Journal of Cosmetic and Laser Therapy, 2015; Early Online: 1–4

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healthcare

ORIGINAL RESEARCH REPORTS

Intense focused ultrasound for facial tightening: Histologic changes in 11 Patients

DONG HYE SUH[1], BYOUNG JOON SO[2], SANG JUN LEE[1], KYE-YONG SONG[3] & HWA JUNG RYU[2]

[1]*Department of Dermatology, Arumdaun Nara Dermatologic Clinic, Seoul, Republic of Korea,*
[2]*Department of Dermatology, Korea University College of Medicine, Danwon-ku, Ansan, Republic of Korea, and* [3]*Department of Pathology, Chung-ang University College of Medicine, Seoul, Republic of Korea*

Abstract

Introduction: Intense focused ultrasound (IFUS) is a novel modality for treating skin laxity that produces thermal effects at various depths while sparing the overlying tissue. This study assessed histologic changes and the safety and efficacy of intense focused ultrasound (Doublo^{TM}, HIRONIC Co., Sungnam, Korea) for tightening of facial skin in Asian patients. *Methods:* Eleven patients with facial laxity were treated with IFUS and evaluated before and after treatment. Mean age was 46 years (range, 35–64 years). Two available hand-pieces with different focal depths (3 mm and 4.5 mm) were used with three to five passes 1–2 mm apart. Outcome assessment included photographic evaluation by two blinded investigators, skin biopsies before and two months after treatment, and patient satisfaction. *Results:* Subjective and objective analyses showed 63.6% and 72.7% improvement at the two-month evaluation, respectively. Histologic evaluation by hematoxylin and eosin (H&E) and Masson's trichrome staining showed increased collagen fibers in the lower dermis and between fat layers. *Discussion and conclusions:* Intense focused ultrasound can be used as a non-invasive skin tightening technique in Asian patients. It induced collagen generation in the dermis and fat layers and was effective and safe in our study population.

Key Words: *tightening, ultrasound, laxity*

Introduction

As the average life expectancy increases, there are more people who wish to undergo cosmetic procedures for skin rejuvenation and tightening. Although ablative laser treatment is effective for rejuvenation, there is a long down time after the procedure. There are also risks of texture change, hypertrophic scarring, hyperpigmentation and hypopigmentation. An alternative treatment using a non-ablative rejuvenation (NAR) laser has become popular in aesthetic medicine. The NAR devices have been designed to induce thermal injury within the dermis while sparing the overlying epidermis. The problem with NAR devices, however, is that they are not effective as a conventional ablative treatment. Therefore, a non-ablative rejuvenation procedure with an efficacy comparable to that of ablative treatment is needed.

Ultrasound-based imaging systems have been used for clinical diagnoses for several decades. Intense focused ultrasound (IFUS) is an energy modality that can propagate through tissue up to several millimeters (1). IFUS has been used in the treatment of benign and malignant tumors for several years (2). By applying this technology, new devices have recently been developed for skin tightening. These devices are known to induce molecular vibration leading to the generation of thermal energy and formation of a thermal injury zone in the dermis and superficial musculo-aponeurotic system (SMAS) (1). This mechanism is different from that of other NAR devices in that the thermal lesion is made deeper in the tissue (1,3).

There are several reports describing a novel IFUS approach in human cadaveric facial tissue and porcine tissue. IFUS was reported to produce focused thermal collagen denaturation in the SMAS to induce shrinkage and tissue tightening. Alam et al. reported clinical results of ultrasound tightening of facial and

Correspondence: Correspondence: Dr. Hwa Jung Ryu, Department of Dermatology, Korea University College of Medicine, No. 516, Gojan-1-dong, Danwon-ku, Ansan, 425-707, Republic of Korea. E-mail: dermhj@naver.com

(Received 5 November 2014; accepted 5 January 2015)

ISSN 1476-4172 print/ISSN 1476-4180 online © 2015 Informa UK, Ltd.
DOI: 10.3109/14764172.2015.1007065

neck skin (4). The present study was performed to demonstrate the safety and efficacy of intense focused ultrasound (Doublo^{TM}, HIRONIC Co., Sungnam, Korea) in Asian skin and to closely observe the histologic changes in the dermis after IFUS treatment.

Materials and methods

Eleven patients with facial laxity, diagnosed based on clinical findings, were enrolled in this study. All patients were treated with intense focused ultrasound. After having had the purpose and protocol of the study explained to them, all patients gave written informed consent to participate and for the use of their clinical photographs and biopsy specimens. The study protocol conformed to the guidelines set forth in the 1975 Declaration of Helsinki.

