New-Generation Radiofrequency Technology

Nils Krueger, PhD; Neil S. Sadick, MD

Radiofrequency (RF) technology has become a standard treatment in aesthetic medicine with many indications due to its versatility, efficacy, and safety. It is used worldwide for cellulite reduction; acne scar revision; and treatment of hypertrophic scars and keloids, rosacea, and inflammatory acne in all skin types. However, the most common indication for RF technology is the nonablative tightening of tissue to improve skin laxity and reduce wrinkles. Radiofrequency devices are classified as unipolar, bipolar, or multipolar depending on the number of electrodes used. Additional modalities include fractional RF; sublative RF; phase-controlled RF; and combination RF therapies that apply light, massage, or pulsed electromagnetic fields (PEMFs). This article reviews studies and case series on these devices. Radiofrequency technology for aesthetic medicine has seen rapid advancements since it was used for skin tightening in 2003. Future developments will continue to keep RF technology at the forefront of the dermatologist's armamentarium for skin tightening and rejuvenation.

Cutis. 2013;91:39-46.

Radiofrequency (RF) energy is a type of electromagnetic wave emitted and absorbed by charged particles that will exhibit wavelike behavior. It oscillates in the range of 3 kHz to 300 GHz, which corresponds to the frequency of radio waves. Electric currents oscillating at these frequencies have properties that are not shared by direct currents or alternating currents of lower frequencies. Radiofrequency energy can be transferred from an electric field to charged particles in the target tissue via 3 mechanisms: the orientation of electric dipoles that already exist in the atoms and molecules in the tissue, polarization of atoms and molecules to produce dipole moments, or displacement of conduction electrons and ions in the tissue. In all 3 mechanisms, heat is generated by the movement of particles in response to an electric field respectively by the collisions between the transmission charges and immobile particles.[1]

In 2003, Ruiz-Esparza and Gomez[2] described the use of RF for skin tightening. The technique is based on volumetric heating of dermal tissue to initiate denaturation of collagen accompanied by an immediate contraction of the fibers and subsequent neocollagenesis.[3,4] The shrinkage of collagen is not dependent on reaching a specific temperature but rather is determined by combining time and temperature.[5] For example, longer passes with target temperatures of 60°C to 65°C as well as shorter millisecond passes with target temperatures of 85°C can both be effective.[6] Radiofrequency-based systems are appropriate for treatment of all skin types, as heat generation is not diminished by tissue diffraction or absorption by epidermal melanin.[7,8]

In aesthetic medicine, RF technology has become a standard treatment with many indications due to its versatility, efficacy, and safety. It is used worldwide for cellulite reduction[9]; acne scar revision[10]; and treatment of hypertrophic scars and keloids,[11] rosacea,[12] and inflammatory acne in all skin types.[13] However, the most common indication for RF technology is the nonablative tightening of tissue to improve skin laxity and reduce wrinkles.[14,15]

Radiofrequency devices can be classified by the geometry of their electrodes, as this factor has a determining influence on the distribution of the electrical current. The different systems are defined as

Dr. Krueger is from the Division of Cosmetic Science, University of Hamburg, Germany. Dr. Sadick is from the Department of Dermatology, Weill Cornell Medical College, New York, New York.
Dr. Krueger reports no conflict of interest. Dr. Sadick is a consultant for and received honoraria from Solta Medical; received research grants from Syneron Medical Ltd; and owns stock in, is a consultant for, and received research grants from Venus Concept.
Correspondence: Neil S. Sadick, MD, 911 Park Ave, Ste 1A, New York, NY 10075 (nssderm@sadickdermatology.com).

unipolar, bipolar, or multipolar devices depending on the number of electrodes used. Additional modalities include fractional RF; sublative RF; phase-controlled RF; and combination technologies that add light, massage, or pulsed electromagnetic fields (PEMFs) (Table). This article reviews studies and case series on these devices.

