SCIENTIFIC & TECHNICAL REPORT CONCERNING THE CLINICAL-PHYSICAL STUDY OF EFFECTIVENESS AND SAFETY OF "RADIO 4" EQUIPMENT

Purchaser: NOVAVISION Group

Date of issue: April 21st, 2011

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1 Introduction

The Centre has conducted a research study with the purpose of evaluating both the effectiveness and safety of RADIO4 equipment in relation to the operator's and customer's safety as requested by "Novavision Group s.r.l." Company. The Centre has been entrusted with this task by "Novavision Group s.r.l." Company, with their registered office in Milan, Via Aurelio Saffi 29, P. I. IT02164550960, following the signature of the regular agreement stipulated on 9.9.2010. This piece of equipment is a radiofrequency generator, classified as Class IIa equipment, to be used as indicated by the manufacturing company for the non-invasive treatment "of blemishes caused by wrinkles, of skin tension and cellulite reduction".

RADIO 4 relies on another worldwide patented technology from the Novavision Group Company, the so-called RSS ™ (Radiofrequency Safety System), that makes use of a group of 4 electrodes that are set up automatically and in a dynamic way by a control software in order to let the radiofrequency current circulate between them.

The variable configuration of the electrodes allows creating the creation of electric fields which, once set in the ideal combination, direct the energy deeply in the tissues by electrically overheating them.

In order to allow the above-mentioned evaluations to be carried out, Novavision company delivered a model of RADIO 4 to the Centre, the so-called RADIO4M, that is able to emit the maximum power (100%) of 55W; the Company also supplied a copy of the User Manual and an adequate quantity of aqueous gel to be regularly interposed between the skin and the radiofrequency generator handpieces during the treatments.

Clinical trials were carried out in two concurrent phases: a clinical-experimental phase and an evaluation phase of physical parameters for safety.

The clinical-experimental phase has been carried out under the guidance of Dr Antonia Icaro Cornaglia, tenured Researcher of Histology at the University of Pavia and permanent member of the Centre and under the guidance of Dr Silvia Scevola, Plastic Surgery Specialist and co-opted member of the Centre.

The evaluation phase of physical parameters for safety has been carried out under the guidance of Dr Antonio Coppola, Physicist Specialist in Environmental Health Physics, Qualified Expert (EQ III degree) in Radiation Protection (no. 418 on National Register) and co-opted member of the Centre.

CLINICAL RESEARCH & EXPERIMENTAL STUDIES

2 Experimental clinical study preliminary remarks

The study has been conducted in two stages:

- ***ex vivo* phase:** on body parts removed during surgery
- ***in vivo* phase:** on healthy volunteers.

3 *Ex vivo* study

The purpose of the first leg of the study was to identify the safety limits of the equipment. Therefore its effects were tested by delivering power at different growing levels until the maximum bearable power and the maximum time of application in terms of safety of such amount of energy were tested. Being a test carried out on *ex vivo* samples, thus without thermoregulation, this procedure is to be considered as performed under the worst possible conditions.

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13 Summary conclusions

The following conclusions can be drawn from the analysis of the data found on *ex vivo* samples, during *in vivo* treatments and on histological preparations.

The power energy emitted by Radio 4 is delivered in the form of heat generation. The significant changes in temperature noticed in *ex vivo* samples are partially compensated *in vivo* by the thermoregulatory mechanism. Under no circumstances can power emissions ≥ 50% (values referred to the medical software) be used.

The biological effect of the temperature rise is proportional to the application time.
The tolerability shown by patients during *in vivo* trials faithfully reflects the anatomic-pathological effects noticed under the microscope.
Those areas with a greater sensitive innervation cannot tolerate higher levels of power energy for longer times.

With power emissions tolerated by the subjects, only the denser tissues seems to be affected (dermis, inter-adipose connective septa); while the epidermis does not seem to be damaged, it only appears erythematous at the end of the treatments. Any effects on the subcutaneous adipose tissue can be only related to the thickening and shortening of connective septa and not to a direct effect on adipocytes.
The 2 x 2 configuration of electrodes seems to be less tolerable - for the same power level, - in comparison with the 1:3 configuration.

In order to obtain more safe results, it would be advisable to increase the treatment time rather than to increase power emissions.
After only 2 treatments, the treated subjects report a smoother and softer skin in the treated areas, while the underlying panniculus adiposus did not show any changes even after 4 treatments.
Both *ex vivo* and *in vivo* histological corroborations show large disarranged bundles of collagen fibers, with more evident alterations of the dermis reticular layer (small clots), visible up to approximately 1,5 cm depth. These alterations seem to be proportional to the intensity of the treatment and to the number of applications. Adipose tissue, vascular endothelium, nerve endings and cutaneous annexes seem intact up to 75% of power. The epithelium seems present and intact up to 50% of power.

As regards the effects of the treatments on the *in vivo* response, a minimum cellular response can be detected even after 3 months from the beginning of treatment, after 3 applications during 1 month. It exclusively consisted in a moderate activation of the sole macrophages activity, which revealed the presence of material to be reabsorbed, that would most likely be represented by coagulated collagen fragments. No changes were detected either in other cells indicating an inflammatory response or in connective cells (fibrocytes and fibroblasts) whose qualitative and quantitative characteristics appear unchanged at the end of the cycle of the performed treatments.

As regards the described changes sustained by the elastic fibers – which can be already noticed one month after starting treatment, after 2 applications performed within 2 weeks, - the increase in fibers thickness, involving both the papillary dermis and the reticular dermis, is an event that can be usually observed in skin subject to photodamage after exposure to UV radiation. In a similar way, the increase in thickness of elastic fibers is a constant feature of skin aging, which corresponds, in clinical terms, to a loss of elasticity. On the other hand, it can be noticed that the elastic fibers thickened after the Radio 4 treatment maintain a reticular pattern, typically seen in young people: this ostensible contradiction could be probably interpreted by bearing in mind that Radiofrequency, as thoroughly described in the physical-medical part of this report, induces connective fibers to cluster together by means of a physical mechanism only, connected to the increase in energy potential of the aqueous environment where these highly hydrophobic structures were placed.

The comprehensive interpretation of the evidence involving connective fibers would lean toward a process of spatial rearrangement, without any signs of scar formation. Any clinical-esthetic relapses of these biologic processes in time, especially with regard to a possible stimulation of regenerative processes, cannot be determined on the basis of data collected until now.

The results of the physical tests carried out until now show an overall substantial safety of the equipment, provided that it is used at a power not exceeding 50% using the medical software and sticking to the restrictions widely described above.

Moreover, the manufacturing Company guarantees that RADIO4 equipment is put on the market of non-surgical cosmetics supplied with a software that automatically limits the power to 25W (this corresponds to 45% of the power emitted by the medical equipment tested by us (RADIO4M), which has a maximum power of 55W).

Anyway, the operators working both in the medical field and in the cosmetic field shall pay utmost attention when they treat areas where the increase in temperature might induce adverse side effects. In particular, the application on the movable part of eyelids in direct contact with the eyeball should be banned, as any increase in heat of the eyeball causes opacity of the crystalline lens.

In witness thereof,
Prof. Angela FAGA
Director of the Interdepartmental Research Center "T.A.Me.Ri.Ci."
University of Pavia

Pavia, 21.4.2011

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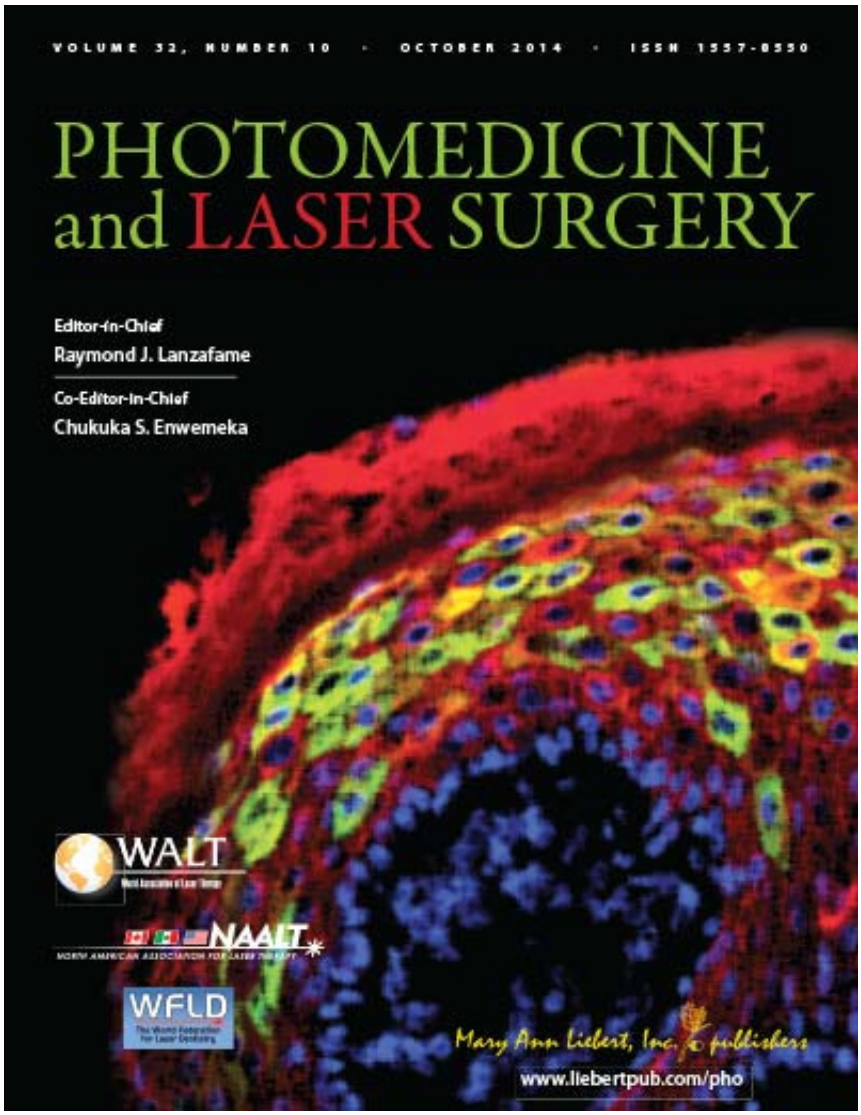
RADIOA™

RSS™
Radiofrequency Safely System

RADIOP™

SCIENTIFIC PUBLICATION



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The Biological Effects of Quadripolar Radiofrequency Sequential Application: A Human Experimental Study

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Abstract

Objective: An experimental study was conducted to assess the effectiveness and safety of an innovative quadripolar variable electrode configuration radiofrequency device with objective measurements in an *ex vivo* and *in vivo* human experimental model. ***Background data:*** Nonablative radiofrequency applications are well-established anti-ageing procedures for cosmetic skin tightening. ***Methods:*** The study was performed in two steps: *ex vivo* and *in vivo* assessments. In the *ex vivo* assessments the radiofrequency applications were performed on human full-thickness skin and subcutaneous tissue specimens harvested during surgery for body contouring. In the *in vivo* assessments the applications were performed on two volunteer patients scheduled for body contouring surgery at the end of the study. The assessment methods were: clinical examination and medical photography, temperature measurement with thermal imaging scan, and light microscopy histological examination. ***Results:*** The *ex vivo* assessments allowed for identification of the effective safety range for human application. The *in vivo* assessments allowed for demonstration of the biological effects of sequential radiofrequency applications. After a course of radiofrequency applications, the collagen fibers underwent an immediate heat-induced rearrangement and were partially denaturated and progressively metabolized by the macrophages. An overall thickening and spatial rearrangement was appreciated both in the collagen and elastic fibers, the latter displaying a juvenile reticular pattern. A late onset in the macrophage activation after sequential radiofrequency applications was appreciated. ***Conclusions:*** Our data confirm the effectiveness of sequential radiofrequency applications in obtaining attenuation of the skin wrinkles by an overall skin tightening.

Introduction

Over the past decade, radiofrequency (RF) has become an important and frequently used technology in aesthetic medicine. The mechanism of action of RF is based on an oscillating electrical current (2,000,000–3,000,000 times/sec) forcing collisions between charged molecules and ions, which are then transformed into heat.[1] A further contribution to the increase in the local temperature is provided by the radiation component of the RF field, with electromagnetic energy transfer to the water-rich dermal matrix.

Noninvasive delivery of RF energy to collagen and subcutaneous tissues produces collagen remodelling, therefore, achieving noninvasive tightening of lax skin and body contouring.[2,3] RF-treated skin displays an immediate and temporary change in the helical structure of collagen, with fibrils showing a greater diameter than that of fibers pretreatment.[4]

It is also thought that RF thermal stimulation results in a microinflammatory stimulation of fibroblasts, which produces new collagen, new elastin, and other substances, to enhance dermal structure.[1,5]

The depth of penetration of RF energy is inversely proportional to the frequency. Consequently, lower frequencies of RF are able to penetrate more deeply. The currently available devices work with frequencies within the 1 Hz to 40.68 MHz range.

Two different forms of RF delivery have been developed so far: monopolar and bipolar. Monopolar systems deliver current through a single contact electrode with an

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accompanying grounding pad that serves as a low resistance path for current flow to complete the electrical circuit; the active electrode concentrates most of the energy near the point of contact, and energy rapidly diminishes as the current flows through the body toward the grounding electrode. As a result, the tissue in the treated area is heated rather deeply (usually up to 20 mm) and intensely.[2]

Bipolar devices pass electrical current between two electrodes closely positioned to the skin; no grounding pad is necessary with these systems because no current flows throughout the rest of the body. The depth of penetration is approximately half the distance between the two electrodes.[3]

As a result, the tissue in the treated area is heated less deeply (usually up to 2–4 mm in depth) and less intensely than with the monopolar RF devices.[6]

Despite its lesser absolute effectiveness, the bipolar technology is currently gaining an increasing popularity, as it allows fair outcomes with significantly less invasive applications.[7]

Nowadays, patients asking for cosmetic medical treatments expect perfect results, with a minimum of work and social downtime. Therefore, such innovative noninvasive treatments have been progressively replacing the traditional and time-honored surgical procedures for skin tightening.

The increasingly large number of technological innovations proposed on the global market require rigorous study protocols for the assessment of safety and effectiveness prior to authorization for human use. As a group of academic plastic surgeons actively involved in aesthetic surgery and medicine research, we were commissioned to assess the effectiveness and safety of an innovative quadripolar variable electrode configuration RF device.

Materials and Methods

The study was conducted at the Advanced Technologies for Regenerative Medicine and Inductive Surgery Research Center of the University of Pavia, Italy, in cooperation with the Plastic and Reconstructive Surgery Unit of the Salvatore Maugeri Research and Care Institute, Pavia, Italy, and the Histology and Embryology Unit, Department of Public Health, Neuroscience, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy.

The study was approved by the University of Pavia Ethical Committee. A formal informed written consent was obtained from all of the patients and the study conformed to the Declaration of Helsinki.

