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Research Article

Radiofrequency *vs.* Synchronized Radiofrequency and Targeted Ultrasound Technology for Enhanced Skin Hydration

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ABSTRACT

Objective: Skin aging is characterized by significant changes including the loss of collagen, elastin, and Hyaluronic Acid (HA), impacting skin moisture, elasticity, and overall health. Radiofrequency (RF) and Ultrasound (US) are well-recognized modalities, typically utilized as independent procedures. Due to the novel device allowing simultaneous delivery of both energies in a single applicator, this study compares the effects of RF as a standalone treatment to simultaneous RF and Targeted Ultrasound (TUS) treatment

Methods: A prospective multi-center, two-arm study was conducted with forty-one (41) subjects (3 males, 38 females, 26-77 years, skin types I-VI), randomly allocated into two groups: Group A (N=21) treated with monopolar Radiofrequency+Targeted Ultrasound (RF+TUS), and Group B (N=20) treated with monopolar RF only. In each group, subjects received four (4) full-face treatments delivered once per week. Skin hydration was measured with a moisture meter following the final treatment session. Digital photographs were scored by three independent evaluators using the Global Aesthetic Improvement Scale (GAIS scale) and 3D analysis was performed. Additionally, subject satisfaction and therapy comfort were assessed.

Results: At 3 months, group A achieved a marked improvement in the GAIS scale by +1.3 ± 0.1 points. 3D photographs demonstrated more profound results in Group A, achieving a skin texture improvement of +7.3 points (41.6%, $p<0.05$) at 3 months *vs.* Group B by +5.3 points (28.5%). While almost all subjects found both treatments comfortable, treatment satisfaction outcomes were higher in the RF+TUS group. The study demonstrated the synergistic effects of RF and TUS in enhancing skin hydration and overall quality, with no adverse events reported.

Conclusion: Analysis of facial skin hydration, and skin quality showed that simultaneous RF+TUS treatment has significantly better outcomes than single modality RF for improving the overall facial appearance. The results suggest that this novel treatment offers a potential non-invasive approach to skin rejuvenation, with implications for broader application in dermatological and aesthetic practices. However, further research addressing limitations like subject variability and long-term hydration effects is necessary to validate and expand upon these findings.

Keywords: Skin hydration; Radiofrequency; Ultrasound; Healthy skin; Radiofrequency; Skin rejuvenation; Facial aging

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INTRODUCTION

The complex process of skin aging results in significant changes within the skin, including the loss of collagen, elastin, and Hyaluronic Acid (HA) [1]. HA is a naturally occurring glycosaminoglycan found in the human body, particularly in the skin, connective tissues, and eyes [2]. In the skin, hyaluronic acid plays a important role in maintaining moisture, elasticity, and overall skin health, as it is responsible for skin hydration and increasing moisture content due to its water-binding capacity [3,4]. HA has been also implicated as a regulator of cell proliferation and motility, thereby promoting wound healing [5-7]. The enzymatic processes that are needed for normal skin desquamation are impaired when moisture levels in the skin are reduced, leading to the appearance of dry, flaky skin [8]. Therefore, maintaining optimal levels of HA over time is essential for preserving a healthy, youthful, and plump appearance of the skin. As we age, our skin undergoes various changes, including a decrease in the amount of HA in the skin. This leads to reduced hydration levels and gradual development of fine lines and wrinkles, skin dryness, dullness, and tired appearance [9-11]. Hydration of the skin diminishes due to various external factors with one of the most significant contributors being daily exposure to sun leading to prominent changes on the facial skin [12]. Safer non-invasive methods for treating facial wrinkles and improving skin quality, such as Radiofrequency (RF) and ultrasound, are preferred as all skin types can be treated with few complications. However, despite efforts to non-invasively stimulate natural HA production studies have been inconclusive or have shown only minimal effects when treated with single modality technology. Despite the widespread use of both RF and ultrasound, research investigating the synergistic effect is lacking. Recent histologic evaluation has already shown that RF treatment can increase the collagen and elastin in the skin [13-18], the primary structural proteins in the skin, responsible for skin elasticity, firmness, resilience, and structure [19-23]. Hence, it seems that the key to enhancing the production of HA, collagen, and elastin, lies in applying both of these energies simultaneously.

