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Case Series

Bipolar Radiofrequency Combined with Non-Crosslinked Hyaluronic Acid Mesotherapy: A Protocol for Skin Enhancement

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ABSTRACT

Changes associated with aging, such as alterations in epidermal hydration, pigmentation, thickness, and cell renewal, impact skin appearance and may result in laxity, dryness, and uneven skin tone. This case series aimed to evaluate the combined effects of bipolar radiofrequency and non-crosslinked hyaluronic acid mesotherapy on skin appearance, with the goal of achieving synergistic benefits. This retrospective data analysis included subjects aged 33-67 years with facial skin dryness and laxity. Subjects received treatment with a bipolar radiofrequency device on the face, followed immediately by mesotherapy with 2.5 ml of non-crosslinked hyaluronic acid. Photographic documentation and skin analysis were conducted before treatment and 30 days post-treatment. Fourteen subjects with a mean age of 45 years (range 33-67) and presenting with dry, lax facial skin were included. All measured indicators showed significant improvement following the combined radiofrequency and mesotherapy protocol. The combined protocol also correlated with greater improvement in both patient and physician satisfaction, observed immediately after the procedure and at 30 days post-procedure. The treatment was well tolerated, and no adverse events were reported. The combination of bipolar radiofrequency and non-crosslinked hyaluronic acid mesotherapy resulted in significant improvements in skin appearance, firmness, tone, and overall subject satisfaction compared to the baseline condition. The treatments were well received, leading to noticeable enhancements in facial aesthetics. No adverse events were reported, confirming the safety of the protocol.

INTRODUCTION

Skin aging is one of the most prominent signs of growing older, typically manifesting in facial changes starting from the third decade of life (1). This has led to a substantial demand among consumers for anti-aging solutions across all age demographics. There is a rising trend of individuals seeking aesthetic treatments aimed at enhancing skin quality as part of a comprehensive facial rejuvenation strategy, addressing concerns such as skin laxity, hydration, overall tone, and the reduction of lines and wrinkles.

The aging process of human skin is complex, influenced by a combination of genetically determined intrinsic factors and age-related hormonal shifts. These effects are compounded by cumulative exposure to external environmental stressors, primarily ultraviolet (UV) light, along with air pollution, smoking, and inadequate nutrition (2). The skin is composed of two main layers: the dermis and the epidermis, which cover an underlying layer of subcutaneous tissue.

Within the dermis, fibroblasts produce a significant portion of the extracellular matrix (ECM), primarily composed of collagen, elastin, and glycosaminoglycans. This ECM forms a dense network of interconnected collagen (types I and III) and elastin fibers, interspersed with water-retaining proteoglycans. These structural elements collectively provide the skin with mechanical strength and flexibility (2). The epidermis, the outermost layer of the skin, is connected to the dermis through specialized proteins in the basement membrane. It is a stratified epithelium primarily composed of keratinocytes, which mature into the outermost layer, known as the stratum corneum. This layer serves as a protective barrier, shielding the skin from environmental damage. Intrinsic skin aging involves a gradual decline in tissue density, leading to thinning across all skin layers (2, 3). As skin ages, the dermis undergoes significant changes due to its slower turnover rate compared to other layers (4). These changes include decreased levels of collagen and elastin, a shift from type I to type III collagen, and a decline in ECM proteoglycans. These alterations contribute to the visible signs of aging. Similarly, in the epidermis, the turnover of keratinocytes slows down with age. This results in thinner epidermal layers, a flattened dermal-epidermal junction, and a reduced ability to repair the skin barrier quickly (2, 3).

Extrinsic aging exacerbates the deterioration of skin structure, leading to disorganized and fragmented collagen networks, as well as increased levels of abnormal and disordered elastin. With aging, maintaining optimal skin hydration becomes increasingly challenging. Preventing transepidermal water loss (TEWL) relies on two key factors: the presence of natural hygroscopic agents, such as hyaluronic acid (HA), and the effectiveness of the stratum corneum epidermal barrier. Older individuals are often more susceptible to dry, rough, and fragile skin due to the degradation and slower recovery of the skin's epithelial barrier function (5, 6).

