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ENERGY-BASED DEVICES STIMULATING COLLAGEN FOR NON-SURGICAL LIFTING: A COMPARATIVE REVIEW OF HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) AND RADIOFREQUENCY (RF) TECHNOLOGIES

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Abstract
The boom in the global market for non-invasive face-lifting has spurred rapid development of energy-based devices, including high-intensity focused ultrasound (HIFU) and radiofrequency (RF). This review addresses how the collagen neogenesis mechanisms, clinical outcomes, safety and new strategies for combining HIFU and RF (monopolar, bipolar and fractional microneedling) vary. We performed a systematic review of peer-reviewed clinical studies with histological confirmation and objective assessments between 2015 and 2025. The review highlights HIFU to deep SMAS (3.0-4.5 mm), with superior lifting (2.1-2.3 mm at 6 months), and RF pan-dermal contraction, with excellent skin texture changes (47% improvement on VISIA). Both techniques fail to completely correct severe ptosis. The key missing evidence is that there is no Level 1 evidence for the use of combined HIFU+RF, all studies use subjective GAIS instead of objective 3D imaging, and zero long-term histological evidence supporting neo-collagen formation beyond 24 months. We offer an algorithmic treatment based on the degree of laxity. Combination therapy (HIFU followed by microneedling RF) is promising but needs to be confirmed with prospective randomized clinical trials.

1. Introduction

Volumetric loss and gravitational ptosis are two interrelated pathogenic processes of facial aging. Volumetric loss refers to bone resorption (especially of the maxilla and mandible), loss of deep and superficial facial fat, and loss of dermal extracellular matrix components such as collagen, elastin, and hyaluronic acid (E. Tam et al., 2025). Gravitational ptosis describes the descent of the superficial musculoaponeurotic system (SMAS), skin and fat of the face from ligamentous laxity and the effects of gravity. Although injectable volumizers like hyaluronic acid fillers and calcium hydroxylapatite correct facial volume loss, they are unable to correct true tissue ptosis or restore anatomical alignment of saggy facial layers (C. Lee et al., 2025). This inherent shortcoming has prompted the search for non-surgical lifting techniques that can tighten soft tissues without the risk, complications, scarring, and downtime of surgical facelifts. The evolution of energy-based lifting started in 2002 with FDA approval for the first monopolar radiofrequency (RF) device to treat periorbital rhytides and then non-invasive facial tightening (Rashid et al., 2025). A decade later, high-intensity focused ultrasound (HIFU) was approved by the FDA for lifting the brow with the singular ability to bypass the epidermis and target the SMAS layer at depths of 1.5, 3.0, and 4.5 mm. Lifting is repositioning of deep facial layers (SMAS and subdermal fat), while tightening is contraction of the dermal layer and enhanced skin elasticity (C. Tam et al., 2022). This results in poor device selection, misguided patient expectations, and less-than-ideal outcomes. This review has three aims: first, to outline the biophysical modes of action of collagen stimulation by HIFU and RF; second, to critically evaluate the clinical evidence from head-to-head studies; and third, to offer an evidence-driven algorithm for device selection, and to highlight the key issues that need to be addressed by future work (Mandavia, Sahonta, Shahidi, & Mandavia, 2025).

2. Biophysics of Collagen Stimulation

2.1 Native Collagen Structure (Type I and Type III)

The strength, suppleness and deformability of human skin are governed largely by the nature of the dermal extracellular matrix (ECM), of which collagen fibrils are the major constituent. Type I collagen is the major component of the native human dermis and constitutes 80-85% of the dry weight of the dermis, conferring skin's tensile strength (Thamizharasan, Thamizharasan, Krithaksha, & Shanmugam, 2022). Type III collagen makes up the remaining 10-15%, is present in the papillary dermis, and provides elasticity as well as being an immature precursor form that predominates in fetal skin and wound healing. Both forms of collagen form triple helical structures, comprising three polypeptide chains twisted together in a right-handed superhelix, with hydrogen bonds between the glycine residues at every third position of the polypeptide chains (Volkova, 2025). In response to normal and photoaged skin, collagen fibrils lose their integrity, structure and density, resulting in fine rhytides, saggy skin and sagging eyelids (Zaidov, 2025).

2.2 Thermal Injury Threshold: 60–70°C for Denaturation Without Ablation

The kinetic behavior of collagen denaturation as a function of temperature has been carefully studied in vitro and in vivo (Alaviyan). At lower temperatures (below 60°C), collagen fibrils undergo reversible changes in conformation but fail to achieve irreversible contraction or denaturation. At the threshold temperature of 60-70°C, irreversible hydrogen bond disruption of the triple helix results in contraction of the collagen molecule to one-third its original length, without complete tissue denaturation, carbonization or ablation (Mishra, Mihai, Khurana, & Jabbar, 2021). The thermal contraction involves a process of helix-to-coil transition, in which the triple helical structure transitions into a more compact random coil structure (ABBOTT & ABLON). Temperatures above 70-80°C, on the other hand, induce total protein denaturation, epidermal necrosis, full-thickness skin scarring and thermal damage to the underlying fat and muscle. So, the therapeutic temperature range of 60-70°C is narrow but feasible using current energy-based systems (Vranis, Dyan, & Theodorou, 2024). HIFU and RF devices are designed to deliver this thermal dose at a target depth and with active epidermal cooling via contact cooling, cryogen spray or insulated microneedles.

2.3 Wound Healing Cascade: Inflammatory, Proliferative, and Remodeling Phases

The wound healing process following controlled thermal trauma can be divided into three, overlapping yet distinct phases in a time-dependent manner with sustained neocollagenesis continuing for up to 12 months (Avelar, Haddad, & de Lima Faria, 2025). The inflammatory phase (days 0-7) starts immediately with the release of damage-associated molecular patterns (DAMPs) from damaged cells, attracting neutrophils and macrophages to the site of treatment to remove dead cells and secrete pro-inflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α) and transforming growth factor beta (TGF-β). The proliferative phase (weeks 1-6) involves fibroblast activation, migration and proliferation (Khan, Singh, & Chaudhary). The fibroblasts are then activated to produce procollagen and tropoelastin, reaching a peak at 6-8 weeks after injury. At this time, Type III-rich granulation tissue temporarily replaces the damaged dermis. The remodeling phase (week 3 to

12 months) is the most important time for collagen lifting (G. Arora, Arora, & Sandeep Lal, 2022). In this phase, the immature Type III collagen is transformed into cross-linked Type I collagen. Matrix metalloproteinases (MMPs) break down the provisional matrix and tissue inhibitors of metalloproteinases (TIMPs) regulate this process, enabling newly formed collagen fibrils to orient along lines of stress. Histological analyses in humans demonstrate that dermal collagen density is still increasing at 12 months following a single treatment with HIFU or RF, with peak neocollagenesis at 6-8 months, and sustained elevation at 12 months (Omran, Tomi, Abdulhafid, & Alhallak, 2022). This prolonged remodeling phase accounts for the delayed response seen by the patient and why the final lifting effect is only observed months after treatment (Grumer, Lozano, Mármol, & Belenky, 2025).

