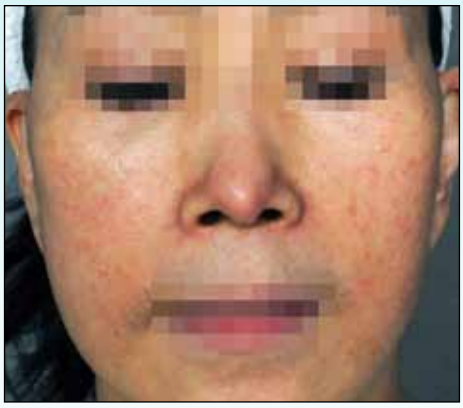
Doublo Achieves Significant

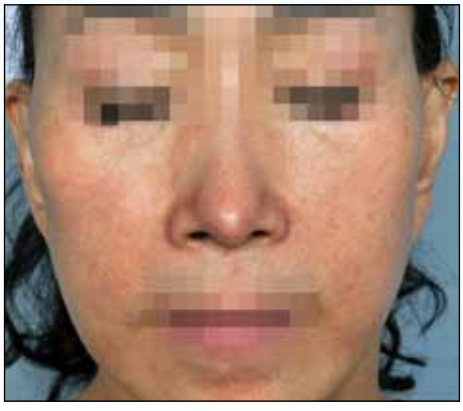
Non-Invasive Skin Rejuvenation and Face-Lifting

Jie Hoon Kim, M.D.
Chairman
Dermatology Clinic at Dr. Kim's Skin & Laser Clinic
Suwon, South Korea

"One of the central advantages of the Doublo is that it allows the clinician to perform a non-invasive face-lift without damaging the epidermis."



Before Tx



After Doublo Tx

Photos courtesy of Jie Hoon Kim, M.D.

By Ilya Petrou, M.D., Contributing Editor

Non-invasive skin rejuvenation procedures have become extremely popular in aesthetic medicine, as new and exciting treatment modalities continue to evolve, offering patients excellent outcomes, in many cases circumventing the need for traditional cosmetic surgery. Since its inception several years ago, the Doublo from Hironic (Sungnam, South Korea) has proven itself as an impressive aesthetic device achieving significant skin tightening and lifting effects in the face and neck regions.

"Compared to other skin rejuvenation devices and technologies, the Doublo can achieve good aesthetic outcomes while limiting unwanted side effects," said Jie Hoon Kim, M.D., chairman of the Dermatology Clinic at Dr. Kim's Skin & Laser Clinic in Suwon, South Korea. "The large majority of my patients are satisfied with the outcomes and improvements achieved in the signs of aging."

Among the different energy-based technologies currently used in skin rejuvenation devices, ultrasound energy is considered by many experts as a safe and effective approach to treating aging and sagging skin. Powered by second generation high-intensity focused ultrasound (HIFU) technology, the Doublo targets the deep dermis and SMAS, creating thermal coagulation zones in the targeted tissues, while largely sparing the surrounding structures. This focused energy causes a contraction of the SMAS, as well as a denaturation and remodeling of the targeted collagen fibers resulting in neocollagenesis, which then produces significant skin tightening and lifting of the targeted tissues.

In Dr. Kim's opinion, "One of the central advantages of the Doublo is that it allows the clinician to perform a non-invasive face-lift without damaging the epidermis. Other rejuvenation modalities such as radiofrequency (RF) and lasers also aim to stimulate the deep dermis, but these treatments often result in unavoidable damage to the epidermis. Doublo's high-intensity focused ultrasound energy avoids damage to the epidermis."

Doublo procedures are quick, safe and painless, said Dr. Kim. Since there is no downtime associated with treatment, patients can return to daily social activities immediately following the procedure.

"Most patients are very satisfied with the results and return for additional sessions," Dr. Kim reported. "Treatments are comfortable and the rejuvenation effects are very noticeable; therefore, patients who know the procedure well, often recommend it to others."

With a 128 CH high resolution image probe, the Doublo offers precise and real-time imaging of the targeted structures before and during a treatment session. It is also equipped with a larger treatment tip, allowing the physician to perform quicker treatments.

In addition, the Doublo was recently upgraded to include a 5,000 shot cartridge (more than double the capacity of the previous cartridge). This improvement allows physicians to treat more patients than ever before with a single cartridge, further underscoring the higher efficiency of the Doublo compared to other devices.

"In my experience, one can achieve the best clinical result if Doublo treatment is combined with another rejuvenation modality such as RF or fractional lasers," Dr. Kim noted. "Since it appeared on the aesthetic market five years ago, I believe Doublo has developed a solid reputation in the rejuvenation field."

Clinical Reviews from Doctors

Date: July 4, 2012

1. SMAS vs Sub Q

"Face lift by HIFU seems not only result from tightening the SMAS layer but result from subQ fat reduction." (By Doctor Kim, Jong Gu from Oracle Clinic)

"Reason for doublo having less possibilities of side effect than Ulthera is because of its precise and wider dot size. Ulthera dot is vertically larger and sharper which cause sharp pain when doublo isn't. Despite this fact, doublo shows better effect because it causes larger thermal coagulative zone on the subQ layer and SMAS surrounding area." (By Doctor Choi, Wonwoo from Well's Clinic)

2. doublo Vs Ulthera

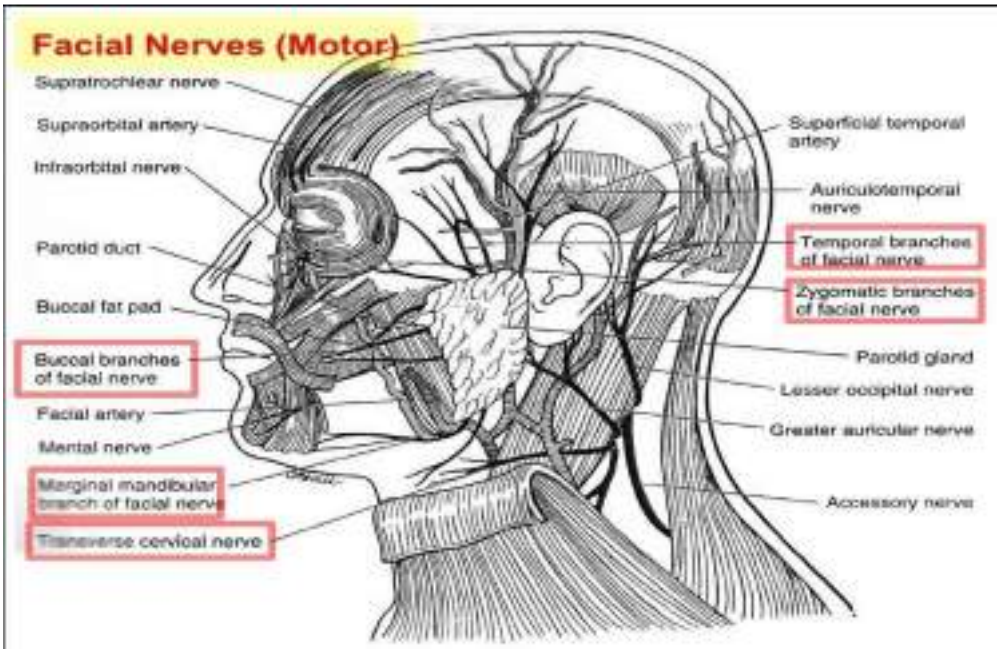
"In the term of 'FACE LIFT', I have experienced much better results with doublo than Ulthera."
(By Doctor Kim, Jong Gu from Oracle Clinic)

"It is impossible to adjust higher energy with Ulthera due to its automatic lock on the energy setting. This point must be rectified." (By Doctor Kim, Jong Gu from Oracle Clinic)

3. Nerve

"The most frequently occurred nerve damage by HIFU energy would be 'facial nerve madibular branch'. The reason is because the ultrasound hits the bone and is reflected to the other direction or creates secondary wave. Therefore, it requires attention on the facial nerve of bony prominence area on the mandible." (By Park, Jae-woo from Dr. Park Plastic Surgery)

Reference: Picture of anatomy that is related to facial motor nerve



"Important thing to remember during HIFU treatment is to consider the direction of relaxed skin tension line and wound healing by secondary intension." (By Dr. Kim, Jie-Hoon from Dr Kim's Skin&Laser Clinic).

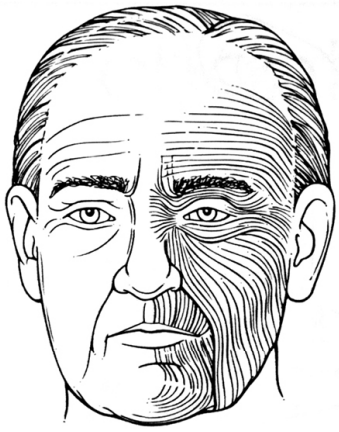


FIGURE I–6. Relaxed skin tension lines of the face at rest with gravitational forces exerted from a seated position. With aging and sun exposure the lines become more pronounced.

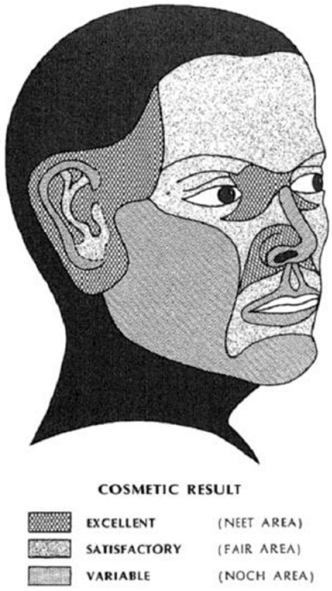


Fig. 1. The cosmetic result of wounds healed by secondary intention according to anatomic site. Healed wounds are often imperceptible in NEET areas (*concave* surfaces of the *n*ose, *e*ye, *e*ar, and *t*emple). In NOCH areas (*convex* surfaces of the *n*ose, *o*ral lips, *c*heeks and chin, and *h*elix of the ear) superficial wounds heal with an acceptable appearance, but deep wounds heal with depressed or hypertrophic scars acceptable only to some patients. Wounds healed in FAIR areas (*f*orehead, *a*nthelix, eyelids [*l*], and *r*emainder of the nose, lips, and cheeks) result in flat hypopigmented scars acceptable to many patients.

4. Treatment of D4 and M7

When combining D4 and M7, 'the ratio of D4:M7 on each treatment area' is as follows.

(1) low face

This area is mostly important for face lifting. Since SMAS is the important factor for lifting and as this area needs to be tightened, D4 should be the main cartridge to use. For the low face lifting, the optimum ratio of D4:M7 would be 6:4 or 7:3. For the power, emit relatively strong energy of 1.3~1.5J. But simply lower the power on the bony prominence like mandibular rim to avoid thermal injury.

(2) mid face

Reason for nasolabial folds is because the structures of mid face have laxity and becomes downwards. In this case, to do skin tightening on mid face, it is important to tighten the deep dermis structures. So it is optimum to use D4:M7 ratio of 5:5.

Also for Mid face, use the relatively strong power, but pay attention on the bony prominence like zygoma. It might cause bruise around the eyes. Therefore, it is recommended not to use D4 and D7 but to use only M7 on the forehead and eye surroundings.

(3) upper face

Even though HIFU device got approved for eyebrow lifting, it requires a lot of attention during this area treatment. For the forehead, there are risks of side effect so the energy should be lowered or use the

only M7 cartridge.
D4:M7 ratio would be 3:7 to make fewer side effects. Since the forehead nearly does not have subQ fat, D4 cartridge depth would probably target not SMAS layer but muscle or periosteum. And so there are some cases with patients having headaches after treatment.

(4) Neck

As the SubQ fat will get less on the neck and SMAS will be combined with platysma muscle, it is required to lower the energy to avoid any side effects. Comparing to face, neck has 1) less *dermal capillary vessel blood flow rate* which causes difficulty in thermal diffusion and 2) thin subQ layer causing high possibilities of side effect.
For the neck, recommended ratio of D4:M7 is 4:6 so mainly use M7 cartridge. Power should be lowered and especially use lower than 1.2J with D4 cartridge.

5. Spacing

Spacing is important.
In the past, D4-1.7mm/M7-1.4mm was the fixed spacing setting and I have been increasing only the energy. I always thought Spacing is an important factor but as I am afraid, I used to make narrow for one or two levels only. Then as Dr. Kim, HS saw Ulthera having up to 1.2mm spacing, he considered to narrow doublo spacing to 1.4-1.5mm as well. The PT Slides from Ulthera shows 1.5mm but some actual users use 1.2mm. In this case, it would mean 1.5mm is the safe & standard spacing for Ulthera recommendation and 1.7mm for doublo, meaning these two devices have different energy concentration. And I considered the possibilities of damaging tendency on important structures due to narrow spacing.
So recently, I have been narrowing the spacing to 1.3mm with doublo and done several cases. Comparing to the last 1.7mm spacing treatment, I could clearly see strong effect. M7 used 1.1mm spacing. From my view, as spacing becomes narrow, the dots of thermal injuries become connected as a long treatment line, and in this case vector direction treatment is more effective. But, this might also affect risks of damaging lower structures. Severe pain after treatment or swallow symptom might occur but this way can show definitely better effect. Of course, patient with more laxity will have difference in results.

6. Ulthera

It is a known fact that Ulthera helps to improve about 50-70% of the wrinkles and skin laxity on the face and neck. But it is difficult to treat skin laxity completely using only this Ulthera treatment. To expect better results, it requires combination therapy. To maximize the HIFU treatment effect, I think it is too dangerous to narrow the spacing to 1.1mm~1.3mm or increase the power energy to 1.7J. Too narrow spacing or too strong energy will cause not only the burns but will cause nerve damage leading peripheral type of facial palsy. I believe it is safe to use treatment that causes no side effect if Ulthera or HIFU can expect more than 90% of the treatment effect. Here is my Ulthera treatment procedure and method.

1) Both Cheek: 4MHz 4.5mm probe from ears - 55lines:1.2J
2) Neck area: 4MHz 4.5mm probe - 50 lines:1.2J
3) Forehead area: 7MHz 3.0mm probe - 20 lines: 0.45J

4) lateral orbital areas: 7MHz 3.0mm probe - 10 lines: 0.45J
5) below infraorbital areas: 7MHz 3.0mm probe - 9 lines: 0.45J
6) lower face area : 7MHz 3.0mm probe - 40 lines: 0.45J
7) Neck area : 7MHz 3.0mm probe - 50 lines: 0.45J (Neck area proceed dual layer therapy)

If the hospital has Thermage, Polaris, Nd-YAG laser;

1) UL + thermage + Polaris
2) UL + thermage + polaris + DLT (If you proceed this kind of combination therapy, you will expect good result for wrinkles and skin laxity.

Doublo; “Clinical study of non-invasive face-lifting treatment in application of HIFU”

Presenter: Dr Jie Hoon Kim,(Dr, Kim’s Skin & Laser Clinic)

Date: 25th March 2012

Place: The Association of Korean Dermatologists Spring Symposium 2012 in Grand Hilton

Organiger: The Association of Korean Dermatologists

[Doctor Profile]

Doctor: Jie Hoon Kim

Profile:

Graduate School of of Suncheonhang University - Medical School

Trained in Ajou University Hospital Department of Dermatology

Graduate School of Ajou University - Dermatology Major(Year 2001)

Member of The Association of Korean Dermatologists

Member of Korean Dermatological Association

Publication Committee Member of the Association of Korean Dermatologists

Planning & Policy Making Committee Member of the Association of Korean Dermatologists

Executive Secretary of the Korean Society for Dermatologic Laser Medicine

Member of The Korean Society for Laser Medicine and Surgery

Member of The Korean Society for Dermatologic Surgery

Member of The Korean Society for Cosmetic Dermatology

Member of Acne Research Team of Korean Dermatological Association

Member of The Korean Hair Research Society

Board Member of CCLMS, 孔林高手 cafe Co-Operator

Currently a member of a board of education in the Association of Korean Dermatologists.

Publication director of Korean Skin Dermatology Laser Society(KSDLS)

Director of Korean Society of Pigment Cell Research (KSPCR)

Awards: Achievement award from the Association of Korean Dermatologists(in 2007)

Health Professions Achievement award from Suwon District (in 2011)

[Abstract]

Doublo: Clinical study of non-invasive face-lifting treatment in application of HIFU

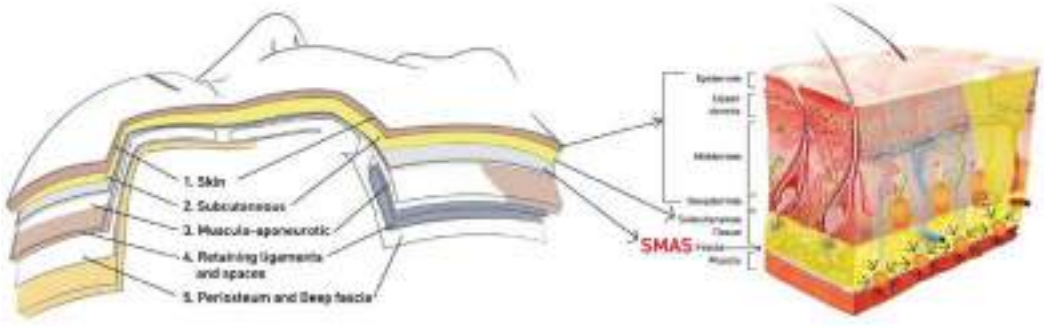
Contents:

(Face Lifting & Rejuvenation)

Face Lifting & Rejuvenation

1. Introduction

As human gets older, skin and its under structure tissues constantly get ageing process. Typically, number of fibroblast on the skin decreases and collagen synthesis also decreases. And functions and numbers of many skin appendage are also dropped. For under tissues of the skin that maintain the face contour also form laxity due to the aging process. Before learning more about face lifting using HIFU (High Intensity Focused Ultrasound), it is necessary to understand the face anatomy. Face and scalp are composed of several layers and these can be specifically composed into five standard layers(Figure 1).



[Figure 1. 5 Layers to compose face and scalp]

1) Skin
2) Subcutaneous layer
3) Musculoaponeurotic layer (SMAS: Superficial MusculoAponeurotic System)
4) Loose areolar tissue (ie, spaces and retaining ligaments)
5) Fixed periosteum and deep fascia

So far in the laser treatment area of dermatology, the epidermis and dermis were the main interested therapeutic areas for the skin treatment. However, collagen remodelling on deep dermis slightly helps to regain some degree of skin elasticity but it is difficult to improve its own fundamental face contour.

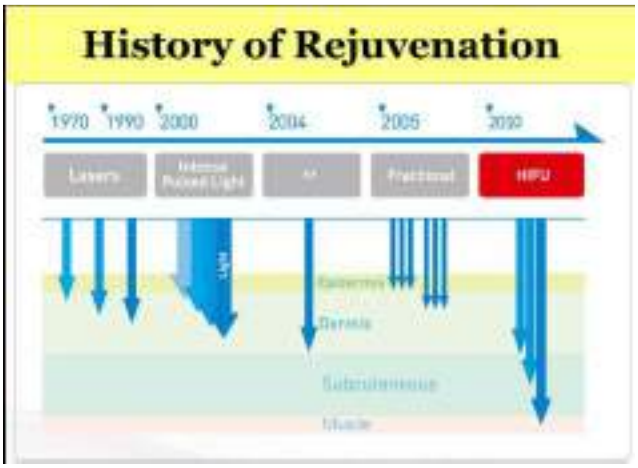
2. History of Face Lifting & Tightening

The Latin word ‘Rejuvenation‘ is the compound word of 'Re' and 'Juvenile' which can be interpreted ‘as a kid again’ or ‘be young again’. The proposition of ‘becoming young again’ is a human desire of all time. Also such development of the laser was developed to meet the wishes of human, and ‘rejuvenation’ is still somewhat a question to dermatologists.

The development of laser and other medical equipment for rejuvenation can be classified in many different ways but can be largely categorized in five (Table 1, Figure 2).

1	Ablative Resurfacing with Lasers
2	Photorejuvenation with IPL
3	Rejuvenation with Electrical Current (RF)
4	Rejuvenation with Fractional Laser
5	New Generation Rejuvenation with HIFU

[Table 1. Developmental history of facial rejuvenation]



[Figure 2. History of Rejuvenation Devices (History of the device development by time frame and describes each device covering area)]

When the laser technology was not developed in old days, ablative laser or chemical peeling was used for face lifting. It was the time when we had to face all side effects through laser treatment. All these experiences and trials affect in the later days the development of next generation lasers. Due to serious side effects and downtime, these are narrowly treated nowadays. Along with development of IPL, interests were focused on 'photorejuvenation' but the effect was insignificant and it soon was dismissed in the market. But IPL has several advantages that it is still widely used in pigmentation, vascular, and hair removal.

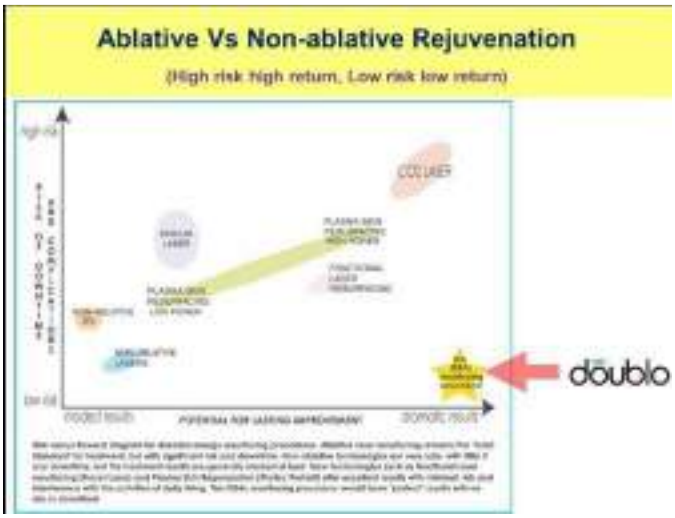
The item that has been used for longest time in Rejuvenation is the 'Radiofrquency' of using electrical energy. It is either divided into MONOPOLAR or BIPOLAR. Only the RF was applied for the treatment or it was developed into a 'hybrid form' of adding other lasers like diode laser, IR, and IPL. In domestics, RF needle is now widely used as method of transferring electrical current fractionally. Most of Korean laser companies are manufacturing this 'needling RF'.

Fractional laser is also the 'rejuvenation item' that has long run. There are many factional lasers with different wavelengths, such as 1,550nm(Er:glass fiber), 10,600nm(CO2), 2,940nm(Er:YAG) that are developed and applied for treatments.

‘HIFU’ is a new spotlight concept in these days. Without damaging the skin or the subcutaneous layer and its surrounding tissues, it makes ‘selective thermal coagulative zone’ on the subcutaneous layer and SMAS layer improving the skin aging. HIFU is a high intensity focused ultrasound that is transferred into deep structures, such as deep dermis, boundary layer of deep dermis and subcutaneous fat, fibrous tissues of subcutaneous fat, SMAS layer and fascia. And over the wound healing process for several months, a gradual face lifting effect can be achieved.

3. Conditions to the Ideal Rejuvenation Equipments

The most important condition to the rejuvenation equipment is ‘to minimize the side effect and to maximize the effect’. But so far, those of equipments showing dramatic results had relatively high risk of side effect (Figure 3).



[Figure 3.] Each Rejuvenation Device’s Correlation of Dramatic Result and Complication Risk:

So far, those of equipments having higher risk of side effects showed dramatic result. The development target of rejuvenation equipment is to minimize the side effect while maximizing the effect.

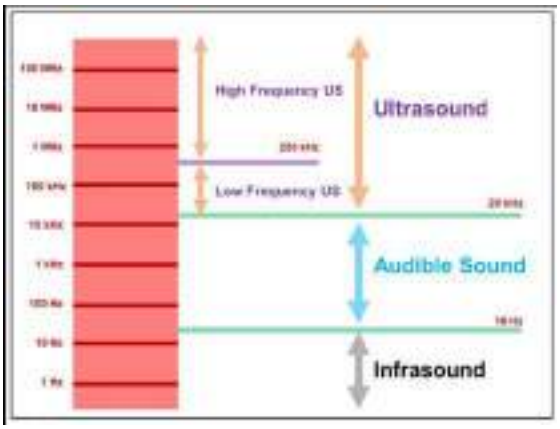
For the full face resurfacing using laser or chemical peeling, effect is positive in case of successful treatment but there were risk of nearly 100% side effects. As a result, high risk is high return.

Thus, far the most important matter in developing rejuvenation equipment is to minimize the side effect while maximizing the effect. And the closest equipment of this can be said as HIFU.

Concepts of HIFU

1. Ultrasound

‘HIFU(High Intensity Focused Ultrasound)’ is not using the ‘light’ like other standard lasers but is using ‘sound waves’ and is a new method in medical device. Frequency of the sound that human ear can hear is generally in the range of 16Hz~20kHz. If frequency exceeds 20kHz, it is called ultrasonic wave(Figure 4).



[Figure 4] Classification of Sound wave For Each frequency area:

If frequency exceeds 20kHz it is classified as ‘ultrasound’ , and ultrasound over 250kHz is classified as ‘high frequency ultrasound’. Ultrasound has a tendancy to transmit water and that allowed to use in ultrasound diagnostic units for long period of time in medical field. Recently ultrasound is widely used in not only the diagnostic unit but in therapy equipment.

The principles of ultrasonic applied in the treatment area is the physical effects of its ultrasound(Table 2).

[Table 2. Three Types of Physical Effects of Ultrasound]

1) Mechanical Effect
2) Cavitational Effect
3) Thermal Effect

2. History of HIFU

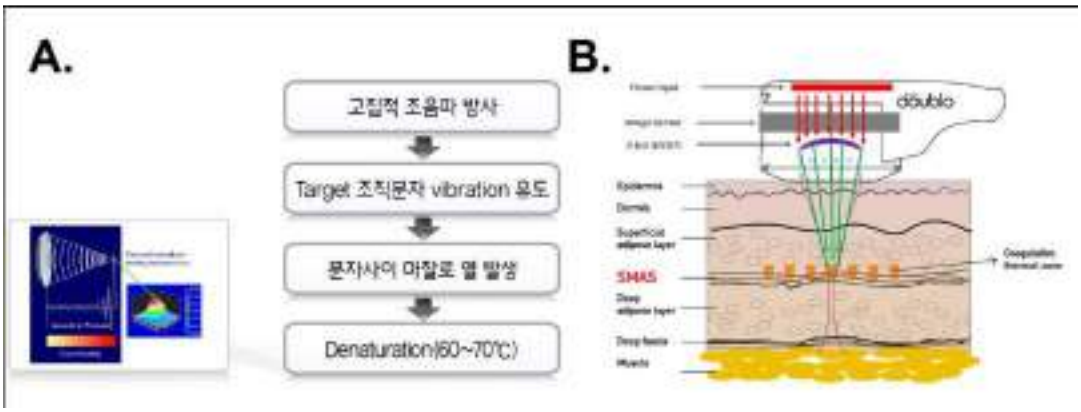
HIFU is to treat various cancers like liver cancer, uterine cancer, and breast cancer through thermal energy which is created in the focal point of supersonic wave, collected from the ultrasound transducer. At first it is developed to treat solid tumor but in later days it could get attention as non invasive treatment modality(Foster RS et al. High-intensity focused ultrasound in the treatment of prostatic disease. *Eur Urol* 1993;23:29–33).

3. Apply to the Skin Rejuvenation

HIFU makes ‘selective thermal coagulative change’ on subcutaneous layer and SMAS layer without damaging surrounding tissues. For other light based devices or RF devices, it was unavoidable to damage the epidermis and upper dermis to stimulate the deep dermis. However, HIFU does not effect the skin and subcutaneous layer at all but forms ‘thermal coagulative zone’ on only the deep dermis.
The first time of applying HIFU to skin rejuvenation was in 2007 by Gliklich(Gliklich RE et al. Clinical pilot study of intense ultrasound therapy to deep dermal facial skin and subcutaneous tissues. *Arch Facial Plast Surg* 2007; 9(2): 88–95). It begins to attract attention in detail when research data using body tissues was released in 2008 at Harvard Wellman Center(Laubach HJ et al. Intense focused ultrasound: evaluation of a new treatment modality for precise microcoagulation within the skin. *Dermatol Surg* 2008; 34(5): 727–34). Research on facial skin tightening was announced but it was a limited research mainly on eyebrow-lifting (Alam et al. Ultrasound tightening of facial and neck skin. *J Am Acad Dermatol* 2010; 62(2): 262–9).

4. Principle of ‘Face Lifting’ using HIFU

When electrical energy is transferred to the ceramic of HIFU transducer, electrical energy transforms into ultrasound. And when this created ultrasound is focused, it generates thermal energy at ‘maximum focusing point’. (Figure 5).



[Figure 5. Diagram of thermal energy emited by HIFU]

A. Diagram of thermal effect of HIFU
B. Diagram of forming thermal coagulation zone on SMAS layer when HIFU is emited
Such thermal effect of the ultrasound within the tissues is observed as the following(Figure 6).
In other words, it only generate thermal energy on the ‘maximum focusing point’ and create ‘selective thermal coagulative zone’ on SMAS layer without damaging epidermis and subcutaneous tissues. These thermal coagulation zones react to high energy of over 60˚C. This causes the sagging skin tissues to contract and give skin tightening and lifting effects.

[Figure 6. Principle of generating thermal coagulation zone using HIFU]

A. Image of 7.5MHz concentrated ultrasound using Schlieren method

B. Histology of energy desposed in human skin tissue

The actual coagulation zone after HIFU applied to real tissues

cf) Schlieren method: A way of making the light visible pattern of wave which is reflected by the change of density based on sound wave

To prove this, a test was carried out on a micro pig(femaile) having the most similar skin to human by emitting HIFU (Figure 7). Even in this animal experiment, selective coagulation zones from thermal damage were found.

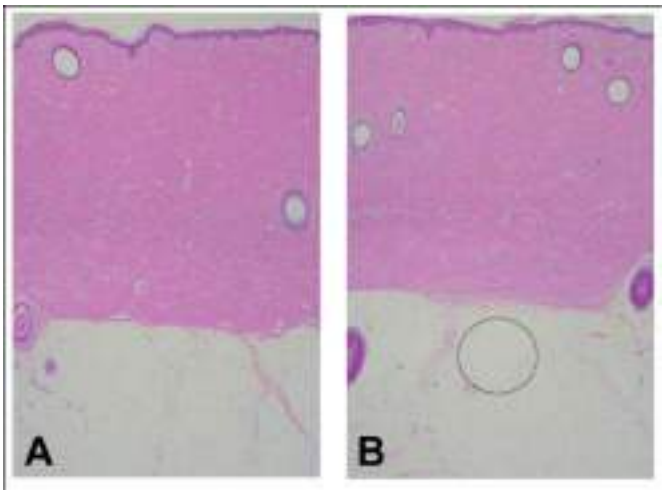


Figure 7. HIFU Emitting pictures of before & after on 'micro pig(female)' tissues (H&E, stain X50)

A. Before Emitting HIFU

B. After Emitting HIFU : There is no damage on epidermis and tissues above dermis, and there is coagulation zone formed on subcutaneous layer where HIFU was emitted.

HIFU is high intensity focused ultrasound energy which is transferred fractionally to depth of skin that creates thermal damage on the deep structures like deep dermis, subcutaneous layer, fascia and

SMAS layer. And it will gradually lead to face lifting effect through few months of wound healing process.

Unlike the general HIFU of treating solid tumor, the HIFU that is used on the skin for rejuvenation purpose has very short exposure duration (in mili second). So the energy delivered to the target is also low(below 15J per pulse). As the ultrasonic is emitted in short time, it does not damage on epidermis and upper dermis but able to target the SMAS layer and deep dermis.

If exposure time(same as pulse duration) gets longer, thermal zone will be created on the skin surface in axial direction. Therefore, when it becomes longer, damages on skin surface is unavoidable. And so short exposure time is very important to treat the target more effectively by not hurting epidermis and upper dermis.

The biggest difference of HIFU from other lasers or light is that it is not related to skin color or chromophore(color blind). It is an advantage that it can do effective rejuvenation even on the dark skin, which was difficult to treat with light based treatment.

HIFU is the new concept therapy equipment for a truly 'non invasive rejuvenation'.

About Hironic Co.

Hironic Co., Ltd is the new global name of BSP Medical which is well known as New MIDAS. It is a total laser company of selling various laser equipments and it is procuring users in domestics but also as globally in more than 30 countries worldwide. Currently their main products are Greenxel, New MIDAS, Doublo, MIDEPI, MIXEL.

In 2011, awarded 3million export tower from the Kyunggi Province and is selected as Small-Gient Enterprise in 2012.

Advantages of doublo

Figure 8. doublo unit composition and specicifaction

(1) More precise and safe

Unlike the existing HIFU equipment using single transducer to generate ultrasonic, doublo is equipped with two ‘multi transducer’. This allows to have precise focusing and reduce damage of surrounding tissue, and also can reduce the consumables cost due to long lifespan of the transducer.

(2) Real-time high resolution: High resolution image probe

Existing HIFU equipment has 16CH image probe. Innovatively, doublo improved the imaging. Using 128CH allows to provide clear and high resolution allowing precise and safe treatment.

(3) Double control system

The existing HIFU equipment has image probe and transducer as one inside the cartridge. But doublo separated these image probe and transducer. So HIFU energy from the cartridge is independent from the skin imaging area.

Actually consumed part is only the HIFU generating device and image probe can be used semi-permanent. When exchanging the cartridge, there is no need of changing the image probe but only need changing the HIFU generating device. It can lower the manufacturing cost on cartridge and leads to more effective device operation. Also it is possible to continue the treatment when image is not monitored.

