Study Book

EMFACE®


EMFACE


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Simultaneous Emission of Synchronized Radiofrequency and HIFES™ for Non-invasive Facial Rejuvenation

A unique combination of RF and HIFES

Facial aging is a complex process resulting not only from skin aging but also from changes in the volume and density of the underlying structures, including the fascial system, facial ligaments, and facial muscles.[1] EMFACE is the first device in the non-invasive facial aesthetic segment that utilizes the simultaneous application of Synchronized RF and HIFES technology to treat multiple facial layers simultaneously.

EMFACE effect on facial skin

The loss of the amount of elastin and collagen and quality impairment of the remaining fibers contribute to the worsening of skin quality and skin aging.[2] EMFACE uses unique Synchronized RF along with the real-time impedance-based system to quickly heat the skin tissue to 40-42°C[3], the temperature needed to stimulate an increase in fibroblast activity, leading to an increased synthesis of new collagen and elastin fibers.[4] In addition, the old collagen and elastin fibers decompose and denature and are rebuilt again.[4]

Clinical studies on EMFACE focusing on structural changes demonstrated a prominent skin remodeling effect. These studies found that collagen increase ranged between 26 - 27% and elastin increase ranged between 110-129% two to three months following the procedure.[3,5] Additional study[6] investigating changes in skin texture and facial appearance reported a 36.8% wrinkle reduction and 25.3% skin evenness improvement three months post procedure.

Although Synchronized RF heating ensures skin texture improvement, treating only textural concerns is not enough. As we age, facial tissue becomes saggy due to changes in the facial musculature and laxity in the connective tissue. Therefore, it is necessary to target the underlying structures to achieve a more youthful appearance.

EMFACE effect on facial muscles

To achieve a complete and more targeted approach to treating all facial layers, the EMFACE utilizes HIFES technology, specifically designed to target the small delicate facial muscles. Facial muscles undergo atrophy and loss of muscular tone due to aging, similarly to the skeletal muscle, and also due to the long-term use of neurotoxins.[7,8]

HIFES technology selectively induces supramaximal contractions in the facial elevator muscles. The intense contractions are strong stimuli that trigger a tissue response leading to promotion of muscle protein synthesis[9,10] and to myofiber renewal[11]. Such processes lead to structural remodeling of the targeted muscles, which has been seen in EMFACE study[12] showing 19.2% increase in muscle density and 21.2% increase in number of myonuclei, which provide the muscle with nutrition. These results were coupled with reduced fibrotic and fat infiltration within the muscle tissue at two months post-procedure.

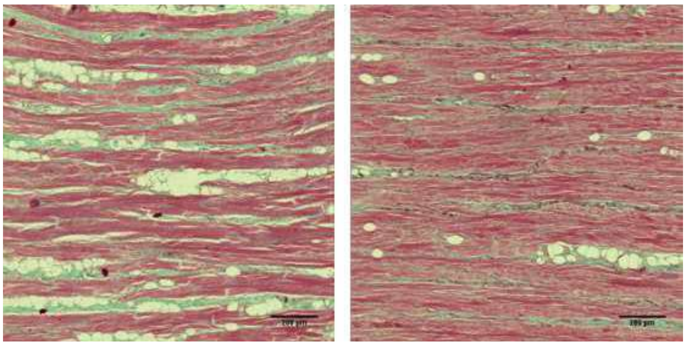

Figure 1: Histologic images of muscle tissues before (left panel) and 2 months after (right panel) the treatment with the EMFACE device.

The structural changes do manifest as increased resting muscular tone, which is necessary for maintaining the lifted facial appearance. The weaker the facial muscles are, the higher muscle effort is needed to avoid sagging and to hold the overlying tissues in place.[13] When being too weak, they become unable to hold the tissue, resulting in e.g. eyebrow drop or cheek sagging. When the resting muscle tone is increased, the muscles have the strength large enough to hold the overlying tissue in place without dropping and without the need to stay contracted.[13] EMFACE was found to increase the muscle tone by 30%[14] which was then shown to lead to an overall lifting effect by 23.1%.[6]

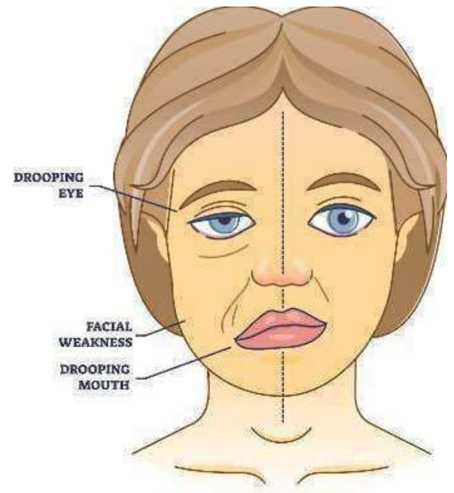

Figure 2: Visualization of the effect caused by weakened facial muscles on the left in comparison to healthy muscles on the right.

The synergy of RF and HIFES

The expression of HSP or SC is higher when the muscle is exposed to the simultaneous delivery of heating of around 40°C and supramaximal contractions compared to individual or consecutive energy applications.[15,16] This simultaneous delivery induces a strong signal, which is followed by a stronger response in the skin, muscle and fascial tissue, leading to more pronounced structural remodeling. [9,10,17-19]

Aside from the muscle and skin tissues, the EMFACE also affects the subdermal connective tissue. The facial fascial framework is largely composed of elastin, collagen, and connective tissue, and their degradation is part of the aging process. Synchronized RF heating with EMFACE may support the fascial framework via collagen and elastin remodeling, similar to what has been documented in previous skin tissue studies. In addition, the fascial support structures have also been found responsive to mechanical stimuli, which in case of EMFACE is delivered with HIFES stimulation.[20] The combination of both the heating and mechanical stress on the fascial support structures may lead to fascial remodeling, leading to increased fascial tightness and elasticity.[20]

Clinical effects

Due to the unique design and energy delivery, EMFACE applicators do not induce the stimulation of the depressors since the stimulation of the depressors could potentially lead to a worsening of rhytides. The forehead application targets the frontalis muscle (brow elevator) and corresponding fascias while avoiding the depressors in the glabella. Restoring the tonus of the frontalis muscle and tightening the fascias in combination with the skin remodeling leads to reduced horizontal forehead lines, brow elevation, and skin texture improvement.

The cheek application primarily targets the more superficial muscles of the cheeks (zygomaticus major/minor & risorius), which are all interconnected elevating units. In contrast, other deeper muscles, such as masseter m. are unaffected. Stimulation of these superficial muscles leads to an elevation of the entire cheek, increasing the midfacial volume and improving the nasolabial fold. Increasing the pull of these elevators further leads to a repositioning not only of the midface but of the lower facial soft tissues. The resulting clinical effect is a reduction in jowls and an increase in jawline contouring. The combined effect of HIFES with Synchronized RF manifests as an overall textural improvement of the skin.

Concluding comments

EMFACE uses Synchronized RF and HIFES energies simultaneously to target all facial layers; skin, fascia, connective tissue framework, and facial muscles to achieve full-face aesthetic remodeling. Affecting all these layers in a noninvasive manner leads to a textural improvement of the skin, wrinkle reduction, and an overall lifting effect visible in the cheeks and the forehead. Aside from multiple clinical studies using various evaluation methods, the results of the procedure are supported by a high patient satisfaction rate of 91.2%[21].

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The mechanism of EMFACE stimulation of muscle after the application of botulinum based neurotoxin

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***Abstract* — EMFACE is a new device that induces supramaximal muscle contractions of delicate facial muscles while heating the skin and underlying tissues. However, many EMFACE patients are users of botulinum based neurotoxins that are used to immobilize facial muscles in order to prevent repetitive skin folding. As such, facial muscles of these patients should not be contrated during EMFACE treatments. However, clinical studies have shown that it is possible to induce contractions of these muscles by external stimulation such as during EMAFCE. However, the mechanism of how it is possible is not entirely known.**

Keywords—Botulinum toxin, BOTOX, HIFES, EMFACE, Stimulation, Facial, Muscle

I. INTRODUCTION

Neuromodulators in aesthetic medicine, such as Botox, Dysport, Xeomin or Jeuveau have become the most frequently sought nonsurgical aesthetic procedure[1]. Type A botulinum-based neurotoxins have a myriad of clinical indications[2]. They are most frequently utilized to treat dynamic facial rhytides[3] involving the glabella, frontalis and periocular regions. Botulinum neurotoxins block neurotransmitter release in the synaptic neuromuscular junction to block voluntary muscle contraction. With blocked contractions, wrinkle formation is prevented as the overlying skin is not being repetitively folded during daily activities and thus aids in maintaining a more youthful skin appearance.[4,5] By decreasing the contraction strength of some facial depressor muscles, there is temporary increased tone of elevating facial muscles. There are also secondary effects such as reduction in erythema which may allow greater light reflection.

Recently, a novel device EMFACE was introduced to stimulate botulinum neurotoxin-blocked muscles to prevent muscle atrophy. EMFACE is able to stimulate the blocked facial muscle even though it is not possible voluntarily. In fact, the use of external stimulation on neurotoxin-blocked muscles has already been documented in multiple studies [6,7], however, the mechanism of how it is possible is not exactly known.

Although it is not entirely clear, all these suggest that external stimulation has the ability to bypass the effect of botulinum neurotoxins. The goal of this paper is to summarize existing knowledge on the topic and provide a viable hypothesis that could explain why such an effect is demonstrated during an EMFACE treatment.

II. THE PHYSIOLOGY OF MUSCLE CONTRACTION

To better understand the effect of botulinum neurotoxin, it is necessary to first explain the standard function of the neuromuscular junction and muscle contraction. The neuromuscular junction is responsible for the chemical transmission of an electrical impulse from the nerve to the muscle, to produce a muscle contraction. When a nerve impulse in the form of action potential reaches a nerve ending, voltage-gated calcium (Ca2+) channels are activated, which causes an influx of Ca2+ ions into the presynaptic neuron from the extracellular space. In the presynaptic neuron, the calcium cations interact with synaptic vesicles and enable their association with the presynaptic membrane. After the fusion of synaptic vesicles with presynaptic membrane, the content of the vesicles – neurotransmitter acetylcholine (Ach) is released into the synaptic cleft - quantal release.[8]

Under normal conditions, the released Ach transmits the electrical signal to the muscle fiber by depolarizing the muscle fiber membrane. Depolarized muscle membrane activates sarcoplasmic reticulum where Ca+ ions are stored and releases them.[8] The presence of the Ca+ ions in the muscle fiber results in a sliding process between actin and myosin filaments which slide alongside each other resulting in muscle contraction. The muscle contraction lasts as long as the Ca+ ions are present in the muscle fiber, however, Ca+ ions are quickly (fraction of second) returned into the sarcoplasmic reticulum unless there is another action potential that again increases the level of Ca+ ions or keeps it at the same level.[8] The collective shortening of the sarcomeres is the molecular mechanism behind a muscular contraction.[9]

III. THE EFFECT OF BOTULINUM NEUROTOXIN

Botulinum based neurotoxin is affecting the process of muscular contraction at the level of neuromuscular junction. When applied, it works as a protease and prevents the fusion of the vesicles with the presynaptic membrane[10]. Without this fusion, the Ach cannot be released into the neuromuscular junction and trigger the muscle contraction as described above. It is a chemical denervation that causes partial paralysis of the innervated muscle. However, such paralysis is not causing any damage to the nerve or the neuromuscular junction and is not permanent[11].

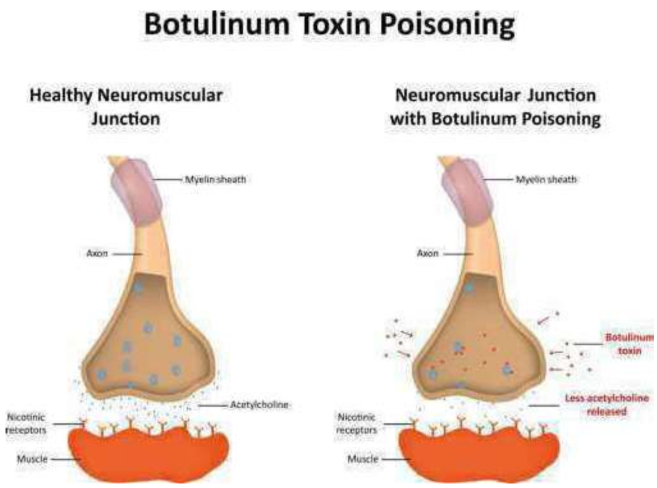

Figure 1: Botulinum toxin blocks the release of acetylcholine to neuromuscular junction, which does not allow the signal transmission into the muscle and thus blocks the muscle contraction.

IV. External stimulation of botulinum-paralysed muscle

There are two approaches to induce muscle contraction externally. First, muscles can be stimulated by applying an external electrical field to the muscle innervating neuron, where it induces an action potential, which is then carried to the neuromuscular junction.[12] Muscle can also be stimulated directly, as the muscle itself is an electrically excitable tissue.[13] If the muscle is stimulated through the neuron and, the whole muscle or all muscles innervated by this neuron are stimulated and contracted. With direct stimulation of the muscle tissue, only those muscle fibers in the electrical field are affected and a high stimulation intensity is needed to induce such contraction.[14] To contract the entire muscle by direct stimulation of the muscular tissue, a critical number of muscle fibers must be recruited.[13]

Multiple studies have shown it is possible to stimulate even the botulinum-paralysed muscles [7,15]. However, it is not entirely clear how such stimulation overcomes the barrier made by the botulinum neurotoxin. Upon the application of botulinum toxin, the membrane of the presynaptic neuron should be practically impermeable to Ach molecule due to its size as the the fusion of vesicles and presynaptic membrane ("quantal release") is blocked. Yet, the clinical trials are showing that externally it is possible to overcome this barrier and although the mechanism of how this happens is not entirely clear, several hypotheses were proposed to explain such mechanism:

Non-quantal Ach release

One of the possible explanations could be the non-quantal Ach release. It has been shown that aside from the above-described quantal release of Ach, also a non-quantal release occurs at the neuromuscular junction[16].

Non-quantal Ach release was proposed to be caused by the high-affinity choline transporter, which under normal physiological conditions returns the inactivated Ach (choline) from the synaptic cleft back to the nerve ending. Experimental findings indicate that this transporter may also transport the Ach to the neuromuscular junction. Its activity appears to be dependent on the concentration of calcium in the cytoplasm, which correlates with the firing rate of the neuron (number of induced action potentials)[16–18]. Considering that maximum firing rate of a neuron during voluntary muscle contractions reaches up to 25 Hz[19], while with external stimulation it is possible to induce firing rates in the order of hundreds of Hz, it could be assumed, that with an increased firing rate frequency, also the cytoplasmic calcium concentration increases, thus also increasing the level non-quantal Ach release.

Based on such findings, it could be hypothesized that such a non-quantal release of small amounts of Ach into the synapse still occurs, even in botulinum toxin denervated muscle. However, during voluntary contractions, the amount of the Ach is not sufficient to cause depolarization and the muscles thus remain relaxed. By applying an external high-frequency electrical field that surpasses the frequency of brain signals, the activity of the high-affinity choline transporter could be elevated, leading to exaggerated non-quantal release of Ach in amounts sufficient enough to cause muscle depolarization and contraction.

Additionally, a long-term insufficient concentration of Ach in the synapse, due to the application of botulinum toxin can lead to an increased expression of n-acetylcholine receptor (nAChR) on the postsynaptic membrane and therefore also to increase in the sensitivity of the muscle to Ach [20,21]. A lower amount of Ach would thus be needed to induce such depolarization.

Direct stimulation of the muscle fiber membrane

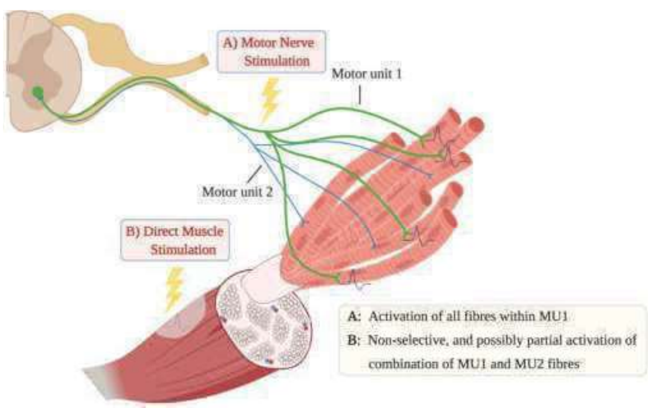

Figure 2: The principle of direct muscle stimulation vs. motor nerve stimulation. With nerve stimulation, the nerve is stimulated and signal propagates towards the muscle, while with direct stimulation the muscle fiber is stimulated directly. Image adopted from Guo et al.[22]

Another possible explanation for the externally induced contraction of botulinum-denervated muscles could be via the direct stimulation of the postsynaptic membrane. The external electrical field could possibly induce action potential directly on the muscle fiber membrane and thus trigger the influx of Ca+ ions into the muscle fiber to contract the muscle.

Nevertheless, multiple studies contradict such hypothesis. Studies investigating the use of external stimulation of muscles fully denervated by physical transection showed that very high intensity (pulses in ms) is needed to depolarize the muscle fiber membrane and induce contractions of these muscles directly, while EMFACE uses lower energy pulses in µs.[23,24] Furthermore, with direct muscle fiber membrane stimulation it is difficult to stimulate the entire muscle, rather it has been shown to stimulate only a portion of the muscle, while with EMFACE the entire muscles are contracted.

However, all these conclusions regarding the direct muscle stimulation are based on studies performed on skeletal muscles only. Facial muscles are of significantly different proportion and are much more superficial located in low depths of 3-8 mm[25]. All this may influence the response. As the facial muscles are more delicate, lower intensity may suffice to irritate the muscle membrane. Since the thickness of some facial muscles may be as small as 0.5mm[26], it may be possible that such stimulation is able to recruit enough muscle fibers to induce contraction of the entire muscle. In addition, this could actually explain the non-stimulation of the masseter muscle during the EMFACE treatment. In the vast majority of patients the masseter is not stimulated and it could be explained by the fact that the neuronal branch innervating the muscle is not in the application field, but also by the fact that masseter muscle is one of the largest facial muscles with thickness of up to 3.5mm[27] and during the treatment not enough muscle fibers are recruited to induce full masseter activation.

V. Summary & Conclusion

It is clear that it's possible to externally stimulate botulinum-denervated muscles, yet, the underlying mechanism is not. Current paper proposes a possible explanation of this phenomenon based on the existing knowledge of the processes on the neuromuscular junction and muscle contraction. However, multiple different factors may play a role in the mechanism. More experimental studies are needed to fully understand why it is possible to externally stimulate the botulinum-paralysed muscles.

In regard to EMFACE specifically, a study by Chilukuri et al.[28] showed that during the EMFACE treatment the botulinum-denervated muscles are being contracted and what is most important, the EMFACE treatment does not interfere with the effect of botulinum toxin itself. No negative effects of the EMFACE stimulation on the efficacy of the botulinum toxin were found.

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Simultaneous Emission of Synchronized Radiofrequency and HIFES for Non-invasive Facial Rejuvenation:

The Mechanism of Action

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Abstract

EMFACE is a unique device specifically developed for non-invasive face lifting and wrinkle reduction by targeting all facial layers; skin, connective tissue framework, and facial muscles. It utilizes both Synchronized RF and HIFES technologies simultaneously. Heating the facial tissue to effective temperatures and HIFES stimulation of only specific facial muscles results in a combined effect that causes textural changes to the skin, smoothing, wrinkle reduction, facial repositioning, and an overall lifting effect. The simultaneous and targeted manner of both technologies yields unique benefits by inducing a synergistic effect in the facial soft tissues that cannot be achieved by using these technologies consecutively or as a standalone procedure.

Keywords: HIFES, Radiofrequency, Simultaneous, Application, Supramaximal, Contraction, Muscle, Fat, Reduction, Hypertrophy, Face, Lift

Introduction

Facial aging is a continuous and unstoppable process resulting from age-related changes in all structures present in the face: skin, fat, muscle, fascia, and bone.[1,2] Age-related changes of all facial soft tissues start at different decades and progress at different speeds, which vary between individuals of different gender and ethnicity. All changes together result in reduced support for the bone-overlying soft tissues, which then follow the effect of gravity. Repositioning and restructuring the affected tissues and layers is the aim of aesthetic procedures via surgical and non-surgical procedures.[1,2]

Amongst non-invasive aesthetic procedures, radiofrequency (RF) is considered the gold standard for facial skin treatment.[3] The effect of RF on the skin tissue is based on dermal heating, which leads to structural changes within the skin and the overall improvement in skin quality.[4] However, these skin heating procedures focus solely on improving skin quality and textural improvement, but not the overall facial appearance.

The overall facial appearance is not only influenced by skin quality but also by the facial volume and density of the underlying structures, including the fascial system, facial ligaments, and facial muscles. Therefore, the extent of facial laxity is a composite effect of all implicated structures of which the facial muscles and their interconnection with the skin play a fundamental role.[5]

The most frequently performed non-surgical treatment to date is the administration of soft tissue fillers, which help to restore facial volume.[6] However, soft tissue fillers only attempt to cover the aging symptoms and do not affect facial muscles, which play a crucial role in natural skin mobility.[7] Currently, the only way to alter facial muscles is through a surgical lift procedure, where the skin and fat tissues are separated from the muscle, and the muscles are then repositioned.[8]

Recently, HIFES technology has been introduced to the market to target the facial muscles and their connective tissue frameworks for lifting and tightening of the facial contours. This novel technology induces electrical fields to contract facial muscles selectively. These delicate facial muscles are crucial for supporting the facial soft tissues and play a structural role in a more youthful appearance.

EMFACE is the first device on the market utilizing the simultaneous application of both the synchronized RF and HIFES technologies for non-invasive facial lifting and wrinkle reduction. While the HIFES technology targets the muscle and overlying fascial tissue, the synchronized RF heating induces structural changes to the dermal and subdermal architecture. This approach ultimately results in an improved appearance through changes in all facial tissue layers.

The Role of Facial Muscles and Fascial Framework in Aesthetic Appearance

It is widely accepted that facial skin changes over time, with facial wrinkles being only the tip of the iceberg. Loss of structural support due to volume depletion and changes to the facial muscles and their connective tissue framework results in an increased soft tissue laxity which is additionally influenced by the effects of gravity. Facial muscles have been found to age through the process of sarcopenia, which manifests as a loss of muscle mass and volume, similar to skeletal muscles.[9,10] Since the facial muscles are interconnected via the fascial system and the overlying skin, weakening of these muscles may result in a visible descent of the tissue sagging as we age. The weaker the facial muscles are and the lower is the resting muscle tone, the higher muscle effort is needed to avoid sagging and to hold the overlying tissues in place. When being too weak, they become unable to hold the tissue, resulting in e.g. eyebrow drop or cheek sagging. When the resting muscle tone is increased, the muscles have the strength large enough to hold the overlying tissue in place without dropping and without the need to stay contracted.

Specifically, the muscles in the cheeks are interconnected by the midfacial superficial musculoaponeurotic system (SMAS).[11] Weakening of the cheek muscles, especially the zygomaticus muscles, allows for the hypothesis that as we age, the resulting facial muscle weakness can promote midfacial soft tissue descent, resulting in the increased severity of the nasolabial fold, formation of jowls, and loss of jawline contour.[12] Targeting these muscles and its surrounding connective tissue architecture might allow for midfacial soft tissue repositioning.

Also, the same muscle weakening could be expected for the frontalis muscles due to aging or long-term use of neurotoxins. The frontalis muscles are largely responsible for eyebrow movements[13]. Their connection with the skin is ensured via the supra-frontalis fascia (located superficial to the frontalis muscle) and the sub-frontalis fascia (located deep below the frontalis muscle). Aging of the forehead structures may result in eyebrow ptosis[14] and heaviness, which along with skin aging, may lead to laxity and wrinkle formation in the region.

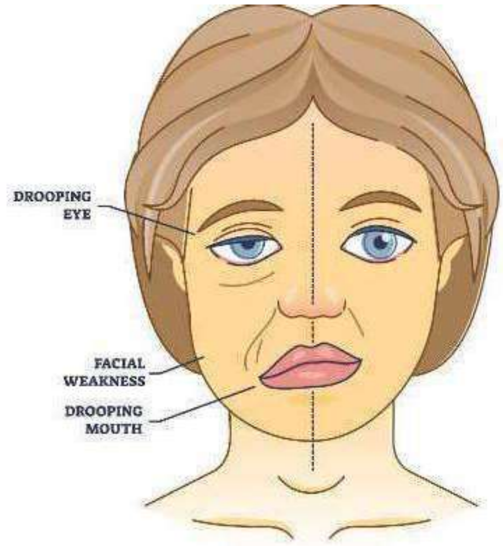

Figure 1: Visualization of the effect caused by weakened facial muscles on the left in comparison to healthy muscles on the right.

In contrast to skeletal muscles, the facial muscles are embedded in a connective tissue framework that interconnects all tissues from bone to skin. Interestingly, in addition, they are connected directly to the brain via the cranial nerves and are responsive to emotional input and the limbic system. Emotional states affect facial contours via resting tone of the muscles and the SMAS. Therefore, the facial muscles need to be seen within their connective tissue environment and addressed accordingly. Assuming that facial muscles affect skin movement alone without the support of a connective tissue environment creates an incomplete picture of facial muscle anatomy.

The combination of age-related facial changes results in an alteration of the facial shape which cannot be improved by targeting the skin alone. Therefore, more **profound treatment algorithms need to be applied to address age-related facial changes.**[15,16] This may include addressing **deeper fascial and muscle layers together**, as they have the ability to promote facial repositioning; treating the skin alone will not have such comparable effects.

How EMFACE Targets Facial Muscle and Fascial Tissues?

The Mechanism of HIFES Stimulation

Increased laxity of the overlying skin and the connective tissue framework increases the disconnect between muscular contraction and skin movement; this is more prevalent as we age. Therefore, inducing positive changes to the connective tissue and facial muscle unit will restore the connection between the layers, rejuvenating all layers, including the skin.

The EMFACE utilizes HIFES technology, specifically designed to selectively induce supramaximal contractions of small delicate muscles in the face. The technology generates strong electrical fields that affect the underlying neuronal and muscle tissue. These electrical fields depolarize the membrane of the motor neurons that innervate the muscle. When the motor neurons are depolarized, a signal is created that travels along the neuron, all the way to the neuromuscular junction - the place where the motor neuron is connected to the muscle. These signals overcome the barrier of the neuromuscular junction and progress to the muscle, which is thus forced to contract. This process bypasses the voluntary intention of the brain, inducing a forced contraction through electrical stimulation.

During each treatment, energy is applied to the facial soft tissues, and muscular contractions are induced. The HIFES technology induces up to 250 energy impulses per second (= 250 Hz), which does not allow any time for the facial muscles to relax in between the individual signals. As the muscle is unable to relax, with additional stimuli it is forced to contract even further which continuously builds up the contraction power with every additional signal. The appropriate selection of these two factors (electrical field strength and frequency) results in the so-called “supramaximal contraction”.

Although it is poorly understood how and to what extent the facial muscles adapt to external stimuli, research studies conducted in skeletal muscles have revealed that heat shock proteins (HSP) and satellite cells (SC) may be activated by intense muscle exercise as a response to the applied stimuli.[17,18] HSP are the signaling molecules playing a crucial role in muscle remodeling through the promotion of muscle protein synthesis.[19,20] SCs are muscle-derived stem cells responsible for myofiber development and renewal.[21] In a resting state, the SCs remain quiescent, ready to be activated, and provide differentiation to create new myonuclei to existing muscle fibers or generate new muscle fibers. Together, HSP and SC activation can support muscle micro-protein structure alterations. In a healthy muscle this may lead to densification of the muscle tissue and to overall improvement of the muscle quality. In atrophied muscle, the muscle structure alteration may lead to hypertrophic response reversing the atrophy. However, it is not only the muscle reacting to the signaling molecules. It has also been documented that the fascial layer remodels itself in response to heat and mechanical stimuli.[22]

Future studies will need to identify similarities between skeletal and facial muscles or provide conclusive evidence that facial muscles behave similarly or differently when targeted by external stimuli.

The Role of Synchronized RF Heating on Facial Muscles and Fascial Framework

Simultaneously with the HIFES stimulation, the EMFACE delivers Synchronized Radiofrequency that heats the facial tissue. Such stimuli affect the connective tissue framework and the facial muscle unit with consecutive adaptive changes to the overlying facial soft tissues.

