# Treatment of Skin Laxity Using Multisource, Phase-Controlled Radiofrequency in Asians: Visualized 3-Dimensional Skin Tightening Results and Increase in Elastin Density Shown Through Histologic Investigation

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BACKGROUND A new multisource phase-controlled radiofrequency (MPCRF) device is widely used for skin tightening and rejuvenation in Asia.

OBJECTIVE To evaluate the efficacy of MPCRF objectively and histologically.

METHODS An MPCRF device with real-time impedance control was evaluated. Ten Japanese patients were treated one side of the face, and the untreated side served as a control. Three-dimensional (3-D) imaging was performed to evaluate the posttreatment volume change. An independent observer assessed the 3-D images. Histologic evaluations of elastin were performed by Victoria Blue staining in 5 Japanese patients.

RESULTS Objective assessments evaluated by a 3-D color schematic representation showed improvement in skin laxity after the final treatment in all patients. The treated side improved markedly compared with the untreated side; however, even the untreated side slightly improved. The elastin density was significantly increased compared with controls in all 5 Japanese patients ($p = .0013$). Induced elastin appeared to be relatively thin elastic fibers without irregular elastic fibers, such as solar elastosis. Side effects were not observed, and the patients reported feeling comfortable throughout the study.

CONCLUSION Multisource phase-controlled radiofrequency treatments provide stimulation of elastin and skin-tightening results safely and effectively, and thus are beneficial for improving skin laxity and rhytides.

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Radiofrequency (RF) devices and nonablative lasers have been widely used for skin rejuvenation and are thought to stimulate dermal collagen remodeling. Nonablative lasers alter dermal collagen structure by thermal induction of collagen neosynthesis and remodeling, as evidenced by increased levels of collagen, elastin, and collagenase.[1,2] We previously reported that near-infrared (NIR) irradiation provides long-lasting stimulation of elastin and skin-tightening results, and thus are beneficial for improving skin laxity and rhytides.[3–11]

One of the thermal effects induced by RF devices is an immediate change in collagen structure, followed by a long-term stimulation of neocollagenesis.[12] Radiofrequency devices are widely used for skin tightening and heat the dermis and subcutaneous tissues, thereby stimulating dermal collagen remodeling. These thermal effects can reduce the appearance of rhytides and laxity and improve contours on both the face and body.

Monopolar and bipolar RF devices have been proven to be beneficial in skin tightening. Nevertheless, these

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effects are often partial or unpredictable because of the uncontrolled nature of energy flow through the body and possible pain produced during monopolar or unipolar RF treatments, and the superficial nature of energy flow for bipolar or tripolar configurations. In addition, these first-generation RF therapy systems delivered frequently unpredictable results, possibly because of the large differences in individual skin impedance.[13] Therefore, a novel multisource phase-controlled radiofrequency (MPCRF) device is used that allows for continuous real-time measurement of skin impedance and delivers constant energy to the patient skin independent of changes in its impedance.

Many studies suggested the efficacy of various types of aesthetic devices, but these studies did not include sufficient objective evaluation. Conventional evaluations using photographs have been widely used, but they do not provide an accurate objective assessment. A 3-dimensional (3-D) color schematic representation can evaluate and objectively present the effectiveness of the results, as well as show patient results that are not demonstrable with standard 2-D photography.[9,14] Therefore, 3-D color schematic representation has been used to objectively evaluate the results in this and in our previous studies.

Furthermore, collagen stimulation has been described in previous studies, whereas stimulation of elastin has not been studied in detail in vivo previously. We hypothesized that MPCRF treatments provide stimulation of elastin and skin-tightening results safely and effectively, and thus are beneficial for improving skin laxity and rhytides. To test this hypothesis, we evaluated the efficacy of the MPCRF treatments and examined changes in the amount of elastin by histologic analysis.