(4) Three types of optimum cartridges for different treatment area

Different cartridges like M7, D4 and D7 are offered depending on the treatment area.

(5) Optimized parameters offered for each treatment area

Parameters saved in the memory setting allow easy and fast treatment. It is also possible to change the values in detail upon the user's decision. Energy setting and spacing are easy to adjust and treatment time is fast.

(6) User-friendly interface

It provides GUI (Grahpic User Interface) that is maximized the convenience for practitioners. This is the biggest merit of Korean lasers. Everyone can easily do the treatment after listening 10 minutes of explanation. Also, there is a foot switch which allow to reduce the practitioner's tiredness.

(7) More resonable comsumables cost

They paid efforts to lower the equipment cost and to meet reasonable cartridge (consumables) cost. This allows to have relatively low treatment cost and so it also allows to offer retouch comfortably if there's dissatisfaction.

Clinical Applications of doublo

Doublo can be applied for tissue tightening and lifting in various ways(Table 3). This will be a good solution to patients who are interested in face lifting but are worried and feel uncomfortable with 'interstitial laser' that needs insertion of cannula into skin hole.

Table 3. Clinical Indications of doublo

Tightening & Rejuvenation

Jowl lifting

Nasolabial fold reduction

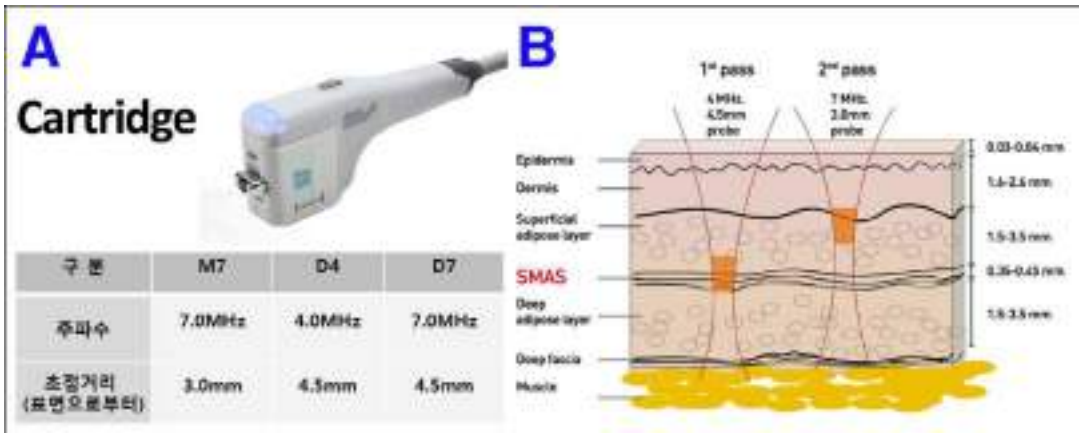
Malar augmentation

Eyebrow lifting

Treatment is very easy and simple, but need to thinkabout several variables(Figure 9).

[Figure 9. Parameters of doublo]

The three variables on the parameter to think of during the treatment are 1) cartridge type, 2) spacing, 3) energy. Spacing means the distance (gap) between the dots. If the spacing is narrow, danger of side effect will increase and the wider spacing can offer the safer treatment. Energy means the intensity of HIFU. The most important thing to consider during treatment is the selection of cartridge(Figure 10A). It is most common to carry out two modes among three types(Figure 10B).



구 분	M7	D4	D7
주파수	7.0MHz	4.0MHz	7.0MHz
초점거리 (표면으로부터)	3.0mm	4.5mm	4.5mm

[Figure 10. Types of Cartridge and applying area]

A. Types of Cartridge and specification
B. Diagram of the applying area on skin with real cartridge

M7 and D4 cartridges are most commonly used. M7 (7.0 MHz) cartridge targets the relatively superficial area like deep dermis and subcutaneous layer, and D4 (4.0 MHz) cartridge targets SMAS layer. M7 targets 3.0mm from the probe. It targets deep dermis which is 3.0mm depth from the

surface of the skin and it leads to strong collagen regeneration. Through the 2-4 weeks of face lifting, collagen and elastine are generated continuously over 3-6 months and is predicted to create tissue tightening.

Destroying subcutaneous fat which is about 3-4mm depth from the surface of the skin can be similar to liposculping concept which can improve the face outline.

D4 targets 4.5mm from the probe. It targets around SMAS layer that is 3.0~4.5mm depth from the surface of the skin. And it generate less than 1mm size of thermal coagulation zone which becomes contraction and relaxation after some time affecting face outline lifting effect.

It is even more effective to use M7 and D4 cartridges as a combination treatment since they tighten specific areas. Below you can find 'Ratio of D4:M7 for each treatment area' when doing combination treatment of D4 and M7.

(1) low face (including jowl)

For lifting, this area is the most important and important factor for lifting is the SMAS. So to tighten the SMAS, D4 should be used as the main cartridge. For low face lifting, D4:M7 ratio should be 6:4 or 7:3. But when it is bottom of the neck, subcutaneous tissues becomes less and SMAS is joined to platysma muscle, so it is recommended to lower the energy to avoid side effect when doing the neck area treatment.

(2) mid face

The mid face structure gets laxity and runs down and becomes the reason for forming nasolabial folds. For this case of skin tightening, it is important to tighten the structure in deep dermis. So for mid face, ratio D4:M7=5:5 should be enough. Eye surroundings are easy to get bruised. Therefore, for around the forehead and eye surroundings, D4 and D7 are not used but recommended to use only M7.

(3) upper face

HIFU got certified for eyebrow lifting but it requires a careful treatment of this area. For forehead treatment, there is danger of side effect so it is better to use M7 or lower the energy. Ratio of D4:M7 should be 3:7 so that it does not induce side effect. Forehead has almost no subcutaneous fat. So actually using D4 would mean to applying energy not to the SMAS layer / fascia but to the muscle or periosteum. And in some cases, patients complain of 'headache' after treatment.

Complications & Managements

(1) Pain

HIFU is a sense of 'shockwave' created by 'soundwaves' but it generates heat through secondary action.

Since generating heat might create pain, it is required to use anesthesia. There are topical anesthesia and nerve block for facial anesthesia. Commonly topical anesthesia is recommended.
During treatment, important thing to remember is the bony prominence which is same as using RF. Areas where bones are protruded have relatively thinner soft tissue, so HIFU can target periosteum or deeper portion. In this case, there is a possibility of accompanying nerve damage, so it requires special attention.
This kind of area on the face is the cheekbone, mandibula surroundings and forehead area. Forehead often carries pain, and as in many cases, this pain is related to side effect. Therefore, it is good to lower the power to 1.2J.
In rare cases, patients complain about toothache. If patients are equipped with prosthetics or tooth braces, reduce the intensity and make enough air space inside the cheek and do the treatment. Then it will reduce the side effect. Also, for the areas nearby mouth and teeth, it is better to use M7 than D4. Specially forehead has bigger pain. This is because the subcutaneous tissue is relatively thinner and so D4 hits the fascia or periosteum.

(2) Nerve injury
Since HIFU targets relatively deep layers like SMAS layer, the possibility of nerve injury should be kept in mind. Even if the nerves are damaged, partial damages such as neurapraxia or axonotmesis can be recovered after a period of time. But in case of neurotmesis, it can lead to permanent disability, so be careful of selecting energy and treatment area.
And also in this case, patients' subjective responses to the pain or the facial nerve response are important indicators for the treatment. Therefore, as mentioned in earlier sentences, nerve block is not recommended.
Important thing to think about for nerve damage is the superfial line coming from the facial nerve branch to the skin. And should take attention on the eye and mouth areas.
Around the mouth, pay attention on the mouth branch of infraorbital n. and mental n.. Nerves around the mouth are superficially ascended in many cases. And especially, those bony prominence compared to other areas will need a special attention. Therefore, do not treat too much on the mouth surrounding wrinkles and will need to turn down the level of patient satisfaction.
Around the eyes, pay attention on the supratrochler n. and infraorbital n..

(3) Thermal injury (Burn)
In case of skin burn is very rare compared to the frequency of burns from IPL, fractional laser or the RF devices. There are two big possibilities of skin burn during the HIFU treatment.
First, when energy is too high, thermal damage area becomes wider and that also burns the skin surface. If energy is high, it is the symptom of thermal coagulation zone being increased to skin

surface in axial direction. Main causes are that 1) energy is too strong 2) energy is applied to the same area continuously or 3) setting for the spacing is too narrow compared to the energy.
Second, due to the improper contact between the skin and the cartridge, ultrasound emitting surface of the cartridge generates thermal and burns the skin.
The thermal is occurred on the boundary surface due to the improper emittion of ultrasound, and this kind of cause and condition is same as the general skin burn from existing devices. In case of using not enough ultrasound gel or making not full contact to the skin, there are chances to get burn but the frequency is very low.

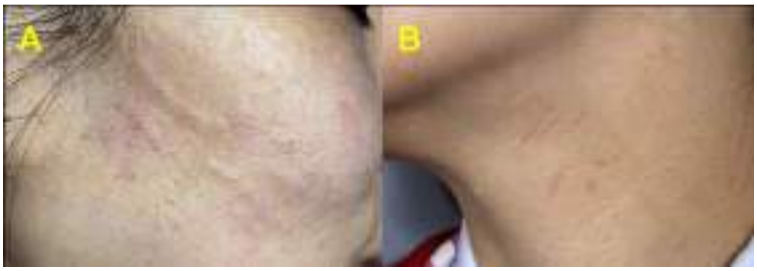


Figure 11. Clinical results of side effects on different treatment area

A. It is edema after treatment using D4 1.7J. It is a temporary phenomenon that it gets better with no scars within 1 week without any extra treatment.
B. It is crust occurred from tiny vesicle on the neck area, which gets better with no scars within 1 week by applying topical steroid.
Cheek has less frequency of side effect during treatment, but neck or the forehead have relatively higher chances of side effect. On the cheek using D4 as standard, there is no problem of using power upto 1.7J except leading temporary edema(Figure 11A). But on the neck, there are higher chances of having blister or crust even when high energy is not used(Figure 11B). The neck comparing to face has higher possibility of side effect because 1) epidermis has little capillary bloodstream that is difficult to thermo diffusion 2) subcutaneous layer is thin. On the bony prominence like forehead or jaw, it is hard to make full contact between cartridge and skin surface, which makes coagulation zone on shallow area than the targeted area. So it is required to pay attention making full contact using M7 cartridge than D4/D7.

Combination Treatment

1.Completion of Rejuvenation: Triple Tightening Rejuvenation (TTR)

Each rejuvenation has all different advantages and disadvantages. As a result in clinical trials, it is the best method to take advantages of various rejuvenation modality and apply to the treatment.

For my case, I would recommend the best treatment method is to combine three methods like fractional laser (1,550 nm Er:glass fiber laser), RF and HIFU. Reasons of using these three devices can be described by following principle of tying up the shoestring.

Figure 12. Rejuvenation principle comparing to a way of tying shoestring

A. Fractional laser or RF

B. HIFU

C. Triple Tightening Rejuvenation

This is a comparison picture of using only the fractional laser or RF (Figure 12A).

It is the case to make surface change on only the epidermis and upper dermis. It makes surface change and improves fine wrinkles on the surface, but it does not correct below the deep dermis even after a long time. Many treatments are required in order to correct the aging of deep dermis and therefore it has disadvantage of long downtime period. Even after many times of treatment,it is hard to do the basic lifting as it does not correct SMAS layer.

This is a comparison picture of lifting deep dermis and SMAS layer by using HIFU(Figure 12B).

It can be felt as if face was lifted up with surgical procedure. It is not to lift the SMAS layer physically but is to create thermal coagulation zones fractionally on SMAS layer which results natural face lifting. But, since it takes some time for lifting result to come out, there are cases with less satisfaction with patients. Then carrying fractional laser or RF at same time might help to increase the patient satisfaction.

The real completion of rejuvenation is to hold and tighten every part of 1) epidermis & upper dermis, 2) deep dermis & subcutaneous layer, 3) SMAS (Figure 12C, Figure 13).

Figure 13. Treatment area of each modality from Triple Tightening Rejuvenation

In the past when laser technology was not developed, it was difficult to transfer energy to SMAS layer without damaging the epidermis. However, this has been solved by the development of HIFU. Thus, the method of tightening all areas from epidermis to SMAS is proposed as 'Triple Tightening Rejuvenation'.

2.Package Composition of Triple Tightening Rejuvenation (TTR)]

It is good to carry HIFU on the first day. Since it does not have downtime during treatment, it is possible to safely treat. And since the results come out in a month or two, it is more effective for package composition to do this treatment in the beginning. Following is my actual package composition, and this program can be changed as per patient's need, skin condition or based on the types of devices in the hospital (Table 4).

[Table 4. Example of package composition on Triple Tightening Rejuvenation (TTR)]

---

1) **HIFU + RF** (HIFU 1 session, RF 3 sessions, SC 7 sessions)

HIFU --> SC --> RF --> SC 2 sessions --> RF --> SC 2 sessions --> RF --> SC 2 sessions

2) **HIFU + RF + FL** (HIFU 1 session, RF 3 sessions, FL 2 sessions, SC 6 sessions)

HIFU --> SC --> RF --> SC --> FL --> SC --> RF --> SC --> FL --> SC --> RF --> SC

cf) Treatment Interval: 1week

SC: skin care (Regeneration or whitening programs)

RF: needling, conventional, hybrid (new Midas, Arneb, Polaris, Aurora)

FL: 1,550 nm Er:glass fiber laser

Conclusion

HIFU is noninvasive and advanced face lifting technology.

Various rejuvenation devices like IPL, RF, and Fractional laser were introduced in the past, but HIFU is a new concept different from existing rejuvenation equipments by tightening SMAS layer for face lifting.

doublo is a safe equipment using high intensity focused ultrasound(HIFU) and obtained the first Korea FDA as eyebrow lifting. It is the second generation as worldwide and is developed in Korean laser manufacturer Hironic.

doublo is targeting on the deep dermis, subcutaneous layer and SMAS layer which are the cause of skin lagging and wrinkles and lead to face lifting and collagen regeneration without any surgical procedure. It is possible to do effective treatment, and is safe from the danger of side effects such as burns and hyperpigmentation.

Journal of Dermatological Treatment

http://informahealthcare.com/jdt
ISSN: 0954-6634 (print), 1471-1753 (electronic)

J Dermatolog Treat, Early Online: 1–5
 DOI: 10.3109/09546634.2013.868862

informa healthcare

ORIGINAL ARTICLE

The efficacy and safety of intense focused ultrasound in the treatment of enlarged facial pores in Asian skin

Hee Jung Lee[1]*, Kyung Real Lee[2]*, Jae Yang Park[1], Moon Soo Yoon[1], and Sang Eun Lee[1]

[1]Department of Dermatology, CHA Bundang Medical Center, CHA University, Korea and [2]Korea Dermatology Research Institute, Bundang-Gu, Seongnam-si, Gyeonggi-do, Korea

Abstract

Background: Intense focused ultrasound (IFUS) has been used successfully for skin tightening.
Objective: To investigate the efficacy of IFUS in treating enlarged pores and to evaluate changes in skin elasticity and sebum production following IFUS.
Materials and methods: Twenty-two subjects with enlarged pores were randomized to receive a single treatment with IFUS using 1.5-mm transducer on one side of the face, and 3.0-mm transducer on the other. Objective clinical assessments were made by blinded photographic evaluation. Subjective satisfaction and adverse effects were evaluated. Measurements of elasticity and sebum were performed at baseline, 3 and 6 weeks post-treatment.
Results: Physicians' evaluation showed clinical pore improvements in 86% and 91% of the IFUS-treated sites using 1.5-mm and 3.0-mm transducer, respectively. The mean improvement scores were 1.7 and 1.9 for 1.5-mm and 3.0-mm transducer, respectively, with no statistical differences. Cutometer measurement demonstrated a significant improvement in skin elasticity. Sebum level showed a reduction without statistical significance. There was a positive correlation between improvement in elasticity and pore improvement grades. All treatments were well tolerated without significant side effects.
Conclusion: IFUS using 1.5-mm or 3.0-mm transducer was safe and effective for reducing enlarged pores in Asian skin with an improvement in skin elasticity.

Keywords

Enlarged facial pores, intense focused ultrasound, skin elasticity

History

Received 1 October 2013
Revised 12 November 2013
Accepted 12 November 2013
Published online 11 February 2014

Introduction

Enlarged facial pores are related to various factors including genetic predisposition, gender, age, sebum secretion, acne, sun exposure, and decreased skin elasticity (1,2).

Topical retinoic acid (3), chemical peeling (4), 1064-nm Nd:YAG laser (5–7), non-ablative fractional 1440-nm or 1550-nm laser (8,9), and radiofrequency (10) have been used to improve the appearance of enlarged pores with limited efficacy. The effect of lasers or radiofrequency on pores can be explained by the thermal damage-induced collagen remodeling adjacent to the pilosebaceous openings (9,11,12).

Recently, intense focused ultrasound (IFUS) has been introduced as a new treatment modality for skin tightening and rejuvenation. IFUS focuses ultrasound energy to produce confined focal zones of coagulation at the deeper tissue plane compared to non-ablative laser systems using transducers with different frequencies, resulting in collagen regeneration (13–19). To date, no clinical studies have evaluated the efficacy of IFUS on enlarged pores. Accordingly, we investigated the efficacy and safety of IFUS treatment in reducing enlarged pores as a prospective randomized clinical trial and evaluated the changes in skin elasticity and sebum production, the two major factors influencing pores, following IFUS.

Methods

Subjects

Twenty-two Korean subjects (3 men, 19 women; aged 22–51; Fitzpatrick Skin Types III–IV) with enlarged facial pores were enrolled in this study. The exclusion criteria included pregnancy, systemic or topical retinoid use, use of hormonal contraceptives, or skin resurfacing treatments within the preceding 6 months. The participants were not allowed to use systemic or topical retinoids and any skin resurfacing treatment during the study. This study was approved by the Institutional Review Board of CHA Bundang Medical Center, CHA University.

Device description and treatment

We used an IFUS device (UltheraTM system, Ulthera Inc, Mesa, AZ). 10-MHz, 1.5-mm and 7.0-MHz, 3.0-mm focal depth transducers were used in this study. Each subject's left and right side of the cheek was randomly assigned to IFUS treatment using 1.5-mm or 3.0-mm transducer. All subjects received one treatment session. One side of cheek was treated with IFUS using 1.5-mm transducer at 0.25 J per pulse and the other side with IFUS using 3.0-mm transducer at 0.63 J per pulse. Topical anesthetic ointment, eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (AstraZeneca AB, Södertälje, Sweden), was

*These authors contributed equally to this work.

Correspondence: Sang Eun Lee, MD, PhD, Department of Dermatology, CHA Bundang Medical Center, CHA University, 351 Yatap-dong, Bundang-Gu, Seongnam-si, Gyeonggi-do 463-712, Korea. Tel: 82 31 780 5240. Fax: 82 31 780 3449. E-mail: sangeunlee@cha.ac.kr

applied to the cheeks under the occlusion for 40–50 min before the treatment. A total of 40 to 50 lines were delivered to each side of the cheek, adjusting to the size variations in each subject's face.

Objective and subjective evaluations

Photographs by digital camera (Nikon D90, Tokyo, Japan) of each subject were obtained by the same photographer, using identical settings, subject positioning, and room lighting at baseline, and at 3 and 6 weeks after treatment. Objective clinical assessments were performed by two blinded dermatologists. They compared the photos obtained at pretreatment and 6 weeks after treatment separately on each side of the face in a non-chronological order using a quartile grading scale scored as follows: grade 1, 0–25% = minimal to no improvement; grade 2, 26–50% = moderate improvement; grade 3, 51–75% = marked improvement; and grade 4, more than 75% = near total improvement. To evaluate subjective satisfaction, subjects were asked to complete a satisfaction questionnaire at each visit. Overall level of satisfaction was categorized as very satisfied, satisfied, slightly satisfied, or unsatisfied. At each follow-up visit, subjects were also asked to report the possible side effects including persistent erythema, edema, pain, post-inflammatory hyperpigmentation, or numbness.

Measurements of skin elasticity and sebum production

Skin elasticity and casual sebum levels of each side of the cheek were measured at baseline and at 3 and 6 weeks after treatment with a Cutometer® MPA 580 and a Sebumeter® SM815 (Courage & Khazaka, Cologne, Germany), respectively. All the measurements were taken from the same area of each central cheek three times and we calculated their average. Each measurement was performed under the constant temperature and humidity condition (25 °C room temperature and 50% humidity). Three different mechanical parameters of the Cutometer used in this study were: R2, the overall elasticity of the skin (Ua/Uf), R5, the net elasticity (Ur/Ue), and R7, the biological elasticity (Ur/Uf).

Table 1. Objectively assessed clinical improvement grades in pore appearance after a single session of intense focused ultrasound (IFUS) treatment using 1.5-mm and 3.0-mm focal depth transducers at 6 weeks after treatment.

Improvement grade assessed by physicians	1.5-mm focal depth transducer	3.0-mm focal depth transducer
Improvement	19 (86%)	20 (91%)
Mild improvement (1–25%)	10 (45%)	6 (27%)
Moderate improvement (26–50%)	5 (23%)	9 (41%)
Marked improvement (51–75%)	2 (9%)	3 (14%)
Very significant improvement (76–100%)	2 (9%)	2 (9%)
No improvement	3 (14%)	2 (9%)
Total	22 (100%)	22 (100%)

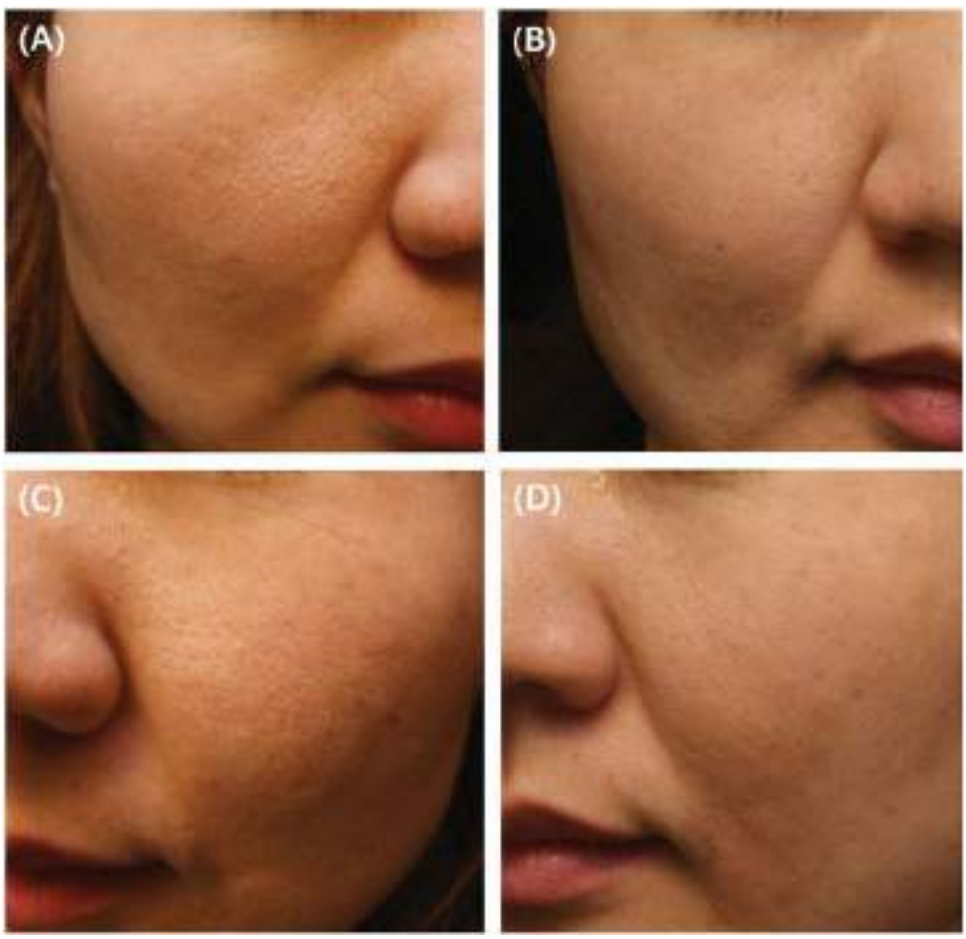


Figure 1. Thirty-nine-year-old woman with enlarged facial pores (A and C) before treatment and 6 weeks after one treatment session of IFUS (B and D). The total number of treatment lines was 50 in each side. The side treated with IFUS using 3.0-mm transducer (B) showed grade 4 improvement in pore size by objective evaluation along with a tightening of the nasolabial fold and marionette line. Subject's satisfaction score was very satisfied. The other side, treated with IFUS using 1.5-mm transducer (D), also showed grade 4 improvement in pore size by objective evaluation and subject's satisfaction score was very satisfied.

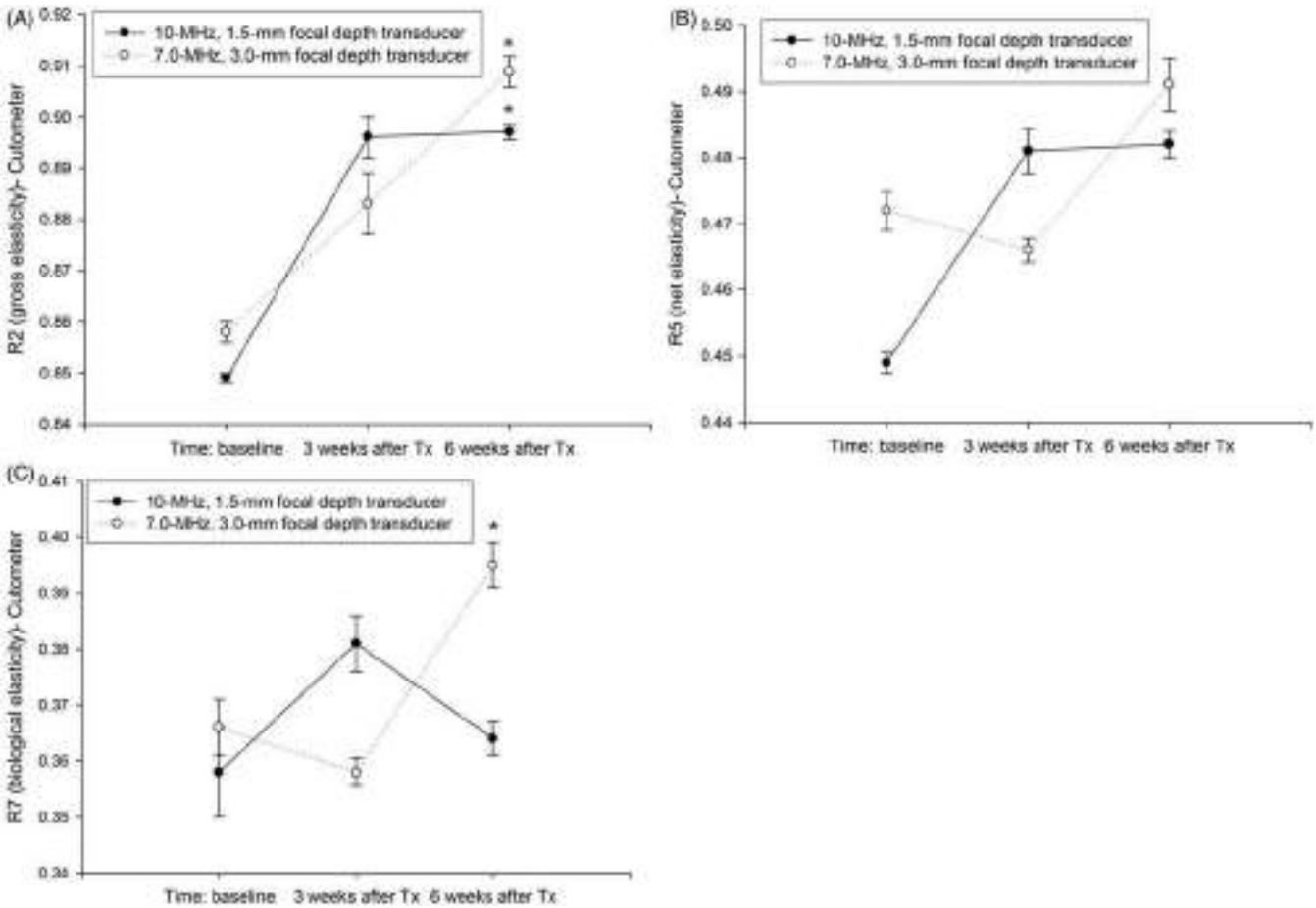


Figure 2. Changes in the skin elasticity as measured by Cutometer following a single session of IFUS treatment using 1.5-mm and 3.0-mm transducers at baseline and at 3 and 6 weeks post-treatment. Results represent mean ± standard deviation. Statistical significance as compared with baseline is indicated as $*p < 0.05$.

Statistical analysis

All statistical analyses were performed using SPSS software (version 12.0, SPSS Inc., Chicago, IL). To compare the post-treatment to baseline values in pore scores, skin elasticity, and sebum production, we used Student's paired *t*-test. Correlations between changes from baseline in elasticity parameters and the clinical improvement grades were tested by calculating the Spearman rank-order correlation coefficients. Statistical significance was defined as a p value of less than 0.05.

Results

At 6 weeks after IFUS treatment, randomized, blinded evaluation by two physicians using a quartile grading scale showed clinical improvements in the overall pore appearance in 19 of the 22 sites (86%) and 20 of the 22 sites (91%) treated with IFUS using 1.5-mm and 3.0-mm transducer, respectively. Four of the 22 sites (18%) and five of the 22 sites (23%) treated with IFUS using 1.5-mm and 3-mm transducer, respectively, demonstrated over 50% improvements (Table 1, Figure 1). The mean improvement scores by physicians were 1.7 ± 1.0 for 1.5-mm transducer and 1.9 ± 0.8 for 3.0-mm transducer, respectively ($p = 0.903$).

Cutometric measurement demonstrated significant improvements in skin elasticity following IFUS treatments. In the sides treated with 1.5-mm transducer, R2 values were significantly increased from 0.849 ± 0.01 at baseline to 0.897 ± 0.02 at 6 weeks after treatment ($p < 0.05$, Figure 2A). R5 and R7 values were also increased at 6 weeks, respectively, however, there was no statistical significance (Figure 2B and C). R2 and R7 values of the sides treated with 3.0-mm transducer were significantly increased from 0.858 ± 0.02, 0.366 ± 0.05 at baseline to 0.909 ± 0.03, 0.395 ± 0.04 at 6 weeks after treatment ($p < 0.05$, Figure 2A and C), indicating that IFUS using 3.0-mm transducer improves the two main parameters of skin elasticity. Furthermore, the clinical improvement grades assessed by physicians in all sites treated with IFUS using both transducers were significantly correlated to the % changes in R2 values (Spearman's $\rho = 0.402$, $p < 0.01$) (Figure 3).

Sebum levels decreased following one session of IFUS, from $44.23 \pm 5.03\,\mu g/cm^2$ and $41.68 \pm 15.26\,\mu g/cm^2$ at baseline to $35.78 \pm 6.04\,\mu g/cm^2$ and $34.52 \pm 14.22\,\mu g/cm^2$ at 6 weeks post treatment using 1.5-mm and 3.0-mm transducer (Figure 4), respectively, but these were not statistically significant.

Subjects' assessment of pore improvement showed that nearly half of the subjects (45.4% and 45.5% for 1.5-mm and 3.0-mm transducer, respectively) reported to be satisfied or very satisfied (Figure 5).

Most subjects experienced transient erythema or edema immediately after treatment. No severe pain but feeling of tightness that lasts about 1–2 weeks was reported in the 3.0-mm transducer-treated sites in six subjects. Edematous striations were noted in the 1.5-mm transducer-treated sites in four subjects, however, the swelling disappeared within 2 weeks. Other possible adverse events such as persistent erythema, bruising, post-inflammatory hyperpigmentation, or numbness were not observed.

Discussion

Loss of skin elasticity and enlarged pores are age-related changes, which can be treated with various skin rejuvenation treatments.

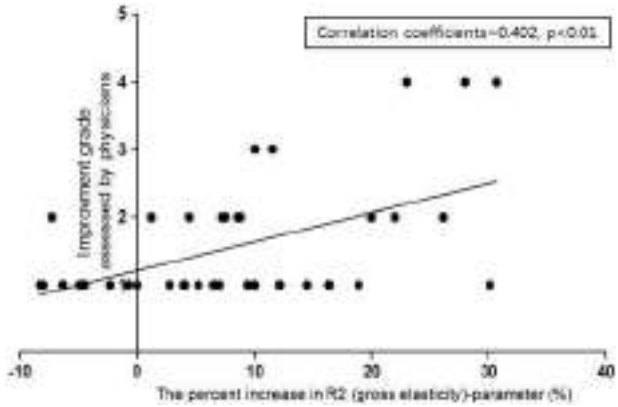


Figure 3. Correlation between the physician's global assessment scores on pore improvements and the percent increase in skin elasticity parameter following IFUS treatment at 6 weeks post-treatment. The association was tested by calculating Spearman's rank order correlation coefficient. A p value < 0.01 was considered to be statistically significant.

