistic activity between the two forms of energy. An alternative to traditional light-based systems, electro-optical synergy has the capability to target specific areas of the dermis, sparing the patient recovery time for treatment.[13] Laser-based systems produce tissue scatter and melanin absorption, which greatly reduces skin penetration. By using electro-optical synergy, low emissions between 400 and 980, 580 and 980, and 680 and 980 are emitted to preheat dermal structures, allowing a temperature change between surrounding tissues. The theory underlying these devices is that selective photothermolysis is used to preheat a target tissue. In doing so, the impedance of the target is altered, and its susceptibility to a subsequent pulse of RF is increased. Warm temperatures of the dermal

structures ease the directed application of RF energy to dermal chromophores with less impedance. Skin precooling and targeted heating create this optimal condition. RF energies up to 25 J/cm^2 can be generated with a dermal penetration of 4 mm.[14] This is intended to reduce complications by using lower optical and RF energies.

The FDA-approved Aurora SR system (Syneron, Inc., Yokneam, Isreal) is used for rejuvenating the skin by reducing rhytides and improving skin texture and tone. The system can treat multiple areas of the body such as facial acne, unwanted hair, and vascular and pigmented injuries.[15,16] Patients are treated with three to four sessions per visit at 3- to 4-week intervals. The system is precise because it does not rely on melanin absorption to target areas in the dermis.

Another system, the Polaris WR (Syneron, Inc.), uses a combined 900-nm diode laser with an RF energy device. Optical energies are delivered through a bipolar electrode tip with fluences ranging from 10 to 50 J/cm^2 and RF energies of 10 to 100 J/cm^3. While the energies are transferred into the tissue, the RF energy penetrates deep and begins collagen production, addressing superficial rhytides, pigmentation, and vascularity. Hair, leg veins, and vascular wounds have been effectively removed using the Polaris WR system.[8,9,17] Furthermore, the 900-nm diode laser targets intravascular hemoglobin or dermal pigment. In contrast, simultaneous RF energies affect the distortion of vascular or hair follicles.

The theory behind combining the optical and bipolar RF energies is that the combination allows for lower energies with both methods to achieve target heating, thereby increasing safety and reducing discomfort and complications.[4,18,19]

Fractional RF

Previous studies have investigated the effects of microneedle-based bipolar RF treatment on joint capsular tissue, but little is known about its effects on human skin. Recently a novel fractional RF device (Renesis, Primavea Medical, Inc., Fremont, CA) that uses a minimally invasive bipolar microneedle delivery system for the treatment of human skin was introduced and demonstrated the ability to produce controlled zones of collagen coagulation in the reticular dermis at the histological level.

Hantash and colleagues[20] developed a minimally invasive investigational device that delivers bipolar RF current through a microneedle electrode assembly. They demonstrated that controlled RF thermal zones (RFTZs) can be deposited in human skin. This fractional RF (FRF) system is capable of achieving fractional and contiguous treatment patterns while sparing the epidermis and key adnexal structures that contribute to rapid healing.

They examined wound-healing response after FRF in human subjects.[21] The FRF delivered RF energy within the dermis five microneedle–electrode pairs. Tissue temperature was held at 72°C for 4 seconds using an intelligent feedback system. The wound-healing response was evaluated histologically and using reverse transcriptase polymerase chain reaction (PCR) up to 10 weeks after RF treatment. Neoelastogenesis and the role of heat shock proteins (HSPs) were assessed using immunohistochemistry. Results showed that a vigorous wound healing response is initiated after treatment, with progressive increase in inflammatory cell infiltration from day 2 through week 10. An active dermal remodeling process driven by the collagen chaperone HSP47 led to complete replacement of RFTZs with new collagen by 10 weeks after treatment. Furthermore, using immunohistochemical and PCR studies, they demonstrated for the first time evidence of profound neoelastogenesis after RF treatment of human skin.[22]

Another device using FRF technology is the Matrix RF (Syneron Medical Ltd.). Matrix RF is the first bipolar RF-based aesthetic device capable of delivering ablative tunable RF energy to the skin in a nonhomogenous fractional manner using an array of multielectrode pins. This results in heating of the

areas in direct contact with the pins and spares the zones between the targeted areas, which helps to maintain the skin integrity and serves as a pool of cells that promote wound healing.[23]