A novel Class I RF generator, RADIO4™, produced by Novavision Group s.p.a., (Via dei Guasti 29, 20826 Misinto, Milan, Italy) was tested. RADIO4 is based on a four electrode system with software-controlled automatic dynamic configuration providing a 1 MHz RF current circulation. The variable electrode configuration allows for creation of custom-made electric fields promoting thermal energy transfer to the tissue from RF current circulation. The device allows three possible electrode configurations within the four electrodes (Fig. 1):

- 1–3: one transmitter electrode and three receiver electrodes
- 2×2: two transmitter electrodes and two receiver electrodes in a cross fashion

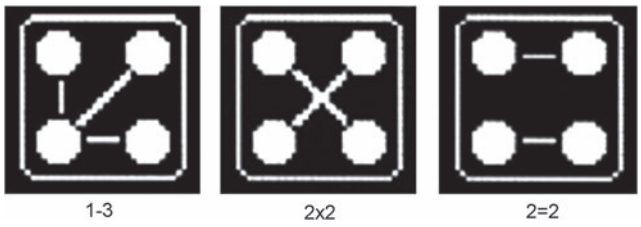

FIG. 1. The three electrode configuration options in the tested device: (1) 1–3, one transmitter electrode and three receiver electrodes; (2) 2×2, two transmitter electrodes and two receiver electrodes in a cross fashion; (3) 2=2, two transmitter electrodes and two receiver electrodes in a parallel fashion.

- 2=2: two transmitter electrodes and two receiver electrodes in a parallel fashion

The single electrode configuration is allowed to swap over at a time interval adjustable between 1 and 9 sec.

The maximum device working power is 55 W adjustable within a 5–100% delivery range. The device is equipped with an original patented safety technology, Radiofrequency Safety System (RSS™), and has been developed for noninvasive treatment of skin wrinkles and cellulite and for skin tightening.

The study was performed in two steps: *ex vivo* and *in vivo* assessments.

Ex vivo assessment

The ex vivo assessment was conducted on eight human anatomical specimens, including full thickness skin and subcutaneous tissue harvested from four female patients during sessions of abdominoplasty. The specimens underwent the experimental process after surgical harvesting, and the average time delay between harvesting the tissue and starting the experiment was 10 min. The tests were conducted in a dedicated air conditioned room at a temperature of 23°C. A control biopsy, including full thickness skin and adipose tissue, was harvested from each specimen before treatment.

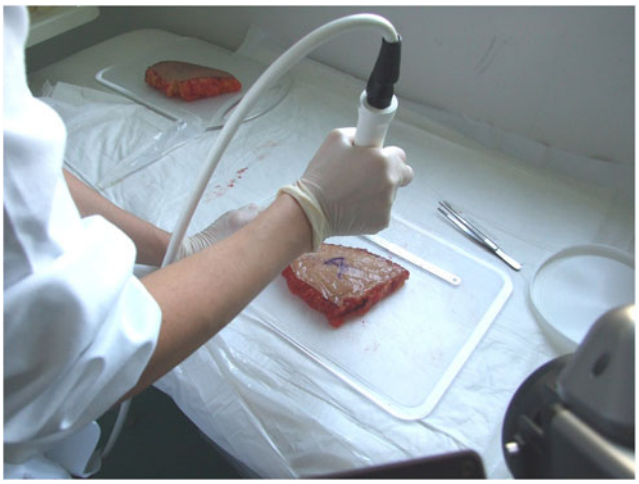

FIG. 2. *Ex vivo* radiofrequency application with the device's probe.

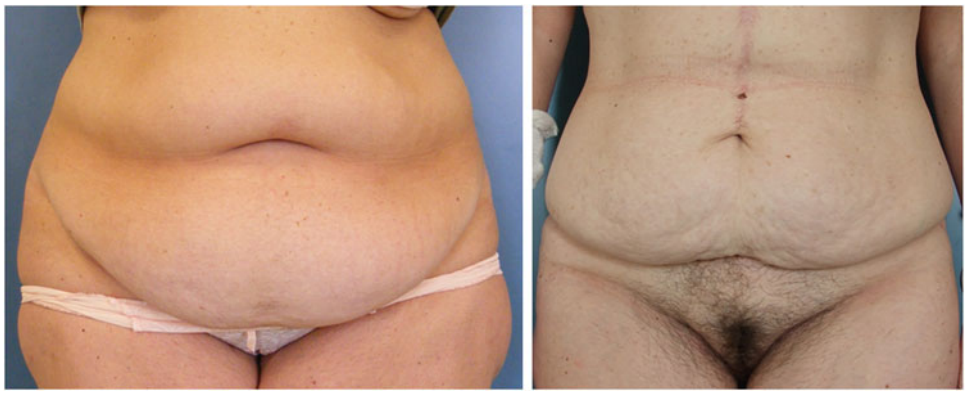

FIG. 3. Areas of abdominal fat that were investigated on the two patients scheduled for abdominoplasty.

The effects of RFs on the specimens were assessed with the association of three different methods:

- Clinical full examination and medical photography
- Temperature measurement in the specimens before and after the treatments with thermal imaging scan using the AVIO Thermal Video System TVS 500 camera with an uncooled infrared sensor with a 8–14 μm spectrum sensitivity, 320 × 240 pixel thermal image resolution, and 0.1°C thermal resolution (Nippon Avionics Co., Ltd. Gotanda Kowa Bldg., 1–5, Nishi-Gotanda 8-chome, Shinagawa-ku, Tokyo, 141-0031 Japan).
- Histological examination at light microscopy. Tissue samples were fixed in a 4% paraformaldehyde solution in phosphate buffer for 6 h, cryoprotected by immersion in sucrose saturated solution, frozen in liquid nitrogen, and finally cut in a cryostat. Finally, tissue sections were routinely stained using hematoxylin and eosin.

A water gel was applied on the skin surface in order to allow an optimal delivery of the RFs from the probe to the tissues (Fig. 2). The gel was stored at room temperature (23°C).

The study was performed using the 1–3 electrode configuration modality, Radio Frequency System (RFS) 1–3, and the configuration swap over time (RFS time) was set at 5 sec.

The eight specimens were divided into four groups of two and the RF was delivered to each group at the following percentages of the maximum device working power: 25% (13.75 W), 50% (27.50 W), 75% (41.25 W), and 100% (55 W). The energy was delivered in continuous mode (duty cycle 100%, time on = 1.000 msec, time off = 0 msec). The scheduled maximum application time was 4 min. As the specimens treated with the maximum device working power displayed clinical evidence of full thickness burn after few seconds, the applications in this group were discontinued at this time.

At the end of the application, a full thickness skin and subcutaneous tissue biopsy was harvested in each specimen from the site of maximum tissue warming, as displayed by the thermocamera scan.

In vivo assessment

The *in vivo* investigations were conducted on two volunteer female patients scheduled for abdominoplasty at the end of the experimental study (Fig. 3). The assessments

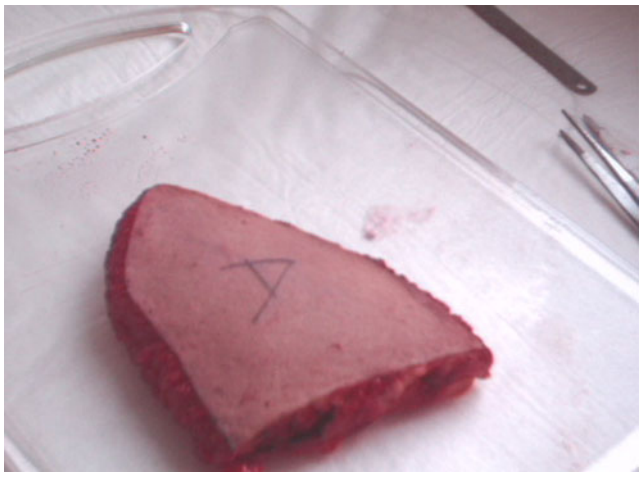

FIG. 4. Human *ex vivo* specimen before treatment: macroscopic view.

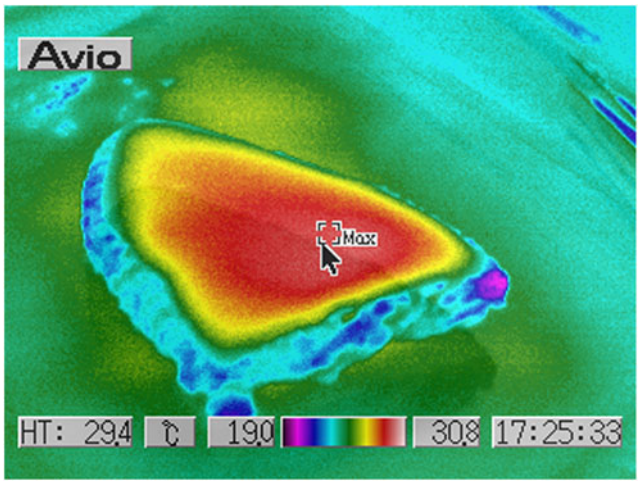

FIG. 5. Human *ex vivo* specimen before treatment: thermal imaging scan.

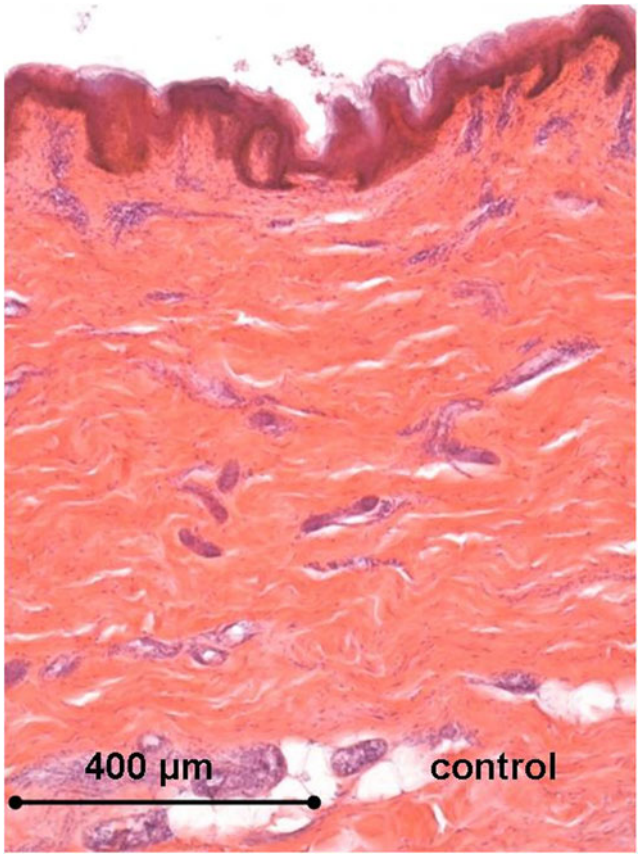

FIG. 6. Histology of the human *ex vivo* specimen before treatment: the epidermis displays a regular multilayered structure, the dermis shows regular dermal papillae with thin collagen fibers and thick collagen bundles in the reticular dermis. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

were performed on the lower abdominal skin area bounded above by the umbilicus, below by the pubis, and on each side by the anterior superior iliac spine. The applications were performed in the same dedicated air conditioned room at a temperature of 23°C, as in the *ex vivo* tests.

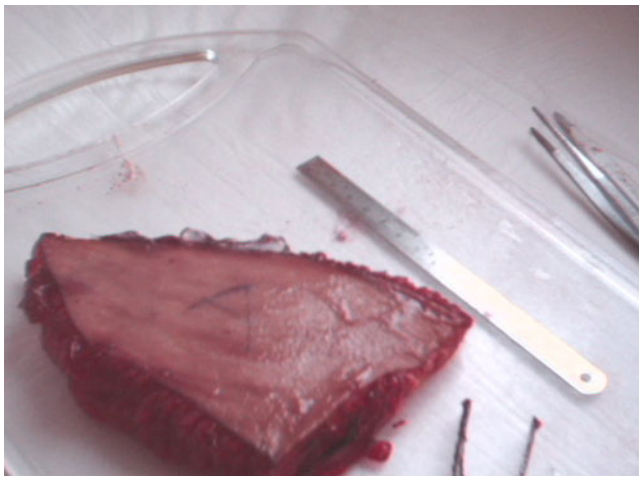

FIG. 7. Human *ex vivo* specimen after treatment with 25% of the maximum device working power (13.75 W): macroscopic view.

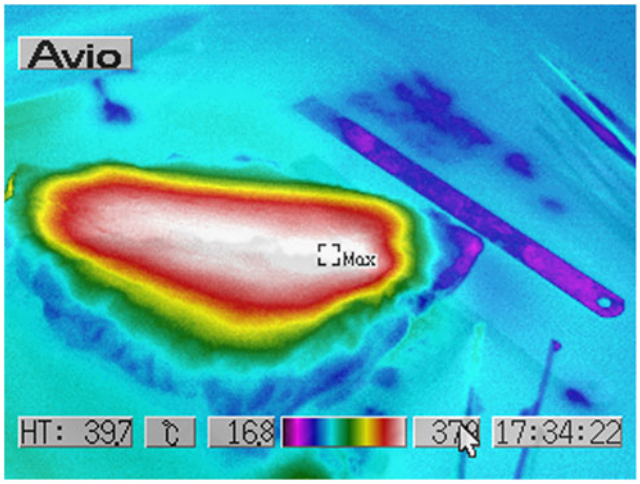

FIG. 8. Human *ex vivo* specimen after treatment with 25% of the maximum device working power (13.75 W): thermal imaging scan.

A control biopsy, including full thickness skin and adipose tissue, was harvested before the treatment. Three sequential treatments were performed with 2 weeks' interval. A water gel was applied on the skin surface in order to allow an optimal RF energy delivery from the probe to the tissues.