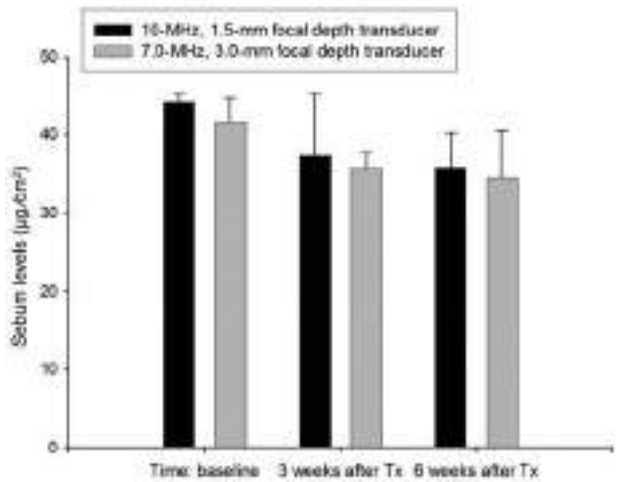


Figure 4. Changes in the sebum production as measured by Sebumeter following a single session of IFUS treatment using 1.5-mm and 3.0-mm transducers at baseline and at 3 and 6 weeks post-treatment. Results represent mean ± standard deviation. A p value < 0.05 was considered to be statistically significant.

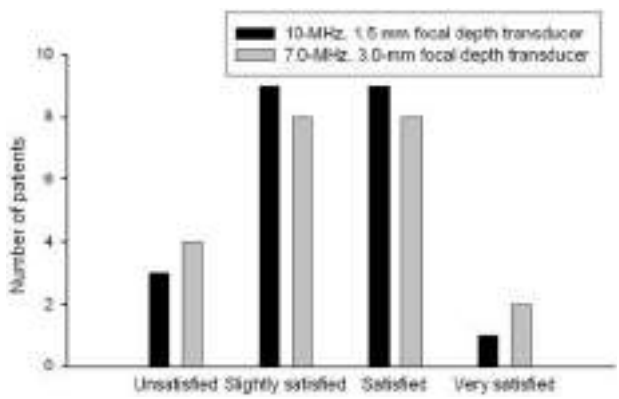


Figure 5. Subjective satisfaction rates after a single session of IFUS treatment using 1.5-mm and 3.0-mm transducers at 6 weeks after treatment.

Our study demonstrated that a single session of IFUS treatment using 1.5-mm or 3.0-mm focal depth transducer is effective for improving the appearance of enlarged pores.

Using the Cutometer, we also demonstrated that IFUS using 1.5-mm or 3.0-mm transducer caused a significant increase in skin elasticity over 6 weeks after treatment. In addition, a positive strong correlation between the clinical pore improvement scores and the post-treatment changes in R2 values suggests that IFUS-induced dermal regeneration and subsequent increases in skin elasticity are major mechanisms involving pore shrinkage and clinical improvement in pore appearance following IFUS.

Previously, Roh et al. (6) reported that five sessions of treatment with Q-switched or long-pulsed 1064 nm Nd:YAG laser were effective in reducing pores and sebum level, suggesting that reducing sebum production may be another possible mechanism of treating pores. We also postulated that IFUS-induced thermal damage may affect sebaceous glands, however, sebum production in both sides of the face showed a slight but statistically insignificant decrease at 6 weeks after treatment compared to baseline. From our results, we suggest that the effect of IFUS on enlarged pores may be attributed to the dermal remodeling at perifollicular area and increased skin elasticity rather than a decrease in sebum secretion. However, thermal injury-induced dermal remodeling may occur for up to 6 months, therefore, further studies are needed to determine the long-term effect of IFUS on the sebum production.

We would like to note that, in our study, a single session of IFUS treatment showed significant objective and subjective improvements in pores along with increased skin elasticity, whereas, in previous studies (5–9) using non-ablative laser resurfacing methods, three to five sessions of treatment were required to produce satisfactory clinical results. In addition, our subjects were all Asian with Fitzpatrick skin type III–IV, however, there were no noticeable adverse events such as post-treatment hyperpigmentation. Different from light-based laser devices, focused ultrasound energy is not selectively absorbed by chromophores such as melanin and hemoglobin (13), suggesting that IFUS may be relatively safe in treating darker skin types. Although our results showed that IFUS treatment improved the enlarged pores along with the increased skin elasticity at 6 weeks after the treatment, a long-term follow-up study is needed to determine the lasting effects of IFUS on reducing pores.

In conclusion, we suggest that IFUS treatment using 1.5-mm or 3.0-mm transducer is safe and effective for improving the appearance of enlarged facial pores with an improvement in skin elasticity in Asian skin.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

References

1. Uhoda E, Piérard-Franchimont C, Petit L, Piérard GE. The conundrum of skin pores in dermocosmetology. Dermatology. 2005;210:3–7.
2. Kim BY, Choi JW, Park KC, Youn SW. Sebum, acne, skin elasticity, and gender difference - which is the major influencing factor for facial pores? Skin Res Technol. 2013;19:e45–53.
3. Phillips TJ, Gottlieb AB, Leyden JJ, et al.; Tazarotene Cream Photodamage Clinical Study Group. Efficacy of 0.1% tazarotene cream for the treatment of photodamage: a 12-month multicenter, randomized trial. Arch Dermatol. 2002;138:1486–93.
4. Grimes PE. The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. Dermatol Surg. 1999;25:18–22.
5. Lee CN, Kim YJ, Lee HS, Kim HS. Effects of Q-switched and long-pulsed 1064 nm Nd:YAG laser on enlarged facial pores. Photodermatol Photoimmunol Photomed. 2009;25:328–30.

6. Roh MR, Chung HJ, Chung KY. Effects of various parameters of the 1064 nm Nd:YAG laser for the treatment of enlarged facial pores. J Dermatolog Treat. 2009;20:223–8.
7. Wattanakrai P, Rojhirunsakool S, Pootongkam S. Split-face comparison of long-pulse-duration neodymium-doped yttrium aluminum garnet (Nd:YAG) 1,064-nm laser alone and combination long-pulse and Q-switched Nd:YAG 1,064-nm laser with carbon photoenhancer lotion for the treatment of enlarged pores in Asian women. Dermatol Surg. 2010;36:1672–80.
8. Saedi N, Petrell K, Arndt K, Dover J. Evaluating facial pores and skin texture after low-energy nonablative fractional 1440-nm laser treatments. J Am Acad Dermatol. 2013;68:113–18.
9. Cho SB, Lee JH, Choi MJ, et al. Efficacy of the fractional photothermolysis system with dynamic operating mode on acne scars and enlarged facial pores. Dermatol Surg. 2009;35:108–14.
10. Cho SI, Chung BY, Choi MG, et al. Evaluation of the clinical efficacy of fractional radiofrequency microneedle treatment in acne scars and large facial pores. Dermatol Surg. 2012;38:1017–24.
11. Goldberg DJ, Silapunt S. Histologic evaluation of a Q-switched Nd:YAG laser in the nonablative treatment of wrinkles. Dermatol Surg. 2001;27:744–6.
12. Schmults CD, Phelps R, Goldberg DJ. Nonablative facial remodeling: erythema reduction and histologic evidence of new collagen formation using a 300-microsecond 1064-nm Nd:YAG laser. Arch Dermatol. 2004;140:1373–6.
13. Laubach HJ, Makin IR, Barthe PG, et al. Intense focused ultrasound: evaluation of a new treatment modality for precise microcoagulation within the skin. Dermatol Surg. 2008;34:727–34.
14. White WM, Makin IR, Barthe PG, et al. Selective creation of thermal injury zones in the superficial musculoaponeurotic system using intense ultrasound therapy: a new target for noninvasive facial rejuvenation. Arch Facial Plast Surg. 2007;9:22–9.
15. White WM, Makin IR, Slayton MH, et al. Selective transcutaneous delivery of energy to porcine soft tissues using Intense Ultrasound (IUS). Lasers Surg Med. 2008;40:67–75.
16. Alam M, White LE, Martin N, et al. Ultrasound tightening of facial and neck skin: a rater-blinded prospective cohort study. J Am Acad Dermatol. 2010;62:262–9.
17. Suh DH, Shin MK, Lee SJ, et al. Intense focused ultrasound tightening in Asian skin: clinical and pathologic results. Dermatol Surg. 2011;37:1595–602.
18. Lee HS, Jang WS, Cha YJ, et al. Multiple pass ultrasound tightening of skin laxity of the lower face and neck. Dermatol Surg. 2012;38:20–7.
19. Gliklich RE, White WM, Slayton MH, et al. Clinical pilot study of intense ultrasound therapy to deep dermal facial skin and subcutaneous tissues. Arch Facial Plast Surg. 2007;9:88–95.

Seminars in
Cutaneous
Medicine
and Surgery

Microfocused Ultrasound for Skin Tightening

Jennifer L. MacGregor, MD,* and Elizabeth L. Tanzi, MD†

The demand for noninvasive skin tightening procedures is increasing as patients seek safe and effective alternatives to aesthetic surgical procedures of the face, neck, and body. Over the past decade, radiofrequency and infrared laser devices have been popularized owing to their ability to deliver controlled heat to the dermis, stimulate neocollagenesis, and effect modest tissue tightening with minimal recovery. However, these less invasive approaches are historically associated with inferior efficacy so that surgery still remains the treatment of choice to address moderate to severe tissue laxity. Microfocused ultrasound was recently introduced as a novel energy modality for transcutaneous heat delivery that reaches the deeper subdermal connective tissue in tightly focused zones at consistent programmed depths. The goal is to produce a deeper wound healing response at multiple levels with robust collagen remodeling and a more durable clinical response. The Ulthera device (Ulthera, Inc, Meza, AZ), with refined microfocused ultrasound technology, has been adapted specifically for skin tightening and lifting with little recovery or risk of complications since its introduction in 2009. As clinical parameters are studied and optimized, enhanced efficacy and consistency of clinical improvement is expected.
Semin Cutan Med Surg 32:18-25 © 2013 Frontline Medical Communications

KEYWORDS microfocused ultrasound, noninvasive skin tightening

Facial and neck skin laxity has traditionally been addressed using surgical lifting techniques. Over the past decade, a wide range of nonsurgical treatments have emerged as an alternative to surgery. Procedures such as radiofrequency (RF) and ablative and fractional laser skin resurfacing provide variable degrees of tissue tightening through the delivery of controlled dermal heating. Although tissue tightening has been shown with these devices, several shortcomings exist, including inconsistent clinical results, extensive recovery requirements after the procedure, and the need for multiple treatment sessions.[1-7] As such, the need for additional noninvasive face and neck rejuvenation procedures with minimal recovery and consistent results that more closely mimic those of traditional surgical techniques continues. In 2009, microfocused ultrasound (MFUS) was introduced to deliver precise focused zones of thermal injury at treatment depths greater than the aforementioned technologies. The MFUS device may be uniquely suited to address the problem of skin laxity owing to its ability to deliver deep thermal energy at tissue planes in the subdermal connective tissue in addition to the superficial dermis to effect more complete collagen remodeling.

Evolution of Nonsurgical Technology and Mechanism of Action

Traditional ablative laser skin resurfacing with carbon dioxide or erbium:yttrium-aluminum-garnet devices selectively ablates the epidermis while delivering significant thermal injury to the dermis sufficient to stimulate a robust wound healing response with subsequent collagen remodeling and contraction.[1-3] However, traditional ablative laser skin resurfacing is associated with extensive postoperative recovery and risk of delayed dyspigmentation.[4] Modest skin tightening can also be induced by RF devices that rely on heat delivery up to 2-4 mm into the dermis to stimulate the wound healing cascade and neocollagenesis without epidermal injury and associated clinical recovery.[5-7] The benefits of this approach are clear—limited downtime, relative safety for use on nonfacial areas and skin of color, and a favorable side effect profile as compared with ablative laser skin resurfacing or surgical lifting procedures. Unfortunately, less invasive

*Union Square Laser Dermatology, Columbia University Medical Center, New York, NY.
†Washington Institute of Dermatologic Laser Surgery, Washington, DC.
Disclosures: The authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest and none were reported.
Correspondence: Elizabeth L. Tanzi, MD, Washington Institute of Dermatologic Laser Surgery, 1430 K Street, NW, Suite 200, Washington, DC 20005. E-mail: etanzi@skinlaser.com

approaches are historically associated with inferior efficacy, inconsistent clinical response, and a less durable tightening effect.

High-intensity focused ultrasound (HIFU) acoustic energy, known to propagate much deeper through tissue than laser or RF energy, has been previously investigated for use in bulk heating for the treatments of solid organ tumors[8-10] and recently adapted for the treatment of subcutaneous lipolysis.[11] The ultrasound waves penetrate into tissue, leading to vibration in molecules at the site of beam focus. The friction between tissue molecules produces heat and thermal injury at the focal site of the beam. Penetration depth is determined by frequency in which higher frequency waves produce a shallow focal injury zone and lower frequency waves have a greater depth of penetration to produce focal thermal injury zones (TIZs) at deeper layers. The treatment of solid organ tumors and adipocytes relies on bulk heating over a larger area (>1 cm^3) to accomplish tissue destruction through thermal effects and the cavitation process. In comparison with HIFU, MFUS allows for more precise energy delivery as a result of advances within the system to better address the needs of skin laxity.[12-14] For transcutaneous treatment, modifications of short pulse durations coupled with higher frequency transducers allow MFUS to deliver precise zones of coagulative necrosis, so-called TIZs. Each TIZ is tightly focused at a given depth and heated precisely using shorter pulses (<150 ms) to produce small zones (1 mm^3) of coagulative necrosis at the site with surrounding tissue and superficial layers essentially unaffected.[12-14] Similar to a laser pulse, the thermal injury is confined by keeping the pulse duration relatively short. The epidermal surface remains unaffected as long as the energy delivered is not excessive for the given focal depth and frequency emitted by a given transducer, eliminating the need for superficial cooling and speeding the recovery process, as healing occurs rapidly from untreated adjacent tissue.[13,14]

The MFUS device is able to penetrate deeper into tissue than its nonsurgical predecessors in an effort to affect superior tissue tightening and longevity of results by selectively targeting the superficial musculoaponeurotic system (SMAS). The SMAS lies deep to the subcutaneous fat, envelops the muscles of facial expression, and extends superficially to connect with the dermis.[15] The SMAS layer is composed of collagen and elastic fibers similar to the dermal layer of the skin; however, it has more durable holding property and less delayed relaxation after lifting procedures than skin alone.[15] Thus, the SMAS is a desirable target for noninvasive skin tightening procedures.

The Ulthera device (Ulthera, Inc, Meza, AZ) has refined MFUS technology using transducer handpieces uniquely capable of imaging mode (lower energy ultrasound for real-time imaging) and treatment mode (delivery of higher energy ultrasound exposures [Fig. 1]). The energy is delivered in a straight 2.5-cm line with TIZs 0.5-5 mm apart at a given depth within the tissue. Short pulse durations (25-50 ms) and relatively low energy (0.4-1.2 J, range depending on the transducer) confine the TIZs to their intended depth. The transducers are fixed at 7.5 MHz (3 and 4.5 mm focal depths) and 4.4 MHz (4.5 mm focal depth) frequencies. Most recently, a 19-MHz transducer capable of delivering TIZ at depths of 1.5 mm into the dermis was introduced to effect more superficial dermal neocollagenesis. Preclinical studies in cadaver, porcine, and prerhytidectomy excision skin have confirmed consistency in the depth, size, and orientation of TIZ created by MFUS in the deep dermis and SMAS (Fig. 2).[12-14,16]

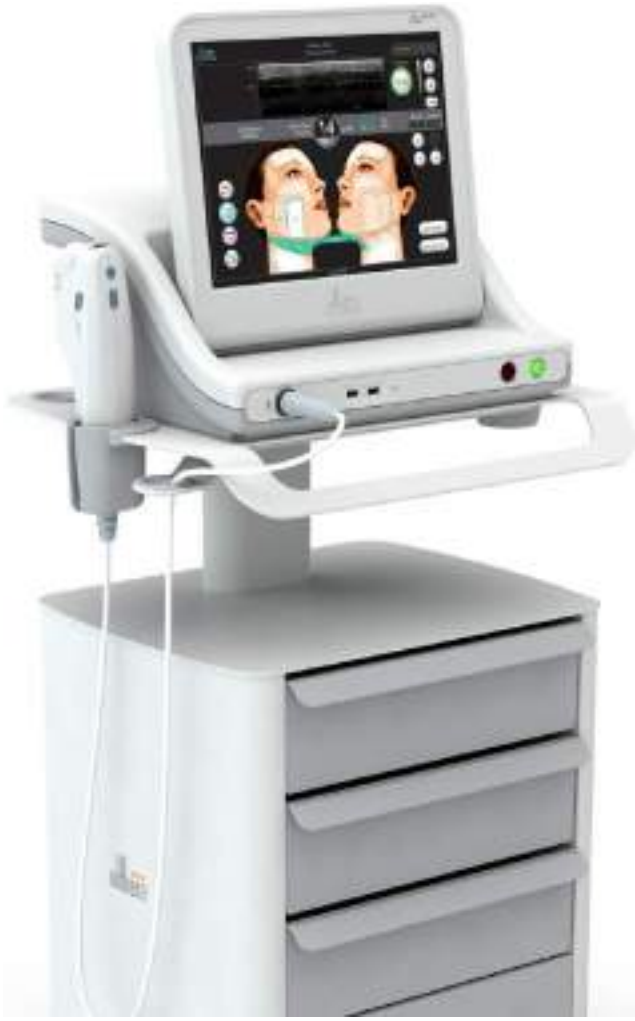


Figure 1 Ulthera microfocused ultrasound device.

Clinical Use for Skin Tightening

Early clinical and preclinical work led to Food and Drug Administration approval of the MFUS device in 2009 for eyebrow lifting. Eyebrow lifting is straightforward to measure using standardized photography, whereas lower face and neck tightening are more difficult to quantify, given the lack of an established and objective grading scale for evaluation of improvement.[17,18] Early studies quantify lower face and neck tightening with a subjective rating of "improved" reported by patient self-assessment and blinded physicians.[19,20] However, subsequent studies and off-label use in the lower face and neck that yielded consistent results led to a Food and

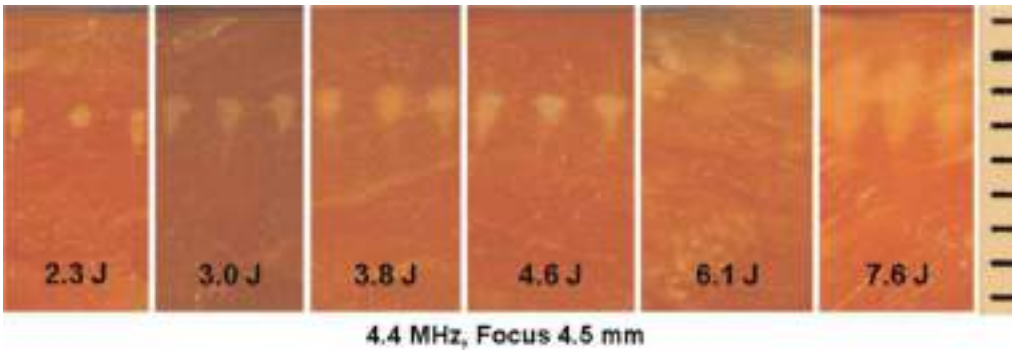


Figure 2 Geometry of thermal injury zones in porcine muscle as delivered energy is increased from 2.3 to 7.6 J. The inverse cone-shaped lesions demonstrate consistent size, depth, and spacing of coagulative necrosis. (Reprinted from White, et al.,[12] with permission, Wiley Periodicals.)

Drug Administration approved indication for "noninvasive lift of lax tissue of the neck and submentum" in 2012.[21]

Alam et al[17] conducted the first clinical study of full-face and neck MFUS treatment in 35 patients, looking at safety and efficacy. In standardized photographs, 86% of the patients achieved significant improvement as measured by blinded physician assessment. Photographic measurements demonstrated a mean brow lift of 1.7 mm.

Chan et al[22] evaluated the safety of MFUS skin tightening in 49 Chinese patients using an advanced protocol. All patients underwent full-facial and neck treatment without significant or persistent adverse effects. Suh et al[19] evaluated 22 Korean patients after full-face treatment and reported 91% of patients improved, as rated on a subjective scale where 1 = improved and 2 = much improved at the nasolabial fold and jaw line (1.77 and 1.72 average improvement, respectively). Skin biopsies obtained from 11 study subjects at baseline and 2 months after treatment confirmed an increase in reticular dermal collagen and dermal thickening, with elastic fibers appearing more parallel and straighter than pretreatment specimens.[19] Lee et al[20] reported subjective improvement in 9 of 10 patients by their own self-assessment, and 8 of 10 patients were rated as "improved" by blinded physician assessment. Suh et al[23] subsequently showed subjective improvement in most patients treated with a single pass to the lower infraorbital region in 15 patients treated with a 7-MHz 3-mm transducer.

Alster and Tanzi[24] established the first report of clinical efficacy in nonfacial areas. Paired sites in 18 women were evaluated on the arms, knees, or medial thighs where dual-plane treatment with the 4-MHz 4.5-mm-depth and 7-MHz 3-mm-depth transducer was compared with single-plane treatment with the 4-MHz 4.5-mm-depth transducer alone. Global assessment scores of skin tightening and lifting were determined by 2 blinded physician raters and graded using a quartile grading scale. At the 6-month follow-up visit, statistically significant improvement was seen at all 3 body sites, with the arms and knees demonstrating more noticeable improvement than thighs. Dual-plane treatment yielded additional benefit in smoothing skin texture, an effect potentially related to more superficial dermal collagen remodeling. When asked to rate their impression of clinical efficacy, 13 of 16 patients reported being "highly satisfied" with the treatment.

Sasaki and Tevez[21,25] have reported on their extensive experience with the use of MFUS for multiple indications. Using the new 19-MHz 1.5-mm superficial transducer, they treated 19 patients in the periorbital region with 45 lines on each side, with another 45 lines using the 7-MHz 3-mm as

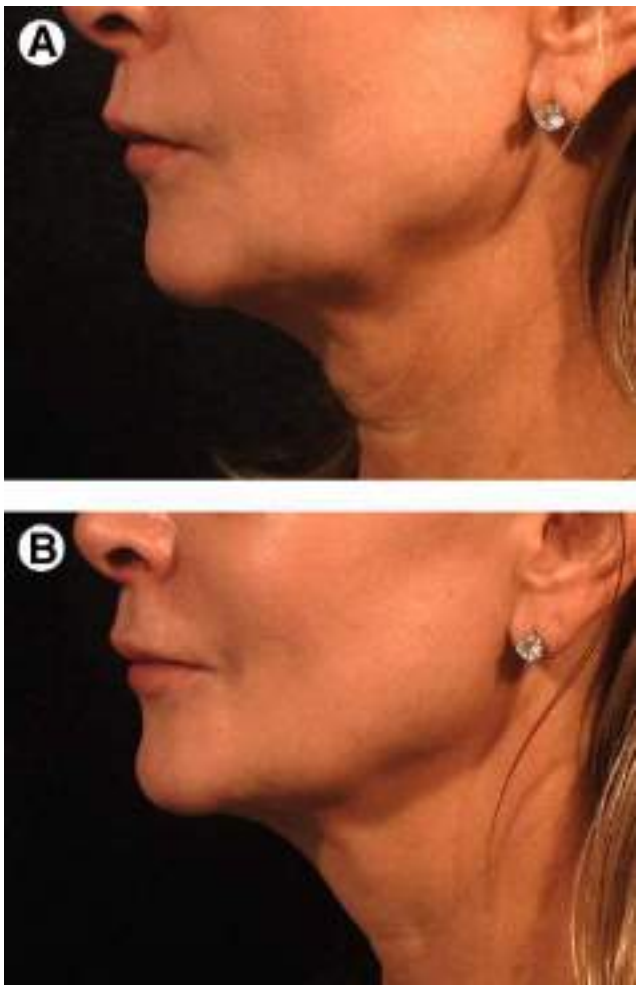


Figure 3 Neck before (**A**) and 6 months after (**B**) a single microfocused ultrasound treatment of the cheeks and neck.

Figure 4 Periocular area before (**A**) and 6 months after (**B**) a single microfocused ultrasound treatment of the brow.

the second depth over the orbital rim.[25] Brow elevation was measured between 1 and 2 mm in each of 19 patients treated, and periorbital skin tightening was rated as moderate between a 3- and 6-month period. Body sites treated in this study included décolletage (5), brachium (44), periumbilicus (6), inner thigh (1), knee (4), hand (1), and buttocks (2). Treatment protocols varied according to skin thickness at the target site. Blinded evaluator assessment scores revealed moderate improvement in the periorbital area, inner brachium, periumbilicus, and knees. Less consistent results were achieved in the décolletage, inner thighs, hands, and buttocks. In a larger series of pilot studies and clinical investigations, the authors compared horizontal and vertical vectors in the brow and marionette regions while keeping depth and energy constant.[21] Vertical vectors were superior in all sites and energy settings evaluated. They also evaluated a larger number of patients to confirm that a higher number of lines and joules would yield significantly superior results at all areas treated. In total, 193 patients were included in the investigations.[21]

Recent presentations at scientific meetings have included additional data supporting efficacy for MFUS treatment of wrinkling around the knee,[26] tightening of the neck,[27] décolletage,[28] and buttock,[29] and the potential to treat axillary hyperhidrosis.[30] Future directions of research include its potential to induce scar remodeling, which would be particularly useful in deep or contracted scars. MFUS has also been reported to soften silicone and associated scarring of the lip.[31] The potential for anti-inflammatory effect and possible use in acneiform disorders is also a current subject of investigation.

Patient Selection and Preparation

The ideal patient for nonsurgical tissue tightening displays mild to moderate skin and soft tissue laxity (Figs. 3 and 4). Severe skin laxity, marked platysmal banding, severe jowling, and low cervicomental angle are problems best addressed by surgical interventions. In the authors' experience, younger patients are more likely to have a good outcome with MFUS, as the wound healing response to thermal injury is vigorous. By contrast, patients with excessively photodamaged skin or a history of smoking are less favorable candidates, as their ability to create collagen in response to thermal injury may be inadequate. The few absolute contraindications include active infection or open skin at the treatment site, cystic acne, and pregnancy. Relative contraindications include medical conditions and medications that alter or impair wound healing.

Another relative contraindication to MFUS skin tightening is the patient with unrealistic expectations of treatment. The overall rate of nonresponse in current published clinical studies is <20%, with the clear advantage of MFUS being a safe and effective alternative to surgical lifting or ablative laser resurfacing with minimal to no recovery. However, clinical improvements are often subtle and do not approach those of surgical lifting procedures. Indeed, modest tightening may be satisfactory for 1 patient, whereas similar improvement would leave another dissatisfied with the procedure. Therefore, before treatment, high-quality medical photographs must be obtained and used in conjunction with a candid physician–patient discussion that includes realistic expecta-

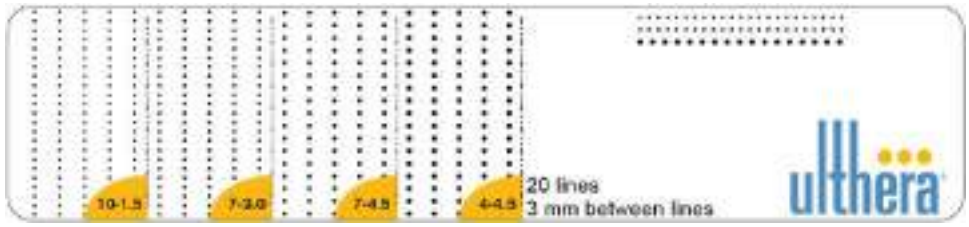


Figure 5 Card for preoperative planning of line placement and marking.

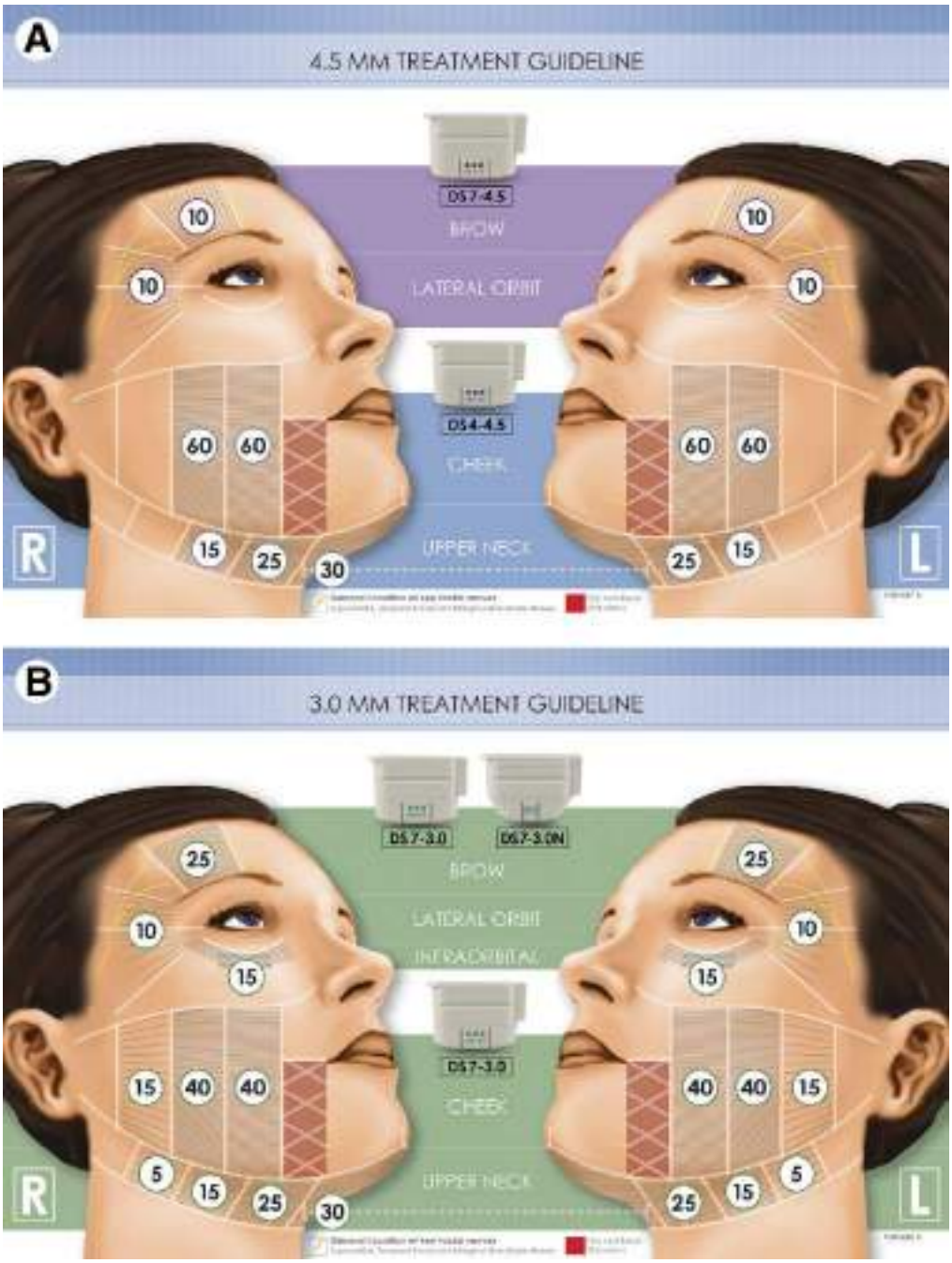


Figure 6 Diagram of dual-plane treatment guidelines. Treatment suggestions for a deep 4.5-mm focal depth transducer (**A**) followed by a superficial 3.0-mm focal depth superficial transducer (**B**). (Reprinted from Ulthera treatment guidelines, Ulthera, Mesa, AZ; with permission.)

tions of improvement, maintenance requirements, limitations in achieving the patient's goal of "lifting" the tissues without surgery, and the possibility of no appreciable clinical improvement.

As with any heat-based cosmetic procedure, there are variable degrees of discomfort associated with MFUS skin tightening. Preoperative planning should include a discussion of the patient's historical pain tolerance and response to anxiolytic and narcotic pain medications. Individual published reports of pain in response to the treatment range from mild to severe. Sufficient pain management is critical to an effective outcome and the overall treatment experience for the patient. As such, the authors use a combination of oral anxiolytics (5-10 mg of diazepam) and intramuscular narcotics (50-75 mg of IM meperidine) 20-30 minutes before treatment to alleviate discomfort in most patients. Other methods of pain management have been described, including high-dose nonsteroidal anti-inflammatory drugs, oral or intravenous narcotics, topical or local injections of anesthetics, conscious sedation, and cold techniques.[32] The deeper probe and higher energy delivery is associated with increased pain. For superficial treatment of periocular and perioral rhytides us-

Table 1 Complications of Microfocused Ultrasound

Mild/Transient	Moderate	Severe/ Prolonged
Erythema	Transient dysesthesia	None reported
Purpura	Motor nerve paresis	
Postinflammatory hyperpigmentation		
Geometrical wheals or striations		
Subcutaneous nodules		
Edema		

ing the 1.5-mm-depth transducer, topical anesthesia alone may effectively lessen treatment-associated discomfort.