This study aimed to investigate the effectiveness of the novel device simultaneously delivering RF and Targeted Ultrasound (TUS), developed to enhance the body's innate capacity to produce HA. To quantitatively measure the increase in hyaluronic acid levels in the skin in this study, a skin hydration assessment was performed after the final treatment.

MATERIALS AND METHODS

Study population and treatment protocol

This is a prospective multi-center, two-arm study. Forty-two subjects (3 males, 39 females, 26-77 years) were recruited and forty-one (N=41, one subject was withdrawn) were randomly allocated into two study groups-group A (N=21) and group B (N=20). The patients' baseline characteristics are shown in Table 1.

Variables	Group A	Group B
Patients	21	20
Sex		
Male	2	1
Female	20	19
Age (years)		
Mean	57.5 ± 2.3	56.3 ± 2.0
Range	26-77*	43-73
Median	56	55.5
Skin types		
I	3	2
II	12	10
III	3	3
IV	2	2
V	1	2
VI	0	1

Table 1: Patients' baseline characteristics. **Note:** *: Only one subject was 26-year old in group A, without this patient the range is 50-77 years.

Group A was treated with a novel EXION (BTL Industries Inc., Boston, MA) device using the Exion Face applicator delivering monopolar RF and TUS energies simultaneously (Group A). Group B was treated with single-modality monopolar RF. By comparing the two treatments, a better understanding of their mechanisms of action may be understood. In each group, subjects received four full-face treatments delivered once per week. A conductive gel was applied to the treatment area to ensure optimal energy flow. During therapies, RF intensity parameters of the therapy were adjusted according to patient feedback (on a scale of 0% to 100%, where TUS was set to 100% by default). The study participants were continuously monitored and assessed for any potential adverse events that might occur during the study.

Data and evaluation

Skin hydration was measured by MoistureMeterSC (Delfin Technologies Ltd.) and assessed at baseline and immediately after the last treatment visit. The MoistureMeterSC measures the combination of the skin's dielectric constant and the changing thickness of the stratum corneum's dry layer. These values are represented on a scale of 0 to 300 points, indicating a relative dimensionless quantity that corresponds to the hydration

level of the skin surface. As the moisture content of the skin surface increases, the measured values also increase.

Digital photographs of the treated areas were taken at baseline, after the last (4th) treatment, at 1-month, 3-month, and 6-month (optional) follow-up visits. These photographs were scored by three blinded independent evaluators using the Global Aesthetic Improvement Scale (GAIS) in order to evaluate the changes in skin quality.

A Three-Dimensional (3D) photographic imaging system LifeViz® Mini (QuantifiCare S.A., France) was used to capture facial 2D photographs from the left, right, and front views of the face at multiple angles, and compiled them into a 3D model by using the Quantificare software suite. 3D models were evaluated for skin quality (e.g. skin creases and evenness). Every analysis was assigned a score ranging from -10 to +10. A negative score means the appearance of an individual is worse than the average and positive scores above 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.

Therapy Comfort Questionnaire (TCQ) using the 5-point Likert scale ("I found the treatment comfortable") and Visual Analog Scale (VAS, 0-no pain, 10-maximum bearable pain) was administered after the final treatment session. The 5-point Likert scale (1-strongly disagree, 5-strongly agree) Subject Satisfaction Questionnaire (SSQ) was administered after the final treatment and at all follow-up visits to assess patients' satisfaction with the therapy results.

Statistical methods

All data was analyzed for statistical significance and the descriptive statistic was calculated (mean, standard error of the mean, and median value). Paired variables measured at multiple time points were tested by non-parametric Friedman's test followed by Nemenyi's test used to analyze the significance of observed changes. Wilcoxon signed-rank test for a single sample was used to determine whether a mean GAIS difference showed a significant improvement compared to "no change" (zero score) and for analyzing significance in hydration assessment. The significance level was set to α=0.05 (5%).

RESULTS

Forty-one (56.9 ± 1.5 years old, skin types I-VI) received the RF +TUS treatment (A group, N=21) or RF-only treatment (B group, N=20).

GAIS evaluation

The majority of patients (94.4%) from Group A achieved a significant (P<0.05) improvement according to the GAIS scale (Table 2). The most prominent difference was observed at 3 months (Figure 1) in Group A by +1.3 ± 0.1 points and was maintained with individual slight decrease at 6 months. In Group B, the GAIS scale difference showed only +0.8 ± 0.2 points at a 3-month follow-up visit.

