



Efficacy and safety of a home-use handheld multi-energy-based device for skin rejuvenation: clinical, ex vivo, and histological studies

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Abstract

Alongside increases in the average lifespan and a growing interest in anti-aging remedies, the demand for at-home skincare devices is rapidly expanding in the cosmetic market. This study aimed to assess the safety and efficacy of a novel home-use handheld multi-energy-based device for skin rejuvenation that simultaneously emits low level light, low-dose radiofrequency, low-energy microcurrent, and low-intensity ultrasonic wave. This prospective, randomized, split-face clinical trial enrolled 36 healthy Korean women. After 8 weeks of device use, parameters associated with skin aging were assessed. Additionally, a preliminary ex vivo study and skin biopsy following device use were performed to confirm safety and efficiency of the device. Parameters associated with skin aging including skin hydration, elasticity, roughness, skin pore size, and eye wrinkle volume showed significant improvements after 8 weeks of the device use, relative to baseline measurements and the control side. No adverse effects were observed during the follow-up period. Results of ex vivo and in vivo skin tissue studies correlated with clinical findings, which showed an increase in the expression of type 1 collagen and a decrease in the expression of matrix metalloproteinase-1, which is related to the skin aging phenotype. The expression of loricrin and involucrin, major components of the epidermal skin barrier, also increased after the use of the device. Multi-energy-based device is effective for skin rejuvenation and tolerable, without any considerable adverse effects.

Keywords Radiofrequency · Low-level light · Microcurrent · Iontophoresis · Ultrasonic wave · Skin rejuvenation

Introduction

The recent growth of the public's interest in anti-aging and skin rejuvenation has fueled market demand for at-home cosmetic devices. Traditional laser equipment is limited to

the clinical setting; however, at-home devices that utilize low-fluency lasers or other energy transfer modes have also demonstrated efficacy for treating various skin conditions and aging skin [1]. Non-invasive energy-based devices such as those based on fractional radiofrequencies (RF), low-level light therapy (LLLT), low-intensity ultrasonic waves, and microcurrents have previously been utilized for skin rejuvenation [2–4].

The device used in the present study (PraL Intensive Multi-care BLP1; LG Electronics, Seoul, Korea) is a novel, handheld, multi-energy-based device developed for at-home use to enhance skin elasticity and achieve wrinkle improvement by emitting low-dose radiofrequencies, low-level light, low-energy microcurrents, and low-intensity ultrasonic waves. This study aimed to evaluate the device's safety and clinical efficacy for skin rejuvenation by assessing biophysical parameters of the skin, appearance of wrinkles, and histological changes before and after device application ex vivo and in vivo.

Sooyeon Choi and Jemin Kim contributed equally to this work.

IRB approval status This study was reviewed and approved by Yonsei University Health System (Approval No.: 4-2021-0349 and 4-2021-0262).

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Methods

Clinical study participants, design, and device information

This study was approved by the Institutional Review Board (IRB) of (anonymized for peer-review), (anonymized for peer-review) College of Medicine (IRB number: 4–2021-0349). The study protocol was initiated after written informed consent was obtained from all participants. The study was performed between May 2021 and January 2022. Healthy adult women aged 20–60 years were eligible for the study. Exclusion criteria were a history of keloid scarring; current inflammatory, infectious, or photosensitive skin diseases; malignant thyroid diseases or hyperthyroidism; pregnancy; and bleeding tendencies following antiplatelet or anticoagulant use.

This was a prospective, randomized, split-face clinical trial. All participants were instructed to divide their face in half; participants used both a moisturizer (LAVIDA calming gel, COREANA Cosmetics, Chungcheongnam-do, Korea) and the at-home multi-energy-based device on one side of their face (test side) and only the moisturizer on the other side of their face (control side). The treatment sites were randomly assigned, and the device was used twice a week for 6 min each time.

The facial area designated as the test side was subjected to the “intensive care mode” of the device. The device was equipped with 24 light-emitting diode (LED) at a wavelength of 630 nm. The total irradiance was 25 mW/cm² (each wavelength emitted 50% of the total irradiance) with a maximum temperature of 35 °C. In addition, two bipolar, non-invasive, 1-MHz RF-emitting electrodes, along with a low-energy (50 Hz, 250 µA) microcurrent, iontophoresis (1 kHz, 4 V at 47 kohm), and low-frequency (355 kHz) ultrasonic wave were delivered concurrently by the device.

Ex vivo skin organ culture, UVB irradiation protocol, and skin penetration study

A preliminary ex vivo study was performed to confirm the safety and efficiency of the device. Residual normal human skin specimens left behind during free transverse rectus abdominis myocutaneous flap breast reconstruction surgery was obtained following the approval from [anonymized for peer-review] Hospital’s IRB (IRB number: 4–2021-0262).

