The Efficacy of Combined Monopolar Radiofrequency and Targeted Ultrasound for Lip Hydration: A Pilot Study

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Abstract

Aging-related changes in the lips, such as dehydration, volume loss, perioral wrinkles, and thinning, primarily result from a decline in hyaluronic acid (HA), collagen, and elastin. Existing treatments, including HA fillers, lip balms and topical lip HA, mainly focus on replacing lost HA rather than stimulating its natural production. This study investigates a novel, non-invasive approach using a patented combination of monopolar radiofrequency (RF) and targeted ultrasound (TUS) to improve lip hydration, potentially associated with increased intrinsic HA production. Despite extensive research on facial rejuvenation, studies specifically targeting lip hydration and wrinkle reduction remain limited. This pilot study evaluates the efficacy of RF+TUS for lip rejuvenation in Asian individuals, specifically targeting lip hydration and wrinkle reduction. Thirty participants underwent four weekly treatment sessions over four months, with assessments conducted at baseline, one month, and three months post-treatment using both objective (MoistureMeter, Antera 3D) and subjective measures (photographs, satisfaction scores, side effects, and pain levels). Results demonstrated a significant increase in lip hydration (MoistureMeter: baseline 42.14 ± 7.28 to Month 1: 48.07 ± 6.44, $p < 0.001$) and a reduction in fine wrinkles (Antera 3D: baseline 24.63 ± 6.87 to Month 1: 23.05 ± 6.04, $p = 0.003$). No serious side effects were reported. Statistical analysis for Month 3 data is pending. This study introduces an innovative approach to lip rejuvenation, shifting the focus from external HA supplementation to methods that may stimulate natural HA production. The combination of RF and TUS offers a safe, effective, and well-tolerated alternative for improving lip hydration and reducing wrinkles, contributing to advancements in minimally invasive aesthetic medicine.

Keywords: *monopolar RF, targeted ultrasound, lip hydration, lip wrinkles, hyaluronic acid*

1. Introduction

The unique structural and physiological characteristics of the vermillion lips make them highly susceptible to dehydration and aging. Composed of thin, non-keratinized epithelium, the lips lack an effective barrier to moisture loss, leading to dryness, rough texture, and increased susceptibility to environmental factors such as UV exposure, temperature fluctuations, and smoking (Subramanyam et al., 2023; Bielfeldt et al., 2019; Trookman, et al., 2009). Studies indicate that lip hydration varies across ethnicities, with Asian individuals generally exhibiting lower hydration levels (Gunt, & Levy, 2019; Gunt, & Levy, 2024). Aging further exacerbates these issues, contributing to volume loss, increased vertical lip lines, thinning, and diminished color (Seo et al., 2024). These changes result from intrinsic factors such as decreased collagen, elastin, and HA, as well as extrinsic influences like repetitive muscle movements and environmental exposure.

Various treatments, including HA fillers, topical lip HA, topical lip balm, and lipstick sunscreen, have been employed to address lip dryness (Makino et al., 2017; Draelos et al., 2021; López-Jornet et al., 2010; Tamura et al., 2020; Gunt et al., 2015; Ribé, 2023). While these approaches offer temporary hydration and structural support, they do not stimulate the body's natural HA production. Monopolar RF and TUS have emerged as

promising non-invasive modalities for enhancing skin quality. RF generates controlled dermal heating, inducing fibroblast activity to stimulate collagen and elastin production, while TUS applies mechanical stress to the reticular dermis, optimizing conditions for HA synthesis. When combined, these technologies synergistically enhance fibroblast function, leading to increased HA levels and improved skin hydration (Duncan et al., 2024).

Previous studies have demonstrated that targeted ultrasound is crucial for HA production. Duncan et al. found that only targeted ultrasound combined with RF significantly increased HA levels, with the RF+TUS group exhibiting up to a 224% increase in HA production. Similarly, Chilukuri & Boyd reported that simultaneous RF+TUS treatment resulted in a 41% improvement in skin texture and a 22.8% increase in skin hydration, which was over three times greater than the improvement observed with RF alone (Duncan et al., 2024; Boyd, & Chilukuri, 2024).

