

Radiofrequency in Cosmetic Dermatology: Recent and Future Developments

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Radiofrequency (RF) technologies are increasingly employed in dermatology to achieve skin rejuvenation with minimal adverse effects and downtime. Radiofrequency enables physicians to augment targeted tissue layers while sparing melanocytes and the cutaneous surface, thereby preventing dyspigmentation and prolonged wound healing. Recent advances in RF have expanded the array of treatment indications and improved cosmetic outcomes. Future developments are likely to further enhance the therapeutic index of RF. This review will shed light on the technical aspects and clinical outcomes of the most recent developments in RF technologies. *Cosmet Dermatol.* 2011;24:565-574.

Radiofrequency (RF) technology was first applied to cosmetic dermatology at the beginning of the 21st century after having been employed in medicine and surgery for numerous indications for years. After RF was found to induce collagen contraction and a wound-healing response, it began to be used for tissue tightening and subsequently was adapted for a variety of other indications, including rhytides, scar revision, vascular lesions, and acne vulgaris.¹⁻⁵ Advances in the understanding of the biophysics of RF have led to adaptations of this technology for a variety of dermatologic indications and dramatic recent improvements in RF devices and treatment techniques.

PRINCIPLES OF RF

A basic understanding of the biophysics of RF technology facilitates an informed discussion of expanding target indications and innovative treatment techniques as well as an appreciation for the vast potential of RF in cosmetic dermatology. Radiofrequency devices utilize electrical energy to transfer heat energy to the dermis at relatively low temperatures. These devices typically are not intended to resurface the skin but rather to induce thermal damage to dermal collagen while sparing the epidermis. Resistance and the resultant degree of thermal damage is determined by the depth and composition of the treated tissue. When applied over a period of time, thermal energy contracts and thickens collagen fibers, disrupts hydrogen bonds, and alters the conformation of the collagen triple helix. It also induces a more prolonged wound-healing effect that is associated with sustained remodeling, reorientation, and formation of new collagen bundles over subsequent months.^{6,7} Because RF energy uses an electrical current rather than a light source, it does not affect epidermal melanin; therefore, patients of all skin types, including darker skin types and those with a predisposition to develop postinflammatory

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hyperpigmentation may be treated with RF. When applied properly, RF denatures dermal collagen and induces a healthy wound-healing response, resulting in effective skin rejuvenation with minimal recovery time.

Radiofrequency devices can be classified into several configurations based on the method by which the electrical current passes through the tissue. The first type to be introduced was monopolar RF, which applies energy to tissue via a single electrode tip and a grounding plate. Bipolar RF applies energy to tissue via 2 points on the tip of a single probe, and penetration depth is estimated at half the distance between the electrodes. Tripolar RF devices recently were introduced; this technology utilizes a multiple electrode configuration to heat superficial and deep skin layers simultaneously. Fractional RF also is a novel technology in which bipolar RF energy is delivered via a minimally invasive approach using a microneedle electrode assembly. This technology generates discrete thermal zones of treated tissue to the depth of the reticular dermis with fractional sparing of the epidermis and adnexa, thereby inducing a rapid and vigorous wound-healing response along with sustained dermal remodeling and profound neocollagenesis (Figure 1).^{8,9}

MONOPOLAR RF

One of the first monopolar RF devices (ThermaCool TC, Solta Medical, Inc) demonstrated to be safe and efficacious

in the treatment of periorbital rhytides in an early landmark study achieved its first US Food and Drug Administration approval in 2002.¹⁰ Unfortunately, early results with this device were somewhat inconsistent and often were statistically insignificant after photographic analysis.¹¹

Monopolar RF is hardly an antiquated technology, as physicians continue to explore and expand its use in dermatology (Table 1). A recent study utilized a new 2.2-MHz monopolar device (RF-ReFACING, Meyer-Haake Medical Innovations) to treat facial laxity and fine wrinkles affecting the lower eyelid, crow's-feet, and jowl line, and reported safe, convenient, and effective therapy for a wide array of patient age groups.¹² Another group helped expand the use of the ThermaCool TC System to the trunk, treating patients with abdominal skin laxity using the Thermage Multiplex Tip, with waist circumference and skin laxity scores decreased at follow-up.¹³