Topical anesthetic cream was applied for 40 mins before treatment. After gently removing the topical anesthetic cream, ultrasound gel was applied to the skin. The probe was then placed firmly on the skin surface with uniform pressure. The forehead, temples, and malar area, which is relatively thin, were treated with the 7 MHz, 3.0-mm probe at the following energy settings: forehead, 0.25–0.3 J; malar, 0.35 J; temple, 0.35 J. The cheeks and submentum were treated with the 4 MHz, 4.5-mm probe at an energy setting of 1.0 to 1.2 J followed immediately by treatment with the 7 MHz, 3.0-mm probe at an energy setting of 0.35 to 0.45 J. The spacing of pulses was set at 1.5–2.0 mm. On average, 100 treatment lines were delivered to the forehead, 30 to each temple, 200 lines to each cheek, and 40 lines to the submentum for a total of about 400 lines per face. After treatment, the ultrasound gel was wiped off and a cooling pack was applied.

Follow-up visits took place eight weeks after treatment. Digital photographic documentation under the same conditions (light source, room, and camera) was obtained before treatment and after eight weeks. Improvement was assessed from comparison of the before and after treatment clinical photographs by two blinded investigators. Subjective and objective scores were assigned as follows: 1, no improvement (0%); 2, mild improvement (1–25%); 3, moderate improvement (25–50%); 4, good improvement (50–75%); and 5, excellent improvement (>75%). The clinical data were gathered by two different observers, the principal investigator and the patient herself or himself. Side effects of the focused ultrasound treatment were documented after treatment and at the follow-up visit. Punch biopsies (2 mm) were taken from the lateral side of the cheek two months after treatment. All specimens were stained with hematoxylin and eosin (H&E), Masson's trichrome and Victoria blue.

Results

All eleven patients (one man and ten women) completed the study successfully. Their ages ranged from 35 to 64 years (mean 46.0). All patients were treated with IFUS. None dropped out of the study due to intolerable pain or side effects. During treatment, patients felt only minimal pain, with an average visual analogue score of 3. No patient reported severe pain requiring additional pain relief with analgesia or sedation. Patients had mild erythema that persisted for two to three days. There were no serious adverse events such as persistent erythema, swelling, bruising, or prolonged numbness. Patients were able to return to their usual activity immediately after treatment.

Compared to before treatment, 54.5% and 63.6% improvements in the subjective and objective scores were noted, respectively (Table I). After treatment, improvements in the appearance of fine wrinkles and dilated pores were prominent in seven patients (Figure 1).

Histopathologic results

Hematoxylin and eosin (H&E) staining of biopsy specimens taken at baseline showed non-specific findings (Figure 2 A1, B1, C1). Eight-week post-treatment biopsy specimens showed increased and thickened collagen in the reticular dermis (Figure 2 A2, B2, C2). Although there was no inflammation or fat necrosis, increased fibrosis was seen between fat layers. There were no significant changes in the epidermis in any of the cases. The increase in collagen in the reticular dermis and between fat layers was confirmed by Masson's trichrome staining (Figure 2 D1, D2).

Discussion

Various devices have been developed to treat skin laxity. Ablative skin resurfacing (ASR) rejuvenates skin by inducing sub-lethal thermal damage, leading to re-epithelialization and new collagen formation (5). Ablative carbon dioxide or erbium lasers are successful treatment devices in the ASR category (6). However, patients treated with ASR devices experience a prolonged recovery time, infection and post-inflammatory hyperpigmentation (7). To overcome these limitations, non-ablative skin resurfacing (NSR) devices including Nd:YAG, radiofrequency, infrared light and intensive focused ultrasound (IFUS) were developed (8).

Table I. Summary of treatment results in 11 patients.