Unipolar RF

Although unipolar RF was the first RF system used in aesthetic dermatology, the technology is far from being outdated. The term *unipolar* can be misleading, as the energy is applied to the skin using a single electrode tip but is conducted to a grounding pad under the patient's body that serves as the opposite pole. This setting leads to a concentration of electrical energy near the tip of the active electrode and a rapid decrease in energy with distance. Sufficient active cooling of the skin surface is necessary to protect the dermis from overheating and subsequent damage. In general, unipolar RF has been shown in several uncontrolled and controlled trials to be efficient for the tightening of facial and nonfacial skin including periorbital wrinkles,[16] cellulite,[9] and facial rejuvenation.[17]

Innovations in unipolar RF aim to decrease pain and discomfort that often is associated with treatment. These effects can be reduced by improving treatment tips and software routines according to findings in pain research. New software routines create a pattern of short RF pulses and cooling bursts, which is confusing to the neural system and therefore reduces pain. This effect is used in transcutaneous electrical nerve stimulation, which is utilized in pain therapy.[33] Supporting this approach is a handpiece that applies vibration to the treatment area to inhibit pain impulses. Based on Melzack and Wall's[34] theory of pain, large nerve fibers that transport a nonpain signal can overrule smaller nerve fibers that carry pain impulses. The new treatment tips also use a thin polyimide film frame to cover a portion of the electrode, resulting in better heat distribution and uniformity and allowing more tissue to be heated to higher temperatures to deliver better results.

Bipolar RF

Radiofrequency devices with a bipolar configuration use 2 electrodes that are both part of the treatment tip; therefore, an additional grounding pad is not necessary. The RF current in bipolar systems has a controlled distribution inside the tissue, as it is limited to the volume of tissue between the 2 electrodes. The penetration depth is equal to half the distance between the electrodes. The effects achieved using bipolar RF and its indications are similar to unipolar RF,[18] but due to the reduced penetration, bipolar RF is less painful.[19]

An important advancement has been multifrequency technology that allows for independent control of the heating depth through the application of 3 separate RF frequencies for deep (0.8 MHz), medium deep (1.7 MHz), and shallow heating (2.45 MHz). Together the 3 frequencies can be used in a single pulse for consistent volumetric tissue heating. With these different frequencies, it is possible to individually control the heating depth depending on the patient and the intended treatment indication. Belenky et al[19] demonstrated that the frequencies of 0.8 and 1.7 MHz are useful for the lower face and perioral regions, while the forehead and cheekbone areas were best treated with a frequency of 2.45 MHz. The combination of all 3 frequencies in a single pulse was the best choice for body areas.[19]

Although RF treatments in aesthetic medicine usually are known for being nonablative, a new technology breaks this rule by creating ablative microspots that are similar to fractional photothermolytic laser irradiation. In contrast with light-based modalities, fractional RF is a safe and effective treatment in patients with skin of color. The fractional RF tip consists of parallel rows of bipolar-arranged electrode pins, forming an array of 64 positively and negatively charged electrodes. These electrode pins form a closed circuit through the irradiated skin, delivering 1 MHz of conducted RF current to the skin. Pulses can be emitted in different programs, giving the operator control of the depth and intensity of dermal heating with minimal epidermal effects. Several case series with 80 patients indicate that this technology is especially useful for the treatment of acne scars in all skin types,[10,21,23,32] but it also is efficient for the treatment of wrinkles.[20,22] To be generally accepted, however, results would have to be confirmed in double-blind randomized clinical trials.

Another development is the use of sublative fractional bipolar RF. This new minimally invasive approach heats up the deep dermis from within using microneedle electrode arrays. Bipolar RF energy is delivered between the microneedle pairs at a depth of 1.5 mm so that the thermal lesions are fractionally generated directly within the deep dermis in a volume defined by the geometry of the microneedle electrode pairs. Sensors in the tips of the microneedle electrodes measure the surrounding temperature in real time, thereby allowing precise delivery of modulated energy. A randomized controlled trial by Alexiades-Armenakas et al[24] showed that sublative fractional bipolar RF is effective for the treatment of facial skin laxity. Uncontrolled studies by Cho et al[25] and Lee et al[13] further indicated that the device could be

