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RESULTS ON SUBDERMAL FAT TISSUE
REDUCTION USING A NOVEL MICROWAVE
BASED BODY CONTOURING SYSTEM

October 2018



Results on Subdermal Fat Tissue Reduction Using a Novel Microwave Based Body Contouring System

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Abstract

Background: Body shaping market has shown a consistent growth in the last decade. In order to improve fat adiposity odds, a novel method for fat reduction has been proven to be specifically focused on subdermal fat.

Objective: This study wants to verify that a novel 2.45 GHz microwave device would provide safer and more consistent visible results on fat.

Materials and Methods: Nineteen healthy patients, 10 women and 9 men (24 to 55, avg. 39) with visible abdominal adiposity, received 3 Coolwaves™ treatment sessions (4 weeks apart) using the new Onda body shaping system (DEKA, Florence - Italy). This device utilizes a 2.45 GHz microwave applicator, internally cooled, to support patient comfort during the application. Appropriate protocol was set and the treatment was delivered in about 10 minutes on each treatment area. Before starting the treatment, all patients have filled out an informed consent form and photographic release form. Before each session the following data were collected: weight, size, circumference of waist as well as photographs (Quantificare, Nice - France). All the areas to be treated were marked with the patient standing still with a dermatologic white pencil. The marked areas are 15 cm x 15 cm. Exclusion regarded obese patients (defined as BMI>30) or with adiposity diffused over the entire body or conditions of irreversible severe skin laxity. For each patient blood examination was performed both before starting the treatment (T0) and at the end of the entire protocol (T3).

Results: All of the patients met the inclusion/exclusion criteria of the study and signed an informed consent form. All of the 19 healthy adults were divided in three Groups in regards of the abdominal pinch size. Group 1 consisted of 4 patients with a pinch greater than 4.5 cm, Group 2 consisted of 10 patients with a pinch included between 2.5 cm and 4.5 cm and last Group 3 consisted of 5 patients with a pinch lower than 2.5 cm. Results showed that all patients reported clinically appreciable abdominal circumference reduction at 3-month follow-up that was of 4.5 cm, 4.0 cm, 2.6 cm for each group respectively.

Conclusions: Novel microwave body contouring system has been found to be safe and effective for abdominal circumference reduction. Neither considerable pain nor noticeable discomfort during each treatment session were reported.

Keywords: Microwave, body contouring, fat adiposity, Coolwaves™

Background

Body shaping market has shown a consistent growth in the last decade due to its continuously demand of nonsurgical, noninvasive treatments on fat adiposities and cellulite odds as well as skin tightening ^[1]. In order to improve body contour, a variety of different methods are nowadays available. Despite the fact many of those equipment might provide a sort of effect on either fat or cellulite, the need of a multi treatment device ensuring

both efficacy and safety as well as low sessions number for all the body contouring needs, is raising consistently^[2-5]. In this light, technology is seeking for new solutions to provide medical users with multiple platforms able to ensure high level of comfort for patients.

Description

Microwave technology is very widely used in the modern society as well as in many branches of

medicine up to now including oncology, surgery and dermatology. After 5 years studies it is believed that the application of non-invasive high-energy 2.45 GHz microwaves [6] to body areas with adiposity may direct a focused action toward the subdermal fatty tissues in order to promote adipocyte cells heating with no interest of the upward dermal epidermal layers. This lead to a totally metabolic compatible macrophage adipolysis with reduction of subdermal fatty tissues and consequential reduction in circumference.

As cellulite is improved by solubilization of the collagen septa in the cellulite, heating the subcutaneous adipose tissue it causes dermal collagen fibers to contract in order to improve the skin's external architecture.