Global Aesthetic Improvement Scale (GAIS)				
	After Tx	1 month	3 months	6 months
Group A	0.6 ± 0.1 (N=19)	0.8 ± 0.1 (N=19)	1.3 ± 0.1 (N=18)	1.1 ± 0.2 (N=9)
Group B	0.5 ± 0.1 (N=19)	0.7 ± 0.1 (N=19)	0.8 ± 0.2 (N=18)	0.7 ± 0.1 (N=6)

Table 2: GAIS difference average ± Standard Error of the Mean (SEM) values after the treatment, 1-month, 3-month, and 6-month (optional) follow-up visits.

Figure 1: A 73-year-old female subject at baseline (left) and at the 3-month follow-up visit after the RF+TUS treatment. Visible improvement of facial appearance by jawline definition, lift of nasolabial and cheeks, and more even skin.

Skin hydration

Up to 71.4% of subjects improved after the RF+TUS treatment. Skin hydration was assessed after the last treatment and increased by +15.4 points (22.8%) in Group A (N=21). Compared to subjects treated with RF only (N=20), a lesser effect was observed (+4.2 points, 7%), pointing out a higher improvement level in group A and healthier-looking skin.

3D analysis of skin texture

Twenty-one (21) patients were included in the 3D analysis, eleven (11) from Group A and ten (10) from Group B. Based on the 3D photo model evaluation with QuantifiCare® software, the more profound skin quality improvement was documented at 1 month and 3 months (Figure 2) in group A against a baseline score of -0.9 ± 1.0 points by +3.5 points (19.3%, P<0.0.5) and +7.3 points (41.6%, P<0.05). This improvement was maintained up to 6 months (+35.1%, P<0.05). The most prominent improvement in Group B (baseline score of 0.1 ± 1.0 points) was documented at 3 months by +5.3 points (28.5%, P<0.05).

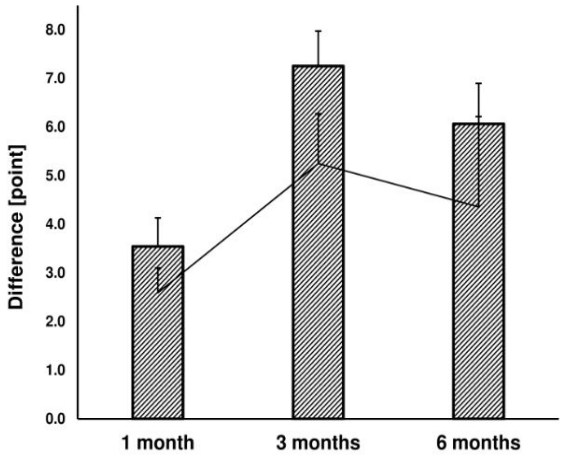

Figure 2: Skin quality by 3D analysis (average+SEM) for Group A (RF+TUS) and Group B (RF only) at 1-month and 3-month follow-up and 6-month optional follow-up visit. **Note:** (▨): RF+TUS; (—): RF only.

Subject satisfaction and therapy comfort

While almost all subjects found the treatment comfortable, the treatment satisfaction outcomes were higher in Group A with simultaneous delivery of RF+TUS. At 3 months, up to 95% of patients from Group A were satisfied with wrinkle reduction and improvement of skin laxity and overall skin appearance after the treatment. From group B, 90% were satisfied with the RF effects. In addition, all patients from both groups agreed the treatment was comfortable showing 4.6 ± 0.1 points in Group A and 4.5 ± 0.1 points in Group B. During the treatment, only low to mild discomfort was documented by a 10-point visual analog scale showing 1.8 ± 0.4 points for Group A and 1.7 ± 0.5 for Group B. No adverse events were observed.

DISCUSSION

This study aimed to investigate the effectiveness of a treatment utilizing RF and TUS compared to single modality RF by examining the overall change in facial appearance through skin hydration levels and overall skin quality. Based on the results from the 3D analysis, GAIS, and skin hydration assessment, a significant improvement in the RF+TUS group was documented, supporting the hypothesis that the synergy of both technologies is essential for an increase in HA production.