Despite the abundance of research on facial skin rejuvenation, studies focusing specifically on lip rejuvenation remain scarce. Most research has centered on perioral treatments rather than directly addressing the vermillion zone. This study aims to bridge this gap by evaluating the effectiveness of RF+TUS in enhancing lip hydration and reducing wrinkles, offering a non-invasive alternative to traditional HA-based treatments.

2. Objectives

1) To study the efficacy of combined monopolar radiofrequency and targeted ultrasound for lip hydration
2) To evaluate patient satisfaction after procedure
3) To examine the side effects on subjects' lips after procedure

3. Materials and Methods

The study was a pilot study, comparing results before the procedure and at 1 month and 3 months after the final treatment. It lasted for 4 months, following approval from the Human Research Ethics Committee of Thammasat University. Participant involvement took place at the Department of Dermatology, Benchakitti Park Hospital, Thailand.

3.1 Patient Selection and Sample Size Calculation

3.1.1 Patient Selection

A total of 30 Thai participants were selected based on the following inclusion criteria:

1) Aged 25 to 60 years
2) Fitzpatrick skin types III-V
3) Willingness to participate in the study

The following exclusion criteria were applied to ensure participant safety and prevent confounding factors:

1) Pregnancy and breastfeeding
2) Recent energy-based device treatment on the lips within the past 12 months
3) Lip filler injection within the past 12 months
4) Active bacterial or viral infection (e.g., oral herpes simplex) in the lip/perioral area
5) History of oral herpes simplex
6) Active inflammation (e.g., sores, eczema, or other skin conditions) on the lip/perioral area
7) Unhealed lip wounds
8) Recent surgical procedure (within 3 months) on the lip/perioral area
9) Metal implants near the treatment area or pacemakers/electrical implants in the body
10) Systemic diseases, including:
    - Impaired immune system

- Skin-related autoimmune diseases
- History or current malignant cancer (including skin cancer)
- History of radiation therapy or chemotherapy
- Cardiovascular disease
- Poorly controlled endocrine disorders (e.g., diabetes)
- Tuberculosis
- Febrile conditions
- Acute neuralgia or neuropathy
- Kidney or liver failure

3.1.2 Sample Size Calculation

To calculate the sample size, the study used the formula referenced from the research of Samadi, Aniseh et al., (2018) The effect size was calculated as follows:

$$d = \frac{\mu_1 - \mu_2}{\sigma} = \frac{11.45 - 8.47}{5.32} = 0.5601$$

The calculated effect size of 0.5601 indicates a medium effect, meaning the intervention has a significant impact. For a one-sample t-test, the sample size was calculated as:

$$n = \left(\frac{2.8}{0.56}\right)^2 = 25$$

Considering a 20% dropout rate, the final sample size was adjusted to 30 participants. This approach is standard for pilot studies, ensuring that the study provides reliable data for future research.

3.2 Materials

1) EXION™ with face applicators (BTL Aesthetic Ltd., Newcastle, England) features a 0.5 cm² tip. The radiofrequency operates at a frequency of 3.25 MHz, while the targeted ultrasound operates at a frequency of 1.9 MHz

2) Ultrasound gel/Conductive gel

3.3 Intervention

1) Position the neutral electrode on the patient's back, avoiding placement across the spine.

2) Apply ultrasound gel to the lip area to facilitate optimal energy transmission.

3) Set up the combined monopolar radiofrequency and targeted ultrasound applicator (Exion face probe), starting with an RF setting of 30-40% to reach the target temperature of 40-42°C.

- If the RF setting at 40% does not reach the target temperature, adjust the RF level in 5% increments until the target temperature is achieved, ensuring the patient can comfortably tolerate the heating sensation.
- The RF setting may vary for each patient.
- The temperature is measured by the tip of the probe and will be displayed on the machine monitor.