According to previous studies on skeletal muscles[19,20,23–25], HSPs can also be activated by heat within the range of 40℃. Together with the muscular contractions, the heat thus may further increase the levels of released HSP[26,27], this effect has been shown in abdominal muscle [28,29], gluteal muscle [30,31], or in the muscles of the upper extremity.[29,30] A recent study by Kinney et al.[32] measured the facial muscle temperature during the treatment with the EMFACE device and showed that the temperatures in the targeted muscle tissues reached up to 40℃, indicating that a similar effect could also be seen in the facial muscles during the EMFACE treatment.

The primary effect of Synchronized RF heating on the subdermal tissues can be seen in the fascial framework. The fascial framework primarily consists of collagen and elastin, which are known to be heat responsive. Therefore, heating to adequate temperatures may induce remodeling of collagen and elastin within the fascial framework, leading to increased elasticity and tightness of the fascial web.[22]

Clinical Effect of EMFACE on Facial Muscles and Fascial Tissues

Forehead application

The EMFACE applicators are designed to target specific muscles of the face. The forehead applicator has been designed to specifically target the frontalis muscle and its surrounding connective tissue environment, composed of the supra-frontalis fascia (located superficial to frontalis muscle) and of the sub-frontalis fascia (deep to frontalis muscle), enveloping the only eyebrow elevator like a sleeping bag. The applied stimulus during the treatment with the EMFACE device affects the connective tissue framework and the facial muscle unit simultaneously, which have a soft tissue thickness in the range of 3 – 7 mm[33] for the forehead. The applied energy induces changes to the entire unit, which results in its structural alteration. A tighter fascia (sleeping bag) allows for the relaxation of the enveloped muscle, which in turn most likely reduces its baseline contractile tonus. The latter effect is clinically visible in the form of reduced horizontal forehead lines. Since the frontalis muscle is an eyebrow elevator, strengthening formerly atrophied frontalis muscle may aid with eyebrow ptosis and lead to brow elevation.

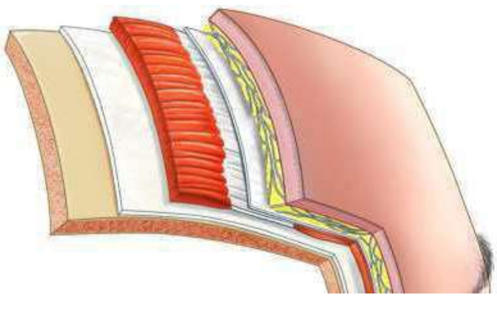

Figure 2: The frontalis muscles is enveloped by the supra-frontalis and sub-frontalis fascias. The condition of both the muscle and the fascias affects the overall appearance of forehead.

Affecting the connective tissue framework and the facial muscle unit of the forehead indirectly influences the glabellar muscles. All upper facial muscles (consisting of frontalis, procerus, corrugator supercilii, and orbicularis oculi) connect with the skin at the level of the upper margin of the eyebrow both in the midline and laterally. Affecting the frontalis m. will indirectly influence the eyebrow depressors and cause, most likely, a **change in their position** (relative to the underlying bone) by being pulled upward. Muscular contractions of the glabellar muscles are not observed during the treatment. The effect is thus indirect, only due to the supporting fascial framework, which stabilizes and guides muscular actions.

Cheek application

The cheek applicators are designed to stimulate the zygomaticus major and minor muscles and the risorius muscle.

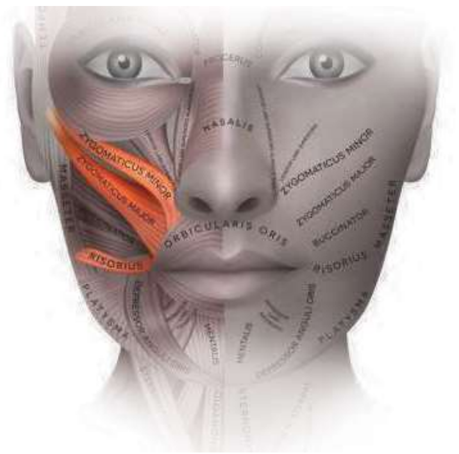

Figure 3: The cheek muscles stimulated by EMFACE cheek applicators: Zygomaticus major & minor muscles and risorius muscle.

The zygomaticus minor muscle is attached to the skin at the nasolabial fold. The zygomaticus major muscle is connected to the underlying maxilla by a connective tissue sheet termed the transverse facial septum.[34] This septum forms the inferior boundary of the midfacial fat compartment and forms a biomechanical unit with the overlying muscle. Stimulating this unit allows for conformational change of the septum, elevating the entire cheek, increasing the midfacial volume[2], and improving the nasolabial fold.[35]

Figure 4: Cadaveric dissection of the left side of the face showing the transverse facial septum connecting the zygomaticus major muscle to the maxilla. Image taken from Cotofana et al.[34]

Repositioning the midfacial soft tissues, especially the superficial fat compartments, influences the balance between total facial elevators and depressors. The platysma is the strongest facial depressor, due to its extent and fascial connection to the SMAS, the superficial temporal fascia, and the orbicularis oculi muscle. Decreasing the caudally oriented vector of the midface will shift the balance toward the zygomatic facial elevators, allowing for repositioning not only midfacial but lower facial soft tissues. The resulting clinical effect is a reduction in jowls and an increase in jawline contouring. In addition, the masseter muscle, deeper muscles of facial expression like the buccinator or levator anguli oris do not display muscular contractions during the treatment.

It is important to note, facial muscles are not expected to increase in their thickness as compared to the structural changes observed in skeletal muscle following strength training. However, these delicate muscles do keep their genetically predisposed thickness: frontalis muscle approx. 3 mm[36], zygomaticus major approx. 3.6 mm[37], and approx. 0.5 mm for the zygomaticus minor[38] and risorius muscles.[39] Future studies will need to identify similarities or differences between these muscle groups.

The effect of EMFACE on muscle structure has been investigated in a study by Kinney et al.[32], who found a 19.2% increase in muscle density and a 21.2% increase in the number of myonuclei after four EMFACE treatments. Structural changes post-EMFACE treatments were also suggested in a study by Halaas et al.[40], who used ultrasound echogenicity to evaluate muscle quality, also called muscle tone. In this study, the muscle quality increased by 30%.

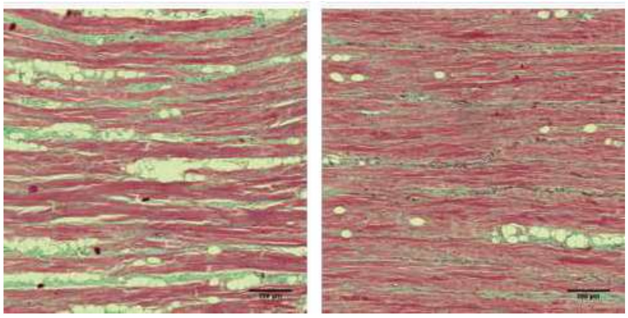

Figure 5: Histologic images of muscle tissues before (left panel) and 2 months after (right panel) the treatment with the EMFACE device[32].

Additionally, clinical studies on the EMFACE device further support the proposed mechanism of action. A clinical study by Kinney and Boyd et al.[41] investigating EMFACE found a brow lifting effect of 23.1% coupled with 91.2% patient satisfaction. In addition, a study by Halaas and Gentile et al.[42] reported a 36.8% wrinkle reduction. These studies additionally revealed that clinical changes peak at approximately 2 to 3 months post-treatment, which is in line with the time frame needed for structural changes to be implemented into the connective tissue framework and the facial muscle unit.

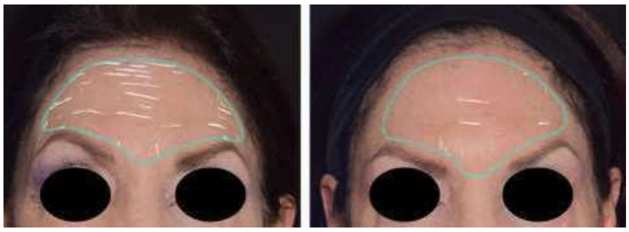

Figure 6: Example of patient results in wrinkle reduction as evaluated by automated software. Baseline on the left and 1 month after on the right. Taken from Halaas et al.[42]

The effect of EMFACE on facial skin tissue

Regarding skin, fine lines and wrinkles accompanied by loss of skin volume are usually the first indicators of skin aging, a normal physiological process influenced by genetic and hormonal changes. However, external factors also influence aging, e.g., exposure to UV radiation, skin[43,44], smoking[45], diet, air pollution[46], or chemicals and toxins.[47,48] During the skin aging process, the dermal blood vessel structure is disrupted, and in turn, the dermis is not supplied with nutrition and oxygen, thus slowing cellular regeneration.

The major building blocks of the skin are collagen and elastin fibers, responsible for skin elasticity and firmness. These components are also affected by aging. During the aging process, collagen and elastin synthesis decreases, collagen bundles lose their extensible configuration and become fragmented[48], and the elastin fiber network is degraded, leading to the loss of structural integrity of microfibrils.[49] As the extracellular matrix is degraded, skin thickness is also reduced.[50,51]

As a result of aging, collagen and elastin deficiencies are the main cause of wrinkle formation. Amount of skin collagen and elastin is deacreasing every year due to aging process. It is estimated that adult skin loses 1%[52] of overal collagen content annualy.

Effect of RF heating

RF heating is known to address aging factors within the skin effectively. EMFACE utilizes a novel Synchronized RF electrode that allows the simultaneous application of an RF field together with HIFES, which is impossible with any other RF technology. During the 20-minute treatment, the skin tissue is heated to 40-42°C. This therapeutic temperature range is reached within the first 2 minutes of the treatment, as documented by the thermal probe measurements and by thermal camera by Kent et al.[53]

Radiofrequency current flow achieves the heating through the dermal and subcutaneous tissues. As the RF current flows through the tissue, a portion of the RF energy is absorbed by the tissue, transforming the energy into heat and the desired thermal effect. The level of RF energy absorption in the tissue depends on the RF frequency[54] and tissue impedance[55], among other factors. Since the skin, muscle, and fat tissues have different impedances[56], it is possible to selectively target the energy and achieve the thermal effect only in the desired tissue(s).

When the therapeutic temperature is reached in the skin tissue for the desired time period, the hydrogen bonds tying the collagen fibers together begin to unwind, and collagen denaturation occurs. However, these temperatures do not lead to permanent damage.[57] As the tissue dissipates the mentioned thermal effect, the bonds begin to renature, and the skin's architecture is changed to a more youthful level.[57] After repeating this process during multiple treatments, the structure of older collagen and elastin fibers is changed. It begins to take on the structure similar to newly formed collagen and elastin fibers.

This thermal effect is also accompanied by a heat-induced wound healing response and increased fibroblast activity. Fibroblasts are the dermal cells responsible for producing new collagen and elastin fibers. As we age, their activity decreases to a level equivalent to an overall "net loss" of fibers. This means that the amount of newly formed fibers does not exceed the number of fibers being degraded, which accelerates the appearance of skin aging. Nevertheless, studies have shown that heat stress increases fibroblast activity, leading to an increased synthesis of collagen and elastin - neocollagenesis & neoelastogenesis.[58]

RF heating supports the skin to regain its volume, elasticity, and a more youthful appearance by restoring the collagen and elastin fiber structure and enhancing the synthesis of new collagen fibers.

Clinical studies on EMFACE, which focused on structural changes, demonstrated a prominent skin remodeling effect. The outcomes of a study performed on a porcine model by Kent et al.[53] correlated with the human histology study by Goldberg et al[59]., as both found that collagen increased by 27% and 26%, respectively. In addition, elastin was found to have doubled in the study by Kent et al.[53], while in the Goldberg study[59], the elastin levels increased by 129%.

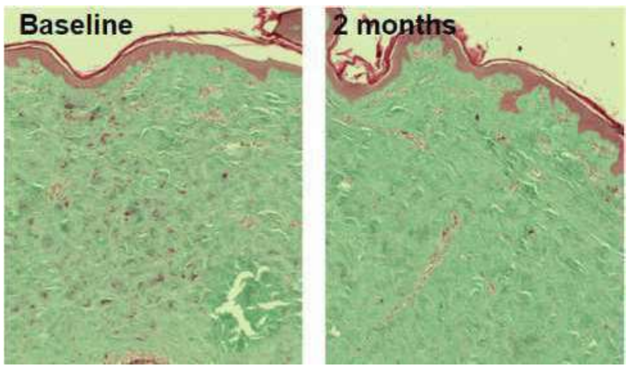

Figure 7: Densification of the collagen fiber network at 2 months post EMFACE treatment (right) in comparison to baseline (left) documented in Kent et al.

The effect on skin has also been documented in additional studies. For example, a study by Halaas and Gentile et al.[42] reported 36.8% wrinkle reduction and

25.3% skin evenness improvement. Wrinkle improvement was also reported in a study by Cohen et al.[60] Similar to the muscle studies, the skin results also peaked at 2 to 3 months post-treatment.

The Effect of EMFACE on Fat Tissue

During the treatment with EMFACE, the temperature in the fat tissue does not exceed the 43°C[61] needed for induction of an apoptotic process. Any direct effects in the fat tissue thus have not been observed.

Summary

EMFACE is a unique device specifically developed for non-invasive face lifting and wrinkle reduction by targeting all facial layers; skin, connective tissue framework, and facial muscles. It utilizes both Synchronized RF and HIFES technologies simultaneously. Heating the facial tissue to effective temperatures and HIFES stimulation of only specific facial muscles results in a combined effect that causes textural changes to the skin, smoothing, wrinkle reduction, facial repositioning, and an overall lifting effect. The simultaneous and targeted manner of both technologies yields unique benefits by inducing a synergistic effect in the facial soft tissues that cannot be achieved by using these technologies consecutively or as a standalone procedure.

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Research

Novel Technology for Facial Muscle Stimulation Combined With Synchronized Radiofrequency Induces Structural Changes in Muscles Tissue: Porcine Histology Study

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Abstract

Background: With age, facial muscles lose the ability to complete contractions properly, resulting in limitation of facial expressions and fat shifting, and leading to skin creases and wrinkling.
Objectives: The aim of this study was to determine the effects of the novel high intensity facial electromagnetic stimulation (HIFES) technology combined with synchronized radiofrequency on delicate facial muscles, using an animal porcine model.
Methods: Eight ($n = 8$, 60-80 kg) sows were divided into the active group ($n = 6$) and the control group ($n = 2$). The active group underwent four 20-minute treatments with radiofrequency (RF) and HIFES energies. The control group was not treated. Histology samples of muscle tissue were collected by a punch biopsy (6 mm in diameter) from the treatment area of each animal at baseline, 1-month, and 2-month follow-up. The evaluation included staining of the obtained tissue slices with hematoxylin and eosin and Masson's trichrome to determine the changes in muscle mass density, number of myonuclei, and muscle fibers.
Results: The active group showed muscle mass density increase (by 19.2%, $P < .001$), together with elevated numbers of myonuclei (by 21.2%, $P < .05$) and individual muscle fibers, which increased from 56.8 ± 7.1 to 68.0 ± 8.6 ($P < .001$). In the control group, no significant changes were seen in any of the studied parameters throughout the study ($P > .05$). Finally, no adverse events or side effects were observed in the treated animals.
Conclusions: The results document favorable changes after the HIFES + RF procedure at the level of the muscle tissue, which may be of great importance in terms of maintenance of facial appearance in human patients.

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Aging is a multifactorial process that affects all body structures, causing emotional distress through altering of the visual appearance and thus self-perception.[1–3] In the face, the skeleton, ligaments, muscles, adipose tissue, and skin undergo age-related changes at a different pace, however all structures interact with each other. Therefore, changes in one structure affect others.[4] Facial muscles are one of the most affected structures. Muscle changes can be promoted by age and gradually lose their mass and function after the third decade of life.[5] The imbalance between the degradation and synthesis of new muscle fibers leads to functional setbacks, recognized as sarcopenia.[6] Atrophic changes in the muscle tissue can also result from neuromodulators such as botulinum toxin type A injections.[7,8] The deconditioned muscles manifest themselves with loss of strength, disorganized sarcomere spacing, and decrease in plasma

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membrane excitability, all of which lead to decreased muscle twitch time and twitch force.[5,6] Because the facial structures are intertwined, changes in one structure can manifest themselves in other structures, and as a result of this deterioration in muscle function certain facial expressions may be limited, and changes in adjacent structures can be seen as well, such as fat shifting and skin wrinkling.[4]

Facial muscles are a type of striated muscles that (in contrast to skeletal counterparts, which facilitate movement of entire body parts) are embedded in a connective tissue framework that interconnects all tissues from bone to skin to perform facial emotional expressions and mastication.[9] Recently high-intensity focused electromagnetic (HIFEM) technology synchronized with radiofrequency (RF) has been proven to be safe and effective in muscle strengthening of the large skeletal muscle groups; however, due to the physiological differences between skeletal and facial muscles, novel high intensity facial electromagnetic stimulation (HIFES) technology with synchronized radiofrequency was developed to strengthen delicate facial muscles to combat the signs of aging.[1,10–12] Regarding muscle action, there is a substantial difference between voluntary and induced muscle contractions. The general mechanism of voluntary muscle contraction starts with a signal from the brain—an action potential. It is essentially an electrical impulse that travels through the motor neuron to the synapses (neuromuscular junction), releasing the neurotransmitter and influencing the membrane's electrical potential, causing depolarization and activation of muscle contraction, followed by the relaxation phase.[13,14] The novel HIFES technology, however, induces so-called supramaximal contractions independent of brain activity. Moreover, due to the tailored stimulation frequency, the muscle contractions are considerably intensified because the relaxation phase does not follow every single stimulus. The synchronized RF aids the effect of the HIFES field by heating the muscle tissue within a safe range of temperatures (below 42°C), activating protein synthesis and increasing the expression of heat-shock proteins, which help with muscle regeneration and growth.[15,16] Additionally, RF heating leads to neocollagenesis and neoelastinogenesis, creating firm, tightened, lifted, and smooth skin.[17]

The HIFES technology synchronized with radiofrequency has the potential to treat the vast majority of facial imperfections because it is able to target both muscle and connective tissues. However, the aim of this animal histology study is to investigate its effects and safe use on muscle remodeling, focusing on the structural organization of this tissue.

METHODS

This prospective, single-center animal study was approved by the Institutional Animal Care and Use Committee and the Ethics Committee for Animal Protection of the Ministry of Agriculture of the Czech Republic. The study was initiated in June 2021 and was completed in September 2021. It was performed in association with and supervised by a veterinary institute certified for good laboratory practice. All animals were stabled at the veterinary institute, so the veterinarian and veterinary staff handled the animal care to ensure animal welfare during the study. After performing all the planned procedures and collection of all samples, the animals were euthanized by an analgesic overdose (T61 a.u.v. inj, Intervet International B.V./MSD AH, Boxmeer, the Netherlands) administered by a veterinarian.

Animal Model and Treatment Settings

Eight large white pigs ($n = 8$ females, 60-80 kg of live weight) were utilized for this trial. Six sows ($n = 6$, active group) underwent four 20-minute treatments on the forehead once a week with simultaneous application of HIFES and RF. Two sows ($n = 2$, control group) were not treated. The control group was established to reduce the number of punch biopsies taken from the treated animals and to allow them to heal properly. In addition, all treated animals had blood tests and were examined to ensure their health and to rule out any possibility of unexpected interference with results. The treatments were delivered by noninvasive self-adhesive, hands-free EMFACE applicators (BTL Industries, Boston, MA) emitting both RF and HIFES energies and covering approximately 53 cm^2 (Figure 1). Both energies were set at 100% intensity. In addition, optical fiber sensors were inserted into the treated muscles under the applicator (LumaSense Flurotropic Thermometer; Lumasense Technologies, Santa Clara, CA) to monitor the temperature during the treatment. An infrared camera measured the skin temperature immediately after the treatments (Fluke Ti300; Fluke Corporation, Everett, WA).

During the treatment and collection of punch biopsies, the animals were kept under general anesthesia for easier manipulation and comfort. At first, the premedication for anesthesia consisting of Tiletamine + Zolazepam (Zoletil 100 Virbac; Carros, France) + Ketamine (Narketan, Vetoquinol; Lure Cedex, France) + Xylazine (Sedazine, Fort Dodge; Overland Park, KS), each medicine dosed at 2 mg/kg, was administered intramuscularly. Then, an intravascular cannula was placed into the ear's vein to infuse propofol 2% MCT/LCT (Fresenius; Bad Homburg, Germany), dosed at 1-2 mg/kg to maintain anesthesia. The animal's heart activity was monitored by electrocardiogram. A certificated veterinarian oversaw the animals during the entire treatment sessions and follow-ups, including assessment of adverse events and side effects related to the study device.

Three samples of muscle tissue per animal were collected by a punch biopsy (6 mm in diameter) taken from the treatment area on the forehead (active group) and a corresponding place on the forehead of those in the control

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Figure 1. Visualization of the self-adhesive, hands-free EMFACE applicator intended to treat the forehead area in human patients.

group. All samples were collected in the anesthetized animals before the first treatment, and at 1-month and 2-month follow-ups, to minimize the suffering of the sows. After the sampling procedure, the wound was disinfected, closed with 2 clamps, and covered with an adhesive bandage to protect the wound from infection.

Evaluation of Muscle Changes

Each muscle sample was stored in a container with 10% neutral buffered formalin (in a sample-to-fixative ratio of approximately 1:30) to preserve the tissue condition at the time of collection. The samples were then embedded in paraffin wax, sliced on the microtome, and stained with hematoxylin and eosin (H&E) and with Masson's trichrome for visualization in longitudinal and transverse cross-sections.

The hematoxylin has to be oxidized into hematein to gain staining abilities, and because it is positively charged it dyes the nucleus in a dark-blue color.[18,19] The eosin is negatively charged and stains the proteins and cytoplasm pink.[20] The staining process starts with immersing the slides in H_2O to clean the formalin and rehydrate the samples. Then, the slides are dyed with hematoxylin, rinsed, and stained with eosin. Next, the dyed sample is dehydrated with alcohol because some substances can be better dissolved. Then the alcohol is rinsed again, and the sample is mixed with a mounting medium and covered with a coverslip.[20] The muscle cells consist of myofilaments and intermediate filaments in the cytoplasm, which after H&E staining appear deep pink, with multiple nuclei dyed in dark blue color, allowing analysis of the morphology of each structure.[19,21]

Masson's trichrome staining consists of 3 dyes, a Weigert hematoxylin that stains the nucleus (dark brown), an acid stain (Ponceau–Fuschin) which stains muscle fibers (red), and a phosphotungstic acid (orange G), a decolorizing agent, which diffuses out of the collagen fiber while leaving the muscle cells stained red.[22–24] Additionally, Goldner's stain III (light green SF yellowish) dye was utilized to stain collagen fibers green and erythrocytes orange.[22,25] The staining process starts with refixing the samples in Bouin solution, which improves the quality of the stain. The slide is rinsed with tap water and stained with Weigert hematoxylin and again rinsed with tap and distilled water. Then it is dyed with an acid stain, rinsed with distilled water, immersed in phosphotungstic acid, and stained with Goldner's stain III. At this point, the sample is rinsed in distilled water and differentiated with 1% acetic acid, washed again in distilled water, dehydrated with alcohol, and cleaned with xylene. The last step is to mount the sample with a mounting medium and cover it with the coverslip.[22]

All stained slices were then visualized under a light microscope and photographed with Hitachi Axio Scan.Z1 (Carl Zeiss AG; Oberkochen, Germany) with a 20×/0.8NA Plan-Apochromat objective. The primary outcome measures included calculating muscle mass, the number of myonuclei located on the periphery of the sectioned muscle fibers, the number of muscle fibers, and the diameter of individual muscle fibers. The evaluation was performed with semiautomatic processing and analytic software ImageJ (National Institutes of Health; Bethesda, MD) in the predefined regions of interest (ROI) of 122,500 μm^2.

The descriptive statistic was calculated (mean, standard deviation) when analyzing the obtained quantitative data. To determine the statistical significance of the changes the Friedman test, followed by the Nemenyi test, for pairwise comparisons was performed. In addition, a Wilcoxon rank sum test was done to compare independent data. For all statistical analyses, the significance level of α=.05 was set.

RESULTS

All animals recovered from the anesthesia without any complications. No treatment-related side effects were observed in any of the animals or on the histological evaluation. In total, 24 muscle samples were collected during the study period, with each sample sliced, stained (3 slices per each staining, 144 slices in total), and evaluated to determine the primary outcomes. In general, there was no difference between the groups (P value > .05) in any of the measured outcomes at baseline. However, as the study progressed, the active group showed significant changes at the follow-ups and when compared with the control group. The temperature measurements revealed elevated

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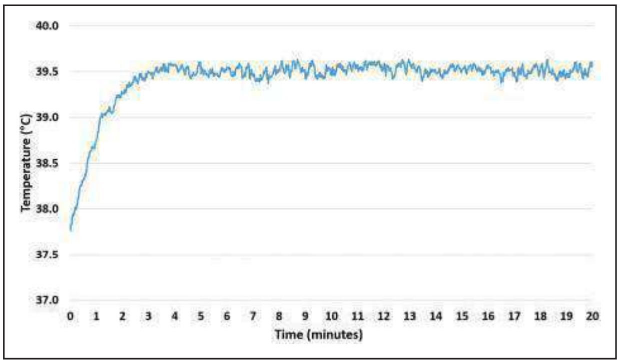

Figure 2. The temperature development in the muscle tissue during the therapy. The temperature rises to 39.5°C within 2 minutes and stays essentially unchanged for the rest of the therapy time.

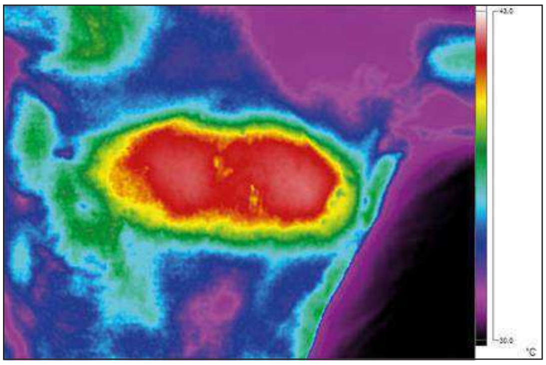

Figure 3. The skin temperature measurements were taken immediately after the treatment. The maximum surface temperature in the treatment area was just above 42°C, not exceeding 42.5°C. A thermal image taken by an infrared camera Fluke Ti300 (Fluke Corporation; Everett, WA).

muscle temperature from the onset of therapy, exceeding the 39°C within 2 minutes and stabilizing at the level of approximately 39.5°C in the third minute of therapy (Figure 2). The skin temperature measurements showed safe values at the level of 42°C (Figure 3).

The Evaluation of Muscle Mass

In the active group, the average muscle area in the ROI was 60810.1 μm^2 at baseline. At a 1-month follow-up visit, the average muscle area had significantly increased to 69223.2 μm^2 (*P* value = .003). Finally, the increase peaked at a 2-month follow-up visit with the average muscle area being 72474.4 μm^2 (*P* value < .001). Compared to baseline, the average muscle density was increased by 13.8% at 1 month and 19.2% at the 2-month follow-up visit in the active group. The observed changes in the examined histology slices are visualized in Figures 4, 5. In the control group, the baseline muscle area was 61711.4 μm^2 and did not show any substantial changes during the 1-month (61455.6 μm^2, *P* value > .05) or 2-month (62076.1 μm^2, *P* value > .05) follow-up.

The Number of Myonuclei

The average number of nuclei in the active group increased from 146.6 ± 24.9 (baseline) to 161.7 ± 26.7 (10.3% increase) at the 1-month follow-up visit, and up to 177.7 ± 30.7 (21.2% increase) at 2-month follow-up. The changes were significant at both follow-up visits (*P* value < .05). In the control group, however, the change in the nuclei count was insignificant (*P* value = .75 at 1 month; *P* value = .57 at 2 months), because it rose slightly from 136.7 ± 21.7 (baseline) to 140.3 ± 20.4 at 1 month and stayed at 140.3 ± 18.8 at 2 months.

The Number and Size of Muscle Fibers

In the active group, the average number of fibers in the ROI was 56.8 ± 7.1 at baseline, gradually increasing to 62.5 ± 9.2 fibers (10.1% increase, *P* value = .03) at 1-month follow-up. Analogous to the muscle density and myonuclei, the fiber count peaked at a 2-month follow-up visit with 68.0 ± 8.6 fibers (19.8% increase, *P* value < .001) per ROI. In the control group, the number of fibers was 56.3 ± 6.5 at baseline, with little to no increase throughout the study (57.3 ± 9.6 at 1 month, *P* value = .48; 58.2 ± 6.7 at 2 months, *P* value = .32). The changes in the number of muscle fibers compared with the control group were significant at the 2-month follow-up (*P* value = .004).