Number	Sex/Age	Subjective satisfaction	Objective satisfaction
1	F/51	Moderate	Good
2	F/44	Moderate	Moderate
3	F/46	Excellent	Excellent
4	F/46	Excellent	Excellent
5	M/49	Moderate	Moderate
6	F/40	Good	Good
7	F/46	Good	Good
8	F/64	Good	Good
9	F/45	Excellent	Excellent
10	F/40	Mild	Mild
11	F/35	Mild	Mild

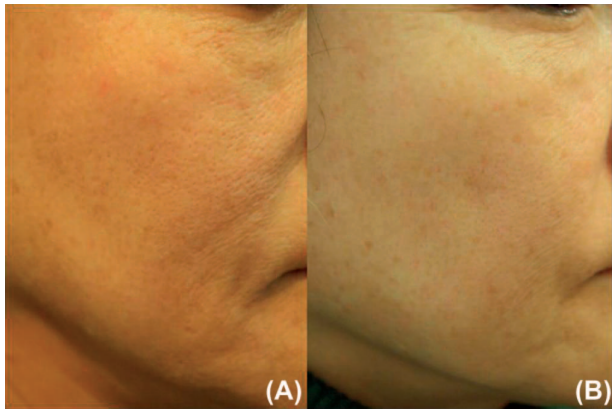

Figure 1. Baseline photograph showing the skin of a 64-year-old women with skin laxity (A). Improvement in fine wrinkles and laxity was seen two months after treatment with IFUS (B).

Intense focused ultrasound is a skin rejuvenation device that is intended to produce thermal effects in the dermis and superficial muscular aponeurotic system (SMAS). The system generates small controlled coagulation points at a certain depth by using short pulses of intense focused ultrasound in the millisecond domain. This technology plays an important role in ensuring both focus accuracy and minimal surrounding tissue damage.

High-intensity focal ultrasound was initially invented as a non-invasive device for the treatment of several benign and malignant tumors and mass reduction in prostate hyperplasia (9). Now it has also been applied for skin rejuvenation applying the concepts of the US-induced thermal treatment zone (9). Ultrasound penetrates the epidermis leading to friction between the cellular molecules. As a result, it generates heat greater than 60°C, which is sufficient for collagen denaturation in a given tissue (1,10). This heat generates a thermal coagulation zone in the target area, inducing a wedge-shaped thermal coagulation zone in the reticular dermis, without damaging the papillary dermis (1). Because melanin is not affected by ultrasound-induced thermal energy, IFUS can be used in a wide range of skin types (11). Furthermore, secondary scatter and absorption in the epidermis does not occur, thereby conferring reduced risk of inadvertent cutaneous injury.

Although previous studies mainly focused on the lifting effect of IFUS, the present study focused on the efficacy of IFUS with regard to collagen and elastic fiber formation in the dermis. We found increased and thickened collagen in the reticular dermis in eight cases after 8 weeks post-treatment. The increase in elastic fibers was not prominent, although some morphologic changes were noticeable, such as elongation. These findings are consistent with those of previous studies describing collagen formation and elastic fiber rearrangement after IFUS treatment (9). Recent studies have also shown that IFUS reduces pore size by inducing collagen formation and subsequent tightening around enlarged pores (12). We also observed improvement in the appearance of fine wrinkles and pores in seven patients. These histologic findings support the clinical finding that IFUS not only has a lifting effect, but also a rejuvenating effect. The lifting effect of IFUS can be explained by the coagulation points made in the SMAS layer. Since tissue only as low as the subcutaneous level is included in punch biopsies, the effect of IFUS on the SMAS layer could not be confirmed in this study. Punch biopsies were done in all cases; part of the fat layer was observed and there was microscopic fibrosis replacing part of the fat lobules after treatment with IFUS. Therefore, we presume that some of the coagulation points were made in the fat layer. Every human has a different dermis thickness, and depending on how much pressure the physician uses when performing IFUS, there can be some coagulation points made in the fat layer. The microscopic fibrosis in the fat layer may contribute to skin tightening. Although this process does not lead to lipoatrophy since the changes are microscopic, if the coagulation points are made repeatedly in the same spot, massive fat necrosis would be possible. However, despite concerns about lipoatrophy after treatment with IFUS, this phenomenon has not been reported in the literature so far. Liposonix®, another high intensity focused ultrasound(HIFU) device that was invented to lyse the fat layer, has a similar mechanism but a different frequency, pulse duration and intensities exceeding 1000 W (13). These parameters cause bulky heating that has a lipolysis effect. Therefore, although IFUS typically results in microscopic coagulation, treatment stacking will result in lipolysis as is seen with Liposonix®. Therefore, stacking should be avoided and repeat treatments with some time interval in between would be better in terms of safety than treatment with many lines at once.

Our results support the clinical effectiveness of IFUS in skin rejuvenation. In a previous clinical study performed by Lee et al., 80% of subjects were found to have clinical enhancement after treatment with IFUS device (Ulthera System, Ulthera, Inc., Mesa, AZ, USA). Our study revealed 63.6% and 72.7% of subjects with clinical improvement. The differences in effectiveness may be due to the fact that we used a different model (Doublo™) of IFUS for treatment.