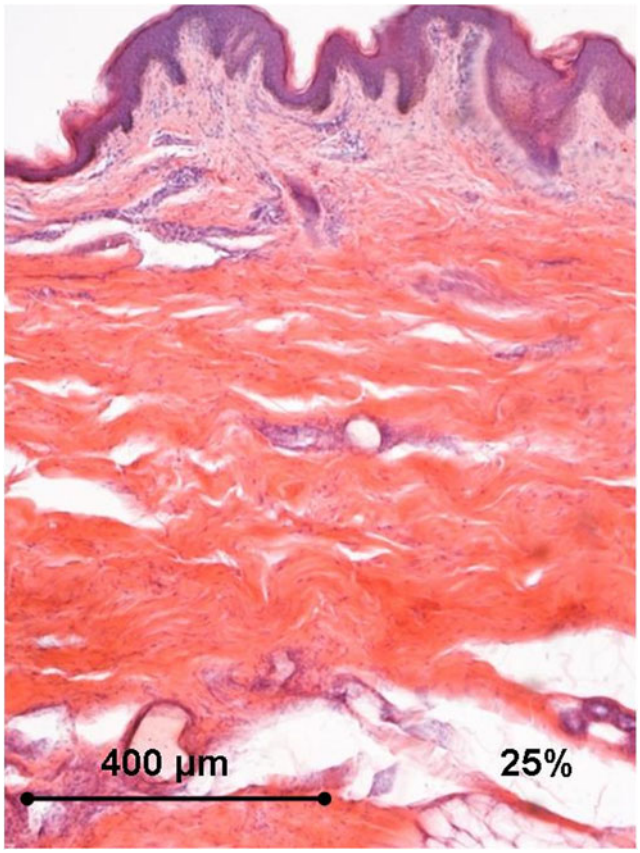

FIG. 9. Histology of the human *ex vivo* specimen after treatment with 25% of the maximum device working power (13.75 W): complete sparing of the epidermis that displays normal structure; an early thickening of the collagen bundles is appreciated in the deep dermal layers. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

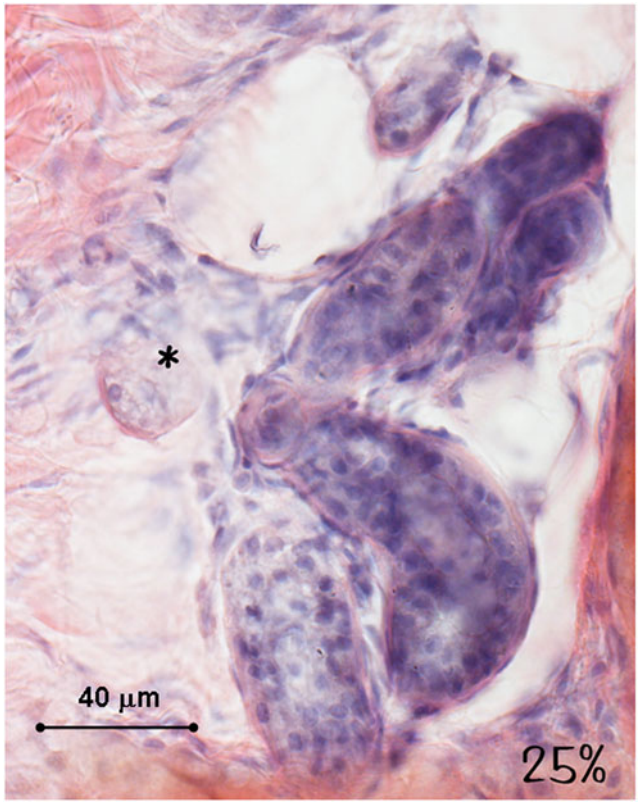

FIG. 10. Histology of the human *ex vivo* specimen after treatment with 25% of the maximum device working power (13.75 W): the sweat glands and the nerves (asterisk) display a normal structure and a regular staining. Light microscopy, hematoxylin and eosin staining, bar 40 μm.

The applied parameters were the same as in the *ex vivo* section of the study: RFS 1–3, duty cycle 100%, RFS time 5 sec.

Three sequential treatments were scheduled with 2 weeks' interval. Each treatment lasted 20 min.

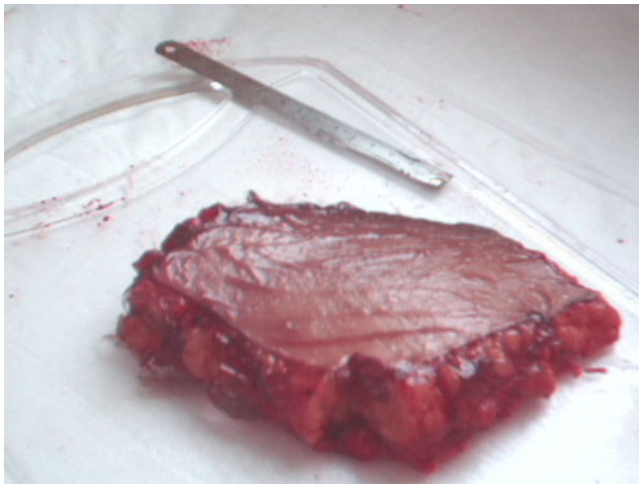

FIG. 11. Human *ex vivo* specimen after treatment with 50% of the maximum device working power (27.50 W): macroscopic view.

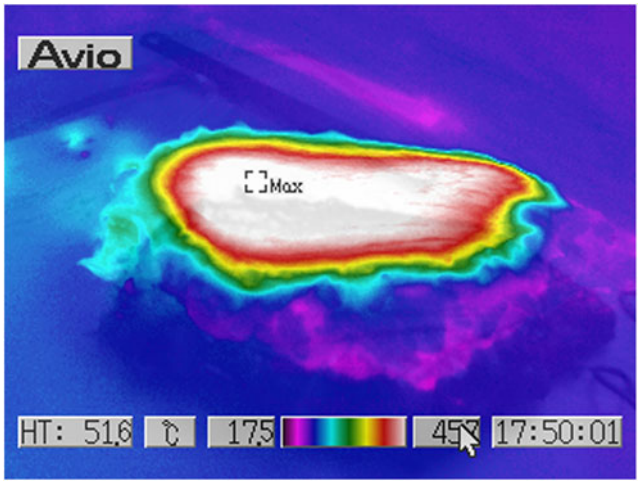

FIG. 12. Human *ex vivo* specimen after treatment with 50% of the maximum device working power (27.50 W): thermal imaging scan.

The initial working power was 45% (24.75 W); however, following a patient's consistent subjectively perceived discomfort, the energy delivery power was reduced to 35–40% (19.25–22 W) in all of the tests, and this level was comfortably tolerated. On occasion of the second treatment in

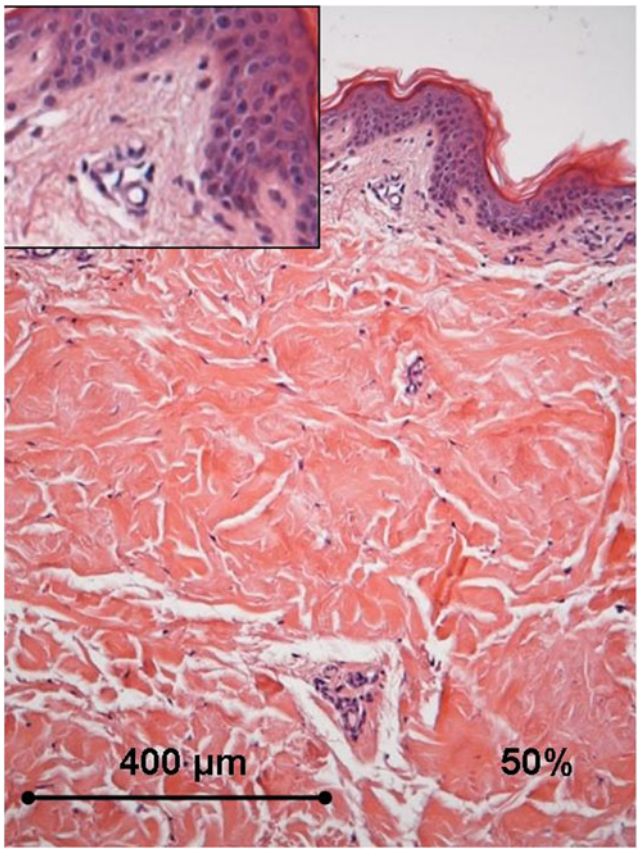

FIG. 13. Histology of the human *ex vivo* specimen after treatment with 50% of the maximum device working power (27.50 W): the thickening of the collagen fibers in the papillary dermis is appreciated, whereas the blood vessels in the dermal papillae do not display any alteration (box). Light microscopy, hematoxylin and eosin staining, bar 400 μm.

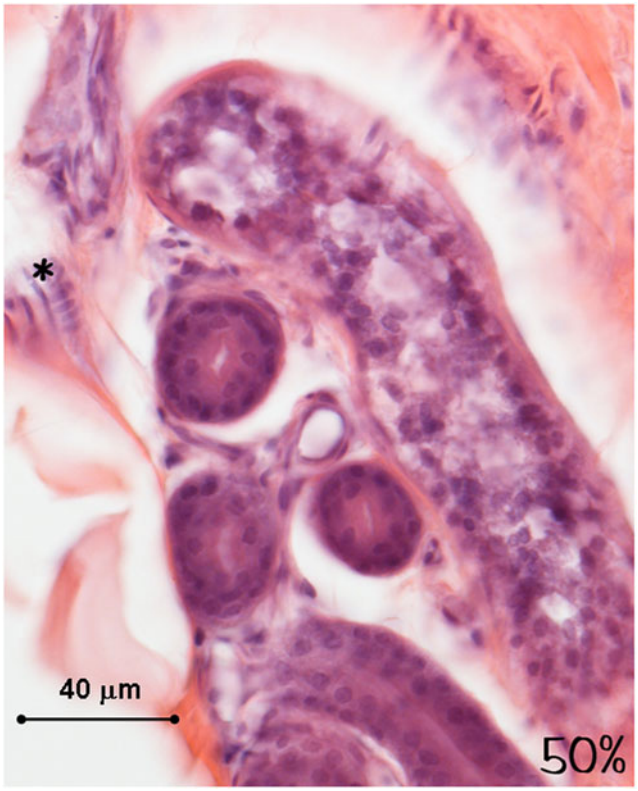

FIG. 14. Histology of the human *ex vivo* specimen after treatment with 50% of the maximum device working power (27.50 W): the sweat glands and the nerves (asterisk) display a normal structure and a regular staining. Light microscopy, hematoxylin and eosin staining, bar 40 μm.

one patient, the energy delivery power had to be reduced to 20% (11 W) in the last 8 min of application, because of severe subjective discomfort.

The effects of the RF applications on the patient were assessed with the same methods used in the *ex vivo* as-

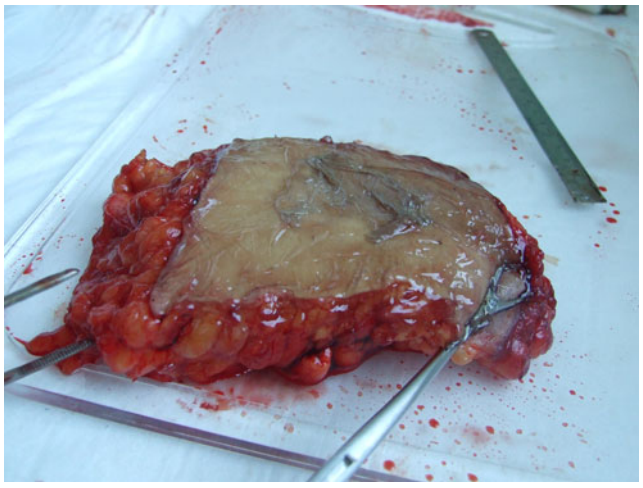

FIG. 15. Human *ex vivo* specimen after treatment with 75% of the maximum device working power (41.25 W): macroscopic view.

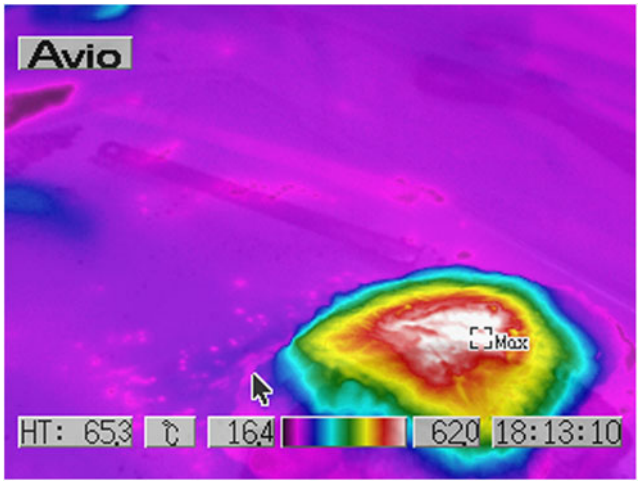

FIG. 16. Human *ex vivo* specimen after treatment with 75% of the maximum device working power (41.25 W): thermal imaging scan.

sessment: clinical examination, thermocamera scan, and histological examination of treated tissue biopsies. Three punch full thickness skin and subcutaneous tissue biopsies were harvested from each treated area. The first biopsy was harvested 2 weeks after the first treatment, the second one 2

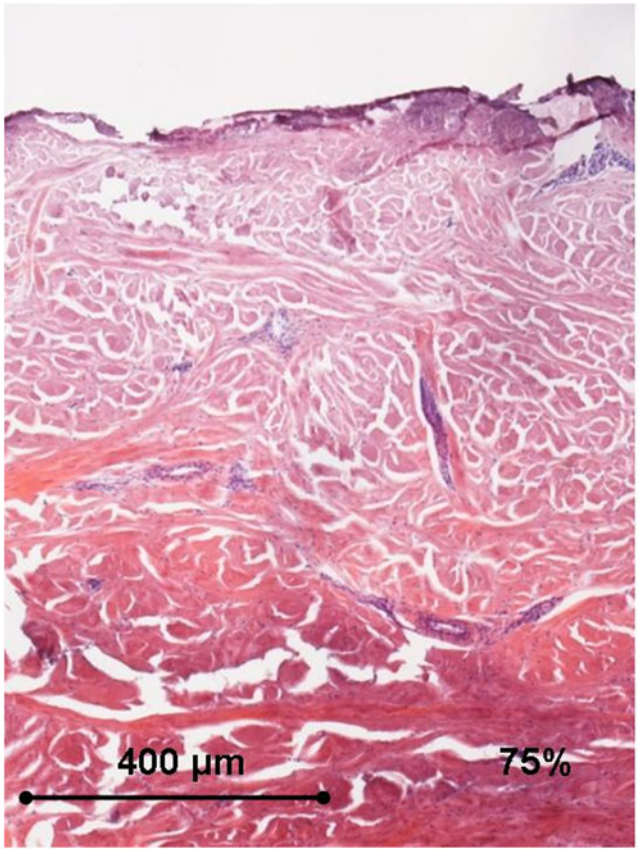

FIG. 17. Histology of the human *ex vivo* specimen after treatment with 75% of the maximum device working power (41.25 W): the epidermis is necrotic, and the collagen bundles display a remarkable diffuse thickening in the whole dermis. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