Hruza and colleagues[23] delivered fractional RF treatment to the abdomen in individuals scheduled for abdominoplasty. They used different tips at varying energy densities and coverage rates. Biopsies were performed ex vivo after abdominoplasty, and tissue samples were routinely processed and stained, using hematoxylin and eosin. Another group of subjects received three facial treatments scheduled at 3- to 4-week intervals. Clinical improvement and response to therapy were evaluated using standardized photography and clinical assessment by the subjects and investigators. Histological findings immediately after treatment revealed demarcated zones of ablation, coagulation, and necrosis and subnecrosis up to a depth of 450 μm. Higher energy levels generated deeper effects. Subjects undergoing facial treatment had minimal pain and no permanent side effects or significant downtime. Investigators' assessments of improvement in skin texture correlated with subjects' evaluations and were greater than 40% for approximately 50% of subjects. Eighty percent of the subjects were satisfied with the results. Higher energy levels and lower coverage rates produced better aesthetic results along with less pain.

Table 1 highlights the major studies on bipolar RF and their results.

Tripolar RF

Recently, a novel system TriPollar radiofrequency device (Regen, Pollogen Ltd., Tel Aviv, Israel) was developed to deliver the effects of RF energies in a nonablative treatment for all skin types. This unique system is based entirely on a different method than previous RF systems, heating superficial and deep skin layers simultaneously by delivering focused RF current to the skin. The Regen system is a RF device that uses a multiple-electrode, TriPollar configuration. The TriPollar design, a third-generation RF technology, is based on three or more electrodes to deliver the focused RF current to the skin tissue. The depth of heat penetration is approximately the average distance between the three electrodes and simultaneously heats the dermal and subcutaneous layers. Because of its design, no active cooling of the electrodes or the skin is required. The regen system delivers RF energy at a frequency of 1 MHz and a maximum power of 30 W. Two applicators are available for body and face treatments. A small number of trials have evaluated the efficacy and safety of tripollar RF systems in skin rejuvenation.[43,44]

One study provided evidence that TriPollar technology is a safe and effective non-invasive solution for skin tightening and body reshaping. The study involved 12 patients who underwent an average of seven weekly treatment sessions on different body areas, including the face, neck, arms, hands, and abdomen. Histopathological examination revealed marked differences between the treated and nontreated abdominal skin areas. An increase of 49% in dermal thickness due to neocollagen regeneration, focal thickening, remodeling of collagen fibers, and focal shrinkage of fat cells were measured after the TriPollar treatments. Patient satisfaction was also measured, and the study confirmed clear satisfaction with clinical results achieved.[43]

The safety and efficacy of the regen system for treatment of skin laxity and circumference reduction on Asian skin was evaluated at the Lyhn clinic in Seoul, Korea. Patients underwent weekly treatment sessions, and results were evaluated quantitatively by measuring circumference and qualitatively through photography and patient satisfaction questionnaire. Healthy female patients aged 18 to 65 were enrolled in the study. Exclusion criteria included pregnancy, any implantable electronic device that could be disrupted by RF energy, and any active dermatological or collagen–vascular disorder. Patients completed a medical history form and signed an informed consent form before commencement of treatment.