The increase in the diameter of the muscle fibers was visible in the active group throughout the study period. At baseline, the average muscle fiber size was 32.6 ± 2.5 μm, with a size of 33.6 ± 2.3 μm at 1-month follow-up and 37.8 ± 5.3 μm at 2 months (*P* value < .05). In the control group, no significant changes were observed (*P* value > .05), because the average muscle fiber size was 32.5 ± 0.31 μm throughout the study. The change in the relative frequency distribution of measured fibers can be seen on the histogram in Figure 6. Results indicate that the number of small-sized fibers considerably decreased over the course of the study. At the same time, there were increased numbers of thicker muscle fibers in follow-up samples from the active group. The histogram shows that the most common fiber size per ROI was between 30-40 μm in diameter at baseline. At the follow-ups, the number of fibers with a diameter greater than 40 μm was most abundant in the ROI.

DISCUSSION

In this study we evaluated the effects of novel HIFES technology combined with synchronized RF on deconditioned

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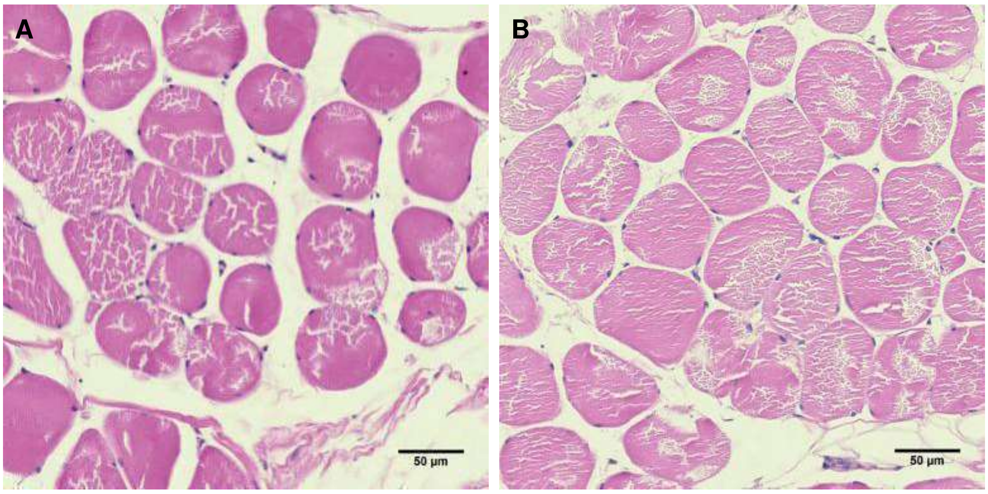

Figure 4. A cross-sectional view of the muscle tissue in the active group stained by hematoxylin and eosin, taken at (A) baseline and (B) 2-month follow-up. The pink represents the muscle tissue with dark purple nuclei at the periphery. The muscle tissue is noticeably denser after treatments in the assessed regions of interest.

muscle tissue. Based on the data obtained, we observed a consistent and significant increase in all studied parameters related to the quality and function of the muscle tissue. During the study, no treatment-related issues or side effects were observed in any of the animals or histological samples. The measured temperatures in the muscle tissue as well as on the surface showed that the heat was within the safe but effective limits. The results indicated that the simultaneous application of HIFES + RF safely and effectively targets the muscle tissue while promoting muscle remodeling and structural improvement.

Facial muscles are subject to the ravages of time together with the rest of the body tissues. Age-related muscle deconditioning and weakening are associated with loss of muscle quality and quantity manifested as a decrease in muscle mass and the number of fibers, and altered myofibrillar protein expression.[26] Therefore, this animal histology study aimed to observe these indices as the main markers for successful treatment of the deconditioned muscle tissue.

Throughout the study, the active group showed significant improvement in all measurements. The overall muscle mass increased by 19.2% at a 2-month follow-up, which may be attributed to the densification of muscle fibers while they increased in diameter at the same time (Figure 4). There is evidence that an increase in muscle mass is correlated with higher muscle strength and function.[27] Such changes can have beneficial implications when it comes to the treatment of human patients and restoration of facial appearance, which relies on the functional muscle tissue that interconnects with the skin. Also, the increased muscle mass indicates the substitution of adipose and connective tissue with muscle tissue (Figure 5), accompanied by muscle fiber growth both in size (+15.9%) and quantity (+19.8%). In human patients, studies have shown that the increase in muscle thickness in the crosswise direction induced by facial exercise has a positive effect on facial rejuvenation because it contributes to firmer and more elastic facial skin with a decrease in mimetic muscles linked to sagging of the face.[28,29] Therefore HIFES facial therapy might provide a first attempt standardized facial protocol to mitigate the loss of bulk and lift in facial aging, as a postoperative treatment or a stand-alone regimen.

The last marker of the changes occurring in the muscle tissue during the study period was the number of myonuclei, which correlates with the size of muscle fibers.[30] The significant increase in the number of myonuclei (+21.2%) may be attributed to satellite cells, which are activated during exercise.[31,32] Because supramaximal muscle stimulation is an effective alternative to exercise, these satellite cells fuse with the muscle fibers and donate their nucleus to the fiber to increase the regenerative and remodeling responses of the muscle fibers.[32–34]

The mild difference in the number of muscle fibers observed at 1-month follow-up when compared to control is most likely due the short observation period. As Kadi et al showed in their review, the effects of satellite cell activation take approximately 50-90 days to propagate fully, which corresponds to our 2-month follow-up observation, when the increase of muscle fibers was found to be highly significant when compared to the control group (*P* value = .004).[35] Nonetheless, all markers increased gradually in the active group and no significant changes were observed in the control group, and we can attribute the results seen in the active group to the HIFES + RF sessions.

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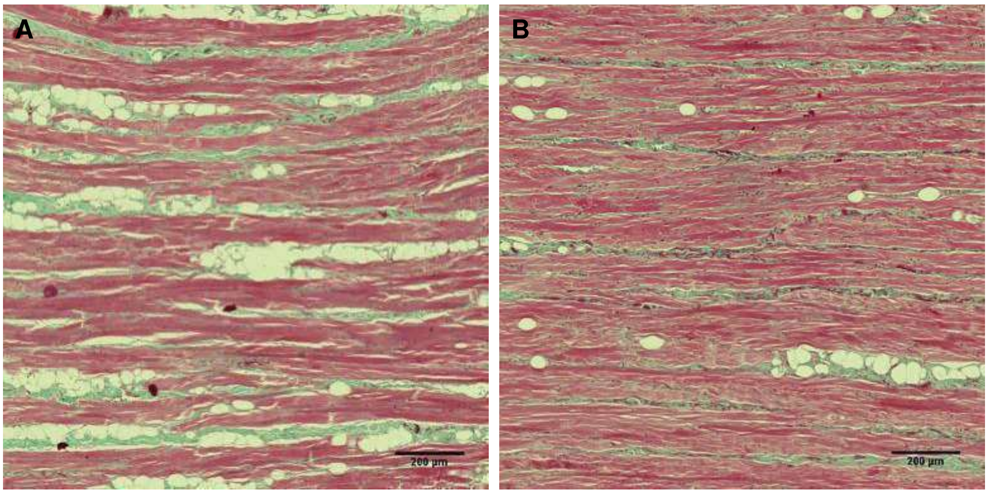

Figure 5. A longitudinal view of the muscle tissue stained by Masson's trichrome, taken at (A) baseline and (B) 2-month follow-up. The red color represents the muscle tissue, whereas the green color documents the presence of the intersected collagen fibers with lipid droplets without color. At baseline, the muscle fibers were relatively sparsely distributed, which changed at the 2-month follow-up. There was a noticeable increase in muscle fiber density together with a decrease in the fat tissue infiltration.

One of the limitations of this study was the use of a porcine animal model instead of human patients. Nonetheless, given the invasive nature of the study procedures, this animal model was found most suitable for the purpose of this study. Pigs have been successfully employed in biomedical research because of their remarkable similarity to humans in anatomy, physiology, immune system, and genome. These similarities provide sufficient insight to consider the biological processes transferable to humans.[36] Another limitation was the treatment area. Although the novel HIFES technology was designed to target all facial muscles, the trial was conducted on the pigs' foreheads only. The sow's cheek area was found to be problematic in terms of applicator placement and biopsy acquisition. However, the forehead area was eligible for treatments, because sow's forehead muscles are not intensively used by the animals, and therefore may correspond with deconditioned human muscles in the face. Also, all procedures were undertaken in a way to minimize animals' suffering. Taking samples from muscles of mastication in pigs may lead to pain during feeding and loss of appetite, resulting in weight loss and compromising the long-term results of the experiment. Nonetheless, we believe that the obtained results can be applied generally to the facial muscle groups because they all are subject to the same processes of deterioration.[37] Regarding the length of the follow-up, the animals were not kept with the general population, to lower the chances of infection or injury and overall bias from keeping them in uncontrolled conditions. Due to a long isolation with only study animals stress was considered a potential risk factor, and so there are no data available later than 2-month follow-up. This study was designed to investigate the immediate to short-term response of the tissue, and the 2-month period was deemed sufficient. The study's focus was to provide a basic understanding of the induced changes, which might provide insight into the effects of the simultaneous use of the investigated technologies with implications for use in human patients. In total, there were 144 evaluated tissue slices in this study, ensuring a reliable data count for conducted statistics. Also, 4 different aspects characterizing changes at the muscle tissue composition level were assessed, providing a comprehensive description of the effects of the investigated technology. In sum, this study offers a new method of noninvasive facial rejuvenation with the potential to contribute to the understanding of facial muscle aging in further detail. Future studies will benefit from using human patients to verify the findings described, and utilizing more objective methods (such as ultrasound) for a comprehensive analysis of the events occurring in the facial muscle tissue related to facial rejuvenation. Future human studies of a noninvasive nature should also consider including muscle testing of facial muscles to measure the improvement of facial expressions after the treatments, while establishing a longer follow-up period to document the long-term effects of the procedure.

CONCLUSIONS

This animal histology study aimed to evaluate the effectiveness and safety of the simultaneous application of novel HIFES technology and synchronized radiofrequency. The results documented by the histological analysis indicate

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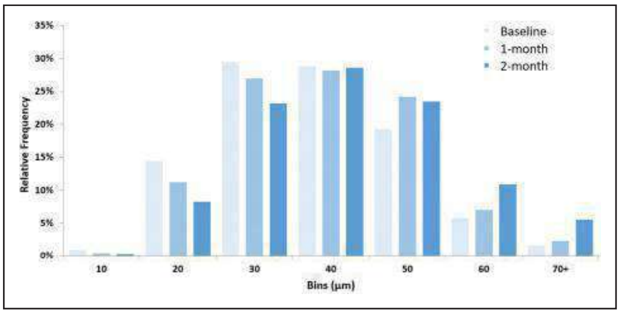

Figure 6. The histogram represents the relative frequency distribution of the muscle fiber sizes in the active group samples. The interval width was chosen to be 10 µm. The muscle fibers of greater diameters were more frequently present at 2-month follow-up.

treatment effectiveness for improving overall muscle quality; the active group significantly improved in all studied parameters. The safe use of this technology was also documented. No adverse effects occurred, and there were no unusual findings when assessing histology samples.

Disclosures

Drs Kinney and Bernardy are clinical investigators for BTL Industries (Boston, MA). Dr Jarošová is an associate of the Veterinary Research Institute (Brno, Czech Republic).

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Novel Approach to Facial Rejuvenation by Treating Cutaneous and Soft Tissue for Wrinkles Reduction: First Experience from Multicenter Clinical Trial

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Abstract

Background: Facial aging is determined by skin quality and the condition of underlying muscles, which contribute to the overall appearance by lifting heavy facial structures.

Objective: This study aims to assess the safety and effectiveness of the novel radiofrequency (RF) and high-intensity facial muscle stimulation (HIFES) technology for treating wrinkles by facial tissue remodeling.

Methods: This trial assessed the 3-month data of 24 subjects seeking facial wrinkles treatment. All subjects received four treatments, with a device utilizing RF and HIFES. The evaluation included a two-dimensional photographs assessment according to the Fitzpatrick Wrinkle and Elastosis Scale (FWES) and a three-dimensional (3D) photograph analysis for facial appearance. Therapy comfort and subject satisfaction were assessed.

Results: Based on the data of 24 subjects (56.5 ± 2.0 years, skin types I–IV), the significant improvement increased up to 3 months (-2.3 points, $p < 0.001$) post-treatment. 3D photographs analysis documented notable cutaneous and structural rejuvenation and coincided with FWES evaluation, underlining the positive subjective appreciation of the results with 20.4% average wrinkle reduction at 1 month, further increasing to 36.6% wrinkle reduction at 3 months.

Conclusion: Documented by both subjective and objective evaluation tools, the RF and HIFES procedure for facial rejuvenation was found to be effective for treatment of wrinkles and skin texture.

ClinicalTrials.gov Identifier: NCT05519124.

Introduction

In recent years, various noninvasive and minimally invasive procedures have been developed, mainly for skin tightening,[1–4] primarily utilizing ultrasound, radiofrequency (RF), or laser energy. The RF modality has become widely adopted due to its ability to induce production of new collagen and elastin fibrils while enhancing the existing connective tissue structures, and cellular metabolism.[5] Nonetheless, when it comes to facial appearance, counteracting only the signs of skin aging is part of the solution.[6–9] The loss of density of underlying muscles plays an important role in overall facial appearance.[10]

The direct relationship between facial muscles and skin appearance is based on the muscle toning effect that improves the density and quality of facial muscles, hence

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KEY POINTS

Question: Is the radiofrequency (RF) and high-intensity facial muscle stimulation (HIFES) technology effective in the treatment of facial wrinkles?

Findings: The significant wrinkle reduction was documented by evaluation of digital photographs using Fitzpatrick Wrinkle and Elastosis Scale and three-dimensional analysis.

Meaning: The findings suggest that the RF and HIFES technology are an effective approach for wrinkle treatment.

making the attached skin firmer and more elastic.[11] Weakening of the cheek muscles (especially zygomaticus muscles) can promote midfacial soft tissue descent, resulting in the increased severity of the nasolabial fold, formation of jowls, and loss of jawline contour.[12] Muscle remodeling can help to change the face contour by lifting effect that highly contributes to the overall facial appearance.[13]

To target both skin and facial muscle, monopolar RF and high-intensity facial muscle stimulation (HIFES) technology are combined in the novel device, which uniquely synchronizes both technologies to address the overall facial appearance. The mechanism of RF treatment is based on the oscillating electrical currents that flow through the skin tissue, where they are transformed into heat.[2,14] The novel HIFES technology generates a strong electrical field that depolarizes the motor neurons innervating the facial elevators: frontalis muscle, zygomaticus major and minor, and risorius muscle.

Depolarization of these motor neurons results in supramaximal contractions of these muscles.[15,16] The selectivity of the technology enabling the stimulation of only the elevator muscles is ensured by the design of the applicators, which contain multiple segments, whereas the HIFES energy is generated only in certain segments overlying the elevator innervating muscles. The repeated application of HIFES results in the initiation of muscle protein synthesis and may lead to the densification of the muscle tissue and its overall improvement.[17–21]

As documented in previous research, neocollagenesis and neoelastinogenesis are initiated after the RF therapy, and the improvements in skin appearance and properties are usually noticeable a few weeks after the treatment.[14,22,23] In addition, the heat delivered by RF supports the effect of HIFES through improved blood circulation, which increases nutrient supply,[24,25] promoting the muscle remodeling and regeneration of existing muscle fibers.[26,27]

This study aims to evaluate the safety and effectiveness of the novel device for facial wrinkles and rhytides treatment. We hypothesize that this novel treatment may facilitate the natural healing process following the thermal effects of RF and workload from HIFES, conceivably resulting in wrinkle reduction and skin tone improvement.[24]

Methods

Study population

Twenty-four subjects (1 male and 23 females, for more details see Table 1) were enrolled at two study sites. At the time of enrollment, the inclusion and exclusion criteria and the subject medical history were reviewed. Inclusion criteria were subjects aged 21 years and older, understanding of the investigative nature of the treatment concerning potential benefits and side effects, presence of clearly visible wrinkles in the treatment area, willingness and ability to abstain from partaking in any facial treatments other than the study procedure during study participation, and willingness to comply with the study instruction to return to the clinic for the required visits and to have photographs of their face taken.

Subjects who met any exclusion criteria, such as metal implants, local infection, or unhealed wounds in the treated area, were excluded from participation in the study.

Ethical consideration

This multicenter single-arm open-label interventional study was approved by the Advarra Institutional Review Board, and its conduct adhered to the ethical principles of the 1975 Declaration of Helsinki. All patients voluntarily provided informed consent before any study-related procedure was performed. Each patient was assigned a unique subject identification number for anonymization.

Treatment protocol

All patients received treatments with the novel EMFACE (BTL Industries, Inc., Boston, MA) device using RF and HIFES technology for the noninvasive reduction of wrinkles, rhytides, and overall improvement in facial contours. The treatment was performed on the forehead and both cheeks at the same time using adhesive single-use applicators. Before each therapy, the treatment area was cleared of any cosmetics, lotions, jewelry, and prominent hairs. The treatment administration phase consisted of four 20-min treatment visits, delivered 5–10 days apart. At each therapy, the intensities of RF and HIFES

Table 1. Baseline patient characteristics ($N = 24$)

	All cases
Patients	24
Gender	
Male	1 (4.2%)
Female	23 (95.8%)
Age (years)	
Mean	56.5 ± 2.0
Range	34–75
Median	59.5
Skin types	
I	1
II	13
III	6
IV	4

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stimulation (on a scale of 0%–100%, where RF was set to 100% by default) were adjusted according to the patient's feedback concerning any possible discomfort.

All patients were required to complete all four treatments and three follow-up visits: immediately after the last treatment, at 1-month, and at 3-month follow-up (±10 days). Patients were monitored and examined for the occurrence of any adverse events throughout the study duration.

Data collection and evaluation

At baseline and all follow-up visits, two-dimensional (2D) photographs of the face were taken and evaluated according to the Fitzpatrick Wrinkle and Elastosis Scale (FWES). Three independent evaluators assigned the FWES score to the subjects' pre- and post-treatment photographs to assess wrinkle severity as per Table 2.

The three-dimensional (3D) automated analysis was performed using two standardized systems to evaluate the severity of wrinkles, skin evenness, and texture. A 3D photographic imaging system LifeViz® Mini (QuantifiCare S.A., France) was used to capture facial images of 13 patients that were to be evaluated.[28] At baseline and both 1- and 3-month follow-up visits, the 2D photographs were taken from the left, right, and front views of the face at multiple angles, and compiled into a 3D model by using Quantificare software suite. 3D models were evaluated for the wrinkle severity and skin evenness by analyzing the combination of depth, length, and width of the wrinkles in the treated areas according to the subject's age, gender, and skin type.

Every analysis was assigned with a score ranging from −10 to +10. A negative score means the wrinkle severity and skin evenness are worse than in the average individual, and positive scores >0 (i.e., average) indicate how much better the patient's result is than in the case of an average individual of similar age, gender, and skin type as a concerned subject.

Similarly, photographs of 11 subjects were taken using the Vectra® H2 camera (Canfield Scientific, Inc.), and were analyzed for wrinkle severity and skin texture using the included Sculptor® software.[29] The results were determined as a score based on the intensity of the measured instance on a scale of 0–100, where 100 means the highest possible score reflecting excellent skin condition.

The 5-point Likert scale Subject Satisfaction Questionnaire (SSQ) was administered after the final treatment and at all follow-up visits to assess patients' satisfaction with the therapy results. The Therapy Comfort Questionnaire including the visual analog scale (0—no pain, 10—maximum bearable pain) and 5-point Likert scale was administered after the final treatment session.

Statistical methods

The descriptive statistic was calculated (mean, standard error mean, and median value). All data were analyzed for statistical significance. Paired variables measured at multiple time points were tested by repeated measures analysis of variance followed by a post hoc Tukey honestly significant difference test used to analyze the significance of observed changes. The significance level was set to $\alpha = 0.05$ (5%).

Results

Out of the recruited 24 subjects (56.5 ± 2.0 years, skin type I–IV), 17 completed the 3-month follow-up visit. All patients received wrinkle treatment with parameters set according to the patient's feedback. During the treatment, the intensities ranged from 50–100% for HIFES and 80–100% for RF.

FWES evaluation

The FWES evaluation resulted in a baseline value of 5.2 ± 0.4 points (class II, median value = 5.0 points). At a 1-month follow-up visit, the FWES score decreased to 3.8 ± 0.5 points (median value = 3.5, −1.4 points, $p < 0.001$; class II). The results peaked 3 months after the last treatment ($p < 0.001$), averaging a score of 2.9 ± 0.4 points (median value = 3.0 points, −2.3 points, class I).

3D analysis

Evaluating 3D photographs with QuantifiCare® software, the patient's baseline average wrinkle score was subaverage with −1.3 ± 0.6 points. Gradually, it improved showing an average difference of +3.1 ± 0.5 points ($p < 0.001$) at 1-month follow-up, as shown in Figure 1. The improvement was maintained up to 3 months with an average score increase of +4.4 ± 0.6 points ($p < 0.001$). The skin evenness (3.5 ± 0.4 points at baseline) of the whole face was enhanced on average by +3.7 ± 0.5 points at a

Table 2. Wrinkle severity according to the Fitzpatrick Wrinkle and Elastosis scale

Class	*Wrinkling*	*Score*	*Description*
I	Fine wrinkles	1–3	Mild: fine texture changes with subtly accentuated skin lines
II	Fine-to-moderate depth wrinkles with a moderate number of lines	4–6	Moderate: distinct popular elastosis (individual papules with yellow translucency under direct lighting) and dyschromia
III	Fine-to-deep wrinkles, numerous lines with or without redundant skin folds	7–9	Severe: multipapular and confluent elastosis (thickened, yellow, and pallid) approaching or consistent with cutis rhomboidalis

Fig. 1. Seventy-five-year-old patients before (left) and at 1 month after (right) the final treatment with the EMFACE device. Photographs were taken using the 3D photograph imaging system LifeViz® Mini (QuantifiCare S.A., France). 3D, three-dimensional.

1-month follow-up visit ($p<0.001$). At the 3-month follow-up, a significant improvement ($p<0.001$) by +5.1 ± 0.6 points was achieved.

The photographs evaluated in Vectra Sculptor software analogically showed a wrinkle improvement noticeable from the 1-month follow-up when the score increased by +11.3 ± 2.2 points ($p<0.001$) against the baseline (53.0 ± 3.7 points). The improvement peaked at 3 months with an average score increase by +17.6 ± 2.8 points ($p<0.001$). The skin texture (75.0 ± 3.8 points at baseline) was enhanced by +11.6 ± 4.1 points at a 1-month follow-up visit, and by +17.7 ± 2.5 points at 3 months (both $p<0.001$).

Despite the use of different 3D analysis software tools, desired changes were observed in all subjects with fine or pronounced wrinkles resulting in fuller and lifted cheeks 1 and 3 months after the final treatment as shown in Figures 2 and 3. Average subject's improvement rate was quite similar for both software, achieving 36.8% (QuantifiCare) and 36.5% (Vectra) improvement at 3 months for wrinkles and 24.2% (QuantifiCare) and 26.2% (Vectra) for skin evenness and texture, respectively.

Subject satisfaction and therapy comfort

The majority of patients (87.5%, $N=21$) agreed that the therapy was comfortable and 91.7% ($N=22$) patients reported no or minimal discomfort during the treatment. There were no negative responses from the SSQ evaluation immediately after the treatment. At 1- and 3-month follow-ups, satisfaction with results was high, achieving 95.5% and 95.0%, respectively. In addition, 87.5% of patients reported more lifted and tighter skin after the treatment during the whole study. The lifting effect is demonstrated in Figure 4. No adverse events or treatment-related side effects were observed.

Fig. 2. Forty-six-year-old patients before (left) and at 3 months after (right) the final treatment with the EMFACE device. Photographs were taken using the 3D photograph imaging system LifeViz® Mini (QuantifiCare S.A., France).

Discussion

The appearance of facial wrinkles and rhytides was significantly ($p<0.05$) improved after the treatment using a novel device combining RF and HIFES technologies. The FWES results showed a shift from class II (5.2 ± 0.4 points) to class I (2.9 ± 0.4 points) indicating only fine wrinkles. The 3D analysis demonstrated a significant wrinkle (36.6%) and skin texture (25.2%) improvement maintained up to 3 months. The majority of patients (90.9%) agreed the therapy was comfortable and there were no negative responses from the SSQ. In addition, patients were satisfied especially with the lifting effect visible after the final treatment and with treatment results (83.3%) in general—outcomes leading to minimization of signs of aging.

Fig. 3. Sixty-two-year-old patients before (left) and 3 months after (right) the final treatment with the EMFACE device showing wrinkle severity improvement with visible jawline definition.

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Fig. 4. Sixty-year-old patient at the 1-month follow-up visit after the final treatment with the EMFACE device with pronounced lifting effect on the cheeks. Photographs were taken using the 3D photograph imaging system LifeViz® Mini (QuantifiCare S.A., France).

In this study, the skin quality, determined by wrinkle, evenness, and texture analysis, improved most at 3 months. These outcomes corresponded with findings of Kent et al.[30] and Goldberg and Lal,[31] confirming the fact that collagen and elastin structural remodeling within 3 months after the RF treatment resulted in skin rejuvenation. In addition, the outcomes demonstrated by Kinney and Jarosova[32] and Halaas[33] presented positive muscle changes, especially densification and overall function improvement shown at the 3 months post-RF+HIFES treatments.

This benefit of synchronized use of RF and HIFES technologies to the overall facial appearance was supported by our findings accompanied by high patients' satisfaction with a lifting effect, reported by 87.5% of the treated subjects. Although our study was not primarily focused on the lifting effect, these findings suggest that remodeling of facial muscles considerably contributes to the lifting of the facial structures. In addition, as heat responsive, the collagen and elastin remodeling was initiated after RF heating and supported the lifting effect by increasing the skin elasticity and tightness.

Current therapies for facial rejuvenation often include invasive surgical facelift procedures, botulinum neurotoxin-based injections, and skin fillers. Despite them being effective, they are still considered (minimally) invasive and could be associated with a number of side effects and drawbacks, such as long recovery, or scarring, and also limited effectiveness on the underlying muscles.[34–36]

The use of a novel device offers a way to overcome most of these disadvantages. The device combines the synchronized effect of RF on the skin tissue with selective stimulation of the underlying fibromuscular tissue and fascia using HIFES technology. This combination poses as an interesting opportunity for targeting facial wrinkles. Moreover, as documented herein, the combined treatment is fully noninvasive and highly comfortable with minimal or mild discomfort.

To achieve reliable wrinkle improvement evaluation, two methods were used—FWES based on blinded evaluators and 3D automated analysis due to the potential limitations of the former. Overall, the considerable consistency of the FWES and 3D analysis results was documented, evidencing the positive effect of the treatment on wrinkles and skin texture. Also, to include a wide range of patients with well-visible facial wrinkles, subjects of varying ages were enrolled (34–75 years). Nonetheless, desired changes were observed in all subjects with fine or pronounced wrinkles resulting in fuller and lifted cheeks after the treatment, regardless of the demography.

Future research on larger and specific patients' groups, for example, those manifesting a certain degree or severity of wrinkles and rhytids, would be of great value to expound on the effectiveness of the treatment by EMFACE device for wrinkle reduction and to improve facial appearance.

Based on our findings, the EMFACE device may be recommended for the noninvasive treatment of wrinkles and overall facial skin appearance. EMFACE offers a noninvasive, pleasant, and fast alternative to current facial therapies or surgeries.

Conclusion

The treatment by a novel EMFACE device simultaneously delivering RF and HIFES resulted in a significant improvement in overall facial appearance. Based on the outcomes from 3D analysis and FWES evaluation, the procedure leads to decreased facial wrinkle severity (36.6%) and improved skin quality (25.2%). The treatment proved its safety since no adverse events were documented.

Authors' Contributions

Conceptualization of the study was carried out by R.G., methodology was by R.G. and Y.H., formal analysis was by R.G. and Y.H., investigation was done by R.G. and Y.H., resources were taken care by R.G. and Y.H., writing—original draft, was done by R.G., writing—review and editing, was by R.G. and Y.H., and supervision was carried out by R.G. and Y.H.