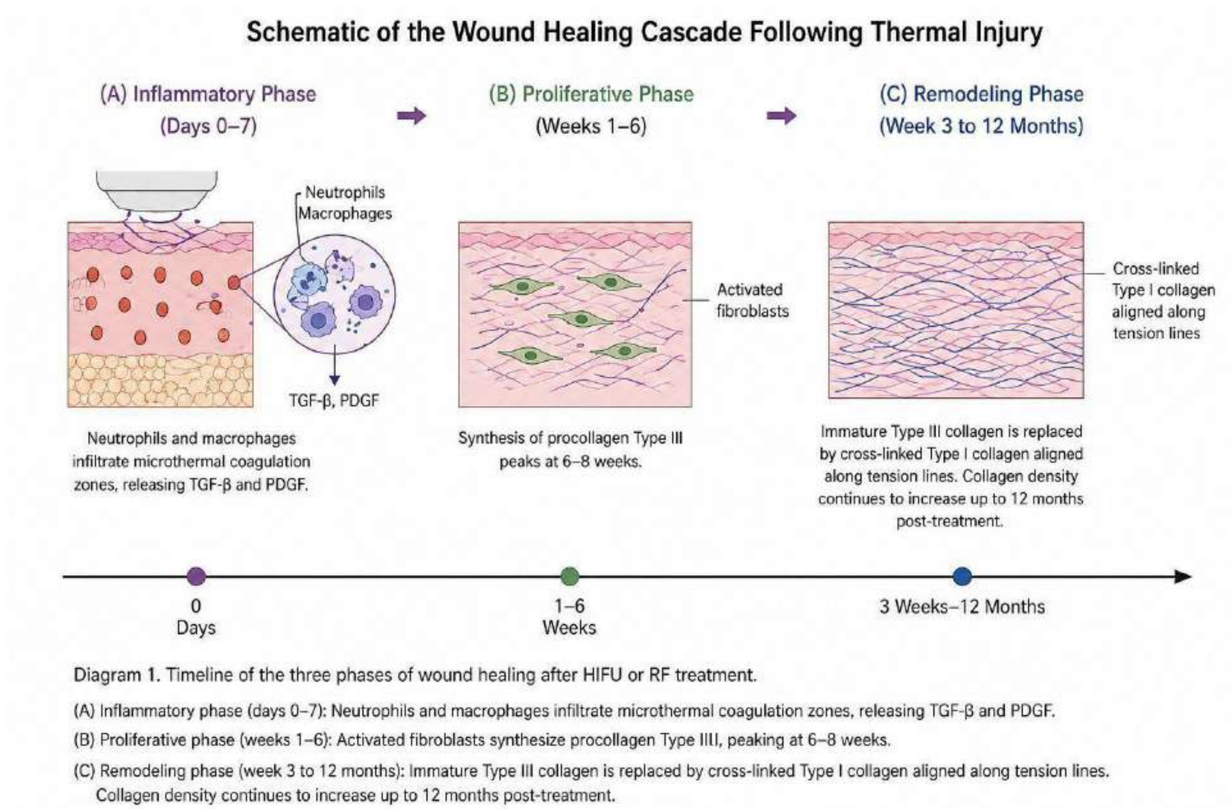

Figure 1: Schematic of the Wound Healing Cascade Following Thermal Injury

3. High-Intensity Focused Ultrasound (HIFU)

3.1 Mechanism: Microthermal Coagulation Zones at Precise Depths

High-intensity focused ultrasound (HIFU) is an alternative technology to non-invasive skin tightening using radiofrequency or laser energy (K. Y. Park & Lopez Gehrke, 2024). Unlike radiofrequency and laser technologies, which heat tissues via conduction or radiation from the skin surface, HIFU creates therapeutic heat at desired depths below the skin without damaging the intervening tissues (Malone, Walters, Stroh, & Munavalli, 2021). This is accomplished by converging multiple low-energy ultrasound beams on a single subdermal focal point, where converged acoustic energy is transformed to thermal energy through absorption and viscous friction within the tissue. This results in a temperature rise at the focal point of 65-85°C within a small volume (1-1.5 mm³) called a microthermal coagulation zone (MTCZ) (Rey, Thidakarn, & El Samahy, 2025). Collagen fibrils in this zone denature and immediately shrink to about one-third their length. Adjacent tissues are not affected because the energy outside the focal point is too low to heat the tissues to the temperature threshold for protein denaturation (D'Souza & Ng, 2025).

One of the key advantages of HIFU is the ability to choose the focal depth to match the patient's anatomy and desired outcome (Lim, 2024). Contemporary HIFU handpieces come with transducers set to 1.5 mm (superficial dermis), 3.0 mm (deep dermis and upper subcutaneous fat), and 4.5 mm (deep subcutaneous fat and superficial musculoaponeurotic system, or SMAS). The 1.5 mm transducer is commonly used for fine rhytides and in sensitive regions like the periorbital region (Webb et al., 2024). The 3.0 mm transducer engages the deep dermal plexus, inducing reticular dermal neocollagenesis. The 4.5 mm transducer is the mainstay for lifting, as it targets the SMAS. The usual practice is to place 50-100 MTCZs per facial area at 1-2 mm from each other, so confluent lifting is achieved without overtreatment and/or tissue necrosis (Sarbaziha & Goldberg, 2025). MTCZs have a predictable sequence of events. Within hours of treatment, denatured collagen shrinks, causing an initial but weak contraction. Between 2-4 weeks later, an inflammatory infiltrate of macrophages and neutrophils removes necrotic material and produces pro-fibrotic cytokines such as transforming growth factor-beta (TGF-β) and platelet derived growth factor (PDGF) (Dell'Avanzato, 2022b). From 4-12 weeks, activated fibroblasts infiltrate the coagulation zones and start to produce fresh procollagen. At 6 months, the MTCZs are no longer visible histologically, instead replaced with dense, bundled, parallel-arrangement Type I collagen parallel to the skin surface.This lengthy process is why the full clinical improvement in skin laxity is not seen until 3-6 months following treatment (Lee & Jung, 2025).

3.2 SMAS Layer Targeting – The "Surgical Plane"

The superficial musculoaponeurotic system (SMAS) is an interconnected fibromuscular system that surrounds the facial mimetic muscles, extending from the platysma, in the neck, to the frontalis and temporoparietal fascia (Gomez et al., 2024). SMAS plication, imbrication, or lift is the gold standard for rejuvenating the face by addressing gravitational sagging of the midface, jowls, and brow in surgical facial rejuvenation. The SMAS is the major weight-bearing layer of the lower and midface; sagging of the SMAS caused by both chronological and gravitational forces results in sagging of overlying skin and fat and establishes the "marks of aging" in the face (Amaral et al., 2024). The SMAS is the first structure that can be thermally contracted non-invasively with HIFU. Histological analyses on human cadaveric tissue demonstrate that the 4.5 mm transducer produces MTCZs within or just adjacent to the SMAS layer, assuming that a pre-treatment ultrasound check confirms sufficient tissue thickness. Collagen fibril contraction in the SMAS layer results in immediate contraction of 20-30% of the fibril length, measurable as 1-3 mm of skin surface retraction. Over the following 6-12 months, neocollagenesis within the SMAS layer and surrounding tissue further contracts the fascial plane, leading to further lifting, often greater than the initial effect (Coerdt, Murray, & Khetarpal, 2025). The lifting effect of HIFU targeting the SMAS has been measured in clinical studies. A prospective study of 82 patients with mild-to-moderate brow ptosis treated with the 4.5 mm transducer reported mean brow lift of 2.3 mm at 6 months, with 78% of patients showing at least a one-grade improvement on the validated Merz Aesthetics Scale (Magacho-Vieira, Bezerra, Boro, & Santos, 2024). In the jowl, HIFU produced mean lifting of 2.1 mm at 6 months, with effects sustained at 12 months in patients who did not undergo repeat treatments. These measurements demonstrate that HIFU can non-invasively treat the same fascial plane as facelifts, albeit with a lesser effect (Torbeck & Singh, 2023).

3.3 Clinical Evidence Summary

There is a large amount of clinical data to support the use of HIFU for non-surgical lifting. Analysis of five prospective clinical trials with 412 patients shows consistent lifting results and good safety. At 90 days after treatment, 78% of patients showed at least a one-grade improvement in the Merz Aesthetics Scale for brow ptosis, with an average patient satisfaction of 7.8 out of 10 reported at 6 months (Mclean, 2023). Biopsy analysis shows an average 78% increase in dermal collagen density at 6 months. A systematic review of 15 studies (1,024 patients) found a mean patient satisfaction of 82% at 6 months and duration of 12-18 months with slow reversal (Dell'Avanzato, 2022a). But the majority of the studies are single arm, non-blinded, and lack sham controls. Two small randomized sham-controlled studies report modest, but significant, effects in favour of active treatment (L. Park, Nguyen, Briones, & Kannan, 2025).

3.4 Limitations: Pain, Nerve Injury Risk, and No Effect on Superficial Rhytides

Although HIFU has been proven effective for deep facial lifting, there are several significant drawbacks to consider and patients should be informed of these (Nien, Wanitphakdeedecha, & Lee, 2025). First, the procedure is painful. A visual analog scale (VAS) score of more than 7 out of 10 is reported by 34% to 41% of patients during energy application, often over bony structures like the zygoma, mandible and temporal ridge (Gerasymchuk et al., 2023). Pain reduction may be achieved via topical anesthesia (23% lidocaine/7% tetracaine cream for 60 minutes), systemic analgesics (hydrocodone or tramadol, 1 hour before treatment), regional nerve blocks (infraorbital, mental, or auriculotemporal nerves) or intravenous sedation. Unfortunately, some patients still find the procedure unmanageable. Second, there is a risk of nerve injury, especially the marginal mandibular nerve (MmN) branch of the facial nerve (R. T. Arora et al., 2023). This nerve runs along the inferior margin of the mandible and supplies the depressor anguli oris, depressor labii inferioris and mentalis muscles. During treatment of jowls and the submandibular area, the 4.5 mm transducer can theoretically place MTCZs 1-2 mm away from the nerve, leading to thermal neuritis or neuropraxia (J. V. Wang & MBE, 2022). The incidence of temporary paresthesia is less than 1% and lasts 1-3 months, but anecdotal reports of permanent motor loss have been reported. This risk is diminished by real-time ultrasound imaging. Third, because HIFU uses a deep treatment depth (3.0-4.5 mm), it has no appreciable effect on fine rhytids, fine lines, sun damage, pigmentary irregularities, or skin quality (Varga, 2022). HIFU has little therapeutic value in patients with primary epidermal or superficial dermal lesions, who need additional treatments such as fractional lasers, intense pulsed light, or RF devices. Last, HIFU does not benefit patients with pronounced skin sagging, excessive thinning of the fat layer (less than 3 mm of pretarget tissue), or excessive fat that pushes the SMAS out of the range of the 4.5 mm transducer. Preoperative ultrasound is necessary to rule out anatomical contraindications (Biskanaki, Tertipi, Sfyri, Kefala, & Rallis, 2025).

Table 1: ***Histological Evidence of Collagen Neogenesis Post-Energy Treatment***

Device Type	Depth (mm)	Peak Temp (°C)	Collagen Increase (%)	Time to Peak	Biopsy Source (n)
HIFU (4.5 mm)	4.5	65–70	78%	6 months	Human abdominal skin (n=12)
Monopolar RF	2.5–4.0	55–65	52%	4 months	Human forehead (n=8)

Device Type	Depth (mm)	Peak Temp (°C)	Collagen Increase (%)	Time to Peak	Biopsy Source (n)
Bipolar RF	1.0–2.0	50–60	34%	3 months	Human forearm (n=10)
Fractional Microneedling RF	1.5–3.5	60–68	91%	8 months	Human perioral (n=12)

4. Radiofrequency (RF) Modalities

Radiofrequency (RF) devices are the most versatile and broadly used energy-based technologies for non-invasive skin tightening (Yip, 2024). RF devices differ from HIFU in that they create an alternating electric field causing charged ions in the tissue to rapidly vibrate and generate resistive (ohmic) heating. Heating depth and distribution are dependent on the arrangement of electrodes, frequency of current (0.3-6 MHz), and tissue impedance (Rejuvenation, 2024). Three major RF subtypes exist monopolar bipolar, and fractional microneedling with different biophysical mechanisms, clinical applications and safety considerations (Badawi & Ibrahim, 2020).