Monopolar RF technology also has been applied to other indications besides skin laxity and rhytides; one report described the successful treatment of steatocystoma multiplex involving the scrotum without infection, scarring, or dyspigmentation.¹⁴ Our understanding of the clinical and histologic changes induced by monopolar RF recently was advanced through the work of el-Domyati and colleagues.¹⁵ They treated participants with Glogau classification I to II facial wrinkles and reported increases

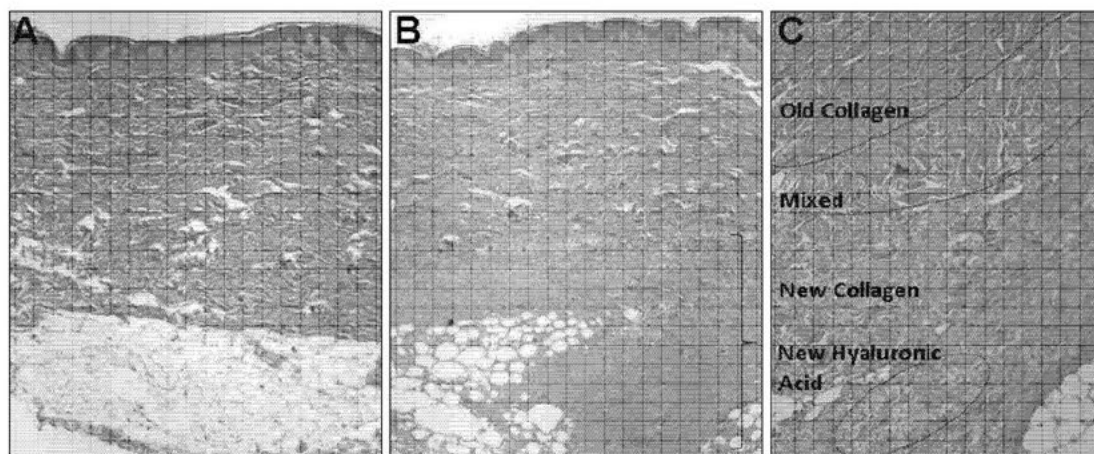


Figure 1. Long-term dermal remodeling and neocollagenesis following fractional radiofrequency treatment at baseline (A) and 10 weeks post-treatment (B) (H&E, original magnification $\times 4$ for both). At 10 weeks, dermal thickness was increased over baseline and subcutaneous interstitial collagen also was thickened with no evidence of fat necrosis. Both observations can be attributed to dermal remodeling and ongoing neocollagenesis following fractional radiofrequency treatment. Higher magnification revealed the presence of a wispy blue-gray staining substance (indicative of de novo hyaluronic acid deposition) in the midst of a high-density field of nucleated cells (C) (H&E, original magnification $\times 10$). This image also indicates 3 distinct zones that typically were observed: an old collagen zone, a mixed transition zone, and a new collagen zone. Reprinted with permission from Hantash et al.⁹

TABLE 1

Novel Uses of Monopolar RF

Reference (Year)	No. of Participants	Study Type	RF Type	Parameters	Indication	Outcome	Side Effects
Wollina ¹² (2011)	20	PCS	2.2 MHz	3 sessions; 2 passes/session; 8–12 W	Facial laxity and fine wrinkles	75% (15/20) rated good or better posttreatment	None reported
Anolik et al ¹³ (2009)	12	PCS	6 MHz	1 session; mean, 42 min; 28–46 J/cm ²	Abdominal skin laxity	Improved waist circumference and skin laxity	Transient erythema
Choudhary et al ¹⁴ (2010)	2	CS	2.4 MHz	1 session; ablation	Steatocystoma multiplex	Resolution	None reported
el-Domyati et al ¹⁵ (2011)	6	PCHS	6 MHz	6 sessions; 2 passes whole face; subsequent periorbital, nasolabial, and forehead passes	Facial wrinkles	35%–40% skin tightening immediately and 70%–75% skin tightening at 3 mo; 0%–45% immediate improvement in rhytides and 90%–95% improvement in rhytides at 3 mo; increased collagen (types I and III)	Transient erythema