Author Disclosure Statement

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Novel Approach to Facial Rejuvenation by Treating Skin and Muscle Tissue for Facial Lifting: Preliminary Data from Multicenter Clinical Trial

Brian M. Kinney, M.D.[1], Charles M. Boyd, M.D., MBA[2]

1. Clinical Associate Professor of Plastic Surgery, USC Keck School of Medicine, Los Angeles, CA, USA
2. Boyd Beauty, Birmingham, MI, USA

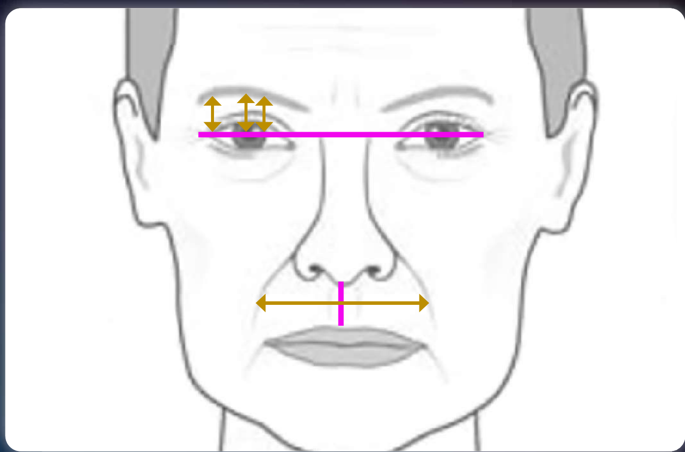
Accepted at American Academy of Facial Plastic and Reconstructive Surgery 2022 Annual Meeting, Washington, DC

+23.1% Lifting Effect

95.2% Patient Satisfaction

Methodology

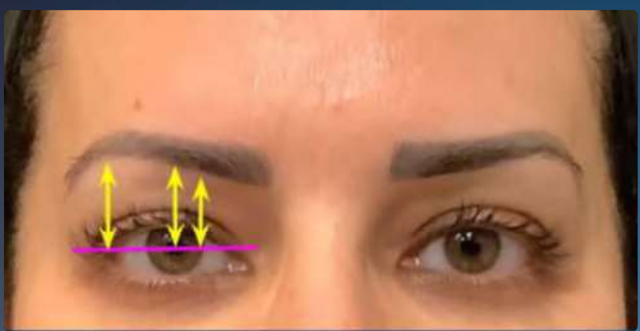
- 24 patients recruited at two sites
- Four 20-minute full face treatments
- Lifting effect assessed as:
  - Brow lift: Distance of eyebrow from the pupils' line at several points
  - Cheek lift: Distance between left and right nasolabial fold
- Patient satisfaction & Treatment comfort



Measurement locations of the lifting effect

Example of eyebrow lift results

44 year old patient
Eyebrow lift +2 mm on average



Baseline

Follow up

Histological Analysis of Human Skin Indicates Quantitative Increase of Collagen and Elastin Fibers after Synchronized Radiofrequency with Facial Muscle Stimulation

Karan Lal, DO, MS[1] and David Goldberg, M.D., J.D.[1]

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Presented at American Society for Dermatologic Surgery (ASDS) Annual Meeting 2022, Denver, CO.

+27% Increase in Collagen

+129% Increase in Elastin

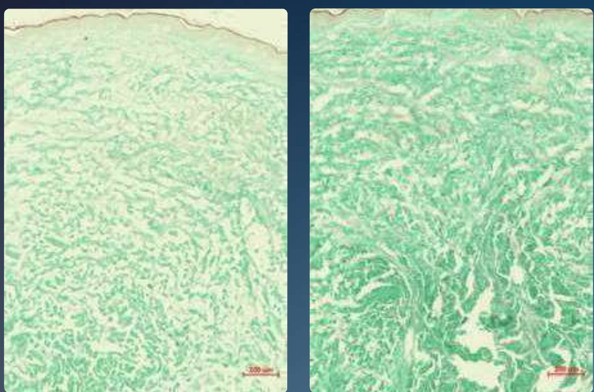
Methodology

- 7 patients allocated to Active (N=6) and Control (N=1) groups
- Active group: Four 20-minute RF+HIFES full face treatments (Control group - no treatments)
- Punch biopsies of skin tissue collected at baseline, 1-month and 3-month follow-ups
- Evaluation of digital photographs, satisfaction, comfort and safety

Preliminary Results

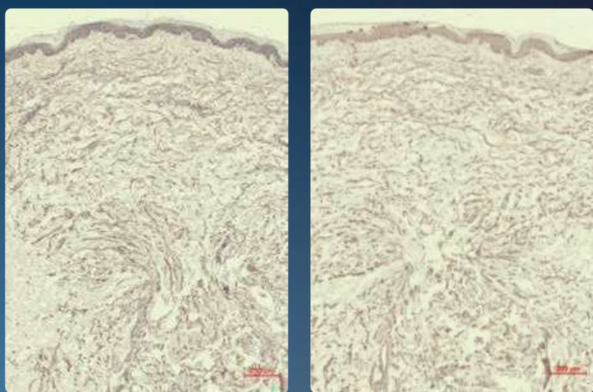
- Increased levels of elastin and collagen at 1-month and 3-month follow-ups
- Visible improved facial appearance
- Patients report high rates of satisfaction with the treatment
- No adverse events

Collagen - Trichrome Stain



Baseline | 3 months

Elastin - Orcein Stain



Baseline | 3 months

Novel technology for Facial Muscle Stimulation Combined with Synchronized Radiofrequency Induces structural changes in Muscles tissue: Porcine Histology Study

Brian Kinney, MD[1]; Jan Bernardy, DVM[2]; Rea Jarosova MSc[2]

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2. Veterinary Research Institute, Brno, Czech Republic

Presented at 41st Annual Conference of the American Society for Laser Medicine and Surgery. 2022; San Diego, CA

+19.2% Increase in Muscle Density

+21.2% Increased nr. of Myonuclei

+19.8% Increased nr. of Muscle Fibers

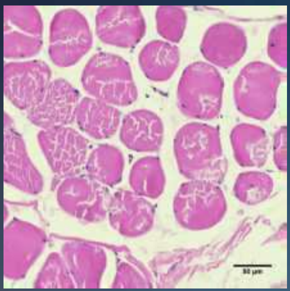
Methodology

- 8 Large white pigs (60-80 kg) divided into 2 groups
- Active group (6 sows): Four 20-minute treatments of forehead
- Control group (2 sows): No treatment
- Punch biopsies of muscle tissue collected at baseline, 1 and 2 months after last treatment

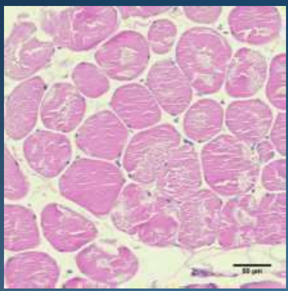
Results

- All results in active group were significant
- Control group showed insignificant changes
- Muscle temperature during treatment up to 39.5°C

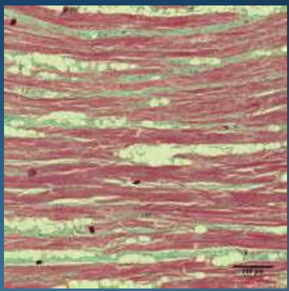
Example of muscle tissue samples



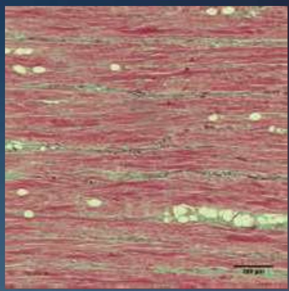
Baseline



2 Months After



Baseline



2 Months After

A Combined Effect of Novel HIFES Technology with Synchronized Radiofrequency for Qualitative Improvement of Facial Muscles

Yael Halaas, M.D., FACS[1]

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Accepted at American Academy of Facial Plastic and Reconstructive Surgery 2022 Annual Meeting, Washington, DC

+30%

Increase in Muscle Tone

Methodology

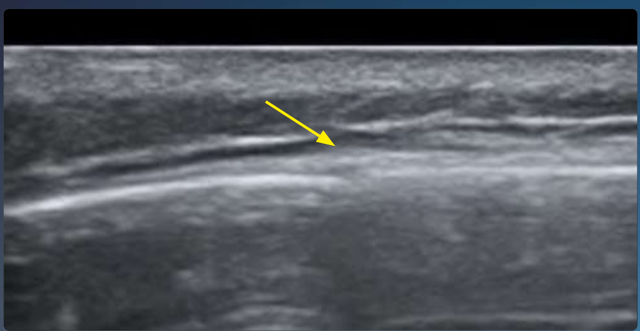
- 10 enrolled patients
- Four 20-minute simultaneous treatments on the forehead and the cheeks
- Ultrasound scans of m. frontalis and m. zygomaticus major taken at baseline, immediately after last treatment, 1 month after last treatment, and 3 months after last treatment
    - Echogenicity measurements
- Subject satisfaction
- Therapy comfort assessment

Results

- Interim findings suggest:
    - Enhanced muscle structure and quality
    - Enhancement of facial visual appearance
    - High patient satisfaction

Ultrasound scans of the frontalis muscle

Darker representation of the muscle at the after scan indicates densification of the muscle and increased muscle tone.



Baseline

After the last treatment

Effects of noninvasive synchronized radiofrequency and novel HIFES: Histological analysis of Porcine dermal Collagen and Elastin

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2. Veterinary Research Institute, Brno, Czech Republic

Accepted for American Society for Dermatologic Surgery (ASDS) Annual Meeting 2022, Denver, CO.

+26% Increase in Collagen

+110% Increase in Elastin

Methodology

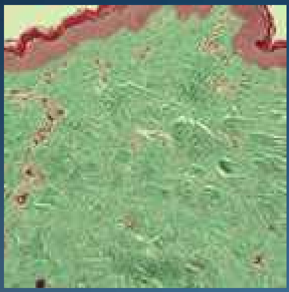
- 8 Large White female pigs, 60-80 kg
- Active (N=6): Four 20-minute treatments on belly
- Control (N=2): Untreated
- Three biopsy explants obtained at baseline, 1 and 2 months post-reatment

Results

- Active group showed highly significant changes
- Elastin and collagen did not change in control group
- Skin temperature was maintained at 40 – 42°C throughout the treatment.
- No adverse events observed

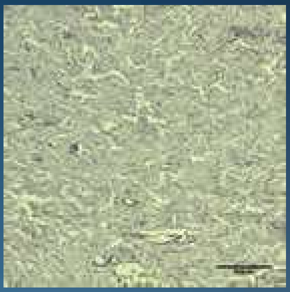
Collagen - Trichrome Stain

Baseline



2 Months After

Elastin - Orcein Stain



Baseline

2 Months After

Novel Approach to Facial Rejuvenation by Treating Skin and Muscle Tissue for Wrinkles Reduction: Preliminary Data from Multicenter Clinical Trial

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Accepted for American Academy of Facial Plastic and Reconstructive Surgery 2022 Annual Meeting, Washington, DC

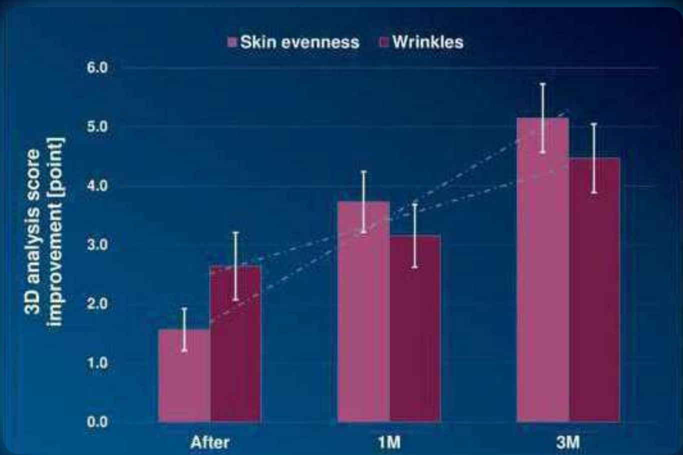
95.0%
Patient Satisfaction

+25.3%
Skin Evenness Improvement

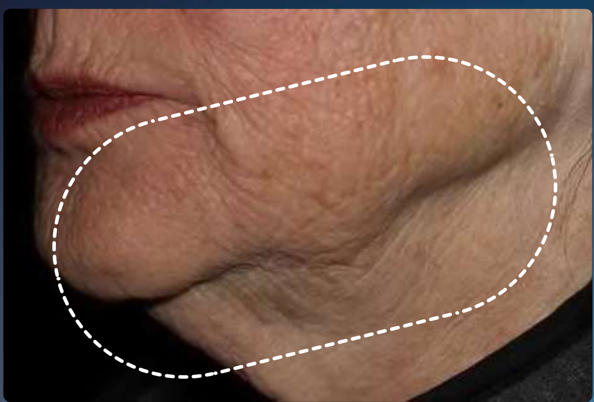
-36.8%
Wrinkle Reduction

Methodology

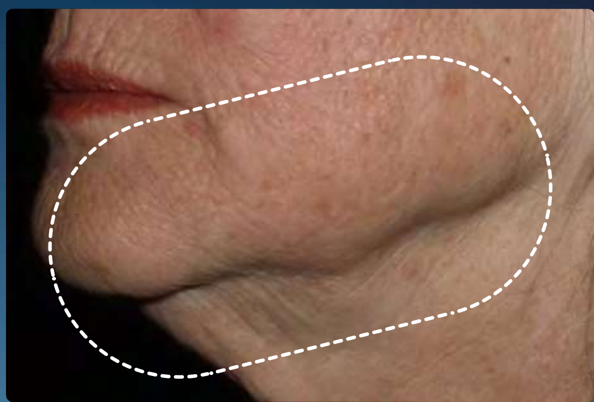
- 24 subjects (23 females, 1 male)
- Four 20-minute full face treatments
- Evaluation of
  - Wrinkle severity via automated 3D photo assessment
  - Patient satisfaction
  - Treatment comfort



Sixty-two year old patient



Baseline



3M FU

Novel HIFES and RF Technology for Comprehensive Facial Enhancement and Volume Improvement in Patients

Yael Halaas, M.D.[1], Charles M. Boyd, M.D.[2], Richard Gentile M.D.[3], Suneel Chilukuri M.D.[4], Lesley Clark-Loeser, M.D.[5]

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+1.65 ml

Average Volume Improvement in Upper Cheeks

-1.08 ml

Average volume change of the lower face (jowls)

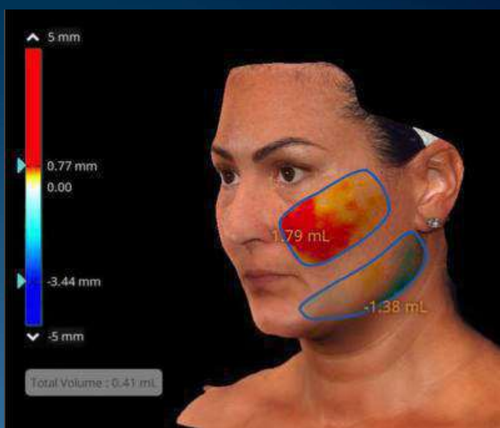
Methodology

- A total of 47 patients from four studies underwent four full-face EMFACE treatments.
- Evaluation of 3D photographs using Quantificare and Vectra systems:
  - Volume change in the upper cheek
  - Volume change in the lower face

Preliminary Results

- Study outcomes have demonstrated a noticeable improvement in facial shape, which can be attributed to the volume shift.

Examples of volume changes observed three months after EMFACE treatments.



Holistic Approach for Noninvasive Facial Rejuvenation by Simultaneous Use of High Intensity Focused Electrical Stimulation and Synchronized Radiofrequency

A Review of Treatment Effects Underlined by Understanding of Facial Anatomy

Suneel Chilukuri, MD

KEYWORDS

• Face • Fillers • High intensity focused electrical stimulation • Radiofrequency • Neuromodulators • Noninvasive

KEY POINTS

- Facial aging is a continuous process resulting from age-related changes in all structures present in the face. Such complex anatomy needs to be considered when it comes to noninvasive treatments for improving facial appearance. The facial muscles especially should be seen within their connective tissue environment and addressed accordingly.
- Novel HIFES and Synchronized RF technology was developed to target facial layers in synergy. Its effects show that it is a viable option for noninvasive face lifting and wrinkle reduction.
- It has been documented that HIFES and Synchronized RF does not interfere with the effects of neuromodulators or dermal fillers and can be safely and effectively used in patients injected with either of them, to deliver satisfactory improvement of overall facial appearance.

INTRODUCTION

Facial aging is a continuous process resulting from age-related changes in all structures present in the face: skin, fat, muscle, fascia, and bone.[1,2] Age-related changes of all facial soft tissues start at different decades and progress at various paces, which vary between individuals of different gender and ethnicity. All changes together result in reduced support for the bone-overlying soft tissues, which then follow the effect of gravity. Thus, a loss of structural support owing to volume depletion and changes to the facial muscles and their connective tissue framework results in increased soft tissue laxity.

The Role of Facial Muscles and Fascia Framework in Aesthetic Appearance

Facial muscles have been found to age through the process of sarcopenia, which manifests as a loss of muscle mass and volume, similar to skeletal muscles.[3] Because the facial muscles are interconnected via the fascial system and the

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overlying skin, weakening of these muscles may result in a visible descent of the tissue as we age (**Fig. 1**). The weaker the facial muscles are, and the lower the resting muscle tone is, the higher that muscle effort is needed to avoid sagging and to hold the overlying tissues in place. When too weak, they become unable to hold the tissue, resulting in eyebrow drop or cheek sagging. When the resting muscle tone is increased, the muscles are then able to hold the overlying tissue in place without dropping and without the need to stay contracted.

Specifically, the muscles in the cheek are interconnected by the midfacial superficial musculoaponeurotic system (SMAS).[4] Weakening of the cheek muscles, especially the zygomaticus muscles, allows for the hypothesis that as we age, the resulting facial muscle weakness can promote midfacial soft tissue descent, resulting in the increased severity of the nasolabial fold, formation of jowls, and loss of jawline contour.[5] Targeting these muscles and their surrounding connective tissue architecture might allow for midfacial soft tissue repositioning. Also, the same muscle weakening could be expected for the frontalis muscle owing to aging or long-term use of neurotoxins. The frontalis muscle is mainly responsible for eyebrow movements. Its connection with the skin is ensured via the suprafrontalis fascia (located superficial to the frontalis muscle) and the subfrontalis fascia (located deep below the frontalis muscle). Aging of the forehead structures may result in eyebrow ptosis[6] and heaviness,

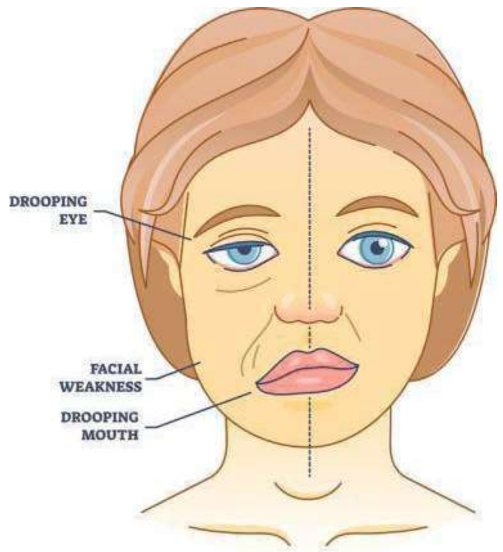

Fig. 1. Visualization of the effect caused by weakened facial muscles on the left in comparison to healthy muscles on the right.

which along with skin aging, may lead to laxity and wrinkle formation in the region.

In contrast to skeletal muscles, the facial muscles are embedded in a connective tissue framework that interconnects all tissues from bone to skin. Interestingly, they are connected directly to the brain via the cranial nerves and are responsive to emotional input and the limbic system. Emotional states affect facial contours via resting tone of the muscles and the SMAS. Therefore, the facial muscles need to be seen within their connective tissue environment and addressed accordingly. Assuming that facial muscles affect skin movement alone without the support of a connective tissue environment creates an incomplete picture of facial muscle anatomy.

Treatment Alternatives

Repositioning and restructuring the facial tissues and layers is the aim of aesthetic procedures via surgical and nonsurgical means.[1,2] Among noninvasive aesthetic procedures, radiofrequency (RF) is considered the gold standard for facial skin treatment. The effect of RF on the skin tissue is based on dermal heating, which leads to structural changes within the skin and the overall improvement in skin quality.[7] However, these skin heating procedures focus solely on improving skin quality and textural improvement, but not the overall facial appearance, which is also influenced by the facial volume and density of the underlying structures, including the fascial system, facial ligaments, and facial muscles. Therefore, the extent of facial laxity is a composite effect of all implicated structures of which the facial muscles and their interconnection with the skin play a fundamental role.[8]

The most frequently performed nonsurgical treatment to date is the administration of soft tissue fillers, which helps to restore facial volume. However, soft tissue fillers only cover the aging symptoms and do not affect facial muscles, which play a crucial role in natural skin mobility.[9] When it comes to muscles, the application of neurotoxins is yet another popular solution, although its primary effects are also limited to one tissue only. Currently, the only way to reliably alter facial muscles is through a surgical lift procedure, where the skin and fat tissues are separated from the muscle, and the muscles are then repositioned.[10]

Overall, the combination of age-related facial changes results in an alteration of the facial shape, which cannot be improved by targeting one type of tissue alone. Therefore, more profound treatment algorithms need to be applied to address age-related facial changes.[11] This may include addressing deeper fascial and muscle layers together, as they have the ability to promote facial repositioning.

Recently, HIFES technology synchronized with RF heating has been introduced with the EMFACE (BTL Industries Ltd, Boston, MA, USA) device, to target the facial muscles and their connective tissue frameworks for lifting and tightening of the facial contours. HIFES technology induces electrical fields to contract facial muscles selectively. These delicate facial muscles are crucial for supporting the facial soft tissues and play a structural role in a more youthful appearance. While the HIFES targets the muscle and overlying fascia tissue, the Synchronized RF heating induces structural changes to the dermal and subdermal architecture. This approach can ultimately result in an improved appearance through changes in all facial tissue layers.

TARGETING FACIAL TISSUES BY NONINVASIVE HIFES AND SYNCHRONIZED RADIOFREQUENCY TECHNOLOGIES

Mechanics of HIFES for Facial Muscle Stimulation

HIFES technology was specifically designed to selectively induce supramaximal contractions of small delicate muscles in the face, namely the frontalis muscle on the forehead and zygomaticus major muscles, zygomaticus minor muscles and risorius muscles on the cheeks (**Fig. 2**). The technology generates strong electrical fields, delivered by its specifically designed applicators, that affect the underlying neuronal and muscle tissue. These electrical fields depolarize the membrane of the motor neurons that innervate the muscle. When the motor neurons are depolarized, a signal is created that travels along the neuron, all the way to the neuromuscular junction—the place where the motor neuron is connected to the muscle. These signals overcome the barrier of the neuromuscular junction and progress to the muscle, which is thus forced to contract. This process bypasses the voluntary intention of the brain, inducing a forced contraction through electrical stimulation.

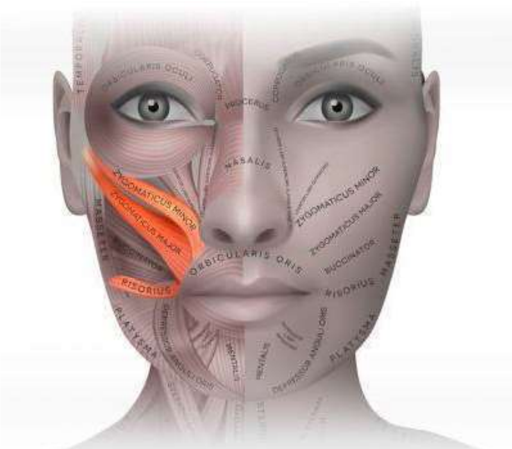

Fig. 2. The cheek muscles stimulated by HIFES technology: zygomaticus major and minor muscles and risorius muscle.

The HIFES stimuli repeat with such frequency that the facial muscles are not allowed to relax in between the individual signals. As the muscle cannot relax, with additional stimuli, it is forced to contract even further, which continuously builds up the contraction power with every additional signal. The appropriate selection of these 2 factors (electrical field strength and frequency) results in the so-called supramaximal contraction. Although it is poorly understood how and to what extent the facial muscles adapt to external stimuli, research studies conducted in skeletal muscles have revealed that heat shock proteins (HSP) and satellite cells (SCs) may be activated by intense muscle exercise as a response to the applied stimuli.[12] HSPs are the signaling molecules playing a crucial role in muscle remodeling through the promotion of muscle protein synthesis.[13] SCs are muscle-derived stem cells responsible for myofiber development and renewal.[14] In a resting state, the SCs remain quiescent, ready to be activated, and provide differentiation to create new myonuclei to existing muscle fibers or generate new muscle fibers. Together, HSP and SC activation can support muscle microprotein structure alterations. In a healthy muscle this may lead to densification of the muscle tissue and to overall improvement of the muscle quality. In atrophied muscle, the muscle structure alteration may lead to hypertrophic response reversing the atrophy. However, it is not only the muscle reacting to the signaling molecules. It has also been documented that the fascial layer remodels itself in response to heat and mechanical stimuli.[15] Nonetheless, the future studies will need to identify similarities between skeletal and facial muscles or provide conclusive evidence that facial muscles behave similarly or differently when targeted by external stimuli.

The Role of Synchronized Radiofrequency Heating on Facial Muscles and Framework

Simultaneously with the HIFES stimulation, the Synchronized RF that heats the facial tissue is delivered. Such stimuli affect the connective tissue framework and the facial muscle unit with consecutive adaptive changes to the overlying facial soft tissues. According to previous studies on skeletal muscles,[13,16] HSPs can also be activated by heat within the range of 40°C. Together with the muscular contractions, the heat thus may further increase the levels of released HSP,[17] although this effect has been shown in abdominal muscle[18] or gluteal muscle.[19] A recent study by Kinney and colleagues[20] measured the facial muscle temperature during the treatment with HIFES and RF and showed that the temperatures in the targeted muscle tissues reached up to 40°C, indicating that a similar effect could also be seen in the facial muscles during the simultaneous treatment.

Furthermore, the primary effect of Synchronized RF heating on the subdermal tissues can be seen in the fascial framework. The fascial framework primarily consists of collagen and elastin, which are known to be heat responsive. Therefore, heating to adequate temperatures may induce remodeling of collagen and elastin within the fascial framework, leading to increased elasticity and tightness of the fascial web.[15]

The Role of Synchronized Radiofrequency Heating on Skin Tissue Rejuvenation

The same effect for the fascia can also be seen in the skin tissue. Regarding skin, fine lines and wrinkles accompanied by loss of skin volume are usually the first indicators of skin aging, a normal physiologic process influenced by genetic and hormonal changes with contribution of external factors.[21] During the skin aging process, the dermal blood vessel structure is disrupted, and in turn, the dermis is not supplied with nutrition and oxygen, thus slowing cellular regeneration.

The major building blocks of the skin are collagen and elastin fibers, which are responsible for skin elasticity and firmness. During the aging process, collagen and elastin synthesis decreases, and collagen bundles lose their extensible configuration and become fragmented. The elastin fiber network is degraded, leading to the loss of structural integrity of microfibrils. As the extracellular matrix is degraded, skin thickness is also reduced. It is estimated that adult skin loses 1% of overall collagen content annually.[22]

The EMFACE device uses a novel Synchronized RF electrode that allows the simultaneous application of an RF field together with HIFES. As the RF current flows through the tissue, a portion of the RF energy is absorbed, transforming the energy into heat and the desired thermal effect. During the 20-minute treatment, the skin tissue is heated to 40°C to 42°C. This therapeutic temperature range is reached within the first 2 minutes of the treatment, as documented by the thermal probe measurements.[23] The level of RF energy absorption in the tissue depends on the RF frequency and tissue impedance, among other factors. Because the skin, muscle, and fat tissues have different impedances,[24] it is possible to selectively target the energy and achieve the thermal effect in the desired tissues.