TABLE 1. Major Studies of Bipolar Radiofrequency (RF) and Skin Tightening

Investigators	*Study Objective*	*Results and Conclusions*
Alexiades-Armenakas[24]	To assess the combination of the three main classes of nonablative rejuvenation, infrared laser, intense pulsed light, and RF energy	The combination technology resulted in a mean improvement per category of 10.9% (95% CI = 8.1–13.7%) per treatment and 26.0% (95% CI = 16.5–35.5%) overall following a mean ± SD of 2.4 ± 1.2 treatments. In addition, patient satisfaction was 71.4%, suggesting that combining nonablative technologies may maximize clinical results and patient detection of improvement.
de Felipe et al[25]	A retrospective review to establish the degree of side effects in 290 patients receiving a total of 757 treatments with monopolar RF	The appearance of second-degree burns occurred in 2.7% of the treatment sessions. Other less-frequent adverse reactions were persistent erythema (1.2%), headache, scarring, edema, fat atrophy, burn in the return pad site, neuralgia, and facial palsy. The occurrence of facial palsy might be a coincidence.
Finzi and Spangler[26]	To determine the safety and report on the efficacy of a RF application that involves a multipass vector technique to target facial and neck skin laxity	All patients experienced some immediate erythema and edema, which had completely resolved in most patients within 48 hours. No scarring or dyspigmentation was noted on follow-up at 6 and 12 weeks. Photographic analysis of pre- and post-treatment digital images revealed cosmetic improvement in facial and neck laxity in 96% of patients. The majority of patients demonstrated moderate or better improvement. Stacked pulses in the submental region were shown to reduce fat.
Sasaki et al[27]	To discover at baseline from patient demographics, skin and fat characteristics, measurable degrees of tissue mobility, and photoaging any predictors of a positive result under a standardized treatment algorithm	At baseline and 3, 6, and 12 months, measurements of skin thickness, subcutaneous fat depth, tissue mobility, and wrinkle and fold depth were obtained at nine reference sites on each patient. Nineteen patients (76%) who progressively responded to nonablative monoradiofrequency energy over 12 months were observed at baseline to have a global mobility score (mean ± SD) of 3.4 ± 0.27 mm; six patients who were assessed to be nonresponders over 1 year of evaluation began with more tissue laxity and exhibited at baseline a higher global mobility score of 4.4 ± 0.60 mm.
Friedman and Gilead[28]	To assess the efficacy and safety of a novel RF device (Accent, Alma Lasers, Ltd., Caesarea, Israel) for the treatment of rhytides and lax skin	For wrinkles and skin laxity, in five patients (42%), the cheeks ($n = 12$) scored 51% to 75% (significant improvement), and in two patients (17%), 76% to 100% (excellent improvement). For the jowl lines ($n = 9$), four patients (44%) scored 51% to 75% (significant improvement), and one patient scored 76% to 100% (excellent improvement) for lax skin. For wrinkles on the periorbital ($n = 7$) and forehead areas ($n = 8$), three patients (37%) scored 51% to 75% (significant improvement).
Sadick et al.[29]	To study the therapeutic effect of a new method of skin renewal: electro-optical synergy, which combines intense pulsed optical energy and conducted bipolar RF energy into a single pulse and has been recently introduced	Overall skin improvement was rated at 75.3%. Overall average wrinkle improvement was 41.2%, with average Class 1 wrinkle improvement of 64.7%, Class 2 wrinkle improvement of 38.6%, and Class 3 wrinkle improvement of 20.4%. Improvement in skin laxity was rated at 62.9%. Skin texture was reported to improve 74.1%. Improvement in the appearance of pore size was rated at 65.1%. Average improvement in erythema and telangiectasia was 68.4%. Average improvement in hyperpigmentation and dyschromia was 79.3%. Overall patient satisfaction was 92%. The overall minor complication rate, including blistering, crusting, and stripping, was 8.3%, and the major complication rate was less than 1%.