4) Initiate the therapy by gently moving the applicator's tip over the lip area for a duration of 4 minutes.

5) If patients experience discomfort, pause the therapy, reduce the radiofrequency setting, and then assess the patient's condition.

6) The participants undergo a total of 4 therapy sessions with a one-week interval between each session. The weekly schedule is based on supporting international research that follows this protocol.

7) Follow-up and assessment are conducted at baseline, 1 month, and 3 months after the last treatment.

3.4 Assessments

This study includes both objective and subjective outcomes, comparing results before and after the procedure within the same individual, without using a control group.

1) Objective Outcomes (at baseline, 1 month, and 3 months after the last treatment)

- MoistureMeter (Delfin®) measures tissue water content by assessing the tissue dielectric constant (TDC), which increases with higher water content. The XS5 probe is used to measure depths ranging from 0.5 to 2.5 mm**.**

- Antera 3D Camera is used to analyze and measure lip wrinkles. Small wrinkles are defined as having a depth ranging from 0.1 to 1 mm, while custom wrinkles are defined as having a depth ranging from 0.1 to 0.5 mm**.**

2) Subjective Outcomes

- Digital Photographs will be taken at baseline (before the procedure) and during each follow-up visit, including close-up images of the lips to monitor changes over time.

- Side Effects will be evaluated based on patient feedback. Possible side effects include a heating sensation, erythema (redness), swelling, and dry skin in the treated area for a few days post-procedure. Rare side effects may include crust formation, blistering, and burns, though these are uncommon due to the safety measures of the device.

- Pain Score will be assessed after each procedure using a scale from 0 to 10, categorized into 5 levels, 0**:** No pain, 1-3: Mild pain, 4-6: Moderate to severe pain, 7-9: Very severe pain, 10: Worst possible pain

- Patient Satisfaction will be evaluated at 1 month and 3 months after the last procedure using a Likert scale from 1 to 5**,** 1: Very dissatisfied, 2: Dissatisfied, 3: Sufficiently satisfied, 4: Satisfied, 5: Very satisfied

The outcomes will be assessed before and after the procedure within the same individual, allowing for a direct comparison of the effectiveness of RF+TUS. No control group is used in this study because the primary goal is to evaluate the efficacy of RF+TUS treatment on lip hydration and wrinkles within the same person. Comparing pre- and post-treatment data in the same individual eliminates variability caused by between-subject differences, providing a more accurate assessment of the treatment's impact.

3.5 Statistical Analysis

We analyzed the data using Linear Mixed Models (LMMs) to evaluate changes in scores from Baseline at Month 1 and Month 3. Each subject was modeled with random intercepts to accommodate intra-subject variability over time. Fixed effects for time points were used to determine changes in scores, with a p-value of 0.05 set as the threshold for statistical significance. The analyses were conducted using the statsmodels package in Python.

4. Results and Discussion

4.1 Results

4.1.1 Demographic Data

Thirty-two subjects were enrolled in the study, but two were excluded due to health issues, leaving a total of 30 subjects. One subject was terminated during the study due to illness. Table 1 presents the baseline demographic characteristics of the study participants. The mean age of the participants was 44.93 years with a standard deviation (SD) of 11.45, indicating a moderately wide age range among the study population. In terms of gender distribution, the majority of participants were female, accounting for 70% of the total sample, while males comprised 30%. Regarding skin type, based on the Fitzpatrick Skin Type classification, the majority of participants had Type 3 skin (51.72%), followed by Type 4 (41.38%). A smaller proportion of participants had Type 5 skin (6.9%).

Table 1 Baseline demographic characteristics of participants

Category	Value (n = 30)
Age (mean ± SD)	44.93 ± 11.45
Gender	
Male	9 (30.00%)
Female	21 (70.00%)
Fitzpatrick Skin Type	
Type 1	0 (0.00%)
Type 2	0 (0.00%)
Type 3	16 (51.72%)
Type 4	12 (41.38%)
Type 5	2 (6.90%)
Type 6	0 (0.00%)

4.1.2 MoistureMeter and Antera Identation

Table 2 presents the results of the Moisture Meter levels and Antera Indentation measurements (small wrinkle and custom wrinkle) at baseline, and at 1 month after the last treatment. Statistical analysis for Month 3 data is still pending.

