Current Otorhinolaryngology Reports (2021) 9:422–435
https://doi.org/10.1007/s40136-021-00371-5

New Technologies in Skin Tightening

C. Helen Malone[1] · Nicole Walters[2] · Rachel Stroh[2] · Gilly Munavalli[3]

Accepted: 27 September 2021 / Published online: 11 October 2021

Abstract

Purpose of Review The skin laxity component of facial aging has been traditionally addressed with surgical intervention. However, demand for alternative treatment options with less associated risk, scarring, downtime, and cost have driven advances in non-surgical tightening techniques. This article explores the recent advances in these non-surgical technologies for skin tightening including microcoring, hydroxyapatite fillers, and energy-based devices (lasers, ultrasound, radiofrequency, and plasma).

Recent Findings Advances in non-surgical skin-tightening devices allow for effective skin tightening. Although fully ablative laser resurfacing devices are often considered the gold standard for non-surgical rejuvenation, important advances in this technology include fractionated energy delivery to decrease risk and shorten treatment recovery. In addition, studies have shown that optimal treatment temperatures for skin tightening are lower than those achieved with CO2, favoring radiofrequency devices as a more optimal choice for tissue tightening in terms of treatment results, skin types amenable to treatment, risks, and downtime. Ultrasound technology has the unique advantage of allowing for real-time tissue assessment and tailored heat delivery. Microcoring and hydroxyapatite treatment stimulate skin tightening without heat production. Advantages and disadvantages of various non-surgical skin tightening are reviewed and summarized in this article.

Summary A wide array of non-surgical skin-tightening techniques provide an attractive alternative to surgical intervention for modern cosmetic patients.

Keywords Skin Tightening · Radiofrequency · Ultrasound · Lasers · Plasma · Hydroxyapatite · Microcoring

Introduction

Halting signs of aging has been an elusive goal for generations. Cutaneous signs of aging such as skin laxity and rhytids are exacerbated both by intrinsic genetic factors, and extrinsic environmental factors including chronic ultraviolet radiation exposure, smoking, diet, and air pollution [1–3, 4•]. Until recently, non-surgical antiaging interventions were unable to achieve significant tissue tightening and were limited to treatment of telangiectasia, mild to moderate rhytids, dyschromia, and epidermal growths. Although surgical intervention remains the gold standard for skin tightening, disadvantages include prolonged downtime, potential surgical complications, cost, and scarring [2, 3, 4•, 5]. Newer non-invasive or minimally invasive techniques can achieve mild to moderate laxity improvement and improve the quality of the skin with less downtime and risk compared to traditional surgical intervention.

Non-surgical skin-tightening techniques include microcoring, hydroxyapatite fillers, and energy-based devices (lasers, ultrasound, radiofrequency, and plasma) [1, 4•, 6]. These non-invasive or minimally invasive techniques share the common aim of improving skin laxity by harnessing the skin's natural wound-healing mechanisms to produce collagen, elastin, and hyaluronic acid [5]. Many

This article is part of the Topical collection on *Facial Plastics: Facial Skin Rejuvenation*

✉ C. Helen Malone
chelenmalonemd@gmail.com

Nicole Walters
Nicole.walters@gmail.edu

Rachel Stroh
Rachel.stroh@bcm.edu

Gilly Munavalli
gmunavalli@carolinaskin.com

1 Cary Skin Center, Cary, NC, USA

2 Baylor College of Medicine, Houston, TX, USA

3 Dermatology, Laser, & Vein Specialists of the Carolinas, Charlotte, NC, USA

patients are willing to compromise on more dramatic results achieved with surgery in favor of a more "natural" approach with lower cost, lower risks, shorter downtime, and minimal potential for permanent side-effects [2, 4•]. In this review, we will discuss the recent developments in non-invasive or minimally invasive skin-tightening techniques (Tables 1 and 2).

Energy-Based Tightening Techniques

Lasers

Mechanism Lasers were first employed for skin tightening and rejuvenation in 1983 [7]. Lasers typically achieve skin tightening by heating the dermis using water as the target chromophore [7, 8]. Heat triggers immediate contraction of collagen fibers and induces delayed biochemical remodeling and neocollagenesis associated with wound healing in the following 3 to 6 months [7–9]. Laser therapy for skin rejuvenation can be categorized into ablative and non-ablative techniques.

Variations Ablative Lasers Ablative CO2 lasers remain the gold standard in non-surgical skin-tightening of photodamaged skin and are characterized by heating the skin to 100 °C [8, 10, 11•]. At this high temperature, the entire epidermis and portions of the underlying dermis are vaporized. The heat partially denatures collagen fibers, leading to contraction and thickening during healing, which creates observable tightening of the skin [8, 10]. Dramatic facial rejuvenation and skin tightening can be achieved with ablative laser resurfacing as seen in Fig. 1. Ablative lasers can be further subcategorized into full-field ablation and fractional ablation.

Full-field ablation resurfaces the skin by removing the entire epidermis and portions of the dermis within the treatment area, and the depth of its penetration is determined by the energy level of the laser employed [7]. While traditional full-field ablation can see benefits in a single treatment session, it puts patients at risk for bleeding, infection, pain, scarring, significant downtime for re-epithelialization, and delayed onset hypopigmentation in the 6 to 12 months following the procedure [7, 8, 10, 12]. Ablative lasers, such as CO2 lasers and Er:YAG lasers, must be used with caution in Fitzpatrick skin types III to VI. Fitzpatrick skin types III and IV have a significantly higher risk of post-inflammatory hyperpigmentation or hypopigmentation, which occurs in 55.5% of this patient population [3]. The risk of dyspigmentation is even higher in Fitzpatrick skin types V and VI, so extreme caution and experience are required [3, 7].

Fractional Ablation

Fractional ablation results in skin tightening by using thermal energy to remove microscopic channels of the epidermis and dermis, while leaving adjacent areas of skin intact [7–10, 11•]. These untreated areas serve as reservoirs of fibroblasts to help accelerate wound healing, and to decrease the risk of scarring even with deeper penetration into the dermis. While fractional ablation achieves more modest results and often requires multiple treatments, it also confers a shorter downtime and lower risk of complications such as scarring when compared to traditional ablation [7–10]. Fractional ablation also spares epidermal melanocytes, which prevents delayed-onset hypopigmentation [8]. Thus, fractional ablation is preferred over traditional ablation in Fitzpatrick skin types IV to VI.

Non-Ablative Lasers

Non-ablative lasers, in contrast to ablative lasers, do not vaporize tissue and only heat the skin to about 70 °C. Non-ablative lasers create zones of partial collagen injury [7, 10]. Epidermal sparing can be achieved through adjustments to laser pulse duration, use of wavelengths of light that are poorly absorbed by melanin, and concomitant application of epidermal cooling with cold air, cryogen, or contact cooling [7, 10, 13]. Non-ablative lasers require more treatments and provide minimal (if any) skin laxity improvement when compared to ablative lasers. However, non-ablative lasers have less downtime, fewer adverse effects, and a better safety profile [7, 10].