Hyaluronic acid is abundant in the dermis and is also found in the epidermis. In addition to its moisturizing properties, it plays a role in preserving the proper structure of the stratum corneum and the function of the epidermal barrier, while also carrying out various bioregulatory functions (7, 8). A healthy epidermis undergoes constant regeneration to maintain its functional barrier and repair skin damage. However, as one ages, the turnover of epidermal cells slows down, resulting in decreased nutrient transfer between the dermis and epidermis. This contributes to a less effective exfoliation process and an increase in skin fragility (9).

The homeostasis of the epidermis depends on the regenerative capacity of cells and the complex signalling pathways that regulate this process. With age, the epidermis undergoes numerous changes in keratinocyte differentiation and function, including delayed regenerative capacity and decreased levels of hyaluronic acid (10, 11). Therefore, the application of hyaluronic acid may stimulate keratinocyte differentiation and lipid production, leading to improved epidermal barrier function (12).

In an effort to combat or slow down skin aging, numerous strategies have been developed with the goal of rejuvenating both the dermis and epidermis, restoring their youthful and healthy appearance (13). While topical products typically aid in enhancing the skin barrier function, technologies that penetrate deeper layers of the skin are necessary to effectively counteract degradation and revitalize essential structural components like collagen and elastin. For this purpose, treatments using visible light, intense pulsed light, ablative and non-ablative laser photo-rejuvenation, radiofrequency, and injectable skin rejuvenation in the form of mesotherapy are employed. Of particular note are protocols utilizing RF and non-crosslinked hyaluronic acid mesotherapy, which offer skin-rejuvenating effects with minimal or no side effects and little to no downtime. The integration of bipolar radiofrequency with HA mesotherapy resulted in more significant improvements in skin hydration, firmness, and tone compared to radiofrequency treatment alone. Furthermore, this combined approach led to notable increases in epidermal thickness and density, along with enhanced keratinocyte differentiation, indicating a synergistic effect on epidermal health and barrier function (14). Radiofrequency treatments alone demonstrated direct collagen contraction and immediate skin tightening. Long-term remodelling and the production of new collagen occur over the months following treatment, leading to improved skin elasticity and aesthetic outcomes (15-18).

Similarly, the use of HA-based dermal fillers in the form of mesotherapy, which involves multiple microinjections, promotes skin hydration and keratinocyte differentiation, creating an optimal environment for maintaining healthy skin homeostasis. This approach helps reduce and protect against external risk factors associated with the aging process (14, 19, 20). Consequently, it is justified to use and combine therapies that address multiple aspects of skin aging, allowing practitioners to target visible signs by understanding their underlying causes. This strategy maximizes results and enhances patient satisfaction. Histological analysis supports this approach by demonstrating an increase in fibroblast activity, leading to the production of Type III reticular collagen, an increased number of blood vessels, and greater epidermal thickness. However, despite these positive changes, ultrasound data analysis before and after treatment revealed no statistically significant difference in skin thickness in the malar area, chin, and mandibular angle (21).

Although skin rejuvenation mesotherapy appears to be a simple, easy, and financially attractive therapeutic option, it remains a controversial cosmetic procedure due to insufficient evidence supporting its efficacy. A review published over a decade ago highlighted the lack of conclusive scientific data on its effectiveness. Despite its ongoing use by both medical and non-medical professionals for anti-aging purposes, no clinically valuable data or significant advancements have emerged since then. According to the American Society of Plastic Surgeons (ASPS) policy statement updated in 2019, mesotherapy for skin rejuvenation is not approved by the Food and Drug Administration. Until more definitive evidence becomes available, skin rejuvenation mesotherapy cannot be recommended for routine clinical application (22).

The main objective of this retrospective analysis of medical data was to evaluate the impact of mesotherapy with non-crosslinked hyaluronic acid and 0.01% calcium hydroxyapatite (CaHA) in combination with bipolar radiofrequency on improving skin appearance.

MATERIAL AND METHODS

This analysis of medical documentation was conducted in compliance with Good Clinical Practices and local regulatory requirements. Each participant received written information regarding the product and procedure and provided consent for both the procedure and the use of their data for scientific purposes by signing an informed consent form.