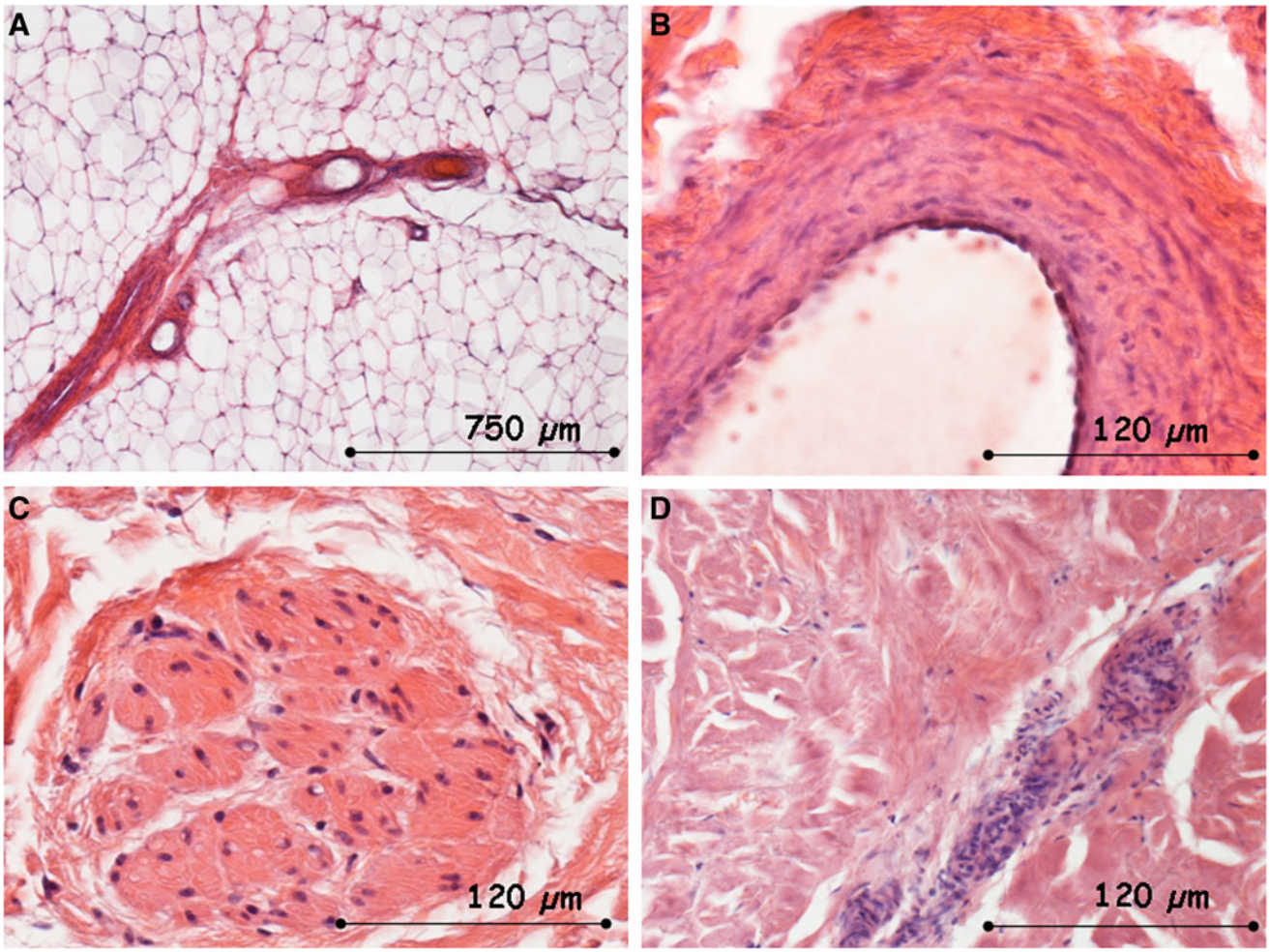

FIG. 18. Histology of the human *ex vivo* specimen after treatment with 75% of the maximum device working power (41.25 W): the subcutaneous tissue (**A**, bar 750 μm), the vascular wall with its endothelial lining (**B**, bar 120 μm), the nerves (**C**, bar 120 μm), and the sweat glands (**D**, bar 120 μm) appear intact. Light microscopy, hematoxylin and eosin staining.

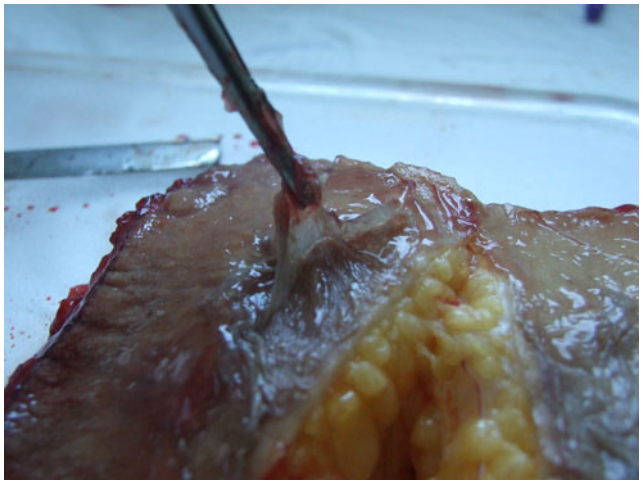

FIG. 19. Human *ex vivo* specimen after treatment with 100% of the maximum device working power (55 W): macroscopic view; after a few seconds of application, the epidermis displays separation from the dermis, and the subcutaneous tissue shows coagulative necrosis in the superficial layer while it appears intact in the deep layer.

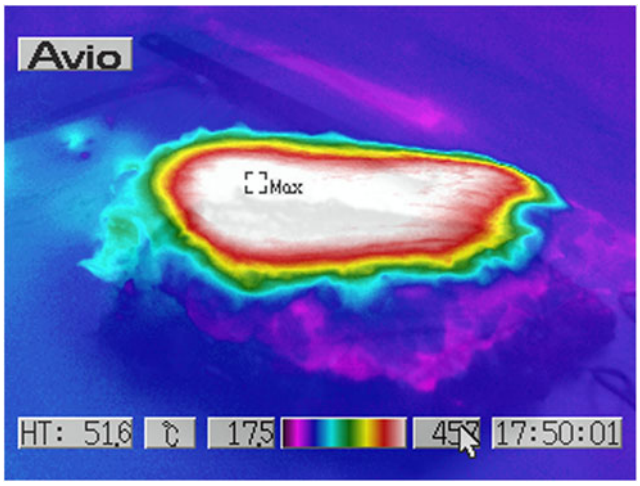

FIG. 20. Human *ex vivo* specimen after treatment with 100% of the maximum device working power (55 W): thermal imaging scan.

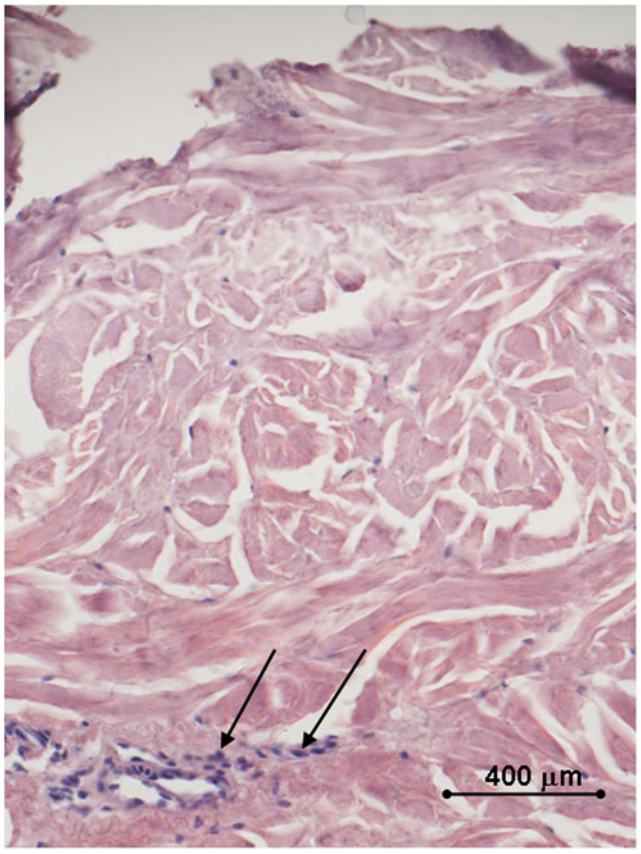

FIG. 21. Histology of the human *ex vivo* specimen after treatment with 100% of the maximum device working power (55 W): a complete loss of the epidermal lining and a massive coagulative dermal necrosis are appreciated; the sweat glands display early signs of necrosis (arrows). Light microscopy, hematoxylin and eosin staining, bar 400 μm.

weeks after the second treatment, and the third one 10 weeks after the last treatment.

Results

Ex vivo assessment (Figs. 4–21)

Clinical examination. At the end of the application, the specimen treated with 25% of the maximum working power did not display any macroscopic skin surface alterations, although the subcutaneous tissue was softer at palpation and displayed some degree of shrinkage.

The specimen treated with 50% of the maximum working power showed a significant wizening of the subcutaneous tissue after 90 sec, whereas the skin showed a remarkable retraction and separation from the subcutaneous tissue in 3 min; after 4 min, the overall appearance was as a deep skin and subcutaneous tissue burn.

The specimen treated with 75% of the maximum working power displayed a total skin retraction and separation from the subcutaneous tissue after 90 sec, with coagulative necrosis of the subcutaneous fat.

The specimen treated with full working power displayed a full thickness burn appearance in a few seconds.

Temperature report. The energy application was followed by an increase of the specimen temperature proportional to the application power and time, with a gradient decreasing from the surface to the subcutaneous adipose tissue (Table 1).

Histological examination. All of the specimens displayed scattering of the collagen bundles that was appreciated from the papillary dermis up to 1.5 cm in depth. Such an alteration was proportional to both time and energy power application. The epithelial superficial lining appeared intact up to the application of 50% of the maximum working power. The subcutaneous tissue, the nerves, and the skin glands appeared intact up to the application of 75% of the maximum working power.

In vivo assessment

Clinical examination. The treatments were well tolerated, and the patients occasionally referred to tolerable local heat sensation, burning pain, and electric shock sensation. At the end of the treatments, no skin lesions were appreciated. After two applications, the patients referred to improved local skin softness and smoothness.

Temperature report. The energy application was constantly followed by an increase of the skin surface temperature (Table 2, Fig. 22).

Histological examination (Figs. 23–29). The *in vivo* findings 2 weeks after the first treatment closely resemble those in the *ex vivo* specimens: the collagen bundles appeared diffusely scattered whereas the epithelial superficial lining, the subcutaneous tissue, the nerves, and the skin glands appeared intact.

Two weeks after the second application, the collagen bundles appeared coagulated in small grumes in the papillary dermis and in larger grumes in the underlying reticular dermis. The epidermis appeared normal. The overall connective cell count and general pattern did not differ from the

TABLE 1. AVERAGE *EX VIVO* SPECIMEN TEMPERATURE VALUES MEASURED AT DIFFERENT WORKING POWER APPLICATIONS

	T pre	*T post 4' 25%*	*T post 4' 50%*	*T post 4' 75%*	*T post 45'' 100%*
Skin surface	25.8°	37°Δ + 11.2°	47.7°Δ + 21.9°	55 Δ + 29.2°	60 Δ + 34.2°
Subcutaneous adipose tissue	27.5°	28.8°Δ + 1.3°	27.5°Δ 0	27.2 Δ − 0.3°	27 Δ − 0.5°

T, temperature in degrees Celsius; Δ, average temperature delta between pre- and post-treatment; ', minutes; '', seconds.

TABLE 2. AVERAGE SKIN SURFACE TEMPERATURE VALUES MEASURED AT THE END OF THE *IN VIVO* TREATMENT

	T pre	*T post*	Δ
Skin surface	29.6°	38.2°	+8.6°

T, temperature in degrees Celsius; Δ, average temperature delta between pre- and post-treatment.

control areas. A remarkable thickening in the elastic fibers with a regular reticular pattern and a definite orientation perpendicular to the basal membrane in the papillary dermis was appreciated in the treated areas versus the controls.

Ten weeks after the third application, the macrophages had moved from the perivascular niche and displayed a slight increase in their count, thus suggesting some sort of functional activation. Such a finding suggests the presence of coagulated collagen fragments and/or other tissue debris.

Discussion

The device used in our study is one of the innovative multipolar developments of the bipolar technology.[8]

As any technical innovation should undergo a rigorous assessment of both safety and effectiveness prior to clinical use, our study provided a prudent design with two different and sequential steps.

The *ex vivo* experimental assessments allowed for identification of the effective safety range for human application, which was established between 11 and 22 W.

We deliberately opted for a random choice of only one electrode configuration out of three potentially available in the device setting, as the rigorous compliance requirements substantially limited the number of patients recruited for the study.

As expected, the biological effects of RF application were related to the thermal energy transfer to the tissues, and were proportional to both local temperature and exposure time.[9] All of the possible typical macro- and microscopic tissue burn features were observed in the *ex vivo* samples in relation to the different levels of applied energy. However, these effects were mainly appreciated in the dermis and subcutaneous tissue, with involvement of the overlying epidermis only for the highest applied energy levels. Such a figure is a peculiar advantage of RF technology that allows selective heat transfer to the dermis and subcutaneous tissue, yielding a controlled collagen alteration.

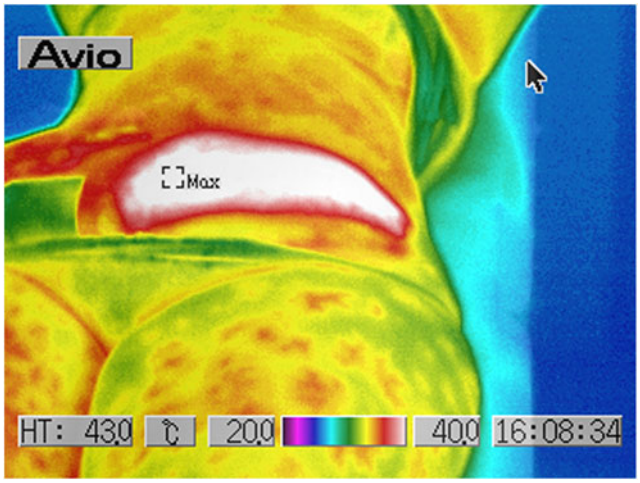

FIG. 22. Thermal imaging scan of the lower abdominal region after the *in vivo* treatment.

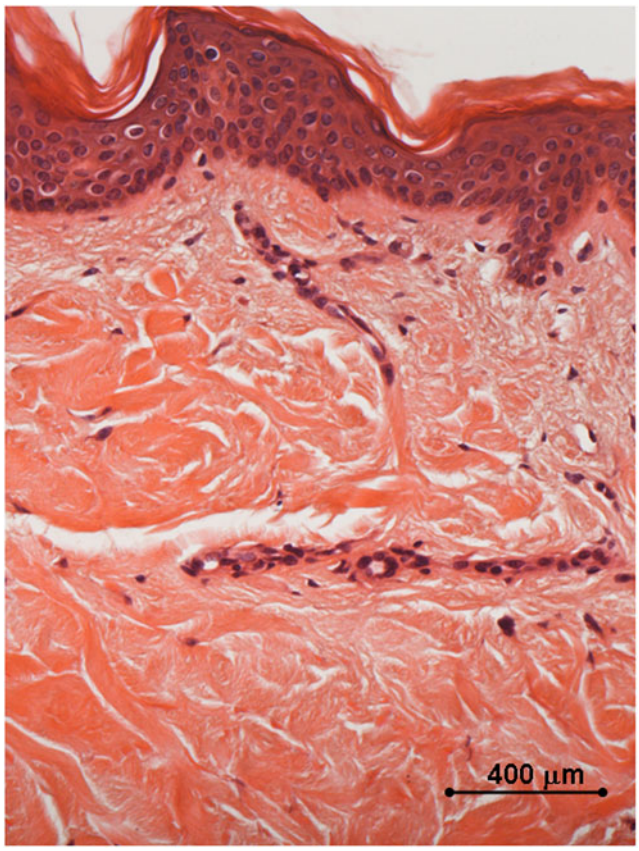

FIG. 23. Histology of *in vivo* control biopsy: the collagen fibers appear thin and outstretched. Light microscopy, hematoxylin and eosin staining, bar 400 µm.