Tissue specimens were cut into 5 × 5-cm² pieces and divided into four groups: control, BLP1, type B ultraviolet (UVB), and UVB + BLP1. In the control group, moisturizer (LAVIDA calming gel) containing fluorescent

material (rhodamine B, 500 µg/mL) was applied without BLP1 device use. In the BLP1 group, moisturizer containing rhodamine B was first spread on skin tissue and BLP1 device’s “intensive care mode” was applied for 6 min. Skin tissue assigned to the UVB and UVB + BLP1 group was irradiated twice using UVB lamps (BLX 312, Vilber Lourmat, Paris, France) with a wavelength of 306 nm at 300 mJ/cm². In the UVB + BLP1 group, the BLP1 device was administered for 6 min following UVB light exposure. The specimens were cultured in a 6-well Transwell plate containing phosphate-buffered saline at 37 °C in a 5% CO₂ atmosphere for 24 or 48 h.

After 24 h, specimens from the control and BLP1 groups were harvested, distribution of the absorbed fluorescent material was evaluated, and fluorescence intensity was measured. The tissue was prepared as a frozen block and sliced into 6-µm thick sections using a microtome (Cryostat; Leica Biosystems, Nussloch, Germany). The sections were attached to a silane-coated slide, and the images were magnified 200 times and observed under a fluorescence microscope (M2; Carl Zeiss, Jena, Germany). Fluorescence intensity was measured using ImageJ software (National Institutes of Health, Bethesda, MD, USA). All experiments were independently repeated three times.

Assessment of the clinical efficacy and safety of the device

Skin status was assessed at baseline, and the clinical efficacy of facial skin rejuvenation was assessed at 4 and 8 weeks after the initiation of treatment. Subepidermal skin hydration was measured using the Moisture Meter-D (Delfin Technologies Ltd., Kuopio, Finland). Skin elasticity was measured using the Dermal Torque Meter (Dia-Stron, Hampshire, UK) and Cutometer Dual MPA580 (Courage Khazaka Electronics, Köln, Germany). The Antera 3D™ (Miravex, Dublin, Ireland) was used to measure and visualize skin roughness, skin pore size, and three-dimensional (3D) volumetric changes in wrinkles. All measurements were performed in the lateral canthus area, except for pore size measurements performed in the cheek. Each measurement was performed in triplicate at each visit, and all participants were allowed to acclimatize to controlled environmental conditions (room temperature: 18–21 °C; relative humidity: 40–60%, without direct light) for 30 min prior to measurements at each visit.

At each visit, a board-certified dermatologist performed a physical examination to evaluate the safety of the device. In addition, participant reports regarding the type and severity of adverse events experienced (e.g., edema, hyperpigmentation, itching, pain, bruising, asymmetry of the facial area, allergic reaction, and scarring) following the use of the device were carefully documented. Skin erythema was

measured at baseline and 8 weeks using the Mexameter MX18 (Courage Khazaka Electronics) to assess the degree of erythema induced by application of the BLP1 device.

Sample acquisition from clinical study participants by skin biopsy

Ten of the participants who had mild-to-moderate degree of facial wrinkles (Lemperle wrinkle assessment scale score, ≥ 2) provided informed consent for sequential skin biopsies during the study. These participants applied the BLP1 device for an additional 4 weeks (total, 12 weeks), and a skin biopsy was performed at baseline and 12 weeks after treatment. Two 4-mm skin tissue specimens were obtained from the adjacent submandibular triangle area to minimize scar formation.

Histology, immunohistochemistry, and immunofluorescence staining

Tissues obtained from ex vivo cultures and skin biopsies were fixed in 10% formalin. Paraffin blocks were cut into 6- μ m thick sections, deparaffinized, and dehydrated using a xylene and ethanol series. We performed hematoxylin–eosin (H&E) staining, Masson trichrome (MT) staining, and Verhoeff–van Gieson staining (EVG). The epidermis and dermis of the stained tissue samples were photographed at 400 $\times$ magnification using an optical microscope (BX43F; OLYMPUS, Tokyo, Japan).

Immunohistochemistry was performed on consecutively sectioned, paraffin-embedded skin tissue samples. First, the slides were processed and subjected to antigen retrieval. Primary antibodies, including anti-collagen 1 (ab34710; Abcam, Waltham, MA, USA) and anti-matrix metalloproteinase (MMP)-1 (MAB901; R&D Systems, Minneapolis, MN, USA), were applied to the samples that were further developed with secondary antibodies (collagen 1: anti-rabbit; k4003; Dako, Carpinteria, CA, USA, and MMP-1:

anti-mouse; k4001; Dako). Finally, the cell nuclei were stained with hematoxylin (SM806; Dako), and the tissues were fixed using a mounting solution. Tissues were observed at 400 $\times$ magnification under an optical microscope. Collagen 1- or MMP-1-positive areas present in the papillary dermis were measured using an image analysis program (Zen image analysis; Carl Zeiss).

For immunofluorescence staining, primary antibodies including anti-filaggrin (ab81468; Abcam), anti-loricrin (ab85679; Abcam), and anti-involucrin (ab68; Abcam) were applied to the samples that were then incubated with secondary antibodies (A11012; Invitrogen, Waltham, MA, USA; ab6717; Abcam; and A11001; Invitrogen). Finally, the cells and tissue specimens were fixed using a fixation solution (VECTASHIELD® mounting medium with 4',6-diamidino-2-phenylindole [Vector Laboratories Inc., Burlingame, CA, USA]). All fluorescence images were acquired using a laser-scanning microscope (LSM 700; Carl Zeiss), and fluorescence intensity was measured using ImageJ software.