Selection of Studies and Case Series Utilizing RF Technology

Reference (Year)	Study Design	No. of Participants	Use	Notable Findings
Unipolar RF				
Fitzpatrick et al[16] (2003)	Multicenter, uncontrolled, investigator blind	86 (119 total treatment areas)	Periorbital tissue tightening	Improvement in 83.2% (99/119) of treated periorbital areas
Ruiz-Esparza et al[12] (2003)	Case series	3	Telangiectatic and papular rosacea	Improvement in papular lesions
Meshkinpour et al[11] (2005)	Controlled clinical and histologic evaluation	10	Hypertrophic and keloid scars, and collagen changes	Increased collagen production but no significant clinical improvements
Alexiades-Armenakas et al[9] (2008)	Randomized, single blind, split design, controlled	10	Cellulite	Improvement in dimple density, distribution, and depth
el-Domyati et al[17] (2011)	Uncontrolled histologic evaluation	6	Photoaging	Increases in types I and III collagen as well as newly synthesized collagen, and decrease in elastin
Unipolar/Bipolar RF				
Alexiades-Armenakas et al[18] (2008)	Randomized, investigator blinded, split face	10	Rhytides and skin laxity	Minimal clinical efficacy with a trend toward improvement in rhytides and skin laxity
Multifrequency Bipolar RF				
Belenky et al[19] (2012)	Uncontrolled	27 (cellulite and body shaping), 16 (skin tightening)	Cellulite and skin tightening	Average cellulite improvement of 55%, improvement of skin appearance from skin tightening procedure in 81% of patients (13/16)
Fractional Bipolar RF				
Hruza et al[20] (2009)	Uncontrolled	35	Skin rejuvenation and wrinkles	Improvement in skin texture and reduction of wrinkles
Ramesh et al[21] (2010)	Uncontrolled	30	Acne scars	20%–70% improvement of acne scars 6 mo after treatment
Lee et al[22] (2011)	Uncontrolled	26	Photoaged skin	Significant improvement of smoothness and tightness, brightness, and overall appearance (P=.049, P=.007, and P=.001, respectively)

TABLE CONTINUED ON PAGE 42

Table (continued)

Reference (Year)	Study Design	No. of Participants	Use	Notable Findings
Fractional Bipolar RF (continued)				
Taub and Garretson[23] (2011)	Uncontrolled	20	Acne scars	Improvement 1 mo after 3 treatments, persisted for at least 12 wk after the fifth treatment
Gold and Biron[10] (2012)	Uncontrolled	15	Acne scars	Significant reduction of scar severity (P=.0019)
Sublative Fractional Bipolar RF				
Alexiades-Armenakas et al[24] (2010)	Investigator blinded, randomized, controlled	15	Skin laxity	Improvement in skin laxity with RF but less than surgical facelift
Cho et al[25] (2012)	Uncontrolled	30	Acne scars and large facial pores	Improvement of acne scars and large pores in >70% of patients
Lee et al[13] (2012)	Uncontrolled, investigator blinded	18	Inflammatory acne vulgaris	Improvement of inflammatory acne lesions in 16 participants
Multipolar Fractional RF				
Sadick et al[14] (2011)	Uncontrolled, investigator blinded	30	Wrinkles and depressed acne scars	Reduction in the depth of wrinkles and acne scars
Phase-Controlled Multisource RF				
Elman and Harth[26] (2011)	Uncontrolled, investigator blinded	30	Wrinkles, skin laxity, and acne scars	Moderate to good improvement in most participants
	Uncontrolled, investigator blinded	23	Body contouring	Improvement in skin laxity, cellulite, and stretch marks
Royo de la Torre et al[27] (2011)	Unblinded, controlled	33	Skin laxity	Greater degree of clinical improvement in participants with surface temperature increases >11.5ºC at the end of the procedure and remaining >4.5ºC 20 min later
Bipolar RF Plus Diode Laser				
Sadick and Trelles[28] (2005)	Uncontrolled	23	Wrinkles and skin texture	Noticeable improvement in wrinkles, skin smoothness, and texture