The analysis included fourteen subjects (13 female and 1 male) aged 33-67 years, with a mean age of 45. All participants were in good general health but exhibited facial skin dryness and laxity. Prior to the procedure, the skin condition of all patients was assessed using the Fitzpatrick Wrinkle Assessment Scale (Wrinkling). The distribution of initial results was as follows: 1 patient was classified as Class 0.5 (very shallow yet visible wrinkle), 1 patient as Class 1 (fine wrinkle with visible wrinkle and slight indentation), 6 patients as Class 1.5 (visible wrinkle with clear indentation and 0.1-mm wrinkle depth), 4 patients as Class 2 (moderate wrinkle with clearly visible wrinkle and 1- to 2-mm wrinkle depth), and 2 patients as Class 2.5 (prominent and visible wrinkle with a depth between 2 mm and 3 mm).

The degree of elastosis was similarly evaluated using the Fitzpatrick Wrinkle Assessment Scale (Degree of Elastosis). Initial results showed that 5 patients were scored as 1-3 (fine texture changes with subtly accentuated skin lines), and 9 patients were scored as 4-6 (distinct papular elastosis with individual papules showing yellow translucency under direct light and dyschromia).

Skin firmness was assessed through facial imaging and palpation. The presence of gravitational wrinkles in the tear trough, nasolabial folds, and marionette lines indicated a reduction in skin firmness.

Treatment protocol

All participants received radiofrequency treatment, administered according to the manufacturer’s instructions and adjusted for each patient. Radiofrequency was performed prior to treatment with the mesotherapy product, using a 480 kHz frequency device, Sectum (Berger & Kraft Medical Sp. z o.o, Poland). The treatment durations for various facial areas were as follows:

- 10-15 minutes for the left and right cheek and chin,
- 10 minutes for the forehead and crow's feet.

The energy level ranged from 10 to 40W, and the temperature ranged from 38 to 42°C, with adjustments made according to patient feedback regarding comfort.

This was followed by needle mesotherapy treatment on the entire face using 2.5 ml of non-crosslinked hyaluronic acid (Neauvia Hydro Deluxe, Matex Lab, Switzerland). The mesotherapy solution contained hyaluronic acid at a concentration of 18 mg/ml, 0.01% calcium hydroxyapatite (CaHA) microspheres, as well as glycine and L-proline. The procedure involved multiple intradermal or subcutaneous injections (ideally at the epidermal/dermal junction) of a total of 2.5 ml of the non-crosslinked HA, administered with a 30G needle and ampoule syringe.

To minimize discomfort, a local anesthetic cream (EMLA®, AstraZeneca, UK) was applied to the treatment area and covered for 30 minutes before initiating the whole procedure.

During the visit, photographic documentation, patient interviews, and skin analysis were performed. The OBSERV520x device (Sylton Diagnostic Systems, Netherlands) was used to assess various skin parameters, including pores, UV pigmentation, redness, skin tone, and UV damage. Additionally, all patients followed a post-treatment protocol using the Anti-OX serum and Rebalancing Light Cream cosmeceuticals (Matex Lab, Switzerland). During the second visit, 30 days post-procedure, repeat photographic documentation, skin analysis using the OBSERV520x device, and patient interviews were conducted.

RESULTS

The case series included fourteen subjects (13 female and 1 male) aged 33-67 years (mean age of 45), with Fitzpatrick skin phototypes III-VI. This case series describes fourteen patients who underwent a procedure involving mesotherapy with non-crosslinked hyaluronic acid and 0.01% calcium hydroxyapatite (CaHA) in combination with bipolar radiofrequency, aimed at improving skin appearance.