## Methods

### *Japanese Patients*

Ten Japanese patients (9 women and 1 man) aged 26 to 51 years (mean age, 37.82 ± 7.37 years) with Fitzpatrick skin Type III-V were enrolled in this study. All 10 patients had visited the Clinica Tanaka Anti-aging Center to achieve skin rejuvenation on their faces. Skin biopsies were taken from 5 Japanese women patients who had visited the Clinica Tanaka Anti-Aging Center to remove some pigmented nevi (more than 1 pigmented nevus on both control side and treated side of the cheek) and achieve skin rejuvenation on their faces. When each pigmented nevus was removed by elliptical excision, the excess skin on either side of the pigmented nevus was submitted for biopsies. None of the patients had a history of any type of skin disease or cosmetic procedure that affected the treatment areas. No topical was used before treatment, and the posttreatment skin care regimen consisted of a gentle cleanser and sunblock. Patients did not use any specific skin care product or did not have any specific diet. We excluded patients who exhibited weight loss during the study period. Control biopsies were taken before MPCRF treatment and received neither treatment nor irradiation. All biopsies were taken at least 1 cm from previous biopsies to ensure that wound healing would not affect the adjacent biopsy sites. All patients gave written informed consent for participation in the study and for taking biopsy samples after reading the experimental protocol and being advised about the risks of treatment.

### *MPCRF Treatment*

An EndyMed PRO (EndyMed Medical Ltd, Caesarea, Israel) that emits at 1-MHz frequency at 1 to 65 W was used as an MPCRF device. Ten Japanese patients were treated on the more ptotic and aged side of the face. The other side of their face was not treated and served as a control. All patients were offered the opportunity to have the untreated side of their face treated after the last follow-up visit of the study. Three rounds of treatment with a 1-week interval between treatments were performed.

Patients were treated at a 33-W output, facial tightening mode, treatment area: cheeks, heating depth: 3, and 12 passes of 30 seconds per area. The target was to maintain constant painless heat sensation with surface skin temperature <43°C. No topical anesthetics or oral analgesics were administered before, during, or after the treatment. In addition, no skin cooling was required. All patients were treated by the same physician.

### *Objective Assessments*

Digital photographs and 3-D imaging were conducted as objective assessments with a Canfield Scientific Vectra camera and software (Canfield Scientific Inc., Fairfield, NJ). This system is designed to accurately capture the surface shape and also 2-D color information of the human body. The capture sequence of Vectra was set to less than 3 milliseconds to capture the shape accurately even if the subject was not perfectly still.

A 3-D color schematic representation indicates the volume changes between pretreatment and posttreatment (3 months after the final treatment) images in the face, and shows the varying degrees of tightening achieved in colors ranging from yellow to red. Green areas indicated no changes to the face. Care was taken to ensure similar nonsmiling facial tone in both pretreatment and posttreatment photographs.

An independent observer was used to assess the clinical results. The observer was blinded regarding the side that was treated, and the 3-D images were randomly displayed in a nonsequential fashion. The observer was asked to score the results after the treatments using the following categories:

(1) Worsening.
(2) No change.
(3) Mild improvement.
(4) Moderate improvement.
(5) Significant improvement.

### *Histologic Assessments*

Human skin specimens (3–5 from each patient) from the face were obtained for microscopic investigation. Biopsies were taken before treatment as a control and at 2 months after the final treatment. The specimens were fixed in 20% neutral buffered formalin, processed for paraffin embedding and serially sectioned along the sagittal plane (3–4-μm thickness). Tissue sections were stained by Victoria Blue staining.

Elastin densities stained by Victoria Blue staining in the dermis were calculated after an optimized color threshold was applied to each image to distinguish between the stained areas and background. Images were scanned and quantified in 5 representative fields per section, and subsequently averaged to obtain a final score. The sections were photographed under an Olympus BX50 microscope (Olympus, Tokyo, Japan). The digital photographs were processed using Adobe Photoshop (Adobe, San Jose, CA).

### *Statistical Analyses*

The differences between groups at each time point were examined for statistical significance using the Wilcoxon signed-rank test. A $p < .05$ was set as a cutoff for statistical significance. The median change and its variability were also illustrated in a box plot graph.

## Results

Objective assessments evaluated by 3-D color schematic representation revealed significant improvement after the treatment (Figures 1 and 2). The treated side improved markedly compared with the untreated side. However, even the untreated side slightly improved. Eighty percent of the patients reported significant improvement, and 20% reported moderate improvement.

The elastin density was significantly increased compared with controls in all 5 Japanese patients ($p = .0013$) (Figures 3 and 4). Induced elastin appeared to be relatively thin elastic fibers without irregular elastic fibers, such as solar elastosis (Figure 3).