Combined Approaches

Approaches combining ablative and non-ablative lasers have also been developed as tools for skin tightening. Combined ablative and non-ablative fractional laser treatment allows for more significant skin tightening than non-ablative lasers alone, while maintaining less downtime than ablative lasers. This combined method may require multiple treatments for significant results [7]. In addition, combination and layered laser treatments also allow a user to address multiple aspects of skin aging, including telangiectasia, actinic damage, dyschromia, rhytids, and skin laxity simultaneously without affecting overall downtime. Although this is an exciting advance in the field of cosmetic rejuvenation, a full discussion of combination laser treatment is outside the scope of this paper.

Table 1 A summary of radiofrequency mechanisms, advantages, and disadvantages

Modality	Variations	Mechanism	Advantages	Disadvantages
Monopolar radiofrequency	**Monoterminal**	Current is delivered using one electrode on the skin, and energy disperses throughout the environment [28]	Depth of penetration is greater than bipolar counterparts [12, 31]	High voltage and low current system [28]. It creates less skin tightening than its biterminal counterpart
	Biterminal	Current is delivered using one electrode on the skin and a grounding pad on the back or leg [4•, 12, 31]	Low voltage and high current system [4•, 12, 31]. It creates greater skin tightening than its monoterminal counterpart. Depth of penetration is greater than bipolar counterparts [12, 31]	Greater depth of penetration is associated with greater pain and risk for burns and scarring [12]
Bipolar radiofrequency		Current is passed between two electrodes placed a short distance apart [4•, 12, 28, 29, 31]	More controlled distribution of energy and less pain than monopolar counterparts [4•, 12, 36]	Limited depth of penetration when compared to monopolar counterparts [12, 31, 36, 37]
Fractionated radiofrequency	**Short-pulse**	Temperature cannot be monitored as well during treatment, so shorter duration pulses are utilized to prevent excessive thermal injury	Improvement in acnes scars and superficial rhytids in addition to skin tightening [2, 3, 5, 6, 12, 28, 29, 31, 33•, 34, 37, 38•]	Requires multiple treatments for significant skin tightening. Transient erythema, edema, and paresthesia [1–3, 5, 12, 28, 29, 30•, 31, 33•, 34, 37, 38•]
	Long-pulse	Treatment temperature and tissue impedance can be precisely measured allowing for optimal heat delivery Optimal treatment settings for tissue tightening: 67 °C and 4-s duration of pulses [1, 5, 32, 35, 38•]	Significant skin tightening after single treatment [31]. Elastic fiber production in addition to collagen and hyaluronic acid [2, 3, 5, 6, 12, 28, 31, 32, 35–37, 38•]	Transient erythema, edema, and paresthesia [1–3, 5, 12, 28, 29, 31, 32, 35–37, 38•]
	Non-insulated	RF energy emitted over the entire needle length [3]	Separate deep and superficial passes are unnecessary [3]. Minimal or no in treatment bleeding [3]. No post-treatment open wound [3]	Epidermis is not protected from the needle, which may result in burns [5, 36]. Transient erythema, edema, and paresthesia [1–3, 5, 12, 28, 29, 31, 32, 35–37, 38•]
	Insulated	RF energy delivered at controlled depths and intensity with insulated needles [1, 5, 30•, 35, 37]	Protects the epidermis from thermal damage [1, 5, 30•, 35–37]	Transient erythema, edema, and paresthesia, more bruising compared to non-insulated [1–3, 5, 12, 28, 29, 31, 32, 35–37, 38•]
Percutaneous radiofrequency		Delivery of energy to hypodermal skin layers via an internal electrode [33•]. Delivery to hypodermal layers results in coagulative necrosis of subdermal fat and contraction of surrounding connective tissues [33•]	Percutaneous RF has more consistent hypodermal delivery than previous generations of RF treatment [33•]	Transient erythema, edema [1–3, 5, 12, 28, 29, 31, 32, 35–37, 38•]

Table 2 A summary of skin-tightening mechanisms, advantages, and disadvantages

Modality	Variations	Mechanism	Advantages	Disadvantages
Lasers	**Ablative**	Traditional ablation removes the entire skin surface in the treatment area [7]. Depth of injury is dependent on the energy level of the laser. Skin is heated to about 100 °C [10]	Ablative CO2 lasers are the gold standard in non-surgical skin-tightening procedures for photodamaged skin [8, 11•]. Benefits achieved in a single treatment [7, 10]	May have significant side effects such as oozing, bleeding, infection, pain, and considerable downtime for re-epithelialization [7, 8, 12]. No new elastin fiber generation. Must be used with caution in Fitzpatrick type IV to VI skin [7]. Delayed onset hypopigmentation is sometimes seen 6–12 months after procedure [8]
	Fractionated ablative	Ablation of a portion of the epidermis and dermis, leaving adjacent skin untreated [11•]. Untreated areas accelerate wound healing [10]	Shorter downtime and lower risk of scarring/complications when compared to traditional ablation [7–10]. Sparing of epidermal melanocytes prevents delayed-onset hypopigmentation [8]	May require multiple treatments for significant results and achieves more modest results than traditional ablation [7–10]
	Non-ablative	Skin is heated to about 70 °C. Epidermis is protected from thermal injury through the application of epidermal cooling [7, 10, 13]	Quicker recovery and lower risk of scarring/complications when compared to traditional ablation [7]. Can be used in all skin types	Requires multiple treatments and minimal laxity improvement [7, 10]
Ultrasound	**MFU-V**	MFU-V delivers low-energy ultrasonic pulses to the dermis and hypodermis [17•]. The heat these pulses create causes thermal tissue damage [17•]. The damage then initiates a wound healing cascade associated with collagen remodeling [17•]	MFU-V is advantageous over HIFU because of its ability to be visualized. Visualization allows more precision when administering ultrasound therapy MFU-V is also very safe and has few side effects [20–24, 25•] Ultrasound in general penetrates deeper than other non-invasive skin tightening treatments [16, 19]	MFU-V is painful relative to other skin tightening modalities [20, 27] MFU-V has a very common side effect of edema and erythema (resolves within 2 weeks) [20–24, 25•]
	HIFU	HIFU delivers high-energy ultrasonic pulses to the dermis and subcutaneous adipose layer that disrupts cell membranes and heats the subcutaneous layer, causing coagulative necrosis [17•]	HIFU is faster than MFU-V due to the lack of visualization Ultrasound in general penetrates deeper than other non-invasive skin tightening treatments [16, 19]	HIFU is not as commonly used in the USA due to its lack of visualization and deeper penetration

Table 2 (continued)