When the therapeutic temperature is reached in the skin tissue for the desired time period, the hydrogen bonds tying the collagen fibers together begin to unwind, and collagen denaturation occurs. However, the above-mentioned temperatures do not lead to permanent damage. As the thermal effect dissipates, the bonds begin to renew, and the skin's architecture is changed to a more youthful level. After repeating this process during multiple treatments, the structure of older collagen and elastin fibers is changed, similar to newly formed collagen and elastin fibers.[25] This thermal effect is also accompanied by a heat-induced wound-healing response and increased fibroblast activity. Fibroblasts are the dermal cells responsible for producing new collagen and elastin fibers. As we age, their activity decreases to a level equivalent to an overall "net loss" of fibers. This means that the amount of newly formed fibers does not exceed the number of fibers being degraded, which accelerates the appearance of skin aging. Nevertheless, studies have shown that heat stress increases fibroblast activity, leading to an increased synthesis of collagen and elastin–neocollagenesis and neoelastinogenesis.[25] Overall, synchronized RF heating supports the skin to regain its volume, elasticity, and a more youthful appearance by restoring the collagen and elastin fiber structure and enhancing the synthesis of new collagen fibers.

CLINICAL EFFECTS OF HIFES AND SYNCHRONIZED RADIOFREQUENCY ON FACIAL TISSUES

Because of the unique design and energy delivery, HIFES does not induce the stimulation of the depressors because it could potentially lead to a worsening of rhytides. The forehead application targets the frontalis muscle (brow elevator) and corresponding fascias while avoiding the depressors in the glabella. Restoring the tonus of the frontalis muscle and tightening the fascias in combination with the skin remodeling thus lead to reduced horizontal forehead lines, brow elevation, and skin texture improvement. The cheek application primarily targets the more superficial muscles of the cheeks (zygomaticus major/minor and risorius), which are all interconnected elevating units. In contrast, other deeper muscles, such as the masseter muscle, are unaffected. Stimulation of these superficial muscles leads to an elevation of the entire cheek, increasing the midfacial volume and improving the nasolabial fold. Increasing the pull of these elevators further leads to a repositioning not only of the midface but also of the lower facial soft tissues. The resulting clinical effect is a reduction in jowls and an increase in jawline contouring. Furthermore, the combined effect of HIFES with Synchronized RF manifests as an overall textural improvement of the skin.

Clinical studies focusing on structural changes after HIFES and RF demonstrated a prominent skin remodeling effect. These studies found that collagen increase ranged between 26% and 27%, and elastin increase ranged between 110% and 129% 2 to 3 months following the procedure.[23,26] Research[27] investigating changes in skin texture and facial appearance reported a 37% wrinkle reduction and a 25% skin evenness improvement 3 months after the procedure. The processes induced in muscle tissue led to structural remodeling of the targeted muscles, which has been documented by Kinney and colleagues,[20] showing a 19% increase in muscle density and a 21% increase in the number of myonuclei. These results were coupled with reduced fibrotic and fat infiltration within the muscle tissue at 2 months after the procedure (**Fig. 3**).

The structural changes do manifest as increased resting muscular tone, which is necessary for maintaining the lifted facial appearance. The weaker the facial muscles are, the higher the muscle effort that is needed to avoid sagging and to hold the overlying tissues in place. When too weak, they become unable to hold the tissue, resulting in, for example, eyebrow drop or cheek sagging.[2] Recently, HIFES and RF was found to increase the muscle tone by 30%,[28] which was then shown to lead to an overall lifting effect by 23%.[29] Aside from multiple clinical studies using various evaluation methods, the results of the procedure are supported by a high patient satisfaction rate of 91%.[29]

APPLICATION OF HIFES AND SYNCHRONIZED RADIOFREQUENCY THERAPY WITH CURRENTLY USED PROCEDURES FOR IMPROVEMENT OF FACIAL APPEARANCE

HIFES Effects on Neurotoxin-Blocked Muscles

Neuromodulators in aesthetic medicine, such as Botox, Dysport, Xeomin, or Jeuveau, have become some of the most frequently sought nonsurgical aesthetic procedures with type A botulinum–based neurotoxins having a myriad of clinical indications. They are most frequently used to treat dynamic facial rhytides[30] involving the glabella, frontalis, and periocular regions. Botulinum neurotoxins block neurotransmitter release (Acetylcholine; Ach) in the synaptic neuromuscular junction and block voluntary muscle contraction. With blocked contractions, wrinkle formation is prevented, as the overlying skin is not being repetitively folded during daily activities and thus aids in maintaining a more youthful skin appearance.

Botulinum-based neurotoxin affects the process of muscular contraction at the level of neuromuscular junction. When applied, it works as a protease and prevents the fusion of the vesicles with the presynaptic membrane.[31] Without this fusion, the Ach

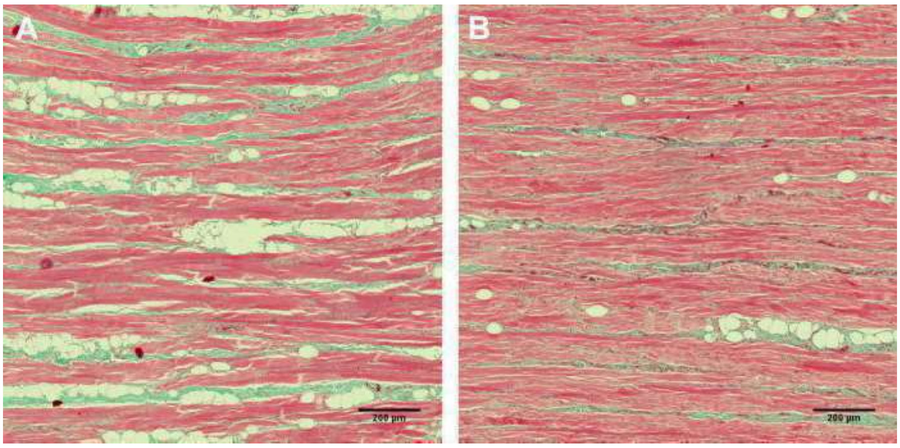

Fig. 3. Histologic images of muscle tissues before (*A*) and 2 months after (*B*) the treatment with the HIFES and RF. Red represents muscle tissue; green represents intersected collagen fibers, and white rounded cells are adipocytes.

cannot be released into the neuromuscular junction and trigger the muscle contraction. It is a chemical denervation that causes partial paralysis of the innervated muscle. However, such paralysis is not causing any damage to the nerve or the neuromuscular junction and is not permanent.[32]

Studies have shown it is possible to stimulate even the botulinum-paralyzed muscles.[33,34] However, it is not entirely clear how such stimulation overcomes the barrier made by the botulinum neurotoxin. Upon the application of botulinum toxin, the membrane of the presynaptic neuron should be practically impermeable to Ach molecules owing to its size as the fusion of vesicles and presynaptic membrane ("quantal release") is blocked. Nevertheless, clinical trials are showing that externally it is possible to overcome this barrier, and although the mechanism of how this happens is not entirely clear, several hypotheses were proposed to explain such mechanism, particularly the nonquantal Ach release[35] and direct stimulation of postsynaptic membrane.[36]

Research has shown that a nonquantal release of small amounts of Ach into the synapse still occurs, even in botulinum toxin denervated muscle. However, during voluntary contractions, the amount of the Ach is not sufficient to cause depolarization, and the muscles thus remain relaxed. By applying an external high-frequency electrical field that surpasses the frequency of brain signals, the activity of the high-affinity choline transporter could be elevated, leading to exaggerated nonquantal release of Ach in amounts sufficient enough to cause muscle depolarization and contraction. In addition, an insufficient long-term concentration of Ach in the synapse, owing to the application of botulinum toxin, can lead to an increased expression of n-acetylcholine receptor on the postsynaptic membrane and, therefore, also to an increase in the sensitivity of the muscle to Ach.[37] A lower amount of Ach would thus be needed to induce such depolarization.

On the other hand, the conclusions regarding the direct muscle stimulation are based on studies performed on skeletal muscles only. Facial muscles are of significantly different proportions and are much more superficially located in low depths. All this may influence the response. As the facial muscles are more delicate, lower intensity of stimulus may suffice to irritate the muscle membrane. Because the thickness of some facial muscles may be as small as 0.5 mm,[38] it may be possible that such stimulation is able to recruit enough muscle fibers to induce contraction of the entire muscle.

Regardless of the mechanism, HIFES technology is seemingly able to stimulate botulinum neurotoxin–blocked muscles in order to prevent risk of muscle atrophy. HIFES stimulates blocked facial muscle even though it is not possible voluntarily. Recent findings[39] showed that during the EMFACE treatment the botulinum-denervated muscles are being contracted, and what is most important, it does not interfere with the effect of botulinum toxin itself. No negative effects of the HIFES and RF procedure on the efficacy of the botulinum toxin were found.

Synchronized Radiofrequency and Dermal Fillers Treatment

Injection of dermatologic fillers is one of the most common procedures that is used in aesthetic medicine for rejuvenation of the face. These gellike substances are used for the treatment of wrinkles by injecting filler beneath the skin so it restores lost volume and more contour to the face. Fillers can be divided into 2 categories. First, the biodegradable fillers that are not permanent and can last up to 12 months, losing their effectiveness with time and eventually being metabolized. Fillers that are currently available stimulate neocollagenesis, so the effect persists longer to some extent.[40] Such dermal fillers that are currently used and approved by the Food and Drug Administration (FDA) are hyaluronic acid, calcium hydroxylapatite, and poly-L-lactic acid. The second group of nonbiodegradable fillers are long-term solutions for wrinkles, but there is a much bigger risk of complications. There are only 2 nonbiodegradable fillers approved by the FDA: polymethylmethacrylate microspheres and liquid injectable silicone (LIS), but LIS was approved only for intraocular use.[41]

Concerns have been voiced among patients and practitioners regarding RF treatments in that dermal filler would break down if they underwent RF treatment, or even worse, that the patient's skin would get damaged under RF applicators. Nevertheless, there exists plenty of evidence in the literature about safety of RF treatment over the area injected with dermal fillers.[42–44] In addition, there even exist devices that are using RF energy during dermal filler injection. In study by Kim and colleagues,[45] it was found that using RF during filler injection is a safe and effective method to treat especially mobile areas like the nasolabial fold. Overall, the findings prove that increasing the temperature of the tissue above normal levels is safe for the filler's stability. Depending on the system used, RF devices for noninvasive skin treatments elevate the tissue temperature no more than 65°C. On the other hand, the current dermal fillers are usually autoclaved, and therefore, bear considerable thermal stability. For instance, hyaluronic acid fillers are usually sterilized at a temperature of 120°C before one can observe negative effects of heightened temperatures.[46] Furthermore, the literature shows that use of RF with dermal fillers is safe for treated tissue itself if using RF treatments at normal clinical temperatures up to 65°C, which is far beyond the temperature range achieved during EMFACE therapy. Nevertheless, more studies are needed to rule out any possible doubt, especially studies using human participants treated with different ranges of RF intensity and time exposure as well as using multiple different commercially available dermal fillers.

SUMMARY

The novel EMFACE device was developed for noninvasive face lifting and wrinkle reduction by targeting all facial layers, framework, and facial muscles by simultaneously using Synchronized RF and HIFES technologies. Heating the facial tissue to effective temperatures and HIFES stimulation of only specific facial muscles result in a combined effect that causes textural changes to the skin, smoothing, wrinkle reduction, facial repositioning, and an overall lifting effect. The simultaneous and targeted manner of both technologies yields unique benefits by inducing a synergistic effect in the facial soft tissues that cannot be achieved by using these technologies consecutively or as a stand-alone procedure. It poses no risk to patients who underwent neuromodulator or dermal filler procedures and can be safely and effectively used in patients injected with either of them to deliver satisfactory improvement of overall facial appearance.

CLINICS CARE POINTS

- In a long-time botox using patients, the visible contractions start at a higher intensity and after a longer period of time, however in all the patients, the visible contractions were always achieved
- It is normal to observe asymmetrical contractions, when in doubt please palpate the subject. You can adjust the HIFES intensity for each applicator separately
- This therapy uses the radiofrequency, therefore be aware of patients' hydration

DISCLOSURE

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OPEN

First Evidence of Cutaneous Remodelling Induced by Synchronized Radiofrequency Aided by High-Intensity Facial Muscle Stimulation: Porcine Animal Model

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BACKGROUND The quality of one's facial appearance diminishes with aging as skin and underlying soft tissues deteriorate. Connective tissue and musculofascial degeneration leads to skin laxity and wrinkles developing.

OBJECTIVE To evaluate the effects of synchronized radiofrequency with high intensity facial stimulation technology on dermal collagen and elastin fibers in a porcine model.

MATERIALS AND METHODS Eight sows were divided into Active (N = 6) and Control (N = 2) groups. Synchronized radiofrequency and high intensity facial stimulation were delivered to the ventrolateral abdomen. The Active group received four 20-minute treatments, once a week. Control group was untreated. Skin biopsy sample were histologically analyzed for connective tissue changes pre- and post-treatment. Data were analyzed statistically ($\alpha = 0.05$).

RESULTS In the Active group: the collagen-occupied area at baseline was $1.12 \pm 0.09 \times 106\ \mu m^2$ and increased by +19.6% ($p < .001$) at 1-month and by +26.3% ($p < .001$) 2 months post-treatment; elastin-occupied area at baseline was $0.11 \pm 0.03 \times 106\ \mu m^2$ and increased by +75.9% ($p < .001$) at 1-month and +110.8% ($p < .001$) at 2-months follow-up. No significant changes ($p > .05$) found in the Control samples.

CONCLUSION Collagen and elastin fiber content increased significantly after treatments. Connective tissue in the treatment area was denser up to 2-months post-treatment.

Facial aging is a complex process involving changes in facial anatomy.[1] Various skin components, underlying muscle, and fibromuscular fascia are involved.[2–4] The fascial framework and the dermis consist of fibroelastic connective tissue primarily composed of collagen and elastin.[5,6] The muscles, fascia, and skin quality degenerate because of intrinsic and extrinsic factors, causing the skin to become slack and fragile.[7–9] Elastin and collagen content decline when there is an imbalance in protein turnover as the degradation of collagen is accelerated, whereas its synthesis is diminished. This lack of balance (dysregulation) causes further deterioration of connective tissue. There is a loss of tissue structural integrity and elasticity because of increased degradation of functional collagen and decreased collagen production. Fine lines (rhytids), wrinkles, and saggy skin are some signs of aging.[10–14]

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Radiofrequency (RF) causes neocollagenesis in the skin at temperatures of 40 to 45°C.[15] Thermal energy destabilizes the collagen fiber.[16] This collagen structure disruption results in the stimulation of fibroblasts needed for increased neocollagenesis and neoelastogenesis.[17]

The HIFES modality aims to remodel and tone delicate facial muscles, counter the sagging appearance of skin, and improve the facial contour with increased volume.[18] To maximize the benefits of facial treatments, a novel device using synchronized RF with HIFES was developed. Combining these 2 different technologies targets superficial (dermal) and deep (muscle and fascia) tissue components. The simultaneous application of RF and HIFES technologies may be useful in improving facial appearance characterized by sagging, wrinkles, and rhytids.

This veterinary study aimed to evaluate the effects of synchronized radiofrequency and HIFES technology on porcine skin, particularly effects of the therapy on collagen and elastin fibers in the dermis, through a noninvasive hands-free applicator.

Materials and Methods

This veterinary study protocol was approved by the Ethics Committee for Animal Protection of the Ministry of Agriculture of the Czech Republic. Before the study, the animals underwent blood tests to assess their condition and health status. Animals were kept at ambient room temperature and fed a cereal diet. The study was conducted on 8 female large white pigs (*Sus scrofa* domesticus),

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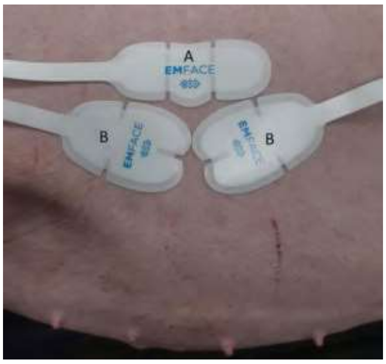

Figure 1. Illustrative set-up of the hands-free, self-adhesive device applicators on the ventrolateral abdomen of a sow that received active simultaneous RF and HIFES treatment. In human subjects, applicator A is intended for the forehead and B for the cheeks.

weighing between 60 and 80 kg. There were 2 study groups, namely, the active group with 6 sows receiving simultaneous RF and HIFES therapy under general settings, and the control group with 2 untreated sows.

The synchronized RF and HIFES treatments were delivered with a study device (EMFACE, BTL Industries Inc, Boston, MA) through noninvasive self-adhesive electrode applicators placed on the ventrolateral part of the abdomen of the sows (Figure 1). The area covered by the electrode applicator had a diameter of 15 cm, and the treatment lasted 20 minutes at 100% power setting. The temperature in the dermis and subcutaneous fat layer was measured using a fiber optic temperature probe (LumaSense Flurotropic Thermometer) inserted into the tissue using an 18-G 1.5-inch injection needle. Treatment was done once per week for a total of 4 weeks. Treated sows were kept under full general anesthesia during the introduction to the surgical hall and the entire treatment phase, which lasted up to approximately 1 hour before awakening again.

Skin samples were collected by punch biopsy (6 mm diameter, Kruse Buster) from the treatment area (in the active group) and in the analogous anatomical area of the untreated control animals. Biopsies were obtained pretreatment (baseline) and post-treatment (1-month and 2-months follow-ups) in all animals including the control. After biopsy sampling, the wounds were dressed.

Histologic Analysis

The tissue samples from the punch biopsy were processed and sectioned in preparation for Orcein and Trichrome staining protocol. After staining, slides were mounted and observed. In total, 6 slices were prepared out of every biopsy sample.

Collagen

Masson's trichrome procedure was followed for collagen-specific staining. Collagen fibers were selectively stained and developed a green color. The stained samples were mounted to a microscopy slide.

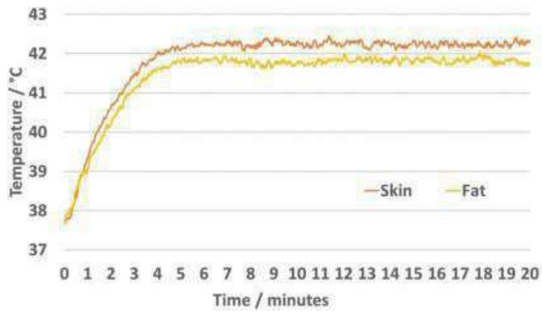

Figure 2. Thermoprobe measurement results during the treatment. The threshold temperature of approximately 40 to 42.5°C was reached in the dermis within the first 2 minutes and maintained in the range for the rest of the treatment time. The temperature in the fat was also monitored, showing about half a degree lower temperatures than the dermis.

Elastin

Visualization of elastin fibers was done with Orcein staining protocol. The elastin fibers were selectively stained and developed a brown-dark color.

The slides were observed and photographed using an automated slide scanning microscope (Hitachi Axio Scan.Z1, Carl Zeiss AG, Germany; 20×/0.8NA Plan-Apochromat objective) in a bright field. Quantitative analysis of collagen and elastin was performed with the Image J software based on semi-automatic segmentation in the Hue-Saturation-Brightness color system. The appropriate threshold differentiating the collagen and elastin fibers from the background was identified in the selected regions of interest (ROI = 1800 × 1,200 μm). After the collagen and elastin fibers were selected, their densities were expressed as the occupied area (square micrometers), which the fibers encompassed in the studied images' ROI.

Statistical analysis Student *t*-test and repeated measures analysis of variance test were performed with significance level set at $\alpha = 0.05$. Post-hoc Tukey honest significant test was conducted for multiple comparisons.

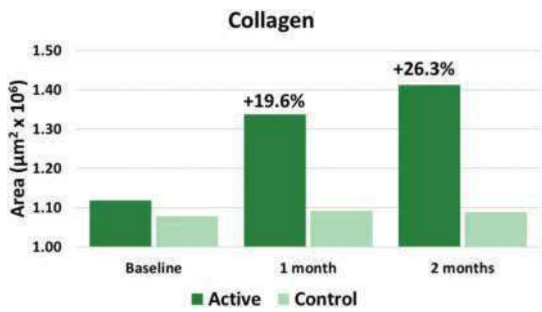

Figure 3. In the active group, the collagen fibers ($p < 0.001$) increased, occupying a greater area after 2 months follow-up compared to baseline. No significant change occurred in the control group.

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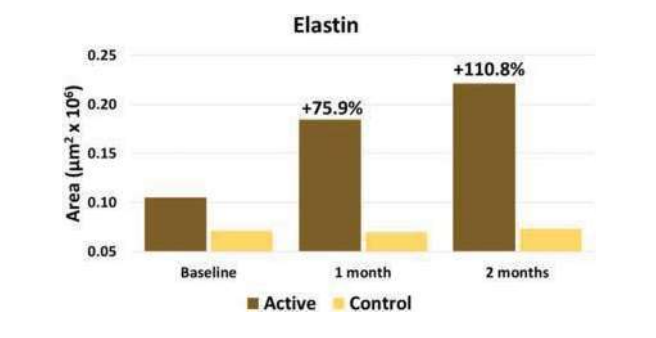

Figure 4. In the active group, the elastin fibers ($p < 0.001$) increased, occupying a greater area after 2 months follow-up compared to baseline. There was no significant change in the control group.

Results

All the sows were in good health and condition before and during the study duration. The animals recovered from anesthesia without any complications. The dermal temperature was maintained slightly above 42°C, although not exceeding 42.5°C. The measurements in the fat layer showed a temperature elevation to approximately 41.9°C, elucidating the nature of the temperature gradient observed during the treatment (Figure 2). There were no side effects or adverse events related to the treatment.

Collagen

In the active group, the average area occupied by collagen was 1.12 ± 0.09 × 106 μm^2 at baseline. The average collagen-occupied area increased to 1.34 ± 0.08 × 106 μm^2 and 1.41 ± 0.07 × 106 μm^2 at the 2-month follow-up. Compared with baseline, in the active group, the average collagen amount increased ($p < .001$) at both post-treatment follow-ups. In the control group, there was no significant difference ($p > .05$) in collagen fibers, because the collagen content fluctuated in the range of 1.08 ± 0.04 to 1.09 ± 0.05 × 106 μm^2 throughout the whole study. There was a significant difference ($p < .001$) in the collagen-occupied sample area at both the 1-month (+19.6%) and 2-month (+26.3%) follow-ups (Figure 3) when comparing treated and control samples.

Elastin

In the active group, the mean elastin-occupied area at baseline was 0.11 ± 0.03 × 106 μm^2. At the 1-month follow-up, the average elastin amount was 0.19 ± 0.02 × 106 μm^2. At the 2-month follow-up, the area encompassed by elastin increased further to 0.22 ± 0.03 × 106 μm^2. Compared with baseline, the average elastin-occupied area increased at both follow-ups ($p < .001$). At both, the 1-month (+75.9%) and 2-month (+110.8%) follow-ups, the amount of elastin was significantly different ($p < .001$) comparing the active and control group (Figure 4). In the control group, there were no significant changes ($p > .05$) in elastin density at the follow-up points, elastin content ranged between 0.71 ± 0.04 × 106 to 0.73 ± 0.06 × 106 μm^2.

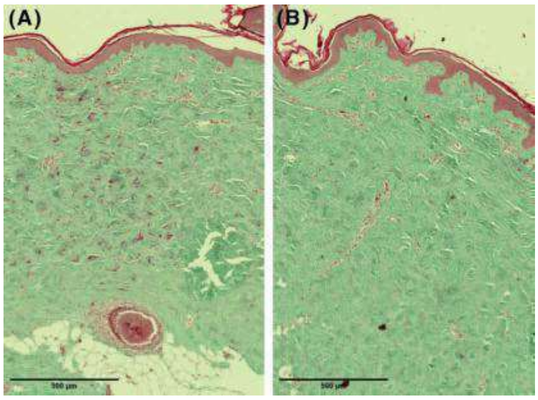

Figure 5. Bright-field visualization of collagen fibers stained by trichrome stain, active group sample. The collagen fibers appear in green color. In the slide on the right (2-months follow-up, B), the collagen fibers are noticeably denser, occupying a greater area when compared to the left (baseline, A).

Exemplary samples of the collagen (Figure 5A,B) and elastin (Figure 6A,B) microscopic evaluation results of the active group are shown below.

Discussion

This study evaluated the effects of synchronized RF and HIFES on porcine skin. Histologic analysis of connective tissue structural proteins in the dermis showed a statistically significant increase in collagen and elastin content at 1 month and 2 months post-treatment. All the treated animals in the study recovered well after each treatment and did not experience any complications or adverse events.

Collagen production and remodeling are vital in tissue regeneration and may be beneficial to promote connective

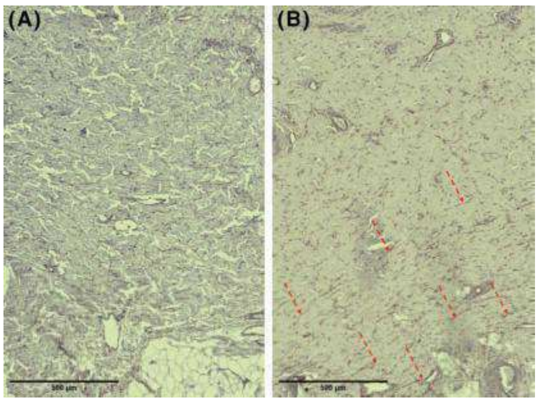

Figure 6. Bright-field visualization of elastin fibers stained by Orcein stain (active group sample). The baseline sample (left, A) has noticeably fewer elastin fibers, observed as dark/brown filaments (indicated by red arrows), than the 2-month follow-up (right, B). The surrounding collagen tissue (pale grey) also appears denser and better organized at 2 months post-treatment.

tissue fascia repair in the skin of the face. In this study, collagen content increased by +19.6% at 1 month and +26.3% at 2 months post-treatment follow-up. Elastin content increased by +75.9% at 1 month and +110.8% at 2 months after treatment, indicating that combined RF and HIFES enhanced expression of both structural proteins. The HIFES modality, in combination with RF, is intended for noninvasive improvement of skin tissue quality. Therefore, if confirmed in human subjects, this treatment method may be an alternative to current, invasive procedures aimed at improving facial appearance.[19–23]

To achieve a therapeutic effect on the skin, reaching the desired tissue temperature is key. Sustaining a lower, moderate therapeutic temperature between 40 and 45°C is essential for treatment effectiveness to circumvent cutaneous tissue necrosis and side effects because of overheating.[24] As shown in Figure 2, the dermal temperature measured via a thermal probe reached 40°C within the first 2 minutes from the start of the treatment and was maintained in the range 40 to 42.5°C for the duration of the treatment. This temperature is the target therapeutic range, which ensures treatment efficacy without affecting the underlying fat tissue, as intended during facial treatments. However, the effect on the fat should be a subject of further studies to fully rule out any alterations in response to the treatment.

The control group and temperature tracking were objective evaluation methods. Alternatively, immunofluorescence and scanning electron microscopy may be used for comprehensive connective and adipose tissue analysis. Gross examination of subcutaneous adipose tissue would expound the knowledge about the effects of sublipolytic temperatures on the underlying fat tissue structure in the treated area.[25,26]

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Conclusion

The novel RF + HIFES technology for targeting facial skin, fascia, and muscles was investigated with a focus on the changes in the skin tissue using a porcine animal model. The study results showed that the procedure induces a denser network of collagen and elastin fibers in porcine skin after treatment with synchronized radiofrequency and HIFES observed through histologic analysis and skin temperature measurement. The enhanced collagen and elastin expression observed in this study may be beneficial for skin remodeling and revitalization if replicated in human subjects.

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ORIGINAL ARTICLE

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Remodeling of facial soft tissue induced by simultaneous application of HIFES and synchronized radiofrequency provides nonsurgical lift of facial soft tissues

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Abstract

Background: The application of radiofrequency (RF) and HIFES on the body provides improvement in skeletal muscle tissue, reduction in fatty tissue, reorganization of connective tissue, and skin texture improvement. However, overall facial appearance relies on both skin and underlying structures, specifically muscles and connective tissue which have to be treated as one unit to achieve proper care while preserving fatty layers that define youth facial appearance.

Aims: The aim of this study is to find whether the effect of novel RF + HIFES is safe and can induce the lifting of soft tissue and overall improvement in facial appearance.

Methods: In this study, 21 subjects were enrolled. The therapy was administered in four 20-min treatments on the forehead and cheeks. Photographs were evaluated by a Global Aesthetic Improvement Score (GAIS) and linear measurements of facial tissue lifting at 1- and 3-month follow-ups. Volumetric changes in the cheek area were investigated as well. The patients' satisfaction, safety, and comfort were documented throughout the study.