Most of the patients did not report feeling pain during the treatment, although it was performed without anesthesia and contact cooling. Side effects, such as epidermal burns, adipose tissue atrophy, and contraction, were not observed, and the patients reported feeling comfortable throughout the study.

## Discussion

This study demonstrated that MPCRF treatment can provide safe and effective stimulation of elastin, and achieve skin rejuvenation by improving skin laxity and rhytides. Radiofrequency treatment has been shown to penetrate deeper than optical light sources

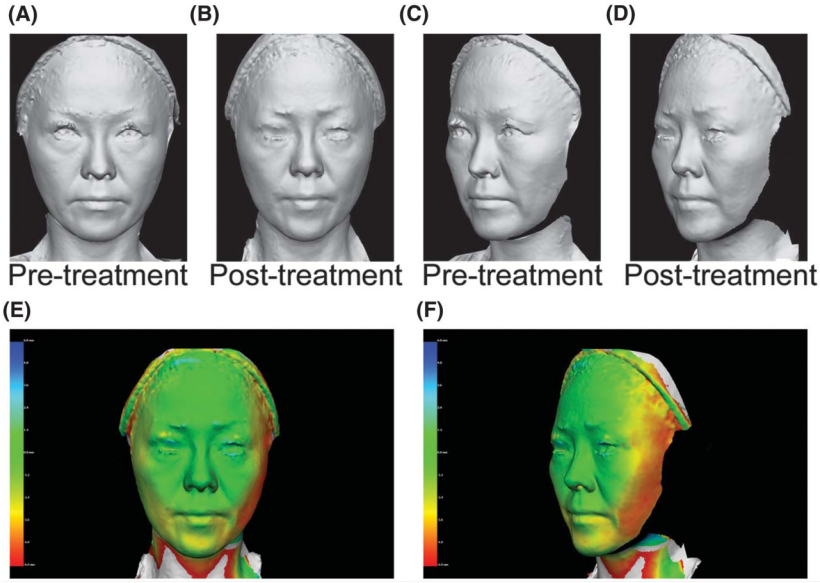


**Figure 1.** A 43-year-old Japanese woman. (A, C) Before treatment; (B, D) 90 days after treatment; (E, F) 3-D color schematic representation; (C, D, F) The treated side (left cheek). The varying degrees of tightening achieved are shown in colors yellow to red. Green areas indicate areas that remained unchanged. Significant improvements in skin laxity were noted in the gray image and 3-D color schematic representation in the treated side.

independent of the skin color and is beneficial for skin tightening. Many studies have shown the efficacy of various types of devices for skin tightening, but did not include a sufficient objective evaluation. We previously described the tightening effects of NIR objectively and histologically, and reported that NIR provides stimulation of elastin and skin-tightening results safely and effectively, and thus are beneficial for improving skin laxity and rhytides.[4–11]

Elastin is one of the major proteins of connective tissue and is produced by fibroblasts. It has an important function in providing elasticity of the skin. Elastin possesses hydrophilicity and enhances water uptake.[15]