TABLE 1. Continued

Investigators	*Study Objective*	*Results and Conclusions*
Hammes et al[30]	To evaluate the efficacy and safety of nonablative wrinkle treatment using combined RF and optical energy (electro-optical synergy; Polaris).	Independent scoring of blinded photographs showed a wrinkle score improvement of at least 1 (0 = no improvement, 1 = medium, 2 = good, 3 = excellent improvement) 3 months after the last of six treatment sessions. There was no difference between periorbital and perioral wrinkle reduction. Fifty-eight per cent (14/24) of the subjects reported notable wrinkle reduction; 16% noted mild to moderate edema and erythema lasting for no more than 1 day. Scarring or pigmentary changes were not detected. The average pain score was 0.6 (0 = no pain, 5 = intolerable pain).
Goldman et al.[31]	To confirm or refute any possible subtractive effects of augmentation of the nasolabial folds when followed by 1,320-nm neodymium-doped yttrium aluminum garnet laser, 1,450-nm diode laser, monopolar RF, IPL treatments, or a combination	There were no statistically significant differences between wrinkle severity or global aesthetic scores for hyaluronic acid gel implantation alone and hyaluronic acid gel with laser–RF–IPL treatment at any time. In a small sample, histologic changes were not apparent after laser–RF–IPL treatment.
Sadick and Mulholland[32]	A two-center study to investigate the safety and effectiveness of combined energies for cellulite treatment using the VelaSmooth system	All study patients showed some level of reduction in thigh circumference after 8 weeks of treatment; 70% of all patients showed such a reduction after 4 weeks of treatment. All patients showed some level of improvement in skin texture and cellulite. The mean decrease in circumference was 0.8 inches. Some patients demonstrated reductions of more than 2 inches. There were minimal complications associated with treatment.
Sadick and Trelles[33]	A two-center study to investigate the safety and effectiveness of combination diode laser (900 nm) and RF for the treatment of wrinkles and skin texture	Twenty-three subjects completed all three treatment sessions, of whom more than 50% had a greater than 50% improvement in the appearance of wrinkles. All subjects reported a noticeable improvement in skin smoothness and texture.
Kushikata et al.[34]	To assess the efficacy and clinical effect of RF in Asian skin, with additional study on the duration of the effect and any complications	RF treatment was effective for nasolabial folds, marionette lines, and jowls. Objective physician evaluation found relatively good improvement at 3 months after treatment and even better improvement at the 6-month evaluation.
Ruiz-Esparza and Gomez[35]	To evaluate the function of a novel technology that tightens tissue, using energy in the RF segment of the electromagnetic spectrum to produce internal heat within the skin	All patients experienced minimal discomfort and were able to return to their normal activities right away. All patients except one had visible results approximately 12 weeks after the treatment session; in one patient, the results started 1 week after treatment. Four independent physicians outside of the study reviewed standardized photographs to evaluate results. The patients were followed for 6 to 14 months.
Alster and Tanzi[36]	To evaluate a novel combination device involving RF, infrared light, and mechanical tissue manipulation for the treatment of cellulite	Ninety percent (18/20) of patients noticed overall clinical improvement, and 17 of these 18 patients reported that they would pursue treatment of the contralateral thigh. Side effects were limited to transient erythema in most patients, and bruising was observed in two patients after the first few treatment sessions but not as the treatment series progressed. Clinical improvement scores averaged 1.82 (corresponding to approximately 50% improvement) after the series of treatments. Circumferential thigh measurements were reduced by 0.8 cm on the treatment side.

TABLE 1. Continued

Investigators	*Study Objective*	*Results and Conclusions*
Bassichis et al.[37]	To evaluate the use of the ThermaCool TC nonablative RF device for rejuvenation of the upper third of the face, as determined by brow elevation	The post-treatment measurements were better than in the control group ($p<.05$). The post-treatment measurements were also improved from pretreatment baseline ($p<.05$). Subjective results obtained from patient satisfaction questionnaires did not correlate to the objective data. The data also showed that improvement in brow elevation was not uniform in each patient.
Nahm et al.[38]	To objectively quantify the effectiveness of volumetric RF application on the face by treating 10 patients on the left side of the face with RF and evaluating the changes in brow position, superior palpebral crease, angle of the eyebrow, and jowl surface area	At the end of 3 months on the side that was treated, patients exhibited on average 4.3 mm of brow elevation and 1.9 mm of superior palpebral crease elevation along the midpupillary line and an average of 2.4 mm of brow elevation along the lateral canthal line. There was no significant improvement of brow elevation along the lateral canthal line on the contralateral side. The peak angle of the ipsilateral eyebrow became slightly more acute by an average of 4.5° after treatments. Moreover, the jowls on the lower part of the face displayed a mean decrease of 22.6% in surface area after treatments. The nontreated side displayed a lack of eyebrow angle and jowl surface area changes.
Fritz et al.[39]	To compare the effectiveness of one and two RF treatments with the ThermaCool TC system on middle and lower face laxity	All subjects experienced mild edema and mild to moderate erythema as an acute clinical response; no patients experienced burns, skin breakdown, or scarring. At 4-month follow-up, patients in the two-treatment group received higher scores in all categories of photographic analysis; the difference in improvement in the nasolabial folds was statistically significant ($p=.04$). In self-assessment ratings, individuals receiving two treatments reported more improvement than subjects in the single-treatment group 4 months after treatment ($p=.03$). In both treatment groups, physician photographic assessment demonstrated continued improvement in all subsites between the 1-month and 4-month assessments ($p<.05$)
Gold et al.[10]	To evaluate the safety and efficacy of a new device that implements an innovative combination of bipolar RF and vacuum	Significant improvement in the skin's appearance and texture was observed during the treatment course and continued to increase during the follow-up period. The mean elastosis score on the wrinkling and elastosis scale before treatment was 4.5 and was less than 2.5 by 6 months after treatment, representing a drop of an entire wrinkle class (from II to I) on this scale.
Montesi et al.[40]	To examine the mechanism of action of a new bipolar RF device that emits RF energy through a handpiece with a bipolar electrode configuration, and assesses the clinical histological and immunohistochemical results on a sample group of patients who underwent a cycle of sessions with this device	All patients showed improvement in treated imperfections from the second session onward and expressed their satisfaction at the end of the treatment cycle. The most notable clinical, histological, and immunohistochemical results were observed in patients with abdominal striae distensae. In most cases, the temporary side effects observed consisted of rashes and ecchymosis.
Narins and Narins[6]	To evaluate the efficacy and safety of RF treatment of the brow and jowls	The technique was found to produce gradual tightening in most patients, and there were no adverse effects.