Operative Technique

Four transducers are available for transcutaneous treatment using the MFUS device. These interchangeable dual-functioning transducers are labeled according to their frequency and focal treatment depth. They include 4-MHz 4.5-mm focal depth (0.75-1.2 J), 7-MHz 4.5-mm focal depth (0.75-1.05 J), 7-MHz 3-mm focal depth (0.4-0.63 J), and 19-MHz 1.5-mm focal depth (0.15-0.25 J). In general, the areas with the thinnest skin, such as the neck and periocular area, should be treated with superficial depth probes; the brow and temple should be treated with superficial and deeper probes; and cheek and submental skin is best treated with the deepest 4-MHz 4.5-mm probe followed by additional treatment with a superficial probe. Multiple treatment protocols using single-, double-, and even triple-depth treatment planes have been reported, and the parameters continue to be refined in different treatment protocols to enhance efficacy. The technique of layering multiple depths of TIZs throughout the treatment area enhances efficacy in both facial and nonfacial treatment sites.[21,24,25]

Before treatment, the skin is freshly cleansed, dried, and cleared free of makeup, sunscreen, or products. Each targeted region for treatment is outlined with a planning card to determine the number of treatment columns required to deliver energy with minimal overlap (Fig. 5). Ultrasound gel is applied to the skin, and the probe is placed firmly and gently on the target site so the entire transducer is evenly coupled to the skin surface. Correct technique is confirmed with visualization of acoustic coupling as seen on the ultrasound images on the monitor. Focal depth is visible on the screen in the corresponding ultrasound image and lined up with the deep dermis to SMAS, depending on the transducer and targeted site. Treatment lines of ultrasound pulses are manually delivered adjacent and parallel to one another with minimal spacing (<3 mm). The overall number of lines placed in a treatment area will depend on the size of the treatment area and chosen protocol (Fig. 6). The most advanced protocols call for the placement of 600-800 lines of ultrasound pulses when treating the full face. Until additional experience with a large cohort of patients confirms its safety, treatment over soft tissue augmentation material and implants should be approached with caution. Because there are no commercially available eye shields known to prevent propagation of ultrasound energy over the globe, treatment inside the orbital rim is not possible. The thyroid gland is palpated and marked before treatment to avoid inadvertent delivery of ultrasound pulses over the area.

Postoperative Management, Side Effects, and Complications

After treatment, ultrasound gel is removed and a bland moisturizer applied. Patients are instructed to care for their skin as they normally would with no restrictions on activity. If systemic pain management was used, the patient is discharged with appropriate transportation. If desired, the patient may apply cold compresses to the treatment area in the hours after the procedure to minimize local edema; however, its use is not mandatory in all patients, as degrees of swelling after treatment are variable.

Noninvasive skin tightening with MFUS produces relatively few expected side effects and transient complications (Table 1). Post-treatment erythema is expected in most patients and typically resolves in the first few hours to days.

Table 2 Prevention of Complications From Microfocused Ultrasound

Motor nerve paresis	Ask patient to report any facial muscle twitching during treatment near superficial motor nerves and apply ice to any red or inflamed areas after treatment
Forehead palsy	Avoid treatment over the temporal branch of the trigeminal nerve
Perioral palsy	Avoid treatment over the marginal mandibular nerve
Nodules	Use appropriate treatment density and technique as confirmed by corresponding ultrasound image on monitor
Bruising	Avoid treating patients on blood thinning medications and administering pulse directly to a visible vessel on the ultrasound image
White striations or geometrical wheals	Typically occur with superficial transducer—ensure proper coupling with corresponding ultrasound image before each pulse delivery

Figure 7 Diagram of proper distribution of line placement and "danger zones" over relative location of temporal branch of trigeminal and marginal mandibular nerves.

Small areas of purpura may develop and are expected to resolve over 1-2 weeks. Linear or geometrical striations seen after treatment with the superficial transducer are treated with topical corticosteroids and followed for rapid resolution.[17,19,21] No permanent textural changes from these lesions have been reported. Lingering mild to moderate skin tenderness and edema in the first 1-4 weeks after treatment is common.[22,24] Transient postinflammatory pigmentation was observed in 2 Chinese patients treated over the brow, but was most likely related to placement of the deep 4-MHz 4.5-mm transducer and was not observed in subsequent treatments.[22] Focal areas of numbness on the brow or perioral area can occur with return of full sensation within several weeks without intervention.[19,21,22]

Although uncommon, more serious complications after MFUS skin tightening can occur, including the development of palpable subcutaneous nodules and/or motor nerve paresis.[33] Fortunately, these effects are temporary and can be avoided with proper operative technique (Table 2). Motor nerve paresis is the most concerning potential complication in the immediate post-treatment period, and its incidence is limited to case reports. The areas at the greatest risk for injury are the temporal branch of the trigeminal nerve as well as the marginal mandibular nerve, where the course of the nerve becomes relatively superficial (Fig. 7). The affected patient will present with an inability to contract the frontalis muscle or perioral asymmetry. Symptoms usually occur within the first 1-12 hours after treatment and are likely related to nerve inflammation. Resolution is expected in 2-6 weeks, and no permanent nerve injury has been reported to date.[33] For patients who notice facial muscle twitching during treatment near "danger zone" regions, ice should be immediately applied and anti-inflammatory medication considered.

Conclusions

MFUS is capable of delivering transcutaneous ultrasound energy to selectively heat dermal and subdermal tissues in a linear array of tightly focused TIZs. As superficial and surrounding tissue is unaffected, rapid clinical recovery is coupled with a favorable side effect profile. Initiation of the wound healing response with subsequent neocollagenesis and tissue contraction leads to gradual lifting and tightening of the skin. As clinical parameters are studied and optimized, enhanced efficacy and consistency of clinical improvement is expected. Future applications and current areas of investigation for MFUS include the targeting of adnexal structures for acne, rosacea, and hyperhidrosis, as well as expanded use for nonfacial skin tightening.

References

1. Ross EV, McKinlay JR, Anderson RR. Why does carbon dioxide resurfacing work? A review. *Arch Dermatol*. 1999;135:444-454.
2. Ross EV, Naseef GS, McKinlay JR, et al. Comparison of carbon dioxide laser, erbium:YAG laser, dermabrasion and dermatome: A study of thermal damage, wound contraction and wound healing in a live pig model: Implications for skin resurfacing. *J Am Acad Dermatol*. 2000;42: 92-105.
3. Fitzpatrick RE, Rostan EF, Marchell N. Collagen tightening induced by carbon dioxide laser versus erbium:YAG laser. *Lasers Surg Med*. 2000; 27:395-403.
4. Tanzi EL, Lupton JR, Alster TS. Lasers in dermatology: Four decades of progress. *J Am Acad Dermatol*. 2003;49:1-31.
5. Alster TS, Tanzi E. Improvement of neck and cheek laxity with a nonablative radiofrequency device: A lifting experience. *Dermatol Surg*. 2004; 30:503-507.
6. Zelickson BD, Kist D, Bernstein E, et al. Histological and ultrastructural evaluation of the effects of a radiofrequency-based nonablative dermal remodeling device: A pilot study. *Arch Dermatol*. 2004;140:204-209.
7. Arnoczky SP, Aksan A. Thermal modification of connective tissues: Basic science considerations and clinical implications. *J Am Acad Orthop Surg*. 2000;8:305-313.
8. Kennedy JE, ter Haar GR, Cranston D. High intensity focused ultrasound: Surgery of the future? *Br J Radiol*. 2003;76:590-599.
9. Mast TD, Makin IR, Faidi W, et al. Bulk ablation of soft tissue with intense ultrasound (IUS): Modeling and experiments. *J Acoust Soc Am*. 2005;118:2715-2724.
10. Van Leenders GJ, Beerlage HP, Ruijter ET, et al. Histopathological changes associated with high intensity focused ultrasound (HIFU) treatment for localised adenocarcinoma of the prostate. *J Clin Pathol*. 2000;53:391-394.
11. Fatemi A. High-intensity focused ultrasound effectively reduces adipose tissue. *Semin Cutan Med Surg*. 2009;28:257-262.
12. White WM, Makin IR, Slayton MH, et al. Selective transcutaneous delivery of energy to porcine soft tissues using intense ultrasound (IUS). *Lasers Surg Med*. 2008;40:67-75.
13. White WM, Makin IR, Barthe PG, et al. Selective creation of thermal injury zones in the superficial musculoaponeurotic system using intense ultrasound therapy: A new target for noninvasive facial rejuvenation. *Arch Facial Plast Surg*. 2007;9:22-29.
14. Laubach HJ, Makin IR, Barthe PG, et al. Intense focused ultrasound: Evaluation of a new treatment modality for precise microcoagulation within the skin. *Dermatol Surg*. 2008;34:727-734.
15. Har-Shai Y, Bodner SR, Egozy-Golan D, et al. Mechanical properties

and microstructure of the superficial musculoaponeurotic system. *Plast Reconstr Surg*. 1996;98:59-70.
16. Gliklich RE, White WM, Slayton MH, et al. Clinical pilot study of intense ultrasound therapy to deep dermal facial skin and subcutaneous tissues. *Arch Facial Plast Surg*. 2007;9:88-95.
17. Alam M, White LE, Martin N, et al. Ultrasound tightening of facial and neck skin: A rater-blinded prospective cohort study. *J Am Acad Dermatol*. 2010;62:262-269.
18. Weiss M. Commentary: Noninvasive skin tightening: Ultrasound and other technologies: Where are we in 2011? *Dermatol Surg*. 2012;38:28-30.
19. Suh DH, Shin MK, Lee SJ, et al. Intense focused ultrasound tightening in Asian skin: Clinical and pathologic results. *Dermatol Surg*. 2011;37: 1595-1602.
20. Lee HS, Jang WS, Cha YJ, et al. Multiple pass ultrasound tightening of skin laxity of the lower face and neck. *Dermatol Surg*. 2012;38:20-27.
21. Sasaki GH, Tevez A. Clinical efficacy and safety of focused-image ultrasonography: A 2-year experience. *Aesthet Surg J*. 2012;32:601-612.
22. Chan NP, Shek SY, Yu CS, et al. Safety study of transcutaneous focused ultrasound for non-invasive skin tightening in Asians. *Lasers Surg Med*. 2011;43:366-375.
23. Suh DH, Oh YJ, Lee SJ, et al. Intense focused ultrasound tightening for the treatment of infraorbital laxity. *J Cosmet Laser Ther*. 2012;14:290-295.
24. Alster TS, Tanzi EL. Noninvasive lifting of arm, thigh, and knee skin with transcutaneous intense focused ultrasound. *Dermatol Surg*. 2012; 38:754-759.
25. Sasaki GH, Tevez A. Microfocused ultrasound for nonablative skin and subdermal tightening to the periorbitum and body sites: Preliminary report on eighty-two patients. *J Cosmet Dermatol Sci Appl*. 2012; 2:108-116.
26. Gold MH. Ulthera—A single center, prospective study on the efficacy of the micro-focused ultrasound for the non-invasive treatment of skin wrinkles above the knee. Data Presented at the American Society for Dermatologic Surgery Meeting, Atlanta, GA, 2012.
27. Elm KDL, Schram SE, Wallander ID, et al. Evaluation of a high intensity focused ultrasound system for lifting and tightening of the neck. Data Presented at the American Society for Dermatologic Surgery Meeting, Atlanta, GA, 2012.
28. Fabi SG, Massaki A, Goldman M. Evaluation of the micro-focused ultrasound system for lifting and tightening of the décolletage. Data Presented at the American Society for Dermatologic Surgery Meeting, Atlanta, GA, 2012.
29. Goldberg D, Al-Dujaili Z. Micro-focused ultrasound for lifting and tightening skin laxity of the buttock. Data Presented at the American Society for Dermatologic Surgery Meeting Atlanta, GA, 2012.
30. Nestor MS. Micro-focused ultrasound for the treatment of axillary hyperhidrosis. Data Presented at the American Society for Dermatologic Surgery Meeting, Atlanta, GA, 2012.
31. Kornstein AN. Ulthera for silicone lip correction. *Plast Reconstr Surg*. 2012;129:1014e-1015e.
32. Brobst RW, Ferguson M, Perkins SW. Ulthera: Initial and six month results. *Facial Plast Surg Clin North Am*. 2012;20:163-176.
33. Missel L. Prevention of potential adverse events associated with use of Ulthera device. *Tech Bull*, 2011.

jected to the described procedure with the natural shape and configuration of their ears (Fig. 1).

The place of incision is difficult to see because it is hidden on the posterior side of the ear, in the sulcus formed by the helical fossa. After surgery, none of our patients had the prominence of the upper part of the ear as a complication.

We place the incision high at the level of retroauricular projection of the fossa helicis so that it is more difficult to notice. In our opinion, excessive retroauricular skin excision should be avoided; otherwise, it will make the auricle tense and the incision visible. We thin out the cartilage by trimming it to make it more compliant, and remove all sharp margins, deepening and modeling the triangular fossa so that the auricle assumes its normal and natural-appearing configuration.

Using this technique, we can very easily shape the cartilage, bringing it into the natural configuration. The prominence of the ear is efficiently resolved by a Y-shaped incision in the region of the new antihelix and the anterior and posterior crura, and subsequent shaping and modeling of the configuration of the cartilage by trimming.

DOI: 10.1097/PRS.0b013e31828278e0

Milan D. Jovanović, M.D., Ph.D.

Miodrag M. Colić, M.D., Ph.D.

Lukas Rasulić, M.D., Ph.D.

Department of Plastic and Reconstructive Surgery
University of Belgrade School of Medicine, and
Institute for Burns, Plastic, and Reconstructive Surgery
Clinical Center of Serbia
Belgrade, Serbia

Correspondence to Dr. Jovanovic
Belgrade University
Faculty of Medicine
Institute for Burns, Plastic, and Reconstructive Surgery
Clinical Centre of Serbia
Zvecanska 9
11000 Belgrade, Serbia
aes.surg@eunet.rs

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

PATIENT CONSENT

Parents or guardians provided written consent for use of the patient's images.

REFERENCES

1. Wolfe SA. Timing of otoplasty for prominent ears. *Plast Reconstr Surg.* 2006;117:680; author reply 680–681.
2. Mustarde JC. The correction of prominent ears by using simple mattress sutures. *Br J Plast Surg.* 1963;16:170–178.
3. Stenstrom SJ. A "natural" technique for correction of congenitally prominent ears. *Plast Reconstr Surg.* 1963;32:509–518.
4. Janz BA, Cole P, Hollier LH Jr, Stal S. Treatment of prominent and constricted ear anomalies. *Plast Reconstr Surg.* 2009;124:27e–37e.
5. Lentz AK, Plikaitis CM, Bauer BS. Understanding the unfavorable result after otoplasty: An integrated approach to correction. *Plast Reconstr Surg.* 2011;128:536–544.

Ultherapy Shrinks Nasal Skin after Rhinoplasty following Failure of Conservative Measures

Sir:

It can take months—and sometimes years—for nasal-tip edema to resolve after rhinoplasty, which can be challenging for patients and surgeons. Although various conventional modalities have been used to counteract edema, they are not successful for all skin types or in all situations.

With the advent of the Ultherapy Ulthera System (Ulthera, Inc., Mesa, Ariz.), the capability now exists to safely and reliably manipulate the contour of the skin to permit the skin to conform optimally to the underlying cartilaginous framework. Thus, the cartilage and skin can work in tandem to create a more ideal nasal-tip configuration.

During the past 18 months, the author has used Ultherapy to control edema and shape the nasal skin after rhinoplasty in 21 patients (19 women and two men, aged 22 to 66 years). Participants were required to have nasal skin types that typically are not amenable to conforming to underlying anatomical structures and thus would preclude an optimal result. The patients had previously undergone conservative attempts to reduce postoperative edema, which were not successful. All patients had been informed that Ultherapy is not a "proven" or U.S. Food and Drug Administration–approved modality for enhancing or expediting the results of rhinoplasty, but that it is U.S. Food and Drug Administration approved for facial skin tightening and brow elevation.

Ultherapy creates microthermal injury in the dermis and subdermis at depths of 1.5, 3, and 4.5 mm. Healing of these lesions, at the consistently spaced locations, leads to skin contraction, remodeling of scar tissue (revisional rhinoplasty), and, when desired, a degree of thermally induced subcutaneous fat loss.

The average number of treatments per patient was 2.1. The average time between rhinoplasty and the initial Ultherapy treatment was 3.22 years. Four nasal-tip skin types are anatomically limiting with respect to achieving optimal postrhinoplasty aesthetic results: large skin sleeve, thick skin sleeve, scarred skin sleeve, and C-shaped curvature. However, Ultherapy proved successful for three of these skin types (Figs. 1 through 3.) All patients were pleased with their result, as measured by a posttreatment survey, and there were no treatment-related adverse effects. Follow-up is ongoing to assess the durability of results, and a full clinical report is planned.

In the author's experience, Ultherapy has been particularly useful for patients who would typically be considered poor candidates for rhinoplasty because of the quality or quantity of their skin. The success achieved in the present series has led the author to use Ultherapy routinely in his practice to reduce tip edema following rhinoplasty.

Fig. 1. Large skin sleeve. (*Left*) Preoperative view of a 19-year-old model with a large skin sleeve who underwent open rhinoplasty with suture techniques on March 3, 2000. (*Center*) A pre-Ultherapy photograph, taken 11.5 years postoperatively, shows only subtle improvement. In addition to elastic taping (performed routinely for at least 3 weeks), this patient received four steroid injections over 19 months postoperatively. Ultherapy was performed on November 22, 2011 (11.5 years postoperatively). (*Right*) A post-Ultherapy photograph, taken 3 months after treatment, shows substantial reduction of edema and improvement in contour.

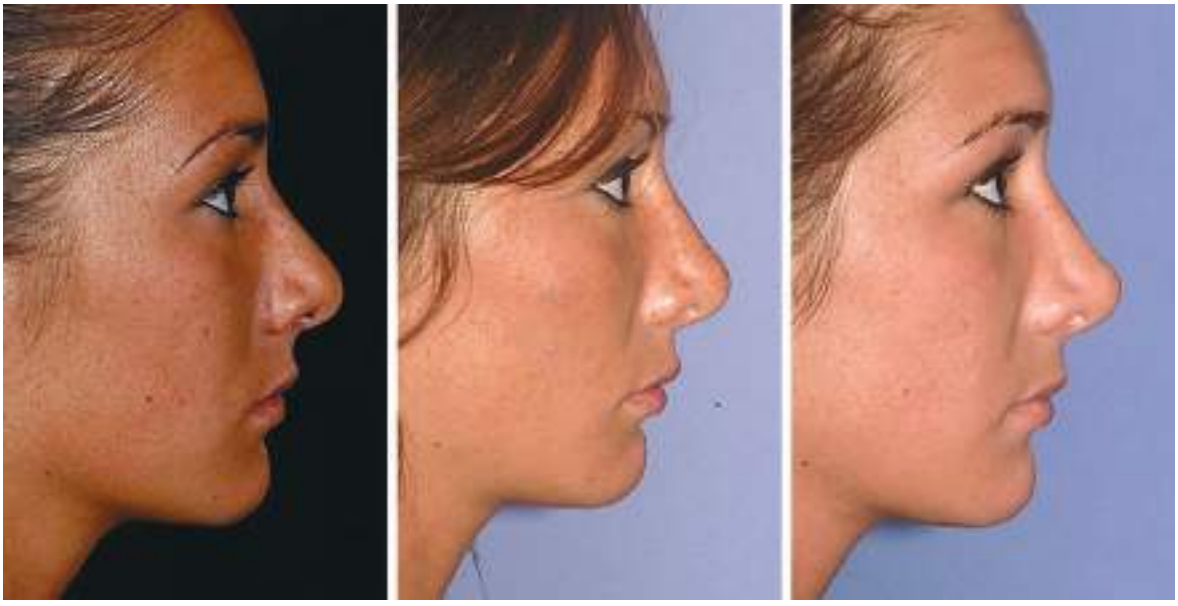


Fig. 2. Thick skin sleeve. (*Left*) Preoperative image of an 18-year-old woman who underwent secondary open rhinoplasty on August 4, 2008. The surgery included a "golf tee" graft for tip projection, definition, and control of a very thick skin sleeve. (*Center*) A pre-Ultherapy photograph, taken 3 years postoperatively, shows significant improvement but poor definition, and waxing and waning tip edema caused by poor skin contraction. Postoperatively, she received four steroid injections and two conventional external ultrasound treatments over 17 months. Ultherapy was performed twice between July 29, 2011, and January 4, 2012 (3 years postoperatively). (*Right*) A post-Ultherapy photograph, taken 4 months after treatment, shows marked improvement in definition.

Ultherapy's mechanism of action appears to be absolute shrinkage of the skin sleeve,[1–3] renewal of the cutaneous structure including enhanced elasticity,[4] and the ability to remodel scar tissue. Ultherapy also has been used successfully to reduce the size of silicone-injected lips nonsurgically. A proposed mechanism of action is remodeling of the silicone bead capsule.[5]

Fig. 3. Scarred skin sleeve from multiple rhinoplasties. (*Left*) Preoperative view of a 31-year-old woman who underwent open tertiary rhinoplasty including alar baton and crushed tip grafts on December 17, 2008. (*Center*) A pre-Ultherapy photograph, taken 18 months postoperatively, shows improved contour but poor definition. In addition to elastic taping, this patient received three steroid injections over 6 months, two radiofrequency treatments, and seven conventional external ultrasound treatments. Ultherapy was performed three times between November 14, 2011, and January 30, 2012 (3 years postoperatively). (*Right*) A postprocedure photograph, taken 4 months after the final Ultherapy treatment, shows substantial improvement in definition.

In postrhinoplasty patients, Ultherapy appears to "shrink wrap" the skin over the underlying cartilaginous framework. With this modality, rhinoplastic surgeons are able to control another anatomical element—the skin—to allow optimal sculpting of the central feature of the human face.

DOI: 10.1097/PRS.0b013e3182827966

Andrew N. Kornstein, M.D.
Museum Mile Surgery Center
1050 Fifth Avenue
New York, N.Y. 10028
info@kornstein.com

DISCLOSURE

The author has no financial interest to declare in relation to the content of this article. No funding was received for the preparation of this article.

PATIENT CONSENT

Patients provided written consent for the use of their images.

REFERENCES

1. White WM, Makin R, Barthe P, Slayton M, Gliklich RE. Selective creation of thermal injury zones in the superficial musculoaponeurotic system using intense ultrasound therapy. *Arch Facial Plast Surg.* 2007;9:22–29.
2. Hinz B. Formation and function of the myofibroblast during tissue repair. *J Invest Dermatol.* 2007;127:526–537.
3. Mulvaney M, Harrington A. Cutaneous trauma and its treatment. In: James WD, ed. *Military Dermatology (Textbook of Military Medicine).* Fort Detrick, Md: Department of the Army, Office of the Surgeon General, Borden Institute; 1994:143–156.
4. Suh DH, Shin MK, Lee SJ, et al. Intense focused ultrasound tightening in Asian skin: Clinical and pathologic results. *Dermatol Surg.* 2011;37:1595–1602.
5. Kornstein AN. Ulthera for silicone lip correction. *Plast Reconstr Surg.* 2012;129:1014e–1015e.

Regenerative Surgery for the Definitive Repair of Chronic Ulcers: A Series of 34 Cases Treated with Platelet-Derived Growth Factors

Sir:

Regenerative surgery is based on the use of stem cells and/or platelet-derived growth factors, which induce stem cell migration to the damaged tissues, stimulating their proliferation and eventually resulting in tissue repair. Platelet gel is a hemocomponent containing numerous growth factors that are potentially useful for tissue repair.[1] Platelet gel is used in oral bone implants[2] and in combined soft- and bony-tissue reconstruction in facial plastic surgery[3]; in tendon and muscle repair[4]; and in the treatment of difficult wounds, ulcers, and injuries.[5,6]

Thirty-four patients, aged 25 to 88 years, with chronic nonhealing ulcers were treated consecutively with platelet gel. Patient characteristics are listed in Table 1. Standard procedures (e.g., skin grafts or flaps) had already been performed to treat the ulcers, but failed.

Platelet concentrate, cryoprecipitate, and thrombin were obtained from 450 ml of whole blood. Platelet gel was prepared by adding 1 cm^3 of thrombin and then 1 cm^3 of calcium gluconate for every 10 ml of platelet concentrate/cryoprecipitate solution. After proper wound bed preparation, platelet gel was layered on the lesion and covered by a patch loaded with platelet-derived growth factors.

Journal of Cosmetics, Dermatological Sciences and Applications, 2012, 2, 108-116
http://dx.doi.org/10.4236/jcdsa.2012.222022 Published Online August 2012 (http://www.SciRP.org/journal/jcdsa)

Microfocused Ultrasound for Nonablative Skin and Subdermal Tightening to the Periorbitum and Body Sites: Preliminary Report on Eighty-Two Patients*

Gordon H. Sasaki[1#], Ana Tevez[2]

[1]Loma Linda University Medical School Private Practice, Pasadena, USA; [2]Sasaki Advanced Aesthetic Medical Center, Pasadena, USA.
Email: #ghsasakimd@drsasaki.com

Received June 30th, 2012; revised July 31st, 2012; accepted August 10th, 2012

ABSTRACT

Lax crepey skin is a major unsightly finding throughout the face and body that occurs from chronological aging and environmental photodamage. Surgical lifting procedures are unable to induce sufficient neocollagenesis and also associated with visible scars, risks and recovery time. In this preliminary report, non-invasive delivery of microfocused ultrasonic thermal coagulation points at two levels of the dermis outside the orbital rims was effective in reduction of crepey, wrinkled and sagging skin for about 1 ½ years in nineteen treated patients. Matched Orientation Mirror Imaging produced an average brow height elevation of 1 - 2 mm. Microfocused thermal coagulation points at multiple tissue levels also induced tissue tightening and reduction of crepey wrinkled skin in the décolletage, brachium, periumbilicus, inner thigh and knees. Investigator and Subject Global Aesthetic Improvement Scale graded responses that correlated to the severity of the degree of crepiness and laxity. Pain management during the procedure included the use of infiltration of local anesthesia. No permanent adverse events were observed. Further innovations in the current technology are needed for more effective and safer delivery of energy to improve the appearance of crepey and lax tissue in the head, neck and body.

Keywords: Crepey; Focused; Imaged; Ultrasound; Noninvasive; Lifting; Tightening

1. Introduction

Microfocused ultrasound energy has been shown to lift and tighten facial and neck skin and subdermal tissue [1,2] by delivering focal thermal coagulation points (TCP) below the skin's surface and targeting foundational layers without affecting intervening tissue [3-6]. These special characteristics present a suitable alternative treatment for thin, crepey and wrinkled eyelid skin outside the orbital rims, inner arm, décolletage, periumbilicus, inner thighs and knees whose management remains resistant to current modalities [7-10]. With the recent development of a 1.5 mm focal depth transducer, which deposits energy more superficially compared to the deeper 3.0 mm and 4.5 mm focal depth transducers, precise heating at three levels is possible now and may provide optimal temperatures for increased collagenesis and elastogenenesis to renew crepey skin.

The purposes of this contribution were 1) To evaluate the effects of dual levels of treatment depths to the dermis surrounding the eyelid skin outside the orbital rims; and 2) To report on the safety and efficacy to body sites with dermal and subdermal treatment depths.

2. Ultrasound System

The focused ultrasound device (FDA-approved September 2009) incorporates on a user interface screen in the visualization mode an ultrasound image of tissue layers to 8 mm depth. On activation of the selected transducer on the skin surface, a horizontal treatment line is displayed either at a 1.5 mm depth within the upper reticular dermis, 3.0 mm depth in the lower reticular dermis, or 4.5 mm depth within the subdermal levels, as determined by the present fixed focal depth of the 1.5 mm, 3.0 mm or 4.5 mm transducers. One of three transducers was chosen to achieve the designated treatment depths and desired amounts of distributed ultrasound energy (joule)/TCP: 1) DS 10 - 1.5 mm, 19 MHz (0.15 - 0.25 joules/TCP); 2) DS 7 - 3.0 mm, 7 MHz (0.25 - 0.45 joules/TCP; 3) DS 4 - 4.5mm, 4 MHz (0.75 - 1.2 joules/TCP. On activation

*Ulthera provided an unrestricted educational grant which was used to support publication costs.
#Corresponding author.

through contact gel, the 1.5 mm and 3.0 mm transducers released a maximum of 23 TCPs, spaced about 1.1 mm apart along a 25 mm line in the superficial and deeper level of the dermis, respectively. Likewise, the 4.5 mm transducer delivered a maximum of 17 TCPs, spaced 1.5 mm apart, along a 25 mm line in the deeper subdermal plane. About ninety-five percent of the vibratory energy creates friction between molecules, which produces an optimal 60˚C - 70˚C in a confined approximate 0.5 × 1.8 mm zone (TCP), depending on the transducer used, for collagen denaturation and eventual tissue tightening [11].

For treatment of crepey skin outside the orbital rims, the operator used a dedicated DS 10 - 1.5 mm, 10 MHz transducer (0.15 - 0.25 joules/TCP) and a DS 7 - 3.0 N mm narrow transducer (0.25 - 0.45 joules/TCP) which delivered a shorter treatment line of 14 mm (13 TCPs) to accommodate the anatomical boundaries of this treatment site. In all other areas, the operator dispensed the maximum treatment length of 25 mm and the highest amount of joules/TCP for potential maximal results.

3. Patient Selection

Adult patients were recruited from the site's data base. Inclusion criteria included mild-to-moderate crepey skin outside the orbital rims. These patients also exhibited mild-to-moderate ptosis of skin folds and orbital portions of the underlying fibro-muscular layer orbicularis oculi muscle. Patients with crepey skin at the décolletage, inner arm, periumbilicus, buttocks inner upper thighs, knees and hands were also included for treatment. Exclusion criteria included active local infections or skin diseases that might alter wound healing; acne or keloidal scarring; significant ptotic skin or subcutaneous fat; pregnant or breast-feeding women; recent ablative or nonablative skin procedures; and surgical procedures within a year to the proposed treatment sites.

4. Photographic and Statistical Analysis

A custom-designed Canfield photographic and lighting system (Canfield Scientific, Inc., Fairfield, NJ) was used for baseline and follow-up standardized photography. Matched Orientation Function of Mirror Software compared baseline to post-treatment distances (mm) between reference points for brow on a standardized facial positioning table for the vertical displacement of each brow (midpupil, lateral canthus, lateral tail of brow) from the intercanthal horizontal axis for the upper periorbital treatments. Each photographic image was automatically tagged with a specific label (metadata) that could not be altered. In each patient, the average of three vertical displacements of each brow (midpupil, lateral canthus, lateral tail of brow) from the intercanthal horizontal axis provided the database for comparison measurements for each subject. Disadvantages of employing the brow as a reference point for measurements were the inherent vagaries for mobile groomed structures. Standardized Photography compared baseline and post-treatment changes in crepiness to the upper and lower periorbital skin and the aforementioned body sites. The validated Fitzpatrick Wrinkle, Fold and Tissue Laxity Scale [12] was used to classify and score patients by two independent investigators: Class I mild, 1 - 3 score; Class II moderate, score 4 - 6; class III severe, score 7 - 9. Aesthetic efficacy from baseline to six months was rated by the same two independent investigators using the Investigator Global Aesthetic Improvement Scale (IGAIS) from standardized photographs (0 = no change; 1 = mild improvement; 2 = moderate improvement; and 3 = significant improvement. Patients used a Subject Global Aesthetic Improvement Scale (SGAIS): (0 = no change; 1 = mild changes; 2 = moderate changes; 3 = significant changes) to assess their results at the six month evaluation period. During their treatments, patients assessed their levels of heat-pain perception on a 10-point scale (0 = no pain; 1 - 4 = mild pain; 5 - 8 = moderate pain; 9 - 10 = severe pain).

5. Treatment Protocol

The usage of topical skin care products such as isotretinoin, glycolic and salicylic acids was discontinued about two weeks prior to treatment. Patients were reminded not to apply facial creams, lotions, powders and foundations on the treatment day. Patients washed their faces with a mild cleanser just prior to their procedure. All metal jewelry was removed from the facial area. Patients with a history of viral infections were placed on prophylactic antivirals two days before and six days after the procedure. Treatment was not recommended directly over those areas with mechanical implants or electrical devices and with soft tissue augmentation material.

After a thin layer of ultrasound transmission gel was applied to the transducer's window, the selected transducer was positioned on the designated treatment sector and activated for imaging of the skin and subdermal structures. On activation of the transducer, a series of thermal coagulation points were deposited at the selected tissue level in a straight line. This sequence was repeated within each treatment sector with the selected number, direction and depth of treatment lines, as recommended in the individualized maps (see below). The refrigerated ultrasound transmission gel was frequently reapplied to the transducer's window to ensure proper tissue imaging and coupling.

For patients who acknowledged their low pain threshold levels or experienced moderate discomfort during treatment, a pain management program was initiated in a

graded fashion beginning with oral non-steroidal anti-inflammatory drugs, pain and sedative medications, distractive hand/foot massages, reducing skin temperatures by an air coolant device, lowering the energy settings either by one level for each transducer, or shortening the length of treatment lines. The usage of topical analgesic gels for an hour prior to treatment lessened pain in a few patients. Finally, infiltration of buffered lidocaine was offered for pain relief during treatment in sensitive sites such as the décolletage, inner arms, hands, abdomen, upper inner thighs or knees.

6. Peri-Orbital Treatment Map

The treatment map recommended for the periorbital area consists of delivering 15 radial lines (14 mm/line) across the upper lid-brow complex, 15 cris-crossing lines at the crow's feet area, and 15 radial lines below the lower lid margin with the DS 7 - 3.0 Nmm transducer (13 TCPs/line, 0.45 joules/TCP), distributing a total of 263.2 joules within the lower level of the dermis (**Figure 1**). Thereafter, the upper dermis was treated with the DS 10 - 1.5 Nmm transducer (13 TCPs/line, 0.25 joules/TCP) that delivered 15 radial lines (14 mm/line) across the upper lid-brow complex, 15 cris-crossing lines at the crow's feet area, and 15 radial lines below the lower lid margin, distributing a total of 146.25 joules. Treatment of periorbital skin at a dual depth was limited to tissue only over the orbital portion of the orbicularis muscle and bone in order to prevent intraocular injury. Currently, there are no commercially available eye shields that have been shown to effectively block ultrasound energy.