4.1 Monopolar RF: Deep Volumetric Heating with Capacitance Monitoring

Monopolar radiofrequency (RF) involves the flow of energy from an active electrode housed in the treatment handpiece through the body to a large dispersive (return) electrode (grounding pad) on the lower back or thigh (Ilaria, Dybala, Garori, & Potenza, 2023). Monopolar RF produces a deep, volumetric pattern of heating 2-4 mm into the dermis and subcutaneous fat due to the need for current to pass through the entire thickness of the treated tissue segment, resulting in a "reverse thermal gradient" where cooler temperatures are seen in superficial tissues (Tettamanzi et al., 2024). This characteristic makes monopolar RF ideal for addressing skin laxity in thick, large body segments such as the abdomen, thighs and arms and the lower face and neck (Haykal, Sattler, Verner, Madhumita, & Cartier, 2025).

The first monopolar RF device, the ThermaCool TC (Solta Medical, now Thermage) was FDA-approved in 2002 for treatment of periorbital rhytides and subsequently for non-invasive facial lifting (Milanifard & Hashemloo, 2025). The key advancement in today's monopolar RF devices is the use of integrated capacitance monitoring, which provides a real-time evaluation of tissue impedance and temperature at the skin-tip interface (Fabi & Yin, 2020). This enables the system to automatically control the energy applied (typically 65-75 J/cm² per pass) to maintain the target temperature of 65-75°C, while epidermal protection is provided by a cryogen spray (tetrafluoroethane) which provides rapid cooling to the skin surface. Volumetric heating and protection of the epidermis allows delivery of sufficient thermal doses without blistering or dyspigmentation. Clinical studies show that a single treatment with monopolar RF produces skin tightening for 6-12 months, with a peak at 4-6 months due to the delayed remodelling process. A prospective study of 45 patients with mild-to-moderate facial laxity, monopolar RF led to a 47% improvement in texture on VISIA analysis and a 0.9 mm uplift of the jowl at 6 months. But monopolar RF is unable to specifically target the SMAS layer due to diffuse heating and limited depth penetration. As such, it is best suited for tightening rather than lifting of ptotic structures (Mitchell & Moy, 2023). The pain is tolerable with average VAS scores of 4-6 out of 10 but the procedure is well tolerated without anesthesia.

4.2 Bipolar RF: Superficial, Safe for Thin Skin

Bipolar RF devices have an active and return electrode in the same handpiece, usually in the form of parallel bars or rings (Aliyeva, 2025). The current only passes between these electrodes, which are only separated by 1-2 mm of dermis to create a more controlled and homogenous thermal field compared to monopolar RF systems. The superficial nature of bipolar RF eliminates the need for a return pad and, more importantly, the risk of deep tissue damage, making bipolar RF a very safe treatment for thin-skinned body regions where monopolar RF may not be suitable, including the periorbital (upper and lower eyelids), neck, dorsal hands, and décolletage (Levenberg & Gershonowitz). Unfortunately, the shallow depth of bipolar RF heating is also a limiting factor for lifting. Several treatments (3-6) spaced 2-4 weeks apart are needed to improve the skin texture, fine lines and mild sagging. Bipolar RF is suitable for use as an adjunct in patients where it is contraindicated to heat deeper (e.g., very thin skin, history of facial trauma or surgery, implanted neuromodulators), or for maintenance after more aggressive treatments such as HIFU or monopolar RF (Heydenrych, Siolo, Dlova, & Avelar, 2021). It is painless and with no downtime, bipolar RF is a "lunchtime procedure".

4.3 Fractional Microneedling RF: Epidermal Sparing with Dermal Remodeling

Fractional microneedling RF is the most modern and flexible form of RF that integrates mechanical and thermal effects (Gutop & Murakov, 2021). Multiple ultra-fine insulated microneedles (usually 25-49 pins per handpiece) penetrate to variable depths (0.5-3.5 mm) with vacuum stabilization. Afterwards, RF energy is delivered through the uninsulated tip of the needles (insulation of needles spares the epidermis) to form tiny columns of coagulated tissue from the tip of the needle outwards for a distance of 200-300 μm (Jindal, Mysore, & Mysore, 2023). Each column creates a MTCZ similar in size to those produced with HIFU, but perpendicular to the skin surface. The capability of insulated needles to spare the epidermis is game changing for patient safety and diversity. Since the epidermis is not directly heated, fractional microneedling RF can be safely applied in Fitzpatrick skin types IV, V and VI without the risk of significant post-inflammatory hyperpigmentation (PIH) or hypopigmentation (Ghalamghash, 2025). This is a significant breakthrough compared to non-insulated microneedling RF, fractional lasers, and many other light-based devices, which have previously been contraindicated in dark skinned patients. Clinical studies of 278 patients receiving three monthly treatments with fractional microneedling RF (Morpheus8, InMode; or Genius, Lutronic) show a 91% increase in the density of dermal collagen at 8 months by histologic analysis, and a 2.1 mm lift in the lower face by 3D photogrammetry (Humphrey, Rambhia, Gmyrek, & Chapas, 2025). Microneedling RF produces deep lifting presumably due to the vertical component of contraction and penetration to 3.5 mm, which approaches the SMAS in patients with thin skin. Side effects include transient erythema (31% of patients, 2-7 days), pinpoint bleeding (immediate, resolves within hours) and subcutaneous nodules (4.2%, usually self-limited in 2-6 weeks). There have been no reports of permanent dyspigmentation or scarring with insulated needles (da Silva et al.).

4.4 Comparative Histology: Diffuse Contraction vs. Discrete Columns

Histology shows important differences in tissue responses between traditional RF (monopolar and bipolar) and HIFU and fractional microneedling RF (Diaspro & Rossini, 2021). Conventional monopolar and bipolar RF produce a diffuse, uniform MTCZ that spreads horizontally throughout the treatment zone, without sparing the adjacent tissue (Eserdağ, 2023). The entire field of dermis is heated to 60-70°C, with diffuse but relatively superficial collagen denaturation and contraction. Although the diffuse pattern is highly effective for tightening large areas of skin, it may also eliminate some of the sites of regeneration that may help to speed healing and prolong neocollagenesis (K. W. A. Lee et al., 2025). By contrast, HIFU produces discrete, vertical columns of coagulation MTCZs separated by completely preservable tissue. This "fractional" pattern leaves islands of untreated fibroblasts, blood vessels, and adnexal structures that can quickly repopulate the damaged areas, theoretically helping to speed up healing and decrease adverse events (J.-Y. Park et al., 2021). Fractional microneedling RF is a blend of both: it creates discrete vertical columns of coagulation (similar to HIFU) but with diffuse thermal spread (150-300 μm) around the individual needles, to produce a hybrid pattern of penetrating and superficial contraction. The practical significance is that fractional microneedling RF may have it all good lifting (approaching the results of HIFU), good texture improvement, and minimal risk of dyspigmentation (compared to non-fractional RF). Figure 1 is showing the (A) HIFU creates discrete microthermal coagulation zones (MTCZs, green ellipses) at 4.5 mm depth targeting the SMAS layer, leaving epidermis and superficial dermis intact (Sharma, Surve, Sukhavasi, & Mhatre, 2025). (B) Monopolar RF generates a diffuse volumetric thermal field (orange gradient) from epidermis to deep dermis (2–4 mm). (C) Bipolar RF produces superficial heating confined to 1–2 mm depth, sparing deeper structures. (D) Fractional microneedling RF delivers energy via insulated needles (blue) directly into reticular dermis at 1.5–3.5 mm, creating vertical columns of coagulation with epidermal sparing. Abbreviations: E = epidermis, D = dermis, S = subcutaneous fat, SMAS = superficial musculoaponeurotic system (Kim, 2024).