1) Lip Hydration (Moisture Meter Measurement)

Lip moisture levels significantly increased from baseline (42.14 ± 7.28) to Month 1 (48.07 ± 6.44, $p < 0.001$). The increase in hydration was statistically significant, with a coefficient of 5.93 (95% CI: 3.66, 8.20), indicating improved lip hydration after RF + TUS treatment.

2) Reduction in Small Wrinkles (Antera Indentation – Small Wrinkle)

Antera Indentation analysis for small wrinkles, defined as wrinkles with a depth of 0.1 to 1 mm, revealed a significant reduction. The mean indentation decreased from 24.63 ± 6.87 at baseline to 23.05 ± 6.04 at Month

1 (p = 0.003), with a reduction coefficient of -1.43 (95% CI: -2.36, -0.49). A negative coefficient in this context indicates a decrease in wrinkle depth, reflecting wrinkle improvement.

3) Custom Wrinkle Indentation (Antera Indentation – Custom Wrinkle)

For custom wrinkles, defined as wrinkles with a depth of 0.1 to 0.5 mm, a slight reduction in indentation was observed. The mean indentation decreased from 11.02 ± 2.90 at baseline to 10.38 ± 2.43 at Month 1 (p = 0.035), with a coefficient of -0.47 (95% CI: -0.90, -0.03). Similar to small wrinkles, the negative coefficient denotes a reduction in wrinkle depth, suggesting a mild improvement.

Overall, the findings indicate that RF + TUS treatment significantly enhances lip hydration and reduces small wrinkles after one month. A mild improvement in custom wrinkles was also observed. The follow-up results at Month 3 in this study will provide further clarity on the treatment's long-term effects.

Note: Negative coefficient values in Table2 indicate a reduction in the measured parameter. In the context of wrinkle analysis, a negative coefficient represents a decrease in indentation depth, signifying an improvement in skin smoothness.
Additional Note on Error Bars in Figure1: The error bars in the graphs represent ***standard deviation (SD)****, which provides an estimate of variability within the dataset. Standard deviation reflects the dispersion of individual values around the mean, indicating the spread of the data points in relation to the average measurement.*

Table 2 The results of MoistureMeter levels and Antera Indentation (small wrinkles and custom wrinkles) on the lips at baseline, and at 1 month after the last treatment

Time Period	Mean ± SD	Coef (95% CI)	p-value
Moisture Meter			
Baseline	42.14 ± 7.28	-	-
Month 1	48.07 ± 6.44	5.93 (3.66, 8.20)	<0.001
Antera Indentation (Small Wrinkle)			
Baseline	24.63 ± 6.87	-	-
Month 1	23.05 ± 6.04	-1.43 (-2.36, -0.49)	0.003
Antera Indentation (Custom Wrinkle)			
Baseline	11.02 ± 2.90	-	-
Month 1	10.38 ± 2.43	-0.47 (-0.90, -0.03)	0.035