Reference (Year)	Study Design	No. of Participants	Use	Notable Findings
Bipolar RF Plus ELOS				
Sadick et al[29] (2005)	Uncontrolled, investigator blinded	108 (540 total treatments administered)	Rosacea, telangiectasia, dyschromia, hyperpigmentation, photodamage, wrinkles, skin texture, and laxity	Improvement in all parameters
Bipolar RF Plus IR and Massage				
Romero et al[30] (2008)	Randomized, controlled, investigator blinded	10	Cellulite	Improvement in overall cellulite appearance and skin condition
Hexsel et al[31] (2011)	Uncontrolled	9	Cellulite	Significant improvement of cellulite on buttocks (left, $P=.002$; right, $P=.038$)
Fractional Laser and RF				
Peterson et al[32] (2011)	Uncontrolled	15	Acne scars and skin texture	Significant improvement in acne scars and skin texture (both $P<.001$)

Abbreviations: RF, radiofrequency; ELOS, electro-optical synergy; IR, infrared light.

effective for the treatment of inflammatory acne, acne scars, and large facial pores. Transient mild to moderate erythema, swelling, and ecchymosis, which all resolve in 5 to 10 days, are common side effects of this treatment. Residual yellow-brown discoloration that resolves 2 to 3 weeks postoperatively is an uncommon side effect.[24] Blisters can occur when treatments are performed at superficial depths.[35]

Multipolar RF

Unlike unipolar or bipolar RF, multipolar systems are based on 3 or more electrodes. While 1 electrode acts as a positive pole, the others act as negative poles. The current that flows through the positive pole is the sum of all the currents flowing through each of the negative poles. To avoid tissue overheating at the positive pole, a sequence of electrical modulation is applied so that each electrode in turn acts as the positive pole. Although the penetration of multipolar RF usually is superficial, the treatment results in volumetric dermal heating with no active cooling needed and is virtually pain free.[26,27]

A new multipolar RF technology employs the use of phase-controlled multisource RF. This approach is based on an array of several RF sources, controlling the phase of current flowing between each pair. The multiple electrical fields that are created repel each other, leading to the precise delivery of energy in different depths. Because adjacent electrodes possess an identical polarity, no current is created between these electrodes on the skin surface. This approach confines the emission of focused and contained energy to a depth of up to 11 mm and makes it possible to apply concentrated heat to the papillary dermis, reticular dermis, and fascia superficialis.[27] An unblinded controlled study of 33 patients by Royo de la Torre et al[27] showed that 6 treatments with phase-controlled multisource RF can substantially improve skin laxity. In another investigator-blinded uncontrolled study of 23 patients, Elman and Harth[26] noted moderate to

good improvement of stretch marks and cellulite in areas treated with this technology.

Combination Therapy

Several aesthetic devices combine RF with 1 or more additional forms of energy to achieve synergistic effects. The most common approach is the combination of RF with optical energy generated by lasers or infrared light sources. In these combinations, selective photothermolysis is used to preheat and thereby alter the impedance of the target tissue to increase its susceptibility to a subsequent RF pulse.[36] This combination allows the usage of lower energies for both modalities, thereby increasing the safety of the procedure and reducing discomfort and complications.[28,29] Another common combination is the use of RF with additional mechanical tissue manipulation from a vacuum or rollers, an approach that often is chosen to improve microcirculation and generate active tissue reaction for cellulite treatment or circumferential reduction. A small investigator-blinded, randomized, controlled trial (N=10) by Romero et al[30] showed improvements in overall cellulite appearance and skin condition at the treatment site compared to baseline in 100% of participants. Another uncontrolled study of 9 patients by Hexsel et al[31] indicated an improvement of cellulite on the buttocks but not on the thighs after treatment with this modality.