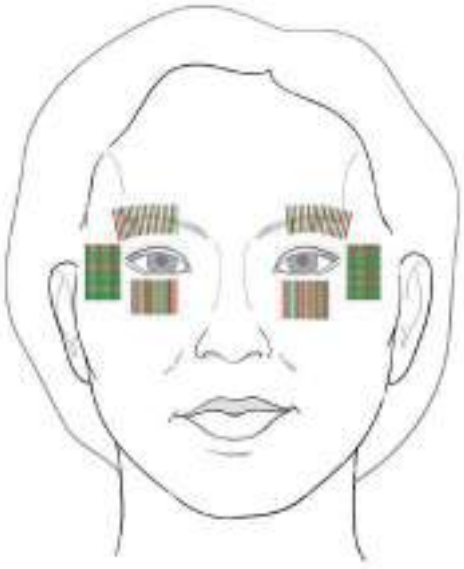


Figure 1. Periorbital Treatment Map with the DS 7 - 3.0 Nmm (13 TCPs/14 mm line) and DS 10 - 1.5 Nmm (13 TCPs/14 mm line) transducers.

7. Body Treatment Map

The treatment maps recommended for the body varied by area sizes, depths of dual treatment, and deposited total energy, as shown in **Figure 2**. Dual treatment began at the subdermal depth and then proceeded to the more superficial dermal level with all treatment lines placed in a vertical (foot-to-head) direction, as listed below in **Table 1**.

8. Results

A total of eighty-two patients (81 females) were treated and evaluated, as listed in **Table 2**. The median age was 51.8 years (range 30 - 72 years). Ethnic backgrounds included 42 Caucasians, 31 Hispanics, 8 Asians, and 1 African-American. Treatment sites comprised the periorbitum, décolletage, brachia, abdomen, inner thighs, knees, hands and buttocks.

Primary outcomes for efficacy of eyebrow lifting after treatments within the upper and lower levels of the dermis were measured by Matched Orientation Function of Mirror Software, comparing baseline to 6 month post-treatment changes (mm) between reference points. A single treatment produced an average elevation between 1 - 2 mm (7% - 8% increase from baseline) in each 19 patients, as depicted in **Figure 3** and **Figure 4**.

Two masked evaluators classified and scored patients' skin and subdermis at the eight sites based on the following clinical gradations of crepiness and ptotic folds: Class I mild, score 1 - 3; Class II moderate 4 - 6. Patients, who presented with Class III severe scores 7 - 9, were excluded from treatments. Investigators and patients compared changes from baseline to six month photographs, listed in **Table 3**

In general, wrinkled and crepey skin of lower grading (Class I and II) in the periorbital region, inner brachium, periumbilicus and knees experienced moderate improvements by IGAIS and SGAIS assessment at 6 months (**Figures 5-8**). Salutary effects were observed as early as 6 weeks (especially to treated eyelid and periorbital skin), but the majority of patients appreciated a smoothing and tightening of the crepey skin between 3 to 6 months. Observed responses lasted about from 6 months to 1 ½ years after a single treatment. In the décolletage, inner thighs, hands and buttocks areas, the frequency of clinical responses was not as great, when compared to the numbers observed in the periorbital region, inner brachium, periumbilical, and knee areas.

9. Side Effects and Complications

All patients developed fleeting erythema immediately after treatment, especially around the upper and lower eyelids. All erythema dissipated within a few hours. Transient edema from therapy was difficult to assess because of

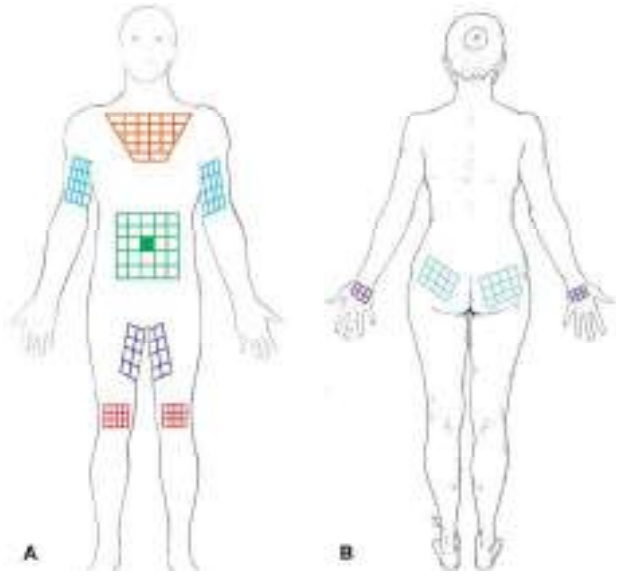


Figure 2. Body Treatment Maps with the DS 10 - 1.5 mm (23 TCPs/25 mm line), DS 7 - 3.0 mm (23 TCPs/25 mm line) and DS 4 - 4.5 mm (17 TCP/25 mm line) transducers.

Table 1. Treatment maps for body sites.

Site(s)	Number of 2.5 × 2.5 cm square	Transducers	Number of Lines (mm length)/square	Total Joules/Squares
Décolletage	21	DS 7 - 3.0 mm DS 10 - 1.5 mm	30 (25 mm) 30 (25 mm)	310.5 172.5
Brachium	16	DS 4 - 4.5 mm DS 7 - 3.0 mm	30 (25 mm) 30 (25 mm)	612 310.5
Periumbilicus	24	DS 4 - 4.5 mm DS 7 - 3.0 mm DS 10 - 1.5 mm	30 (25 mm) 30 (25 mm) 30 (25 mm)	612 310.5 172.5
Inner Thigh	8	DS 4 - 4.5 mm DS 7 - 3.0 mm	30 (25 mm) 30 (25 mm)	612 310.5
Knee	12	DS 4 - 4.5 mm DS 7 - 3.0 mm	30 (25 mm) 30 (25 mm)	612 310.5
Hand	6	DS 7 - 3.0 mm	15 (25 mm)	155.25
Buttock	12	DS 4 - 4.5 mm DS 7 - 3.0 mm	30 (25 mm) 30 (25 mm)	612 310.5

subcutaneous injections of local anesthetic solution for pain management. No other adverse events (such as blistering, ulceration, scarring, dyschromia, numbness, bruising, or striations) were noted at any time point.

In most cases, patients completed treatments to skin outside the orbital rims by implementing the previously mentioned steps for pain-management. Unresponsive patients to these conservative antipain measures may benefit from selective nerve blocks to the supratrochlear, supraorbital, zygomaticotemporal, zygomatico-facial or infraorbital nerves for pain relief. Selective nerve blocks are preferable to local infiltration techniques which potentiates periorbital swelling and edema. In contrast, patients requested infiltration of local anesthesia to body

Table 2. Demographics of treatment groups.

Number (Sex)	81 Females 1 Male
Age	51.8 years (range 30 - 72)
Ethnicity	42 Caucasians 31 Hispanics 8 Asians 1 African American
Number of Patients (Treatment Area)	19 (Periorbitum) 5 (Décolletage) 44 (Brachium) 1 (Hand) 6 (Periumbilicus) 2 (Buttock) 1 (Inner Thigh) 4 (Knee)

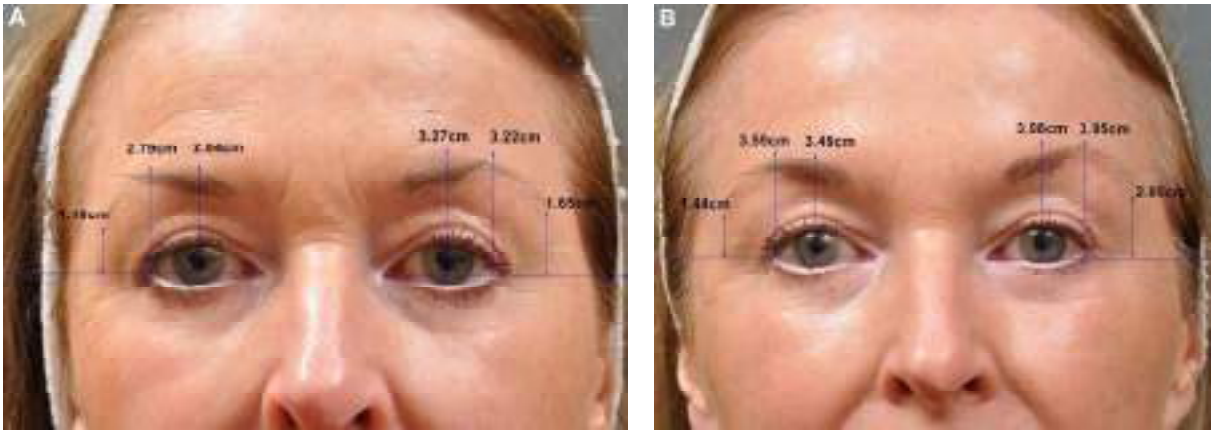


Figure 3. In Panel A, this 67 year old patient presented with crepey periorbital skin and brow ptosis. The lower dermis of the upper lid-brow complex (15 cris-crossing lines), crow's feet area (15 cris-crossing lines) and lower lid (15 cris-crossing lines) was treated with the DS 7 - 30 Nmm transducer (14 mm line; 13 TCPs/line; 0.25 joules/TCP; total 263.2 joules). Thereafter, the upper dermis of the same three areas received treatments (15 lines/site) with the DS 10 - 1.5 Nmm transducer (14 mm line; 13 TCPs/line; 0.25 joules/TCP; total 146.25 joules). In Panel B, 12 months after treatment, each eyebrow was elevated at its three reference points, measured by the Canfield Matched Orientation Mirror Software. There was a noticeable improvement of the crepey periorbital skin from the baseline image.

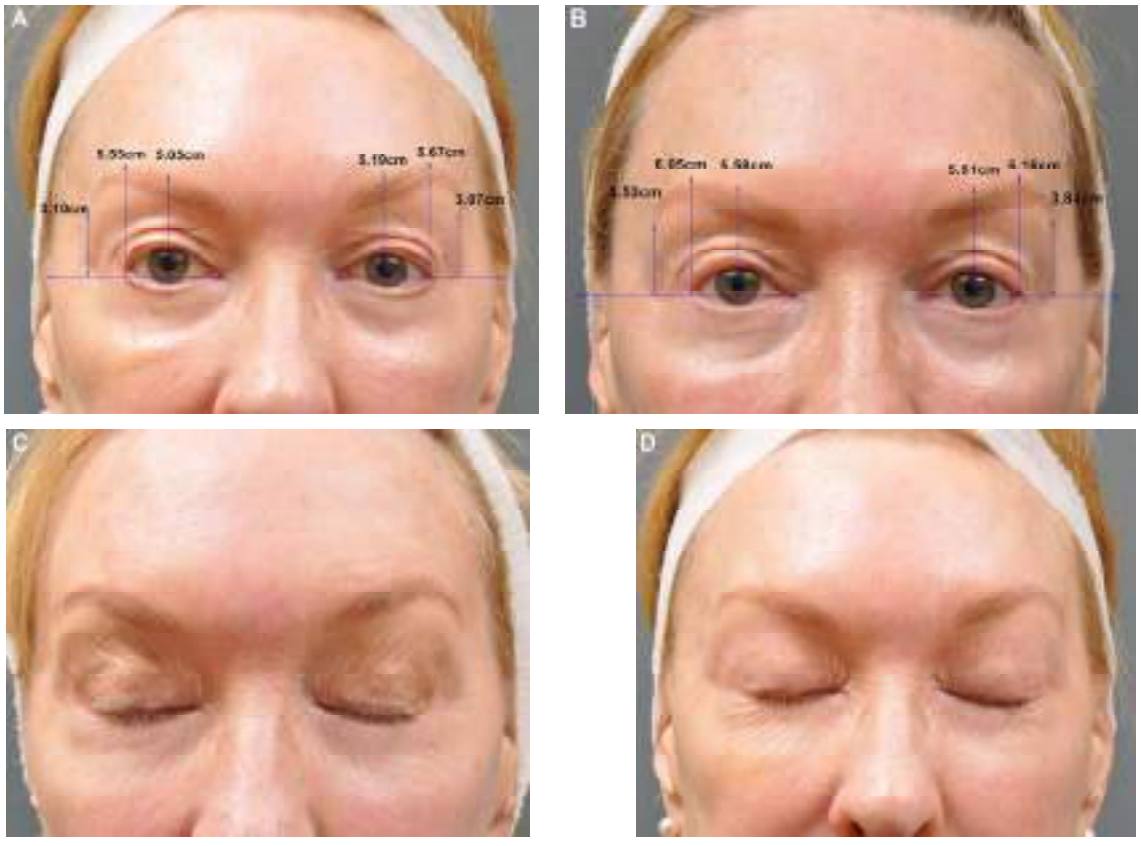


Figure 4. In Panel A, this 60 year old female presented with asymmetric and ptotic right brow relative to her opposite less ptotic side with crepey periorbital skin. Dual dermal treatment was given as listed in the periorbital treatment map with the DS 7 - 3.0 Nmm transducer (14 mm line; 13 TCPs/line; 0.25 joules/TCP; total 263.2 joules) and the DS 10 - 1.5 Nmm transducer (14 mm line; 13 TCPs/line; 0.24 joules/TCP; total 146.25 joules). In Panel B, 12 months after treatment, right brow ptosis was improved from baseline images with elevation of both brows to a more symmetrical level (Mirror Matched Orientation). In Panel C, baseline images showed marked crepey periorbital skin; in Panel D, noticeable improvement of the crepey periorbital skin was documented 12 months after single treatment.

Table 3. Grading of wrinkling, crepey skin and subdermis to evaluation of clinical 6 month responses.

Site	# of Pts (Skin Score)	# of Pts (IGAIS)	# of Pts (SGAIS)
Periorbitum	9 Pts (Class I) 10 pts (Class II)	3 Pts (1); 5 Pts (2); 1 Pt (3) 2 Pts (1); 7 Pts (2); 1 Pt (3)	3 Pts (1); 6 Pts (2) 3 Pts (1); 7 Pts (2)
Décolletage	2 Pts (Class I) 3 Pts (Class II)	1 Pt (1); 1 Pt (2) 1 Pt (1); 2 Pt (2)	1 Pt (1); 1 Pt (1) 1 Pt (1); 2 Pts (2)
Brachium	15 Pts (Class I) 29 Pts (Class II)	1 Pt (0); 2 Pts (1); 12 Pts (2) 3 Pts (0); 7 Pts (1); 19 Pts (2)	2 Pts (0); 3 Pts (1); 10 Pts (2) 5 Pts (0); 4 Pts (1); 20 Pts (2)
Periumbilicus	2 Pts (Class I) 4 Pts (Class II)	2 Pts (2) 1 Pt (0); 1 Pt (1); 2 Pts (2)	2 Pts (2) 1 Pt (0); 2 Pts (1); 1 Pt (2)
Inner Thigh	1 Pt (Class II)	1 Pt (1)	1 Pt (1)
Knees	2 Pts (Class I) 2 Pts (Class II)	2 Pts (2) 1 Pt (1); 1 Pt (2)	2Pts (2) 2 Pts (1)
Hand	1 Pt (Class II)	1 Pt (1)	1 Pt (1)
Buttock	2 Pts (Class II)	2 Pts (1)	1 Pt (0); 1 Pt (1)

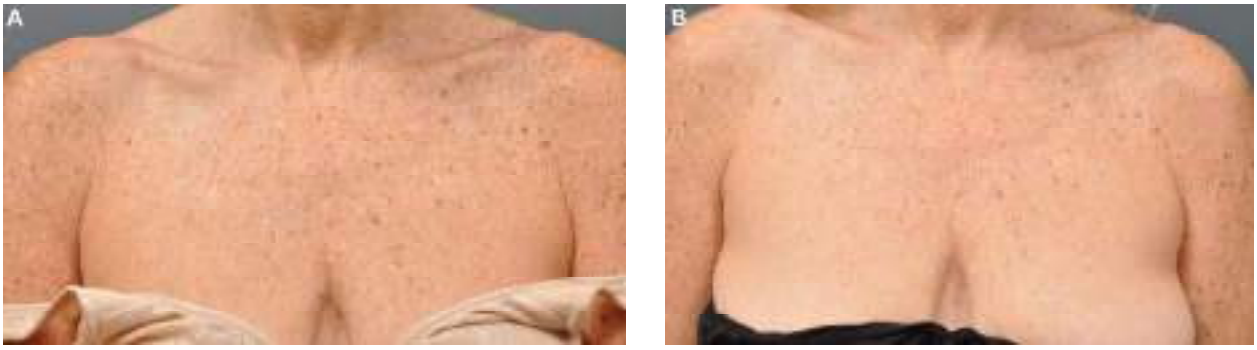


Figure 5. In Panel A, this 50 year old patient had concerns of crepey, pigmented and wrinkled skin in her décolletage and intermammary folds. The exposed region was outlined as an inverted pyramid of twenty-one 2.5 × 2.5 cm squares. Each sector received treatments in the lower reticular dermal plane with the DS 7 - 3.0 mm transducer (30 lines; 25 mm line; 23 TCPs/line; 0.45 joules/TCP; total 6520.5 joules), followed in the upper third of the reticular dermal plane with the DS 10 - 1.5 mm transducer (30 lines; 25 mm line; 23 TCPs/line; 0.25 joules/TCP; total 3622.5 joules). In Panel B, moderate reduction in vertical crinkle lines, superficial pigmentations, thin skin, and also wrinkling within the intermammary folds was observed 9 months after treatment.

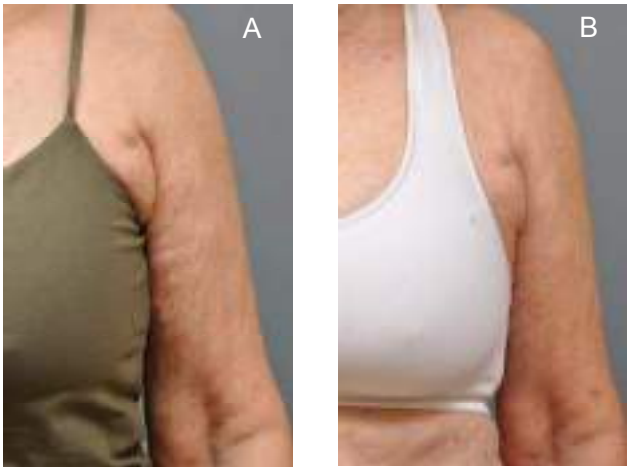


Figure 6. In Panel A, this 65 year old patient presented with generalized creping of the brachial skin. The visible crepey inner brachial skin was marked into sixteen 2.5 × 2.5 cm squares. Each sector was treated in the subdermal plane with the DS 4 - 4.5 mm transducer (30 lines; 25 mm line; 17 TCPs/line; 1.2 joules/TCP, total 9792 joules), followed in the deeper reticular dermal plane with the DS 7 - 3.0 mm transducer (30 lines; 25 mm line; 23 TCPs/line; 0.45 joules/TCP; total 4968 joules). In Panel B, significant improvement was observed 9 months after treatment with smoothing and tightness to the thin crepey skin.

sites because of uncomfortable pain during treatments that were not ameliorated even by topical anesthetic gels.

Patients assessed their perceived pain levels during the initial part of their treatment prior to requests, if needed, for topical anesthetic gels, selective nerve blocks or local subcutaneous anesthetic infiltrations, as listed in **Table 4**.

10. Discussion

Lax crepey skin and localized subcutaneous fat folds on the body occur not only with chronological aging, but also after photoaging, or sequelae after pregnancy and weight loss. Although surgical procedures address these findings more effectively, they carry inherent risks and require recovery times. Non-invasive thermal devices [7-12] have the potential to denature triple helical chains within collagen fibers between 65˚C - 70˚C with immediate recoil and contraction of collagen fibers in the dermis and subcutaneous tissues. Later neocollagenesis and elastogenesis occur at three months with remodeling effects for long-term tissue tightening and improvement of the crepey skin [13-15].

In this preliminary clinical report, non-invasive delivery of microfocused ultrasonic thermal coagulation points to two levels of the dermal skin around the periorbitum,

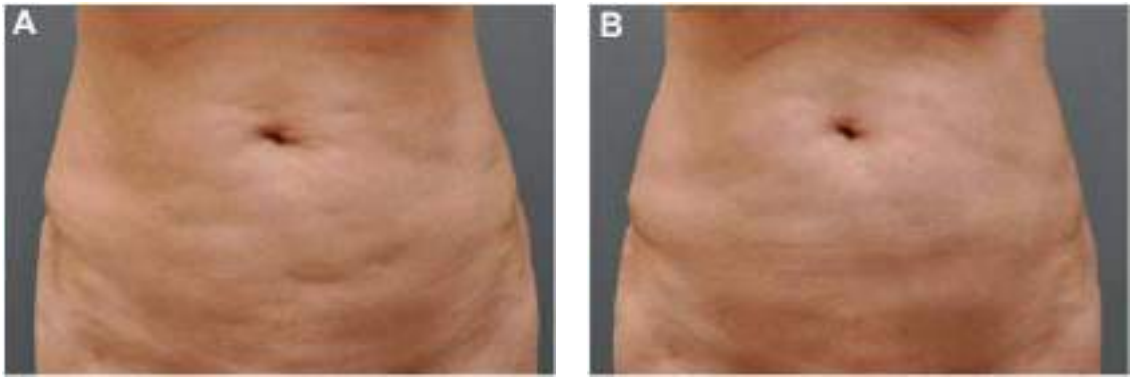


Figure 7. In Panel A, this 72 year old patient (gravida 3, para 3) complained of crepey lines around the periumbilical area and surface irregularities (resembling cellulitic formations) to the remainder of the abdomen. The patient had received no surgical or non-invasive procedures in the past. The periumbilicus and adjacent abdomen was demarcated into twenty-four 2.5 × 2.5 cm squares. Each square received treatment to the subdermal plane with the DS 4 - 4.5 m transducer (30 lines; 25 mm line; 17 TCPs/line; 1.2 joules/TCP; total 14,688 joules), and secondly in the deeper reticular dermis with the DS 7 - 3.0 mm transducer (30 lines; 25 mm line; 23 TCPs/line; 0.45 joules/TCP; total 7452 joules). The third treatment level consisted of treatment in the upper third of the dermis with the DS 10 - 1.5 mm transducer (30 lines; 25 mm line; 23 TCPs/line; 0.25 joules; TCP; total 4140 joules). In Panel B, moderate reduction in the crepey wrinkle lines around the umbilicus as well as the surface depressions/folds to the surrounding treated abdomen was observed 1 year after treatment.

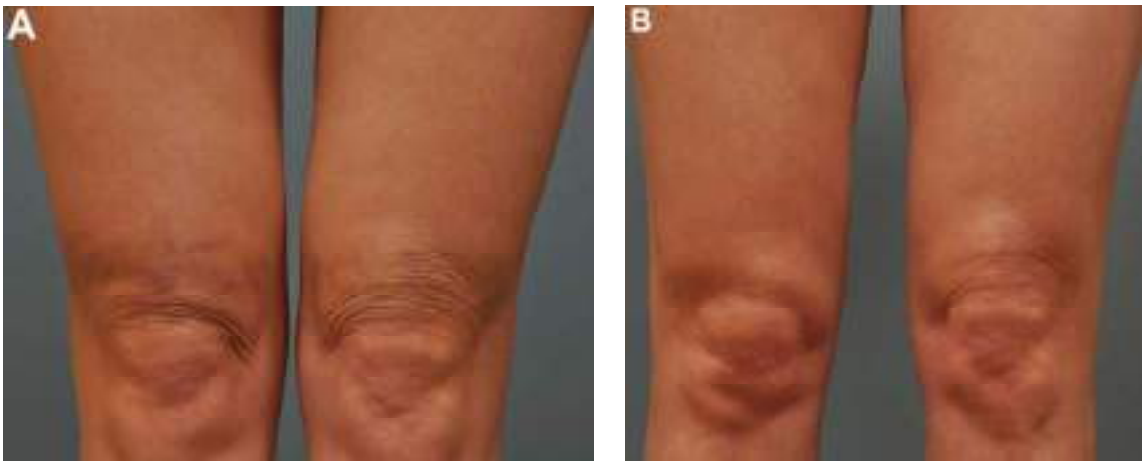


Figure 8. In Panel A, this 39 year old patient sought treatment for crepey transverse lines above the knees. The area of visible lines was marked into twelve 2.5 × 2.5 cm squares. Each sector was treated in the subdermal plane with the DS 4 - 4.5 mm transducer (30 lines; 25 mm line; 17 TECPs/line; 1.2 joules/TCP; total 7344 joules) and subsequently treated with the DS 7 - 3.0 mm transducer (30 lines; 25 mm line; 23 TCPs/line/ 0.45 joules/TCP; total 3726 joules). In Panel B, marked reduction in the gathered crepey lines was noted 9 months after treatment.

Table 4. Pain assessment to each treated site: 0 = no pain 10 = severe pain.

Treatment Site	Number of Assessed Patients	Mild (1 - 4/10)	Moderate (5 - 8/10)	Severe (9 - 10/10)
Periorbitum	19	15	2	2
Décolletage	5	1	2	2
Brachium	44	10	21	13
Hand	1	0	1	0
Periumbilicus	6	0	5	1
Buttock	2	0	1	0
Upper Inner Thigh	1	0	1	0
Knee	4	0	3	1

appeared to be effective in reduction of wrinkles, crepey and sagging skin for about 1 ½ years in all nineteen treated patients. Delayed collagen remodeling is believed to result in a synergistic tightening and elevation of brow-tissues, averaging 1 - 2 mm in all 19 treated patients between six weeks to 1 ½ years, as determined by the Matched Orientation Function of Mirror Software. The degree of response correlated inversely with the severity of classification on the Fitzpatrick Wrinkle, Fold and Tissue Scale, *i.e*., the lower the FWFTLS score for skin aging, the greater the response as determined by the Investigator and Subject Global Aesthetic Improvement Scales. A single treatment produced minimal downtime, moderate discomfort and nominal side effects without epidermal injury.

In areas of the décolletages, brachii, periumbilical sites, and knees, dual treatment levels to the dermis and subdermis transformed crepey and wrinkled skin (Class I and II) in the majority of patients to mildmoderate improvements by IGAIS and SGAIS evaluations. Although there were few patients treated in areas of the décolletage, abdomen, and knees, encouraging responses were observed by the third month and continued for a year after a single treatment.

In the few numbers of patients treated in the upper inner thighs, hands and buttocks, results were modest after high energy density treatments were provided to the dermis and subdermis. Significant degrees of thin crepey skin, as often observed in the dorsum of hands and medial thighs, might have contributed to weak responses after a year follow up.

It is important to note that microfocused ultrasound treatments to tissues of the periorbitum and different regions of the body were more sensitive to thermal coagulation points than previously observed in patients who received high density treatments to the face and neck [1,2]. Moderate to significant intraoperative pain was experienced most commonly to the décolletage, brachium, knee and periumbilical sites. In order to obtain the greatest potential for clinical responses with higher density energy deposition, the addition of small amounts of local anesthesia in the subcutaneous tissue currently is preferable to reducing the total amount of energy delivered by shortening each treatment line per sector (which, in turn, decreases the number of coagulation points per treatment line) or reducing the energy per thermal coagulation point. Notably, the number and degree of clinical responses to dual levels of treatment appear to be directly related to selection of patients who present with mild-to moderate degrees of skin thinness and laxity and smaller amounts of sagging subcutaneous fat.

The limitations of this preliminary report were the unknown optimal treatment parameters in this first ultrasound experience with the current technology to periorbital tissues and differing body sites. Further innovations in the delivery of increased energy to more structural levels and in improvement in the treatment algorithms (higher densities, more passes, vectored treatment lines, different dermal and subdermal depths) may increase tissue tightening and induction of more collagenesis to renew thin and crepey dermis without increasing significant adverse events, costs, and delivery times. Needless to say, greater patient enrollment and longer follow up evaluations by volumetric and measurement advances are needed. In the near future, this novel energy device may be able to visualize and treat more specific structural levels than currently available for tissue tightening but also rejuvenation, volumetric reduction and treatment of troublesome dermal adnexal structures.

11. Conclusions

Microfocused ultrasound for nonablative thermal tightening and rejuvenation of thin crepey tissue to the periorbitum and body sites appears to be safe and moderately effective by outcome evaluations in this small cohort of patients limited to mild-to moderate degrees of tissue wrinkling and laxity. Responders experienced positive effects up to 1 ½ years, especially to crepey skin in the periorbitum, décolletage, brachium and knees. All patients commonly experienced transitory mild swelling and erythema.

Most patients reported moderate-severe pain during treatments in differing body sites that required either local nerve blocks or injections within the subcutaneous tissue. The cumulative effects of upper and lower dermal treatments for improvements in crepey wrinkled skin are encouraging but will require further clinical and objective validations.

12. Acknowledgements

The authors wish to thank Margaret Gaston, BS, for statistical and photographic assistance.

13. Disclosures

Dr. Sasaki is a consultant to Ulthera, Inc. and received limited funding under an unrestricted research grant for the studies. Registered Nurse Ana Tevez has no financial disclosures.

REFERENCES

[1] M. Alam, L. E. White, N. Martin, *et al*., "Ultrasound Tightening of Facial and Neck Skin: A Rater-Blinded Prospective Cohort Study," *Journal of the American Academy of Dermatology*, Vol. 62, No. 2, 2009, pp. 262-269. doi:10.1016/j.jaad.2009.06.039

[2] G. H. Sasaki and Tevez, "Focused Imaged Ultrasound: Clinical Efficacy and Safety (2 Year Experience)," *Aesthetic Surgery Journal*, Vol. 32, No. 5, 2012.

[3] W. M. White, I. R. S. Makin, P. G. Barthe, *et al*., "Selective Creation of Thermal Injury Zones in the Superficial Musculoaponeurotic System Using Intense Ultrasound Therapy," *Archives of Facial Plastic Surgery*, Vol. 9, No. 1, 2007, pp. 922-929.

[4] W. M. White, I. R. S. Makin, M. H. Slayton, *et al*., "Selective Transcutaneous Delivery of Energy to Porcine Soft Tissues Using Intense Ultrasound (IUS)," *Lasers in Surgery and Medicine*, Vol. 40, No. 2, 2008, pp. 67-75. doi:10.1002/lsm.20613

[5] R. E. Gliklich, W. M. White, M. H. Slayton, *et al*., "Clinical Pilot Study of Intense Ultrasound Therapy to Deep Dermal Facial Skin and Subcutaneous Tissues," *Archives of Facial Plastic Surgery*, Vol. 9, No. 2, 2007, pp. 88-95. doi:10.1001/archfaci.9.2.88

[6] D. Manstein, G. S. Herron and R. K. Sink, "Fractional Photothermolysis: A New Concept for Cutaneous Remodeling Using Microscopic Patterns of Thermal Injury," *Lasers in Surgery and Medicine*, Vol. 34, 2004, pp. 426-438. doi:10.1002/lsm.20048

[7] G. H. Sasaki, H. M. Travis and B. Tucker, "Fractional CO_2 Laser Resurfacing of Photoaged Facial and Non-Facial Skin: Histologic and Clinical Results and Side Effects," *Journal of Cosmetic and Laser Therapy*, Vol. 11, No. 4, 2009, pp. 190-201. doi:10.3109/14764170903356465

[8] T. S. Alster and J. R. Lupton, "Nonablative Cutaneous Remodeling Using Radiofrequency Devices," *Clinics in Dermatology*, Vol. 25, 2007, pp. 487-491. doi:10.1016/j.clindermatol.2007.05.005

[9] C. C. Dierickx, "The Role of Deep Heating for Noninvasive Skin Rejuvenation," *Lasers in Surgery and Medicine*, Vol. 38, No. 9, 2006, pp. 799-807. doi:10.1002/lsm.20446

[10] N. Sadick, "Tissue Tightening Technologies: Fact or Fiction," *Aesthetic Surgery Journal*, Vol. 28, 2008, pp. 180-188.

[11] M. L. Elsaie, "Cutaneous Remodeling and Photorejuvenation Using Radiofrequency Devices," *Indian Journal of Dermatology*, Vol. 54, No. 3, 2009, pp. 201-205. doi:10.4103/0019-5154.55625

[12] D. J. Maitland and J. T. Walsh, "Quantitative Measurements of Linear Birefringence during the Heating of Native Collagen," *Lasers in Surgery and Medicine*, Vol. 20, No. 3, 1997, pp. 310-318. doi:10.1002/(SICI)1096-9101(1997)20:3<310::AID-LSM10>3.0.CO;2-H

[13] S. P. Arnoczky and A. Aksan, "Thermal Modification of Connective Tissues: Basic Science Considerations and Clinical Applications," *Journal of the American Academy of Orthopaedic Surgeons*, Vol. 8, No. 5, 2000, pp. 305-313.