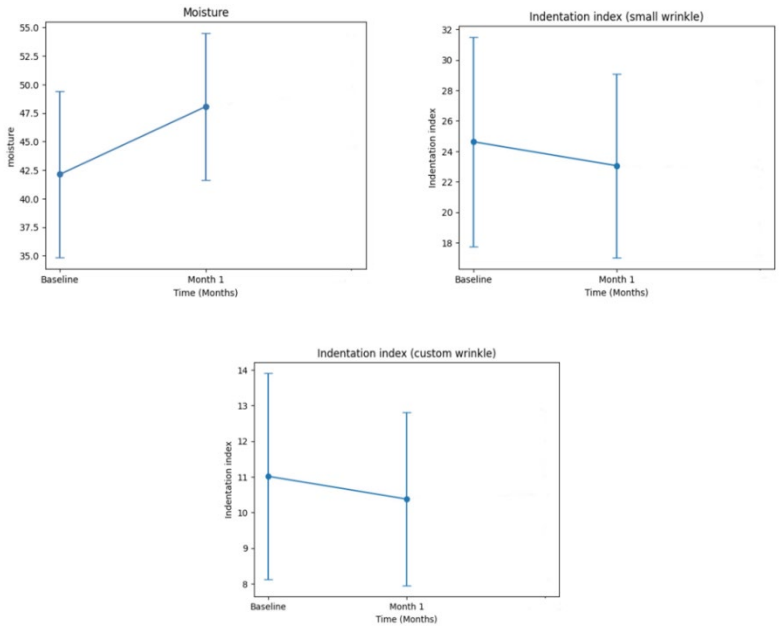

Figure 1 Changes in Moisture Meter levels and Antera Indentation indices

4.1.3 Patient's Satisfaction Score

Patients undergoing the treatment were assessed using a Likert scale satisfaction survey at Month 1 post-treatment. The Likert scale ranged from 1 (very dissatisfied) to 5 (very satisfied). The patient-reported satisfaction scores were analyzed to determine changes in subjective treatment efficacy over time. The majority of patients (around 16) rated their satisfaction as "4 - Satisfied," indicating a generally positive response to the treatment. The second highest group (approximately 7 patients) rated their satisfaction as "3 - Sufficiently satisfied". Around 5 patients gave the highest rating of "5 - Very satisfied," demonstrating a smaller but notable group of highly satisfied participants. Very few patients rated the treatment negatively, with only 1 patient rating it as "2 - Dissatisfied" and none giving the lowest rating of "1 - Very dissatisfied.", indicating that the treatment was well-tolerated with no major negative feedback.

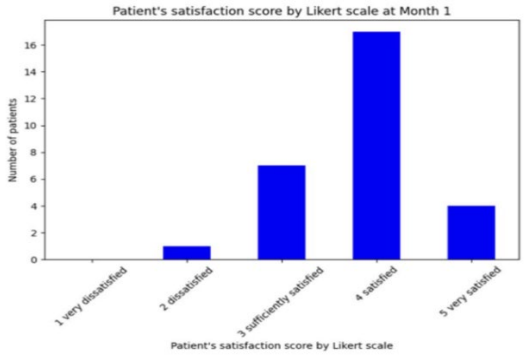

Figure 2 Patient Satisfaction Analysis

4.1.4 Pain Score & Side Effect

1) Pain Score

The pain score was graded using a pain assessment scale ranging from 0 to 10, categorized into 5 levels. Pain level 0 indicates no pain at all, levels 1-3 denote mild pain, levels 4-6 represent moderate to severe pain, levels 7-9 indicate very severe pain, and level 10 signifies the worst possible pain.

The combined monopolar radiofrequency and targeted ultrasound treatment was generally well tolerated by participants. While some reported mild tingling due to heat exposure, pain levels remained low, with most describing the experience as warm rather than painful. Pain scores showed a steady reduction over multiple sessions, with the highest pain score (0.83 ± 1.04) recorded in the first session. Subsequent sessions (Time Points 2, 3, and 4) showed reductions to 0.66 ± 0.90, 0.55 ± 0.74, and 0.52 ± 0.74, respectively, indicating improved tolerance as participants became familiar with the treatment.

The bar graph supports this trend, showing that most participants reported no pain (0) or mild pain (1–3) in all sessions. The number of participants experiencing no pain increased over time, while mild pain decreased. Severe pain (scores 4–10) was rare, highlighting the treatment's high tolerability. The decrease in pain can be attributed to participants becoming accustomed to the treatment over successive sessions, reducing the perception of pain. Repeated exposure likely helped them psychologically adjust, leading to improved comfort and tolerance over time.