A new treatment approach is the combination of multipolar RF with PEMF to increase efficacy and maintain the superior safety and pain profiles of multipolar RF. In clinical studies, the therapeutic effects of PEMF have been shown over time to be safe and effective for treatment of nonhealing bone fractures.[37,38] Further studies of PEMF also show a positive impact on angiogenesis,[39] a process that is critical for successful healing of various tissues, and a stimulating effect on collagen synthesis.[40,41] Because the mechanisms of action and target structures of multipolar RF and PEMF are different, their combination is complementary. The stimulation of neovascularity, fibroblast proliferation, and collagen neosynthesis by PEMF synergizes with the denaturation of existing collagen by RF accompanied by an immediate contraction of the fibers and a delayed synthesis of collagen and elastin fibers. Furthermore, the nonthermal mechanism of PEMF does not interfere with the thermal mechanism of the multipolar RF. A clinical study has shown that the combination of multipolar RF with PEMF is a safe, effective, and painless approach to treat facial rhytides.[42] Further studies are necessary to evaluate the applicability of this technology for skin tightening of nonfacial areas or other indications such as cellulite or stretch marks.

Comment

Since it was introduced in aesthetic medicine, RF technology has been used for many indications, including skin tightening, wrinkle reduction, and treatment of cellulite and acne scars. Nonablative RF technology proved itself in daily practice as a safe and efficient way to stimulate collagen contraction and neocollagenesis without integumentary injury. The lack of chromophore dependence makes nonablative RF a versatile treatment option for every skin type; however, despite its positive role in clinical practice, RF technology remains a field that has been insufficiently researched. Findings often are based on uncontrolled case series with limited validity. More randomized, double-blind, controlled studies are needed to increase the level of evidence and explain the high variability of results often seen in daily practice.

As RF technology continues to rapidly advance, physicians and patients can choose from a sophisticated selection of treatment techniques to improve skin appearance. Smart innovations such as vibrating handpieces and optimized software programs that imitate transcutaneous electrical nerve stimulation have the potential to decrease the pain and discomfort that often is associated with RF treatments. Other innovations are intended to optimize the energy transfer and distribution inside the tissue or implement an additional form of energy to increase efficacy and optimize safety. Some innovations have included new treatment tips that ensure better heat distribution and uniformity; multifrequency and phase-controlled devices that allow for independent control of tissue heating; and the combination of multipolar RF with PEMF, which creates a synergistic effect. These advances along with future developments will continue to keep RF technology at the forefront of the dermatologist's armamentarium for skin tightening and rejuvenation; however, more randomized controlled trials are needed to increase the knowledge about this relatively new and rapidly developing technology.

REFERENCES

1. Stuchly M, Stuchly S. Electrical properties of biological substances. In: Gandhi OP, ed. *Biological Effects and Medical Applications of Electromagnetic Energy*. Upper Saddle River, NJ: Prentice Hall; 1990:76-112.
2. Ruiz-Esparza J, Gomez JB. The medical face lift: a noninvasive, nonsurgical approach to tissue tightening in facial skin using nonablative radiofrequency. *Dermatol Surg*. 2003;29:325-332.
3. Zelickson BD, Kist D, Bernstein E, et al. Histological and ultrastructural evaluation of the effects of a radiofrequency-based nonablative dermal remodeling device: a pilot study. *Arch Dermatol*. 2004;140:204-209.