Abbreviations: RF, radiofrequency; PCS, prospective clinical study; CS, clinical study; PCHS, prospective clinical and histologic study.

in mean collagen types I and III as well as newly synthesized collagen. They also observed higher levels of mean collagen and a lower level of mean elastin at 3 months posttreatment compared to immediately posttreatment, which they attributed to continued dermal remodeling. Participants demonstrated statistically significant improvements in skin tightening ($P=.02$), skin texture ($P=.04$), rhytides ($P=.01$), and participant satisfaction ($P=.001$).¹⁵

BIPOLAR RF

Bipolar RF devices obviate the need for a grounding pad and provide a controlled distribution of thermal energy

within treated tissue by passing current between 2 electrodes applied to the skin. The effect on tissue is otherwise essentially the same as monopolar RF, but bipolar systems typically do not penetrate as deep and are more comfortable than monopolar RF devices. Bipolar RF has been employed for a lengthy and continually expanding list of indications, including skin laxity, wrinkles, vascular lesions, dyschromia, cellulite, and body tightening.¹⁶ Bipolar technologies continue to expand the reach and effectiveness of novel RF devices (Table 2).

Functional aspiration controlled electrothermal stimulation is a recently developed technology that uses a

TABLE 2

Novel Uses of Bipolar RF

Reference (Year)	No. of Participants	Study Type	RF Type	Parameters	Indication	Outcome	Side Effects
Alexiades-Armenakas ¹⁷ (2006)	28	PCS	Combined	Mean, 2.4 sessions; IR/RF/IPL	Photoaging	10% improvement/treatment; 26% mean overall improvement	N/A
Dincer et al ¹⁸ (2010)	15	PCS	1.7 MHz	Electro-coagulation	Xanthelasma palpebrarum	9 patients excellent; 5 patients good; 1 patient moderate	None reported
Foster et al ¹⁹ (2009)	29	PCS	2 Hz	0.5–10.0 mA; pulse width, 0.2 ms	Glabellar furrows	90% (26/29) abrogation; 69% (26/29) with treatment response ≥ 4 mo	None reported
Reich-Schupke et al ²⁰ (2011)	20	HS	N/A	Varied application; 5–25 W	Varicose veins	Necrosis of intima and media at 20–25 W and application time to 400 Ω impedance	N/A

Abbreviations: RF, radiofrequency; PCS, prospective clinical study; IR, infrared; IPL, intense pulsed light; N/A, not available; HS, histologic study.

vacuum to fold target tissue between the 2 bipolar electrodes. This technique allows lower energy levels to be employed while achieving the ideal density at superficial and deep target layers, creating a safe, effective, and virtually painless technique for treating wrinkles and elastosis.²¹

Bipolar RF also has been increasingly combined with other technologies, typically light based, to achieve a synergistic effect between energy types. One such combination employs a 900-nm infrared laser, bipolar RF and intense pulsed light (500–1200 nm), which has been reported to diminish photoaging.¹⁷ A major drawback of this therapy, however, is that it requires numerous treatments at 2- to 3-week intervals, which may ultimately achieve only mild to moderate improvement. Because lower energies are required in combination therapy, patient discomfort

and the risk for complications are reduced, and treatment of a wide variety of indications is possible.^{22–25}

The list of dermatologic indications for which bipolar RF may be effective continues to expand. This technology recently was described for the treatment of xanthelasma palpebrarum, including the effective treatment of lesions close to the eyes.¹⁸ Another novel use of bipolar RF is to eliminate glabellar furrows via the percutaneous ablation of efferent nerves innervating the corrugator and procerus muscles. A 2009 study reported 29 participants undergoing bilateral ablation with this technique, with abrogation of glabellar furrowing achieved in 26 participants (90%) and no major adverse events. The therapeutic effect persisted for 4 months or more in 20 participants (69%).¹⁹ There also have been advances in the treatment of

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unwanted veins utilizing bipolar RF. A recent *ex vivo* study found circumferential necrosis of intima and media was reached by a power of 20 to 25 W and an application time up to an impedance of 400 Ω ; only heterogeneous necrosis was reached with lower power and long application time.²⁰ Finally, RF also has been reported to be efficacious in providing a minimally invasive method for treating chronic plantar fasciitis.²⁶ Bipolar RF continues to be employed in new and effectual methods while also inspiring future generations of RF devices.