Quantitative reverse transcription-polymerase chain reaction (qRT-PCR)

Tissue specimens obtained at 24 and 48 h after application of the test device were homogenized using a TissueLyser II (Qiagen, Hilden, Germany). Total RNA was extracted using the TRIzol reagent (Invitrogen) and subsequently reverse-transcribed to cDNA (EcoDry Premix Kit, Takara Sake, Berkley, CA, USA). The synthesized cDNA, TaqMan Gene Expression Master Mix (Applied Biosystems, Waltham, MA, USA), and TaqMan primers for each target (TGFB1 [TGF- β]: Hs00998133_m1, IL1A [IL-1 α]: Hs00174092_m1, PTGS2 [COX-2]: Hs00606991_m1, and CALCA [calcitonin gene-related peptide (CGRP)]: Hs01100741_m1; Applied Biosystems) were used in the qRT-PCR experiments. The expression level of each gene was normalized to that of the housekeeping gene GAPDH (Hs02786624_g1; Applied Biosystems) and calculated using the $2^{-\Delta\Delta C_t}$ method.

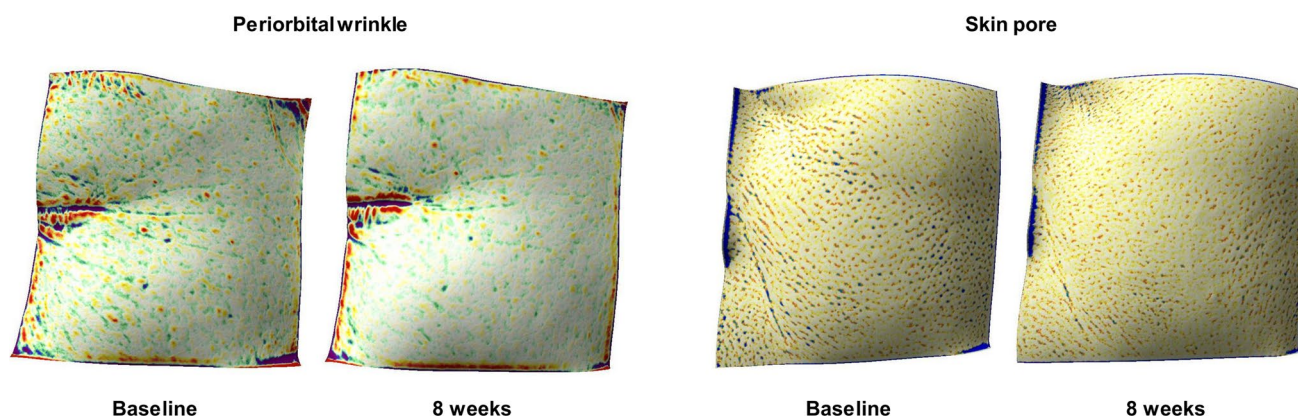


Fig. 1 Periorbital wrinkle and pore size improvements on the test side between baseline and week 8

Statistical analyses

Data are presented as numbers (percentages) or means $\pm$ standard deviations according to the type of data. Data were analyzed for normality using the Kolmogorov–Smirnov test. For time-dependent between-group comparisons, repeated measures analysis of variance (RM-ANOVA) and subsequent post-hoc analysis using the Student's *t* test were performed with Bonferroni correction. For non-parametric independent variables, including the datasets from the ex vivo and skin biopsy studies, the Wilcoxon rank-sum test was used. Statistical significance was set at *p* values < 0.05 . All statistical analyses were performed using SPSS, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Participant characteristics

Thirty-six healthy women were enrolled in this study. Five participants were excluded from the study due to poor compliance with the study schedule. A safety analysis was conducted after all enrolled participants used the test device at least once. Subsequently, assessments for efficacy were conducted on data obtained from 31 participants. The participants' average age was 40.3 ± 11.0 years (range, 22–57 years). Six participants were identified as having sensitive skin through a lactic acid sting test.

Clinical efficacy of the test device for skin rejuvenation and safety profile

During the study, non-invasive biophysical parameters of the skin were measured at baseline and at weeks 4 and 8 after treatment initiation. Skin hydration, especially subepidermal moisture, and skin elasticity increased significantly after 8 weeks of BLPI device use compared with those at baseline (both, $p < 0.001$). Skin roughness, pore size, and eye wrinkle volume were measured using the 3D camera system; these parameters were significantly reduced after 8 weeks of intervention relative to baseline measurements ($p < 0.001$; Fig. 1). Subsequently, we conducted an intergroup comparison between the BLPI and control sides during the 8-week study period. A significant improvement in all measured parameters was noted on the BLPI side compared to the control side (RM-ANOVA, $p < 0.001$ for all parameters). Based on post-hoc analysis, measurements at both weeks 4 and 8 showed significant improvements on the BLPI side compared with the control side (Table 1).