[14] B. M. Hantash, A. A. Ubeid, H. Chang, *et al*., "Bipolar Fractional Radiofrequency Treatment Induces Neoelastogenesis and Neocollagenesis," *Lasers in Surgery and Medicine*, Vol. 41, No. 1, 2009, pp. 1-9. doi:10.1002/lsm.20731

[15] D. Shoshani, E. Markovitz, S. J. Monstrey, *et al*., "The Modified Fitzpatrick Wrinkle Scale: A Clinical Validated Measurement Tool for Nasolabial Wrinkle Severity Assessment," *Dermatologic Surgery*, Vol. 34, No. S1, 2008, pp. S85-S91. doi:10.1111/j.1524-4725.2008.34248.x

Ulthera: Initial and Six Month Results

Robert W. Brobst, MD[a,b], Maria Ferguson, BS[b], Stephen W. Perkins, MD[a,b,*]

KEYWORDS

- Facial rejuvenation • Neocollagen deposition
- Noninvasive facial rejuvenation • Skin laxity
- Ulthera • Ultrasound

Key Points

- For most nonsurgical methods of facial rejuvenation, improvement is dependent on a robust wound healing response consisting of increased expression of reparative mediators and neocollagen deposition.
- The ideal patient has mild to moderate skin laxity and mild lipoptosis. A younger patient typically has a more vibrant wound healing response and an inherent skin elasticity, which leads to better results.
- Limitations of the procedure include patients with extensive skin ptosis/laxity, heavy lipoptosis with jowling, and marked platysmal banding. These patients are better served with surgical interventions.
- Relative contraindications include treatment directly over keloids, implants, and fillers because it may cause further scarring, malfunction, or volume loss, respectively. Judgment should be exercised in patients at risk for bleeding complications, poor wound healing, infection, or exacerbation of an autoimmune disorder.

Video of Ulthera Technique accompanies this article at http://www.facialplastic.theclinics.com/.

EMERGENCE OF ULTHERA

The demand for facial rejuvenation has increased as patients from the baby boomer generation continue to age and subsequent generations find further societal acceptance of such interventions. Traditional surgical techniques and ablative skin resurfacing remain the gold standard for substantial, predicable improvement for those with extensive neck and facial skin laxity, deep rhytids, jowling, platysmal banding, and lipoptosis. Once shrouded in secrecy, master techniques are now readily shared and have become further refined to improve safety and outcomes. However, not all patients present with such extensive aging changes and some cannot accommodate a lengthy downtime in their schedules. In response, a multitude of alternative noninvasive treatment options have evolved to meet the demand of these patients.

These noninvasive treatment modalities include injectable neurotoxins and dermal fillers (hyaluronic acid, calcium hydroxyapatite, and poly-L lactic acid), intense pulsed light, nonablative lasers (infrared 1100–1800 nm, midinfrared 1320-nm neodymium-doped yttrium aluminum garnet, and pulsed dye), and radiofrequency bulk heating (monopolar and bipolar capacitive). Of these treatments, neurotoxins and fillers are the most frequently used and continue to see an exponential growth because of their ability to treat dynamic rhytids and the volume losses of aging, respectively.

Disclosure Statement: Maria Ferguson is a part time consultant for Ulthera, Inc. Drs Brobst and Perkins have no financial conflicts.

[a] Department of Otolaryngology – Head and Neck Surgery, Indiana University School of Medicine, 699 Riley Hospital Drive, RR 132, Indianapolis, IN 46202, USA
[b] Meridian Plastic Surgery Center, 170 West, 106th Street, Indianapolis, IN 46290-0970, USA
* Corresponding author. 170 West 106th Street, Indianapolis, IN 46290-0970.
E-mail address: sperkski@gmail.com

Facial Plast Surg Clin N Am 20 (2012) 163–176
doi:10.1016/j.fsc.2012.02.003
1064-7406/12/$ – see front matter

However, their role in facial tissue tightening and skin rejuvenation is minimal. Common to the other treatment modalities is an attempt to induce this effect through thermal heating of the dermis without injury to the overlying epidermis. This technique largely avoids the negative aspects of the traditional methods (ablative lasers, dermabrasion, and chemical peels), including pigment changes, scarring, infection, and the delay in return of normal activities during reepithelialization. Pain relief is not necessarily eliminated. For instance, early radiofrequency devices were noted to be painful. Later modifications to decrease pain resulted in reduced efficacy and the need for repetitive treatments. As is frequently the case, invasiveness and efficacy are directly related. With nonsurgical methods, improvement is dependent on a robust wound healing response consisting of increased expression of reparative mediators and neocollagen deposition. Quantitative studies have shown that traditional methods can achieve a 1000-fold increase in these factors, whereas noninvasive modalities result in only a fraction of the response.[1] This finding partially explains the more modest results with these noninvasive modalities. The options for nonablative treatments need to continually improve to meet the desires of consumers seeking a low-risk, minimal-downtime procedure with results that closer mimic traditional methods. To this end, a facial application of intense focused ultrasound (IFUS), the Ulthera system (Ulthera, Mesa, AZ, USA), has recently been developed for the goal of improved noninvasive rejuvenation results.

Ultrasound as a Therapeutic Modality

Although more familiar as a diagnostic imaging modality, ultrasonography has been investigated as a therapeutic modality for more than 60 years. Early studies, conducted by Fry and colleagues,[2,3] focused on the biologic effects and neurologic applications of ultrasonography. This early work failed to find clinical usefulness, but in recent decades ultrasonography is finding an emerging role in the treatment of both benign and malignant solid tumors. In 2004, the US Food and Drug Administration (FDA) approved a magnetic resonance imaging-guided focused ultrasonography device for the treatment of uterine fibroids.[4] Clinical trials are active for the management of benign prostate hypertrophy and malignancies of the breast, liver, kidneys, prostate, and brain.[5,6] In addition, nonablative ultrasonography modalities are being investigated for targeted drug delivery and gene therapy.[5,7] In contrast to the applications for high-intensity ultrasonography that accomplish tissue disruption through thermal effects and the cavitation process, IFUS uses heat alone.[5–8] This situation is the result of shorter pulse durations of 50 to 200 milliseconds, a higher frequency of 4 to 7 MHz, and a decreased energy quantity of 0.5 to 10 J administered through the transducer.[8] As a result, more precise energy delivery is achieved with the Ulthera IFUS device during the aesthetic improvement of facial tissues.

In 2004, Ulthera began preclinical trials with a prototype device, followed shortly thereafter by several clinical trials.[9–12] White and colleagues[10] reported the first aesthetic use of focused ultrasonography and its ability to specifically target the superficial muscular aponeurotic system (SMAS). By 2009, the significant results of these studies led to an FDA approval for a browlift indication.[13,14] This approval has fostered the further development of the device as a noninvasive tool for full facial rejuvenation. Moreover, it has created an enthusiastic community of practitioners investing in the device both in the domestic and in the global markets. Therefore, in this article, we further describe the device and mechanism of action, give our impression of its indications and limitations, detail the treatment, review the literature and our results, discuss future trends, and conclude with the pearls and pitfalls we have identified that might help the early user.

Device Details and Mechanism of Action

The Ulthera system is composed of a power unit, a central processor with monitor, and a handpiece with 4 interchangeable dual-functioning transducers (**Fig. 1**). Each handpiece uses high-resolution diagnostic ultrasonography that is capable of clearly imaging the targeted facial anatomy, including the epidermal/dermal unit, subcutaneous fat, and SMAS, facial mimetic musculature, and the underlying osseous structures, up to a depth of 8 mm (**Fig. 2**). This strategy also allows confirmation of coupling between the handpiece and the skin before treatment initiation. In addition, the handpiece hosts the IFUS transducer responsible for energy delivery. The transducer options include the 4-MHz, 4.5-mm focal depth (4-4.5), 7-MHz 4.5-mm focal depth (7-4.5), 7-MHz 3.0-mm focal depth (7-3.0), and the 7-MHz 3.0-mm focal depth narrow (7-3.0N). These options differ in their geometric focus and wavelength configurations, whereby the depth and quantity of energy delivered during treatment can be varied for a desired effect within the target tissue layer.

Each transducer delivers a highly directed, acoustic energy wave to a precise focal point (**Fig. 3**). Energy absorption causes intermolecular vibration and heat production (greater than 60°C),

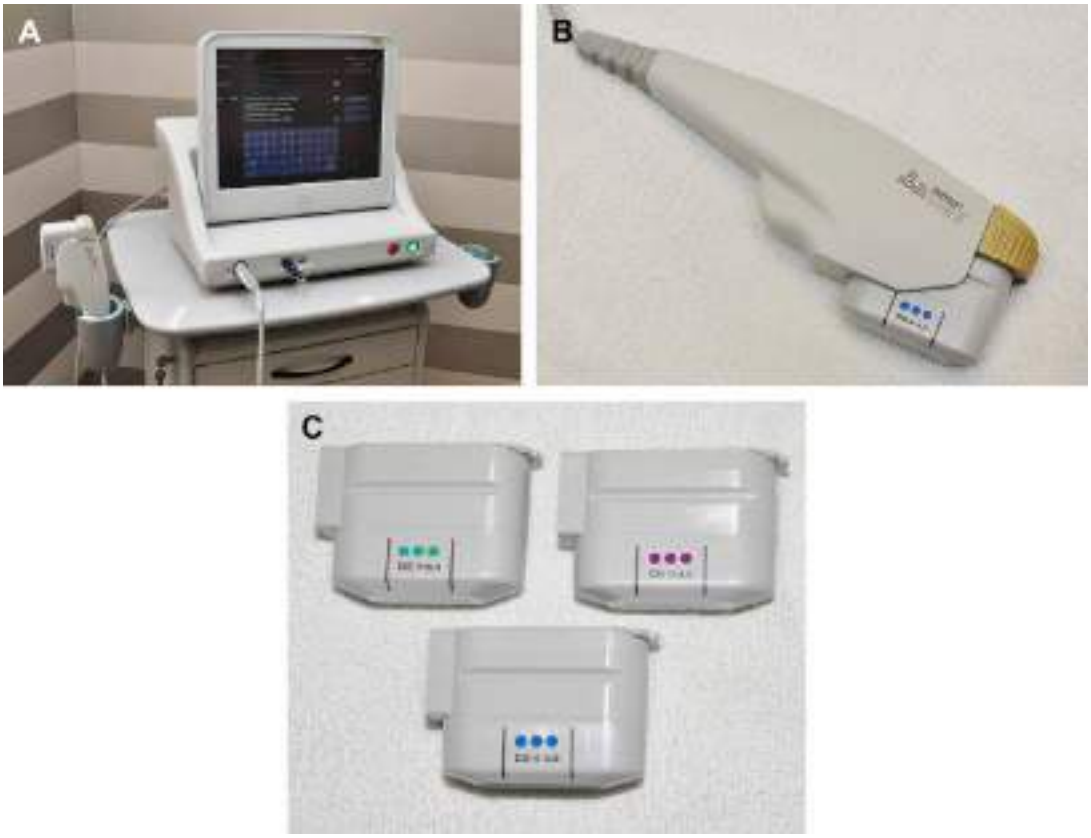


Fig. 1. Ulthera system and components. (*A*) System with monitor. (*B*) Handpiece. (*C*) Transducers (4-4.5, 7-4.5, and 7-3.0).

sufficient for collagen denaturation. This situation creates a thermal injury zone (TIZ) or thermal coagulation point (TCP) of coagulated tissue at the target area. The unfocused acoustic energy surrounding this focal point creates insufficient heat for tissue disruption and therefore limits injury to an approximately 1-mm^3 to 1.5-mm^3 focus. Mathematical modeling and prototype studies agree that as energy is increased, there is deeper penetrance but circumferential enlargement remains minimal.

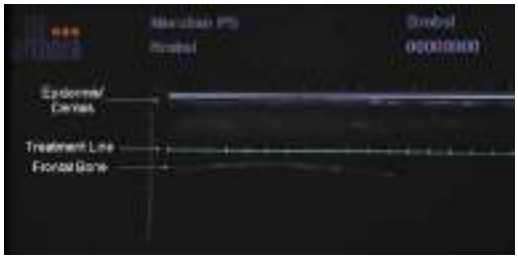


Fig. 2. Ulthera high-resolution diagnostic ultrasonography showing epidermal/dermal unit, subcutaneous fat (not labeled), SMAS (not labeled), treatment line, and frontal bone.

Instead, wedge-shaped TIZs at the focal point elongate toward the epidermis as cigar-shaped lesions (**Fig. 4**). However, even with energy transmission up to 8 J, the epidermis is spared thermal injury.[10,11] The most powerful commercial Ulthera transducer, the 4-4.5, delivers only 1.2 J to its target focus at a depth of 4.5 mm, making epidermal injury unlikely. In addition, wavelength and tissue penetrance are directly related, thus giving the longer wavelength from the 4-MHz transducer, a more robust and deeper treatment depth than the alternative 7-MHz transducer at a 4.5-mm focus. This method allows targeted treatment to the deeper fibromuscular layer of the cheek and jawline, and should be avoided in more superficial tissues. Conversely, the 7-3.0 transducer delivers less energy at a more superficial depth and can be used around the thinner tissue of the eyes. With this knowledge, the handpieces can be selected to treat the fibromuscular SMAS or the deep dermis in a gridlike pattern (**Fig. 5**). Each firing of the device creates a 25-mm linear array of TCPs on the full-sized transducers. The number of TCPs vary from 17 to 22 points per line, with spacing from 1.1 to 1.5 mm

Fig. 3. Schlieren map of intense ultrasound beam profile. Ninety-five percent of the ultrasound energy is delivered to the targeted, approximately 1.5 mm^3, focal point (*bright blue X*). (*Reprinted* and caption *modified from* White WM, Makin IR, Slayton MH, et al. Selective transcutaneous delivery of energy to porcine soft tissues using intense ultrasound. Lasers Surg Med 2008;40:68; with permission. Copyright 2008 by Wiley Periodicals.)

apart depending on the transducer. With parallel lines performed approximately 3 mm apart, a grid of TCPs with untreated intervening tissue is created. This pattern of injury has been related to the model of fractionated lasers. Similarly, the wound healing response is then elicited, leading to collagen remodeling and dermal thickening through inflammatory mediators.[8]

Patient Selection

The ideal patient has mild to moderate skin laxity and mild lipoptosis. In addition, a younger patient typically has a more vibrant wound healing response and an inherent skin elasticity that leads to better results. Similarly, smoking and extensive photoaging decreases the skin quality and elasticity, resulting in less dramatic results when compared with patients with healthier skin.

Contraindications for Ulthera

Few absolute contraindications exist for the device. Patients with open wounds or severe cystic acne fall into this category. Relative contraindications include treatment directly over keloids, implants, and fillers because it may cause further scarring, malfunction, or volume loss, respectively. In addition, because this is a new device, testing has not been performed in many patient populations. Therefore, judgment should be exercised in patients at risk for bleeding complications, poor wound healing, infection, or an exacerbation of an autoimmune disorder or other comorbidity.

Limitations of Ulthera Procedure

Limitations of the procedure include patients with extensive skin ptosis/laxity, heavy lipoptosis with jowling, and marked platysmal banding. These patients are better served with surgical interventions. Patients with mild and moderate findings are more likely to be successful, but appropriate counsel is necessary, because improvement is not seen in every patient. As treatment protocols continue to develop, benefits and limitations will become clearer.

Anesthesia

A degree of discomfort is expected with the Ulthera device, but this is variable in quantity. In the study by Alam and colleagues,[13] which used

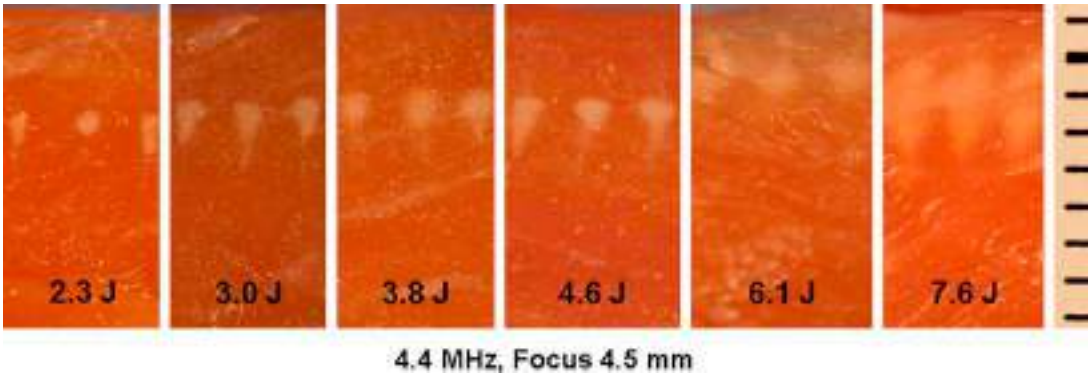


Fig. 4. TIZ geometry. Gross changes in TIZ geometry from a small wedge to an elongated cigar-shaped lesion as energy delivery is increased from 2.3 J to 7.6 J (*left* to *right*) in porcine muscle samples. (*Reprinted* and caption *modified from* White WM, Makin IR, Slayton MH, et al. Selective transcutaneous delivery of energy to porcine soft tissues using intense ultrasound. Lasers Surg Med 2008;40:70; with permission. Copyright 2008 by Wiley Periodicals.)

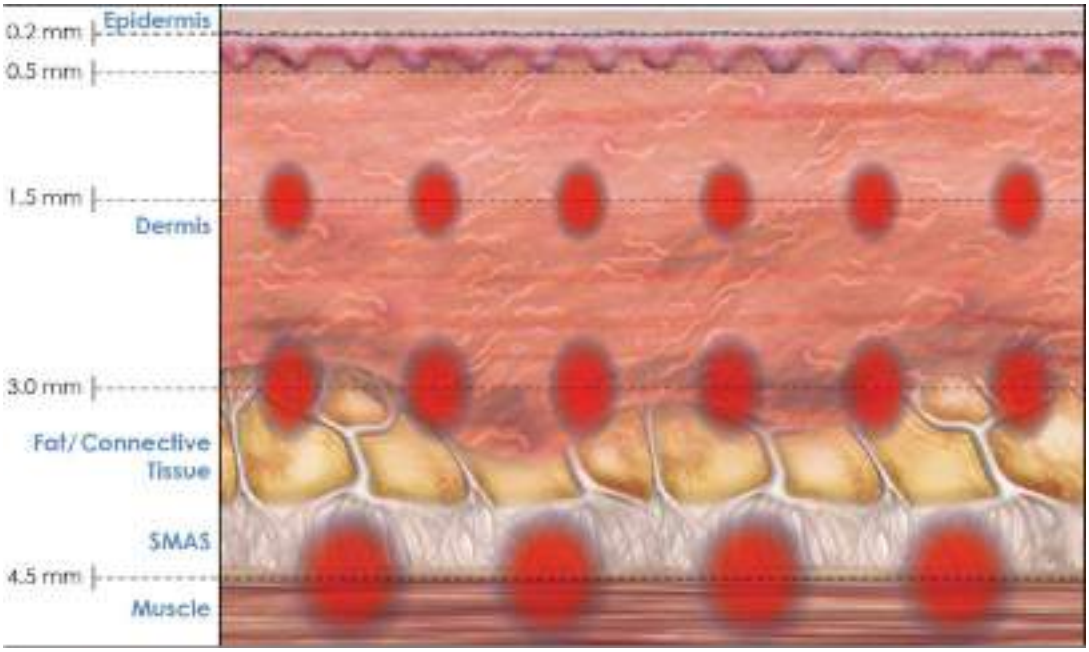


Fig. 5. Skin diagram and treatment depths. Treatment depth is transducer dependent and can focus energy at 1.5-mm, 3.0-mm, and 4.5-mm levels. Specific tissues targeted at these depths vary by regional facial anatomy and should be confirmed with the diagnostic ultrasonography. (*Reprinted* and *adapted from* Ulthera treatment guides, Ulthera, Mesa, AZ; with permission.)

topical anesthetic ointment before treatment, scores of 3 to 4 on a 10-point visual analogue pain scale were most commonly reported. The few patients with increased pain scores were those naive to previous facial cosmetic procedures. In our experience, brief periods of pain are frequently elicited with treatment adjacent to osseous structures such as the mandible, orbital rim, and malar eminence. Also, repetitive regional treatment significantly increases the discomfort level, and therefore changing locations temporarily can be helpful.

Many methods have been described, alone and in combination, to manage pain during the procedure. These methods include antiinflammatory medications, oral and intravenous analgesics, anxiolytics, topical and local anesthetics (infiltration or field blocks), conscious sedation, distraction techniques, and cold techniques.[15] Infiltrative anesthetic should be used judiciously within the areas to be directly treated, because the fluid distortion may alter the cutaneous/subcutaneous level being treated. Our current protocol includes a combination of oral ketorolac 20 mg and diazepam 10 mg initiated before treatment, with distraction and cooling techniques during the procedure. In addition, facial field blocks are performed at the patient's discretion. With this protocol, patient comfort has been significantly improved.

TECHNIQUE

An Ulthera treatment is initiated by adequately cleaning the face and obtaining preprocedure standardized digital photographs (Video 1). The patient is then placed in the supine position and the face is divided into the desired treatment areas (**Fig. 6**). These areas include the neck, cheek, lateral orbit, infraorbital, and brow regions. The thyroid cartilage, inferior mandibular border, zygomatic arch, orbital rim, midpupillary line, and the location of superficial facial nerve branches serve as landmarks in this process. Next, each region

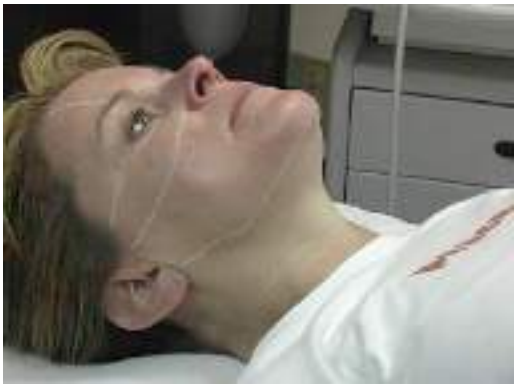


Fig. 6. Facial treatment regions.

is marked with a planning card to determine the number of treatment columns necessary to cover the area with minimal overlap (**Fig. 7**). Then, within each column, the measured density is calculated to quantify the number of lines of treatment (**Fig. 8**). These markings then serve as a guide during the procedure.

The Ulthera device is rapidly learned and is user friendly. Decisions during use are limited to the appropriate transducer selection and the number of lines desired during treatment. Ultrasound gel is first applied and the handpiece is placed perpendicular to the skin (**Fig. 9**). Correct coupling and transducer depth are then verified through the ultrasound images on the monitor. Adjustments should be made before treatment because it can lead to incorrect targeting of energy.[8,13] Unlike the prototype device in which the Joules, pulse duration, and TCP spacing were variable, selection of these variables is now largely irrelevant. Joules delivered is usually set at the default maximum levels, and a change in the energy setting is decided on only if the treatment is poorly tolerated. Treatment is then begun within the neck region and continued upward as each region is completed in a deep to superficial manner. Typically, treatments are performed at 2 depths with 1 pass of a 4.5-mm transducer and then retreating the area with a superficial 3.0-mm transducer (**Fig. 10**). The thin tissue of the infraorbital region is an exception, and is treated only at the superficial focal depth. The narrow transducer is also helpful in this location secondary to its small footprint. In the neck and cheeks, the initial pass is usually with the 4-4.5 transducer. This transducer delivers more energy (maximum 1.2 J/TCP) to the subcutaneous and SMAS layers than is possible with the 7-4.5 transducer (maximum 1.05 J/TCP). In the upper face, the 7-4.5 transducer is more frequently used for the first pass.

Fig. 8. Planning card used for line calculation and marking.

The 7-3.0 transducer is then used to tighten the skin and completes the treatment in most protocols.

Ulthera Aftercare/Complications

No specific aftercare is recommended after this procedure and patients can return to their usual routine immediately. Mild erythema and edema are expected at the completion of the procedure, and in most studies and in our experience this resolves rapidly.[12,13] However, erythema and edema can commonly persist for 48 hours after treatment, as was seen in 22% to 100% of patients studied. In each of these patients, spontaneous resolution occurred by 1 week.[8,13] Also, a small bruise may develop after treatment, but no hematomas or other bleeding events have been reported. Rarely, white wheals can present on the skin surface after use of the superficial transducer. These wheals are attributed to dermal injury secondary to inadequate coupling with the skin. With a topical steroid, the wheals resolve without deleterious effects.[8,13] Temporary numbness within the treatment area has also been reported in up to 18% of patients.[8] This numbness resolves

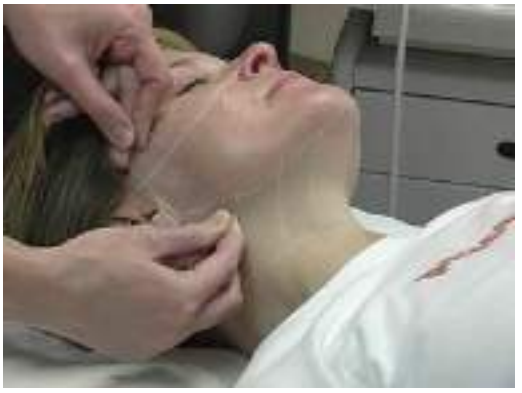


Fig. 7. Marking facial treatment columns with planning card.

Fig. 9. Ulthera treatment with proper handpiece orientation perpendicular to skin surface.

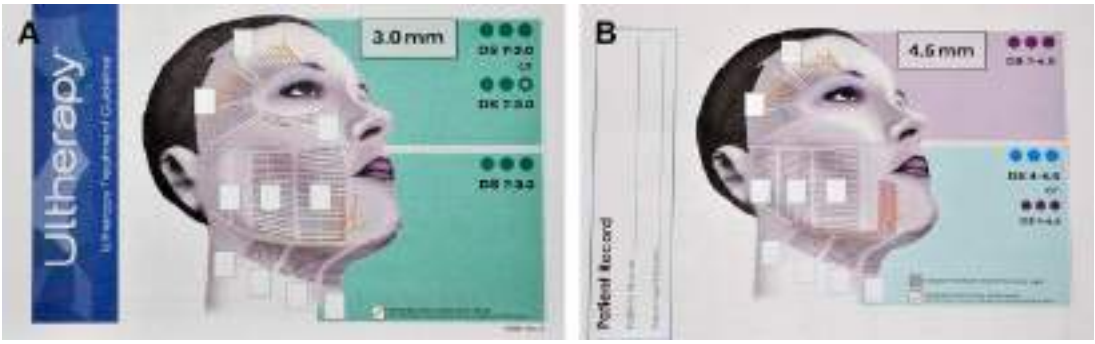


Fig. 10. Treatment diagram. (*A*) Deep treatment. (*B*) Superficial treatment. (*Reprinted* and *adapted from* Ulthera treatment guides, Ulthera, Mesa, AZ; with permission.)

without intervention in 2 to 3 weeks in most instances. Although it has not been described elsewhere in the literature, we observed a temporary frontal branch paresis in 1 patient after using the 4-4.5 transducer, off protocol, on a patient's brow. The brow returned to full function in less than 2 weeks with observation alone.

Ulthera Results in the Literature

As a new therapeutic modality, clinical evidence for Ulthera is limited. An initial pilot study confirming safety (evidence-based medicine level 4) and 2 cohort studies (evidence-based medicine level 2b) for efficacy comprise the clinical literature on the device.

In the pilot study performed by Gliklich and colleagues,[12] reproducible, focal lesions were created within the dermis and subcutaneous tissue without epidermal injury. In the histologic evaluation of excised preauricular skin, findings were consistent with previous animal and cadaveric studies of focal TCPs.

Subsequently, Alam and colleagues[13] performed a full-face Ulthera treatment in a prospective cohort study of 35 patients. Their primary outcome measure was clinical improvement. Using standardized 90-day photographs, assessed by 3 independent physicians, significant improvement was reported in 86% of patients. Attempts at objective measurements of the lower face were not possible, but measured change in eyebrow height from fixed facial landmarks on photographs was possible. Results were consistent with an average of 1.7 mm lift at the 90-day end point. Energy was delivered with the 7-4.5 transducer (1.05 J/TCP) to the brow and temple as a single pass.

In a recent study by Suh and colleagues,[8] an Asian patient population was assessed. Photographic improvement in skin laxity and histologic findings of collagen remodeling were primary and secondary end points, respectively. At 8 weeks, posttreatment photographs were assessed by 2 reviewers and compared with baseline images. In each of the 22 patients, nasolabial fold and jawline improvement was observed. When the patients were asked about their results, 77% and 73% reported improvement in the nasolabial fold and jawline, respectively. At this end point, 11 patients agreed to punch biopsy within the treatment region. Histologic results were assessed for a change in the fraction of collagen and dermal thickness (**Fig. 11**). Findings consisted of patients having 23.7% more dermal collagen fibers and an increased overall dermal thickness. Also, elastic fibers within the upper and lower reticular dermis were more parallel and straighter.

Ulthera Results in Clinical Practice

In our practice, we treated more than 80 patients during a 12-month period. Although a formalized outcome study has not been performed in our practice, patients are largely happy with their results. Some of our patients have had a surprisingly dramatic improvement in their facial contour and general skin tightness after treatment (**Figs. 12** and **13**). Despite similar treatment protocols, most patients instead experience subtle or subclinical changes (**Figs. 14–17**).

Nonideal patients with a heavy neck occasionally request treatment knowing the possible limited benefit they may receive. Sometimes, although less frequently, a clinical improvement can be appreciated (**Fig. 18**). This situation makes counseling patients and predicting expected improvement difficult. However, as mentioned earlier, better results are more likely to occur in the ideal patient who is younger, has slight submental lipoptosis, and early jowling. Alternatively, most patients are candidates for browlifting with the Ulthera device, but calculating those who will see marked improvement is difficult (**Fig. 19**). For this reason, patient selection and managing expectations are

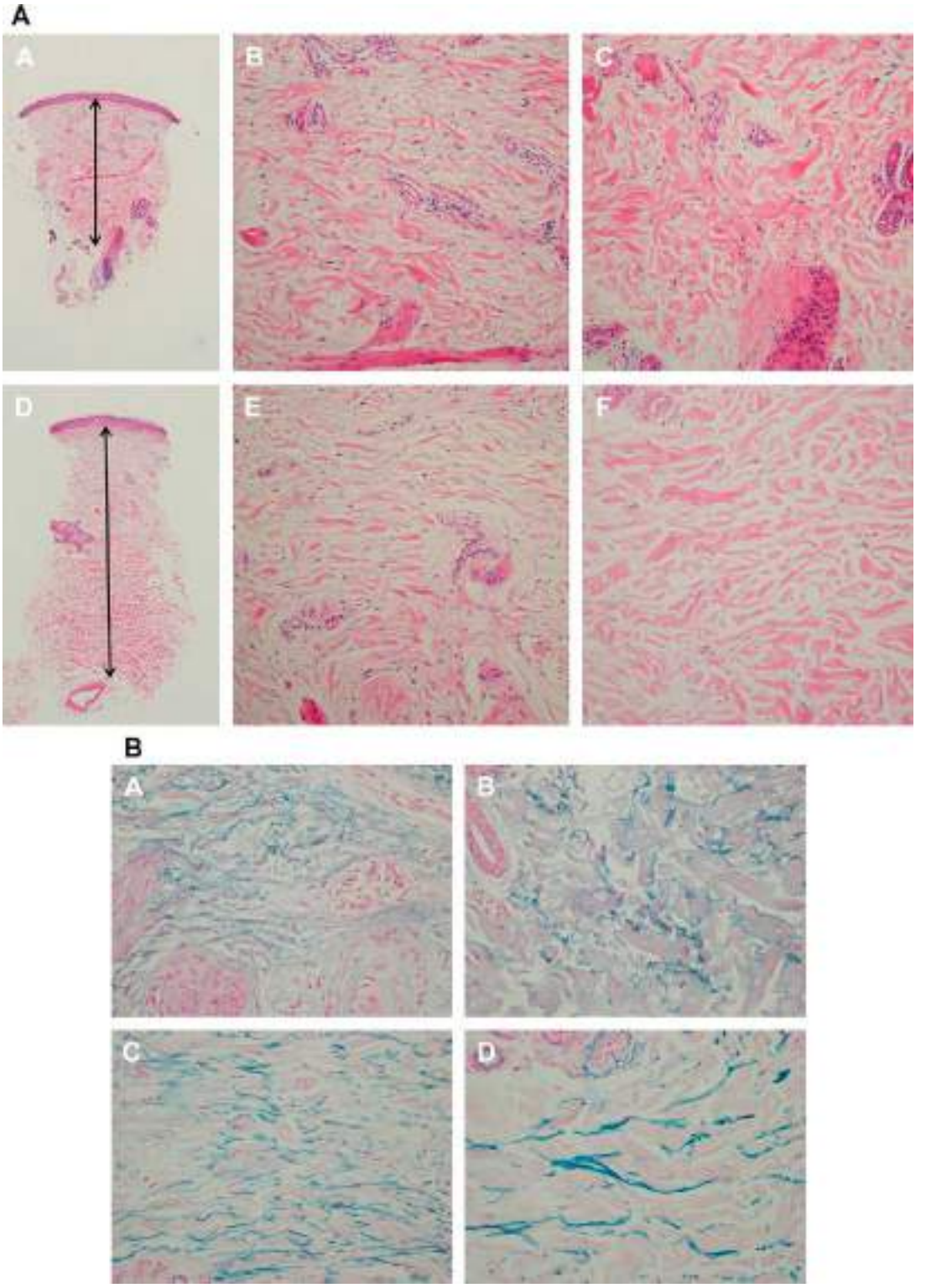


Fig. 11. Collagen and elastic fiber remodeling. Histologic evaluation of a midcheek punch biopsy after dual-energy treatment with 4-4.5 at 1.0 J and 7-3.0 at 0.45 J. (*A*) hematoxylin-eosin staining with collagen straighter and more parallel from pretreatment [*A–C*] to posttreatment [*D–F*]. (*A*/*D* - gross, *B, E* - upper dermis, *C, F* - lower dermis). (*B*) Victoria blue elastic fiber staining with straighter and more parallel elastin from pretreatment [*A* and *B*] to posttreatment [*C* and *D*]. (*A* and *C* - upper dermis, *B* and *D* - lower dermis). (*Reprinted* and caption *modified from* Suh DH, Shin MK, Lee SJ, et al. Intense focused ultrasound tightening in Asian skin: clinical and pathologic results. Dermatol Surg 2011;37:1599, 1600; with permission. Copyright 2011 by Wiley Periodicals.)