After accurate definition of the effective safety range of RF applications on human tissues, the trial proceeded with the *in vivo* assessments.

These tests allowed for demonstration of the biological effects of the device under study at different time intervals.

The temperature changes reported in the *ex vivo* samples were partially compensated *in vivo* by the active thermoregulation and the local temperature increase was proportional to the application time.

A selective effect was appreciated in the more dense and compact tissues, as the dermis and the connective septa of the adipose tissue. The temperature reports and the histological examinations, both *ex vivo* and *in vivo*, consistently demonstrated selective scattering of the collagen bundles in the dermis. The small grumes observed in the reticular dermis of the *in vivo* samples 2 weeks after the second application might have followed local increase of RF current density in sites of enhanced electric conductivity with eventual focal temperature rise.

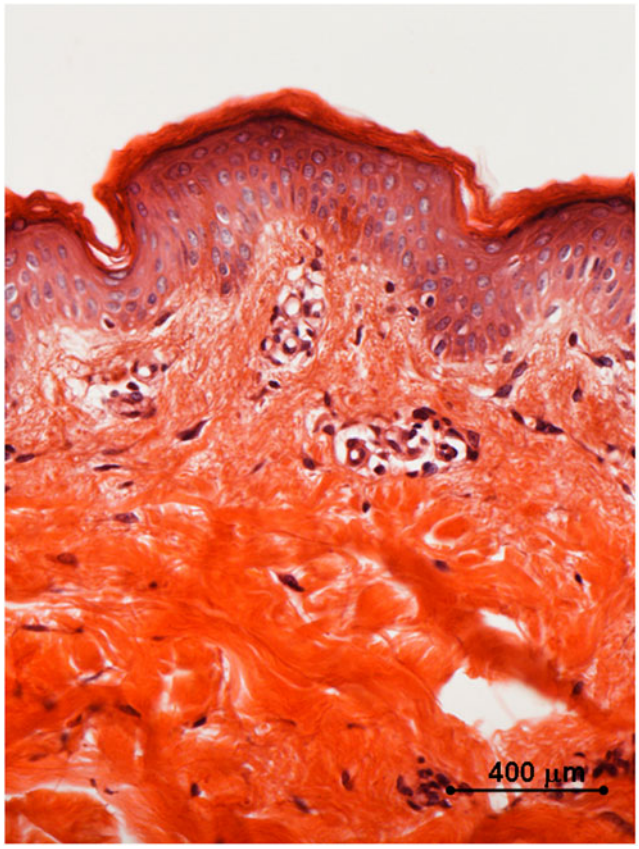

FIG. 24. Histology of *in vivo* sample harvested 2 weeks after the first treatment with 35–40% of the full device working power: early signs of coagulations are appreciated both in the papillary and in the reticular dermis. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

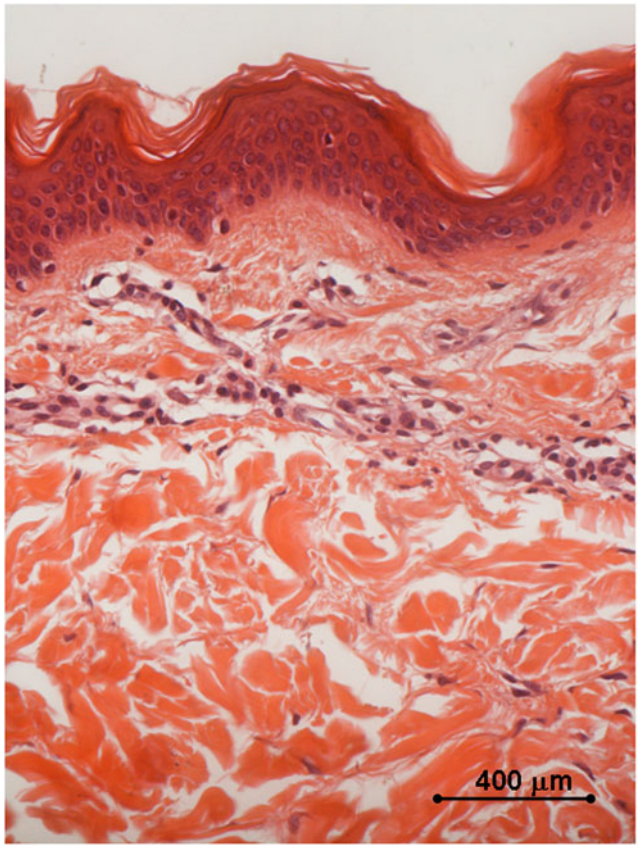

FIG. 25. Histology of *in vivo* sample harvested after two treatments with 35–40% of the full device working power, 1 month after the first treatment: the collagen fibers are coagulated in small grumes in the papillary dermis and in larger ones in the underlying layers; the epidermal lining is intact. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

It is demonstrated that collagen fibers begin to curve at 52–55°C[10] and contract at 65°C,[11] and the denaturation threshold falls between 60° and 70°C.[12] According to the thermal imaging scan in our *ex vivo* and *in vivo* samples, such a temperature threshold was unlikely to have been approached, although it may be theoretically supposed that it occurred in very small and circumscribed tissue spots. We can, therefore, suppose that the observed structural changes of the collagen fibers were not related exclusively to the temperature rise.

The overall effects of the sequential *in vivo* RF applications observed on the connective fibers, both collagen and elastic, might suggest their spatial rearrangement in the absence of complete denaturation: actually, no signs of scarring were observed under the microscope in any of our samples. As the collagen and elastic fibers are highly hydrophobic and are invested by a highly electric conductive water rich matrix, they obviously tend to gather when the temperature in the investing highly hydrophilic matrix rises.

Some interesting changes were observed in the skin elastic fiber network after two sequential applications with 2 weeks' interval 1 month after the first treatment: the elastic fibers appeared thicker both in the papillary and the reticular dermis; however, although thick elastic fibers are a typical feature of skin photo- and chrono-ageing, in our samples their regular network pattern was found more similar to the juvenile one.

Such an interesting figure might also be explained by the shrinkage of the highly hydrophobic elastic fibers with exclusive physical mechanism after increase of the energetic potential in the local water rich environment. These data are consistent with the literature,[13] and are in favor of the bipolar technology, as the elastic fibers seem to significantly decrease after monopolar treatment. [2] The epidermis did not display any significant damage apart from a transient erythema at the end of the *in vivo* treatments.

Adipose tissue, endothelial cells, nerves, and skin adnexa appeared intact with power application up to 41.25 W (Figs. 10, 14, and 18). Such an evidence was consistent with the peculiar temperature gradient figure between the skin surface and the underlying adipose tissue where relevant temperature changes in the dermis were not transmitted to the underlying fat.

These data both confirmed the low thermal conductivity of the human skin and demonstrated the selective superficial distribution of the electromagnetic energy within the treated tissues.

The *in vivo* effects of the RF application included a slight macrophage activation after three sequential applications

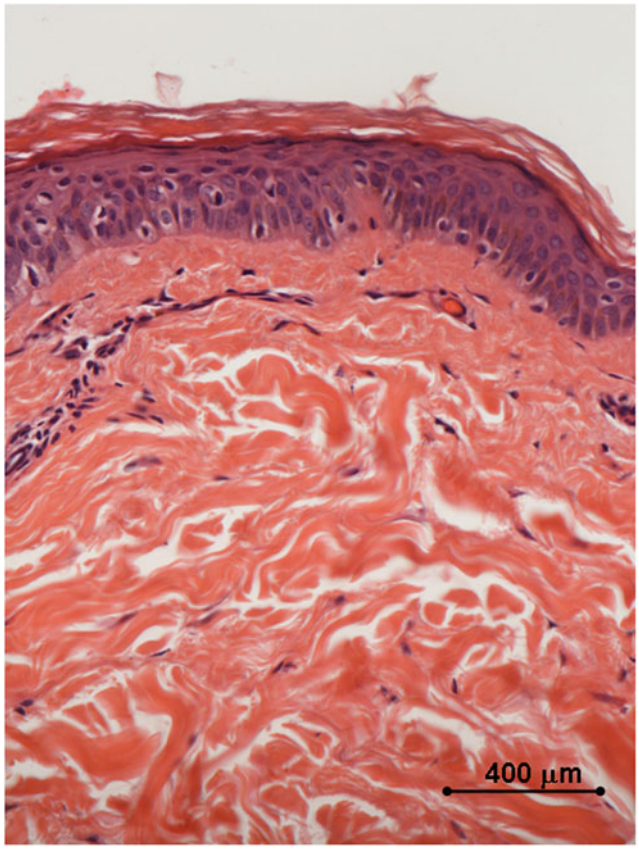

FIG. 26. Histology of *in vivo* sample harvested 10 weeks after the third treatment with 35–40% of the full device working power: the epidermis displays a normal differentiation and layer organization; a remarkable degree of collagen coagulation is appreciated in the papillary dermis, and the collagen bundles in the reticular dermis display a significant thickening as well. Light microscopy, hematoxylin and eosin staining, bar 400 μm.

with 2 weeks' interval, and might suggest the presence of tissue debris and/or coagulated collagen still being metabolized.

Nevertheless, no actual inflammatory cells or fibroblast response was appreciated.

However, a significant cellular response might be expected after further sequential applications, as suggested by the clinical protocols currently in use. The sequential application of RF for the treatment of skin wrinkling would definitely appear as a far different philosophy from the traditional surgical face and body lifting, as it would rely on a progressively induced and gently modulated body biological response. RF might, therefore, be considered an effective alternative for mild cases of skin laxity, and a useful completion of traditional surgical techniques.

Conclusions

The tested quadripolar variable electrode configuration RF equipment can provide selective and favorable changes in the dermal structure without side effects in the epidermis, vessels, and nerves when the energy delivery power ranges between 11 and 22 W.

After a course of RF application, the native collagen fibers underwent an immediate heat- induced rearrangement, and were just partially denaturated and progressively metabolized by the macrophages. Subsequently, an overall thickening and spatial rearrangement was appreciated both in the collagen and in the elastic fibers, the latter displaying a juvenile skin reticular pattern.

Our data demonstrated a late onset in the macrophage activation after sequential RF applications. It might be supposed that such a recruitment might be followed by a fibroblastic response at a later stage,[5] although such a hypothesis would suggest further investigations.

All of our data confirm the effectiveness of the RF applications in obtaining attenuation of the skin wrinkles by an overall skin tightening.

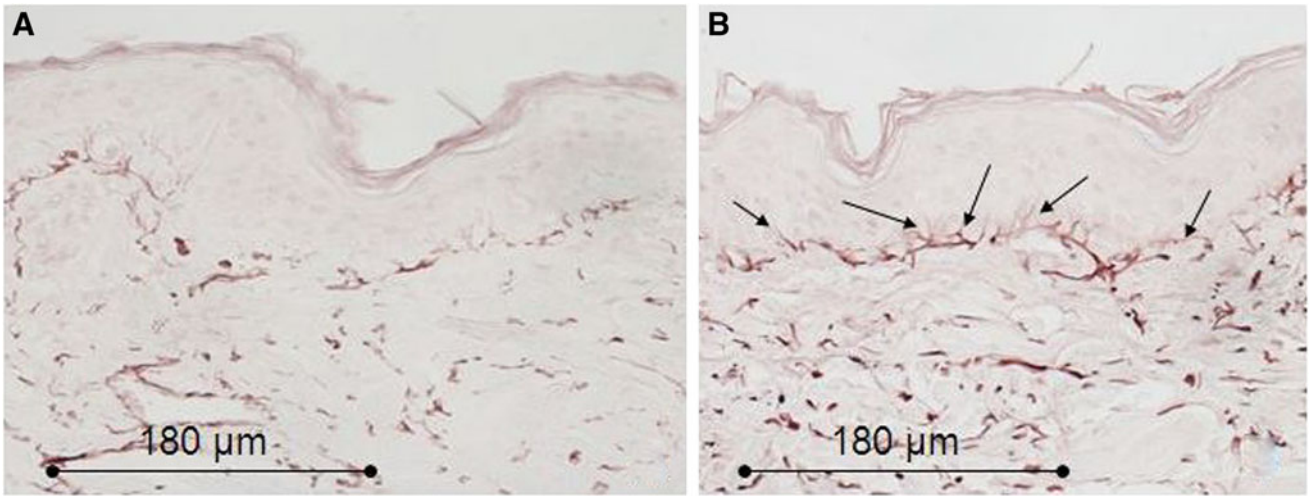

FIG. 27. Histology for elastic fibers of *in vivo* biopsies. **(A)** Control sample: the elastic fibers (purple-brown) show a regular distribution throughout the whole dermis. **(B)** Sample harvested after two treatments with 35–40% of the full device working power 1 month after the first treatment: the elastic fibers show a significant thickening throughout the whole dermis; in the papillary dermis the elastic fibers show a more definite perpendicular orientation to the basal membrane (arrows). Light microscopy, orcein staining, bar 180 μm.