No adverse effects, including edema, pain, bruising, or scarring, were observed during the 8-week follow-up. Notably, even participants who were identified as having sensitive

Table 1 Evaluation of the objective parameters of skin aging during the study

	BLPI side Mean $\pm$ SD, (% change) ^c	Control side Mean $\pm$ SD, (% change) ^c	<i>p</i> value ^a
Subepidermal moisture (PWC, %)			
Baseline	47.0 $\pm$ 3.57	47.3 $\pm$ 3.50	
4 weeks	48.3 $\pm$ 3.64 (2.8)	47.9 $\pm$ 3.48 (1.3)	< 0.001
8 weeks	49.2 $\pm$ 3.73 (4.7)	48.7 $\pm$ 3.50 (2.8)	0.001
<i>p</i> value ^b	< 0.001	0.002	
Skin elasticity, DTM (Ur/Ue)			
Baseline	0.38 $\pm$ 0.05	0.39 $\pm$ 0.06	
4 weeks	0.43 $\pm$ 0.06 (13.4)	0.42 $\pm$ 0.05 (6.9)	0.007
8 weeks	0.44 $\pm$ 0.06 (15.7)	0.42 $\pm$ 0.06 (6.7)	0.001
<i>p</i> value ^b	< 0.001	< 0.001	
Skin elasticity, CM (<i>R</i> ²)			
Baseline	0.71 $\pm$ 0.09	0.71 $\pm$ 0.08	
4 weeks	0.72 $\pm$ 0.09 (2.1)	0.72 $\pm$ 0.08 (1.4)	< 0.001
8 weeks	0.75 $\pm$ 0.09 (5.7)	0.73 $\pm$ 0.09 (3.2)	0.002
<i>p</i> value ^b	< 0.001	< 0.001	
Skin roughness (Ra, AU)			
Baseline	5.69 $\pm$ 1.22	5.70 $\pm$ 1.21	
4 weeks	5.29 $\pm$ 1.06 (−6.9)	5.61 $\pm$ 1.12 (−1.6)	< 0.001
8 weeks	5.10 $\pm$ 0.98 (−10.3)	5.48 $\pm$ 1.11 (−3.8)	< 0.001
<i>p</i> value ^b	< 0.001	< 0.001	
Skin pore size (mm ³)			
Baseline	0.27 $\pm$ 0.15	0.25 $\pm$ 0.15	
4 weeks	0.15 $\pm$ 0.10 (−43.3)	0.18 $\pm$ 0.14 (−29.3)	0.005
8 weeks	0.13 $\pm$ 0.09 (−53.4)	0.16 $\pm$ 0.12 (−36.5)	0.001
<i>p</i> value ^b	< 0.001	< 0.001	
Eye wrinkle volume (mm ³)			
Baseline	0.28 $\pm$ 0.18	0.30 $\pm$ 0.21	
4 weeks	0.24 $\pm$ 0.16 (−13.9)	0.27 $\pm$ 0.19 (−8.8)	0.002
8 weeks	0.23 $\pm$ 0.17 (−18.1)	0.26 $\pm$ 0.18 (−11.8)	0.006
<i>p</i> value ^b	< 0.001	0.007	

PWC percentage of water content, AU artificial unit, *R*², viscoelasticity in %; DTM dermal torque meter, CM cutometer, SD standard deviation

^aComparison between the groups; *p* value according to the post-hoc *t* test with Bonferroni correction

^bComparison within the groups; *p* value according to the paired *t* test (baseline versus 8 weeks)

^cDefined as (8-week measurement – initial measurement)/initial measurement $\times 100\%$

skin through the lactic acid sting test did not complain of irritation after using the device. To assess for unwanted erythema formation caused by the device, the Mexameter erythema index was used. However, the index values decreased from 259.2 ± 46.9 at baseline to 247.2 ± 46.9 at 8 weeks on the BLPI side ($p < 0.001$), and no significant difference was noted between the BLPI and control sides (RM-ANOVA, $p > 0.05$).

Ex vivo study on the effect of BLP1 device application

To confirm the safety of the BLP1 device use on human skin tissue, H&E and MT staining were performed on ex vivo human skin tissue samples following administration of the test device. BLP1-irradiated samples did

not exhibit any notable morphological changes, such as vacuolization of the basal layer of the epidermis, dermo-epidermal separation, homogenization of collagen, thermal coagulation, or dermal vascular damage (Fig. 2a). Compared with that of the control, the BLP1 side showed no significant changes in the thickness and cellularity of the