Modality	Variations	Mechanism	Advantages	Disadvantages
Plasma	**Nitrogen**	RF energy is used as an energy source to convert nitrogen gas to nitrogen plasma in brief energy pulses [43]. Percutaneous application of this plasma energy induces controlled thermal damage which results in neocollagenesis and dermal remodeling [41, 43, 44•]	Chromophore independence lends the ability to treat diverse skin types [43, 44•]. Lack of open wound leads to rapid epidermal recovery (typically within 7 days) [44•]	Inferior in treating moderate to severe rhytids when compared to ablative lasers [44•]
	Helium–Renuvion (Apyx Medical Corporation, Clearwater, FL)	RF energy is used as an energy source to continuously convert helium gas to helium plasma [44•, 45•]. Percutaneous application of this plasma/RF energy induces controlled thermal damage which results in neocollagenesis and dermal remodeling [41, 43, 44•]	High patient satisfaction-comparable results with ablative laser [45•]. Chromophore independence lends the ability to treat diverse skin types [43]. Quick recovery (re-epithelialization typically within 10 days) [45•]. Creates more superficial tissue injury and greater skin contraction when compared to nitrogen plasma [44•, 45•]. Cooling effect of helium gas under the skin lessens risk of thermal burns to the dermis [41, 46]	Side effects include moderate discomfort which largely resolved by day 10, transient erythema, swelling, induration, pruritus, worsening of pre-existing acne, and post-inflammatory hyperpigmentation [44•, 45•]. Rarer side effects included prolonged wound healing and hypertrophic scars [44•, 45•]
Hydroxyapatite filler	**Hyperdilute Radiesse**	Calcium hydroxyapatite is the main bioactive ingredient of Radiesse and forms microspheres when suspended in solution that stimulate collagen production [48, 49, 50•, 51–53]	Modest, consistent results [48, 50•, 51, 52, 54] H&E staining has proven increased collagen deposition around calcium hydroxyapatite spheres [49, 54]	Side effects include bruising, nodules, infection, skin necrosis, and blindness [48, 52, 53]
Microcoring	**Cytrellis**	Microcores of skin are removed from epidermis and dermis, causing the skin to collapse on itself and heal without scarring [55]	Lack of thermal energy limits risks of side effects caused by thermal injury	New technology. Not many studies

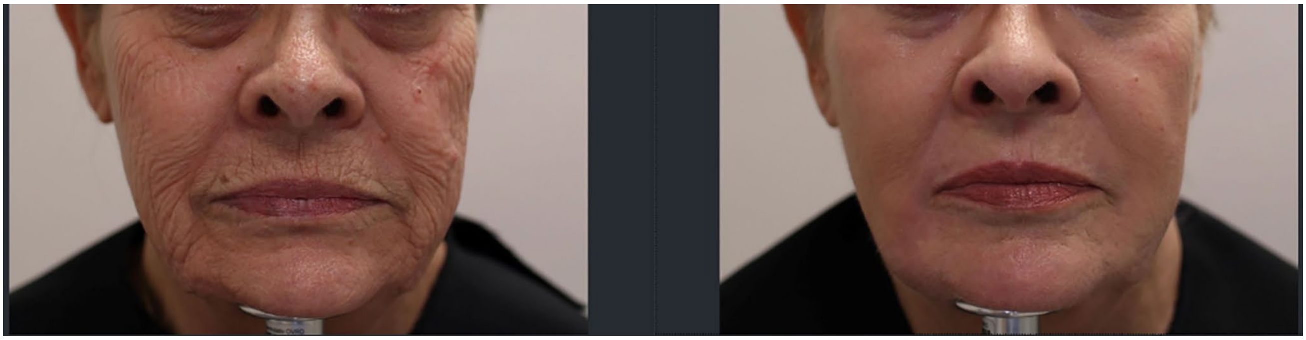

Fig. 1 (Left) Before treatment. (Right) 8 months after full-face treatment with fully ablative Er:YAG and CO_2 laser

Another hybrid approach still in development is the use of ablative conduits for the delivery of non-ablative lasers. This method allows deeper delivery of thermal energy into the dermis, largely bypassing the epidermis. Although similar to fractionated ablation, this new technique offers the benefit of a nearly uniform distribution of the thermal energy in the dermis. Although current results are unimpressive with ablative conduit delivery for non-ablative laser energy delivery, this technology is still under development [13]. Of interest, ablative laser conduits have also been shown to be an effective delivery mechanism for polylactic acid for skin rejuvenation and scar treatment [14].

Ultrasound

Mechanism

Ultrasound technology has a long safety record and is commonly used for medical imaging. Additionally, in 2009, ultrasound technology gained FDA approval for skin tightening [15]. The difference between its use in imaging and skin tightening is the intensity and focus of the ultrasound. Ultrasound can penetrate different layers of the dermis and hypodermis, depending on the length of the probe. The dermis is located approximately 1.5 mm below the surface. The collagen-containing dermis and hypodermis is located between 3 and 4.5 mm below the surface. At 4.5 mm, the ultrasonic waves can reach the superficial muscular aponeurotic system [16]. The application of focused ultrasound at any of these three layers (with the goal of heating to 60–70 °C) will cause thermal injury to the tissue that initiates collagen remodeling and decreases skin laxity [17•].

Variations

The two major types of ultrasound treatment are microfocused ultrasound (MFU) and high-intensity focused ultrasound (HIFU). MFU is more commonly used for skin tightening in the face and neck area, while HIFU is used to contour the body and reduce the appearance of cellulite. MFU-V delivers low-energy ultrasonic pulses to the dermis and hypodermis. HIFU delivers high-energy ultrasonic pulses to the dermis and subcutaneous adipose layer that disrupts cell membranes and heats the subcutaneous layer, causing coagulative necrosis [17•].

There are currently two FDA-approved MFU devices: Ultherapy (Ultherapy, Ulthera, Inc., Mesa, AZ) and Sofwave (Sofwave Medical Ltd., Tustin, CA). Ultherapy allows for variable depths of penetration ranging from the dermis to the superficial muscular aponeurotic system. In comparison, Sofwave only penetrates 1.5 mm below the surface of the skin. This reduces the chance of damaging underlying structures but also limits the range of treatment potential. Sofwave also has a built-in cooling system and a sensor that provides real-time temperature monitoring [18] (Table 3).

Table 3 Summary of FDA-approved ultrasound devices

Device	Mechanism
Ultherapy by Ulthera (Ultherapy; Ulthera, Inc., Mesa, AZ, USA)	Ultrasound waves delivered to desired depth (1.5 mm, 3.0 mm, or 4.5 mm) with visualization MFU-V
Sofwave (Tustin, California, Yokneam Illit, Israel)	No visualization HIFU