Fig. 12. 28-year-old woman with lower face/neck 1-month, 5-month, and 12-month results from a single treatment of 170 lines. (*A*) Before/after frontal images. (*B*) Before/after lateral images.

Fig. 13. 37-year-old woman with submental treatment 13-month result from a single treatment of 180 lines. Before/after lateral images.

Fig. 14. 58-year-old woman with lower face/neck 9-month result from a single treatment of 272 lines. (*A*) Before/after frontal images. (*B*) Before/after lateral images.

of the utmost importance. It is estimated that more than 95% of our patients who are treated with Ulthera are satisfied with their treatment outcomes, and this segment of our practice continues to grow.

Future Directions for Ulthera

The clinical enhancement that was reported in 86% to 100% of patients in the previous studies by Suh and colleagues[8] and Alam and colleagues[13] is more common than our findings. Despite a satisfied patient population, we have found it difficult to routinely appreciate the frequently subtle changes with standard digital photography. Therefore, exploring three-dimensional imaging as a better method to capture small volume and contour changes may be of benefit to further quantify our results and better inform our patients.

Evolution of Treatment Protocol

Over time, patients treated with Ulthera are finding that additional lines of energy in a treatment are necessary to improve patient outcomes. Therefore, an evolution in treatment protocols has occurred from the early, single-pass treatments to later single-session, 2-depth treatments at both 4.5 mm and 3.0 mm. Full-face treatment increased from approximately 110 lines to an average of 350 lines. Most recently, a new Plus protocol has been released, which has increased the average number of lines for a full face at the

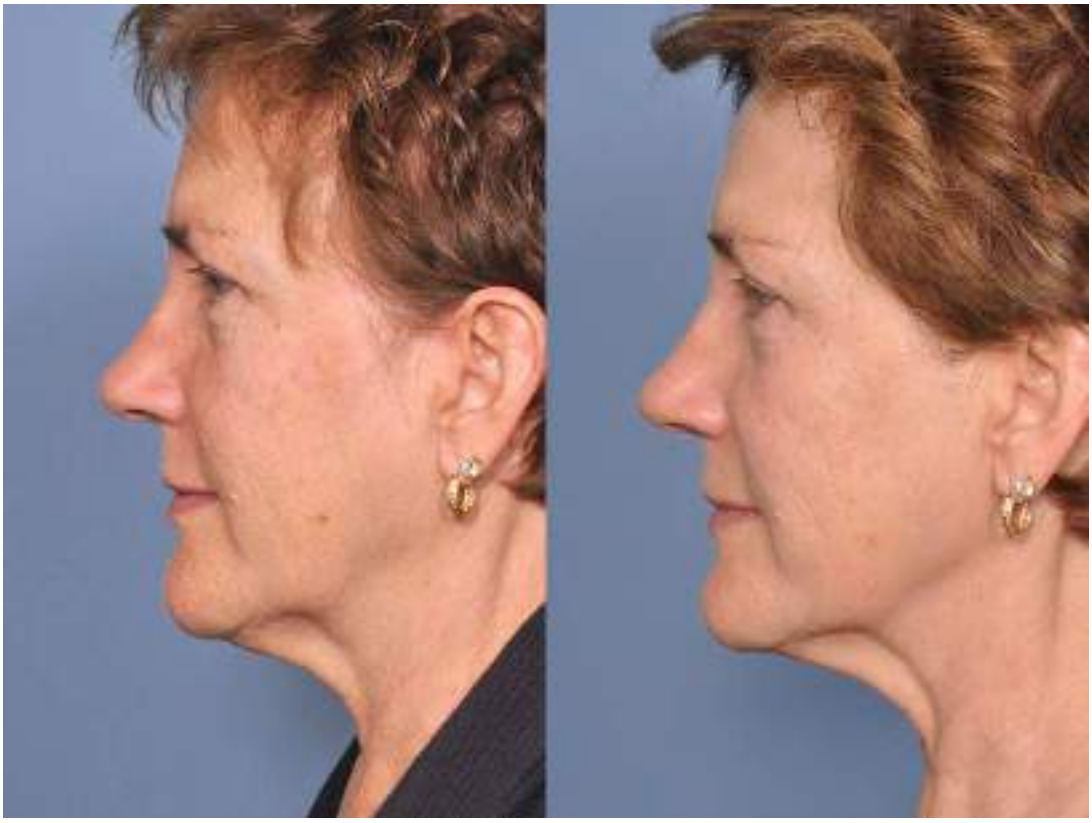


Fig. 15. 61-year-old woman with full-face 9-month result from a single treatment of 422 lines and subsequent intense pulsed light and profractional treatment. Before/after lateral images.

2 depths to 500 lines. Although off protocol, many users, including our practice, are currently increasing to 700 to 800 lines to maximize results on a full-face treatment.

Third Layer of Treatment

Another recent development is the 1.5-mm transducer. This addition offers the potential to better treat the dermis for superficial rhytids. We have

Fig. 16. 41-year-old woman with submental 10-month result from a single treatment of 168 lines. Before/after lateral images.

Fig. 17. 57-year-old woman with lower face/neck 3-month result from a single treatment of 380 lines. Before/after lateral images. (*Courtesy of* Harrison C. Putmann III, MD.)

Fig. 18. 44-year-old man with submental 4-month result from a single treatment of 164 lines. Before/after frontal images.

Fig. 19. 41-year-old woman with brow 3-month result from a single treatment of 96 lines. Before/after frontal images.

NOTES TO EARLY USERS

- Ulthera offers an alternative treatment modality for patients in whom surgery is not indicated or desired.
- Patients are often pleased with their Ulthera result even if the physician appreciates subtle, nonsurgical results.
- Results can be variable and a subset does not obtain a benefit from treatment.
- Careful candidate selection and the management of expectations are paramount to achieving a satisfied patient.
- Used appropriately, Ulthera can supplement a physician's surgical practice.

not had any experience with this transducer, but a few practices have received it and started treatments. It will be interesting to see the clinical benefit of this third layer of treatment.

Increased Lines on Transducers

Ulthera does have a consumables fee for each transducer. The current average cost per line to a practice is $1.16 per line. The company recently increased the lines on their consumable transducers from 1200 lines to 1800 lines without a price increase to aid users with their return on investment (ROI) numbers. The benefit of using more lines in a treatment is clear, and Ulthera plan to increase the lines on their transducers to 2100 lines. To further support the increased line protocol, no changes in transducer prices are expected. Across the country, the average price of a full-face treatment is $3500. With an 1800-line transducer, a 500-line Plus protocol treatment would cost a practice $580, yielding a return of $2920. Overall, this is an attractive ROI that should remain stable even with newer treatment protocols incorporating additional lines.

SUMMARY

Ulthera offers a new treatment modality for noninvasive skin tightening that has been well received by our patients. In addition, the technology continues to undergo further refinement and is supported by its early preclinical and clinical studies. Outcomes of an Ulthera treatment can vary from person to person, and are subtle in most instances. Further studies with objective outcome measures are necessary to quantify treatment success and guide future treatment recommendations. Until these studies have been completed, patients should be counseled as to their likelihood of improvement based on their age, skin laxity, tissue volume, skin quality, rhytids, and general health.

REFERENCES

1. Orringer JS, Kang S, Johnson TM, et al. Connective tissue remodeling induced by carbon dioxide laser resurfacing of photodamaged human skin. Arch Dermatol 2004;140:1326–32.
2. Fry WJ, Wulff VJ, Tucker D, et al. Physical factors in ultrasonically induced changes in living systems: I. Identification of non-temperature effects. J Acoust Soc Am 1950;22:867–76.
3. Fry WJ. Intense ultrasound: a new tool for neurological research. J Ment Sci 1954;22:85–96.
4. US Food and Drug Administration, Center for Drug Evaluation and Research. ExAblate 2000 System P040003 approval letter. 2004. Accessed at: http://www.accessdata.fda.gov/cdrh_docs/pdf4/P040003a.pdf. Accessed November 1, 2011.
5. Jolesz FA. MRI-guided focused ultrasound surgery. Annu Rev Med 2009;60:417–30.
6. Jolesz FA, Hynynen K, McDannold N, et al. MR imaging–controlled focused ultrasound ablation: a noninvasive image-guided surgery. Magn Reson Imaging Clin North Am 2005;13:545–60.
7. Clement GT. Perspectives in clinical uses of high-intensity focused ultrasound. Ultrasonics 2004;42:1087–93.
8. Suh DH, Shin MK, Lee JS, et al. Intense focused ultrasound tightening in Asian skin: clinical and pathologic results. Dermatol Surg 2011;37:1595–602.
9. White WM, Makin IR, Slayton MH, et al. Selective transcutaneous delivery of energy to porcine soft tissues using intense ultrasound. Lasers Surg Med 2008;40:67–75.
10. White WM, Makin IR, Barthe PG, et al. Selective creation of thermal injury zones in the superficial musculoaponeurotic system using intense ultrasound therapy: a new target for noninvasive facial rejuvenation. Arch Facial Plast Surg 2007;9:22–9.
11. Laubach HJ, Makin IR, Barthe PG, et al. Intense focused ultrasound: evaluation of a new treatment modality for precise microcoagulation within the skin. Dermatol Surg 2008;34:727–34.

12. Gliklich RE, White WM, Slayton MH, et al. Clinical pilot study of intense ultrasound therapy to deep dermal facial skin and subcutaneous tissues. Arch Facial Plast Surg 2007;9:88–95.
13. Alam M, White LE, Martin NE, et al. Ultrasound tightening of facial and neck skin: a rater-blinded prospective cohort study. J Am Acad Dermatol 2010;62:262–9.
14. US Food and Drug Administration, Center for Drug Evaluation and Research. Ulthera K072505 approval letter. 2009. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf7/K072505.pdf. Accessed November 1, 2011.
15. Ultherapy User Group Meeting. Informal communications. Rosemont, September 19, 2011.

ORIGINAL ARTICLE

Selective Creation of Thermal Injury Zones in the Superficial Musculoaponeurotic System Using Intense Ultrasound Therapy

A New Target for Noninvasive Facial Rejuvenation

W. Matthew White, MD; Inder Raj S. Makin, MD, PhD; Peter G. Barthe, PhD; Michael H. Slayton, PhD; Richard E. Gliklich, MD

Objectives: To transcutaneously deliver intense ultrasound (IUS) energy to target the facial superficial musculoaponeurotic system (SMAS), to produce discrete thermal injury zones (TIZs) in the SMAS, and to demonstrate the relative sparing of adjacent nontargeted layers superficial and deep to the SMAS layer.

Methods: In 6 unfixed human cadaveric specimens, the SMAS layer was visualized and targeted using the ultrasound imaging component of the IUS device. Using 2 IUS handpieces, 202 exposure lines were delivered bilaterally in multiple facial regions by varying combinations of power and exposure time (0.5-8.0 J). Tissue was then excised and examined grossly and histologically for evidence of thermal injury using nitroblue tetrazolium chloride viability stain.

Results: Reproducible TIZs were produced selectively in the SMAS at depths of up to 7.8 mm, and sparing of surrounding tissue including the epidermis. Higher energy settings and high-density exposure line pattern produced a greater degree of tissue shrinkage.

Conclusions: In human cadaveric facial tissue, IUS can noninvasively target and selectively produce TIZs of reproducible location, size, and geometry in the SMAS layer. The ability to produce focused thermal collagen denaturation in the SMAS to induce shrinkage and tissue tightening has not been previously reported and has significant implications for aesthetic facial rejuvenation.

Arch Facial Plast Surg. 2007;9:22-29

Author Affiliations: Division of Facial Plastic and Reconstructive Surgery, Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, and Department of Otology and Laryngology, Harvard Medical School, Boston (Drs White and Gliklich); and Ulthera Inc, Mesa, Ariz (Drs Makin, Barthe, and Slayton).

THE SUPERFICIAL MUSCULOAPONEUROTIC SYSTEM (SMAS) is a continuous fibrous network that envelops the muscles of facial expression and extends superficially to connect with the dermis of the skin.[1,2] The function of the SMAS is to transmit the activity of the facial mimetic musculature to the facial skin to coordinate facial expression. The SMAS is composed of collagen and elastic fibers in similar proportions to the skin dermis.[3,4] The SMAS and facial skin exhibit viscoelastic properties, but it has been demonstrated that the SMAS has much greater holding properties and more delayed stress relaxation after a surgical "lifting" procedure.[5]

Several nonsurgical modalities have been developed in an effort to treat facial rhytids (peels, microdermabrasion, and lasers).[6,7] These modalities have primarily focused on treating the superficial layers of the skin owing to limitations in penetration depth. One of the most effective treatments for facial rhytids has been ablative skin resurfacing with carbon dioxide or erbium lasers, which creates a sublethal thermal injury in the skin, causing removal of the epidermis and contraction and remodeling of the dermis. Although ablative skin resurfacing has proved efficacious in the treatment of superficial rhytids, its use has been limited by the adverse effects of treating the superficial skin, including prolonged erythema and possible permanent pigmentary changes. For this reason, nonablative skin resurfacing devices (intense pulsed light, light-emitting diode, radiofrequency [RF], Nd:YAG, and pulsed dye lasers) have been designed in an effort to reduce some of the unwanted adverse effects of ablative skin resurfacing.[8] Although these nonablative skin resurfacing modalities have fewer adverse effects than ablative skin resurfacing, the efficacy is less than desirable. Furthermore, neither modality is designed to specifically address the SMAS layer.

Intense ultrasound (IUS) is an energy modality that can propagate through tissue up to several millimeters. However, for skin tissue when the beam is directed in

a tight focus at a given depth, thermal coagulative necrosis occurs in that focal volume of tissue, leaving the superficial layers unaffected.[9-11] Ultrasound waves induce a vibration in the composite molecules of a given tissue during propagation, and the thermoviscous losses in the medium lead to tissue heating. It has been well established in the literature that IUS fields transcutaneously directed into whole-organ soft tissue can produce coagulative necrosis, resulting primarily from thermal mechanisms.[9,10] During the past decade, the clinical use of focused IUS has been investigated as a noninvasive surgical tool to treat whole-organ tumors, such as liver, breast, and uterus.

Working in conjunction with the manufacturer (Ulthera Inc, Mesa, Ariz), a novel IUS approach has been developed specifically for treating facial soft tissues and targeting the SMAS. The prototype focuses energy in tissue to produce a 25-mm line of discrete lesions spaced 0.5 to 5.0 mm apart (**Figure 1**). Furthermore, imaging and targeted energy exposure can be accomplished using the same handpiece. Preclinical studies conducted by our group[11] using porcine skin, a model with skin structure similar to humans, have demonstrated that the IUS system reliably creates small, well-defined, controllable thermal injury zones (TIZs) in dermal or subdermal soft tissues.

The ability to achieve noninvasive thermal injury and reproducible precise and selective collagen denaturation in the SMAS has not been previously reported, to our knowledge. The potential of this approach to cause selective SMAS contraction might have important implications for treatment of the aging face. We postulate that this device is capable of delivering energy to the deep soft tissue layers of the face, such as the subdermal connective tissues (the SMAS). The objectives of this study are, therefore, to deliver IUS energy to targeted areas of the subcutaneous facial tissue, in particular, the SMAS; to produce discrete lesions from thermal injury in the SMAS; and to demonstrate the relative sparing of adjacent nontargeted layers, such as the epidermis and deeper tissues.

METHODS

Approval for this experiment was obtained from the Massachusetts Eye and Ear Infirmary institutional review board. Six nonfixed, frozen, whole cadaveric head specimens were obtained from a tissue bank supplier (International Biological Inc, Gross Pointe, Mich). The cadavers consisted of 2 males and 4 females aged 49 to 72 years. None of the specimens had evidence of previous facial surgical procedures. The specimens were stored in a freezer and could be identified by a serial number tag.

IUS SYSTEM

The IUS system (Ulthera Inc) is a device designed to target and deliver focused IUS in human tissue. The IUS handpiece contains a transducer that has 2 functioning modes: imaging (which is used to image the region of interest before the therapeutic ultrasound exposures) and treatment (which is the mode that delivers a series of higher-energy ultrasound exposures). In treatment mode, the transducer delivers a series of precise ultrasound pulses along a linear path. The handpiece is designed to mechanically slide in a straight line to deliver a series of ultrasound exposures. For each series of exposures, the following source conditions can be varied: power output, exposure time, length of exposure line, distance between exposure zones, and time delay after each exposure. In this manner, thermal injury can be produced in selective zones in a straight line at a given depth in the tissue (a 25-mm line of discrete lesions spaced 0.5-5.0 mm apart).

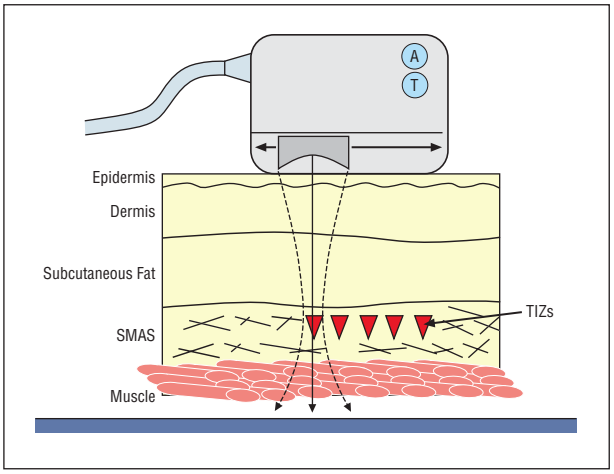


Figure 1. Schematic of intense ultrasound exposures. The intense ultrasound handpiece focuses energy at depths to create thermal injury zones (TIZs) in the superficial musculoaponeurotic system (SMAS) layer. The parabolic transducer slides in the handpiece to create multiple TIZs at a fixed depth in tissue. As an added safety feature, the intense ultrasound device cannot be deployed without first arming the device. This is similar to a laser in the "standby" mode. A indicates arm; T, treat.

Penetration depth of energy is primarily affected by ultrasound source frequency. The preclinical experiments[11] in ex vivo porcine tissues have shown that handpieces with higher ultrasound frequency combined with a shallower focal depth in tissue produce lesions more superficial in tissue, whereas lower-frequency handpieces tend to penetrate deeper in tissues. The results of this study are from handpieces operating at 7.5 and 4.4 MHz, with the focal depth in tissue for each handpiece being 4.5 mm.

IUS EXPOSURE PROCEDURE

Experiments were conducted with the cadaveric specimens at room temperature (20°C) after they had been thawed overnight in a water bath. Multiple facial areas were selected bilaterally: cheek, preauricular area, temple, frontal area, and neck. In the planned treatment area, the skin was tattooed (India ink) to the level of the SMAS using a preconstructed grid (**Figure 2**A). Each microtattoo was placed 10 mm apart in horizontal and vertical lines to create a permanent grid over the proposed treatment area.

Facial areas of treatment were then selected. A range of source conditions was selected and planned for each area. Before each treatment, ultrasound imaging was performed to identify the target tissues. Ultrasound imaging was performed on each planned treatment area, and still images were captured and stored. The superficial and deep skin layers, fat, SMAS, parotid fascia, and parotid gland were discernible during the ultrasound imaging mode.

All the treatments were performed perpendicular to the relaxed skin tension lines of the cadaveric face. The IUS exposure lines were delivered using 2 methods: (1) up to 7 horizontal rows of exposures spaced 10 mm apart at varying energy levels or (2) in a "high-density line" pattern achieved by placing multiple parallel exposure lines (n=15-20) at a fixed energy level 2 to 3 mm apart. Immediately after IUS exposure lines were delivered, the handpiece was left in place, and the axis of

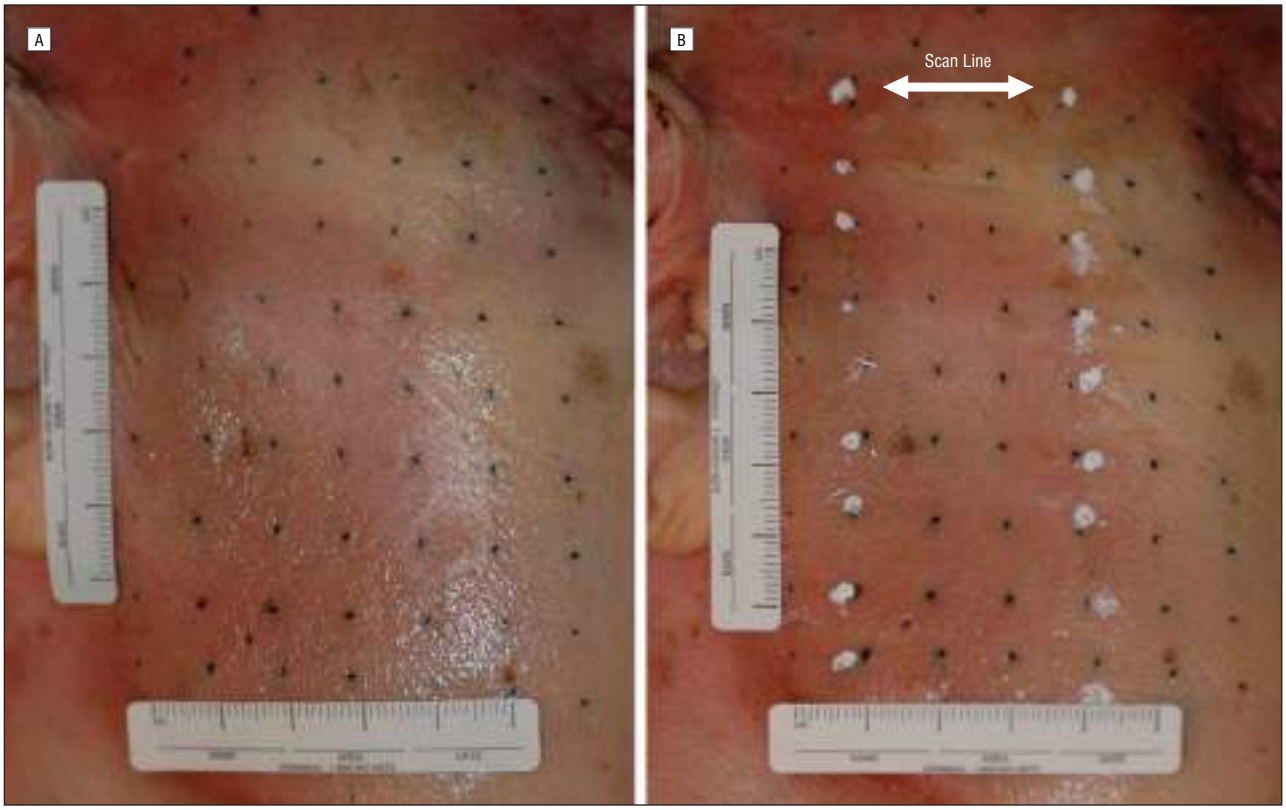


Figure 2. Digital photographs of the intense ultrasound exposure area: right preauricular area. A, Before the exposures, grids were created using India ink tattoos. The intense ultrasound exposures were delivered horizontally along these treatment grids and, therefore, perpendicular to relaxed skin tension lines. B, Immediately after treatment the exposure lines were marked using correction fluid to aid in localizing the lesions.

the exposure line delivered was marked using correction fluid (Wite-Out; Bic Corp, Milford, Conn) (Figure 2B).

After all IUS exposures for a given cadaveric specimen had been completed, each treated facial region was excised en bloc up to the subperiosteal level. The tissue bloc was then placed on an acrylic glass (Plexiglas; Arkema Group, Philadelphia, Pa) tray and kept in a –15°C freezer for approximately 2 hours. Using a surgical blade, fine 1-mm-thick sections were cut perpendicular to the IUS exposure lines. These grossly sectioned thin strips of tissues were then placed in nitroblue tetrazolium chloride (NBTC) stain overnight for viability staining.[11,12] The remaining exposed tissue was embedded and submitted for frozen-section histologic processing and staining.

A digital single-lens reflex camera (Nikon D-70; Nikon USA, Melville, NY) was used for high-resolution photographs of IUS-exposed areas. Standardized conditions for distance and lighting were used for photography. Photographs were taken of the left and right side profiles of the face before and after IUS exposure (Figure 2). Digital photographs were also taken of the gross tissue sections after they had been stained with NBTC.

HISTOLOGIC ANALYSIS

Unfixed cadaveric tissue was used to more readily approximate human facial skin and to allow for evaluation in collagen by the NBTC viability stain.[12] When frozen tissue sections are stained, the reduction of nitroblue tetrazolium chloride (a redox indicator) by nicotinamide adenine dinucleotide (NADH) diaphorase produces an intense blue cytoplasmic pigment. The activity of nicotinamide adenine dinucleotide diaphorase has been shown to decrease immediately on cell death. Therefore, blue staining of cells on frozen sections using NBTC confirms viability, and the absence of blue staining is indicative of an area of coagulative necrosis.[13] We also performed routine hematoxylin-eosin regressive staining, which has also been used previously to demonstrate thermal denaturation of collagen for laser hair removal and ablative resurfacing.[14] Both of these staining methods allow for accurate determination of the location and extent of the TIZs.

IMAGE ANALYSIS

Using image processing software (NIH ImageJ, available at http://rsbweb.nih.gov/ij/), postexposure digital photographs were compared with pretreatment images. The length of each horizontal and vertical line of the grids was then measured, recorded, and compared. The magnitude of thermal-induced immediate contraction was calculated by subtracting the postexposure distance from the preexposure distance, and then this number was divided by the preexposure distance and expressed as a percentage. Thermal-induced immediate contraction was compared parallel and perpendicular to the line of treatments to determine the maximum vector of collagen contraction. Depth and dimensions of TIZs were evaluated using digital photographs of gross tissue strips after NBTC staining.

RESULTS

A total of 202 IUS exposure lines (10 IUS pulses per line) and 2020 individual IUS pulses were delivered to the 6 cadaveric heads. After each exposure line, no noticeable surface changes were seen using either handpiece. Source conditions were varied across a range of 0.5 to 8.0 J for both handpieces. Viability staining (NBTC) identified le-

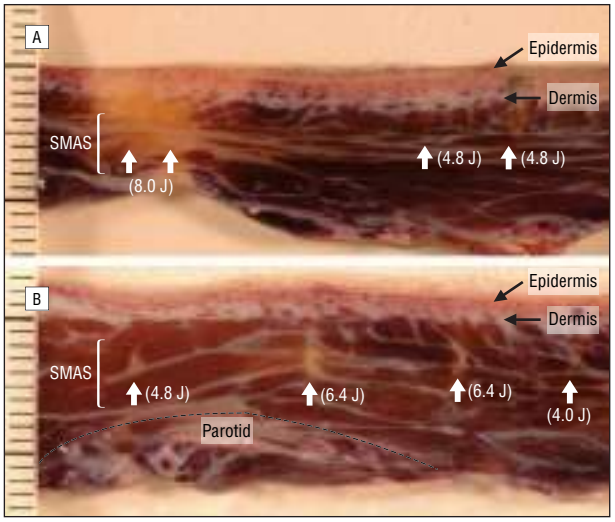


Figure 3. Zones of thermal injury: right preauricular area. Gross nitroblue tetrazolium chloride–stained sections of preauricular tissue after a set of intense ultrasound exposures using the 4.4-MHz/4.5-mm handpiece and 4.8 to 8.0 J of energy (A) and 4.0 to 6.4 J of energy (B). Arrows indicate thermal injury zones; SMAS, superficial musculoaponeurotic system. Scale indicates 1 mm per division.

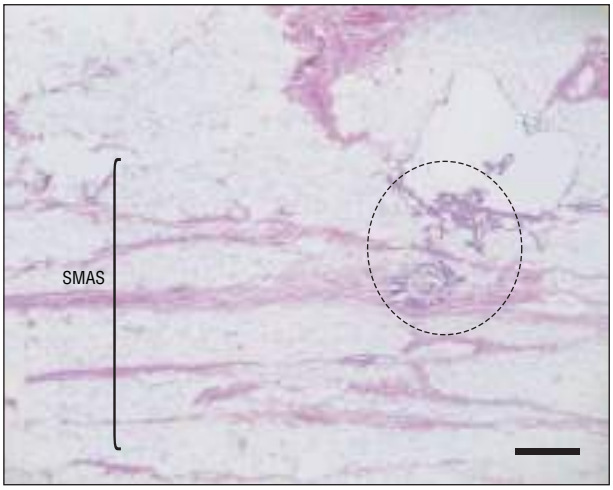


Figure 4. Histologic analysis of tissue taken from the right preauricular area. A discrete, intensely eosinophilic lesion (dotted circle) is seen in the superficial musculoaponeurotic system (SMAS) layer in this histologic section (regressive hematoxylin-eosin staining, original magnification ×20; 4.4 MHz/4.5 mm; 3.2 J). Scale bar indicates 0.5 mm.

sions on gross strips of cadaveric tissue as a lack of blue staining and pale color of the TIZs. Frozen-section histologic analysis of the same tissues also demonstrated the TIZs by lack of blue staining and morphologic evidence of thermal-induced coagulative necrosis, such as thickening of collagen fiber bundles. Thermal injury zone locations and dimensions were observed to be related to particular source conditions, such as energy and focal depth in tissue for a particular handpiece.

QUALITATIVE ANALYSIS OF TIZs

Visual analysis of the digital images of grossly sectioned strips of cadaveric tissues confirmed a dose-response relationship between energy and TIZ size. In the preauricular region, energy was varied between 3.2 and 8.0 J using the 4.4-MHz handpiece, and a dose-response effect of thermal modification was observed. Discrete cigar-shaped lesions can be seen in the SMAS layer without damage to surrounding tissues above or below (**Figure 3**). In this figure, small TIZs are easily identified at the lowest energy level of 4.0 J (Figure 3B). As the source energy is increased to 4.8 and then 6.4 J, the lesions become larger and more elongated. Further increases in energy lead to overtreatment as energy is increased to 8.0 J (Figure 3A). In this area in Figure 3A, 2 IUS exposure lines at an energy setting of 8.0 J are placed adjacent to one another. One can easily see the thermal damage extending proximally toward the source to involve the dermis and epidermis. No gross thermal lesions were seen at energy levels below 4.0 J (additional gross tissue strips from the same location not displayed in Figure 3). However, regressive hematoxylin-eosin–stained histologic slides of areas exposed to 3.2 J of energy confirmed the well-demarcated TIZs as evidenced by deep purple staining and thickening of the collagen bundles (**Figure 4**).

In the forehead region, when IUS exposures were delivered using the 4.4-MHz handpiece at similar energies (2.3-6.1 J), overtreatment occurred at lower energy levels. At 3.8 J, the TIZs can be seen propagating superficially toward the dermis (**Figure 5**). As energy levels were increased further, the TIZs became thicker (Figure 5A). Conversely, when the energy settings were decreased, the TIZs became more slender (Figure 5B). This dose-response pattern could be observed in all of the NBTC-stained gross sections of tissues from all facial regions but was much more apparent in the forehead region. At the highest energy level of 6.1 J, NBTC histologic analysis revealed a lesion that extended from the mid dermis down through the subcutaneous fat to the level of the SMAS (**Figure 6**). In the middle dermis, thickening of collagen fibers is seen, with a loss of blue staining in the subdermis and SMAS that easily demarcates the lesion. The basement membrane revealed a cleft that separated the epidermis from the dermis (Figure 6).

In **Figure 7**, multiple TIZs can be seen discretely in the SMAS. In this region of the temple, a high-density line pattern was created using the 4.4-MHz handpiece. In this high-density pattern, multiple consecutive parallel exposure lines were delivered at the same unique power setting such that an array of densely spaced TIZs were deposited per unit volume of tissue. Relatively lower energy levels (3.0 J) compared with the cheek area were required to produce these well-defined lesions. In this gross tissue section, excellent consistency is demonstrated regarding TIZ depth and dimension. The NBTC-stained histologic analysis confirmed the successful targeting of the SMAS layer and the consistency of the closely spaced TIZ (**Figure 8**).

Intense ultrasound exposures using the higher-frequency 7.5-MHz handpiece with a 4.5-mm focal depth in tissue required much lower energy levels to create TIZs. Also, a much narrower window existed between creating discrete lesions in the SMAS and overtreatment. In **Figure 9**, we see a thin, well-demarcated lesion at 2.2 J; increasing the energy levels quickly results in over-

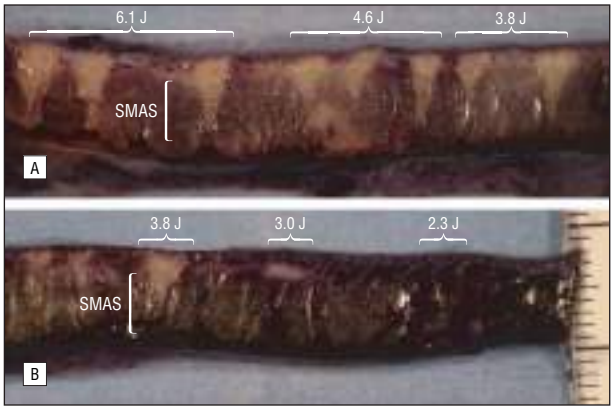


Figure 5. Zones of thermal injury: forehead area. Gross nitroblue tetrazolium chloride–stained sections of forehead tissue after a set of intense ultrasound exposures using the 4.4-MHz/4.5-mm handpiece and 3.8 to 6.1 J of energy (A) and 2.3 to 3.8 J of energy (B). SMAS indicates superficial musculoaponeurotic system. Scale indicates 1 mm per division.