TABLE 1. Continued

Investigators	*Study Objective*	*Results and Conclusions*
Weiss et al.[41]	To establish the rate and degree of side effects in clinical experience using a retrospective chart review	The most common immediate and expected clinical effects were erythema and edema lasting less than 24 hours, although six patients reported edema lasting for up to 1 week. There were no permanent side effects. In total, 2.7% of treatments resulted in temporary side effects, the most significant of which was a slight depression on the cheek ($n=1$), which completely resolved within 3.5 months. Other side effects included localized areas of acneiform subcutaneous erythematous papules ($n=4$) and a linear superficial crust ($n=1$) with the original tip, all of which resolved within 1 week. One patient reported small erythematous subcutaneous nodules resolving in 17 days. Tenderness of the neck lasting from 2 weeks ($n=2$) to 3 weeks ($n=1$) was also reported.
Abraham et al.[42]	To evaluate the clinical efficacy of nonablative cutaneous RF facial rejuvenation	At 12 weeks, a statistically significant increase in mean vertical brow height of 1.6 to 2.4 mm was observed in patients treated exclusively with the RF device ($p<.001$). All skin parameters (laxity, wrinkles, clarity, pore size) were improved. Complications and side effects were minimal. Patients were uniformly satisfied.
Hantash et al[21]	To evaluate the wound healing histologically and using a RT-PCR response created by a fractional RF system using five microneedle electrode pairs in 20 healthy subjects undergoing abdominoplasty or surgical face lift	Heat shock protein 47 expression increased progressively through 10 weeks. Reticular dermal volume, cellularity, hyaluronic acid, and elastin content increased. RT-PCR studies revealed an immediate increase in interleukin-1, tumor necrosis factor alpha, and matrix metalloprotein 13.
Hruza et al[23]	To analyze the degree of tissue ablation, coagulation, and heating; and to evaluate the clinical efficacy and safety of a fractional radiofrequency (RF) device, for the treatment of wrinkles with fractional skin ablation and coagulation.	Histological findings immediately after treatment revealed demarcated zones of ablation, coagulation, and necrosis and subnecrosis up to a depth of 450 m. Higher energy levels generated deeper effects. A tunable balance was noticed between ablation and coagulation/necrosis. These effects were coverage mode and energy density dependent. Subjects undergoing facial treatment had minimal pain and no permanent side effects or significant downtime. Investigators' assessment for improvement in skin texture correlated with subjects' evaluation and was greater than 40% for approximately 50% of subjects. Eighty percent of the subjects were satisfied with the results. Higher energy levels and lower coverage rates produced better aesthetic results along with less pain.