Table 4 Summary of ultrasound studies

Authors	Modality	Area	# of Patients	Results	Pain/adverse effects
Lin [27]	1.5-mm, 3.0-mm, and 4.5-mm transducers	Lower abdomen of postpartum patients	20	Investigator GAIS showed 50% of patients were assessed as being "improved" at 6 months, with 40% "very improved" and 10% "unchanged." Ten percent of patients regarded the result as "exceptional" improvement, 60% of patients were "very improved," 25% of patients were "improved," and 5% were "unchanged."	Topical anesthesia pain: 7.6/10 Subscarpal anesthesia: 3.7/10 No significant adverse effects
Araco [16]	1.5-mm, 3.0-mm, and 4.5-mm transducers	Face	50	Average surgeon reported improvement = 80/100 Average patient reported improvement = 7.28/10	Average pain of procedure: 3/10
Vachiramon et al. [21]	Single plane on one arm (4.5 mm) and dual plane on another arm (3 and 4.5 mm)	Arm	30	Single plane was statistically superior to dual plane from physician perspective No statistical difference between single and dual plane from patient perspective	Erythema (subsided within 1 day) Edema 1–3 days Pain 2.6/8 for single plane and 1.9/8 for dual plane ($P = 0.136$)
Vachiramon et al. [22]	Single plane (3.0 mm) on one side of the abdomen and dual plane (3.0 and 4.5 mm) on the other side of the abdomen	Abdomen	30	There was no statistically significant difference between single- and dual-plane treatment at each time point	Pain 5.25/10 for single plane 4.29/10 for dual plane Pain scores not statistically different Erythema and edema were noted in all treatment sites, which resolved in 1–2 weeks Skin tenderness which resolved in 2 weeks
Kerscher et al. [25•]	3.0 and 4.5 mm	Face and jawline	22	No change in skin temperatures, water loss/hydration. Gross and net elasticity values greatly decreased after 4 weeks and significantly increased at 12 and 24 weeks	Erythema Edema

Advantages

Ultrasound technology has several advantages including a wide range of treatment depths, ability to analyze tissue thickness, and epidermal sparing. A major advantage of ultrasound energy is the ability to direct heat energy deeper than other non-invasive skin-tightening procedures. The ability to deliver energy to the superficial muscular aponeurotic system is unique to ultrasound technology. Most radiofrequency devices can penetrate to a maximum depth of 4 mm and ablative lasers can penetrate to a maximum depth of 1.5 mm [19]. Percutaneous radiofrequency is a notable exception and can also target tissue effectively in the subcutaneous space. Ultrasound technology also has the unique ability to analyze tissue thickness. This allows the clinician to customize the depth of energy penetration based on an individual patient's anatomy and the area being treated [20].

Ultrasound technology has few reported adverse effects, and the most common side effects include edema and erythema [20–24, 25•]. These side effects generally resolve within 2 weeks [21]. Other less common side effects include paresthesia [23].

Disadvantages

Disadvantages of ultrasound technology include inconsistent treatment results and pain during the treatment. Results from ultrasound cosmetic rejuvenation are often user-dependent, and the learning curve for consistent results can be an issue for some users. One study found that 48.8% of patients did not have any improvement with ultrasound therapy [24] while another noted improvement in 95% of patients [26]. Previous studies evaluating ultrasound technology use different metrics to evaluate results and patient satisfaction making it challenging to establish the actual efficacy of this technology (Table 4). Another disadvantage of ultrasound as a method of skin tightening is the pain level during treatment. While pain level varied depending on the method of analgesia, pain ratings reached as high as 7.6/10 [27] in one study and 20% of patients had severe pain in another [20].

Radiofrequency

Mechanism

Radiofrequency (RF) treatment, while first developed in 1920 for electrosurgery, is now a popular non-invasive, non-ablative alternative to a facelift [12]. Like lasers, RF stimulates tissue remodeling through the generation of heat in the skin. RF involves passing electrical current through tissues with variable resistance (impedance), resulting in heat generation. Controlled tissue heat application partially denatures and contracts collagen in the dermis [1–3, 4•, 6, 12, 28, 29, 30•, 31, 32, 33•, 34, 35]. Partially denatured collagen triggers an inflammatory response that stimulates dermal remodeling and upregulation of HSP47 leading to the production of collagen I and III, elastin, and hyaluronic acid [1–3, 4•, 12, 29, 31, 32, 33•, 34–37].

As seen in wound healing literature, continued improvement in rhytids and skin laxity is also seen for up to 12 months after treatment [2, 5, 6, 12, 28, 29, 32, 33•, 34–37, 38•]. There are a variety of RF treatment devices on the market that can be subcategorized as monopolar, bipolar, fractionated, and percutaneous modalities. Some RF devices use concomitant cooling to spare the epidermis from thermal injury, decreasing the risk for adverse events such as blistering and scarring [2, 5, 6, 12, 29, 30•, 31, 34–37]. Real-time feedback sensors used in some RF technology allow for precise control of location, duration, and temperature of energy delivery and achieve consistent results with minimal associated risk [2, 5, 12, 29, 31, 32, 33•, 34, 36, 37].

RF devices have a broader safety profile across all skin types compared to laser technology. Some lasers must be used with caution in Fitzpatrick skin types IV to VI due to variable absorption by melanin and higher treatment temperatures. In contrast, RF is considered a safer treatment modality in darker skin types due to decreased risk of temporary and permanent dyschromia [1, 3, 12, 28, 30•, 31, 33•, 35].

Variations

Monopolar Radiofrequency

Monopolar RF uses one electrode to deliver RF treatment and can be further divided into monoterminal and biterminal systems. In the monoterminal system, the environment is used to disperse the RF energy, creating a high voltage, low current system [28]. Biterminal instead uses a grounding pad on a patient's back or leg to absorb the RF energy, creating a more powerful skin-tightening system that operates with a higher current and lower voltage compared to monoterminal devices [4•, 12, 31]. The main advantage and disadvantage of monopolar RF systems are the depth of energy penetration [12, 31]. Although significant skin tightening can be achieved, monopolar RF systems are often limited by significant pain during treatment and risk side effects including burns and scarring [12, 36]. The use of larger and faster tips accompanied with lower RF energy levels and multiple passes during treatment has improved treatment-associated pain [12, 36].

A widely used biterminal monopolar RF therapy, Thermage CPT (Solta Medical, Hayward, CA), obtained FDA approval in 2005 for treatment of rhytids. The use of feedback sensors and cryogen cooling spray for before, during, and after treatment minimizes epidermal complications such as infection, scarring, and dyspigmentation. Thermage achieves significant skin tightening by heating the dermis to 65–75 °C. Combination treatment with botulinum toxin injections, filler injections, and lasers can enhance cosmetic results [39].

Bipolar Radiofrequency

Bipolar RF allows for improved control over energy delivery, but it is limited by depth of energy penetration [4•, 12, 31, 34, 36]. In bipolar RF, two electrodes are placed a short distance apart, bordering the targeted treatment area [4•, 12, 28, 29, 31]. The electrical current passes between the two electrodes and penetrates the skin at a depth of about half of the distance between the two electrodes [4•, 12]. Bipolar RF energy is mainly limited by the depth it is capable of penetrating in the skin, so bipolar RF treatment is often coupled with light devices in an effort to overcome this limitation [12, 31, 36, 37]. One such light system is electro-optical synergy (ELOS) (Aurora SR, Syneron, Yokneam, Israel), which preheats the target tissue, subsequently lowering its impedance and priming it to be selectively targeted with RF energy [12, 31, 36]. Another strategy to overcome bipolar RF's limited penetration is functional aspiration controlled electrothermal stimulation (FACES) (Aluma System Lumenis, Inc., Santa Clara, CA), which employs a vacuum to fold the skin to a specific depth, optimizing depth of penetration and enhancing control of treatment [12, 31, 37]. With both ELOS and FACES, lower levels of bipolar RF energy are needed to obtain significant effects, which also decreases risk of adverse events and pain associated with treatment [12]. It should be noted that the FACES system is no longer on the market.