Results: The data indicated improvement in overall facial appearance, and 23% of average lifting was found in brows ($p = 3.14 \times 10^{-12}$) and cheeks ($p = 6.00 \times 10^{-15}$). The assessment of digital photographs showed an improvement in 100% of patients at 3-month follow-up. The treatments were safe, accompanied by high therapy comfort and subject satisfaction of 98%.

Conclusions: The treatment by simultaneous RF and HIFES technology produces significant changes to the overall facial appearance, characterized by the lifting of facial tissues.

KEYWORDS
facelift, facial muscles, HIFES, noninvasive, RF

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1 | INTRODUCTION

Perception of human beauty changes over time and differs by culture. Nevertheless, there is a particular trait that we rely on despite the history or socio-geographical factors—the youthful facial appearance. Facial tissue changes, marked as aging of the face, are continuous and complex biological processes that never stop progressing. There is a constant demand for innovative approaches to influencing facial aging and slow down the biological clock.

Various extrinsic factors, as well as intrinsic ones, are involved in facial aging. Typical environmental outside factors are pollution,[1] sun exposure—specifically ultraviolet radiation, and gravity. Overall, these factors lead to pigmentation spots and wrinkles.[2] Diet, smoking, and lifestyle are, to a certain extent, involved.[3] Oppositely, intrinsic factors are linked with different facial compartments that undergo anatomical and physiological changes over time.

Various structures of the face undergo different aging processes; these compartments are skin, muscle, ligaments, and bone. Among the most noticeable manifested aging signs are the appearance of wrinkles, sagging skin, and loss of facial contours and volume. These changes occur due to decreased collagen and elastin content and the dissimilar aging progress in different face compartments. Alteration in facial structure and appearance is also notably exacerbated by elevator muscle deconditioning. The loss of support for facial tissues results in a shift in position and modified structure of soft tissues with their abovementioned compartments.[4] The focus should be placed on each facial compartment, but with an emphasis on the muscle tissue. The midface is linked by a superficial musculoaponeurotic system (SMAS), with zygomaticus muscles playing a dynamic role.[5] Weakening of these muscles can lead to gradual atrophy and sagging, resulting in nasolabial folds, marionette lines, and jowls.[6] By activating these muscles and associated connective tissue, their original form can be improved or preserved, and the midfacial soft tissue can be repositioned.

To achieve specific effects, numerous surgical and nonsurgical aesthetic procedures have been developed to combat facial aging.[7] Among noninvasive procedures, radiofrequency (RF) is considered the gold standard for skin treatment. The principle of technology is based on dermal heating providing structural changes, thus resulting in an overall improvement in skin texture and quality.[8] However, this modality does not target the underlying structures that lift and tighten the overlying tissues. To overcome this limitation, minimally invasive treatments used for volume restoration are utilized; however, they do not provide an effect on underlying muscles crucial for natural skin mobility as well.[9] The most efficient but radical approach is rhytidectomy, the surgical facelift that brings the post-operational drawbacks, counting a lengthy recovery period, scarring, and other related risks.[10]

The latest advancement in noninvasive facial aesthetic treatments is HIFES technology which can target the delicate muscle tissue and connective tissue framework of the tissues of facial expression (SMAS and perhaps to some extent the muscles of mastication and their fascia).[11,12] The HIFES technology generates strong electrical fields, that affect the underlying neuronal and muscle tissue. These electrical fields depolarize the membrane of the motor neurons that innervate the muscle. When motor neurons are activated, a signal travels to the neuromuscular junction, where the neuron connects to the muscle. This signal makes the muscle contract involuntarily, bypassing the brain's control. High-intensity facial stimulation prevents the facial muscles from relaxing between signals, causing continuous contractions. Adjusting the electrical field strength and frequency leads to a "supramaximal contraction."

A holistic solution emerged in applying RF and HIFES to treat skin and muscles in one procedure, aiming for noninvasive skin rejuvenation and lifting of facial structures. The HIFES technology induces electrical fields to contract facial muscles selectively,[13] since the tonus of facial muscles is crucial to ensure the support to surrounding soft tissues. Repeated application of HIFES initiates muscle protein synthesis and can induce the densification of the muscle tissue.[14] By contrast, changes induced by RF heating involve dermal structure and subdermal architecture.[15] As was found with previous research specifically neocollegenesis and neoelastogenesis occur a few weeks after the RF therapies which are recorded as overall improvement in skin appearance and its properties.[16] The application of these two modalities in one treatment has a positive effect on improved blood circulation, leading to a boost in nutrient supply caused by the supportive effect of RF andHIFES.[17] Combining these technologies targets all-important facial tissue compartments, aiming to maintain a youthful appearance.

The study objective was to evaluate the safety and efficiency of the novel technology combining Sync RF and HIFES. During the therapy, synchronized radiofrequency (skin and underlying connective tissue heating) and HIFES (muscle toning) are simultaneously administered. The aim is to document the changes to facial tissues, namely the lifting of facial structures resulting in a naturally youthful appearance.

2 | MATERIALS AND METHODS

2.1 | Study population

This single-arm, open-label study enrolled 21 (three males and 18 females) patients in the age range of 24–60 years (45.17 ± 11.20 on average) with Fitzpatrick type ranging from I to V, at two sites. Selection criteria included healthy adult subjects (over 21 years old) of any gender with clearly visible sagging skin in the treated area. The main exclusion criteria were metallic implants, local infection, or unhealed wounds in the treated area. Limits were not applied to ethnic backgrounds or skin types, all adults seeking treatment who fall within inclusion criteria, and do not meet any of the exclusion criteria, were eligible for enrollment. Detailed instructions about the study were given to all enrolled subjects after providing written consent. The study design and treatment protocol were approved by the Advarra Institutional Review Board and followed the ethical guidelines of the 1975 Declaration of Helsinki.

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2.2 | Study design

Therapy consisted of four 20-min treatments given once a week. The HIFES and RF energies were administered simultaneously on all treated areas (i.e., both cheeks and forehead) by self-adhesive, single-use applicators connected to the EMFACE device (BTL Industries Ltd., Boston, MA). The parameters of the therapy were adjusted according to patient feedback and tolerability on a scale 0%–100% separately for both RF and HIFES. Patients were treated in the supine position without the use of anesthesia. Before the treatment, the face was cleared of cosmetic products, jewelry, or prominent hair.

2.3 | Data collection and evaluation

The 2D digital photographs were evaluated at baseline, and at 1- and 3-month follow-up visits. The photographs were graded for the magnitude of change in facial appearance by three independent evaluators, using the GAIS score based on a 5-grade scale (−1—worse, 0—no change, 1—improved, 2—much improved, 3—very much improved).

The lifting effect was assessed by the measurements of eyebrow lift in 2D digital photographs (front view), based on the methodology described by other authors,[18] (Figure 1). Additionally, the cheek lift was assessed by measuring the width of the line between both nasolabial creases at the middle level between the upper line of the lip and the crease root of the nose in front and side view (Figure 2). Safety and adverse events were monitored throughout the study.

Secondary outcomes included the measurement of volumetric changes in the cheek and mandibular region based on the 3D models reconstructed from photographs taken by VECTRA® H2 camera (Canfield Scientific Inc., US). Particularly, the measured areas (bilaterally) were the malar part of the face, specifically around the occurrence of the malar eminence,[19] and the inferior part between the cheekbone and mandibular area in the buccal region.[20]

The subject's satisfaction with the results was documented throughout the study by the 5-point Likert scale Subjects' Satisfaction Questionnaire consisting of four questions related to facial appearance improvement, lifting of facial tissues, perception of appearance improvement, and overall satisfaction with treatment results. Additionally, a Therapy Comfort Questionnaire (combining a 5-point Likert scale and 10-point Visual Analog Pain scale) was given to the subjects after the last treatment.

For the evaluation of obtained data, the descriptive statistics (mean and standard deviation), together with repeated measures ANOVA were used followed by Tukey HSD tests. The statistical tests were run at the level of significance $\alpha = 0.05$ (5%).

Written consent was provided, by which the patients agreed to the use and analysis of their data.

3 | RESULTS

Of 21 subjects, 18 completed all the scheduled treatment sessions and follow-up visits. The treatment settings were well tolerated achieving 35%–75% for HIFES and 100% of RF (with one subject tolerating 75% of the RF output).

3.1 | Subjective outcome scoring

The evaluation of 2D digital photographs according to GAIS showed significant ($p < 0.05$) gradual improvement with the peak at 3-month follow-up when 100% of patients were graded at least as improved. An average improvement of 0.9 ± 0.3 points was achieved when rating 1-month photographs, which further increased to 1.1 ± 0.3 points at the 3-month follow-up visit (Figure 3).

3.2 | Evaluation of the lifting measurement

Assessment of the lifting effect showed significant ($p < 0.05$) improvement for every measurement compared in each of the follow-up visits to the baseline. Both the midpart (cheek lift) and upper part of the face (brow lift) showed the peak of the treatment effect at the 3-month follow-up visit. The average eyebrow lift was 16.5% at 1-month follow-up (+2.58 ± 0.66 mm; $p = 1.07 \times 10^{-8}$)

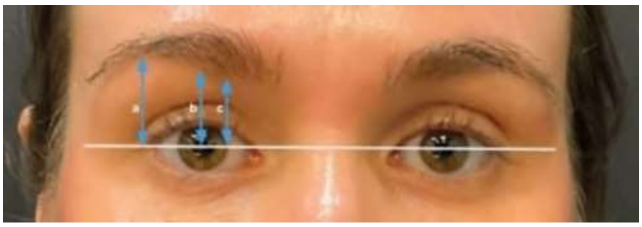

FIGURE 1 Visual guidance to the eyebrow lift effect measurements: different distances from reference line intersecting left and right lateral canthus from (a) lateral canthus, (b) medial limbus, (c) center of the pupil to lower line of the eyebrow.

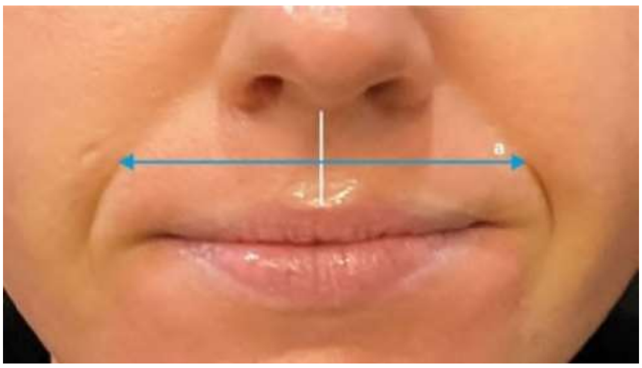

FIGURE 2 Visual guidance to cheek lift effect measurements: (a) distance between nasolabial creases in half line root of nose and lip crease, intersecting a white reference line in the middle.

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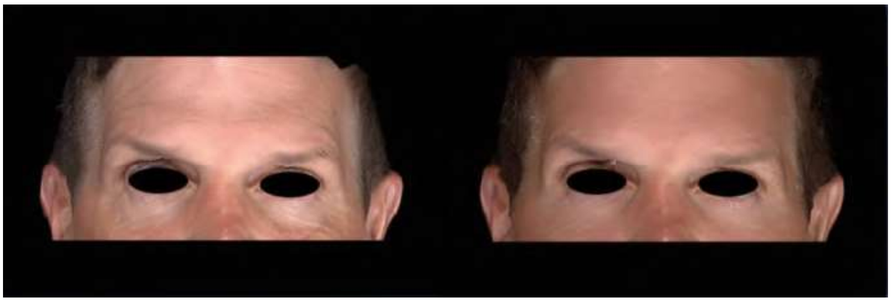

FIGURE 3 Comparison of the baseline (left) and after-the-treatment visit photographs. Improved suppleness of skin and reduction in wrinkles in the periorbital area and forehead can be seen.

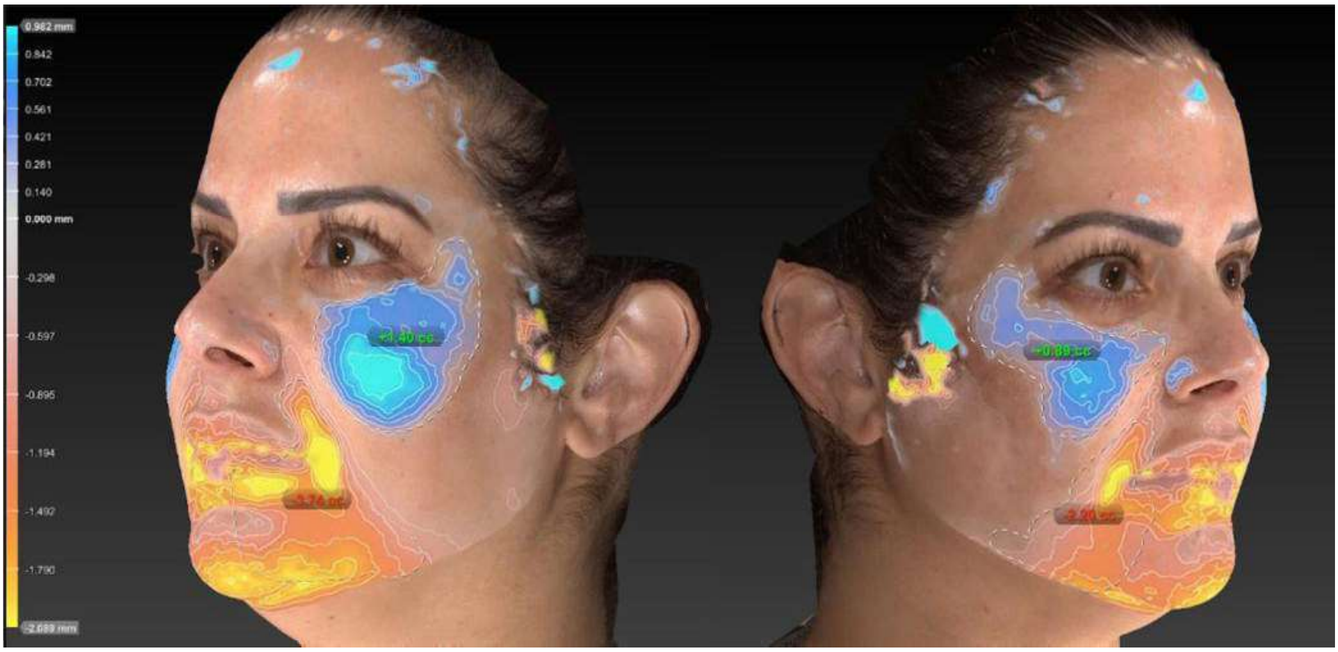

FIGURE 4 Vectra 3D photograph volumetric analyses: the change of volume in face at baseline and 3 months follow-up visit measured on left and right side.

and 22.2% (+3.25 ± 0.74 mm; $p = 3.14 \times 10^{-12}$) at 3 months. The maximum average increase in eyebrow lift at 3 months was measured from the medial limbus distance with a value of 3.79 mm. Conversely, the changes of the least magnitude were detected from the point of the center of the pupil, which was 2.41 mm at 3 months. The average cheek lift effect measured from the frontal view progressed from 1 to 3 months, reaching +3.09 ± 1.96 mm ($p = 2.08 \times 10^{-11}$) to +3.83 ± 1.80 mm ($p = 6.00 \times 10^{-15}$), respectively (Figure 4).

3.3 | Computed 3D photograph volumetric analysis

An increase of volume in the upper part of the midface in the region of malar eminence reached, on average, +0.95 ± 0.38 mL in 1 month and + 1.27 ± 1.08 mL in the 3-month follow-up visit. Conversely, the decrease was detected in the lower part of the midface in the buccal region where it reached −1.35 ± 0.86 and − 1.06 ± 0.5 mL on average at 1 months and 3 months. Both volume changes were counted for each side of the face and averaged. Total volume gain for both sides was 2.53 ± 2.1 mL at 3 months on average.

3.4 | Subject comfort and satisfaction

The presented data are consistent with the results obtained from 18 patients at the 3-month follow-up visit. Satisfaction of the patients was reported as very high, remaining constant during the study, resulting in average satisfaction of 98.2%. All subjects agreed that their appearance in the treatment area improved after the treatments. A more lifted feeling of skin in the treatment area was reported from 94.4% of subjects. Most patients (85.7%, $n = 18$) agreed the therapy was comfortable, with an average pain score of 1.4 ($n = 18$) on the visual analog scale, classifying the treatment as not painful. None of the patients perceived the therapy as uncomfortable. No adverse events or side effects occurred during the treatment.

4 | DISCUSSION

According to the findings of this study, based on both objective and subjective means of evaluation, the noticeable enhancement to sagging facial soft tissues and gradual restoration of facial contours was documented after the simultaneous application of HIFES+RF.

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It is crucial to target all facial layers with a preferred focus on muscle tissue when it comes to noninvasive facial treatments. These muscles are weakened with age, causing specific manifestations in each part of the face. In the midface, the cheeks are interconnected by the midfacial superficial musculoaponeurotic system,[7] where the zygomaticus muscles are involved. Deconditioned and atrophied muscles can progressively cause the descent of soft tissues, which externally appear as nasolabial folds (marionette lines) and jowls.[8] Stimulating muscles and related connective tissue matrix can help secure its original position and shape or allow for midfacial soft tissue repositioning.

Similarly, in the upper third part of the face, the frontalis muscle is the primary determiner of eyebrow movements.[21] Frontalis is interconnected to other supra-frontalis layers, including the skin, and sub-frontalis fascia to deeper layers.[22] Aging-related changes of this complex may lead to eyebrow ptosis[23] and connective tissue degeneration resulting in laxity and wrinkle formation.

The anatomical structures in the mid and upper face crucial for the overall facial appearance are specifically targeted by the EMFACE device due to the unique synergy of HIFES and synchronized RF. This procedure allows for comfortable facial treatments, delivered noninvasively while addressing the key tissue layers. The magnitude of achieved results accompanied by very high patient satisfaction suggests that HIFES+RF constitutes in some circumstances a feasible alternative to current solutions such as rhytidectomy or microinvasive neurotoxin-based injections and fillers, which attract increasing attention nowadays.[3] Although the concurrent approaches possess high efficiency, the long recovery period, non-negligible risk of adverse effects, and lesser comfort level may not be acceptable for all patients. In addition, invasive procedures may cause scarring, and neurotoxin overuse may build up a resistance to active substances.[24] On the contrary, noninvasive treatment by RF and HIFES avoids any downtime or unpleasant risks, as documented in this study.

The different evaluation methods used in this study pointed to consistent results regarding favorable changes in facial appearance. These changes, captured by digital photographs, were expressed in objective linear measurements of lifting effect amounting to +23% at 3 months. Correspondingly, an overall improvement in facial appearance was seen in 100% of patients, as documented by subjective visual scoring with GAIS.

The outcomes from 2D photograph analyses indicated a considerable shift in soft tissues that resulted in volume changes in the face. 3D photographs evaluation showed volume shifts and reduction in the jowl region and, conversely, a volume increase in the zygomatic part of the face. This positive volume shift in the malar regions accounted for an absolute average difference of 2.5 ± 2.1 mL in total. Such results approximate the effect of fillers and limited autologous fat grafting, which have mainly a local effect fixed on application placement not involving different parts and tissues of the face. Additionally, the effect is unstable over time and must be revived to gain desired results. Generally, the best outcome can be achieved by a combination of different approaches; with invasive procedures, the positive volume gain can reach up to 5.7 ± 2.9 mL on average in the midface region[20]; however, the risks connected to invasive procedures are present.

The combination of invasive and noninvasive methods is also efficient. RF and HIFES can be successfully combined with neurotoxin therapy in which induced paralysis of muscles in one area, to avoid formation of wrinkles, is supplemented by HIFES energy stimulation in another.[15] The prevention from dropping and loss of tonus in the face, especially in the forehead area where the frontalis muscle is conditioned, may be ensured.

Simultaneous application of HIFES and RF induces changes in the soft tissues and stimulates directly or indirectly the different compartments of the face bringing a holistic approach to the rejuvenation of the face. Concretely, the densification and muscle function improvement by HIFES produce a more contoured and compact visual appearance of the face.[6] Coupling with the heating effect of RF inducing structural changes originating from collagen and elastin remodeling,[25] overall skin revitalization due to synergistic effect, occurs. In addition, the therapy was perceived as comfortable and not painful, accompanied by high patient satisfaction of 98.2% in this study.

Although positive and consistent results from various measurements suggest the efficacy of the investigated technology for facial soft tissue lifting and rejuvenation, the sample size of 17 patients at 3 months may lead to underpowered statistics. Also, the utilization of 2D and 3D photographs does not provide further insight into changes in delicate facial anatomy induced by the simultaneous application of HIFES+RF. Therefore, further investigation is needed to correlate data from 2D and 3D analyses related to volumetric changes in the midface and lifting effect with the functional changes in facial tissues. This can be achieved by assessment of the entire cheek volume change to insight comprehensive changes. Future research would benefit from studies comparing RF+ HIFES with standalone HIFES or standalone RF to find whatever is the specific effect of combined or standalone modalities to provide thorough guidance to practical application. The longevity of the effects at 6 and 12 months post procedure is currently unknown. In addition, augmentation of the volume effects would be a possibility with more treatment sessions.

5 | CONCLUSION

Simultaneous noninvasive treatment by Synchronized RF and HIFES facilitates changes to the overall facial appearance by targeting both skin and delicate facial muscles. Specifically, the therapy induces favorable volumetric changes to the cheek and mandibular area while delivering a considerable lifting effect to the sagging facial contours. Since being safe and accompanied by high satisfaction, it poses a valuable alternative or complementary solution to current mini-invasive and invasive procedures.

AUTHOR CONTRIBUTION

All authors contributed equally.

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CONFLICT OF INTEREST STATEMENT

The authors have declared they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The Investigation Review Board (IRB) approved the study and registered at ClinicalTrials.gov (NCT05525026). All subjects voluntarily signed a written consent form to have their faces photographed and published.

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Treating Facial Palsy

Aesthetic nurse prescriber Michelle McLean provides insight into facial palsy and treatment options within aesthetic medicine

Facial paralysis, or facial palsy, is a common neuropathy with an annual incidence of 70 cases per 100,000 members of the population in the UK.[1] It may be more following COVID-19 infection and its reported possible side effects, although more research is needed into this area to confirm any hypothesis.[2,3]

Patients with concerns about facial paralysis frequently present to aesthetic clinics hoping to achieve better facial balancing through aesthetic treatments. Increased patient knowledge and awareness of non-surgical procedures and the advancement of injection techniques have led to a significant shift from surgical to non-surgical and combined approaches.

As a clinician, a sound understanding of facial paralysis is essential when treating patients presenting with facial palsy, and considerations should be made to ensure that treatment positively impacts both the physical and psychosocial care of patients.

Causes of facial palsy

Facial paralysis, or facial palsy, generally refers to weakness or total loss of movement of the facial muscles resulting from temporary or permanent damage to the facial nerve.[4] Facial palsy can be a congenital disorder, meaning it presents at the time of birth due to delivery traumas and genetic or malformative diseases.[5] It can alternatively be acquired, possibly appearing at any time during life due to infective, inflammatory, neoplastic, traumatic or iatrogenic causes, and affecting people of any age.[5]

Site	Aetiology
Intracranial	• Acoustic neuroma • Stroke (forehead spared) • Brain stem tumour

Intratemporal	• Bell's palsy (diagnosis of exclusion Herpes zoster oticus, Ramsay-Hunt syndrome)
	• Middle ear infection
	• Trauma:
	  • Surgical
	  • Temporal bone fracture
	  • Lacerations anterior/inferior to the tragus

Extratemporal	• Parotid tumours
Miscellaneous	• Sarcoidosis, polyneuritis

Table 1: Causes of facial nerve palsy[10]

The most common known cause of facial paralysis is generally idiopathic with no apparent reason: Bell's palsy.[6] Other facial nerve palsies can be related to several conditions: Ramsay-Hunt syndrome (caused by herpes zoster outbreak), cholesteatoma, parotid gland tumours, Lyme disease, otitis media, HIV, leprosy, amyloidosis, Guillain-Barré syndrome and sarcoidosis (autoimmune diseases), diabetes and strokes (**Table 1**).[6-8] Infection reports account for 7% of presenting cases, trauma 10-23% and tumours 2-2.5%.[9]

When facial paralysis presents, there is damage or injury to a particular branch of the facial nerve and the correlated muscles.[1] Facial nerve damage can result from various causes frequency of these is as yet unknown.[1]

Facial paralysis can be identified as unilateral (affects one side of the face), which is most commonly seen, or bilateral (affects both sides) – a rarer presentation.[1] The symptoms of facial palsy can vary between patients depending on the underlying cause and severity of the condition.[1]

In some cases, the weakness or paralysis may be mild and only affect certain areas of the face, such as the mouth or eyelid. In more severe cases, the entire face may be affected, including the ability to close the eye on the affected side.[11]

Medical treatment for facial palsy depends on the underlying cause of the condition. In some cases, the condition may improve on its own over time. In the UK, patients experience a considerable variation in care pathways, including medication, physical therapy and surgery.[12] A face-to-face consultation should establish if the patient has a confirmed diagnosis of facial palsy, and the severity of their condition. In the absence of a confirmed diagnosis, the clinician must refrain from treatment and refer the patient back to their GP for further investigation.

In an upper motor neurone palsy, the frontalis is spared, and the patient can still wrinkle the forehead on the affected side. There is no effect on the eyelid or closure of the eye itself. Various causes of upper motor neurone facial palsy include multiple sclerosis, stroke, intracranial tumours, HIV and infections such as syphilis.[13]

Lower motor neurone lesions are associated mostly with Bell's palsy, and around 10 to 40 people per 100,000 are affected annually.[14] A lower motor neuron palsy presents with a total unilateral palsy presentation.[14] Other lower motor neuron lesions are associated with Ramsay-Hunt Syndrome.[14]

It is important for clinicians to refrain from attempting to diagnose patients with facial palsy. Diagnosis should be established through the patient's GP/NHS secondary care pathway to determine the condition's underlying cause. These individuals possess extensive training and experience in this field, so patients should be referred on to them.

Successful treatment of patients relies on assessing the individual's presentation in-clinic, rather than focusing solely on the cause of paralysis. An all-encompassing understanding of the patient is essential for effective treatment since symptoms are unique to each patient and a generalised approach will not suffice. Analysing the patient's psychosocial wellbeing and the impact of paralysis on their daily life is crucial in identifying their specific concerns and objectives.

Damage to the facial nerve CN VII, whether inflammation or compression, can trigger substantial variable symptoms depending on the lesion site and the branch affected, which can be permanent or reversible.[15,16] Symptoms can include a visible mouth droop, flattening of the nasolabial fold, inability to close the eye and smoothing of the brow on the damaged side.[15,16]

The main causation of Bell's palsy suggests it relates to the herpes simplex virus.[15] Therefore, understanding the facial nerve complexity and its variability is pivotal for clinicians in the non-surgical medical aesthetics arena to treat nerve-related injuries/conditions, and prevent damage whilst providing satisfactory results to patients.

Aesthetics as a potential cause of facial paralysis

From an aesthetic perspective, nerve injury secondary to dermal fillers, although rare, can occur, whether it be through blunt or sharp force. The facial nerve can undergo trauma through direct injection into a nerve by needle or cannula, or through compressing and excessive massaging of dermal fillers, which can result in sensory or motor deficit.[17] Threads and dental block procedures can also result in nerve injury.[18,19]

Whilst sound anatomical knowledge is pivotal and will help to reduce the risk and potential of nerve-induced trauma, practitioners should acknowledge that anatomical variations do exist.

If a patient presents with paralysis or weakness following an aesthetic procedure, it is vital that a full face-to-face consultation, medical history analysis and examination of ocular and perioral musculature is sought, as this will greatly assist in the effective and appropriate management of onward secondary care referral.

Figure 1: 56-year-old female patient at baseline in 2019, and at 2022 following botulinum toxin treatment

Facial paralysis caused by dermal fillers is extremely rare, and in my 12 years of aesthetic practice, I have never encountered this complication. Studies in this area are limited, and it would be beneficial for it to be recorded in the future. To ensure the safety of the patient, it is important to have a reliable referral system in place. The use of ultrasound scanning can provide valuable information about the placement of dermal fillers, which can be shared with emergency services if immediate treatment is needed.[20] If the clinician lacks relevant experience or cannot provide treatment, it is necessary to refer the patient for emergency treatment via the NHS Emergency Department or with a complications management specialist.