SD, standard deviation; CI, confidence interval; RT-PCR, reverse transcriptase polymerase chain reaction

Immediate visible results were noticed from the first treatment. The patients' results, observed gradually over the full course of treatment, revealed a significant circumference reduction and observable lifting of sagging skin. Patient self-assessment after the full course of the treatment was "excellent." This patient experienced no adverse side effects during or after any of the treatments. Furthermore, throughout the study, none of the patients experienced any need for downtime after the treatments.[45]

Fibroblasts, which synthesize three polypeptide chains that wrap around one another in a triple helix, produce collagen molecules. The phenomenon

of thermal shrinkage of collagen begins with denaturation of the triple helix of the collagen molecule. When collagen is heated, the heat-labile intramolecular cross-links are broken, and the protein undergoes a transition from a highly organized crystalline structure to a random gel-like state (denaturation). Collagen shrinkage occurs through the cumulative effect of the "unwinding" of the triple helix, due to the destruction of the heat-labile intramolecular cross-links and the residual tension of the heat-stable intermolecular cross-links.[22] Heated fibroblasts are also implicated in new collagen formation and subsequent tissue remodeling, which can also contribute to the final cosmetic result. The precise heat-induced behavior of connective tissues and the extent of tissue shrinkage depend on several factors, including the maximum temperature reached, exposure time, tissue hydration, and tissue age.

Most of these reports are about randomized noncomparative clinical trials with subjective evaluation of results and thus cannot be considered as strong evidence. Even if the clinically favorable reports are taken at face value, many questions remain about optimal treatment parameters.

Side Effects

In general, incidence of side effects is low with RF. Those reported include transient post-treatment erythema and edema, which are expected immediately after treatment. It is rare to see superficial burns or persistent erythematous papules. These are mainly attributed to uneven electrode contact with the skin, which sometimes becomes unavoidable because of uneven facial contours and results in arcing of the monopolar RF energy and epidermal burning.

Overtreatment with RF may cause depressions on the skin. Subcision and autologous fat transfer has been used to correct these dermal depressions.[46] The combination of bipolar RF with diode laser device is well tolerated. Some patients (3–10%) may develop vesiculations due to inadequate epidermal cooling during treatment. This generally clears without dyspigmentation or textural irregularities.[47]

Numbness of skin in the distribution of the greater auricular nerve can occur. This resolves with time because there is no anatomical damage to the nerve.[45] Inflammation of the underlying platysma muscle causing ridging has been reported with use of higher energies in the neck.[48,49] Other less frequent adverse reactions could be headache, scarring, fat atrophy, and burns in the return pad site.

Future

In spite of the developments, there is still much room to enhance RF technology and achieve the ultimate goal of precise contouring and lifting of ptotic skin and underlying structures, providing a truly nonsurgical lifting and tightening effect that may match surgical results.

There is also great interest in combining monofrequency RF with other modalities such as superficial and standard laser resurfacing, fractional lasers, botulinum toxin, and fillers.[50] Additionally, research directed toward developing a treatment tip that precisely determines individual patient's resistance at different treatment sites so that the exact amount of energy required to achieve a desired treatment end point is applied should be performed. This should include low risk of adverse effects. A special device that uses RF technology with fine needle electrodes has been tried for skin tightening. These electrodes have an electrically isolated shaft and a fine, nonisolated tip. A probe holder allows the distance between the electrodes to be varied.[51] Further research on this device could offer new treatment concepts with distinct advantages in nonablative skin tightening.

Conclusion

With the approval of mono- and bipolar RF therapy, new possibilities to treat visible signs of skin aging are available for dermatologists. Nonablative

skin rejuvenation with RF-based systems produces skin tightening through controlled dermal collagen contraction and neocollagenesis without integumental injury. This nonsurgical approach to rhytid reduction thereby avoids many of the inherent risks associated with surgical rhytidectomy. First studies have showed an improvement in appearance and reduction in quantity of wrinkles in the face and even lifting effects on the eyebrows on the basis of demonstrable molecular alterations of collagen. The use of such systems demands comprehensive physician qualification and training, and because facial skin is primarily addressed, a high level of damage is experienced in this sensitive area, and the danger of permanent complications exists, the indication for therapy should be considered. An emerging tripolar RF technology achieves immediate visible results.

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