Previous histologic studies have consistently shown the potential of RF+TUS treatment to increase skin hydration *via* hyaluronic acid production. Based on the Matrix Assisted Laser Desorption Ionization-Time of Flight mass spectrometry (MALDI-TOF) evaluation Duncan DI. [24], presented that the amount of HA in the sample showed a gradual increase by 79% at the 1-month follow-up and by 224% at the 2-month follow-up (p-value=0.022) after the RF+TUS treatment. Compared to RF treatment alone, the synchronized application of RF+TUS resulted in more pronounced enhancement, and no clear trend in the HA changes was observed in the RF group only (14% at the 1-month follow-up, and 11% at the 3-month follow-up visit). These results were accompanied by confocal microscopy pictures visualizing the increased amount of HA in the dermis where HA is produced by fibroblasts. Similar results were documented in Fritz K, et al. [25], study which showed an increase in HA production evaluated by ELISA and light microscopy.

Our study aligns with these findings and further contributes to the existing body of knowledge in this field. The findings of our study highlight the benefits of improved skin hydration. Adequate skin hydration is important for maintaining skin health and function. By enhancing skin hydration levels, our findings suggest potential benefits such as improved barrier function, and a more youthful appearance. These results were quantitatively supported by a detailed 3D analysis of skin quality, which revealed a notable decline in natural skin aging indicators following the treatment. Importantly, increased skin hydration has been linked to the enhancement of collagen and elastin production, both of which are important for maintaining skin structure and elasticity. Furthermore, the mechanical effects of TUS, such as acoustic microstreaming, also contribute to stimulating fibroblast repair and consecutive HA production, collagen synthesis, and tissue regeneration, ultimately resulting in improved skin quality and a more youthful appearance [26]. Our study suggests that the observed increase in skin hydration may potentially lead to enhanced collagen and elastin synthesis, thereby contributing to overall skin quality improvement. Treatment with RF+TUS primarily boosts HA production and secondarily increases skin hydration thereby making the whole tissue more viable while the collagen and elastin structural remodeling propagates within 3 months [27,28].

The biggest limitation of the study was identifying suitable subjects. Patients' skin properties differ due to individual hydration levels, age, or the specific conditions in which the subject lives. The uniformity in subjects would provide a more comprehensive understanding of the treatment's effectiveness. It is also worth noting that the 3D analysis of skin quality was not conducted at one site due to technical issues, which limits the generalizability of the findings and a more robust assessment of the treatment's impact on skin quality. Further, the moisture meter measurement proved challenging.

Moisture meter measurements mainly focus on evaluating the epidermal layer (up to 2 mm) while only partly providing information about the subcutaneous area. Due to this limitation, skin hydration was only evaluated immediately after the final treatment. Skin hydration levels can fluctuate over time and are influenced by various factors including environmental conditions (low humidity, surfactants, wind, and sun) and individual differences. Although such variations may potentially influence the study findings in long-term observations, there is current evidence that skin hydration increases with HA production in the dermal layer [24,25]. The real-life effects that the increase of HA levels has on the skin were observed in this study. The sustained effects of the treatment on long-term skin hydration need to be further investigated. Despite the aforementioned limitations, the observed outcomes provide valuable quantifiable findings through GAIS evaluation and 3D analysis.

CONCLUSION

Overall, no study-related adverse events or side effects were observed in the subjects. Our study demonstrates the efficacy of a novel RF+TUS device in significantly improving skin hydration levels and enhancing overall skin quality. By employing synchronized treatment involving RF+TUS, our findings suggest an even greater potential for skin improvement than RF standalone only. However, future studies addressing the above-mentioned limitations are warranted to validate and expand upon our findings, ultimately advancing the field of skin rejuvenation and hydration.

ETHICAL STATEMENTS

This study was approved by the Advarra Institutional Review Board (ClinicalTrials.gov Identifier: NCT05929625), and its conduct adhered to the ethical principles of the 1975 Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

Conceptualization, C.B.; Methodology, C.B. and S.C.; Formal analysis, C.B. and S.C.; Investigation, C.B. and S.C.; Resources, C.B. and S.C.; Writing–Original Draft, C.B.; Writing – Review & Editing, C.B. and S.C.; Supervision, C.B. and S.C.

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CONFLICT OF INTEREST

The study was sponsored by BTL Industries. The investigators may be contracted to speak or present this work on behalf of BTL Industries.

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