The facial nerve is a vital structure for emotion and communication, and impairment can cause a substantial decline in a patient's quality of life.[14] The impact of the inability to smile and express emotion is the main distressing aspect of facial palsy, and such individuals fear being negatively evaluated by others, which has a detrimental impact on their social interactions.[21]

Aesthetics as a treatment for facial paralysis

The administration of botulinum toxin can play a crucial role in improving quality of life in facial palsy patients. A recent study showed that a single dose of botulinum toxin administered on the unaffected side of 18 patients with acute facial paralysis generated momentous improvement in facial symmetry four weeks post-treatment.[21] Individualised botulinum toxin injection patterns are critical for optimal unilateral synkinesis and contralateral hyperkinesis success. It is important to note that synkinesis treatment aims to target accurate, viable synkinesis muscles and not stimulate flaccid muscles.[21]

When it comes to individualising treatment for patients with facial paralysis, it is crucial that the clinician is well-trained and highly experienced. They should have received ample training and gained experience by shadowing other specialist practitioners who regularly treat facial palsy. In addition to having a thorough understanding of facial anatomy, clinicians should also take a holistic approach to treatment and be familiar with various options such as surgery, therapy, rehabilitation and more. If a clinician is not experienced in treating facial paralysis, referring the patient to a specialist practitioner or back through their NHS pathway is recommended.

Those seeking to expand their knowledge can refer to courses like 'A Multidisciplinary Approach to the Management of Facial Palsy' developed by Catriona Neville (ESP Physiotherapist at Queen Victoria Hospital NHS Foundation Trust) and Sally Glover (Clinical Specialist Physiotherapist, University Hospitals Birmingham NHSFT).[22]

Botulinum toxin can be administered into the non-paralysed facial muscles for successful hyperkinesis treatment to help relax the activity and improve symmetry. Clinicians must carefully consider the precise injection location, depth and angle of treatment, as unnecessary side effects can harm such patients and further exacerbate facial asymmetry. To help minimise such risks, under-correction is essential in the initial treatment plan, as additional injections can be made during the review appointment.[23]

Figure 2: 35-year-old female patient at baseline, after botulinum toxin treatment in 2023 and after EMFACE treatment in 2023

Case study one

This case looks at a 56-year-old female patient. The patient has attended my clinic for regular treatment over the past four years. She has Ramsay Hunt syndrome, and had previously accessed toxins for palsy from the NHS. Free NHS treatment is limited, so additional treatment at my clinic has been used to maintain results in between. Following a recent appointment with her NHS consultant, she was highly dissatisfied with the results, noting that the results seemed to emphasise asymmetry. The patient's wedding was imminent and following successful treatment at my clinic in the past, she returned to discuss possible options before her big day.

A consultation was conducted before treatment to assess suitability and manage the patient's expectations. It was explained that a conservative approach with a view to subsequent top-ups would be the best approach, as in patients with facial palsy, higher doses of botulinum toxin can lead to difficulty talking, eating and drinking.[24]

Treatment

Botulinum toxin type A (Azzalure from Galderma) was injected into the depressor anguli oris (5 Speywood units) and the upper horizontal fibres of the platysma (20 s.U) on the contralateral side to the facial palsy to decrease the tone of the muscle and improve symmetry. This reduced the downward force of zygomaticus major, zygomaticus minor, levator labii superioris and levator labii superioris alaeque nasi, and provided an elevation of the tissue.

Azzalure was also injected into the mentalis (10 s.U) to enable oral commissure elevation, and the orbicularis oculi (20 s.U) and corrugator supercilia (20 s.U) on the unaffected side to improve symmetry and balance. Vivacy Stylage dermal filler was combined with botulinum toxin to improve zygomaticus function and balance as well as improve lip symmetry at rest. Stylage S (1.2ml) was used to augment the lip and soften perioral lines on the hyperactive side. Stylage M (1.3ml) was used to soften and reduce static line activity in the nasolabial fold areas and to support oral commissure elevation.

Results

The patient results show facial balance and harmony have been restored (**Figure 1**), and she reported that her wellbeing had significantly improved. Aftercare advice was general for any patient undergoing toxin and dermal filler treatment; no aftercare specific to facial paralysis was necessary. The patient will next attend the clinic four months after treatment for a new assessment and potential continued treatment.

Case study two

This case looks at a 35-year-old female patient. She suffered facial palsy due to nerve damage from surgical operations on the jaw. Her wellbeing was deeply affected by the physical effects of facial paralysis, meaning she was sometimes withdrawn from society.

Treatment

Initially, toxin was chosen as the management plan to relax unwanted muscle activity on the unaffected side. Azzalure was injected into the corrugator supercilia (20 units s.U), frontalis (15 units s.U) and orbicularis oculi (15 units s.U) on the unaffected side to achieve symmetry and facial harmony by reducing unwanted tension and hyperactivity due to synkinesis. Four months following toxin treatment, we utilised this patient as part of a small study using EMFACE technology. The patient underwent four sessions of EMFACE, each session one week apart. In EMFACE, three facial applicator pads simultaneously emit both synchronised radiofrequency and high intensity facial electromagnetic stimulation (HIFES) energies, causing stimulation on the elevators of the facial muscles – the frontalis, the zygomaticus major and minor and the risorius muscles.[25] The treatment resulted in significant improvements in facial symmetry even after one session.

Results

The patient results show facial balance and harmony have been restored (**Figure 2**), and she reported her wellbeing and mental health had significantly improved. Aftercare advice was general for any patient undergoing toxin or EMFACE treatment; no aftercare specific to facial paralysis was necessary. Toxin results typically last around four months, so the patient will next attend the clinic in four months for a new assessment for toxin management.

Improving patient wellbeing

When carrying out aesthetic treatments, sound anatomical knowledge is required to minimise the risk of nerve injury/neurapraxia, which can be linked to dermal fillers and thread administration, resulting in facial palsy. When it comes to facial palsy patients, whether the condition is related to Bell's palsy, Ramsay Hunt Syndrome etc., experienced clinicians can play a pivotal role in improving patients' quality of life through the successful administration of botulinum toxin and other aesthetic treatments.

Michelle McLean is the founder and medical lead for Aesthetically You, a 'good' rated CQC clinic in the Northwest of England. She has more than 12 years of experience in the industry and is a regional leader for the BACN. McLean is currently completing a second Master's in Cosmetic Medicine.
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Simultaneous Emission of Synchronized Radiofrequency+ and HIFES for Non-invasive Submental Volume Reduction: The Mechanism of Action

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Abstract
An EMFACE submentum applicator is revolutionizing the non-invasive treatment of the submental area. Utilizing the simultaneous emission of Synchronized RF+ and HIFES, the submental applicator targets three layers in the submental region; HIFES selectively tones the strategic submental muscles, and simultaneously RF heating induces lipolysis of the fat depots in the region and tightens fascias and the overlying skin. With two energies targeting all layers from muscle to skin, this novel EMFACE submentum applicator promises a new and strategic approach in improving the appearance of the submental region.

Keywords: HIFES, Radiofrequency, Synchronized RF+, Simultaneous, Application, Supramaximal, Contraction, Muscle, Fat, Reduction, Hypertrophy, Face, Lift, Double chin, Pseudo-double chin, Digastric muscle,

Introduction

The submental region is one of the most critical areas regarding the overall aesthetic of the face. Both aging and lifestyle can be reasons for changes in submental volume, making it a problem for people of all ages. Submental fullness affects how others perceive us. The holy grail of measurement determining submental aesthetics is the angle formed by the submental and cervical planes. This angle is called the submental-cervical angle. Studies reported that the submental appearance is considered attractive and youthful when the submental-cervical angle is between 90°-105°.[1] When below this range, the aesthetic look is perceived as unnatural. When the angle is above this "ideal" range, the submental region is perceived as too volumized and unattractive.

From the anatomical standpoint, the submental region is a multilayered unit where each layer significantly contributes to the degree of the submental-cervical angle. The uppermost layer is the skin covering the subcutaneous fat layer, under which is located the thin platysma muscle. Under the platysma is usually a thin layer of subplatysmal fat that covers the muscles of the submandibular triangle. The outermost muscle of the submandibular triangle is the digastric muscle, which keeps and elevates the position of the hyoid bone as well as all other submandibular muscles.[2,3]

A change in one of these layers affects the submental-cervical angle. However, during aging all of these layers undergo changes, leading to a large impact on the overall submental appearance.

Submental skin layer

As in all body areas, the skin of the submental region undergoes age-related changes due to the continual loss of collagen and elastin.[4,5] Due to the loss of these crucial skin proteins, the skin loses its elastic properties and firmness, which inevitably leads to skin sagging and the formation of wrinkles. However, submental skin experiences sagging more than wrinkles. Gravity pulls lax skin down, and this downward repositioning thus increases the submental-cervical angle. Skin sagging is the predominant submental concern for older patients but can also result from rapid fat loss in the region, either because of weight loss or by aesthetic procedures not followed by skin tightening. [6,7]

Submental fat layer

An increase in the volume of the submental region is often the first noticeable change and is commonly called "double chin." One of the reasons for increased volume is the accumulation of submental fat formed superficially over the platysma. Importantly, there is also fat located under the platysma.[3] Aesthetic treatments target the superficial compartments, which Larson et al. reported as the location where the majority of the fat is located and which highly affects the submental cervical angle.

Submental muscles' relation to the submental cervical angle

Weakened submental muscles are another reason for increased submental volume and have long been neglected. To truly comprehend the muscle contribution to the submental volume it is necessary to understand the anatomy of the submental region.

The muscles of the anterior upper neck, including the submandibular and submental triangle, are arranged in two layers separated by fat. The superficial muscular layer is formed by the platysma, a muscle of facial expression, whereas the deep muscular layer is formed by the suprahyoid muscles which contribute to swallowing and head movement. The platysma muscle covers the entire anterior and lateral neck region and extends from its attachments at the mandible to its continuation with the superficial fascia of the chest; the transition from muscle to fascia occurs approximately at the clavicles. Age-related features of the platysma include platysmal banding, which is visible at rest and is referred to clinically as Turkey neck deformity. This age-related feature must be differentiated from platysmal bands that are visible only during muscular contractions and can be treated with neuromodulator injections, which were shown to decrease the appearance of contraction-related banding and improve lower face and neck contouring.[8–11] In addition to the inhibition of the platysma muscle to reduce platysma bands, there are surgical options for aesthetic improvement of the submental-cervical angle through platysma manipulation, such as a "neck-lift". During this procedure, the platysma muscle is repositioned upward, contributing to the elevation and support of the underlying tissues in the submental cervical area.[12–15]

The deep muscular layer of the upper neck consists of two muscles, which together form the submandibular triangle. A pair of anterior bellies of the digastric muscle, which creates borders of the submandibular triangle and the mylohyoid muscle located deep to the anterior bellies of the digastric, form the floor of the submental area. Both of these muscles most likely undergo a process termed sarcopenia which results potentially in a reduction of their baseline tone and maximal contraction strength.[16] However, only the anterior bellies of the digastric muscle are deemed to significantly contribute to the submental fullness due to their more superficial position and place of attachment.[17,18]

It has been observed that the anterior belly of the digastric muscle might "bulge" more anteriorly therefore increasing the submental cervical angle. The etiology of this problem was previously incorrectly labeled as digastric muscle hypertrophy. Multiple surgical interventions were designed to target the “bulky” digastric muscle. However, recent MRI findings do not support the theory of muscular hypertrophy with aging but rather indicate muscle laxity of the digastric muscle that affects submental fullness. [16,19]

The most likely explanation of this phenomenon is that the weakened digastric muscle loses its muscle tone resulting in its increased laxity. In conjunction with changes in the surrounding tissue, the lax digastric muscle allows for the movement of the surrounding fat compartments in a downward direction, making the digastric muscle “bulge out” consequently increasing the submental-cervical angle. This condition is called the pseudo-double chin (Figure 1). A weak digastric muscle is unable to hold the weight of accumulated fat and reposition itself inferior and anterior, thus changing the aesthetic appearance of the neck as a whole.[16,20]

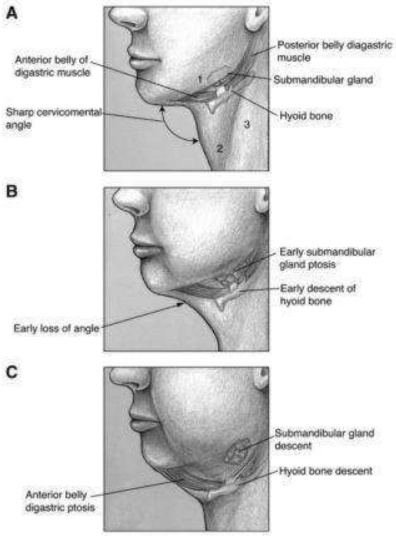

Figure 1: Progression of pseudo double chin (Ptosis of the anterior belly of Digastric m.)A - Ideal Digastric m., B - Erly stage of ptosis of anterior belly Digastric muscle, C - Anterior belly of Digastric m. ptosis (Source: DeFatta and Ducic 2007)

The aging of the digastric muscle is well known to plastic surgeons who commonly suture the weak anterior bellies of the digastric muscle together and suspend them to the mylohyoid muscle. The reason is that although the mylohyoid muscle does lose its tone, it is immune to sagging due to its flat structure and long insertion along the mandible and thus provides good support to the sutured digastric.[2,20–23]

Age-related digastric sagging is not the only concern associated with the digastric muscle. Because the anterior and posterior bellies of the digastric muscle are attached to the hyoid bone, they also have a significant role in keeping the hyoid bone in place. While other bones are directly articulated with other bones the hyoid bone does not have such articulation, and its position is solely given by attached muscles, ligaments, and fascias.[24]

Weakening and laxity of the digastric muscle both create an imbalance in the forces maintaining the hyoid position, which gradually leads to its descent and thus to an increase in the submental-cervical angle. [24–27]

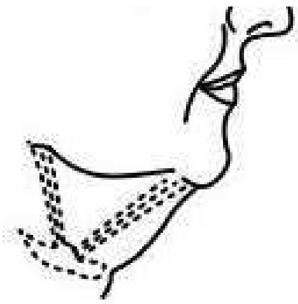

Figure 2: Low-laying hyoid bone (Source: Dedo 1980)

Digastric muscle ptosis and laxity, together with a consequent descent of the hyoid bone, might most likely play a major role in the creation of the so-called pseudo-double chin. The issue is well known to plastic surgeons who attempt to resolve the issue via surgery. However, up to date, there is no non-invasive way to modulate the digastric muscle to regain its condition and thus its ability to maintain a low submental-cervical angle. Noninvasive aesthetic approaches focused on the submental region should aim at digastric muscle condition to prevent or resolve this issue.

Multiple layer approach

As explained above, the submental layers age differently; nevertheless, they are still part of one submental unit and can mutually influence one another. Due to the complexity of the submental unit, patients may experience an increase in submental volume involving one or multiple layers (see Figure 3), yet there is no non-invasive solution that would be able to target three layers that contribute to the submental fullness.

Figure 3: Profile of a patient with increased skin laxity, fat accumulation, and Digastric muscle weakness

EMFACE submentum applicator

The EMFACE submentum applicator is the first non-invasive solution designed to address all submental layers, skin, fat, and muscle tissues. Addressing these three complex targets simultaneously provides a novel solution for enhancing the submental appearance. The applicator uses two technologies, HIFES and Synchronized Radiofrequency plus (Synchronized RF+) to affect all three tissues.

HIFES submental stimulation

EMFACE placed in a submental area is the first device that can address submental muscle aging. HIFES is placed over the mylohyoid nerve which innervates the anterior bellies of Digastric m. and, through neuromuscular stimulation, provides supramaximal contraction. This mechanism of action has been proven to stimulate muscles to increase their tone.[30,31] By increasing the tone of digastricus m. it is tightened, thus decreasing its ptosis and preventing it from bulging out. As a result, the toned digastric muscle can hold the hyoid bone in the right position at C4 thus improving the submental-cervical angle.

HIFES stimulation occurs in the midline of the submental region. This design is crucial to specifically target the Digastric muscle and not the platysma muscle which has more lateral innervation. As previously described the platysma muscle and Digastric m. need a completely different approach to treating signs of aging. Platysma muscle treatment can consist of botulinum toxin-based muscle inhibition to treat platysma bands. However, inhibition of the Digastric m. in this way could lead to dysphagia. The Digastric m. is already weakened by aging and therefore needs to be stimulated to regain strength and reverse ptosis.. [32–34]

Synchronized RF+

Synchronized RF+ is a high power Synchronized RF technology used in other EMFACE applicators that is exclusively implemented in submental applicator. RF+ is simultaneously emitted with HIFES and provides homogenous heating over the whole submental area. Synchronized RF+ increases the temperature in the fat layer to induce apoptosis levels while simultaneously keeping the therapeutic temperatures in the skin to induce neocollagenesis and neoelastinogenesis.

Additionally, tissue heatings might enhance HIFES toning abilities, as has been demonstrated in numerous skeletal muscle studies, which is the group that also includes Digastric. It is well known that heating-stimulated muscle increases the expression of heat shock proteins and satellite cells, both of which are necessary for muscle remodeling and development.[35–38]

Clinical evidence of submental applicator

The efficacy of Submental applicator has been validated in pilot studies on animal subjects showing a significant increase in the fat apoptotic levels by 4.8 times. Furthermore, skin histology showed an increase in collagen and elastin content by 33% and 113%, respectively.

The results seen in animal studies were replicated in human testing, where histology, MRI, 3D photos, and Ultrasound were used to evaluate treatment efficacy. Histology shows a significant increase in apoptotic cells. MRI evaluation on a 1-month follow-up showed a decrease in submental fat volume by 25%. Furthermore, this study also incorporated the cheeks applicators with Synchronized RF, and MRI evaluation showed no significant decrease in cheek fat volume thus proving the important difference between Synchronized RF and Synchronized RF+ effect on adipose tissue. In addition to the volume of the fat layer the, area of "double-chin" with all layers was identified and evaluated. This approach emphasizes the importance of the multimodal approach to submental volume reduction with a volume reduction of the "double-chin" by 31%. This reduction was reflected by 3D photo evaluation with a reduction of 5.78 ml in the submental area.

Summary

As stated in the introduction the submental area is a complex problem that needs to be addressed by a complex and cohesive solution. A non-invasive, multiple-modality approach that would lead to significant changes in all anatomically relevant layers was missing until now. The Synchronized RF+ and HIFES together yield the combined effects needed for complex double chin reduction. When these two modalities are used in conjunction, the reduction effect is amplified. In this way, the connective tissue is rejuvenated, the fat layer is reduced, and the muscle is toned, thus lifting the whole submental area with a reduction of muscle bulging.

Conclusion

EMFACE submentum applicator is the first non-invasive device that affects the submental area problems by incorporating two modalities with effects on skin, fat, and muscle.

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ORIGINAL ARTICLE

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Treatment with synchronized radiofrequency and facial muscle stimulation: Histologic analysis of human skin for changes in collagen and elastin fibers

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Abstract

Background: Skin's exposure to intrinsic and extrinsic factors causes age-related changes, leading to a lower amount of dermal collagen and elastin.

Aim: This study investigated the effects of a novel facial muscle stimulation technology combined with radiofrequency (RF) heating on dermal collagen and elastin content for the treatment of facial wrinkles and skin laxity.

Methods: The active group subjects ($N=6$) received four 20-min facial treatments with simultaneous RF and facial muscle stimulation, once weekly. The control subject ($N=1$) was untreated. Skin biopsies obtained at baseline, 1-month and 3-month follow-up were evaluated histologically to determine collagen and elastin fibers content. A group of independent aestheticians evaluated facial skin appearance and wrinkle severity. Patient safety was followed.

Results: In the active group, collagen-occupied area reached $11.91 \pm 1.80 \times 10^6\,\mu m^2$ (+25.32%, $p<0.05$) and $12.35 \pm 1.44 \times 10^5\,\mu m^2$ (+30.00%, $p<0.05$) at 1-month and 3-month follow-up visits. Elastin-occupied area at 1-month and 3-month follow-up was $1.64 \pm 0.14 \times 10^5\,\mu m^2$ (+67.23%, $p<0.05$), and $1.99 \pm 0.21 \times 10^5\,\mu m^2$ (+102.80%, $p<0.05$). In the control group, there was no significant difference ($p>0.05$) in collagen and elastin fibers. Active group wrinkle scores decreased from 5 (moderate, class II) to 3 (mild, class I). All subjects, except the control, improved in appearance posttreatment. No adverse events or side effects occurred.

Conclusion: Decreased dermal collagen and elastin levels contributes to a gradual decline in skin elasticity, leading to facial wrinkles and unfirm skin. Study results showed noticeable improvement in facial appearance and increased dermal collagen and elastin content subsequent to simultaneous, noninvasive RF, and facial muscle stimulation treatments.

KEYWORDS
collagen, elastin, radiofrequency, rejuvenation

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1 | INTRODUCTION

Facial aging is a complex process that is a result of alterations in multiple layers of the face: the skin, subcutaneous fat, superficial musculoaponeurotic system (SMAS), muscle, and bone.[1,2] The facial muscles tend to lose their resting tone, especially when affecting the elevator muscles such as zygomaticus major muscles or frontalis muscles, leading to the repositioning of facial tissue. The elevator's inability to hold the overlying tissue in place inevitably results in soft tissue sagging. The skin and SMAS are affected by the loss of collagen and elastin, the principal structural and connective tissue proteins. Depletion of these proteins leads to wrinkle formation, reduced elasticity, and sagging appearance. Additionally, thinning of the SMAS layer contributes to laxity and jowling.[3,4] As such, when approaching facial aging, it is necessary to take into account all of the factors and ideally target all involved components. However, current noninvasive approaches focus solely on treating the skin or artificially providing facial volume to compensate for the repositioned tissue or inhibiting certain muscles to balance the loss of tone in others.

Yet, recently a novel approach has been introduced, a novel device using a noninvasive applicator that administers HIFES technology and synchronized radiofrequency (RF) simultaneously has been proposed to enhance the facial appearance.[5] HIFES selectively stimulates the elevator muscles by inducing supramaximal, involuntary, muscle contractions by generating strong electrical currents.[1] The electrical current depolarizes the motor neurons' membrane creating a signal for the muscle to contract. The recruited heat shock proteins and satellite cells can support muscle microprotein structure alterations.[6] Studies have shown that repeated application of HIFES induces muscle protein synthesis, which may result in an increase in muscle tissue density and overall enhancement of muscle tissue together with increasing the resting tone of carefully selected facial muscles in the forehead (frontalis muscle) and cheeks (zygomaticus major, zygomaticus minor, and risorius muscles).[7–10] The monopolar RF is an oscillating electrical current that is partially absorbed by the tissue, where it creates heat. The heating for a period of time is able to increase fibroblast activity and unwind the H-bonds to denaturate the collagen. After the heating stimuli stops, the body starts to induce normal regenerative process, which lead to the neocollagenesis and neoelastinogenesis. With repetition the collagen and elatine is rebuilded repeatedly.[11]

This study includes histological examination of facial skin tissue collected from the foreheads and cheeks of patients who underwent treatment using the non-invasive HIFES and RF applicator. The study objective was to assess changes related to the connective tissue structural proteins—collagen and elastin—and to evaluate the effectiveness of this combined treatment modality in enhancing the structural integrity of the skin (as shown in previous animal model studies)[12,13] and aesthetic facial appearance.

2 | MATERIALS AND METHODS

2.1 | Study design and subject population

This prospective, single-center, interventional, two-arm, open-label design study enrolled seven (7) female subjects interested in participating in a clinical study with a device intended for noninvasive facial rejuvenation. Six (6) subjects in the active group [39–62 (55.83 ± 8.56) years old, BMI 22.73–38.59 (27.65 ± 5.87) kg/m^2, Fitzpatrick skin types I to IV], received active treatment with simultaneous HIFES + RF to the cheeks and forehead. One (1) subject served as a control and was not treated [62 years old, BMI 36.9 kg/m^2, Fitzpatrick skin type IV].

The subjects from the Active group (N = 6) received four 20-min facial treatments, 1 week apart, with single-use, self-adhesive, noninvasive applicator electrodes (EMFACE device BTL Industries Ltd., Boston, MA). The whole face (i.e., forehead and cheeks simultaneously; see Figure 1 for applicator placement) was treated. Subjects

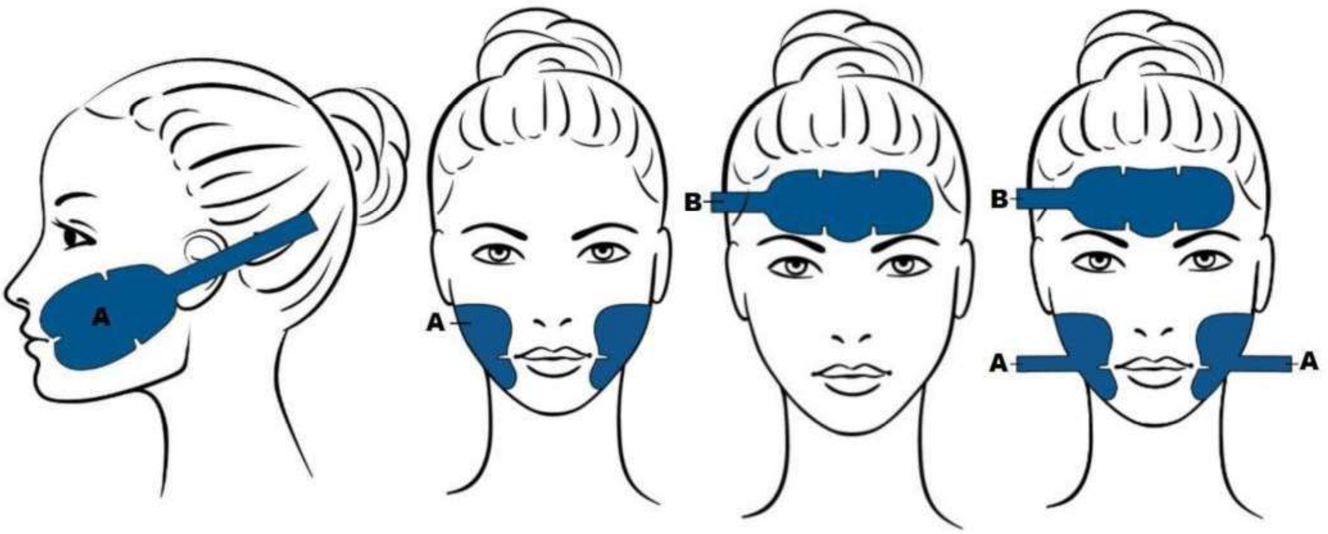

FIGURE 1 Illustration of the noninvasive, self-adhesive, hands-free device applicator placement during the therapy (A = cheek, B = forehead). The patient is treated in the supine position. The forehead and both cheeks are treated simultaneously for a 20-min duration.

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were in a supine position, anesthesia was not required. Both energy intensities (HIFES and RF) were individually set according to patients' feedback and tolerability on a scale of 0%–100%. Jewelry and prominent hair were removed from the face and the skin before the treatment.

Punch biopsies of the skin tissue from the periauricular area were performed at baseline, followed by 1-month and 3-month follow-up visits. All biopsies, 3 mm in diameter (Kruse Buster), were obtained full-thickness (approximate depth 2.0–3.0 mm) at the investigator's site. Local anesthetic was used to numb the biopsy collection area. The biopsy wounds were subsequently closed and disinfected, and the healing process was monitored throughout the study. Participants received detailed instructions for home wound care to ensure proper healing. Inclusion criteria were healthy subjects aged over 21 years, with clearly visible wrinkles on the cheeks and forehead (face) when relaxed, who were willing to abstain from any facial treatments other than the study procedure during study participation. Exclusion criteria prohibited subjects with any active psoriasis, eczema, local infection in the treatment, neurological disorders, or electroanalgesia. The study was IRB approved and registered on clinicaltrials.gov (NCT05524662).

2.2 | Histological evaluation

The obtained skin tissue samples were processed for histological examination. All samples were correctly labeled using subject ID and the description of the corresponding visit—pretreatment (baseline) and posttreatment (1-month and 3-month follow-up visits). The samples were sliced, and the sections were then stained to visualize and examine collagen and elastin under a microscope.

A clinical histologist analyzed the stained samples to evaluate the changes in the tissue, including any pathological changes to rule out potential skin damage resulting from treatment with HIFES and RF noninvasive electrode applicators.

The staining process employed conventional Masson's trichrome procedure, which enables a detailed visual assessment of collagen and the general tissue structure. Collagen fibers developed a green color. Orcein staining was used to specifically visualize elastin in the samples. The elastin fibers developed a brown-dark color. The stained samples were mounted to microscopy slides.