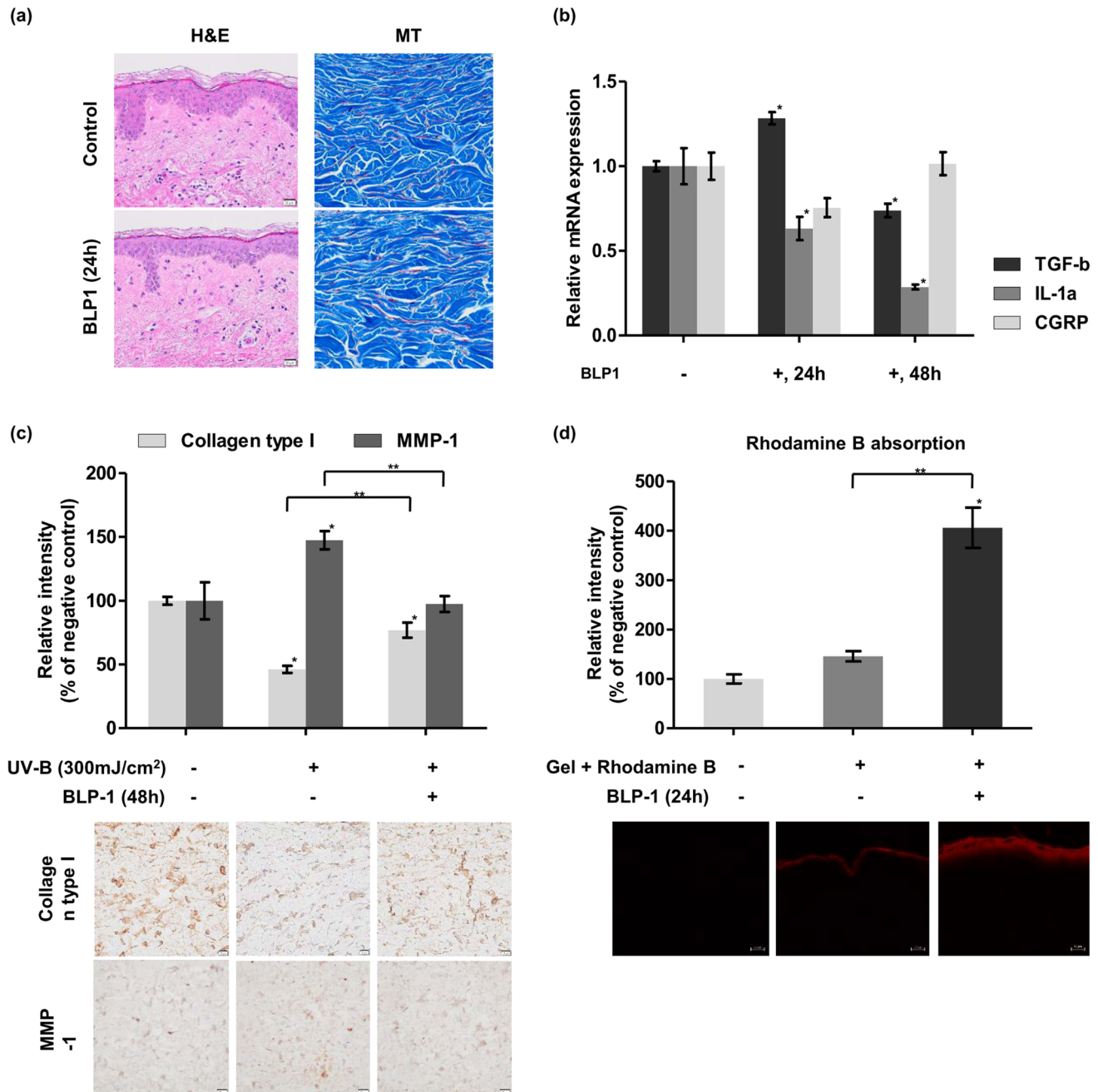


Fig. 2 Effects of the BLP1 device application on ex vivo skin tissues. **a** No significant histological damage was observed based on the hematoxylin–eosin (H&E) staining and Masson trichrome (MT) staining 24 h after using the test device. **b** Real-time quantitative polymerase chain reaction results show decreased pro-inflammatory marker levels, transforming growth factor (TGF)-β, and interleukin (IL)-1α. **c** Immunohistochemical staining results show increased

expression of the collagen-I protein in the treatment samples compared with that in the type B ultraviolet (UVB) light control samples. **d** Distribution of the fluorescent material (rhodamine B) indicates that skin absorption was increased. CGRP, calcitonin gene-related peptide; MMP, matrix metalloproteinase. *p* values < 0.05 according to the Mann–Whitney *U* test, compared to the negative control (*) or positive control (**)