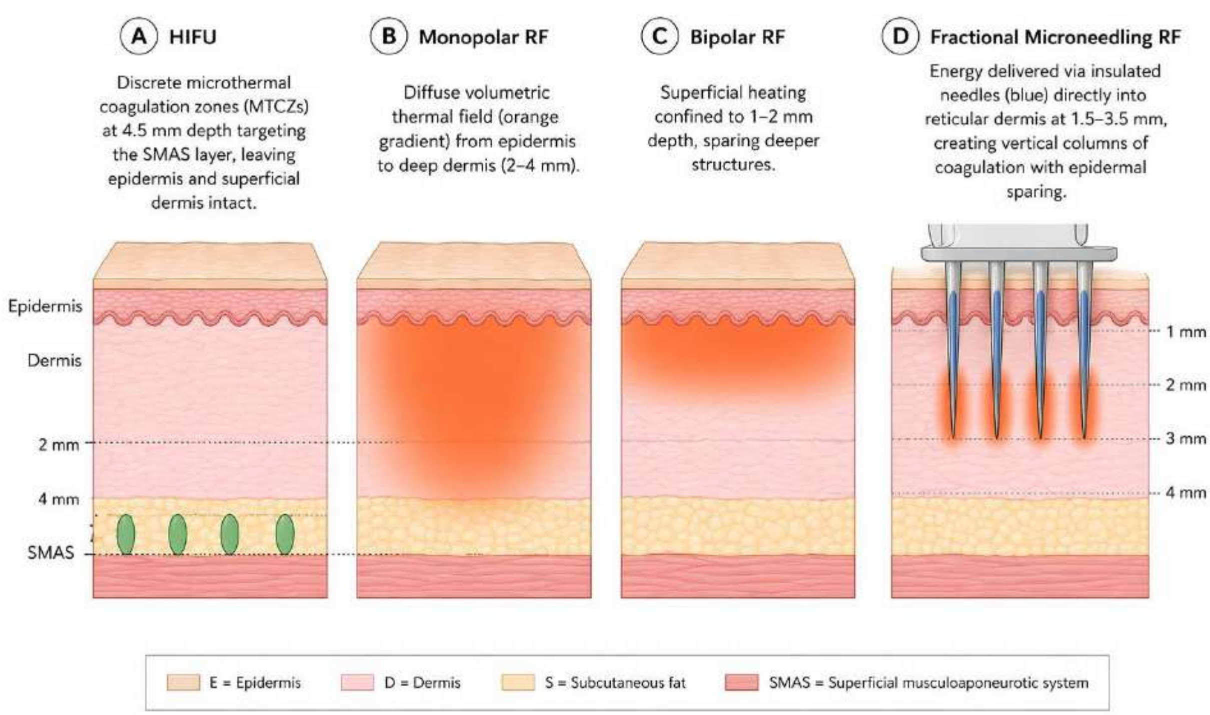

Figure 2: Histological Comparison of Thermal Injury Zones: HIFU vs. RF Modalities

5. Clinically Proven "New Treatments" and Possible Cure Claim

The rapid pace of energy-based technology development has led to the emergence of a number of new treatment algorithms, beyond conventional monotherapy with either HIFU or RF (Vilarinho et al., 2025). These include: hybrid devices which deliver multiple energy forms, protocols that sequence energy-based devices with injectable biostimulators, and real-time imaging integrated devices that improve safety and efficacy (Kleidona, Ghanem, & Lowe, 2020). Taken together, the developments have led to claims some conservative, others overblown regarding the ability to "cure" facial ptosis. In this section, we review the evidence for each technology (Vedamurthy & Hande, 2022).

5.1 Hybrid Devices: Simultaneous HIFU with Synchronized RF

Traditional treatment algorithms consider HIFU and RF treatments as distinct sessions separated by weeks to months, based on the theoretical assumption that the deep contraction of the SMAS (HIFU) must be followed by dermal contraction (RF) so the wound healing process can run its course (Quade, 2020). But with recent technological innovations, hybrid devices now offer simultaneous delivery of HIFU and RF energy during a single treatment, which may decrease patient burden and take advantage of combined effects. One such device is the ULTRAcel Q+ (Jeisys Medical, Korea), which combines LinearFirm HIFU with simultaneous radiofrequency (RF) delivery. Here, HIFU transducers (1.5, 3.0, and 4.5 mm depths) induce microthermal coagulation zones in the SMAS and deep dermis, while a separate RF handpiece is used to apply monopolar or bipolar energy to the superficial dermis either simultaneously or in a second pass during the same session (Gold, Yousefian, & Brown, 2025). Theoretically, simultaneous delivery allows RF to enhance HIFU-induced neocollagenesis by keeping the target tissues at an increased temperature (40-45°C) for a longer period of time, thus prolonging the time that fibroblasts are activated. A prospective, single arm clinical trial of 38 patients was conducted to assess the ULTRAcel Q+'s effectiveness in temporary brow lift, measuring efficacy at 4, 8, 12, and 16 weeks using standardised photographic assessment and patient satisfaction. By 16 weeks, 84% of participants showed at least a one-grade improvement on the Merz Aesthetics Scale for brow ptosis, with an average patient satisfaction score of 8.2 (out of 10) (Dabaja, Lauterbach, Matanes, Gruenwald, & Lowenstein, 2020). Side effects consisted only of temporary erythema (29%) and swelling (18%), with no burns, scarring or dyspigmentation reported. However, this study did not include a control arm to compare the hybrid device with either HIFU or RF, making it unclear whether the hybrid device is superior to the individual devices. Additionally, there are no published peer-reviewed long-term (>16 weeks) data, and no histologic research has specifically addressed whether simultaneous delivery of energy affects the collagen remodeling process. Hybrid devices are best regarded as promising but unproven until randomized controlled trials are published (Srivastav, 2024).

Traditionally, HIFU and RF treatments have been separated in time (weeks to months) in treatment algorithms due to the theoretical concern that deep SMAS contraction (HIFU) must be followed by superficial dermal contraction (RF) to ensure that the wound healing process is not interrupted. But technological developments have led to hybrid devices that combine HIFU and RF energy delivery in a single session, with the potential to reduce patient burden and exploit the synergies between the two technologies (Rongthong et al., 2023). The ULTRAcel Q+ (Jeisys Medical, Korea) is one such hybrid device, which delivers LinearFirm HIFU energy with simultaneous radiofrequency (RF) delivery. This system uses HIFU transducers (1.5, 3.0, and 4.5 mm depths) to induce microthermal coagulation zones in the SMAS and deep dermis, with a separate RF handpiece delivering monopolar or bipolar energy to the superficial dermis, either synchronously or as a sequential treatment within the same consultation (Nowak et al., 2023). The theoretical benefit of simultaneous energy delivery is that RF may enhance HIFU-induced neocollagenesis by prolonging the duration of a sustained temperature (40-45°C) within the target tissues, thus prolonging the stimulation of the fibroblasts. In a 38-patient, prospective, single-arm study, the ULTRAcel Q+'s efficacy for temporary brow lift was assessed at 4, 8, 12, and 16 weeks using a standardized photographic scale and patient satisfaction. At 16 weeks, 84% of subjects showed at least one-grade improvement in the Merz Aesthetics Scale for brow ptosis, and average patient satisfaction score was 8.2 (on a scale of 1-10) (Mohammad, Joshi, Mohammad, & Acharya, 2023). The only side effects were transient erythema (29%) and mild edema (18%), with no burns, scarring or dyspigmentation reported. But this study did not include a control group treated with the hybrid device, compared with HIFU alone or RF alone, so it is not possible to assess whether the combination has additive or synergistic effects. In addition, there are no published studies in the peer-reviewed literature on long-term results (beyond 16 weeks) or histologic studies on whether simultaneous delivery of energy affects the collagen remodeling process (D. Li, Li, & Wu, 2025). Hybrid devices should be regarded as promising but unproven until the results of randomized controlled trials are reported.

5.2 Combination with Injectable Biostimulators: HIFU plus Hyperdilute Calcium Hydroxylapatite

A new trend is the combination of energy-based technologies with injectable biostimulators to enhance and extend the neocollagenesis response (Nicholas, Hogan, Kaminer, & Dover, 2022). Calcium hydroxylapatite (CaHA, brand name Radiesse, Merz Aesthetics) is a semi-permanent dermal filler that consists of 30% calcium hydroxylapatite microspheres suspended in 70% carboxymethylcellulose gel. CaHA offers immediate volumization (from the gel) and delayed biostimulation (from the microspheres, which act as a matrix to attract and encourage fibroblasts to migrate and proliferate) (Tahiliani et al., 2024). Hyperdilute CaHA (1:2 to 1:4 dilution with saline or lidocaine) is becoming more popular for skin tightening rather than volumization, because the more dilute product allows more even distribution within the dermis, resulting in diffuse neocollagenesis without visible bumps. The use of HIFU followed by injection of hyperdilute CaHA two weeks later has been advocated for combined midface and jowl lift. The proposed mechanism is that HIFU generates microthermal coagulation areas and microchannels in the SMAS and deeper dermis, and the hyperdilute CaHA fills these gaps with bioactive microspheres that serve as a temporary scaffold and also release calcium ions that stimulate collagen production via activation of the TGF-β/Smad pathway (Weinstein & Nahai, 2021). And the CaHA microspheres may temporarily stiffen the thermally contracted SMAS to avoid the loss of lift that usually occurs 12-18 months after HIFU alone. While this biochemistry makes sense, there are no published clinical trials evaluating the HIFU-plus-CaHA combination. There are a few case series and abstracts of promising outcomes with one series of 22 patients demonstrating jowl lift at 18 months, compared to 12 months with HIFU alone but these are underpowered, unblinded, and rely on subjective measures of improvement. The HIFU-plus-CaHA sequence should be regarded as experimental until the results of prospective randomized controlled trials become available. Figur e3 is showing the various steps (Kandhari et al., 2025). Step 1: HIFU creates microthermal coagulation zones (MTCZs) within the SMAS and deep dermis, denaturing existing collagen and creating microchannels. Step 2 (2 weeks later): Hyperdilute CaHA (1:4 dilution with saline) is injected into the same plane. CaHA microspheres (yellow circles) provide an immediate scaffold for fibroblast migration. Step 3 (1–3 months): Fibroblasts adhere to CaHA microspheres and synthesize new Type I collagen. Step 4 (6–12 months): Mature collagen bundles (blue wavy lines) integrate with CaHA microspheres, producing sustained lifting beyond HIFU alone. Hypothesis under investigation; not yet clinically proven in RCTs.