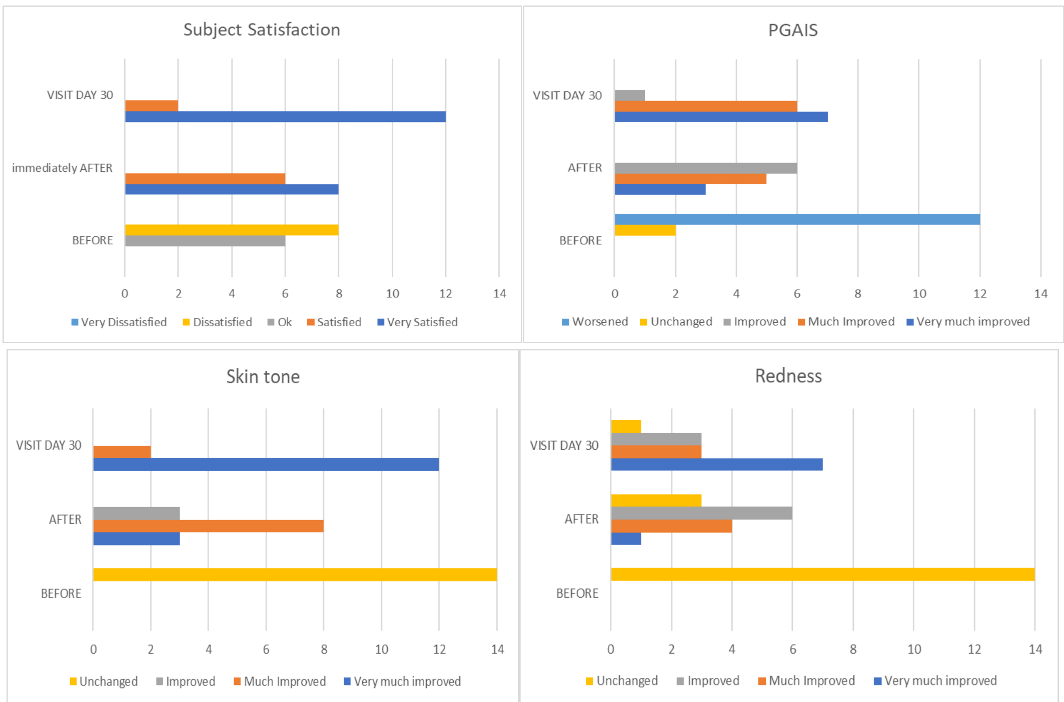
Thirty days after the procedure, the skin condition of all patients was assessed using the Fitzpatrick Wrinkle Assessment Scale (Wrinkling). The distribution of results was as follows: 1 patient was classified as Class 0 (no wrinkle; continuous skin line), 9 patients were classified as Class 0.5 (very shallow yet visible wrinkle), 2 patients as Class 1 (fine wrinkle with visible wrinkle and slight indentation), and 2 patients as Class 1.5 (visible wrinkle with clear indentation and 0.1-mm wrinkle depth).

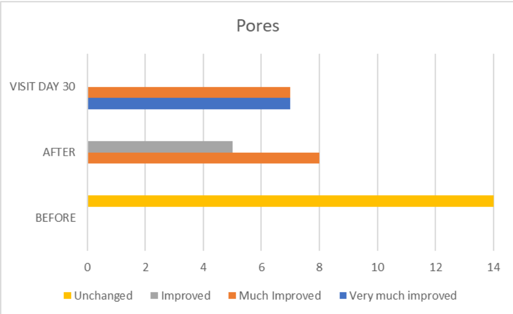
The degree of elastosis was similarly evaluated using the Fitzpatrick Wrinkle Assessment Scale (Degree of Elastosis). Initial results showed that 5 patients were scored as 1-3 (fine texture changes with subtly accentuated skin lines), and 9 patients were scored as 4-6 (distinct papular elastosis with individual papules showing yellow translucency under direct light and dyschromia). Thirty days after the procedure, all patients were scored as 1-3 (fine texture changes with subtly accentuated skin lines). The results for these patients are summarized in Table I and Table II. Regarding safety, no adverse events associated with any of the products used in this case report were reported.