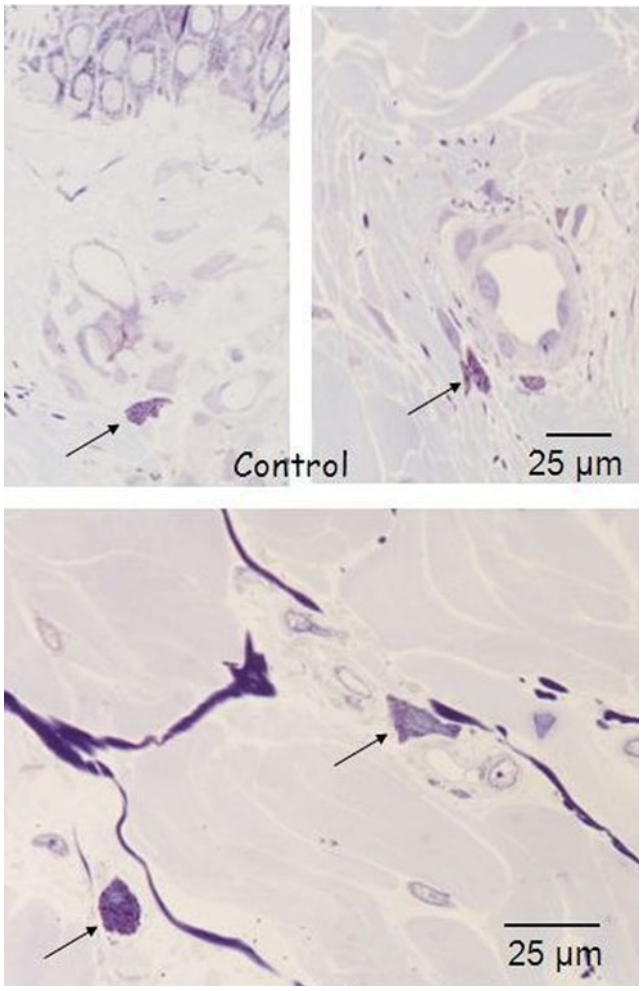

FIG. 28. Histology for macrophages of *in vivo* control biopsy: the arrows highlight the macrophages in quiescent status around the vessels. Light microscopy, toluidine blue staining, bar 25 μm.

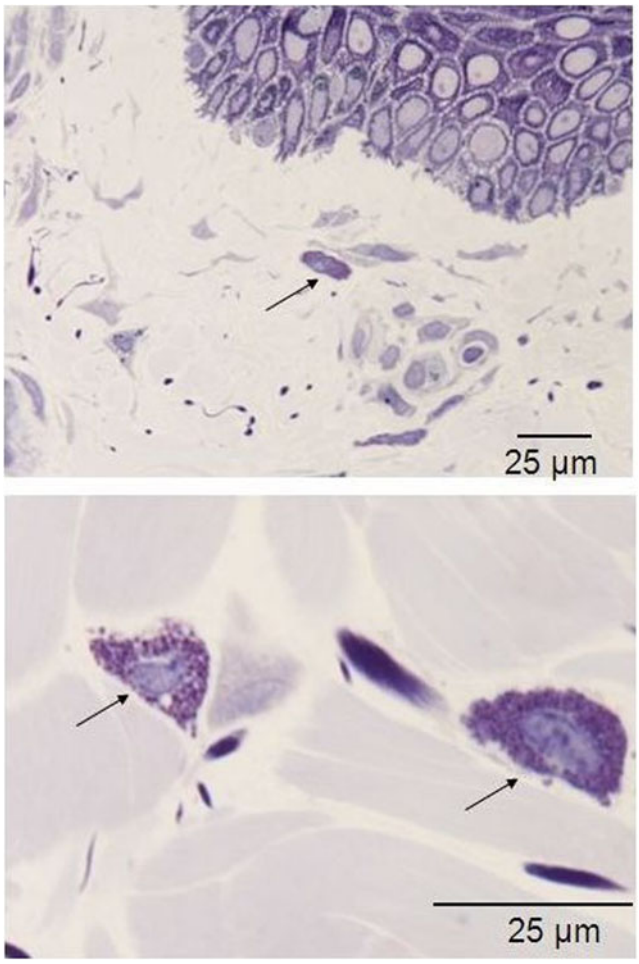

FIG. 29. Histology for macrophages of *in vivo* biopsy harvested after three treatments with 35–40% of the full device working power: the arrows highlight the macrophages that have moved from the perivascular niche, and display a slight increase in their count, thus suggesting an active status. Light microscopy, toluidine blue staining, bar 25 μm.

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Author Disclosure Statement

No competing financial interests exist.

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Case Report

Evolutions in diagnosis and treatment of vaginal laxity

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Abstract

Introduction:

The use of Dynamic Quadripolar Radiofrequency (DQRF) is a new therapy for the treatment of vulvovaginal conditions such as laxity and sexual dysfunctions, while Vaginal tactile imaging allows biomechanical assessment of vaginal tissues and pelvic floor muscles.

The purpose of this study is to explore changes in vaginal tissue elasticity, pelvic floor support and muscle strength after applied vaginal radiofrequency treatments.

Case Report: In January 2017, a 42-year-old Caucasian Patient was treated for vaginal laxity. She had given birth to three children, the most recent being six years before vaginal rejuvenation was performed. She had experienced no previous non-surgical vaginal rejuvenation treatments and no past medical history that would be significant to this procedure such as recent surgical labiaplasty, etc., no known drug allergies, no sexual health history until the procedure, and cervical smears has never shown any abnormalities. DQRF procedures were performed at 2 week intervals for 4 consecutive treatments. The Vaginal Tactile Imager (VTI) was used to assess the vaginal walls, pelvic floor support structures and pelvic floor muscle (PFM) contractions before and and two weeks after the final DQRF treatment. The VTI probe allows for an estimation of: a) vaginal tissue elasticity as a pressure gradient under vaginal wall deformation, b) pelvic floor support conditions as a pressure gradient under deformation of the posterior compartment, and c) PFM strength as a pressure feedback under voluntary and involuntary (cough) contractions.

Conclusion: Dynamic Quadripolar Radiofrequency treatment is a promising novel technology with clinical results improving tissue elasticity, pelvic floor support and PFM strength upon assessment with tactile imaging. VTI allows monitoring of biomechanical transformation of tissues before and after the radiofrequency treatment and may predict the effectiveness of therapy for individual patients.

Keywords: *Vaginal Tactile Imaging, Radiofrequency, Vaginal Laxity, Vaginal Rejuvenation*

Introduction

The use of Dynamic Quadripolar Radiofrequency (DQRF) is a new therapy. for the treatment of vulvovaginal conditions, while Vaginal tactile imaging (VTI) allows biomechanical assessment of vaginal tissues and pelvic floor muscles.

The purpose of this study is to explore changes in vaginal tissue elasticity, pelvic floor support and muscle strength after vaginal DQRF treatments upon assessment with tactile imaging.

Standardized instruments for assessing biomechanical conditions of the pelvic floor and all urogynecologic aspects of female sexual dysfunction are lacking. In the last decade, a new modality for tissue characterization termed Elasticity Imaging (EI) or Elastography has emerged. EI allows visualization and assessment of mechanical properties of soft tissue. Mechanical properties of tissues (elastic modulus, viscosity), are highly sensitive to tissue structural changes in several physiological and pathological processes. Evaluating the biomechanical properties of the vaginal wall and its immediate surrounding connective tissue has been particularly difficult. The specific goal of VTI is to provide a reproducible and quantifiable means to visualize and measure vaginal tissue elasticity. VTI most closely mimics manual palpation because the TI probe, with a pressure sensor array, acts like human fingers during a clinical examination. The probe slightly compresses soft tissue and detects changes in the pressure pattern (“stress imaging,” “computerized palpation,” or “mechanical imaging”).

Case Report

Methods

In January 2017, a 42-year-old Caucasian Patient was treated for vaginal laxity. She had given birth to three children, the most recent being six years before vaginal rejuvenation was performed. She had no previous non-surgical vaginal rejuvenation treatments and no past medical history that would be significant to this procedure such as recent surgical labiaplasty, etc., no known drug allergies, no sexual health history, until the procedure, and cervical smears has never shown any abnormalities. DQRF procedures were performed at 2 week intervals for 4 consecutive treatments.

The Vaginal Tactile Imager (VTI) developed by Egorov et al. was used to assess the vaginal walls, pelvic floor support structures and pelvic floor muscle (PFM) contractions before and and two weeks after the final DQRF treatment.

VTI is performed on a patient the dorsal lithotomy position with empty bladder and rectum. The full VTI examination takes 2 to 3 minutes to complete. The VTI probe is calibrated before every clinical application. The VTI procedure consists of 3 independant parts (i) probe insertion, (ii) probe rotation, and (iii) muscle contractions, with 8 different tests listed below.

VTI allows the acquisition of pressures applied to the vaginal walls and the acquisition of probe location to visualize vaginal and pelvic floor support structures and to record pelvic floor muscle contractions. The VTI software provides visualization, analysis, information, and reporting tools. The acquired data and analysis information can be used for quantitative assessment of the vaginal and pelvic floor conditions. The VTI device is associated with a movable computer display cart. The VTI probe is equipped with 96 pressure sensors along both sides of the probe, an orientation sensor, and temperature sensors with micro-heaters. During the patient examination procedure, data are sampled from the probe sensors and displayed on the VTI computer display in real time. The probe surfaces that contact the vaginal walls are preheated to human body temperature. A lubricating jelly is used for patient comfort and to provide reproducible boundary-contact conditions with deformed vaginal tissue.

The VTI probe allows for an estimation of: a) vaginal tissue elasticity as a pressure gradient under vaginal wall deformation, (test 1 and 2), b) pelvic floor support conditions as pressure gradient under a deformation of the posterior compartment (test 3), and c) PFM strength as a pressure feedback under voluntary and involuntary (cough) contractions (tests 4 to 8). Orthogonal cross-sections of the 3-D tactile image allow visualization of anatomy and elasticity distributions. Tactile imaging reveals not only the elasticity conditions of vaginal wall itself, but the elasticity distribution of underlying tissue structures. These images may be considered as documentation of the current elasticity state of the vaginal walls and surrounding
support tissues. 8 VTI parameters were proposed to characterize vaginal conditions:

Test 1 allows the calculation of: 1.Maximum resistance force to insertion (Fl_{max} in newtons, N); 2.Insertion work (Wl in millijoules, mJ); 3.Maximum stress-to-strain ratio, ie gradient, elasticity (Gl_{max} kilopascals per millimeter, kPa/mm). Test 2 allows the calculation of: 1.Maximum intravaginal pressure at rest (kilopascals, kPa);2.Anterior vs posterior force at rest (newtons, N);3.Left vs right force at rest (newtons, N)
Test 3 allows the calculation of: 1.Maximum intravaginal pressure at pelvic muscle contraction (kilopascals, kPa);2.Muscle contraction force (newtons, N).
A Standard Vaginal Laxity Questionnaire (VLQ) translated in French was also used. It obtains perceptions on level of vaginal laxity/ tightness assessed with 7-level ordered responses (very loose, moderately loose, slightly loose, neither loose nor tight, slightly tight, moderately tight, or very tight).

The patient was successfully treated with 4 consecutive DQRF treatments with 15 days interval.

The non parametric Wilcoxon Signed Rank Test for repeated measurements on single populations was applied to both repeated measures in Improvement in Elasticity and Pelvic Floor Muscles Strength after treatment, and average calculation of vaginal elasticity. Two-sided levels were used for all statistical tests with $p<0.01$ as cut-off for significance.

Results

The vaginal tissues elasticity improved from a VLQ score of 1 (very lose) to 6 (moderately tight), and improved in pressure and calculated pressure gradients with color map going wider in yellow and red colours for pressure in test 1 (figure 1), gradient and pressure in test 2 (Figure 2) and pressure in test 3 (Figure 3). There are statistically significant improvements in pressure at test 1 by 100%, from 20% to 500% in gradient in test 2, and 60% in test 3 (Table 1). The PFM strength for voluntary muscle contractions (figure 4) and PFM strength for involuntary contractions (contraction with a cough, figure 5) showed higher peak pressures after treatment. PFM increased respectively by 242% and 172% (table 1).

The measurement of elasticity (Gradient in kPa/mm in test 1) of the underlying tissues surrounding the vagina, significantly improved by 88%. Maximum intravaginal pressure at pelvic muscle contraction (kPa) increased by 10.5% and muscle contraction force (N) increased by 8.3%. (Table 2)

Comfort level of the VTI examination procedure was classified as more comfortable as manual palpation; No report for the VTI exam as painful.

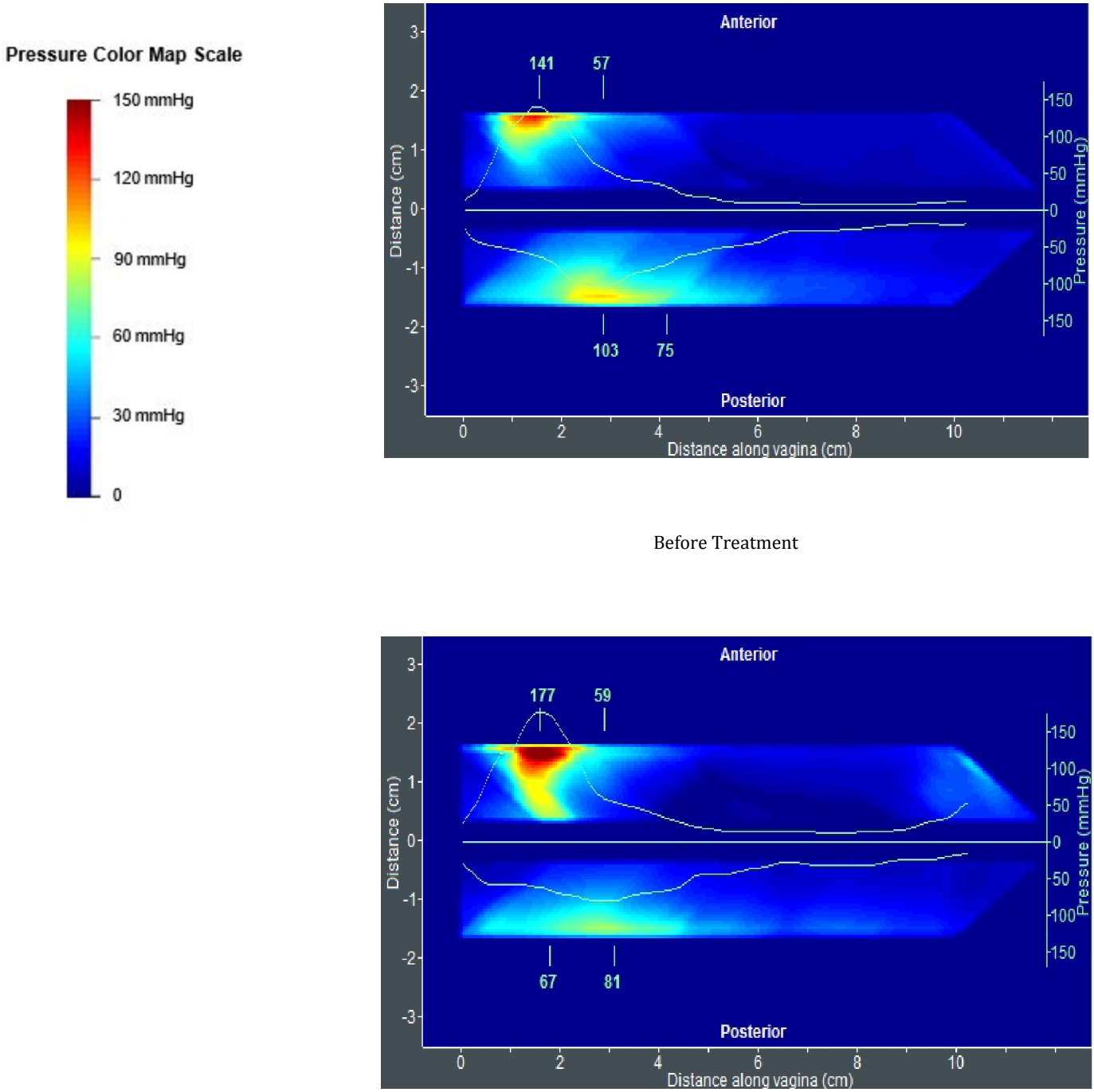


Figure 1: *Pressure patterns for vaginal tactile imaging probe elevation (test 1) and calculated pressure along the anterior and posterior compartments before and after radiofrequency treatment*