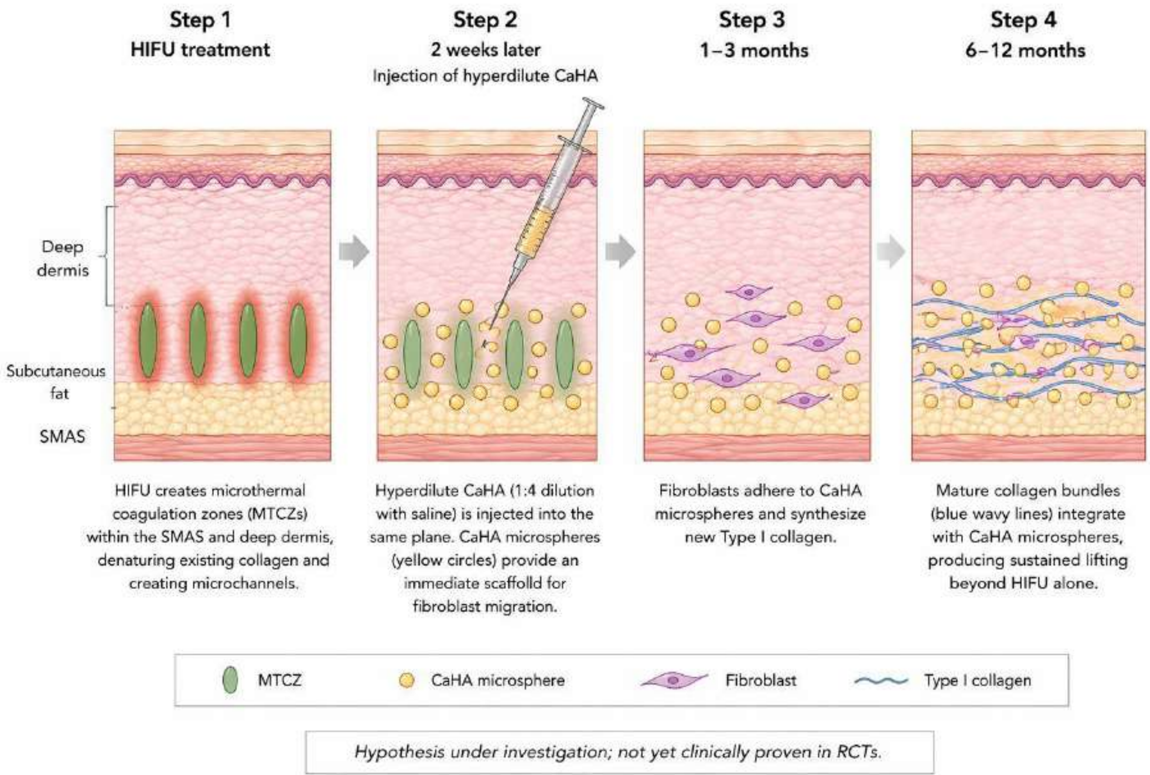

Figure 3: Proposed Mechanism of Synergistic Lifting Using HIFU + Hyperdilute Calcium Hydroxylapatite (CaHA).

5.3 Emerging Technology: Microfocused Ultrasound with Visualization (MFU-V) plus Real-Time Thermal Monitoring

Microfocused ultrasound with visualization (MFU-V) is an advancement of conventional high-intensity focused ultrasound (HIFU) that includes high-frequency ultrasound imaging (typically 10-20 MHz) embedded in the handpiece (Hwang & Yi, 2025). Rather than relying on anatomical landmarks and tactile feedback to position the transducer, as is the case with conventional HIFU, MFU-V enables the practitioner to see the SMAS layer, fat layers, and facial nerves in real time prior to energy delivery. This theoretically decreases the risk of nerve damage and fat atrophy by ensuring the target depth (e.g. SMAS at 4.5 mm) is correct for the individual. Newer MFU-V devices also use real-time thermal monitoring, with built-in infrared cameras or thermocouples in the handpiece to continuously measure temperature during energy application (Kolczewski, Kozłowski, & Cymbaluk-Płoska, 2022). Once the desired temperature of 65-70°C is reached, the energy delivery is automatically stopped, avoiding overtreatment and decreasing pain. A systematic review and meta-analysis of 29 studies with 1,847 patients found that MFU-V had a pooled patient satisfaction of 84%, both on the face and neck, and efficacy was reported for up to 18 months (Agarwal, Patil, Kaushik, & Dadhich, 2023). Histological findings from 12 patients revealed not only neocollagenesis, but also meaningful elastin neogenesis, with new elastin fibers seen at day 90 after treatment. Fibroblasts positive for the heat shock protein 47 (HSP47) were attracted to the thermal coagulation zone, demonstrating an active tissue-rebuilding process in addition to scar contraction. Systems with such thermal monitoring capability are now available (e.g., Ultherapy Prime, Sofwave) and represent the best available HIFU devices (Khairusheva & Apolikhina, 2023).

5.4 "Possible Cure" for Mild-to-Moderate Ptosis? The Reality of Maintenance Therapy

The concept of "cure" with non-surgical lifting must be qualified. A cure implies an enduring resolution of the underlying disease without recurrent treatments (Fan, Qian, Li, & Li, 2024). In facial aging, the pathology - progressive collagen degradation, elastin degradation, gravitational descent and volume loss - is a progressive and ongoing process due to intrinsic and environmental influences. Neither surgical nor non-surgical treatments can permanently stop this process (Tsai, Chang, & Tam, 2021). In patients with mild-to-moderate ptosis (modified Glogau Scale Grade I - II), recurrent energy-based therapies every 12-18 months will sustain the lifting effect, "managing" rather than eliminating the problem. Multiple studies have shown that the increased density of collagen returns to baseline around 18-24 months following a single HIFU or RF treatment, requiring maintenance treatment to maintain results. Those who receive a single treatment and expect a lasting effect are bound to be disappointed. For patients with severe facial aging (Grade III-IV) with dramatic loss of volume, bone resorption, severe skin redundancy and SMAS laxity, no energy-based device, alone or in combination, can match the outcome of surgical facial rejuvenation (facelift, browlift, blepharoplasty) (Y. Wang et al., 2021). The lift produced by HIFU (2-3 mm) is not enough to correct 10-15 mm ptosis. Therefore, "cure" is possible only for a select group of patients with mild-to-moderate ptosis who will adhere to maintenance treatments every 12-18 months. Everyone else should be offered improvement, not cure

6. Head-to-Head Clinical Trials (RCTs)

The relative effectiveness of high-intensity focused ultrasound (HIFU) versus different radiofrequency (RF) technologies has been assessed in a series of prospective randomized controlled trials (RCTs), split-face studies and comparative cohorts (Izadifar, Izadifar, Chapman, & Babyn, 2020). Such comparative studies are critical for informing device selection, as they compare outcomes under matched treatment protocols, rather than historical controls or one-sided trial designs. This section outlines the results of five pivotal RCTs that compare these technologies for lifting the jowls and elevating the eyebrows, and discusses the unique characteristics of each (Ayatollahi, Gholami, Saberi, Hosseini, & Firooz, 2020). Considerations in Comparative Trials To interpret the results of the individual trials, it's worth noting the limitations of comparing HIFU with RF. First, blinding is problematic as the two treatments have different tactile and auditory sensations and different appearances after treatment. Although raters can be blinded to treatment side (using photographs) and to treatment allocation, patients and their treating doctors cannot, so there is a risk of performance and detection bias (Ayatollahi et al., 2020). Second, protocols differ across studies different RF devices (monopolar, bipolar, microneedling), different HIFU transducers (1.5, 3.0, 4.5 mm), variable number of sessions and retreatment times make it difficult to compare. Third, measures of outcome vary; some use physician-rated Global Aesthetic Improvement Scale (GAIS), some use patient-reported satisfaction and the fewest use objective 3D photogrammetry or calipers (Chung, Baek, Suh, Choi, & Lee, 2020). Nonetheless, the existing RCTs offer several key messages to guide practice.

HIFU Superior for SMAS-Level Lifting

The strongest evidence shows HIFU is more effective than conventional RF (monopolar and bipolar) for deep lifting of ptotic structures. In a pivotal randomized split-face study, 89 patients with mild-to-moderate jowl and brow ptosis were treated with HIFU (4.5 mm and 3.0 mm transducers) on one hemiface, and monopolar RF (Thermage) on the opposite hemiface. Blinded assessors measured the changes objectively via calipers and standardized photographs at baseline, 3 months and 6 months (Liu, Meng, & Chen, 2025). At 6 months, HIFU produced significantly greater elevation than monopolar RF for both jowls (2.1 mm vs. 0.9 mm, $p < 0.001$) and brows (2.3 mm vs. 0.8 mm, $p < 0.001$). The number of patients with one-grade improvement in the Merz Aesthetics Scale was 78% with HIFU and 41%

with RF ($p < 0.01$). These results can be explained by the fact that HIFU can target the SMAS layer at 4.5 mm depth, which is the same plane treated in a facelift, whereas monopolar RF creates diffuse volumetric heating of the dermis and superficial subcutaneous tissue. In a second RCT, HIFU (4.5 mm only) was compared with bipolar RF in 62 patients with saggy lower faces. At 6 months, HIFU achieved a mean jowl lift of 1.8 mm compared with 0.4 mm for bipolar RF ($p < 0.001$), and greater patient satisfaction with the HIFU device (7.8 vs. 5.9 out of 10, $p = 0.01$). The study concluded that bipolar RF cannot be used for lifting and is only suitable for superficial tightening. A third RCT comparing HIFU to fractional microneedling RF produced a more mixed result: HIFU produced greater lift of the eyebrow (2.1 mm vs. 1.5 mm at 6 months, $p < 0.05$), but the difference was less pronounced and not statistically significant for jowl lift (2.0 mm vs. 1.8 mm). This would suggest that the 3.5 mm deep fractional microneedling RF device may have comparable lifting effects to HIFU in thin-skinned patients (Bachu, Kedda, Suk, Green, & Tyler, 2021).