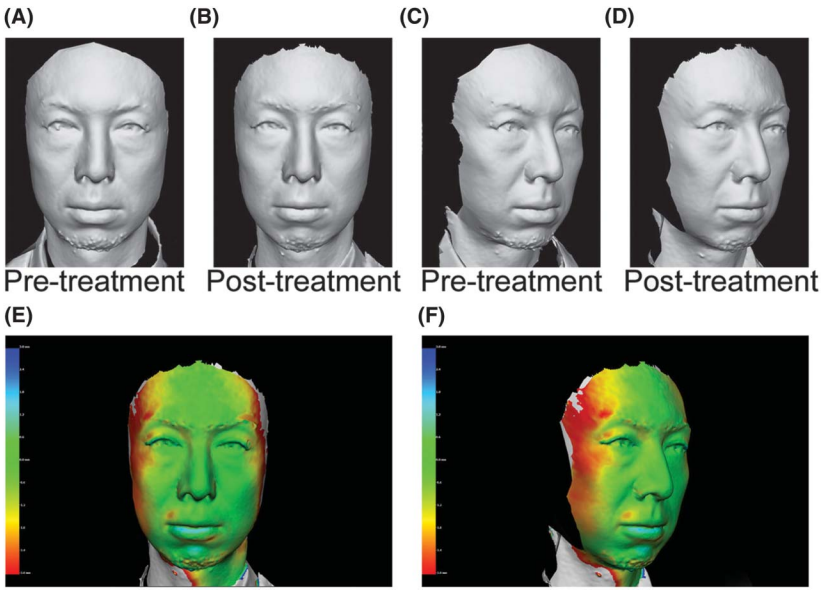


**Figure 2.** A 37-year-old Japanese man. (A, C) Before treatment; (B, D) 90 days after treatment; (E, F) 3-D color schematic representation; (C, D, F) The treated side (right cheek). The varying degrees of tightening achieved are shown in colors yellow to red. Green areas indicate areas that remained unchanged. Significant improvements in skin laxity were noted in the gray image and 3-D color schematic representation in treated side.

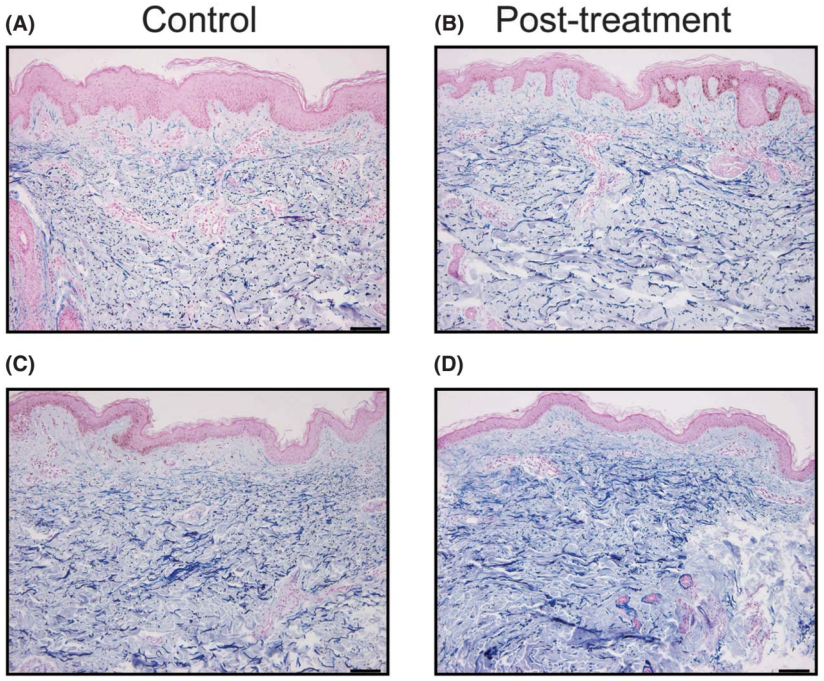


**Figure 3.** A representative histology of Japanese patients' cheek skin evaluated by Victoria Blue staining. (A, B) A 32-year-old Japanese woman; (C, D) A 43-year-old Japanese woman. The amount of elastin stained in blue was significantly increased after treatment (B, D) compared with controls (A, C). Scale bars = 100 μm.

The loss of normal elastic fiber functions is a common age-associated feature of both photoaging and intrinsic aging processes. The accelerated aging and sagging of the skin seen in several hereditary disorders involves collagen or elastin deficiency.[16–19] Because an increase in relatively thin elastic fibers without irregular elastic fibers, such as solar elastosis, was evaluated in this study, this MPCRF treatment seemed to be beneficial for skin rejuvenation.

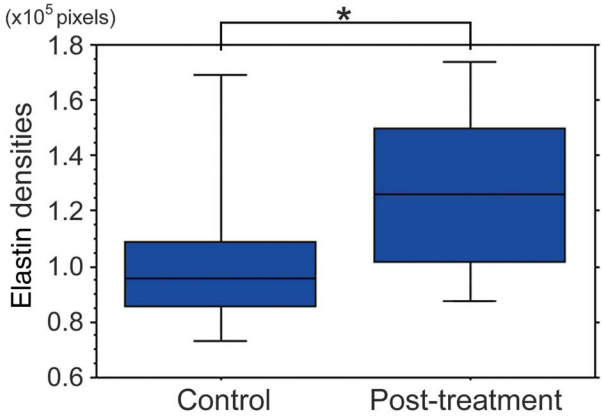


**Figure 4.** The median densities of elastin in the dermis. The box illustrates the interquartile range extending from the 25th percentile to the 75th percentile with a line at the median (50th percentile). The bottom and top end of whiskers show the minimum and maximum data points, respectively. The elastin densities were significantly increased compared with controls ($p = .0013$). Significant differences compared with control are indicated (*$p < .05$).