The slides were observed and photographed using an automated slide scanning microscope (Hitachi Axio Scan.Z1, Carl Zeiss AG, Germany; 20×/0.8NA Plan-Apochromat objective) in a bright field. Collagen and elastin quantification was performed with the Image J software based on semi-automatic segmentation in the HSB (Hue-Saturation-Brightness) color system. The appropriate threshold differentiating the collagen and elastin fibers from the background was identified in the selected regions of interest (ROI = $1800 \times 1200\,\mu m$; $2.16 \times 10^6\,\mu m^2$) at a defined scale, allowing for the quantification of the area covered by collagen and elastin within the tissue sections. After selecting the collagen and elastin fibers, their densities were expressed as the occupied area (square micrometers) encompassed by the fibers in the evaluated images' in the ROI.

Statistical analysis Student's *t*-test and Friedman's one-way repeated measures ANOVA test were performed with significance level set at $\alpha = 0.05$. Post hoc Tukey HSD test was done for multiple comparisons.

This process was repeated for the seven subjects included in this two-arm study design, which consisted of one control subject and six active treatment subjects. The changes in the average areas representing elastin and collagen content before and after treatment were compared for the active group subjects and the control subject.

2.3 | Aesthetic improvement and wrinkle severity

Subjects had digital photographs of their faces taken before treatment (baseline) and at the follow-up visits. Three reviewers, independent of each other and the clinic, evaluated the facial skin appearance according to the Global Aesthetic Improvement Scale by comparing the before and after photos marked by follow-up visit.

A different trio of evaluators received the same set of photographs and evaluated the extent of skin wrinkles and lines (wrinkle severity) according to the Fitzpatrick Wrinkle Elastosis Scale (FWES). The evaluators were blinded to the follow-up stage (i.e., the photos were not labeled according to the follow-up visit and the order in which the evaluators were shown the photos was randomized). Each evaluator assigned a FWES grade per photograph.

2.4 | Safety

The occurrence of treatment or study-related adverse events and side effects was followed/monitored during the course of the trial.

3 | RESULTS

3.1 | Collagen

In the Active group, the average area occupied by collagen was $9.50 \pm 1.77 \times 10^5\,\mu m^2$ at baseline. The average collagen-occupied area increased to $11.91 \pm 1.80 \times 10^6\,\mu m^2$ ($p < 0.05$) and $12.35 \pm 1.44 \times 10^5\,\mu m^2$ ($p < 0.05$) at the 1-month and 3-month follow-up visits. Compared to baseline, in the active group, the average collagen amount increased ($p < 0.05$) at both posttreatment follow-ups. In the control group, there was no significant difference ($p > 0.05$) in collagen fibers, since the collagen content fluctuated in the range of $9.68 \pm 0.45 \times 10^5\,\mu m^2$–$9.51 \pm 0.23 \times 10^5\,\mu m^2$ throughout the study. There was a significant difference ($p < 0.05$) in the collagen-occupied sample area at both the 1-month (+25.32%) and 3-month (+30.00%) follow-ups (see Figure 2) in the treated (active) group.

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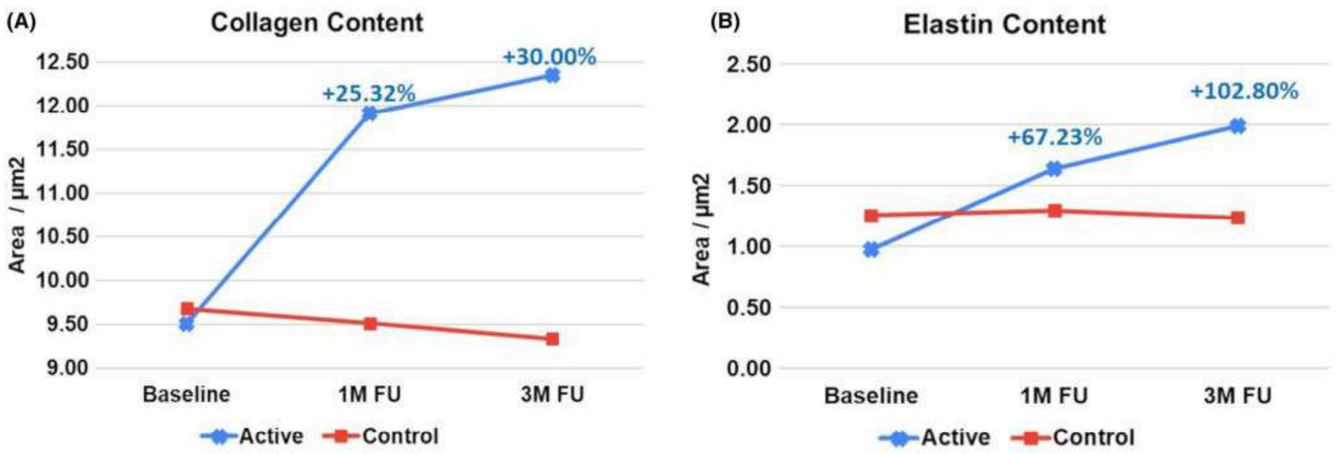

FIGURE 2 Bright-field visualization of collagen fibers by Masson's Trichome method. In the active group, the collagen fibers (A) and elastin fibers (B) increased significantly ($p < 0.05$) and occupied a greater area after 3 months follow-up compared to baseline. No significant change occurred in the Control group. (1M FU: 1-month follow-up; 3M FU: 3-month follow-up).

3.2 | Elastin

In the Active group, the mean elastin-occupied area at baseline was $0.98 \pm 0.34 \times 10^5\,\mu m^2$. At the 1-month follow-up, the average elastin amount was $1.64 \pm 0.14 \times 10^5\,\mu m^2$. At the 3-month follow-up, the area encompassed by elastin increased further to $1.99 \pm 0.21 \times 10^5\,\mu m^2$. Compared to baseline, the average elastin-occupied area increased at both follow-ups ($p < 0.05$). At the 1-month (+67.23%) and 3-month (+102.80%) follow-ups, the amount of elastin was significantly different ($p < 0.05$) comparing the active and control group (Figure 2). In the control group, there were no significant changes ($p > 0.05$) in elastin density at the follow-up points, elastin content ranged between $1.26 \pm 0.16 \times 10^5\,\mu m^2$–$1.30 \pm 0.12 \times 10^5\,\mu m^2$.

Exemplary samples of the collagen (Figure 3) and elastin (Figure 4) microscopic evaluation results of the Active group are shown below (Figure 5).

3.3 | Safety

No adverse events or side effects related to the treatment occurred. Histopathological analysis of the biopsy sample did not reveal any complications or unwanted and unexpected effects.

3.4 | GAIS & FWES results

Overall, the average score of the GAIS evaluation reported that all subjects, except the control, had an improved appearance post-treatment.

The average scores of the active group decreased by 2 grade points on the FWES and GAIS from 5 (moderate, class II wrinkles) to 3 (mild, class I fine lines). The evaluators did not find any change in the control subject's appearance.

Detailed results of the GAIS and FWES independent reviewers' evaluations can be found in Tables 1 and 2.

4 | DISCUSSION

This study demonstrates that noninvasive facial treatment with simultaneous HIFES and RF can induce collagen and elastin expression. In this study, a significant increase ($p < 0.05$) of collagen (+30%) and elastin (+103%) content was observed in dermal biopsy analysis 3 months posttreatment.

The observed increase in elastin content surpasses that of collagen by a factor of around three, marking a noteworthy finding. Upon initial observation, one might perceive the response to changes in elastin levels as deviating from the usual. However, upon examining the baseline data of the active group, it becomes apparent that the levels of elastin are significantly diminished, accounting for approximately 3.5% of the total cross sectional area. In contrast, typical physiological levels of elastin typically fall within the range of 5%–10%. Following the administration of the therapies, there was a twofold increase in elastin levels, resulting in the occupation of 7% of the slice area. This observation indicates a restoration of skin elastin levels to a state consistent with healthy physiological levels.[14–16] Additionally, as SMAS is a tissue that is intertwined with the rest of the facial structures and is made of collagen and elastin, we believe the SMAS layer was also affected and helped with the results.[17] Furthermore, the observed outcomes should not be regarded as a malfunction (e.g., flawed staining process) or an uncommon occurrence. This is supported by the findings of a study conducted by Kinney et al., which examined the effectiveness of HIFES+RF technology on an animal model. In their study, they reported a significant 110.8% increase in elastin levels, which aligns with the outcomes of our own investigation. A similar trend is observed in the case of collagen, as reported by Kinney et al., where there was a notable increase of 26.3%.[5]

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JCD Journal of Cosmetic Dermatology

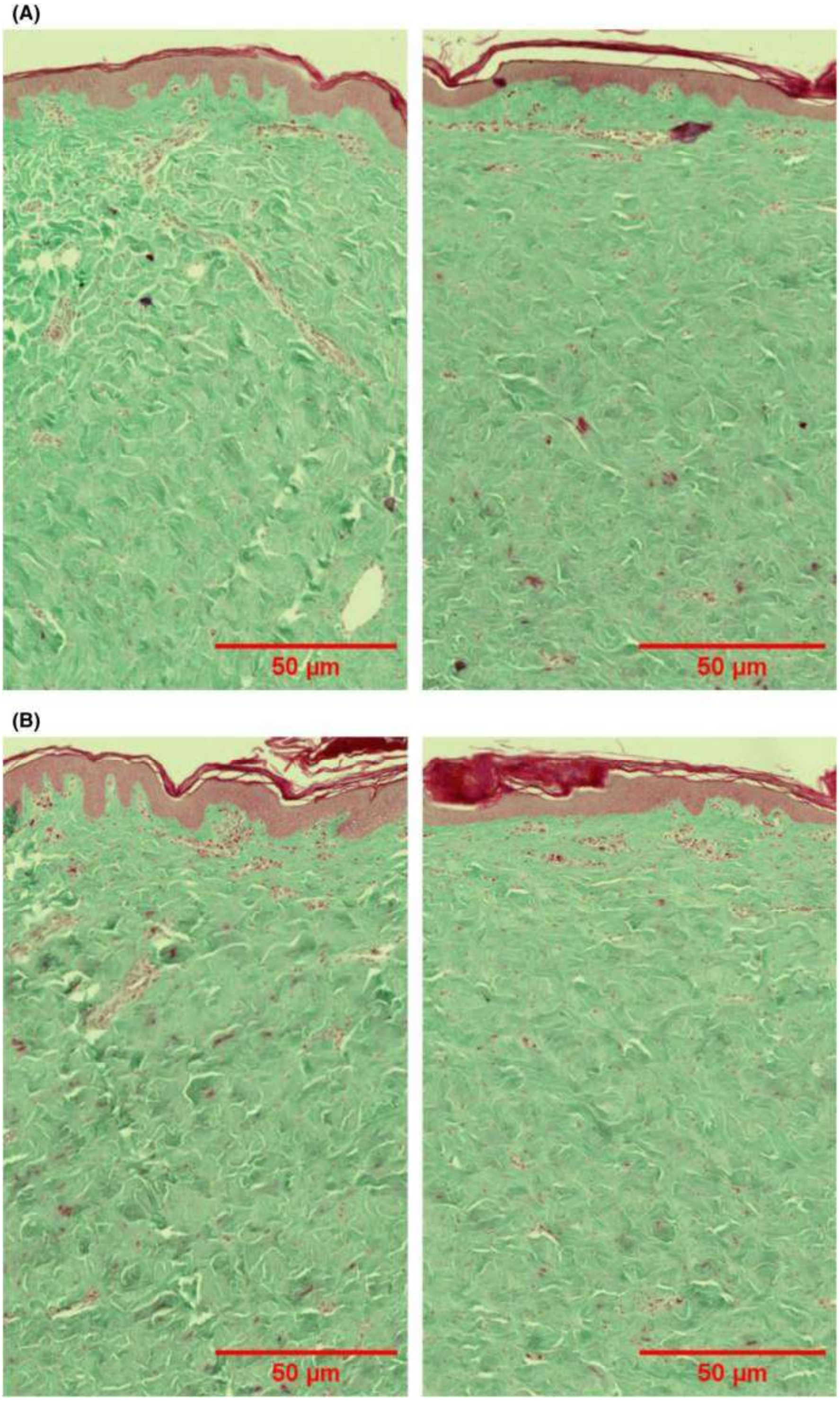

FIGURE 3 Bright-field visualization of collagen fibers stained by trichrome stain, active group samples of two patients (A, B). The collagen fibers appear in green color. At the 3-month follow-up (right), the collagen fibers are noticeably denser, occupying a greater area when compared to the baseline (left).

The substantial increase in the production of elastin and collagen could be attributed to the multimodal approach of the HIFES+RF technology. The application of RF energy has been found to elicit a thermal response in fibroblasts, whereas the HIFES technology induces muscle contractions that mechanically stimulate the skin. These processes have been shown to cause similar responses in fibroblast cells.[18–21] The findings of the study demonstrate a consistent elevation in the concentrations of collagen and elastin, which reached their highest point after a period of 3 months. This aligns with existing understanding on the time it takes for fibroblasts to react to external stimuli of this nature. However, additional research is required to examine the longevity of such an increase.

Besides histological methods, this study further incorporates FWES and GAIS evaluations (by six qualified, independent, clinical aestheticians), all objective basis. As such, the objective evaluation of patient appearance provides insight on significant increase in crucial skin components, namely elastin and collagen. The results

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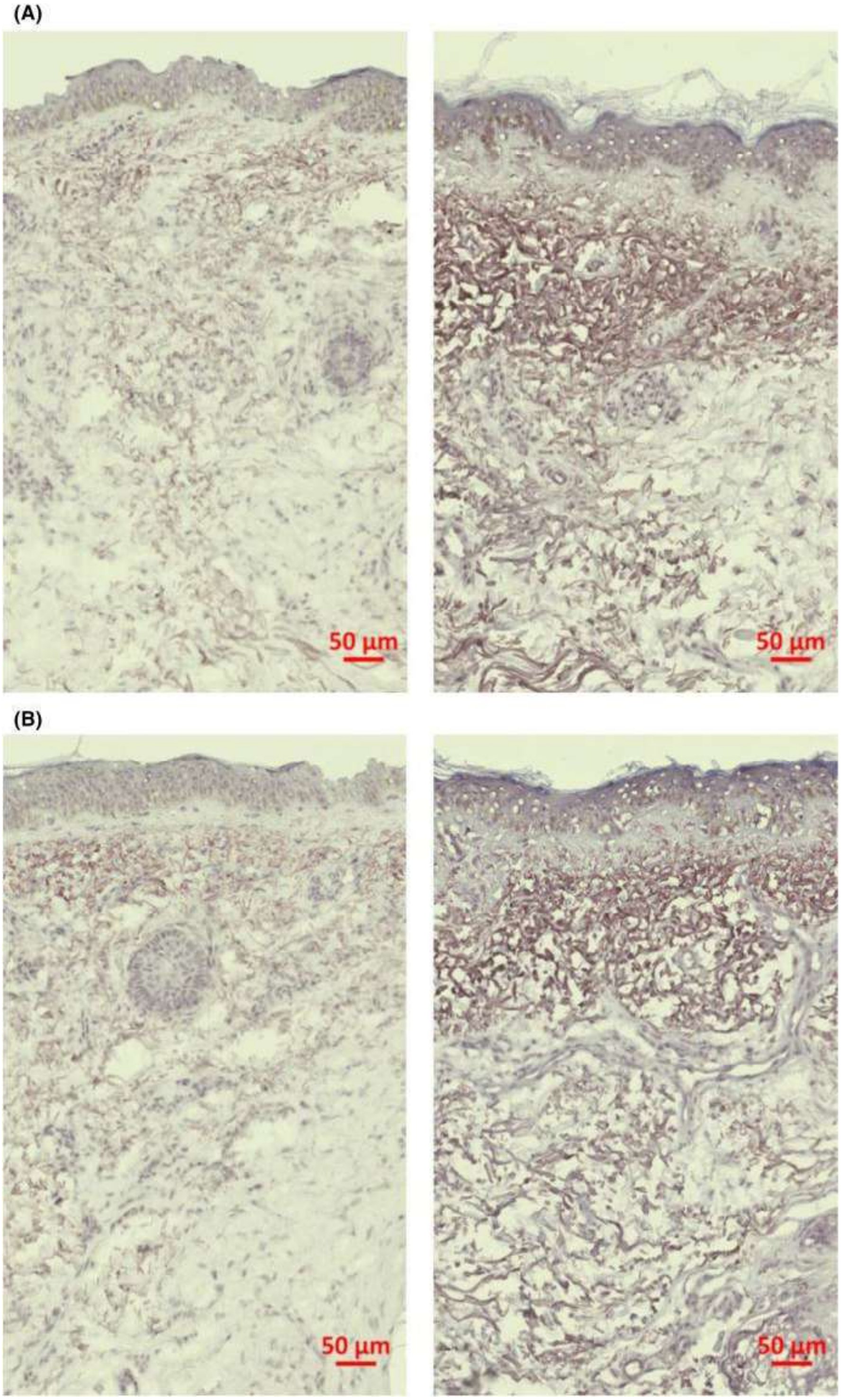

FIGURE 4 Bright-field visualization of elastin fibers by Orcein staining (active group samples of two patients, A and B). The baseline sample (left) has noticeably fewer elastin fibers, observed as dark/brown filaments, than the 3-month follow-up (right). 3-month follow-up shows elastotic fibers replaced with new, longer elastic fibers.

of both evaluation scales indicate a substantial enhancement in the active group, but the control group exhibited no change. These findings provide empirical support for the rejuvenation effect of the HIFES+RF modality.

This objective evaluation approach exhibited a favorable outcome. The findings from the Facial Wrinkle Evaluation Scale (FWES) demonstrate that patients who had scores of 6 or above, indicating moderate to severe wrinkles, experienced more substantial improvements (see Table 1). Comparable results have been observed when comparing the FWES findings to the Global Aesthetic Improvement Scale (GAIS), (Table 2). In contrast, subject number 2, who had only minor wrinkles at the baseline, did not have a major improvement according to the FWES. However, evaluators rated this subject best possible score on the GAIS. The observed discrepancy indicates that the involvement of facial muscles in the aging process holds considerable importance in the context of face rejuvenation, as outlined in the introductory section. The findings of this study may indicate that the utilization of both modalities (RF and HIFES) in combination is

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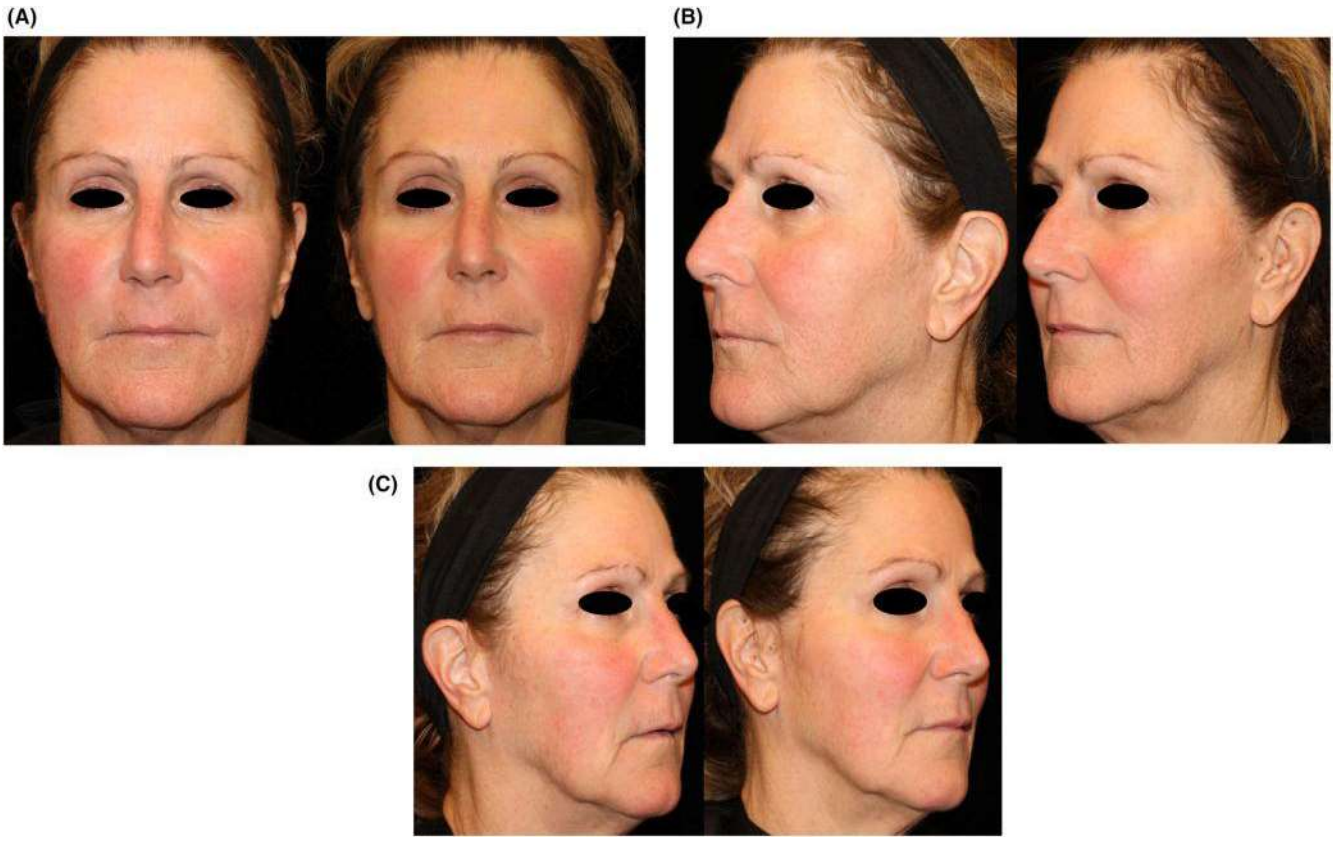

FIGURE 5 Female patient (Skin Type I, 60 years old, BMI 22.6 kg/m^2) at baseline (left) versus 3 months (right)—frontal view (A), left (B) and right (C) lateral oblique angles. The fine lines around the eyes present at baseline have reduced in severity and are less prominent, as well as lifted brows are visible after the treatments. GAIS score = 2 (i.e., much improved), FWES score decreased from 6 (moderate, class II) at baseline to 4 (moderate, class II) at 3-month follow-up.

TABLE 1 Fitzpatrick Wrinkle Elastosis Scale evaluation.

Subject ID	EV 1	EV 2	EV 3	Average	EV 1	EV 2	EV 3	Average
Subject 1	6	5	6	6	4	3	4	4
Subject 2	3	2	2	2	2	1	1	1
Subject 3	4	4	5	4	3	3	4	3
Subject 4	5	5	5	5	4	4	4	4
Subject 5	6	6	6	6	3	3	3	3
Subject 6	7	6	7	7	4	5	4	4
Subject 7[a]	6	5	6	6	6	5	6	6
	Average of active group			5	Average of active group			3

[a]Control subject.

more effective compared to therapies that solely incorporate either one of them.

Furthermore, the study device's practicality increases the comfort for both the operator and patient. The hands-free, self-adhesive applicator provides a significant enhancement in terms of safety and comfort aspects. Operator fatigue is eliminated, and the patients underwent the facial rejuvenation procedures without recovery time or impact to their daily routine. Adverse effects common with some facial rejuvenation therapies such as hyperpigmentation, dyschromia, hematoma and nerve damage did not occur in this study.[22–24]

This clinical study was limited due to the low subject count. Despite that the all-female patient set is also a limiting factor, it must be considered that real-world data have shown women as the vast majority seeking facial cosmetic and rejuvenation procedures.[25] This may be driven by an increased interest and diversity of the patients motivated to undergo treatments aimed at regenerating the body in a more natural way, as opposed to augmentative and

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TABLE 2 Global aesthetic improvement score evaluation.

Subject ID	EV 1	EV 2	EV 3	Average
Subject 1	2	2	2	2
Subject 2	3	3	2	3
Subject 3	1	1	1	1
Subject 4	1	2	2	2
Subject 5	3	3	3	3
Subject 6	3	3	2	3
Subject 7[a]	1	0	0	0

[a]Control subject.

invasive procedures, which provide a different less appealing result. Nonetheless, further in-vivo investigations of this method are warranted to expound the clinical aspects.[26]

5 | CONCLUSION

The cumulative effects of reduced collagen and elastin, lead to an overall loss of skin elasticity, resulting in skin laxity or loose skin. This is especially noticeable in the face, where laxity leads to sagging, the formation of wrinkles and fine lines, and a generally "aged" appearance. This study histologically evaluated facial skin tissue samples for collagen and elastin content pre and post-treatment with the simultaneous HIFES and RF noninvasive. Results demonstrated increased levels of dermal collagen and elastin at the 3-month follow-up.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received. The study was conducted in line with Good Clinical Practice and the Decalaration of Helsinki. The study protocol and informed consent form were approved by the Advarra IRB institutional review board on the 3rd of May 2022 (reference number Pro00063141). Prior to enrolment, subjects provided voluntary written informed consent (date and signature). Subjects further provided voluntary written consent (date and signature) to have photographs of their face taken for the study records, publication and marketing purposes.

CONSENT STATEMENT

Prior to enrolment, subjects provided voluntary written informed consent (date and signature) to have photographs of their face taken for the study records and publication.

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EMFACE in Asian Population

Evaluating the Efficacy and Safety of Combined Synchronized Radiofrequency and HIFES Stimulation for Facial Lifting in Asians: A 6-Month Analysis

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Presented at the American Society for Laser Medicine and Surgery (ASLMS), Baltimore, Maryland, April 11, 2024

Highlights

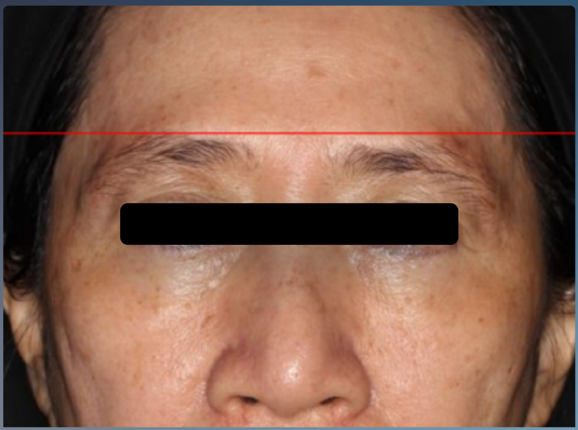
- 15 Asian subjects (skin types III-V) received four 20-min treatments (EMFACE Forehead & Cheeks)
- Results were evaluated using 2D and 3D imaging techniques, cutometer as well as patients' self-assessments at 1M, 3M and 6M post-treatment
- Results show significant lifting of the eyebrow, forehead, and cheeks up to 2.14 mm
- Results were maintained for up to 6 months

93%
Patients Reported Improvement at 6 Months

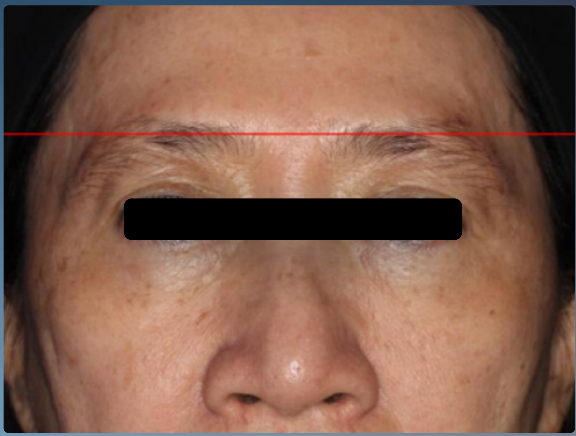
81%
Skin Firmness Improvement at 6 Months

Results after 4 treatments show a significant lifting effect

Baseline



1 Month



Long-Term Efficacy of EMFACE

Evaluation of Synchronized RF and HIFES Efficacy One Year Post-Treatment: A Case Study

Yael Halaas, M.D., FACS

New York, NY, USA

Highlights

- 3 subjects (skin types II-IV) evaluated
  1 year after their original series of four 20-min treatments
  (EMFACE Forehead & Cheeks)
- 3D camera imaging was used to calculate volumetric changes
- All 3 patients maintained post-treatment volume changes at 1Y FU

68%
Maintained Improvement of the Original 3-Month Follow-up

+2.6 ml
Volume Improvement in Upper Cheeks Compared to Baseline

-2.7 ml
Volume Reduction in Jowls Compared to Baseline

Patients Demonstrated Volume Shift Towards Upper Cheek One Year Post-Treatment

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