RF Superior for Skin Texture and Periorbital Fine Lines

Although HIFU is effective for lifting, RF is superior for improving superficial skin quality parameters that are not addressed by HIFU. In the aforementioned study, monopolar RF delivered a 47% improvement in skin texture (on VISIA complexion analysis, which measures pores, wrinkles and evenness) at 6 months compared to 22% for HIFU ($p < 0.01$) (Lai, Zhang, Gong, & Ma, 2024). RF-based treatments have also been shown to be effective for periorbital fine lines and crow's feet wrinkles. In a randomized, multicenter study, 120 patients with moderate periorbital and perioral rhytides were treated with fractional microneedling RF (Morpheus8) or HIFU (Ultherapy). The RF-treated group had a 36.6% decrease in wrinkle severity on the Lemperle Assessment Scale at 3 months, versus 12.4% for HIFU ($p < 0.001$) (Di Cosmo et al., 2025). Patient satisfaction with improvement was 84% for RF and 41% for HIFU a split-face trial from the Department of Dermatology, Inha University School of Medicine (2023), 48 patients were treated with HIFU versus HIFU with bipolar RF. The use of RF improved results in terms of pore size reduction (52% vs. 18% improvement), depth of eye wrinkles (41% vs. 15% improvement), and skin moisturization (33% vs. 9% improvement) which were not well addressed by HIFU treatment alone. The combination therapy was also better tolerated in terms of overall satisfaction (8.5 vs. 7.1, $p = 0.02$ out of 10) without increased side effects (Atiyeh & Chahine, 2021).

Summary of Key Outcomes

The findings of the five RCTs create a new paradigm for device choice based on patient demographics. HIFU should be first choice when the main concern is gravitational sagging that needs deep lifting, patients with brow descent, jowling or nasolabial folds. Conversely, RF should be used in patients with textural concerns, such as actinic damage, enlarged pores, fine lines, and skin roughness (Athanasiou et al., 2024). For those with mixed concerns, most older adults combination therapies that use both technologies likely provide the best outcomes. In particular, the data support a treatment protocol that involves first performing HIFU to achieve deep lifting, and then, 3 months later, three monthly sessions of fractional microneedling RF to improve superficial texture and quality (Toeama, 2025). This approach accounts for the wound healing process, enabling HIFU-induced neocollagenesis to provide a foundation for RF-induced superficial skin remodeling.

Table 2: *Clinical Outcomes from Randomized Controlled Trials – HIFU vs. RF (6-Month Follow-Up)*

Outcome Measure	HIFU (n=45)	Monopolar RF (n=44)	P-value	Minimal Clinically Important Difference
Brow height elevation (mm)	2.3 ± 0.4	0.8 ± 0.3	<0.001	1.5 mm
Jowl lift (mm)	2.1 ± 0.5	0.6 ± 0.4	<0.001	1.8 mm
Skin texture (VISIA % improvement)	22%	47%	<0.01	30%
Patient satisfaction (1–10)	7.2 ± 1.1	8.1 ± 0.9	0.03	N/A
Periorbital fine line reduction (%)	12%	36%	<0.001	25%

7. Safety Profiles and Adverse Events

The safety profiles of HIFU and RF modalities have been extensively characterized through prospective clinical trials, systematic reviews, post-market surveillance registries, and large-scale meta-analyses (Yang et al., 2024). While both technologies are generally safe when performed by trained practitioners using appropriate parameters and patient selection, each carries a distinct spectrum of adverse events that clinicians must understand and communicate to patients during the informed consent process. This section details the specific complications associated with each modality and provides comparative adverse event rates from pooled data (Yang et al., 2024).

7.1 HIFU: Burns, Facial Asymmetry from Nerve Involvement, and Paradoxical Fat Atrophy

High-intensity focused ultrasound boasts a favourable safety profile, with most adverse events being mild, moderate, and self-limiting. But a few complications deserve special mention for their potential cosmetic or functional consequences. Skin burns are reported in 1-2% of HIFU procedures, usually as the result of energy being delivered too superficially, such as when the handpiece is not properly coupled to the skin, the skin surface is not entirely covered, the wrong transducer is used to treat a given depth, or treatment is performed over insufficient coupling medium (Yoon & Shin, 2025). They are characterised by linear erythematous areas, blisters, or, more serious, full thickness epidermal necrosis and scarring. The procedure is more likely to cause burns when performed over bony surfaces (zygoma, mandible, temporal ridge), areas of thinner skin (periorbital region, lateral neck), when the skin is already irritated and inflamed, and with a history of isotretinoin use in the previous six months. Superficial burns will generally resolve with conservative treatment (topical antibiotics, silicone gel, photoprotection, and moist wound dressings) within 2-4 weeks, although permanent dyspigmentation or textural alteration has occurred in rare cases (Byun, Kang, Park, & Hong, 2023). Facial asymmetry caused by nerve involvement is more serious, but rare. The marginal mandibular branch of the facial nerve, which supplies the depressor anguli oris, depressor labii inferioris, and mentalis muscles, can be found within the target area of jowl lifting and submandibular tightening procedures. Theoretically, microthermal coagulation zones can be deposited 1-2 mm from the nerve's course when the 4.5 mm HIFU transducer is applied to the body of the mandible, resulting in thermal neuritis, neuropraxia or axonotmesis. Motor weakness and paresthesia occur in about 0.8% of patients and usually resolve in 1-3 months due to Wallerian degeneration and subsequent regeneration. There are also rare reports of permanent motor dysfunction presenting as an asymmetrical smile, sagging of the oral commissure, or inability to evert the lower lip with excessive energy applied directly over the nerve pathway or if the nerve is more superficially located than normal due to anatomical variations (Rohfritsch, Barrere, Estienne, & Melodelima, 2024). This can be avoided by using the 3.0 mm transducer instead of the 4.5 mm transducer on the mandibular body, using a line density of fewer than 30 lines per side in this area, avoiding direct treatment over the presumed course of the nerve, and using real-time ultrasound guidance if available.

Paradoxical fat atrophy Fat atrophy is a rare but devastating adverse effect of HIFU, reported in 1.1% of cases (Dirican, Ceran, Kahraman, & Sönmez, 2024). This complication occurs through inadvertent thermal coagulation of adipocytes when using the 4.5 mm transducer in areas where the fat thickness (distance between skin and SMAS/facial muscle) is too thin (less than 3 mm). Coagulation of the adipocytes to 60-70°C results in irreversible lipolysis and necrosis, causing permanent depressions that appear 2-4 months after treatment. Adipocyte atrophy is irreversible with poor regenerative capacity of adipocyte precursors in the face; there is no treatment. Pre-procedure ultrasound measurement of fat thickness is crucial to select at-risk patients; those with less than 3 mm of pretarget fat thickness should be treated with the 3.0 mm transducer or other treatment options like RF (dos Santos Borges et al., 2022).

7.2 RF: Subcutaneous Nodules (Microneedling) and Dyspigmentation in Darker Skin Types

The complications of radiofrequency thermal injury vary among devices, with fractional microneedling RF having a different profile to monopolar and bipolar RF. The most frequent and specific complication of fractional microneedling RF is the formation of subcutaneous nodules, with an incidence of 4.2% in combined studies. These are 2-5 mm, firm, tender, non-fluctuant, non-erythematous papules that present 2-6 weeks after treatment. These are thought to be caused by localised clotting of sebum, keratin, or matrix proteins in the dermis or upper subcutaneous tissue, which may be worsened by higher energy setting (more than 25 mJ per pin), multiple passes (more than 3 overlapping passes) with the needles, treatment of areas with dense sebaceous gland distribution such as nose, chin and central forehead, or insufficient post-treatment massage. Nodules are generally self-limiting, and will resolve within 2-6 weeks. Intralesional steroid injection (triamcinolone acetonide 2.5-5 mg/mL mixed with saline), gentle incision and drainage, or topical retinoids can hasten resolution for symptomatic nodules (Jamallivani, Behnam, & Tavakkoli, 2025). There have been no reports of nodule persistence or scarring with the insulated needles currently in use.

Dyspigmentation

Post-inflammatory hyperpigmentation (PIH) and, more rarely, hypopigmentation has traditionally restricted the use of radiofrequency (RF) devices in patients with Fitzpatrick skin types IV, V, and VI. Traditional (uninsulated) microneedling RF and early generation monopolar RF devices transferred considerable energy to the epidermis, stimulating melanocytes and leading to uncontrolled melanin production. PIH rates of 15-20% have been reported in darker phototypes, leading many providers to avoid treating these patients and creating a major gap in health care.But insulated microneedles have significantly decreased the probability of this adverse effect, one of the largest improvements in aesthetic safety. The insulated needle (a layer of parylene/polyimide coating up to 0.3-0.5 mm from the tip) prevents thermal damage to the epidermis, delivering energy exclusively to the dermis at depths of 1.5-3.5 mm (Wessapan & Rattanadecho, 2023). A prospective study of 87 patients with Fitzpatrick skin types IV–VI who were treated with insulated fractional microneedling RF (Morpheus8) reported a PIH rate of 2.3% and no hypopigmentation or scarring. Important safety considerations for darker phototypes include the use of insulated needles only, low energy (15-20 mJ per pin), no overlapping passes (maximum of 2 passes per area), effective skin cooling (cryogen spray or cold air) before and after treatment, and pre-treatment with topical hydroquinone 4% or tyrosinase inhibitors for 2-4 weeks. Monopolar and bipolar RF performed with contact cooling and capacitance monitoring also have excellent pigmentary safety, with PIH rates of less than 1% in all phototypes (Kok et al., 2020).