Overall, the treatment was considered comfortable, with warmth being the predominant sensation. The reduced pain scores and trends reinforce the procedure's feasibility for repeated sessions with minimal discomfort, making it a well-tolerated aesthetic procedure.

Table 3 Pain score measurements over four different time points

Pain score	
Time Point	**Mean ± SD**
1	0.83 ± 1.04
2	0.66 ± 0.90
3	0.55 ± 0.74
4	0.52 ± 0.74

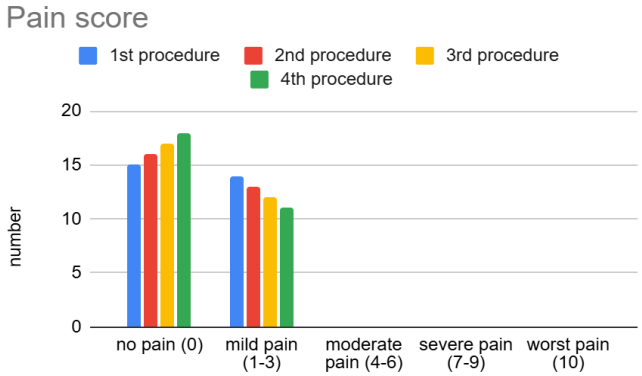

Figure 3 Pain Score Distribution Across Multiple Procedures

2) Side Effects

The side effects observed in this study were primarily a heating sensation, erythema (redness), and dry lips, which lasted for 2-3 days after the procedure. Overall, the procedure was well tolerated, with most participants reporting warmth rather than pain, and only mild tingling or occasional discomfort.

4.2 Discussion

A recent study explored how combining the benefits of two technologies can enhance skin hydration by increasing hyaluronic acid (HA) production. The first study, conducted by Diane Duncan et al. (2024), investigated HA production in the skin following monopolar radiofrequency (RF) and targeted ultrasound (TUS) treatment in a porcine model. Twelve animals were divided into two groups: (1) RF + non-targeted ultrasound and (2) RF + targeted ultrasound. Each group received four 30-minute treatments on one side of the abdomen, while the opposite side served as a control. Punch biopsies were taken at baseline, after the final session, and at 1- and 2-month follow-ups. Results showed a significant HA increase in the RF + TUS group after two months, confirmed by three methods: a 98% increase via PCR, a 224% increase via MALDI-TOF, and improvements observed in confocal microscopy. In contrast, the RF + non-TUS group showed no significant changes.

Another study by Chilukuri & Boyd (2024) examined the simultaneous application of monopolar RF and targeted ultrasound for improving skin hydration and texture in 41 patients. Participants were randomly assigned to two groups: Group A (RF + TUS, 21 patients) and Group B (RF only, 20 patients). Each received four treatments spaced 7–14 days apart, with follow-ups at baseline, 1 month, 3 months, and an optional 6-month visit. Skin hydration was measured by moisture levels, and skin texture was assessed using 3D imaging via the Quantificare software suite. Results showed that the RF + TUS group had a threefold greater improvement in skin hydration than the RF-only group. Skin texture improvement peaked at 3 months, with a 41% increase in the RF + TUS group. Overall, the findings indicate that simultaneous RF + TUS treatment provides significantly better outcomes than RF alone.

This pilot study aimed to evaluate the effects of monopolar radiofrequency (RF) and targeted ultrasound (TUS) on enhancing lip hydration and improving wrinkle appearance. The results at Month 1 demonstrated a significant improvement in lip moisture and a reduction in small wrinkles. The moisture meter data showed a clear increasing trend in lip hydration, with mean values rising from 42.14 ± 7.28 at baseline to 48.07 ± 6.44 at Month 1 ($p < 0.001$). This statistically significant improvement suggests that RF and ultrasound treatment may effectively enhance lip hydration in the short term.