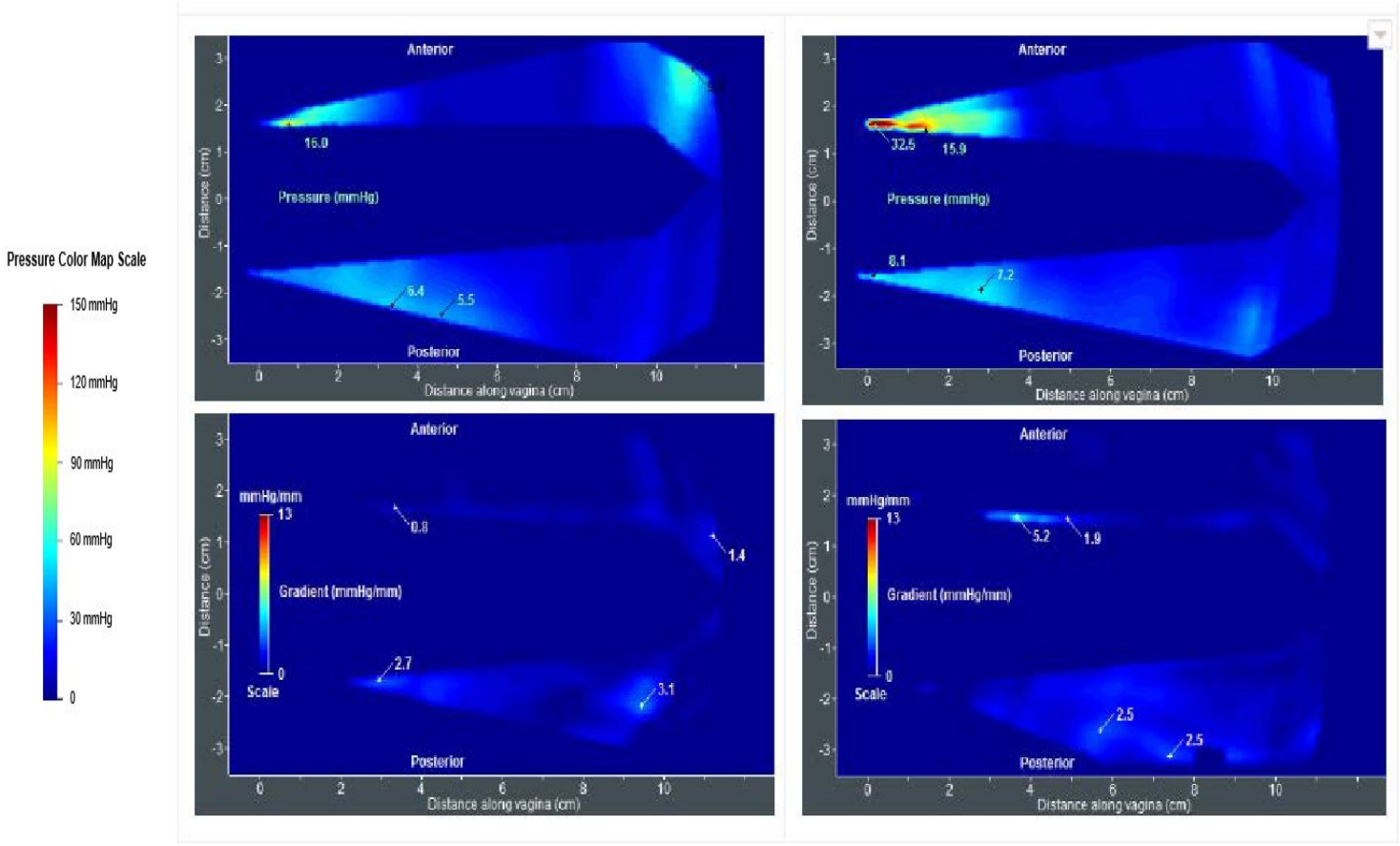
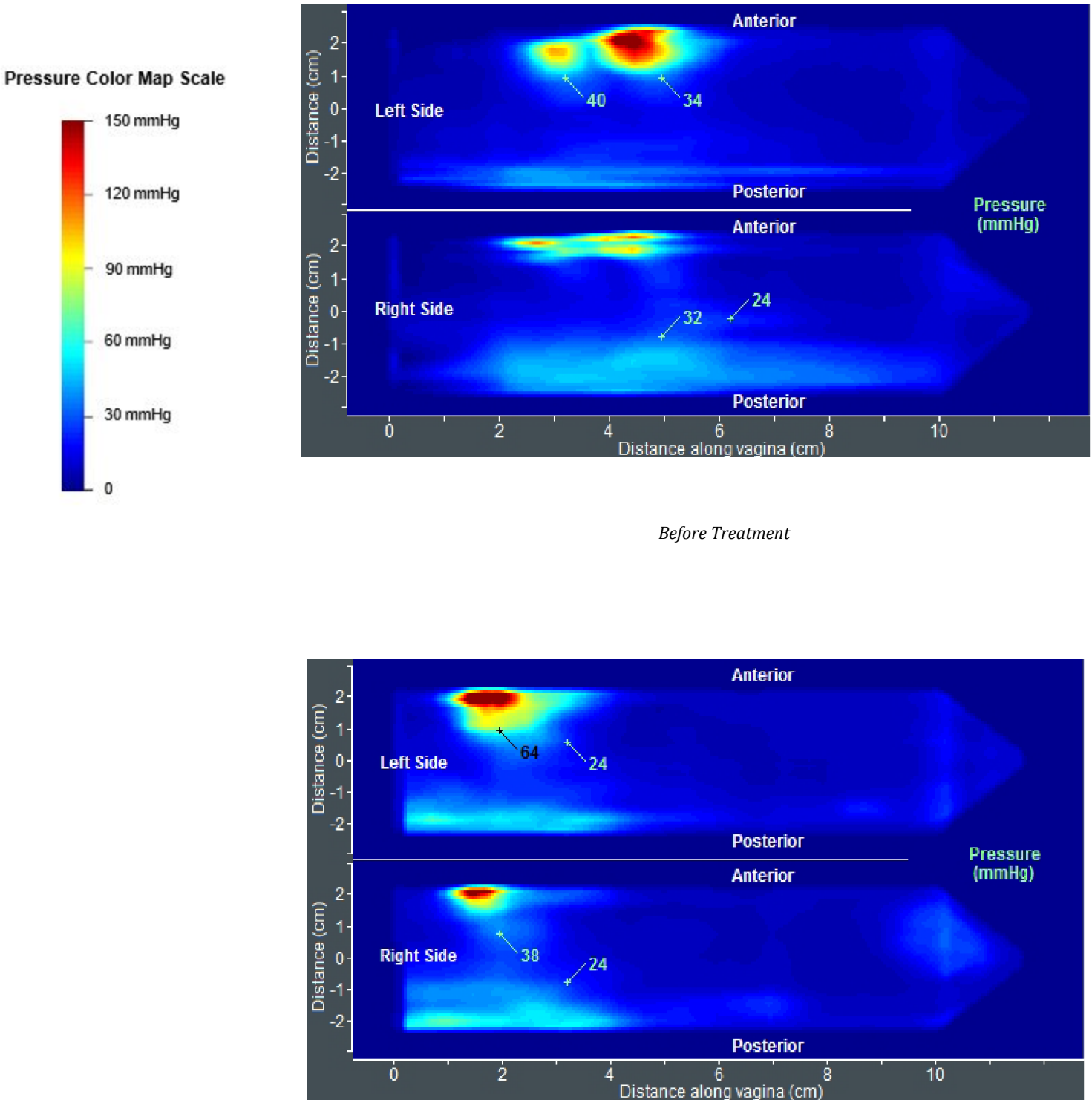


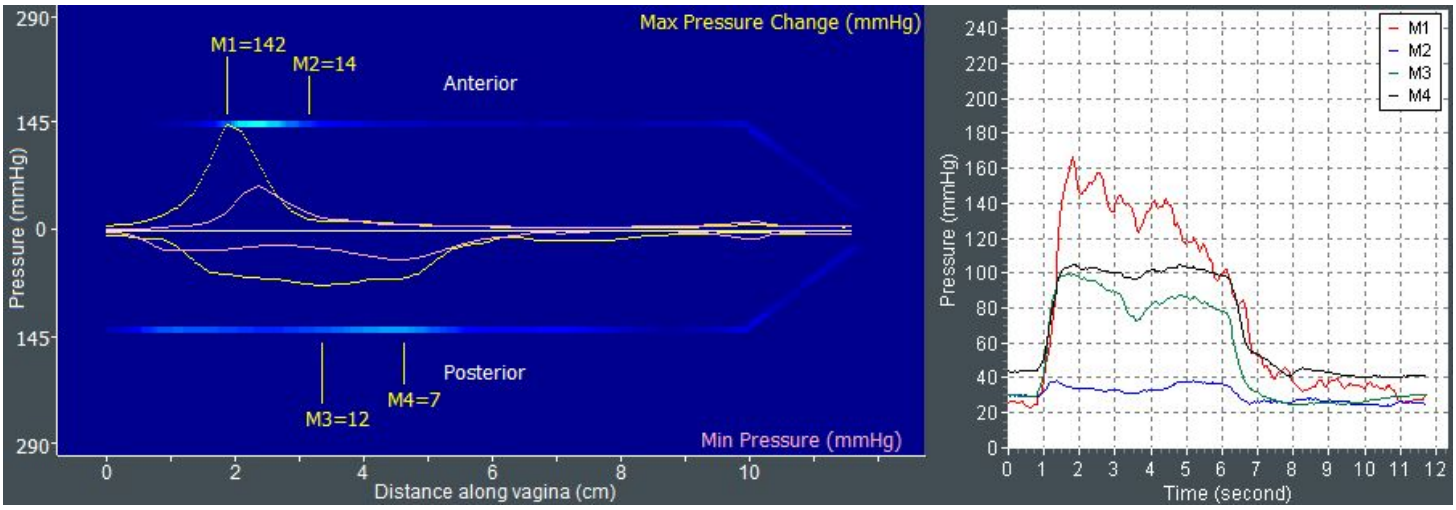
Figure 2: *Pressure patterns for vaginal tactile imaging probe elevation (test 2) and calculated pressure and pressure gradients along the anterior and posterior compartments before and after radiofrequency treatment*



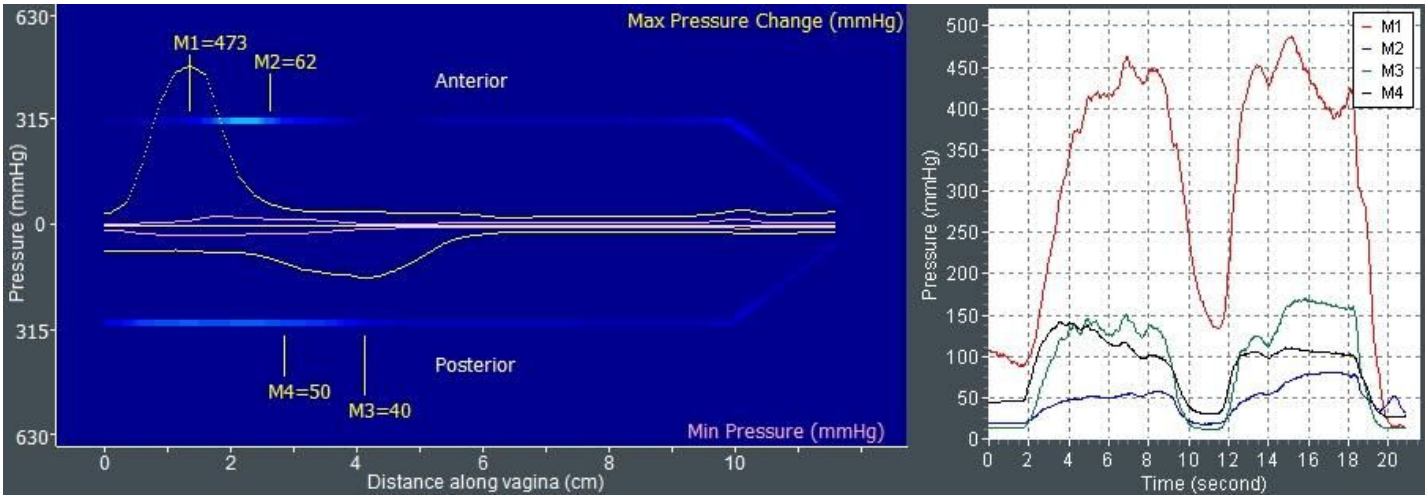
Before Treatment

After 4 sessions of treatment

Figure 3: *Pressure patterns for vaginal tactile imaging probe rotation (test 3) and calculated pressure along the vaginal walls before and after radiofrequency treatment*