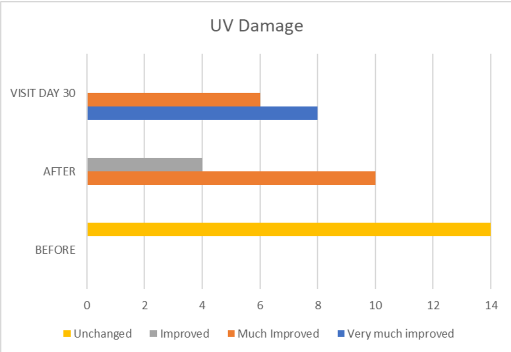
Table I. *Treatment results: based on pre-treatment, immediately after treatment, and 30 days post-treatment.*

	Immediately after	Follow up 30 Days
Physician Global Aesthetic Improvement Scale (PGAIS) Very much improved & Much Improved	57%	93%
Subject Satisfaction Very satisfied & satisfied	100%	100%
Fitzpatrick Wrinkle Assessment Scale (Wrinkling) a change of at least one degree	21%	86%
Fitzpatrick Wrinkle Assessment Scale (Degree of Elastosis) a change of at least two degree	38%	67%
Skin tone Very much improved & Much Improved	79%	100%
Redness Very much improved & Much Improved	36%	71%
Pores Very much improved & Much Improved	57%	100%
Pigmentation changes Very much improved & Much Improved	21%	79%
UV Damage Very much improved & Much Improved	71%	100%

Table II. *Treatment results: based on pre-treatment, immediately after treatment, and 30 days post-treatment for all 14 subjects included in the case series.*







The photos below show patients before and 30 days after the procedure (Fig. 1 a, b, c).

Fig. 1a. *From left to right: before and 30 days after the RF and HA treatment.*

Fig. 1b. *From left to right: before and 30 days after the RF and HA treatment.*

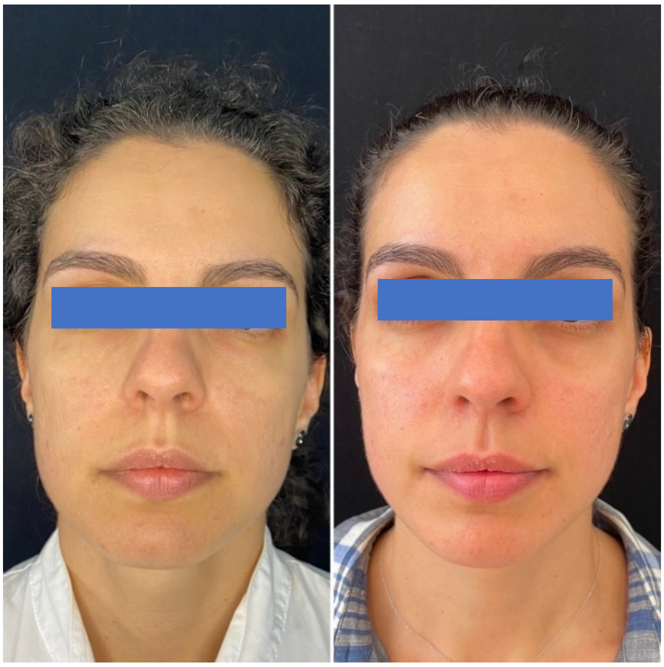


Fig. 1c. *From left to right: before and 30 days after the RF and HA treatment.*

DISCUSSION

Aging skin undergoes numerous cellular and functional changes that affect its quality and appearance, necessitating appropriate treatment. In this series of cases, a treatment protocol combining bipolar radiofrequency with mesotherapy using non-crosslinked hyaluronic acid demonstrated a significant impact on skin quality and appearance in all subjects.

Mesotherapy with hyaluronic acid, as part of the procedure, supplements endogenous hyaluronic acid levels, which decrease with age. Its moisturizing properties are essential for maintaining adequate skin hydration (14, 19). Hyaluronic acid can also enhance the biochemical response of skin cells, which fibroblasts require for optimal collagen and elastin homeostasis. As age advances and HA levels decrease, collagen production in the skin becomes disordered and reduced. By administering HA fillers, we increase the mechanical tension applied, which may induce mechanical stretching and promote collagen production in the extracellular matrix of the skin (23). Additionally, with age, there is a gradual decrease in the number of melanocytes, which, combined with changes in interactions between melanocytes and keratinocytes, leads to dysfunction of the protective barrier against UV (24).