Fractionated Radiofrequency

Fractionated RF has the advantage of precisely controlled energy delivery but with more variable depth of penetration compared to bipolar RF. Often referred to as "RF microneedling," RF energy is delivered among various combinations of electrodes or microneedles to a controlled depth [1–3, 5, 6, 12, 28, 30•, 31, 32, 35–37, 38•]. Fractionated RF selectively heats the areas in contact with or below the microneedles, while leaving adjacent areas intact [12, 28, 31, 35, 36]. Thermal damage to the target areas results in collagen contraction, neocollagenesis, hyaluronic acid formation, and dermal remodeling as seen in other forms of RF [1–3, 5, 6, 12, 28, 30•, 31, 32, 35–37, 38•]. As with fractionated laser treatments, adjacent, intact areas serve as reservoirs that accelerate wound healing [12, 28, 35, 36]. Optimal results are seen in fractionated RF with a temperature of 67 °C and a pulse duration of 3 to 4 s [1, 5, 31, 34, 38•]. One advantage of fractionated RF is the production of new elastic fibers which has been confirmed with histologic studies [2, 3, 5, 6, 12, 28, 29, 31, 33•, 34, 37, 38•]. Fractionated RF can be further subdivided into non-insulated or insulated microneedles. Non-insulated microneedles deliver RF energy along the entire length of the needle which generates tissue tightening in addition to superficial rhytid improvement [3]. Non-insulated microneedles benefit from a lack of bleeding during treatment and post-procedure bruising compared with insulated microneedle treatments [3]. However, non-insulated needles pose an increased risk for epidermal burns [5, 29]. Insulated needles protect the epidermis during RF energy delivery to the dermis or subcutaneous tissue [1, 5, 29, 31, 32, 37]. Increased bruising seen with insulated fractionated RF can be prevented by simultaneously layering treatment with an infrared laser that targets water such as CO_2, Er:YAG, or 1927-nm lasers [40•]. Edema generated at the level of the papillary dermal plexus is thought to tamponade red blood cell extravasation and prevent bruise formation [40•].

Fractionated RF devices can be categorized as either long or short pulse treatments. Most fractionated RF products on the market are short pulse devices which require multiple treatments for significant skin tightening while producing superior results for acne scar treatment and more superficial rhytids. FDA-approved RF devices currently in use are summarized in Table 5.

Table 5 Summary of FDA-approved radiofrequency devices

Devices	Mechanism
Thermage CPT (Solta Medical, Hayward, CA)	Biterminal monopolar radiofrequency
Profound (Candela Corp, Wayland, MA)	Bipolar insulated fractionated long pulse radiofrequency
Secret RF (Cutera, Ilooda, Suwon-si, Korea)	Fractional radiofrequency
Fraxis Duo (Rohrer Aesthetics, Homewood, AL)	Combination CO2 laser and fractional radiofrequency
Morpheus8 (InMode Aesthetic Solutions, Lake Forest, CA)	Insulated fractionated short pulse radiofrequency [28]
Legend Pro (Lumenis LTD, Yokneam, Israel)	Tripollar short pulse radiofrequency
3 DEEP (EndyMed, Caesarea, Israel)	Multisource phase-controlled radiofrequency [58]
INTRAcel (Jeisys, Korea)	Insulated monopolar fractionated radiofrequency [59]
INFINI (Lutronic Corporation, Goyang, South Korea)	Insulated multipolar fractionated radiofrequency [60]
Vivace (SHENB Co., Ltd., Seongsui-Ro, Seongdong-Gu, Seoul, Korea)	Insulated or non-insulated fractionated radiofrequency [61]
Scarlet (Viol, Korea) Agnes (Gowoonsesang Cosmetics Co, Seongnam, Gyeonggi, Korea)	Insulated fractionated radiofrequency [30•]

Long-pulsed fractionated RF is one of the most promising non-surgical skin-tightening technology currently on the market, with one study showing 37% of the results of a traditional facelift with a single treatment [2, 5, 32, 35, 38•] (Fig. 2). Currently, there is only one long pulse fractionated RF device available in the USA (Profound, Candela Corp, Wayland, MA). Some surgeons combine a conservative surgical facelift or submental liposuction with long pulse fractionated RF treatment to achieve more impressive results. Significant cosmetic improvement in the midface can also be achieved with long-pulsed fractionated RF (unpublished results). The volumizing effect of long-pulsed fractionated RF on the midface is thought to be due to resuspension of superficial facial fat pads.

Fractionated RF has a favorable side effect profile with a low risk of scarring [1, 12, 32, 33•, 35, 36]. The most common side effects consist of transient erythema and edema [1–3, 5, 12, 28, 29, 31, 32, 35–37, 38•]. Rarely, transient paresthesia in the treatment area is seen [35, 38•]. With appropriate use of topical and injected lidocaine patient treatment with fractionated RF is well tolerated [1, 3, 12, 29, 31, 32, 36, 37].

Percutaneous Radiofrequency

Percutaneous RF skin-tightening results rival those of long-pulsed RF devices but involves a more invasive treatment application. Percutaneous RF involves delivery of energy to hypodermal skin layers via an internal electrode. Delivery to hypodermal layers results in coagulative necrosis of subdermal fat and contraction of surrounding connective tissues [33•]. The adjustable depth of percutaneous RF coupled with bipolar RF allows for effective treatment of challenging areas [28]. Percutaneous RF has the additional advantage of effective adipose tissue removal compared with other RF devices that have more limiting depths of penetration.

Plasma

Mechanism

Plasma technology is the final energy-based skin-tightening technique discussed in this article. RF energy is passed through nitrogen or helium gas to create plasma. In addition, heat energy is emitted as a byproduct of ionization and subsequent neutralization of the nitrogen or helium gas [41, 42•, 43]. As with other forms of energy-based skin-tightening technology, percutaneous heat application induces neocollagenesis and dermal remodeling [41, 43, 44•].

Variations

Nitrogen plasma is a non-ablative, non-fractionated, and chromophore-independent treatment that delivers thermal energy in the form of microwaves to the dermis [43, 44•]. Nitrogen gas has a greater ability to store heat than helium gas, which allows nitrogen plasma treatment to deliver energy to the dermis in single, short, Gaussian energy pulses [43]. Nitrogen plasma preserves the upper layers of skin, which promotes rapid recovery and minimal risk of infection [44•]. Nitrogen plasma can also be used to treat all Fitzpatrick skin types with minimal risk of dyspigmentation [43, 44•].

Helium plasma treatment produces more superficial thermal damage and generates a higher degree of skin tightening than nitrogen plasma. RF energy, when applied to helium gas, produces a small, continuous, and non-Gaussian

Fig. 2 (Left) Before treatment. (Right) Four months after one treatment of the mouth and jowls with long pulse fractioned radiofrequency

stream of helium plasma. The helium plasma, in turn, acts as a radiofrequency bridge, allowing RF energy to travel with the helium plasma, continuously creating more helium plasma along the beam of energy [44•, 45•]. Renuvion (Apyx Medical, Clearwater, Florida) is a helium plasma device that is coupled with concomitant cooling to decrease the risk of burns [46].