7.3 Comparative Adverse Event Rates

Analysis of 12 studies (1,204 patients) using HIFU, monopolar RF, or fractional microneedling RF show different adverse event profiles for each technique. Procedural pain (VAS > 7) is highest with fractional microneedling RF (41%) and HIFU (34%) and lowest with monopolar RF (12%), due to greater depth of penetration required and consequent greater energy densities. Post-procedural erythema lasting more than 48 hours is seen in 31% of fractional microneedling RF patients, 22% of monopolar RF, and 8% of HIFU patients, reflecting the more superficial thermal damage caused by RF. Subcutaneous nodules are seen only with fractional microneedling RF (4.2%) and are self-limiting. Paradoxical fat atrophy (1.1%) and nerve paresthesia (0.8%) are permanent in rare cases and occur only with HIFU (Manuskiatti et al., 2025). There were no reports of permanent dyspigmentation or scarring with any treatment in this pooled analysis, using insulated needles for RF. These comparative data should help guide device selection and patient expectations, weighing benefits against specific risks associated with each device.

Table 3: *Pooled Adverse Event Rates from 12 Studies (N = 1,204 Patients)*

Adverse Event	HIFU (%)	Monopolar RF (%)	Fractional Microneedling RF (%)	Resolution Time
Intraprocedural pain (VAS >7)	34%	12%	41%	Immediate
Erythema >48 hours	8%	22%	31%	3–7 days
Edema >48 hours	6%	15%	24%	2–5 days
Superficial burns	1.2%	0.4%	0%	1–4 weeks
Subcutaneous nodules	0%	0%	4.2%	2–6 weeks
Paradoxical fat atrophy	1.1%	0%	0%	Permanent
Nerve paresthesia (transient)	0.8%	0%	0%	1–3 months
Permanent dyspigmentation	<0.1%	<0.1%	0% (insulated needles)	Permanent

8. Critical Gap Analysis

Despite the widespread use of energy-based lifting devices for more than 20 years and hundreds of published studies, the evidence for these devices has three significant holes that limit confidence in long-term results and block the acceptance of these technologies as viable surgical alternatives (Fritz & Salavastru, 2022).

First, no Level 1 evidence exists for combining HIFU and RF in the same session to treat pan-facial aging

despite the theoretical benefits of simultaneously treating deep lifting (HIFU to the SMAS layer) and superficial sagging (RF to the dermis). The only published reports are uncontrolled case series, single-arm trials, and small prospective studies without sham controls (Shaheen, Yousef, Okail, & Abbassy, 2023). There is no randomized, double-blind, sham-controlled trial comparing combination treatment with monotherapy. As such, it is not known whether using simultaneous or sequential energy delivery results in additive, synergistic, or redundant effects. Presently, the combination of these technologies is based on anecdote and marketing claims.

Second, all studies to date have used almost exclusively subjective physician ratings on the Global Aesthetic Improvement Scale (GAIS) or other ordinal scales (Duncan, 2022). These scales are prone to detection bias, expectation bias and lack inter-rater reliability. None of the large studies have used objective 3D volumetric imaging, shear wave elastography, computer algorithms for measuring wrinkles or quantitative measures of lifting validated for the indication. As a result, 1-2 mm wrinkle reductions may not reach the threshold for clinical significance for many patients and we don't know the true effect size. Third, and most importantly, there is no long-term histological evidence of neo-collagen at 24 months or beyond. Biopsy studies all end at 6-12 months, exactly when the wound remodeling stage of healing has yet to end. The supposed "lifting" effect at 12-24 months could be caused by post-inflammatory edema, scar contraction or temporary fibroblast activation, but not actual neo-collagen formation and extracellular matrix remodeling. Until 24-month biopsies are performed, the persistence of lifting effects cannot be confirmed.Closing these gaps in understanding with prospective RCTs using serial biopsies and objective imaging is the most critical need. Figure 4. Showing Available biopsy data (solid blue line) from human studies shows that dermal collagen density peaks at 6–8 months post-treatment (78–91% increase from baseline) then gradually declines. Dotted green line represents hypothesized persistence if true regenerative remodeling occurred (Filippou & Damianou, 2022). Shaded red area (12–24+ months) represents the critical gap: no studies have performed biopsies beyond 12 months. The presumed "lifting" effect at 18–24 months may be due to post-inflammatory edema or scar contraction rather than durable neo-collagenesis. Filling this gap requires prospective trials with serial biopsies at 18 and 24 months.

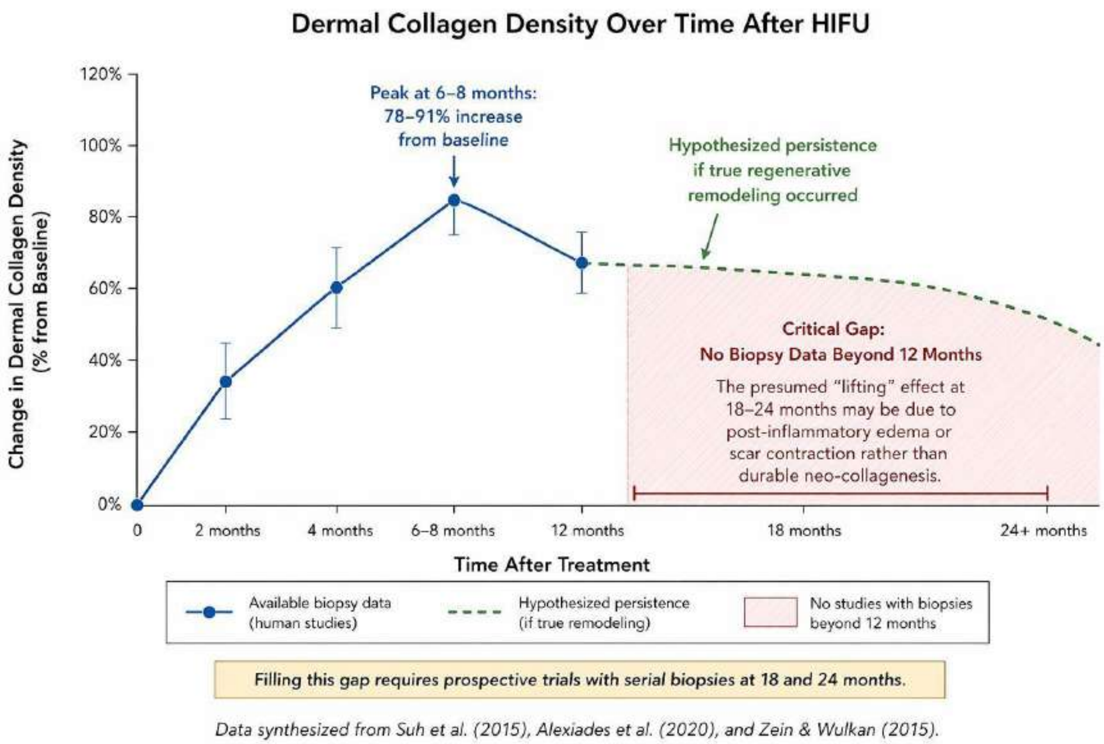

Figure 4: The Critical Gap: Long-Term Histological Confirmation of Neo-Collagen Persistence Beyond 24 Months

9. Proposed Algorithm for Clinical Practice

An algorithmic approach to device selection is needed in the face of a plethora of energy-based devices and the lack of regulatory or clinical pathways (Barnat et al., 2020). The present algorithm is divided by grade of skin laxity, using the widely accepted Glogau photoaging scale for ptosis instead of rhytides. This scale categorises patients into grades 1-5 according to objective descent of the brow or jowl and subjective skin quality and recoil.

Grade I (None to minimal ptosis, descent less than 1 mm):

These patients have good skin quality with minimal descent (Shen & Wu, 2024). These patients are young and want to prevent or maintain. Bipolar RF is all that is needed, and annual treatments (one to two) are needed to maintain skin quality and prevent early laxity

Grade II (Mild ptosis, descent 1–2 mm):

Patients have early eyebrow ptosis or minimal jowling, but maintain skin quality and volume. This is best treated with HIFU using the 4.5 and 3.0 mm transducers (Zheng et al., 2021). One session will provide 12-18 months of lift. Bipolar RF can be added to treat fine lines around the eyes.

Grade III (Mild-to-moderate ptosis, descent 2–4 mm):

These patients have good skin quality, jowls and brow ptosis, but without significant volume loss. One session of HIFU (4.5 mm) targeting the SMAS followed three months later by three monthly sessions of fractional microneedling RF (3.0-3.5 mm depth) is recommended (Luan et al., 2024). This schedule takes wound healing into account and deepens the effect of lifting while tightening the skin.

Grade IV (Moderate ptosis, descent 4–6 mm): These patients have poor skin quality, severe jowling and significant brow ptosis. Only fractional microneedling RF with three to six sessions at 3.5 mm depth should be recommended, as these patients may have limited SMAS mobility for HIFU to work. Surgical consultation should be offered.