4. Drew PJ, Watkins A, McGregor AD, et al. The effects of temperature and time on thermal bond strength in tendons. *Lasers Med Sci*. 2001;16:291-298.
5. Atiyeh BS, Dibo SA. Nonsurgical nonablative treatment of aging skin: radiofrequency technologies between aggressive marketing and evidence-based efficacy [published online ahead of print May 13, 2009]. *Aesthetic Plast Surg*. 2009;33:283-294.
6. Ruiz-Esparza J. Near [corrected] painless, nonablative, immediate skin contraction induced by low-fluence irradiation with new infrared device: a report of 25 patients [published correction appears in *Dermatol Surg*. 2006;32:preceding 773]. *Dermatol Surg*. 2006;32: 601-610.
7. Alster TS, Lupton JR. Nonablative cutaneous remodeling using radiofrequency devices. *Clin Dermatol*. 2007;25: 487-491.
8. Man J, Goldberg DJ. Safety and efficacy of fractional bipolar radiofrequency treatment in Fitzpatrick skin types V-VI. *J Cosmet Laser Ther*. 2012;14:179-183.
9. Alexiades-Armenakas M, Dover JS, Arndt KA. Unipolar radiofrequency treatment to improve the appearance of cellulite. *J Cosmet Laser Ther*. 2008;10:148-153.
10. Gold MH, Biron JA. Treatment of acne scars by fractional bipolar radiofrequency energy [published online ahead of print May 30, 2012]. *J Cosmet Laser Ther*. 2012;14: 172-178.
11. Meshkinpour A, Ghasri P, Pope K, et al. Treatment of hypertrophic scars and keloids with a radiofrequency device: a study of collagen effects. *Lasers Surg Med*. 2005;37:343-349.
12. Ruiz-Esparza J, Barba Gomez JM, Rosales Berber I. A possible role for non-ablative radiofrequency in the treatment of rosacea. *J Drugs Dermatol*. 2003;2:621-623.
13. Lee SJ, Goo JW, Shin J, et al. Use of fractionated microneedle radiofrequency for the treatment of inflammatory acne vulgaris in 18 Korean patients [published online ahead of print December 30, 2011]. *Dermatol Surg*. 2012;38:400-405.
14. Sadick NS, Sato M, Palmisano D, et al. In vivo animal histology and clinical evaluation of multisource fractional radiofrequency skin resurfacing (FSR) applicator. *J Cosmet Laser Ther*. 2011;13:204-209.
15. Javate RM, Cruz RT Jr, Khan J, et al. Nonablative 4-MHz dual radiofrequency wand rejuvenation treatment for periorbital rhytides and midface laxity. *Ophthal Plast Reconstr Surg*. 2011;27:180-185.
16. Fitzpatrick R, Geronemus R, Goldberg D, et al. Multicenter study of noninvasive radiofrequency for periorbital tissue tightening. *Lasers Surg Med*. 2003;33:232-242.
17. el-Domyati M, el-Ammawi TS, Medhat W, et al. Radiofrequency facial rejuvenation: evidence-based effect. *J Am Acad Dermatol*. 2011;64:524-535.
18. Alexiades-Armenakas M, Dover JS, Arndt KA. Unipolar versus bipolar radiofrequency treatment of rhytides and laxity using a mobile painless delivery method. *Lasers Surg Med*. 2008;40:446-453.
19. Belenky I, Margulis A, Elman M, et al. Exploring channeling optimized radiofrequency energy: a review of radiofrequency history and applications in esthetic fields [published online ahead of print February 29, 2012]. *Adv Ther*. 2012;29:249-266.
20. Hruza G, Taub AF, Collier SL, et al. Skin rejuvenation and wrinkle reduction using a fractional radiofrequency system. *J Drugs Dermatol*. 2009;8:259-265.
21. Ramesh M, Gopal M, Kumar S, et al. Novel technology in the treatment of acne scars: the matrix-tunable radiofrequency technology. *J Cutan Aesthet Surg*. 2010;3:97-101.
22. Lee HS, Lee DH, Won CH, et al. Fractional rejuvenation using a novel bipolar radiofrequency system in Asian skin [published online ahead of print August 29, 2011]. *Dermatol Surg*. 2011;37:1611-1619.
23. Taub AF, Garretson CB. Treatment of acne scars of skin types II to V by sublative fractional bipolar radiofrequency and bipolar radiofrequency combined with diode laser. *J Clin Aesthet Dermatol*. 2011;4:18-27.
24. Alexiades-Armenakas M, Rosenberg D, Renton B, et al. Blinded, randomized, quantitative grading comparison of minimally invasive, fractional radiofrequency and surgical face-lift to treat skin laxity. *Arch Dermatol*. 2010;146: 396-405.
25. Cho SI, Chung BY, Choi MG, et al. Evaluation of the clinical efficacy of fractional radiofrequency microneedle treatment in acne scars and large facial pores [published online ahead of print April 9, 2012]. *Dermatol Surg*. 2012;38(7, pt 1):1017-1024.
26. Elman M, Harth Y. Novel multi-source phase-controlled radiofrequency technology for non-ablative and micro-ablative treatment of wrinkles, lax skin and acne scars. *Laser Ther*. 2011;20:139-144.
27. Royo de la Torre J, Moreno-Moraga J, Muñoz E, et al. Multisource, phase-controlled radiofrequency for treatment of skin laxity: correlation between clinical and in-vivo confocal microscopy results and real-time thermal changes. *J Clin Aesthet Dermatol*. 2011;4:28-35.
28. Sadick NS, Trelles MA. Nonablative wrinkle treatment of the face and neck using a combined diode laser and radiofrequency technology. *Dermatol Surg*. 2005;31: 1695-1699.
29. Sadick NS, Alexiades-Armenakas M, Bitter P Jr, et al. Enhanced full-face skin rejuvenation using synchronous intense pulsed optical and conducted bipolar radiofrequency energy (ELOS): introducing selective radiophotothermolysis. *J Drugs Dermatol*. 2005;4:181-186.
30. Romero C, Caballero N, Herrero M, et al. Effects of cellulite treatment with RF, IR light, mechanical massage and suction treating one buttock with the contralateral as a control. *J Cosmet Laser Ther*. 2008;10:193-201.
31. Hexsel DM, Siega C, Schilling-Souza J, et al. A bipolar radiofrequency, infrared, vacuum and mechanical massage