Advantages

Helium plasma treatment has a high level of patient satisfaction [45•]. One study found a 90.9% patient-reported improvement in appearance 3 months post-treatment [45•]. Plasma treatment can also be used to treat a variety of skin tones due to its chromophore independence [43, 44•].

Disadvantages

A significant disadvantage to nitrogen plasma treatment is that it produces milder skin-tightening results when compared to ablative lasers [44•]. Common side effects of plasma treatments include pain after treatment for up to 10 days, transient erythema, edema, induration, pruritus, exacerbation of acne, and post-inflammatory hyperpigmentation. Less common side effects include prolonged wound healing and scars [44•, 45•]. Nitrogen and helium plasma have similar downtime and risk of adverse effects [45•].

Non-Energy Based Tightening Techniques

Hyperdilute Radiesse

Mechanism

Dilute calcium hydroxyapatite (CaHA) filler treatment is currently gaining in popularity as an off-label skin-tightening solution for the face and body with recently published consensus guidelines [47]. CaHA filler (Radiesse, Merz North America, Inc., Raleigh, NC, USA) is a mixture of CaHA suspended in water, glycerin, and carboxymethylcellulose. CaHA filler provides an immediate volume increase and delayed volume improvement from collagen stimulation. CaHA is the main bioactive ingredient and forms microspheres that simulate collagen production [48, 49, 50•, 51–53]. Histological analysis has shown an increase in collagen types I and III, 6 month after injection [49, 54]. CaHA filler can also be safely combined with microfocused ultrasound with visualization (MFU-V) [50•].

Advantages

CaHA both induces new collagen production and provides immediate volume improvement. Most other techniques discussed only promote new collagen formation but do not achieve volume improvement. The results of CaHA also appear to be significant and consistent [48, 50•, 51, 52, 54]. One study in which CaHA filler was injected into the arms of participants reported that 100% of both the subjects and evaluators were satisfied or very satisfied with treatment [52].

Disadvantages

As with all fillers, CaHA filler potential side effects include bruising, infection, nodules, skin necrosis from arterial injection, and blindness [48, 52, 53].

Microcoring

Microcoring is a relatively new concept in the field of skin tightening. Cytrellis Biosystems (Cytrellis Biosystems Inc., Boston, MA) was the first company to begin testing microcoring for skin rejuvenation. The lead study author, Roy G. Geronemus, MD, explained at the American Society for Laser Medicine and Surgery that the mechanism is something like taking a "punch biopsy" [55]. This technology was first tested on pigs. Both studies treated one site with microcoring needles and another site with a control, standard hypodermic needle [56, 57]. With microcoring removal of 10% the skin, the treated area shrunk by 9% [56]. Histological examination showed increased fibroblast activity and increased collagen at microcoring sites [57]. Three months after treatment, an 89% increase in collagen was confirmed using an enzyme-linked immunosorbent assay [57].

Microcoring findings on human patients were presented at the American Society for Laser Medicine. Twenty-three women were treated in the mid and lower face area, removing 5% and 7.5% of skin, respectively [55]. The average pain reported was 0.36 on the Wong Baker 0–10 Scale [55]. Ninety-three percent of investigators and subjects scored "improved to very much improved" on the Global Aesthetic Improvement Scale [55]. No serious adverse effects occurred [55].

Conclusion

Non-surgical skin-tightening technology continues to improve and provides a viable alternative for patients who are unwilling or medically unsuitable for surgical intervention. In addition, demand for non-invasive and minimally invasive skin-tightening procedures continues to increase. Patients want natural results and cost-effective interventions with minimal risk and downtime. Although surgical intervention remains the gold standard for laxity correction, non-invasive and minimally invasive skin-tightening procedures are quickly becoming an essential part of a surgical cosmetic practice.