Monopolar and bipolar radiofrequency devices have been shown to provide measurable improvements in skin laxity with an acceptable adverse event profile (25). Additionally, studies on radiofrequency at frequencies around 400 kHz have revealed that electrostimulation promotes proliferation and/or migration in keratinocytes and fibroblasts. The electrically induced changes in these proteins are consistent with the effects of capacitive-resistive electric transfer (CRET) on the proliferation and migration of keratinocytes and fibroblasts, which are crucial for skin repair and regeneration (26). In our case series, we utilized bipolar radiofrequency, specifically targeting the more superficial layers of the skin compared to monopolar treatment, and paired it with non-crosslinked HA mesotherapy. This combined therapy had a positive impact on various epidermal issues, including enlarged pores, pigmentation spots, and UV radiation-induced damage, compared to the baseline condition. Additionally, uneven skin tone resulting from melanin deposition and erythema improved after the application of mesotherapy combined with RF. We also observed enhancements in skin appearance, such as increased firmness, a more even skin tone, and reduced dryness, along with improvements in epidermal barrier function and skin homeostasis, which support optimal skin renewal.

The protocol was also very well-received and evaluated positively by both patients and the performing physicians. Our observations from applying the combination of HA mesotherapy with 0.01% CaHA and RF confirm the results of other studies, where an increase in epidermal density, a reduction in transepidermal water loss (TEWL), and an improvement in skin hydration were also observed (14). It is worth noting that these two procedures may act synergistically, increasing the level of hyaluronic acid in the epidermis and improving skin hydration. In our case series, no adverse events related to the treatment were reported. This case series was limited by its relatively small sample size and the short follow-up duration, which was insufficient to evaluate the long-term effects of the combination treatment involving 480 kHz RF and HA mesotherapy. To confirm the efficacy and safety of this treatment, further studies with larger sample sizes and extended durations are necessary. It would also be valuable to observe and compare the effects of monotherapies with HA and RF separately, as well as their combination, to validate potential synergistic effects.

The examinations performed in this study allowed for differentiation between granulomas and persistent deposit nodules. They revealed the presence of massive fibrosis and labial glands displaced by these abnormalities, with the glands appearing as hypoechoic oval areas. Histopathological examination confirmed that the morphology of the labial glands, reported by patients as uncomfortable lumps on the mucosal side, closely resembled persistent deposit nodules or granulomas.

High-frequency ultrasound proved essential for accurately differentiating complications related to tissue filler procedures, which facilitates appropriate treatment. This study demonstrated for the first time that lumps reported by patients after lip-filling procedures might be caused by labial glands being displaced by deposits, granulomas, or massive fibrosis—complications associated with such procedures (27).

Various approaches have been proposed for soft tissue augmentation using injectable materials due to their physical and biological properties. Hyaluronic acid, a natural component of connective tissues involved in wound healing and skin regeneration, was specifically investigated for lip augmentation. In this research, eight patients underwent lip augmentation with cross-linked hyaluronic acid, followed by a clinical follow-up period of 60 days. Histological evaluation after this period showed no inflammatory response, tissue contractions, or local inflammatory evidence in the treated areas, and the filling volume appeared to be maintained. The 60-day histological assessment revealed evidence of filler resorption with minimal inflammatory cell infiltration. These findings suggest that cross-linked hyaluronic acid is a safe and effective tool for lip augmentation (28).

CONCLUSION

In this case series involving subjects with dry and lax facial skin, we explored a combined treatment approach using 480 kHz radiofrequency devices and a mesotherapy product containing 18 mg/ml of non-crosslinked HA and 0.01% CaHA. This treatment protocol demonstrated significant effects, leading to notable improvements in both visual outcomes and patient satisfaction, which remained consistently high post-treatment. Moreover, the protocol was well tolerated and resulted in significant enhancements in facial appearance. The presented case series provides further evidence for the clinical utility of combination treatments and highlights the need for additional evaluation. Given the limited number of patients in this series, further research is necessary to assess both the immediate and long-term outcomes of using hyaluronic acid and radiofrequency in combination.

Consent for publication

Informed consent was obtained from the subject involved in the report. Written informed consent has been obtained from the patient to publish this paper.

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