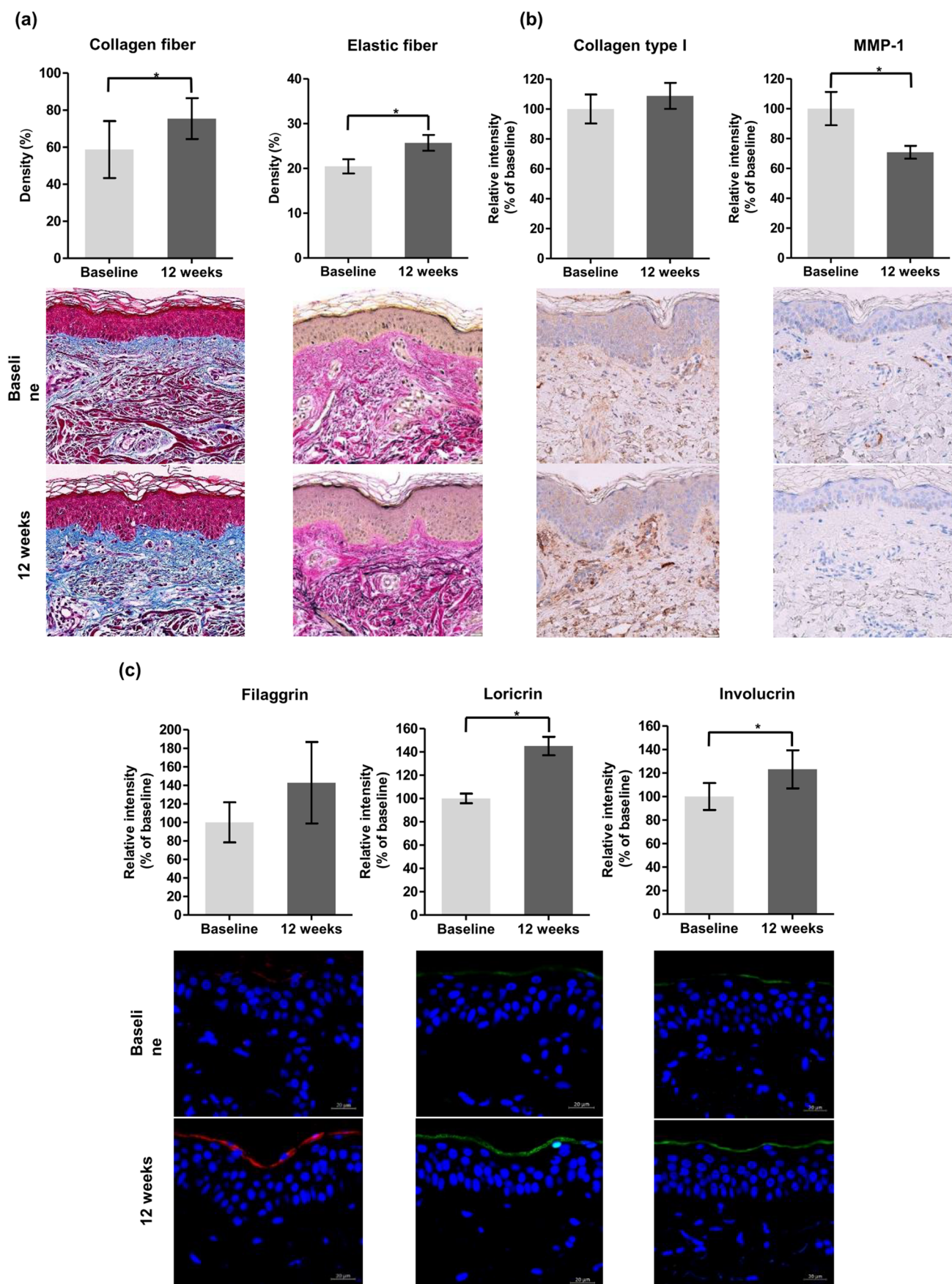


Fig. 3 Effects of BLP1 device application for 12 weeks on in vivo human skin tissue. **a** Masson trichrome staining revealed a significant increase in collagen fiber density, and the Verhoeff-van Gieson staining also revealed a significant increase in elastic fiber density after the use of the device. **b** Immunohistochemical staining results showed increased expression of the collagen-1 protein and decreased expression of the matrix metalloproteinase-1 after the use of the device. **c** After 12 weeks of device application, only loricrin and involucrin expressions were significantly increased compared with those at baseline. * $p < 0.05$ according to the Mann–Whitney U test, compared with baseline

epidermis and dermis (data not shown). To analyze the relative gene expression levels of inflammation-related factors, qRT-PCR was performed. After 48 h, the gene expression levels of TGF- β and IL-1 α were statistically significantly lower in the BLP1 treatment samples than those in the control samples ($p < 0.05$). There was no statistically significant difference in CGRP levels between the BLP1 treatment and control group samples (Fig. 2b).

To assess the effect of the BLP1 device on aging skin, we irradiated ex vivo skin samples with UVB light and applied the test device (Fig. 2c). Immunohistochemical staining revealed a significant decrease in dermal collagen type I protein after UVB light exposure and showed a significant increase in MMP-1 protein levels in the UVB-positive control compared with the negative control (46.2% and 147.4%, respectively). However, with the subsequent BLP1 device application, the type I collagen protein level recovered to 77% of the negative control value, and the MMP-1 level decreased to 98% of the baseline (both $p < 0.05$, compared to the UVB-positive control).

To confirm the enhancement of transepidermal absorption by the BLP1 device, a moisturizer with fluorescent material (rhodamine B) was applied to the skin tissue samples. Without the application of the BLP1 device, rhodamine B was confined to only the stratum corneum. After application of the test device, rhodamine B was completely absorbed into the layers of the epidermis and even reached the upper dermis, with a significant increase in the fluorescence intensity ($p < 0.05$; Fig. 2d).