Additional limitations include the fact that assignment of the subjective and objective scores based on the pre- and post-treatment photographs was not a quantitative evaluation of skin rejuvenation. More precise measurements should be utilized in future studies. Furthermore, if the depth is controlled by the physician and the skin level and structures are seen clearly with high quality ultrasound imaging, even better results can be expected.

To conclude, IFUS has many benefits for skin rejuvenation. It induces thermal damage in the deep dermis that leads to enhancement of collagen synthesis without disrupting the epidermis. We

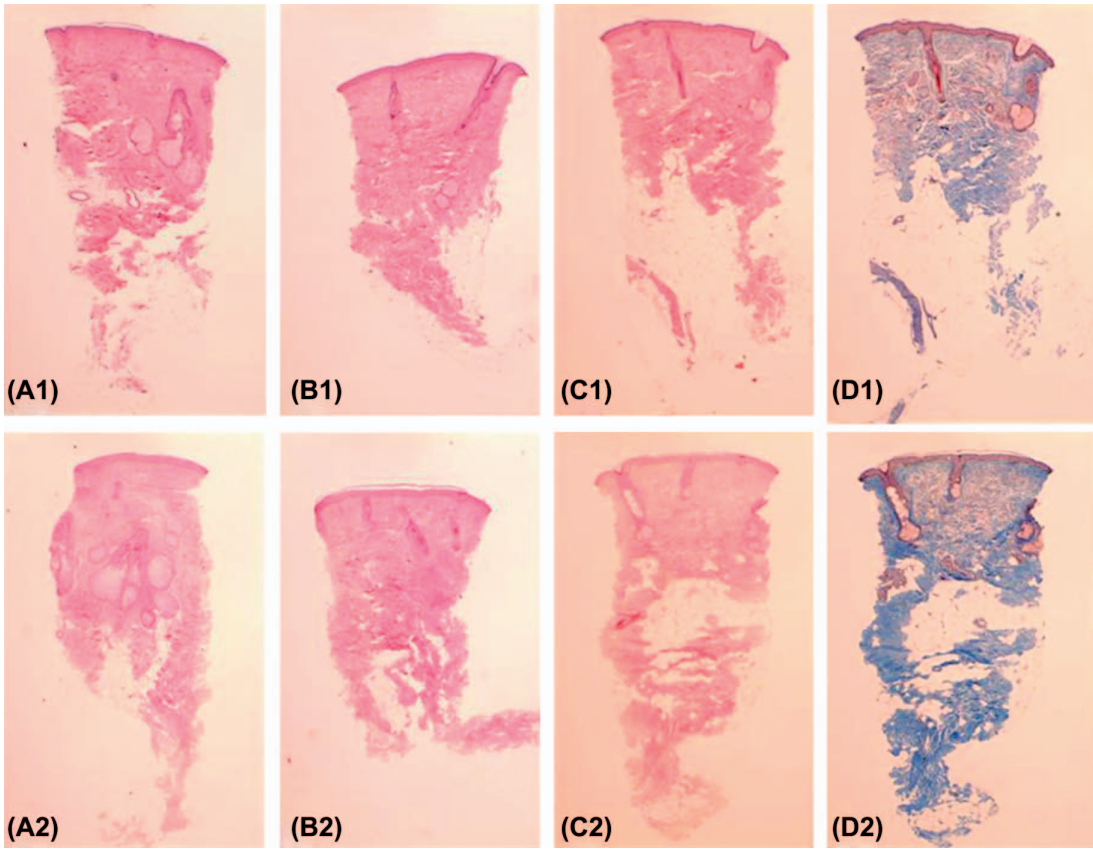

Figure 2. Skin histology of three different patients before treatment with IFUS (A1, B1, C1) and two months after treatment (A2, B2, C2). After treatment with IFUS, the lower layer of the dermis showed increased collagen density, and fibrosis was noted between fat layers. These findings were more evident on Masson's trichrome staining (D1, D2). (H&E × 20, Masson's trichrome × 20).

provide important data that HIFU treatment for skin rejuvenation might be a valuable procedure in Asian patients due to its safety and successful outcomes. Further studies are needed to achieve more effective strategies for skin rejuvenation with IFUS.

Acknowledgements

This work was supported by a Korea University Grant(K1422341).

Declaration of interest: The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

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