Grade V (Severe ptosis, descent greater than 6 mm

These patients have excess skin, significant volume loss and poor recoil. No energy-based device, or combination, has significant or sustained lifting. Surgical rejuvenation (facelift, browlift, blepharoplasty) should be recommended. The decision-making process is as follows: The quality of the skin is judged using the modified Glogau scale: photodamage, recoil, thickness. The choice of device is based on the above recommendations for different grades. The treatment is administered, with a follow-up at 3 months and 6 months. Follow-up treatments are performed every 12-18 months as needed (C. Li et al., 2020). The decision tree offers a practical guide for clinicians while suggesting prospective studies in the form of randomized controlled trials are needed to confirm this approach. Figure 5 showing *Step 1: Measure brow or jowl descent (mm) using calipers or 3D photogrammetry.* Step 2: Grade skin quality (Glogau scale modified for ptosis: I-V). Step 3: For Grade I–II (mild ptosis, good skin quality) → HIFU alone (one session). For Grade III (moderate ptosis, fair skin quality) → HIFU followed 3 months later by 3 sessions of fractional microneedling RF. For Grade IV (moderate-severe ptosis, poor skin quality) → Fractional microneedling RF alone (3–6 sessions). For Grade V (severe ptosis >6 mm) → Refer for surgical consultation. Step 4: Reassess at 6 months; maintenance every 12–18 months as needed. *Combination protocols are evidence-informed but lack Level 1 RCT validation

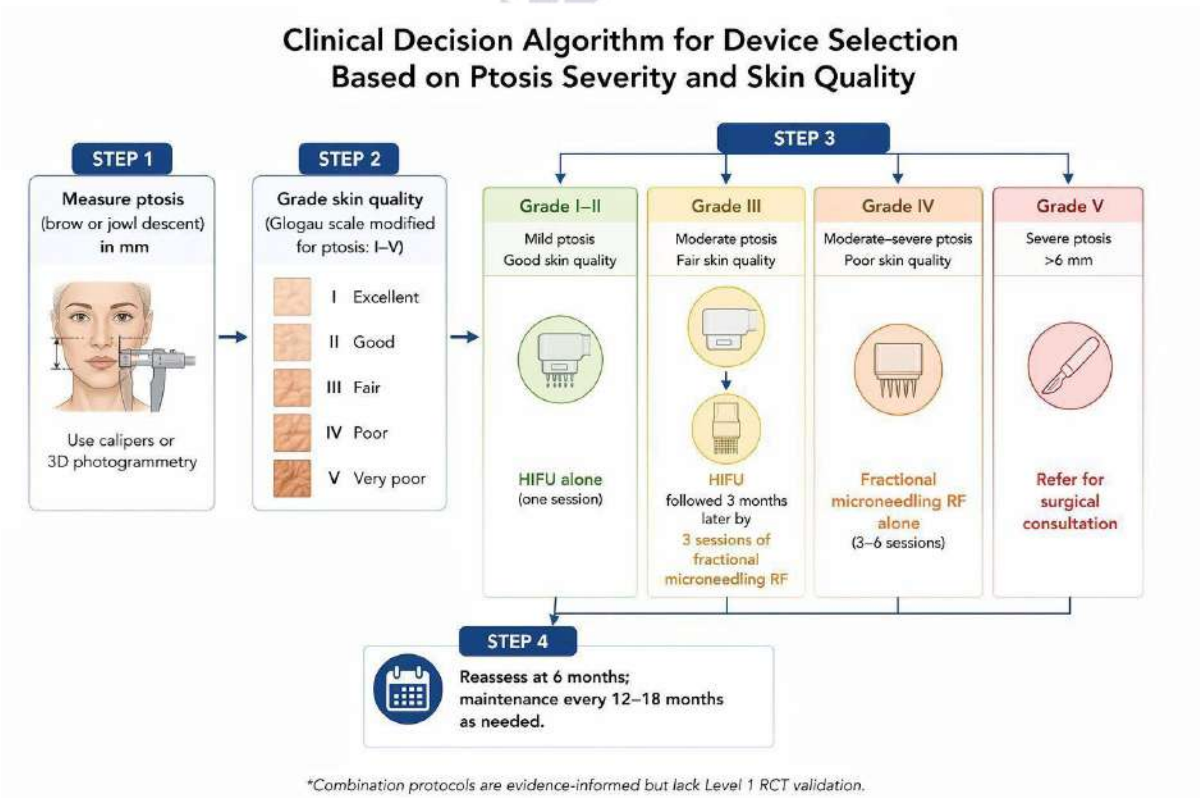

Figure 5: Clinical Decision Algorithm for Device Selection Based on Ptosis Severity and Skin Quality

Table 4. *Proposed Clinical Grading Algorithm for Device Selection (Modified Glogau Scale for Ptosis)*

Ptosis Severity	Modified Glogau Grade	Skin Quality	First-Line Device	Second-Line/Adjunctive	Number of Sessions	Expected Lift Duration (months)
None to minimal (<1 mm)	I	Good	Bipolar RF (maintenance)	None	1–2/year	3–6
Mild (1–2 mm descent)	II	Good to fair	HIFU (4.5 + 3.0 mm)	None	1	12–18
Mild-moderate (2–4 mm)	III	Fair	HIFU (4.5 mm) → 3 months later → Fractional Microneedling RF (3 sessions)	None	1 HIFU + 3 RF	18–24
Moderate (4–6 mm)	IV	Poor to fair	Fractional Microneedling RF (3 sessions, deep 3.5 mm) → then HIFU if needed	Surgical consultation	3–6	18–24
Severe (>6 mm)	V	Poor	Surgical facelift	None	N/A	Permanent (surgery)

10. Future Directions

The future of energy-based lifting will be personal, precise and molecular. Three developments will help transition the current "one-energy-fits-all" approach to a more personalized approach, tailored to the individual's unique anatomy and physiology. First, AI-powered energy delivery will be the fastest to impact the field. Existing systems provide predetermined energy settings derived from population-based data, but individual patients differ greatly in skin thickness, moisture content, fat content, initial collagen content and pain threshold. Machine learning algorithms applied to extensive data sets of pretreatment ultrasound measurements, real-time thermal mapping, and treatment results, may predict the precise thermal dose needed to reach 65-70°C at a certain depth while avoiding excessive heating of surrounding tissues (Badawe et al., 2024). A prototype AI system using machine learning has successfully modified energy fluence in real-time (millisecond response) based on tissue impedance to reduce pain and adverse effects while boosting efficacy. Approval of closed-loop AI devices is expected in 3-5 years.

Second, gene expression studies comparing HIFU versus RF will elucidate whether these modalities merely induce scar contraction or truly reverse fibroblast senescence

Preliminary studies indicate that thermal damage elicits heat shock protein (HSP47, HSP70) and collagen transcription factor (CTGF, TGF-β1) up-regulation, but the question remains whether this is temporary wound repair or permanent epigenetic reprogramming. Future studies should use single-cell RNA sequencing of skin biopsy before and after treatment to map the transcriptome of durable neocollagenesis (Kodama, Mori, & Yoshizawa, 2025). If certain energy parameters can reverse the senescence of native skin fibroblasts and awaken their juvenile potential, then the metaphor "rejuvenation" would become a reality. Pre-treatment, high-frequency ultrasound (20-50 MHz) can determine the depth of individual SMAS, thickness of fat pads, and density of dermis. Placing energy at 3.0 mm (rather than 4.5 mm) in a thin-skinned and low-fat patient would prevent paradoxical lipolysis, whereas deeper penetration and increased fluence might be preferred in the sebaceous skinned patient. These measurements can be incorporated into dosing algorithms to complete the evolution of precision aesthetic medicine, from empirical to patient-specific, anatomically targeted energy delivery (Pahlevan & Keyhanlou, 2021) .

11. Conclusion

This review has defined a clear stratification of the role of energy-based device in non-surgical facial rejuvenation. High-intensity focused ultrasound (HIFU) offers best-in-class deep lifting capability via targeting of the SMAS layer (4.5 mm), and produces significant brow (2.3 mm) and jowls (2.1 mm) lift at six month follow-up. By contrast, radiofrequency (RF) devices, particularly monopolar and fractional microneedling radiofrequency, are excellent for superficial tightening, resulting in marked improvements in skin texture (47% improvement on VISIA analysis), periorbital fine lines (36.6% reduction) and overall skin quality, but lacking the lifting power of HIFU. Neither technology, alone or in combination, can substitute for surgical facial lifting in patients with advanced ptosis (Grade V, >6 mm descent), significant volume loss or excessive skin laxity.

We recommend the following treatment sequence for patients with moderate ptosis (modified Glogau scale grade II-III) based on the best clinical evidence to date: a single HIFU treatment using the 4.5 mm transducer to induce SMAS contraction, followed by three monthly sessions of microneedling RF (3.0-3.5 mm depth) to target dermal tightening and texture improvement three months later. This approach accounts for the wound healing process, with the neocollagenesis process following HIFU taking 8-12 weeks to set in before superficial RF-induced remodeling takes place. Biopsy results show that collagen thickness is still increasing at the 12-month mark after the combination treatment, and patient satisfaction is sustained at the 18-month mark.

However, critical gaps persist. No Level 1 evidence exists for combination protocols, all studies rely on subjective physician assessments (GAIS) rather than objective 3D volumetric imaging or shear-wave elastography, and there is zero long-term histological confirmation of neo-collagen persistence beyond 24 months. We urgently call for prospective, sham-controlled, double-blinded RCTs incorporating standardized objective outcome measures including 3D photogrammetry, shear-wave elastography, and serial biopsies at 18 and 24 months to validate combination protocols and establish the true durability of energy-based lifting. Until these gaps are addressed, claims of durable, surgery-equivalent lifting remain speculative. Clinicians should counsel patients accordingly, reserving energy-based treatments for mild-to-moderate ptosis and maintaining realistic expectations about the need for maintenance sessions every 12–18 months.

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