Skin biopsy and histologic study after BLP1 device application

To further assess the effect of the BLP1 device on human skin tissue in vivo, we performed a skin biopsy at baseline and 12 weeks after treatment. Like the ex vivo study, there were no notable morphological changes in the skin tissue related to thermal damage after 12 weeks of device application (data not shown). MT staining revealed a significant increase in collagen fiber density by 128.5% after device application. EVG staining also showed a significant increase in elastic fiber density by 125.6% after device application ($p < 0.05$; Fig. 3a).

Immunohistochemistry revealed a slight increase in the expression of collagen type I (108.7% of the baseline intensity), but the difference before and after BLP1 device application was not statistically significant. In contrast, MMP-1 protein expression showed a significant decrease ($p < 0.05$; 70.8% of the baseline intensity) compared with that at baseline (Fig. 3b). In addition, the expression levels of filaggrin, loricrin, and involucrin measured by immunofluorescence staining showed an increasing trend after the 12-week application of the test device (Fig. 3c), but statistical significance was achieved only for loricrin and involucrin (both, $p < 0.05$).

Discussion

Our trial revealed that a multi-energy-based device that concurrently emits a low-level light, low-dose RF, low-energy microcurrent, and low-intensity ultrasonic waves was effective for skin rejuvenation. After the 8-week application of the device, parameters associated with skin aging, including skin hydration, elasticity, roughness, and skin pore size, were improved on the treatment side compared with those at baseline. The skin pore size, eye wrinkle volume, skin elasticity measured by a Dermal torque meter, and skin roughness showed an improvement of $> 10\%$ compared with those on the control side (Fig. 4). The results of our ex vivo and in vivo skin tissue studies correlated with the clinical findings, showing an increase in the expression of collagen type 1 and decrease in the expression of MMP-1, related to the phenotype of skin aging. The expressions of loricrin and involucrin also increased after application of the device, suggesting its contribution to enhancing skin barrier function. In addition, the ex vivo skin penetration study using rhodamine B confirmed that the application of the device enhanced transepidermal absorption, suggesting that the device could be used as a potential platform for transepidermal drug delivery.

Among the multimodal energy transfer modules in the BLP1 device, RF is one of the most widely used non-invasive procedures for treating skin wrinkles and laxity [5]. In an animal skin tissue model, the amount of collagen, elastin fibers, and blood vessels in the upper dermis increased following the application of RF on the skin surface [6]. A non-invasive RF device consisting of bipolar electrodes created a closed electrical circuit that allowed the directed transfer of heat energy to the dermis, promoting neocollagenesis while sparing the epidermis [7].

LLLT has been widely used for wound healing and the treatment of various skin diseases. The red LED increases collagen type 1 and MMP-9 expression, which allows the degradation of fragmented collagen, leading to neo-collagenesis [8]. Kim et al. revealed that the 633-nm LED

promotes the synthesis of type 1 procollagen and decreases the expression of MMPs 1 and 2 in skin fibroblasts [9]. These studies suggest possible mechanisms for the effects of LED irradiation on skin rejuvenation.

Low-energy microcurrents promote wound healing of ischemic ulcers and chronic diabetic foot ulcers, and electric stimulation increases blood flow to the wound [10–12]. Low-intensity ultrasounds promote wound healing by increasing nitric oxide levels, which leads to enhanced vasodilation, blood flow, oxygenation, and supply of nutrients [13–15]. Ultrasounds also allow increased movement of substances through the skin, called sonophoresis, by loosening the surrounding matrix and causing cavitation [16].

The distinct characteristic of BLP1 compared to other pre-existing home-use devices is that various energy transfer modalities are combined into one device and concurrently irradiated. The advantages of multimodal low-intensity energy transfer were previously reported in the cellular and animal skin models; one study demonstrated that a combination of ultrasound, iontophoresis, microcurrents, and electroporation enhanced fibroblast proliferation and collagen synthesis more than any individual application [17]. Furthermore, concurrent application of low-intensity sonophoresis and iontophoresis achieved significant penetration enhancement of various hydrophilic and lipophilic molecules in the porcine skin model [18].

When comparing BLP1 with conventional lasers, it appears that ablative and non-ablative lasers are more effective in improving skin elasticity than BLP1 [19, 20]. BLP1 emits various types of low-level energy simultaneously, which may result in a limited effect compared to conventional lasers that use high energy with a single wavelength. However, caution should be exercised when directly comparing efficacy, as different study designs, such as treatment sessions, follow-up periods, and demographic conditions, might affect the measurement outcome. One potential advantage of BLP1 over conventional lasers is its suitability for home-use due to its lower energy output. This feature may allow for more consistent and convenient treatments, ultimately leading to better outcomes.

It is important to confirm the safety of this device in terms of transferring different energies to the human body at the same time. During the 8–12-week clinical study, no device-related adverse effects were reported, and patients with sensitive skin did not experience any problems, such as skin irritation. In our ex vivo and in vivo skin tissue studies, tissue thermal damage was not observed, and markers related to skin inflammation did not increase, supporting the safety of the device.