FRACTIONAL RF

The recent development of fractional radiofrequency (FRF), or minimally invasive RF, represents an important advancement in the field of RF technology. Using a minimally invasive approach, FRF devices such as Renesis (Primaeva Medical, Inc) and eMatrix (Syneron Medical Ltd) generate RF thermal zones with fractional

sparing of the epidermis and adnexa. The Renesis device delivers a bipolar current via a microneedle electrode assembly and produces controlled zones of collagen coagulation in the reticular dermis while sparing key structures that promote rapid healing.⁸ An intelligent feedback system offers real-time feedback of skin temperature within the developing lesion. Wound-healing response after FRF therapy was evaluated histologically and using reverse transcriptase-polymerase chain reaction, and neoelastogenesis and heat shock protein response were analyzed using immunohistochemistry (Table 3).⁹ Ten weeks after treatment, histology revealed neoelastogenesis, neoelastogenesis, increased dermal cellularity, and deposition of hyaluronic acid. Radiofrequency thermal zones were completely replaced with new collagen via an active dermal remodeling process driven by the collagen chaperone HSP47 (Figure 2).⁹ A model that can accurately predict the thermal response of human skin

TABLE 3

Response to FRF Treatment of Wound-Healing Genes Affected by Dermal Remodeling^a

Gene	0 Days		2 Days		14 Days		28 Days	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
TNF- α	43.5	15.7	46.8	18.7	17.7	24.7	62.9	9.9
IL-1 β	41.7	20.5	50	5.6	58.3	21.1	112.5	19.6
TGF- β 1	0	26.8	58.5	18.5	68.3	10.1	85.4	13.2
MMP-1	-3.03	15.6	30.3	20.9	42.4	12.8	78.8	11.9
MMP-3	-7.5	13.5	-7.5	16.2	7.5	18.6	62.5	10.8
MMP-9	11.8	15.7	69.1	20	114.7	17.1	194.1	8.5
MMP-13	48.6	15.4	91.4	19.4	117.1	23.7	182.9	15.2
HSP72	14.5	36.8	65.1	21.2	47	18.9	73.5	6.9
HSP47	11.9	19.1	145.2	6.8	259.5	1.3	345.2	3.7
Fibrillin	10	28.3	64.4	5.4	73.3	16	95.6	6.3
Tropoelastin	17.6	7.5	188.2	5.1	338.2	2	391.2	1.8
Procollagen I	55.1	22.3	57.7	25.2	89.7	25	202.6	13.1
Procollagen III	9.9	42	7.7	19.4	22	25.2	113.2	14.4

Abbreviations: FRF, fractional radiofrequency; SEM, standard error of the mean; TNF- α , tumor necrosis factor α ; TGF- β 1, transforming growth factor β 1; MMP, matrix metalloproteinase; HSP, heat shock protein.

^aValues are shown as percentage control at the relevant time point. Zero days corresponds to immediately posttreatment.

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in vivo during treatment with a bipolar FRF system also has been developed, which may be employed to aid physicians in parameter selection to achieve improved efficacy and safety profiles, particularly because no consensus recommendations for treatment of patients with minimally invasive bipolar RF currently exist.²⁷

The relationship between subjective clinical improvement and changes in objective measures of mechanical skin properties was investigated by Willey and colleagues.²⁸ They compared elastometry measurements with clinical results after treatment of the lower face with bipolar FRF. At

3 months after therapy, elastometry measurements showed statistically significant improvement for pressure measurements ($P < .05$) but not retraction times ($P > .05$). Physician grading revealed statistically significant improvements of wrinkles and laxity ($P < .001$ for both) (Figure 3). Approximately 90% of treated patients were satisfied or very satisfied with the procedure at 3- and 6-month follow-up.²⁸