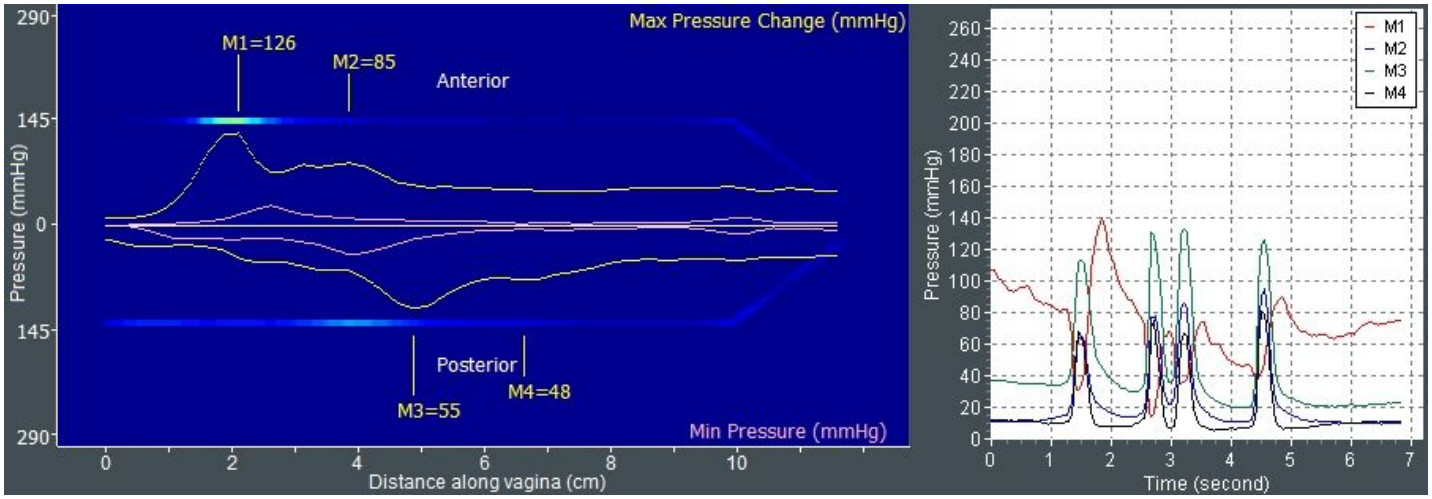


Before treatment

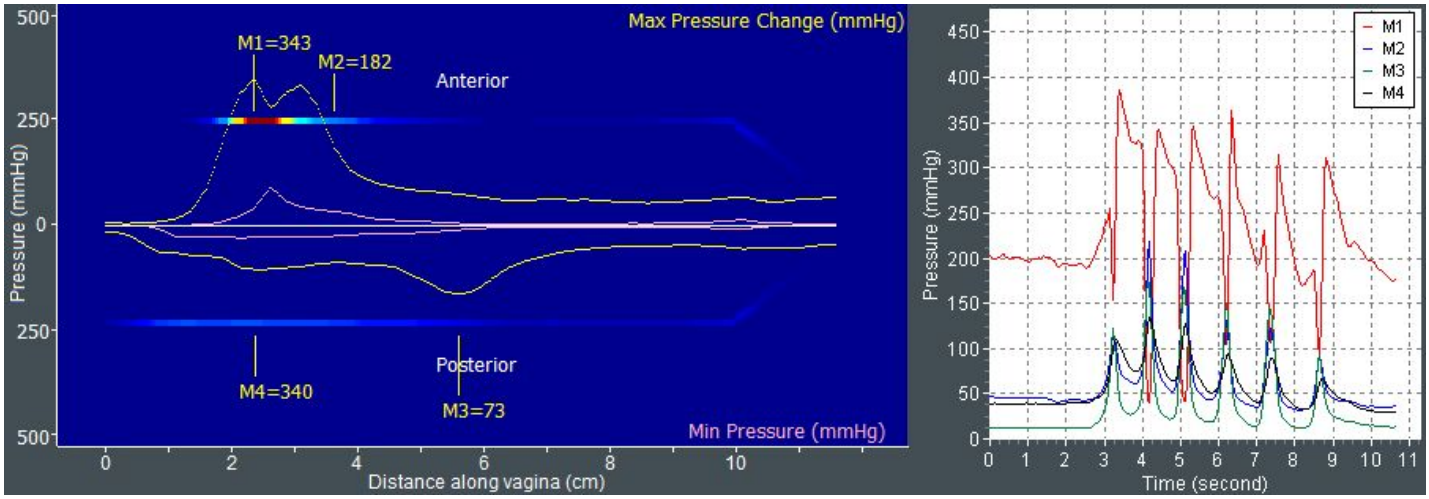


After 4 sessions of treatment

Figure 4: *Pelvic Floor muscles strength for voluntary contraction (test 5)*



Before treatment



After 4 sessions of treatment

Figure 5: *Pelvic Floor muscles strength for involuntary contraction (test 5)*

	Before treatment	After 4 sessions of treatment
Pressure at VTI Test 1	141	177
Pressure at VTI Test 2	16	32.5
Gradient at VTI Test 2	0.8	5.2
Pressure at VTI Test 3	40	64
PFM strength voluntary contraction	142	473
PFM strength involuntary contraction	126	343

Table 1: Improvement in Elasticity and Pelvic Floor Muscles Strength after treatment
Numbers in red shows statistical significance (p<0.01)

	F_{max} (N)		W (mJ)		Gradient (kPa/mm)	
	Before	After	Before	After	Before	After
Test 1	0.665	**0.928**	32.9	**39.9**	0.98	**1.84**

	P_{max} at rest (N)		F (N) at rest vert		F (N) at rest horiz	
	Before	After	Before	After	Before	After
Test 3	23.76	**26.24**	1.56	**1.69**	0.69	0.68

Table 2: *Average calculation of Vaginal Tissue Elasticity*
Numbers in red show statistical significance (p<0.01)

Discussion

Increasingly, thermal non invasive treatments are used for vaginal modification. However, objective assessment of vaginal conditions before and after the applied treatment does not exist yet. Objective anatomic measures, biomechanical, and functional characterization are essential to understand the difference between normal and abnormal conditions. The VTI approach resembles soft tissue palpation, which has been the most prevalent medical diagnostic technique for accessible human organs and the musculoskeletal system. but clinical examination cannot be translated into objective and comprehensive information for a medical report for other clinicians. And that's where tactile imaging acquisition with stored data has a great interest in translating the sense of touch into a digital image.

Tactile imaging displays tissue anatomy and elasticity distribution by keeping the stress-strain relation for deformed tissue. The 3-dimensional tactile image can be transformed into an elasticity image with the use of a linear transformation for a region of interest. Functional tactile imaging is a translation of muscle activity into a dynamic pressure pattern. VTI allowed in our report better comprehension of vaginal walls and pelvic floor muscle changes, when Vagina Laxity Questionnaire (or other questionnaires) is not enough accurate for detailed analysis. It is always useful to have reproductible, stored DATA for comparison and further studies.

Vaginal laxity is common symptom in urogynecology everyday practice. It is often associated with younger age, vaginal parity, symptoms of prolapse. Vaginal laxity occurs in all women in the weeks after vaginal childbirth and after menopause. The stretching of the dense connective tissue of the vaginal walls and introitus during delivery varies in degrees of laxity and can worsen with successive deliveries. Although it may be considered physiological vulvovaginal laxity may deeply affect self-esteem and quality of life, due to discomfort in everyday life, and to negative impact on sexual relationships. Then, loss of sensation is common in women with vaginal laxity. and vaginal laxity is described my practitioners as the most important change of body integrity experienced by women after vaginal childbirth.

Radiofrequency (RF) used for medical treatments is an advanced technology based on converting the energy of an electromagnetic wave into heat: radiofrequency waves interact with the tissues, generating controlled thermal change. Unlike lasers, which produce heat by selectively targeting a specific chromophore, non ablative radiofrequency generates heat as a result of the tissue's resistance to movement of the electrons subject to the RF field.

As also suggested for other thermal therapy technologies, DQRF vaginal rejuvenation in introital and vaginal laxity implies re-activation of fibroblast and connective tissue function and development of new networks of collagen and elastin fibers in the subepithelial layers of introitus and vagina.

One of the current gold standard treatments for after childbirth abnormal conditions are daily sessions of pelvic floor training (PFT). Significant improvement are mostly usually noticed after 2 months. Targeting continent antenatal women early in pregnancy and offering a structured PFT programme may prevent the onset of urinary incontinence in postpartum. However, the cost-effectiveness of this is unknown. Population approaches (recruiting antenatal women regardless of continence status) may have a smaller effect on urinary incontinence, although the reasons for this are unclear. It is uncertain whether a population-based approach for delivering postnatal PFT is effective in reducing urinary incontinence. The new DQRF technique can bring valuable clinical outcomes for patients because of less discomfort for women and less disruption of their daily life and routine. This may require further investigations to compare both methods.

DQRF seems to hold advantage regarding it's non ablative characteristics compared to CO2 lasers, and deeper effects in the dermis compared to Erbium Lasers. Comparative studies could be interesting to conduct to assess these differences.

Conclusion

Dynamic Quadripolar Radiofrequency treatment seems promising to improve tissue elasticity, pelvic floor support and PFM strength upon assessment with tactile imaging. VTI allows monitoring of biomechanical transformation of tissues before and after the radiofrequency treatment and may predict the effectiveness the therapy for individual patients.

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The Biological Effects of Quadripolar Radiofrequency Sequential Application: A Human Experimental Study G. Nicoletti, A. Cornaglia, A. Faga, S. Scevola,*Photomedicine and Laser Surgery Volume 32, Number 10, 2014*

NOVAVISION White Paper 04/2013

DYNAMIC QUADRIPOLAR RADIOFREQUENCY WITH BIOSTIMULATION

AESTHETIC MEDICINE HAS CHANGED A LOT IN THE LAST FEW YEARS.

This has happened because the approach, but above all the way of thinking of its interpreters, has changed and has affected the shift from a very limited as well as a bit unique view of things to a much broader one. There is no longer just the aesthetic aspect, and our attention to the patient moves from a curative medicine in the narrow sense of the word - that is certainly aesthetic - to a medicine that, in our opinion, will be the one of the future: the regenerative medicine.

This broader vision allows us to get much more satisfactory results in a much more natural way and, above all, in the respect of our patients.

The aesthetic physician can fight the signs of skin aging by means of many tools, whether they are injectable, pharmacological or instrumental materials, and each of them has specific usage instructions with specific targets, that are well known by the medical community and that have to be achieved.

Indeed, technology has widely contributed to this development and currently there are many companies that invested lots of time and money in order to develop high-technology tools to be used in the aesthetic medicine field.

This is the case of **NOVACLINICAL** which developed a series of equipment – such as radiofrequency - able to act on the skin quality; what we want to emphasize is that not all devices are the same. First of all, it is important to remember that there are purely aesthetic devices used in beauty centres by non-medical personnel and medical devices that have particular characteristics and that, therefore, require to be used, and above all managed, by people with a medical experience.

Any device produced by these companies is tested and cannot harm patients health; anyway, obviously, each of these devices will present side effects significantly different according to the device type and the patient's sensitivity.

Radiofrequency is a treatment that has been used for a long time in the fight against aging in dermatology and aesthetic medicine with the aim of creating a stimulus for tissue regeneration.

In particular, radiofrequency is a technology exploiting electromagnetic waves that are transferred from the device to the patient's tissue in a more or less deep way. The waves used have different features and vary according to their frequency, to the wavelength and to the power which can be adjusted by means of the device settings.

The target of the emitted waves is to stimulate specific parts of our cellular system through heat; these are fibroblasts that are simply responsible for the production of the elements that form the dermis and that provide the important substances necessary to maintain the cell viability. Hence fibroblasts, that have been dormant over the years, are stimulated by radiofrequency waves in order to produce collagen, glycoproteins, and hyaluronic acid. This triggers a system that is able to execute a skin tissue regeneration that results in a much brighter, rested and healthy appearance of the skin. Therefore, radiofrequency is able to give back tone and elasticity to the dermis, to redefine the features of the treated area, to reduce fine roughness and to improve the texture and thus to slow aging, at the same time.

RADIOFREQUENCY HAS DIFFERENT FORMS: NON- ABLATIVE AND ABLATIVE.

The ablative radiofrequency form is a bit more invasive because its usage causes a limited destruction of the top layer of the tissue on which it is applied, whereas the non-ablative form does not imply any relevant alteration

and it allows to create a stimulus by producing a controlled heat source which can act also at deep dermis level. This radiofrequency type is mainly used in aesthetic medicine with the aim of improving various anatomical areas of the face and body in order to tone and reshape them.

Depending on the device you use, the radiofrequency device can emit waves that can be monopolar, bipolar, three-polar or quadripolar. The monopolar form involves the usage of two electrodes: one placed on the handpiece and one on a plate applied to the patient, which becomes an integral part of the circuit. Obviously, the bipolar device includes two electrodes placed on the handpiece, therefore the area hit by waves will be very limited and superficial.

The latest jewel developed by **NOVACLINICAL** is a dynamic quadripolar radiofrequency with fractionated **4RFH** handpiece, i.e. a latest generation handpiece for dynamic fractionated quadripolar radiofrequency.

It is a non-invasive device mainly used for skin laxity and tissue rejuvenation. The treatment consists in moving a handpiece which originates electric arcs that are a few microns away from each other and that selectively vaporize some skin cells; this energy hits only some of them and leaves undamaged the surrounding ones.

The **4RFH** handpiece of **RADIO4** was developed so that the dynamism of the pins creates a matrix in the considered area of the dermis surface and stimulates the progressive reparative process of epidermis by favouring the production of healthy cells.

The 32 gold-plated pins with 12µNeedles allow to penetrate the stratum corneum through a pressure system calibrated for a more direct power, comfort and efficiency.

As stated above, it is a non–invasive procedure and the patient can resume his/her social activities immediately after the treatment that is not particularly painful. It is safe and it gives excellent results already after the first session with an overall rejuvenation and improvement of the skin quality, i.e. of the texture, of the superficial wrinkles and of the periorbital and perioral ones.

It therefore allows to fight Aging at face, neck and décolleté level, and to improve other imperfections such as stretch marks or scars.

There are no risks in using this device and, the RSS technology in the dynamic fractionated quadripolar radiofrequency 4RFH handpiece monitors the movement of the handpiece and constantly controls the position by ensuring a comfortable, safe and effective treatment.

What we really love and that, in our experience, has given and gives great results with regard to rejuvenation – i.e. the tissue bio-dermal regeneration - is the usage of a multidisciplinarity of techniques and biochemical principles to be introduced at tissue level.

Many scientific clinical studies have shown that cells attacked by free radicals and by the action of metalloproteinase send a message of help to survive and remain viable. This message of help is shown at receptor level through receptor units allowing the transductions of the signal that is the cornerstone of the intercellular communication.

In our opinion, what happens is that such cell condition is not homogenous since the action of aging is very slow and progressive.

The intuition was to create an external stimulus that enables a pathophysiological regeneration and that, through limited damages, allows to develop this message of help sent by the cells in a much stronger and homogeneous way.

Hence, for example, through a thermal stimulus, such as the one originated by radiofrequency, it is possible to stimulate the receptor system (CD44, RHAMM, icam-1) as well as different control systems at cellular level as the one provided by the heat shock proteins, a family of molecular chaperone proteins that are triggered when the cells subjected to thermal stress undergo a protein denaturation and their action allows the usual protein folding. This folding will be codified for new intracellular messages at nuclear level as well as at level of cytosol, endoplasmic reticulum, mitochondria and chloroplasts in addition to

the request to activate cellular units that allow a secondary cell revitalization.

The synergy of a condition such as the one originated by radiofrequency, that enables to create the limited thermal damage which "triggers" all cells of the area treated with an endogenous stimulation carried out through nutrients such as hyaluronic acid, polynucleotides, amino acids or better through the platelet growth factors, is extremely successful and, at biochemical and aesthetic level, the result does not just increase, but it multiplies. In our studies, we draw up various protocols related to the tissue bio-dermal regeneration, and radiofrequency - together with injections of platelet rich plasma at intradermal level - is certainly the one on which we place great reliance in terms of achievable results because it directly stimulates the collagen fibers thanks to the thermal effect and it simultaneously prepares the cell receptivity for growth factors released by platelet elements prepared through specific sterile kits which enable an intensive repair and cell regeneration activity.

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