Regarding wrinkle improvement, both the Antera Indentation (small wrinkle) and custom wrinkle indices showed a slight reduction in wrinkle depth over time. The indentation index for small wrinkles (depth: 0.1–1 mm) decreased from 24.63 ± 6.87 at baseline to 23.05 ± 6.04 at Month 1 ($p = 0.003$), indicating a statistically significant improvement. Similarly, the custom wrinkle index (depth: 0.1–0.5 mm) decreased from 11.02 ± 2.90 to 10.38 ± 2.43 at Month 1 ($p = 0.035$).

The results of this pilot study align with previous research, such as the study by Chilukuri & Boyd, which indicated that RF + TUS technology can significantly improve skin hydration. Interestingly, the observed increase in lip hydration in this study suggests that RF + TUS may potentially stimulate endogenous hyaluronic acid (HA) production. This presents a distinct advantage over topical treatments, such as lip balms or topical HA, which primarily provide external hydration. While both approaches address similar concerns, RF + TUS offers a non-invasive method that may support the body's natural mechanisms, potentially leading to longer-lasting improvements in lip moisture and fine line reduction.

Additionally, compared to lip HA filler injections, which are based on external HA, RF + TUS provides the benefit of enhancing natural hydration and wrinkle reduction without introducing foreign substances. However, HA fillers remain more effective in increasing lip volume and defining lip contours. While this study demonstrates promising results for RF + TUS in improving hydration and reducing lip wrinkles, further research

is needed to evaluate its long-term effects and compare the efficacy of RF + TUS with topical lip treatments and HA fillers.

In conclusion, this study provides preliminary evidence that combined RF and targeted ultrasound treatment significantly improves lip hydration and reduces small wrinkles after one month. While the current results show promising short-term benefits, the Month 3 data are pending for a clearer answer to the long-term effects of this treatment.

Limitations

This study has several limitations. Firstly, the small sample size limits the statistical power and generalizability of the findings. Additionally, while the results at Month 1 indicate a significant improvement in lip hydration and a reduction in wrinkle depth, the full extent of the treatment's effects may require a longer follow-up period to be fully assessed.

Although data collection at Month 3 has been conducted, the analysis is still pending. Since the stimulation of collagen production and hyaluronic acid synthesis by RF and ultrasound treatments is a progressive process, the potential long-term benefits may become more evident over time. Future analysis of the Month 3 data may provide additional insights into the durability and sustained efficacy of this combined approach.

Additionally, external factors such as seasonal variations in temperature and humidity were not controlled in this study and may have influenced the results, particularly in relation to lip hydration. Furthermore, individual differences in baseline hydration levels, lifestyle habits (e.g., water intake, lip care routine), and natural skin variability were not controlled. These could contribute to variability in the observed outcomes.

Despite these limitations, the findings at Month 1 demonstrate significant short-term improvements in lip hydration and wrinkle reduction following RF and ultrasound treatment. Further research with a larger sample size is needed to confirm these preliminary findings and evaluate the long-term benefits of the treatment.

Future Directions

Further studies with larger sample sizes and longer follow-up periods are recommended to confirm the potential benefits of these treatments. Future research could also explore different treatment parameters, such as adjusting the frequency or intensity of RF and ultrasound applications, to optimize outcomes for lip hydration and wrinkle reduction. Moreover, future studies should account for seasonal variations by either adjusting the treatment schedule or including environmental controls to minimize potential confounding effects from changes in temperature and humidity.

5. Conclusion

In conclusion, this pilot study demonstrates that RF + TUS can be a promising new non-invasive lip rejuvenation procedure for individuals experiencing dry lips or age-related lip wrinkles. The treatment achieved statistically significant results in improving lip hydration and reducing fine wrinkle depth. It offers a viable alternative for those who seek improvement in lip hydration and wrinkle reduction without invasive procedures or significant discomfort. The results suggest that RF + TUS can be an effective, well-tolerated, and minimally painful solution. However, data analysis for the third month is still pending to provide a clearer answer regarding the long-term efficacy of this treatment. Larger and more comprehensive studies are required to fully validate these preliminary findings and explore the therapeutic potential of RF + TUS more thoroughly.

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