Declarations

Conflict of Interest G. Munavalli is an investigator and on the Speakers Bureau for Candela. C. Helen Malone and Nicole Walters declare that they have no conflict of interest.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Kleidona IA, Karypidis D, Lowe N, Myers S, Ghanem A. Fractional radiofrequency in the treatment of skin aging: an evidence-based treatment protocol. J Cosmet Laser Ther. 2020;22:9–25. https://doi.org/10.1080/14764172.2019.1674448.
2. Alexiades-Armenakas M, Rosenberg D, Renton B, Dover J, Arndt K. Blinded, randomized, quantitative grading comparison of minimally invasive, fractional radiofrequency and surgical face-lift to treat skin laxity. Arch Dermatol. 2010;146:396–405. https://doi.org/10.1001/archdermatol.2010.24.
3. Gold M, Taylor M, Rothaus K, Tanaka Y. Non-insulated smooth motion, micro-needles RF fractional treatment for wrinkle reduction and lifting of the lower face: International study. Lasers Surg Med. 2016;48:727–33. https://doi.org/10.1002/lsm.22546.
4.• Bonjorno AR, Gomes TB, Pereira MC, de Carvalho CM, Gabardo MCL, Kaizer MR, et al. Radiofrequency therapy in esthetic dermatology: a review of clinical evidences. J Cosmet Dermatol. 2020;19:278–81. https://doi.org/10.1111/jocd.13206. (**This article details the mechanism and advantages of RF therapy for skin tightening**).
5. Alexiades-Armenakas M, Newman J, Willey A, Kilmer S, Goldberg D, Garden J, et al. Prospective multicenter clinical trial of a minimally invasive temperature-controlled bipolar fractional radiofrequency system for rhytid and laxity treatment. Dermatol Surg. 2013;39:263–73. https://doi.org/10.1111/dsu.12065.
6. Hantash BM, Ubeid AA, Chang H, Kafi R, Renton B. Bipolar fractional radiofrequency treatment induces neoelastogenesis and neocollagenesis. Lasers Surg Med. 2009;41:1–9. https://doi.org/10.1002/lsm.20731.
7. Britt CJ, Marcus B. Energy-based facial rejuvenation: advances in diagnosis and treatment. JAMA Facial Plast Surg. 2017;19:64–71. https://doi.org/10.1001/jamafacial.2016.1435.
8. Ortiz AE, Goldman MP, Fitzpatrick RE. Ablative CO2 lasers for skin tightening: traditional versus fractional. Dermatol Surg. 2014;40(Suppl 12):S147-151. https://doi.org/10.1097/DSS.0000000000000230.
9. Russe E, Purschke M, Limpiangkanan W, Farinelli WA, Wang Y, Doukas AG, et al. Significant skin-tightening by closure of fractional ablative laser holes. Lasers Surg Med. 2018;50:64–9. https://doi.org/10.1002/lsm.22748.
10. Geronemus RG. Fractional photothermolysis: current and future applications. Lasers Surg Med. 2006;38:169–76. https://doi.org/10.1002/lsm.20310.
11.• Ha L, Jaspan M, Welford D, Evers M, Kositratna G, Casper MJ, et al. First assessment of a carbon monoxide laser and a thulium fiber laser for fractional ablation of skin. Lasers Surg Med. 2020;52:788–98. https://doi.org/10.1002/lsm.23215. (**In ex vivo samples, CO laser was shown to achieve deeper ablation than the $CO_2$2 laser, which may be desirable depending on the clinical goal**).
12. Lolis MS, Goldberg DJ. Radiofrequency in cosmetic dermatology: a review. Dermatol Surg. 2012;38:1765–76. https://doi.org/10.1111/j.1524-4725.2012.02547.x.
13. Tanghetti E, Mirkov M, Sierra RA. Delivery of light to the skin through ablated conduits. Lasers Surg Med. 2017;49:69–77. https://doi.org/10.1002/lsm.22533.
14. Rkein A, Ozog D, Waibel JS. Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid. Dermatol Surg. 2014;40:624–31. https://doi.org/10.1111/dsu.0000000000000010.
15. Fabi SG. Noninvasive skin tightening: focus on new ultrasound techniques. Clin Cosmet Investig Dermatol. 2015;8:47–52. https://doi.org/10.2147/CCID.S69118.
16. Araco A. Prospective study on clinical efficacy and safety of a single session of microfocused ultrasound with visualization for collagen regeneration. Aesthet Surg J. 2020;40:1124–32. https://doi.org/10.1093/asj/sjz363.
17.• Juhász M, Korta D, Mesinkovska NA. A review of the use of ultrasound for skin tightening, body contouring, and cellulite reduction in dermatology. Dermatol Surg. 2018;44:949–63. https://doi.org/10.1097/DSS.0000000000001551. (**This study provides a summary of the benefits and drawbacks to the use of ultrasound for skin tightening**).
18. Ultrasound Beam Technology for treating wrinkles and fine lines. Sofwave n.d. https://sofwave.com/physicians/int/ (accessed 12 April 2021).
19. Dobke MK, Hitchcock T, Misell L, Sasaki GH. Tissue restructuring by energy-based surgical tools. Clin Plast Surg. 2012;39:399–408. https://doi.org/10.1016/j.cps.2012.07.008.
20. Shome D, Vadera S, Ram MS, Khare S, Kapoor R. Use of microfocused ultrasound for skin tightening of mid and lower face. Plast Reconstr Surg Glob Open. 2019;7:e2498. https://doi.org/10.1097/GOX.0000000000002498.
21. Vachiramon V, Triyangkulsri K, Iamsumang W, Chayavichitsilp P. Single-plane versus dual-plane microfocused ultrasound with visualization in the treatment of upper arm skin laxity: a randomized, single-blinded, controlled trial. Lasers Surg Med. 2020a. https://doi.org/10.1002/lsm.23307.
22. Vachiramon V, Triyangkulsri K, Iamsumang W, Chayavichitsilp P. Efficacy and safety of microfocused ultrasound with visualization in abdominal skin laxity: a randomized, comparative study. Lasers Surg Med. 2020b;52:831–6. https://doi.org/10.1002/lsm.23234.
23. Yalici-Armagan B, Elcin G. Evaluation of microfocused ultrasound for improving skin laxity in the lower face: a retrospective study. Dermatol Ther. 2020;33:e14132. https://doi.org/10.1111/dth.14132.
24. Friedman O, Isman G, Koren A, Shoshany H, Sprecher E, Artzi O. Intense focused ultrasound for neck and lower face skin tightening a prospective study. J Cosmet Dermatol. 2020;19:850–4. https://doi.org/10.1111/jocd.13313.
25.• Kerscher M, Nurrisyanti AT, Eiben-Nielson C, Hartmann S, Lambert-Baumann J. Skin physiology and safety of microfocused ultrasound with visualization for improving skin laxity. Clin Cosmet Investig Dermatol. 2019;12:71–9. https://doi.org/