Fractional RF technology was compared with a surgical face-lift, which is considered the gold standard for treatment of skin laxity, in a blinded randomized study.²⁹ Participants who were treated with minimally

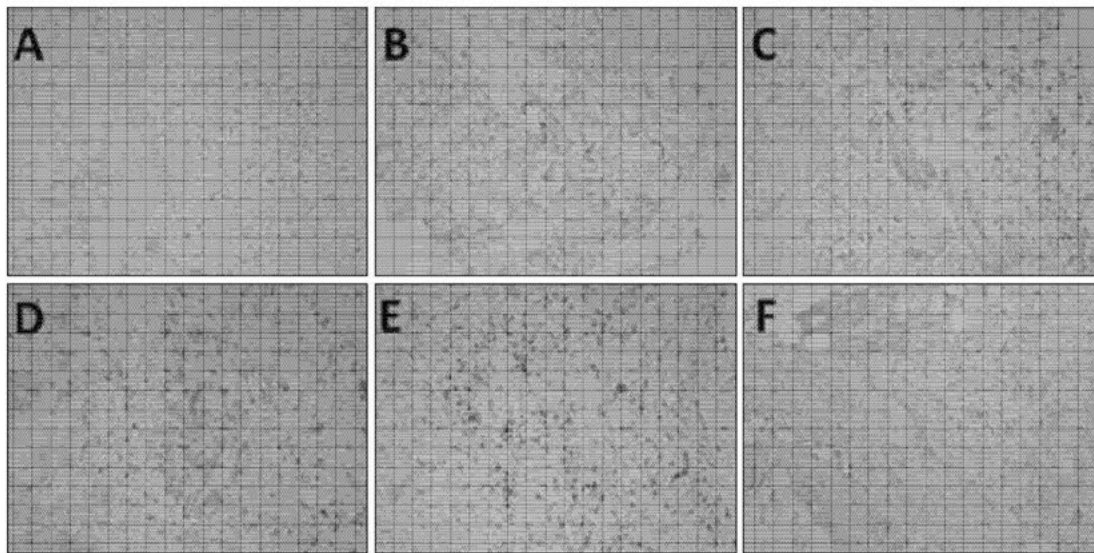


Figure 2. HSP47 (heat shock protein 47) response to fractional radiofrequency treatment. Human abdominal skin was stained with antihuman HSP47 antibody. At baseline (A) (original magnification $\times 4$) and immediately posttreatment (B) (original magnification $\times 4$), there was minimal HSP47 expression in the dermis. Increased HSP47 expression was first detected at day 2 (C) (original magnification $\times 4$), but unlike HSP72, remained elevated from day 14 onward (D-F) (original magnification $\times 4$ for all). At day 28 and 10 weeks posttreatment, HSP47 staining became diffuse throughout the dermis and was not restricted only to the peri-radiofrequency thermal zone regions. Reprinted with permission from Hantash et al.⁹

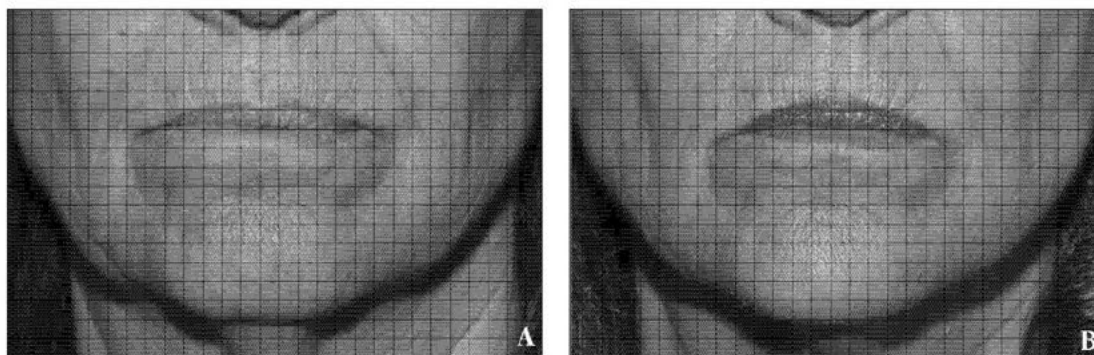


Figure 3. A patient at baseline (A) and 3 months following fractional radiofrequency treatment (B). The patient received bilateral treatment of the lower face with 25% to 30% skin coverage and lesion temperature of 68°C for 5 seconds. Reprinted with permission from Willey et al.²⁸