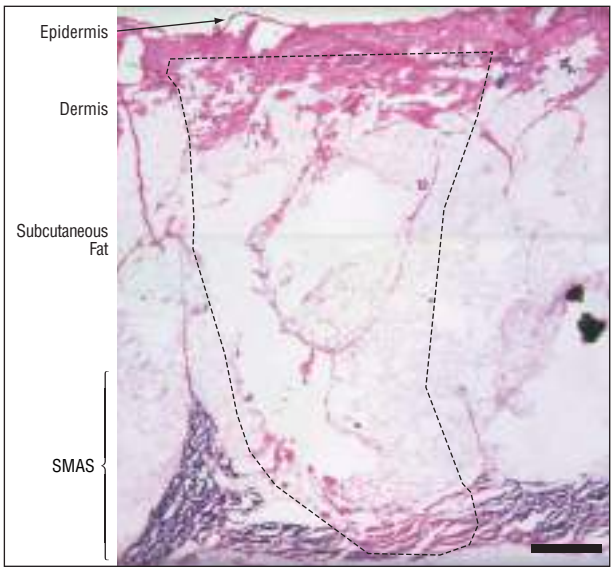


Figure 6. Nitroblue tetrazolium chloride histologic analysis: forehead area. Two photomicrographs were merged together to view a thermal injury zone (dotted line) extending from the mid dermis to the superficial musculoaponeurotic system (SMAS) layer (4.4 MHz/4.5 mm, 6.1 J, original magnification ×20). Scale bar indicates 0.5 mm.

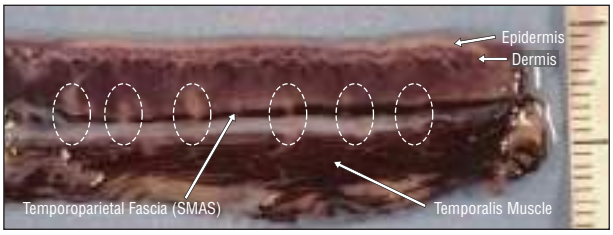


Figure 7. High-density line pattern of intense ultrasound exposures: left temporal area. The line of exposures is confined to the superficial musculoaponeurotic system (SMAS) layer (4.4 MHz/4.5 mm, 3.0 J). Dotted circles indicate thermal injury zones. Scale indicates 1 mm per division.

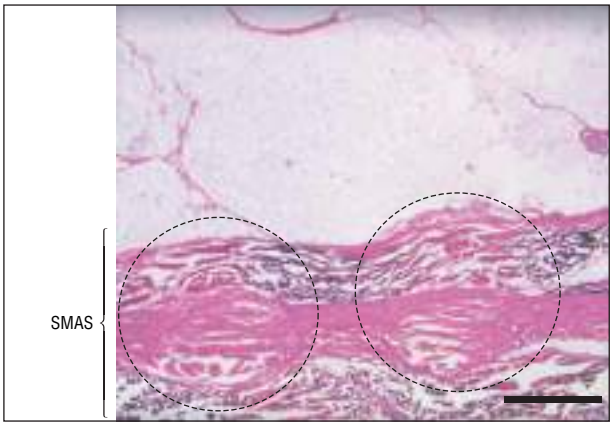


Figure 8. Nitroblue tetrazolium chloride histologic analysis: left temporal area. Two separate thermal injury zones (dotted circles) can be seen confined to the superficial musculoaponeurotic system (SMAS) layer (4.4 MHz/4.5 mm, 3.0 J, original magnification ×40). Scale bar indicates 0.5 mm.

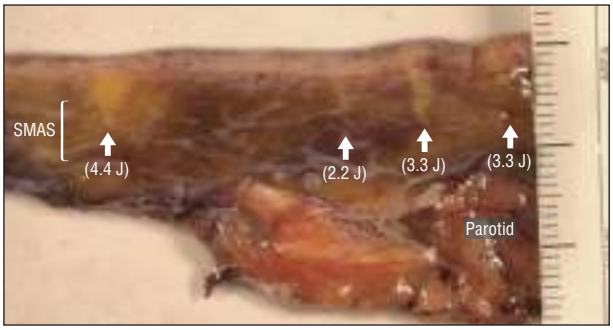


Figure 9. Zones of thermal injury: right cheek area. Gross nitroblue tetrazolium chloride–stained section of the cheek after a set of intense ultrasound exposures (7.5 MHz/4.5 mm, 2.2-4.4 J). Arrows indicate thermal injury zones; SMAS, superficial musculoaponeurotic system. Scale indicates 1 mm per division.

treated regions, as the 3.3 and 4.4 J exposure lines create lesions that approach the skin epidermis (tadpole phenomenon).[9] At an energy exposure level of 1.6 J no gross lesion was produced; however, on NBTC histologic analysis, a discrete lesion was seen in the SMAS and connective tissue septae (**Figure 10**).

QUANTITATIVE ANALYSIS OF TIZs

Measurements were performed to quantify TIZ dimensions and depth of penetration in tissues as source energy settings were varied. Analysis of the digital images of grossly sectioned strips of cadaveric tissues after exposure using the 4.4-MHz handpiece confirmed a dose-response relationship (**Figure 11**). Figure 11A shows that TIZs at all energy levels were usually 0.5 mm below the tissue surface (top) and penetrated, on average, 5 mm deep into tissues (bottom). This corresponded closely to the preset focal depth of the 4.4-MHz handpiece (ie, 4.5 mm). A dose-response effect could be observed: as energy levels were increased from 3.8 to 8.0 J, TIZ dimensions increased proportionally (Figure 11B).

Using the 7.5-MHz handpiece, as energy levels were increased, the TIZs were close to the tissue surface (**Figure 12**A), which is what could be appreciated visually on the NBTC-stained gross cadaveric sections (Figure 9). Depth of penetration in tissue was variable but averaged 5.25 mm, which corresponded to the preset focal depth of the 7.5-MHz handpiece (4.5 mm) (Figure 12A). Analysis of the lesion size created (area in square millimeters) showed a close dose-response rela-

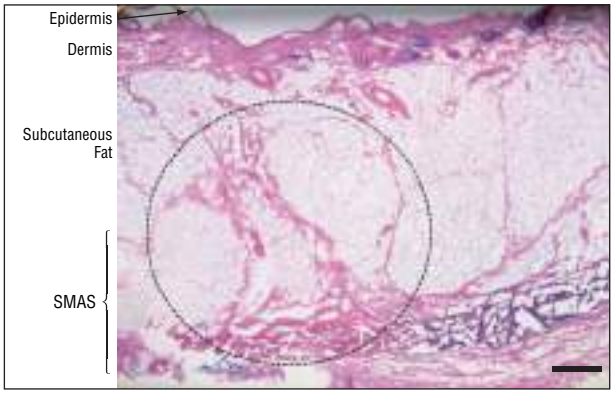


Figure 10. Nitroblue tetrazolium chloride histologic analysis: right forehead area. A well-defined thermal injury zone (dotted circle) is seen involving the superficial musculoaponeurotic system (SMAS) and overlying connective tissue septae. No gross lesion was identified in the tissue at this energy level (original magnification ×20). Scale bar indicates 0.5 mm.

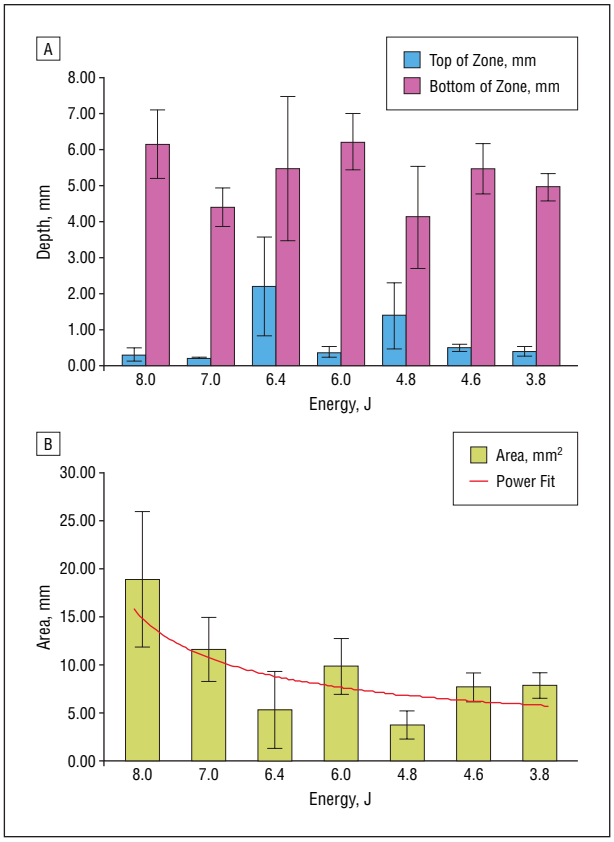


Figure 11. The dose response of the 4.4-MHz handpiece. A, Mean depth of lesions relative to the surface of the tissues. B, Mean changes in the dimensions of the lesion with decreasing energy levels. Error bars represent SD.

tionship: as the energy was increased, the TIZs became larger (Figure 12B).

THERMAL-INDUCED IMMEDIATE COLLAGEN CONTRACTION

Treated facial regions were observed to have small but reproducible degrees of collagen contraction. In general, the greater the energy levels delivered to tissues, the greater

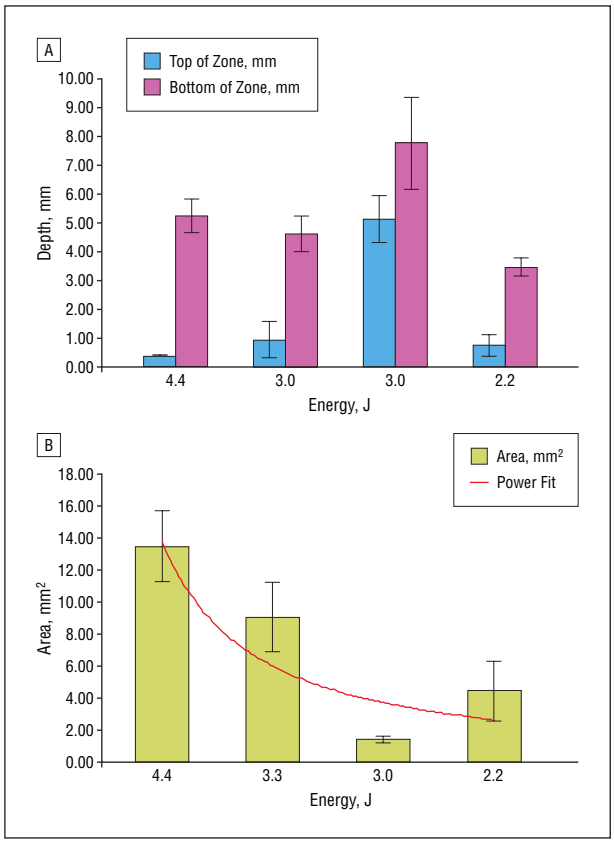


Figure 12. The dose response of the 7.5-MHz handpiece. A, Mean depth of lesions relative to the surface of the tissues. B, Mean changes in the dimensions of the lesion with decreasing energy levels. Error bars represent SD.

was the percentage contraction. In **Figure 13**A, we see that as the energy is increased from 3.1 to 6.7 J in these single-line exposures, the shrinkage increases. However, when multiple (n=20) IUS exposure lines are delivered, even at a much lower energy level (1.3 J), the shrinkage increases dramatically. As seen in the specimens, the high-density line pattern of exposure produces a greater number of TIZs per unit volume of soft tissue. When facial areas with a high-density line pattern were analyzed, the greatest degree of shrinkage occurred in the horizontal dimension, which was along the same axis as the greatest number of IUS exposures delivered (Figure 13B).

COMMENT

In this article, we introduce a novel technology with the potential for use in facial rejuvenation. We demonstrated that IUS is capable of creating zones of thermal injury (or areas of coagulative necrosis from heat) in the SMAS in human cadaveric soft tissues. These lesions are targeted, predictable, and reproducible in terms of depth, size, and shape based on handpiece frequency and source conditions (power, exposure time, and energy). Within the source conditions used in this study, the epidermis was spared even with increasing energy levels. Structures deep to the SMAS also were spared.

It is well established that IUS fields directed in soft tissue can produce ablation resulting primarily from thermal mechanisms.[9] The energy from the ultrasound beam

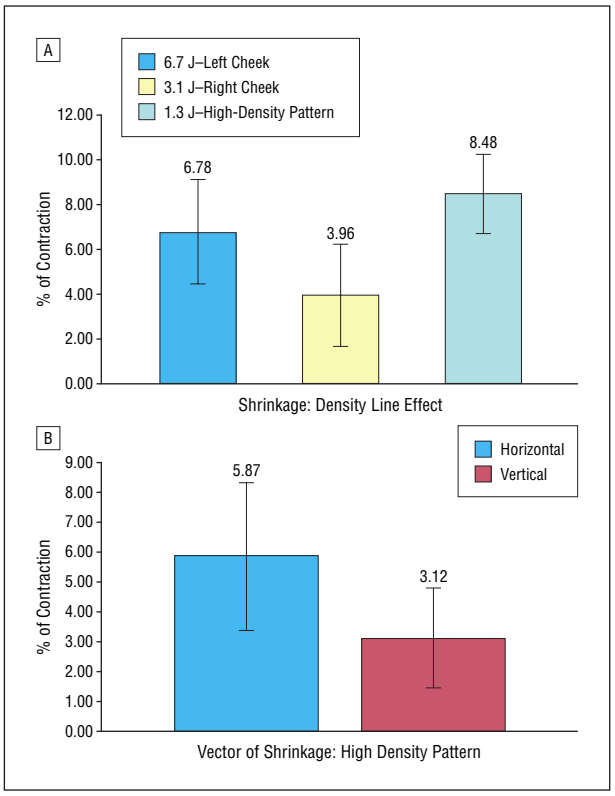


Figure 13. Thermal-induced immediate collagen contraction. A, As you increase the number of thermal injury zones per unit volume, you dramatically increase the amount of contraction (6.7 J, n=6; 3.1 J, n=6; and 1.3 J, n=20). B, In areas where a high-density line pattern was delivered, most shrinkage occurs along the horizontal direction, which was the same direction as the intense ultrasound exposures were delivered (n=65 per bar). Error bars represent SD.

is absorbed in the soft tissue and is converted primarily into heat. The increased temperature, in turn, results in distinct areas of coagulative necrosis of the tissue. In the case of skin tissue, the collagen is denatured (melted), and it loses its organized structure. This tissue response (thermal ablation) achieved by an IUS field is similar to that from other energy-based devices used in the cosmetic arena, such as lasers, RF, and combination laser-RF devices.[6] However, in contrast to the other known energy-based devices used for cosmetic applications, the IUS field is sharply focused; thereby, most of the energy is deposited in the form of heat in the focal zone of the beam, leaving the surrounding regions unaffected. With RF delivery, thermal imaging has revealed that this energy is much more diffuse and tends to affect the dermis and travel along connective tissue septae in the subdermis.[15]

It has been demonstrated in this experiment that it is possible to create well-circumscribed TIZs selectively in the SMAS. No surface changes were noted on the cadaveric skin after exposure, and qualitative views of grossly stained tissue strips and histologic slides revealed no epidermal disruption. However, some overtreated areas revealed a characteristic cleft of the basal layer that is also seen immediately after laser therapy.[16] Because this cleft was detected in untreated areas on histologic analysis, we believe that this may be a processing artifact.

The IUS system has been shown to produce a precise and reproducible line of lesions in tissues at a depth that corresponds well to that handpiece's given fixed focal depth in tissue. The depth measurements of the TIZs were, on average, slightly deeper than the 4.5-mm focus. However, this may be the result of tissue swelling after immersion of the gross tissue strips in the NBTC stain. The depth of soft tissue also can affect lesion geometry. For example, in the preauricular region the soft tissue layer is comparatively thicker than other facial regions. As seen in Figure 3, IUS exposures using the 4.4-MHz handpiece produce discrete TIZs in the SMAS. However, in the forehead region the soft tissue layer is relatively thinner, and Figure 5 reveals overtreatment, or "tadpole formation" (a phenomenon that has been well documented for whole-organ ablation using IUS).[17] This is likely due to reflected ultrasound waves from the periosteum and bone.

Although we demonstrated a small degree of immediate shrinkage after IUS exposure, this study is limited in the fact that the experimentation performed on cadaveric tissue is focused on evaluation of the immediate contraction induced by thermal denaturation of the collagen tissue. When tissue is heated to 65°C, there is a disruption of the intermolecular peptide bonds of the collagen triple helix (denaturation).[7] As these bonds dissociate, the 3-dimensional structure unwinds, and an immediate collagen contraction ensues.

The use of ultrasound imaging to visualize the facial nerve and to direct therapies in the region, including the parotid gland, while avoiding the facial nerve has been successfully reported in Nd:YAG treatments of hemangiomas and vascular malformations of the head and neck.[18] The subdermal delivery of energy in the face and neck has been reported with monopolar RF treatment (Thermage; Thermage Inc, Hayward, Calif) such as the nonsurgical facelift procedure. However, these treatments do not produce focused lesions in a planned and targeted distribution, as demonstrated in this study. Furthermore, the simultaneous use of ultrasound for imaging and treatment of the SMAS has not been previously reported, to our knowledge.

This study suggests that IUS may have several characteristics that are particularly well suited to facial treatment. First, the technology leverages high-resolution ultrasound for imaging and treating the region in the same imaged field. The images generated provide a clear representation of the facial layers, including the skin, subcutaneous tissue, SMAS, and parotid. Second, we demonstrated that the lesion generated is highly selective regarding depth and size because these are directly related to the source frequency and the energy delivered. The handpieces used for this study are at a set frequency (7.5 or 4.4 MHz) and have a fixed focal depth in tissue (4.5 mm), limiting the nominal depth to which most of the energy is delivered in the tissue to approximately 5 mm. Higher energy levels produce lesions that are generally shallower and progress superficially. Lesions produced are consistent for a given region of facial tissue and source conditions, including the frequency and focal depth in tissue of a handpiece (which determines the depth of the lesion) and source energy of the pulse (which determines the size and shape of the lesion).

As a result, we can (1) image an appropriate area of interest and (2) deliver energy limited to a specific depth.

The mean ± SD depths of the facial nerve in this area have been previously described in the literature[19] as follows: main nerve trunk, 20.1 ± 3.1 mm, and nerve exit from the parotid edge, 9.1 ± 2.8 mm for temporal, 9.2 ± 2.2 mm for zygomatic, 9.6 ± 2.0 mm for buccal, and 10.6 ± 2.7 mm for mandibular branches. These are all deep to the greatest depth produced in this study using the 2 handpiece frequencies and source configurations.

Histologic examination of IUS exposures demonstrated coagulative necrosis induced by thermal damage to the SMAS region while sparing the epidermis in a narrow range of energy levels. The characteristics of each of these histologic findings are similar to those of thermal ablation using other energy-based modalities, such as lasers and RF.[15] The maximal area estimated for the zones of ablation achieved in this investigation are approximately 0.5 to 18 mm^2.

This study was limited by the fact that the human ambient body temperature is higher than the temperatures of the cadaveric tissue used in this experiment. Therefore, treatment levels in patients may require less energy to produce the same TIZs. Future clinical investigation in vivo is necessary to understand the effects of other factors, such as blood flow and immediate and delayed inflammatory reactions of the SMAS layer to TIZs.

In conclusion, we demonstrated in human cadaveric facial tissue that IUS energy can noninvasively image and selectively produce TIZs of reproducible location, size, and geometry in the SMAS layer. The ability to transcutaneously target the SMAS and to produce patterns of focused collagen denaturation to induce shrinkage has significant implications for aesthetic facial rejuvenation.

Accepted for Publication: October 1, 2006.
Correspondence: Richard E. Gliklich, MD, Division of Facial Plastic and Reconstructive Surgery, Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston, MA 02114 (Richard_Gliklich@meei.harvard.edu).
Author Contributions: Drs Gliklich and White had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* White, Makin, Barthe, Slayton, and Gliklich. *Acquisition of data:* White, Makin, Barthe, Slayton, and Gliklich. *Analysis and interpretation of data:* White, Makin, Barthe, Slayton, and Gliklich. *Drafting of the manuscript:* White, Makin, Barthe, Slayton, and Gliklich. *Critical revision of the manuscript for important intellectual content*: White, Makin, Barthe, Slayton, and Gliklich. *Statistical analysis:* White, Makin, and Gliklich. *Obtained funding:* White and Gliklich. *Administrative, technical, and material support:* White, Makin, Barthe, Slayton, and Gliklich. *Study supervision:* White, Slayton, and Gliklich.

Financial Disclosure: Drs Makin, Slaton, and Barthe are Ulthera Inc stockholders and technology developers.
Funding/Support: This study was supported in part by funding from Ulthera Inc (Drs White and Gliklich).
Role of the Sponsor: This study was conducted in collaboration with Ulthera Inc, which had a role in the study design, data collection, data analysis, and writing of the manuscript.

REFERENCES

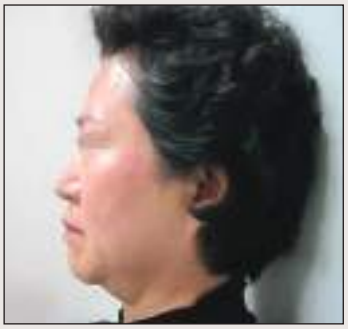
1. Mitz V, Peyronie M. The superficial musculo-aponeurotic system (SMAS) in the parotid and cheek area. *Plast Reconstr Surg*. 1976;58:80-88.
2. Ghassemi A, Prescher A, Riediger D, Axer H. Anatomy of the SMAS revisited. *Aesthetic Plast Surg*. 2003;27:258-264.
3. Har-Shai Y, Sele E, Rubinstien I, Lindenbaum E, Mitz V, Hirshowitz B. Computerized morphometric quantification of elastin and collagen in SMAS and facial skin and the possible role of fat cells in SMAS viscoelastic properties. *Plast Reconstr Surg*. 1998;102:2466-2470.
4. Thaller SR, Kim S, Patterson H, Wildman M, Daniller A. The submuscular aponeurotic system (SMAS): a histologic and comparative anatomy evaluation. *Plast Reconstr Surg*. 1990;86:690-696.
5. Har-Shai Y, Bodner SR, Egozy-Golan D, et al. Mechanical properties and microstructure of the superficial musculoaponeu
rotic system. *Plast Reconstr Surg*. 1996;98:59-70.
6. Hruza GJ. Rejuvenating the aging face. *Arch Facial Plast Surg*. 2004;6:366-369.
7. Ross EV, Naseef GS, McKinlay JR, et al. Comparison of carbon dioxide laser, erbium:YAG laser, dermabrasion, and dermatome: a study of thermal damage, wound contraction, and wound healing in a live pig model: implications for skin resurfacing. *J Am Acad Dermatol*. 2000;42:92-105.
8. Kim KH, Geronemus RG. Nonablative laser and light therapies for skin rejuvenation. *Arch Facial Plast Surg*. 2004;6:398-409.
9. Kennedy JE, ter Haar GR, Cranston D. High intensity focused ultrasound: surgery of the future? *Br J Radiol*. 2003;76:590-599.
10. Mast TD, Makin IRS, Faidi W, Runk MM, Barthe PG, Slayton MH. Bulk ablation of soft tissue with intense ultrasound (IUS): modeling and ablation. *J Acoust Soc Am*. 2005;118:2715-2724.
11. White WM, Makin IRS, Barthe PG, Slayton MH, Gliklich RE. Selective transcutaneous delivery of energy to facial subdermal tissues using the ultrasound therapy system [abstract]. *Lasers Surg Med*. 2006;suppl 18:113.
12. Neumann RA, Knobler RM, Pieczkowski F, Gebhart W. Enzyme histochemical analysis of cell viability after argon laser-induced coagulation necrosis of the skin. *J Am Acad Dermatol*. 1991;25:991-998.
13. Chung JH, Koh WS, Youn JI. Histological responses of port wine stains in brown skin after 578 nm copper vapor laser treatment. *Lasers Surg Med*. 1996;18:358-366.
14. Majaron B, Kelly KM, Park HB, Verkruysse W, Nelson SJ. Er:YAG laser skin resurfacing using repetitive long-pulse exposure and cryogen spray cooling, I: histological study. *Lasers Surg Med*. 2001;28:121-130.
15. Abraham MT, Ross EV. Current concepts in nonablative radiofrequency rejuvenation of the lower face and neck. *Facial Plast Surg*. 2005;21:65-73.
16. Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR. Fractional photothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury. *Lasers Surg Med*. 2004;34:426-438.
17. Meaney PM, Cahill MD, ter Haar GR, Cranston D. The intensity dependence of lesion position shift during focused ultrasound surgery. *Ultrasound Med Biol*. 2000;26:441-450.
18. Werner JA, Lippert BM, Gottschlich S, et al. Ultrasound-guided interstitial Nd:YAG laser treatment of voluminous hemangiomas and vascular malformations in 92 patients. *Laryngoscope*. 1998;108:463-470.
19. Rudolph R. Depth of the facial nerve in face lift dissections. *Plast Reconstr Surg*. 1990;85:537-544.

Doublo Carves Its Niche in the Non-Invasive Skin Rejuvenation Market

By Ilya Petrou, M.D., Contributing Editor

Choi Won-woo, M.D.
Director
Wells Dermatology Clinic
Seoul, South Korea

"In my opinion, the Doublo can more effectively treat the dermis, subcutaneous fat and the superficial muscular aponeurotic system. Treatments with the device result in tightening, as well as lifting."



Before Tx

After Doublo Tx

Photos courtesy of Hironic

With today's aesthetic patient seeking improved treatment outcomes with less downtime, non-invasive skin rejuvenation procedures are in high demand. The Doublo from Hironic (Sungnam, South Korea) is an innovative device using state-of-the-art ultrasonic energy to provide solutions for facial and neck skin laxity.

"The aesthetic market is booming and the number of patients who desire skin rejuvenation treatments has increased significantly, particularly in the non-invasive arena," said Choi Won-woo, M.D., director of the Wells Dermatology Clinic in Seoul, South Korea. "Here, the popularity of aesthetic treatments using high intensity focused ultrasound (HIFU) for the improvement of facial contours continues to enjoy great popularity due to its high efficacy, safety and patient satisfaction."

Powered by second generation HIFU technology, the Doublo is an ideal solution for patients requiring facial and neck skin tightening and rejuvenation, periorbital wrinkle reduction, nasolabial fold reduction, as well as jowl and eyebrow lifting.

According to Dr. Won-woo, the Doublo appears to be a superior choice for skin rejuvenation treatments, a belief that is supported by numerous clinical studies. "In my opinion, the Doublo can more effectively treat the dermis, subcutaneous fat and the superficial muscular aponeurotic system (SMAS). Treatments with the device result in tightening, as well as lifting," Dr. Won-woo said.

Dr. Won-woo also pointed out that the Doublo device has received approval from the Korean Food & Drug Administration following its use in South Korea's first 'eyebrow lifting' procedure using HIFU technology. "The Doublo device is said to achieve remarkable tightening and lifting outcomes after only a single treatment session, with some outcomes reminiscent of those only achievable with surgical face- and neck-lifting procedures," Dr. Won-woo reported.

As Dr. Won-woo explained, the tightening of skin and regeneration of collagen is made possible by the creation of focal thermal zones where HIFU energy is focused deeper into the targeted dermal and SMAS tissues. Targeting of the deep dermis not only results in significant neocollagenesis and subsequent skin tightening over two to four weeks, but collagen and elastin neogenesis will continue for the next three to six months following treatment.

Compared to a conventional 16 CH probe, Dr. Won-woo feels that, "the Doublo's state-of-the-art 128 CH image probe surpasses all expectations regarding efficacy and safety, not only offering precise real-time, high resolution imaging before and during treatment, but also diverse applications and analysis with high performance software.

Clinical data shows that patient satisfaction regarding facial profile and contour improvements are about 80% higher one month after a single treatment with the Doublo. Moreover, Dr. Won-woo said that Doublo provides less painful treatments, even though higher energy is used than the suggested guideline energy. "The new and improved Doublo cartridge handpiece has a proven efficacy and much greater safety, even at high energy levels, compared to its predecessor."

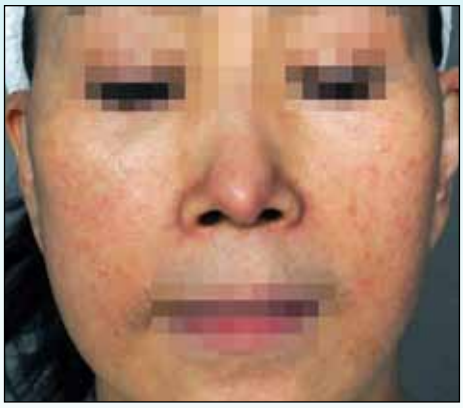
In Dr. Won-woo's opinion, the Doublo stands strong in this competitive market and rivals other HIFU-based devices with its user-friendliness, treatment options and the aesthetic outcomes achieved, backed by a strong safety profile.

Doublo Achieves Significant

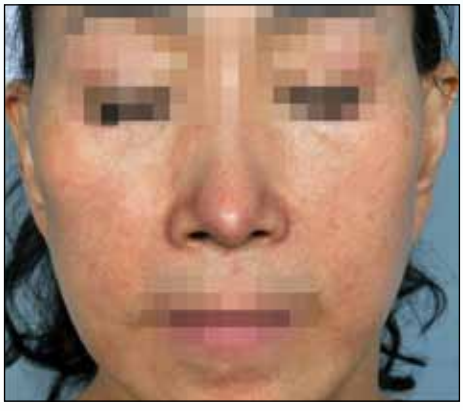
Non-Invasive Skin Rejuvenation and Face-Lifting

Jie Hoon Kim, M.D.
Chairman
Dermatology Clinic at Dr. Kim's Skin & Laser Clinic
Suwon, South Korea

"One of the central advantages of the Doublo is that it allows the clinician to perform a non-invasive face-lift without damaging the epidermis."



Before Tx



After Doublo Tx

Photos courtesy of Jie Hoon Kim, M.D.

By Ilya Petrou, M.D., Contributing Editor

Non-invasive skin rejuvenation procedures have become extremely popular in aesthetic medicine, as new and exciting treatment modalities continue to evolve, offering patients excellent outcomes, in many cases circumventing the need for traditional cosmetic surgery. Since its inception several years ago, the Doublo from Hironic (Sungnam, South Korea) has proven itself as an impressive aesthetic device achieving significant skin tightening and lifting effects in the face and neck regions.

"Compared to other skin rejuvenation devices and technologies, the Doublo can achieve good aesthetic outcomes while limiting unwanted side effects," said Jie Hoon Kim, M.D., chairman of the Dermatology Clinic at Dr. Kim's Skin & Laser Clinic in Suwon, South Korea. "The large majority of my patients are satisfied with the outcomes and improvements achieved in the signs of aging."

Among the different energy-based technologies currently used in skin rejuvenation devices, ultrasound energy is considered by many experts as a safe and effective approach to treating aging and sagging skin. Powered by second generation high-intensity focused ultrasound (HIFU) technology, the Doublo targets the deep dermis and SMAS, creating thermal coagulation zones in the targeted tissues, while largely sparing the surrounding structures. This focused energy causes a contraction of the SMAS, as well as a denaturation and remodeling of the targeted collagen fibers resulting in neocollagenesis, which then produces significant skin tightening and lifting of the targeted tissues.

In Dr. Kim's opinion, "One of the central advantages of the Doublo is that it allows the clinician to perform a non-invasive face-lift without damaging the epidermis. Other rejuvenation modalities such as radiofrequency (RF) and lasers also aim to stimulate the deep dermis, but these treatments often result in unavoidable damage to the epidermis. Doublo's high-intensity focused ultrasound energy avoids damage to the epidermis."

Doublo procedures are quick, safe and painless, said Dr. Kim. Since there is no downtime associated with treatment, patients can return to daily social activities immediately following the procedure.

"Most patients are very satisfied with the results and return for additional sessions," Dr. Kim reported. "Treatments are comfortable and the rejuvenation effects are very noticeable; therefore, patients who know the procedure well, often recommend it to others."

With a 128 CH high resolution image probe, the Doublo offers precise and real-time imaging of the targeted structures before and during a treatment session. It is also equipped with a larger treatment tip, allowing the physician to perform quicker treatments.

In addition, the Doublo was recently upgraded to include a 5,000 shot cartridge (more than double the capacity of the previous cartridge). This improvement allows physicians to treat more patients than ever before with a single cartridge, further underscoring the higher efficiency of the Doublo compared to other devices.

"In my experience, one can achieve the best clinical result if Doublo treatment is combined with another rejuvenation modality such as RF or fractional lasers," Dr. Kim noted. "Since it appeared on the aesthetic market five years ago, I believe Doublo has developed a solid reputation in the rejuvenation field."