Limitations of our study included a small sample size and short follow-up period. Only a portion of the study participants underwent histological examination due to their

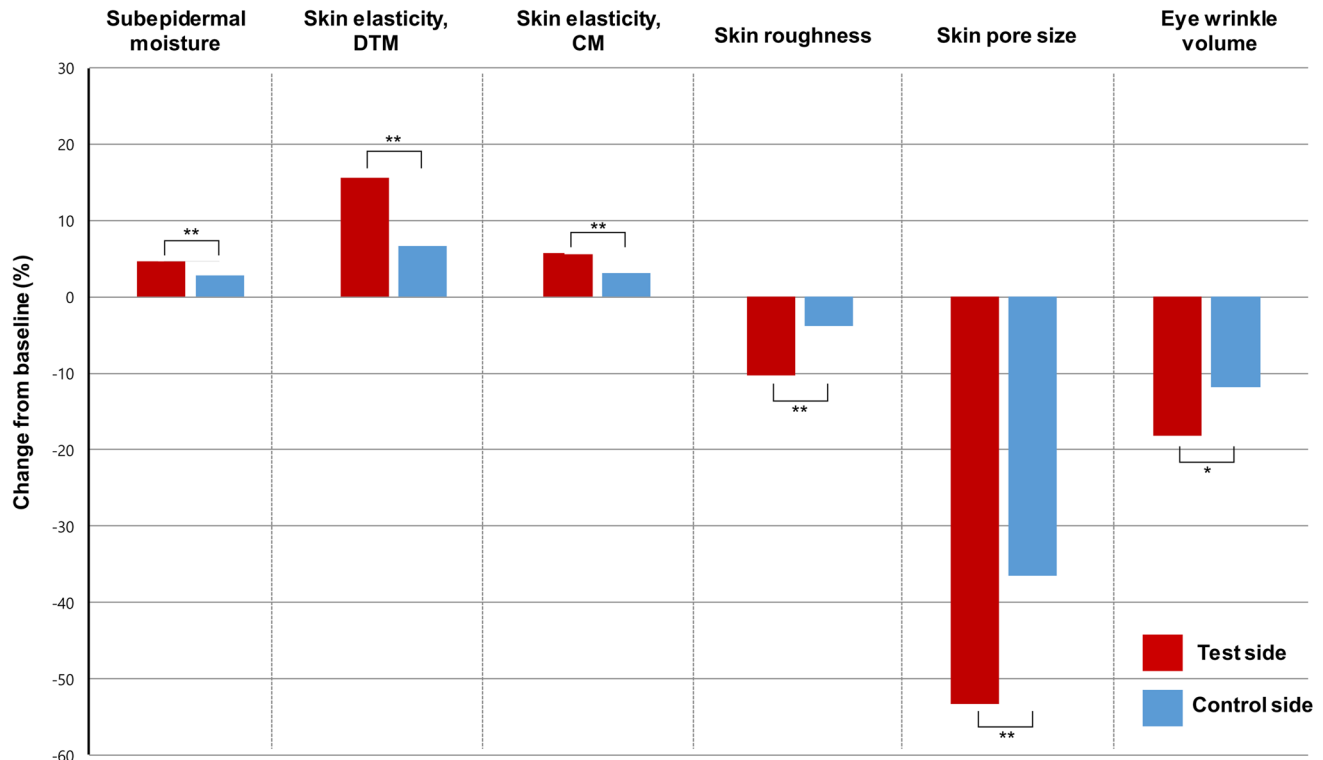


Fig. 4 Change in objective parameters of skin aging from baseline after 8 weeks of test device use. DTM, dermal torque meter; CM, cutometer (* $p < 0.05$ and ** $p < 0.005$)

cosmetic concerns. Additionally, efficacy of the device was not confirmed in various ethnicities because study participants were limited to Koreans. Although we observed changes in the expression of factors related to skin aging and skin barrier function in both in vivo and ex vivo experiments, we did not study their underlying molecular pathways. Further studies are needed to investigate whether a synergistic effect for anti-aging and skin barrier function occurs for simultaneous irradiation of various energies at a low intensity.

Conclusion

The present study found that a multi-energy-based at-home device that emits low-level light, radiofrequency, microcurrent, and ultrasonic waves simultaneously is effective for skin rejuvenation from the perspective of clinical, ex vivo, and in vivo analysis. Moreover, the device enhanced skin barrier function and could potentially be used for transepidermal drug delivery.

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Author contribution Conceptualization: Young In Lee and Ju Hee Lee; data curation: Sang Gyu Lee; formal analysis: Jangmi Suk and Inhee Jung; validation: Young In Lee and Sooyeon Choi; visualization: Jemin Kim; writing—original draft: Sooyeon Choi and Jemin Kim; writing—review and editing: Ju Hee Lee; funding acquisition: Ju Hee Lee; supervision: Ju Hee Lee.

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Declarations

Conflict of interest The authors declare no competing interests.

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