10.2147/CCID.S188586. (**This study confirms the safety of microfocused ultrasound when analyzing skin physiology and barrier function**).
26. Werschler WP, Werschler PS. Long-term efficacy of microfocused ultrasound with visualization for lifting and tightening lax facial and neck skin using a customized vectoring treatment method. J Clin Aesthet Dermatol. 2016;9:27–33.
27. Lin FG. Nonsurgical treatment of postpartum lower abdominal skin and soft-tissue laxity using microfocused ultrasound with visualization. Dermatol Surg. 2020;46:1683–90. https://doi.org/10.1097/DSS.0000000000002576.
28. Dayan E, Chia C, Burns AJ, Theodorou S. Adjustable depth fractional radiofrequency combined with bipolar radiofrequency: a minimally invasive combination treatment for skin laxity. Aesthet Surg J. 2019;39:S112–9. https://doi.org/10.1093/asj/sjz055.
29. Kaplan H, Kaplan L. Combination of microneedle radiofrequency (RF), fractional RF skin resurfacing and multi-source non-ablative skin tightening for minimal-downtime, full-face skin rejuvenation. J Cosmet Laser Ther. 2016;18:438–41. https://doi.org/10.1080/14764172.2016.1228981.
30.• Shin J-W, Park J-T, Chae J-B, Choi J-Y, Na J-I, Park K-C, et al. The efficacy of micro-insulated needle radiofrequency system for the treatment of lower eyelid fat bulging. J Dtsch Dermatol Ges. 2019;17:149–56. https://doi.org/10.1111/ddg.13736. (**This study outlined the advantages and safety behind micro-insulated needle RF systems in skin tightening**).
31. Weiss RA. Noninvasive radio frequency for skin tightening and body contouring. Semin Cutan Med Surg. 2013;32:9–17.
32. Alexiades M, Berube D. Randomized, blinded, 3-arm clinical trial assessing optimal temperature and duration for treatment with minimally invasive fractional radiofrequency. Dermatol Surg. 2015;41:623–32. https://doi.org/10.1097/DSS.0000000000000347.
33.• Locketz GD, Bloom JD. Percutaneous radiofrequency lower face and neck tightening technique. JAMA Facial Plast Surg. 2019;21:71–2. https://doi.org/10.1001/jamafacial.2018.0917. (**This article details the advantages of percutaneous RF when compared to other RF modalities**).
34. Mazzoni D, Lin MJ, Dubin DP, Khorasani H. Review of non-invasive body contouring devices for fat reduction, skin tightening and muscle definition. Australas J Dermatol. 2019;60:278–83. https://doi.org/10.1111/ajd.13090.
35. Malone CH. Fractional radiofrequency. The Dermatologist 2019:27.
36. Hantash BM, Renton B, Berkowitz RL, Stridde BC, Newman J. Pilot clinical study of a novel minimally invasive bipolar microneedle radiofrequency device. Lasers Surg Med. 2009;41:87–95. https://doi.org/10.1002/lsm.20687.
37. Willey A, Kilmer S, Newman J, Renton B, Hantash BM, Hantash B, et al. Elastometry and clinical results after bipolar radiofrequency treatment of skin. Dermatol Surg. 2010;36:877–84. https://doi.org/10.1111/j.1524-4725.2010.01563.x.
38.• Ukoha U, Malone CH, Munavalli G. Nonsurgical brow lift with a temperature-controlled, fractionated radiofrequency needle device. Dermatol Surg. 2021;47:296–8. https://doi.org/10.1097/DSS.0000000000002280. (**This study outlined the efficacy and safety of long-pulsed RF technologies in achieving a non-surgical browlift**).
39. Polder KD, Bruce S. Radiofrequency: thermage. Facial Plast Surg Clin North Am. 2011;19:347–59. https://doi.org/10.1016/j.fsc.2011.04.006.
40.• Alkul S, Poliner A, Malone CH, Munavalli G. Layered 1927-nm laser for prevention of postprocedural bruising. Dermatol Surg. 2020. https://doi.org/10.1097/DSS.0000000000002841. (**Increased bruising seen in insulated fractionated RF was shown to be prevented by concomitant treatment with an infrared laser that targets water**).
41. Doolabh V. A single-site postmarket retrospective chart review of subdermal coagulation procedures with renuvion. Plast Reconstr Surg Glob Open. 2019;7:e2502. https://doi.org/10.1097/GOX.0000000000002502.
42.• Ruff PG. Thermal effects of percutaneous application of plasma/radiofrequency energy on porcine dermis and fibroseptal network. J Cosmet Dermatol. 2020. https://doi.org/10.1111/jocd.13845. (**This study noted similar depth of penetration of thermal energy in a plasma/RF system when compared to a monopolar temperature-controlled RF device. This indicates that a plasma/RF system may be an effective and safe alternative for skin tightening**).
43. Theppornpitak N, Udompataikul M, Chalermchai T, Ophaswongse S, Limtanyakul P. Nitrogen plasma skin regeneration for the treatment of mild-to-moderate periorbital wrinkles: a prospective, randomized, controlled evaluator-blinded trial. J Cosmet Dermatol. 2019;18:163–8. https://doi.org/10.1111/jocd.12767.
44.• Holcomb JD, Schucker A. Helium plasma skin regeneration: evaluation of skin tissue effects in a porcine model and comparison to nitrogen plasma skin regeneration. Lasers Surg Med. 2020;52:23–32. https://doi.org/10.1002/lsm.23167. (**This study found helium plasma to have reduced depth of penetration, greater skin tightening, and similar acute and chronic histopathological findings when compared to nitrogen plasma**).
45.• Holcomb JD, Kelly M, Hamilton TK, DeLozier JB. A prospective study evaluating the use of helium plasma for dermal resurfacing. Lasers Surg Med. 2020;52:940–51. https://doi.org/10.1002/lsm.23257. (**This study found significant skin tightening from a single pass with Helium plasma treatment, and reported no serious adverse events**).
46. Gentile RD. Renuvion RF-Helium plasma for subdermal skin tightening, facial contouring and skin rejuvenation of the face and neck. Facial Plast Surg Aesthet Med. 2020;22:304–6. https://doi.org/10.1089/fpsam.2020.0070.
47. de Almeida AT, Figueredo V, da Cunha ALG, Casabona G, Costa de Faria JR, Alves EV, et al. Consensus recommendations for the use of hyperdiluted calcium hydroxyapatite (Radiesse) as a face and body biostimulatory agent. Plast Reconstr Surg Glob Open 2019:7:e2160. https://doi.org/10.1097/GOX.0000000000002160.
48. Wollina U, Goldman A. Long lasting facial rejuvenation by repeated placement of calcium hydroxylapatite in elderly women. Dermatol Ther. 2020;33:e14183. https://doi.org/10.1111/dth.14183.
49. Marmur ES, Phelps R, Goldberg DJ. Clinical, histologic and electron microscopic findings after injection of a calcium hydroxylapatite filler. J Cosmet Laser Ther. 2004;6:223–6. https://doi.org/10.1080/147641704100003048.
50.• Casabona G, Nogueira TD. Microfocused ultrasound in combination with diluted calcium hydroxylapatite for improving skin laxity and the appearance of lines in the neck and décolletage. J Cosmet Dermatol. 2018;17:66–72. https://doi.org/10.1111/jocd.12475. (**This article found that combining microfocused ultrasound and calcium hydroxyapatite is an effective treatment for increasing skin elasticity and reducing visible rhytids**).
51. Wasylkowski VC. Body vectoring technique with Radiesse for tightening of the abdomen, thighs, and brachial zone. CCID. 2015;8:267–73. https://doi.org/10.2147/CCID.S75631.
52. Amselem M. Radiesse(®): a novel rejuvenation treatment for the upper arms. Clin Cosmet Investig Dermatol. 2016;9:9–14. https://doi.org/10.2147/CCID.S93137.
53. Carruthers JDA, Carruthers JA, Humphrey S. Fillers and neocollagenesis. Dermatol Surg. 2014;40(Suppl 12):S134-136. https://doi.org/10.1097/DSS.0000000000000227.
54. Berlin AL, Hussain M, Goldberg DJ. Calcium hydroxylapatite filler for facial rejuvenation: a histologic and

immunohistochemical analysis. Dermatol Surg. 2008;34(Suppl 1):S64-67. https://doi.org/10.1111/j.1524-4725.2008.34245.x.
55. Brunk D. Novel dermal coring device effective for facial rejuvenation without using thermal energy. MD Edge: Dermatology 2018. https://www.mdedge.com/dermatology/article/164683/aesthetic-dermatology/novel-dermal-coring-device-effective-facial (accessed 12 April 2021).
56. Russe E, Purschke M, Farinelli WA, Wang Y, Doukas AG, Limpiangkanan W, et al. Micro-fractional, directional skin tightening: a porcine model. Lasers Surg Med. 2016;48:264–9. https://doi.org/10.1002/lsm.22444.
57. Fernandes JR, Samayoa JC, Broelsch GF, McCormack MC, Nicholls AM, Randolph MA, et al. Micro-mechanical fractional skin rejuvenation. Plast Reconstr Surg. 2013;131:216–23. https://doi.org/10.1097/PRS.0b013e3182789afa.
58. Sundaram H, Kiripolsky M. Nonsurgical rejuvenation of the upper eyelid and brow. Clin Plast Surg. 2013;40:55–76. https://doi.org/10.1016/j.cps.2012.08.009.
59. Lee SJ, Kim J-I, Yang YJ, Nam JH, Kim W-S. Treatment of periorbital wrinkles with a novel fractional radiofrequency microneedle system in dark-skinned patients. Dermatol Surg. 2015;41:615–22. https://doi.org/10.1097/DSS.0000000000000216.
60. Chun S. Fractional microneedling radiofrequency and fractional 1927 nm thulium laser treatment offer synergistic skin rejuvenation: a pilot case series. Laser Ther. 2018;27:283–91. https://doi.org/10.5978/islsm.27_18-OR-26.
61. Wootten S, Zawacki ZE, Rheins L, Meschter C, Draelos ZD. An evaluation of electrocoagulation and thermal diffusion following radiofrequency microneedling using an in vivo porcine skin model. J Cosmet Dermatol. 2021;20:1133–9. https://doi.org/10.1111/jocd.13690.