device for treatment of cellulite: a pilot study. *J Cosmet Laser Ther*. 2011;13:297-302.
32. Peterson JD, Palm MD, Kiripolsky MG, et al. Evaluation of the effect of fractional laser with radiofrequency and fractionated radiofrequency on the improvement of acne scars [published online ahead of print August 11, 2011]. *Dermatol Surg*. 2011;37:1260-1267.
33. Kocyigit F, Akalin E, Gezer NS, et al. Functional magnetic resonance imaging of the effects of low-frequency transcutaneous electrical nerve stimulation on central pain modulation: a double-blind, placebo-controlled trial. *Clin J Pain*. 2012;28:581-588.
34. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150:971-979.
35. Hantash BM, Renton B, Berkowitz RL, et al. Pilot clinical study of a novel minimally invasive bipolar microneedle radiofrequency device. *Lasers Surg Med*. 2009;41:87-95.
36. Elsaie ML, Choudhary S, Leiva A, et al. Nonablative radiofrequency for skin rejuvenation [published online ahead of print April 2, 2010]. *Dermatol Surg*. 2010;36:577-589.
37. Sharrard WJ. A double-blind trial of pulsed electromagnetic fields for delayed union of tibial fractures. *J Bone Joint Surg Br*. 1990;72:347-355.
38. Ryaby JT. Clinical effects of electromagnetic and electric fields on fracture healing. *Clin Orthop Relat Res*. 1998;355(suppl):S205-S215.
39. Tepper OM, Callaghan MJ, Chang EI, et al. Electromagnetic fields increase in vitro and in vivo angiogenesis through endothelial release of FGF-2 [published online ahead of print June 18, 2004]. *FASEB J*. 2004;18:1231-1233.
40. Murray JC, Farndale RW. Modulation of collagen production in cultured fibroblasts by a low-frequency, pulsed magnetic field. *Biochim Biophys Acta*. 1985;838:98-105.
41. Soda A, Ikehara T, Kinouchi Y, et al. Effect of exposure to an extremely low frequency-electromagnetic field on the cellular collagen with respect to signaling pathways in osteoblast-like cells. *J Med Invest*. 2008;55:267-278.
42. Krueger N, Levy H, Sadick NS. Safety and efficacy of a new device combining radiofrequency and low-frequency pulsed electromagnetic fields for the treatment of facial rhytides. *J Drugs Dermatol*. 2012;11:1306-1309.