TABLE 4

Summary of Studies With FRF

Reference (Year)	No. of Participants	Study Type	Device (Manufacturer)	Parameters	Indication	Outcome	Side Effects
Hantash et al ⁸ (2009)	15	PCS	Renesis (Primaeva Medical, Inc)	1–25 s; 60–80°C	Healthy volunteers	Delivery of controlled heating to dermis; creation of RFTZ	Transient erythema and pinpoint bleeding
Hantash et al ⁹ (2009)	22	PCHS	Renesis (Primaeva Medical, Inc)	5 sessions; 4 s at 72°C	Healthy volunteers	Marked neolastogenesis and neocollagenesis	N/A
Willey et al ²⁸ (2010)	44	PCHS	Miratorne (Primaeva Medical, Inc)	3–5 s at 62–78°C	Fine wrinkles and facial laxity	96% (42/44) with improvement; In wrinkles, 91% (40/44) with improvement in laxity	None reported
Alexiades-Armenakas et al ²⁹ (2010)	15	RCT	Miratorne (Primaeva Medical, Inc)	3 s at 62°C; 5 s at 68–78°C	Skin laxity	16% mean improvement after FRF	Transient erythema and edema
Hruza et al ³⁰ (2009)	35	PCHS	eMatrix (Syneron Medical Ltd)	N/A	Skin laxity	Controlled creation of RFTZ; 49% (17/35) of participants with >40% improvement in skin texture	Pain and transient erythema
Ramesh et al ³¹ (2010)	30	PCS	eMatrix (Syneron Medical Ltd)	<5 sessions; 10–20 J	Acne scarring	>60% improvement in 4 participants; 35%–60% improvement in 18 participants; <35% improvement in 8 participants	None reported

Abbreviations: FRF, fractional radiofrequency; PCS, prospective clinical study; RFTZ, radiofrequency thermal zone; PCHS, prospective clinical and histologic study; N/A, not available; RCT, randomized controlled study.

invasive bipolar FRF showed 16% improvement in skin laxity over baseline as compared to 49% improvement in participants treated with a surgical face-lift. Participants treated with FRF returned to normal activities within 24 hours, while participants in the surgical face-lift

group returned to normal activities in 7 to 10 days. Participant satisfaction in the FRF treatment group was high, with 93% (14/15) of participants reporting they were satisfied or very satisfied and no participants dissatisfied with FRF.²⁹

TABLE 5

Novel Uses of Tripolar RF

Reference (Year)	No. of Participants	Study Type	RF Type	Parameters	Indication	Outcome	Side Effects
Kaplan and Gat ³² (2009)	12	PCHS	1 MHz	Mean, 7 treatments	Skin tightening and body shaping	49% increase in dermal thickness; focal thickening of collagen fibers	None reported
Manuskiatti et al ³³ (2009)	17	PCS	1 MHz	6 weekly treatments	Striae distensae	50% (17/34) of participants with >25% improvement	None reported
Manuskiatti et al ³⁴ (2009)	37	PCS	1 MHz	8 weekly treatments	Skin tightening and cellulite	3.5-cm mean abdominal circumference reduction; 1.7-cm mean thigh circumference reduction	None reported
Levenberg ³⁵ (2010)	37	PCS	1 MHz	Multiple treatments	Localized fat and facial skin tightening	3.6-cm mean circumference reduction (abdomen, buttocks, thighs); improvement of perioral and periorbital wrinkles	None reported
Boisnic et al ³⁶ (2010)	20	PCHS	1 MHz	Home treatment; 2–3 sessions weekly; 2–3 months	Skin laxity and fat reduction	2.4-cm mean thigh circumference reduction; no significant reduction in abdomen; 31% increased collagen synthesis	None reported

Abbreviations: RF, radiofrequency; PCHS, prospective clinical and histologic study; PCS, prospective clinical study.