One of the major issues in all skin-tightening clinical studies is the lack of an accepted standard regarding the accurate assessment of the degree of skin tightening.[20] Conventional evaluations using photographs have been widely used, but do not provide accurate objective assessment. In this study, a 3-D color schematic representation objectively evaluated and presented the effectiveness of the results and showed patients results that are not demonstrable with standard 2-D photography.

Although the volume measurement was performed 3 months after the final treatment, improvement in skin laxity of the treated side compared with the untreated side was proven by 3-D color schematic representation in all patients. In our previous study, the volume reduction as well as improvement of skin laxity and rhytides were observed after this MPCRF treatment.[14] These results suggest that MPCRF treatment may affect the skin as well as subcutaneous tissues. Because the effects of this MPCRF treatment are

clinically observed for at least several months after the treatment, further studies of volume measurements with a longer follow-up time are needed.

Interestingly, skin laxity was slightly improved even on the untreated side of the face, which suggests that it may be affected by the skin-tightening effects of the treated side. This phenomenon should be investigated in future studies.

In this study, a novel MPCRF system was used that allows for continuous real-time measurement of skin impedance and the delivery of constant energy to the patient skin independent of changes in its impedance. Using the MPCRF system, less thermal damage of dermis and subcutaneous tissues occurs compared with monopolar or unipolar RF treatments. Multisource phase-controlled radiofrequency technology is based on the fact that flow of energy on the surface is minimal, whereas most of the energy is directed to the depth of the tissue. Each generator is phase controlled, allowing a complex 3-D interaction between the electromagnetic fields produced in the tissue. Because adjacent electrodes, on each side of the handpiece, possess identical polarities, no current is created between these electrodes on the skin surface and most of the energy is driven deeper into the skin with minimal epidermal flow. This is achieved by repulsion between electrical fields of the same polarity on each side of the handpiece.[14] Because the MPCRF handpiece delivers energy in constant circulatory motion, the effect will be an average lower temperature on the epidermis (<43°C) and higher temperature in the lower skin layers, without the need for cooling.[14]

Furthermore, most of the patients did not report feeling pain during the treatment, although it was performed without anesthesia and contact cooling. A 33 W output was used, which was low enough to produce a painless sensation of heat. A significant improvement was observed after 3 rounds of treatment at this output. However, more rounds of treatments or a higher output may enhance the effects.

Side effects, such as epidermal burns, adipose tissue atrophy, and contraction, were not observed, and the patients reported feeling comfortable throughout the study. Further studies are necessary to determine whether a higher output, increased frequency of treatments, or longer periods of treatment may be even more effective in skin tightening.

It should be noted that this was a preliminary study based on fairly small number of skin biopsies. The number of biopsies was small in this study because of practical limitations in the number of serial biopsy specimens that could be obtained from the face.

When removing several biopsies within proximity, it is possible that previous biopsies subtly influence new biopsies because of wound healing. However, there is no evidence that biopsies next to the pigmented nevus would not have been affected by the pigmented nevus, nor is there evidence to suggest that biopsies next to the pigmented nevus would be affected by the pigmented nevus. Thus, these histologic findings would be acceptable for RF research on elastin using in vivo human tissue investigation. Furthermore, we cannot exclude the possibility that ultraviolet and NIR exposure in everyday life may affect the changes demonstrated in this study. Process between the volume reduction and increase of elastin should be investigated in future studies, which would be beneficial for the improvement and development of treatment parameters and methods.

In conclusion, using this approach, we found significant improvements in skin laxity through objective and histologic assessments after MPCRF treatments. The advantages of MPCRF treatments are reduced discomfort and side effects. Our results indicated that MPCRF provides safe and effective stimulation of elastin, which is beneficial for skin rejuvenation by improving skin laxity and rhytides.

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