The eMatrix device delivers nonhomogeneous fractional ablative energy using an array of multielectrode pins. Fractional RF has been demonstrated to induce improvement in skin texture and reduced wrinkles in both abdominal and facial skin, with greater than 40% improvement in skin texture achieved in approximately 49% (17/35) of participants. Other than pain and transient erythema, no adverse events were reported.³⁰ This FRF technology also appears to provide a safe and effective treatment option for acne scars.³¹ Table 4 summarizes studies on FRF.

TRIPOLAR RF

Tripolar RF expands on the bipolar configuration, employing 3 or more electrodes to deliver current to skin tissue. The TriPollar RF device (Regen, Pollogen Ltd) is able to simultaneously heat superficial and deep skin layers by delivering a focused current to the skin, delivering energy at a frequency of 1 MHz and a maximum power of 30 W, with no active cooling system needed. Several small trials have evaluated this technology, reporting clinical efficacy and a favorable side-effect profile (Table 5). In one study, 12 patients underwent an average of 7 weekly treatment sessions on various body areas, with subsequent histologic analysis revealing an increase in dermal thickness in treated areas due to collagen regeneration and remodeling and a focal shrinkage of fat cells.³²

The safety and efficacy of using the TriPollar RF device for the treatment of striae distensae was evaluated by a pilot study in which 50% (17/34) of participants reported greater than 25% improvement in their striae at 1-week follow-up, and a higher percentage were found to have improvement at 6 weeks posttreatment. No significant adverse events were reported.³³ TriPollar RF technology also has been applied to circumference reduction, cellulite treatment, and localized fat with some success.^{34,35}

OTHER DEVELOPMENTS

A novel RF device based on tripolar technology recently has been produced for at-home use (Pose, Ultragen) with a built-in automatic temperature sensor and relatively slow rate of heating to serve as guards against adverse events. An ex vivo study utilizing this device reported lipolytic activity and increased collagen synthesis in treated abdominal skin. Additionally, 20 participants completed a clinical protocol of at-home treatment, achieving significant circumference reduction of treated thighs ($P=.021$) and improved overall abdominal skin laxity.³⁶

Limitations in current RF methods, including the somewhat uncontrolled nature of monopolar RF and the somewhat superficial treatment level of some bipolar and

tripolar configurations, have been attributed to a lack of adaptation of delivered energy to differences in individual skin impedance. These perceived shortcomings recently were addressed by the development of a method for real-time impedance measurement during skin tightening treatments. The EndyMed Pro system (Eclipse Aesthetics, LLC) allows continuous measurement of skin impedance and delivery of continuous target energy to skin independent of changes in impedance. Harth and Lischinsky³⁷ reported that the real-time customization of energy according to skin impedance allows a more accurate and safe method of skin tightening with consistent and predictable outcomes. Thirty patients with facial skin aging were treated with this device with results that were reported as good or better in 86.7% (26/30) of cases at the 3-month follow-up.³⁷

CONCLUSION

Radiofrequency technology continues to advance rapidly, providing dermatologists with an expanding array of skin rejuvenation techniques that result in few adverse effects and minimal downtime for patients. Radiofrequency treatments allow physicians to augment targeted tissue layers while also sparing melanocytes and the cutaneous surface, thereby preventing dyspigmentation and delayed wound healing. Most recent studies that evaluate novel implementations of RF technology are noncomparative clinical trials with subjective outcome measures and should be viewed with a healthy skepticism. Nevertheless, RF technology is an exciting and expanding sector of cosmetic dermatology. Future developments likely will continue to enhance the therapeutic index of RF by tailoring treatment to the individual patient, combining RF with other treatment modalities, and exploring and expanding indications for therapy.

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