Microwave Technology Rationale

The rationale behind the use of microwaves for the reduction of the subcutaneous fat lays in their selectivity toward the fat when applied to cutaneous tissue[6]. In fact, microwaves are expression of an electromagnetic field and when applied to a biological tissue they provoke some oscillation and vibration effects phenomena in the cutaneous molecules they are applied on. Microwaves are considered safe because they attenuates significantly before they might reach internal organs and such characteristic allow treatments for fat reduction purposes[6]. A frequency of 2.45 GHz (Coolwaves™) has been proven to be the proper one to reach in depth subcutaneous tissue with no substantial power loss density[6]. Such a frequency has been discovered to make both epidermal and dermal tissue to be almost "transparent" to the passage of the energy so to work almost totally over the subdermal fat layer specifically. This preserves the superficial layers of the dermis from unwanted heating, avoiding unwanted burns.

Whenever an electromagnetic energy (either radiofrequency, laser or microwaves) is applied to a

biological tissue, some different results are obtained, all depending on the different frequencies applied (technically: dielectric behaviour). There are two parameters that identify the skin dielectric behaviour: Skin Conductivity (SC) and Skin Permeability (SP). SC identifies the property of a biological tissue to transfer (transmit) the energy received from an outer source (microwave handpiece) to surrounding tissues. This parameter increases as the applied frequency decreases and vice versa. In these terms skin offers more resistance to low frequency energies (less conductivity) while skin offers less resistance (more conductivity) to higher frequency energies. SP identifies the property of a biological tissue to absorb energy and thus to get heated by the energy received from an outer source (microwave handpiece). This parameter decreases as the applied frequency decreases and vice versa. In these terms skin absorbs more energy (i.g. generates more heat) to lower frequency energies than to higher. SP and SC are linked together by the formula following formula:

$$\epsilon_{r,eff}(\omega) = \epsilon_r'(\omega) - j\left(\epsilon_r''(\omega) + \frac{\sigma_{dc}}{\omega\epsilon_0}\right) = \epsilon_r'(\omega) - j\left(\frac{\sigma_{ac}(\omega) + \sigma_{dc}}{\omega\epsilon_0}\right)$$

Figure 1. Electrical Permittivity and Conductivity Formula[7]. Where: $\epsilon_{r,eff}$ = effective permittivity; ω = angular frequency; ϵ_r' and ϵ_r'' = real and complex parts of relative permittivity; ϵ_0 = absolute permittivity; σ_{dc} and σ_{ac} = static and alternate conductivity

If several frequency values are considered (from radiofrequency to microwaves) to have a visual idea of the energy engagement in the skin, it is noticed that most of the electromagnetic energy gets stuck in the epidermis and dermis rather than penetrates into the subdermal fat layer. These energies heats the dermo-epidermal layer to such an extent that there is a risk of tissue damage. Differently from the radiofrequency energy that mostly remains close to the surface, Coolwaves™ specifically reach the hypodermis where the fat cells are located in order for the treatment to be effective (figure 2):

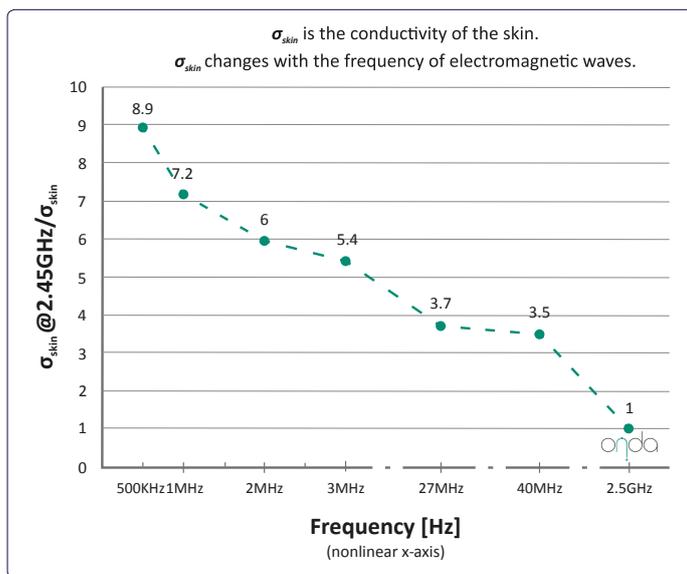


Figure 2. This graph indicates the differences in conductivity at different value of frequency delivered vs Onda. As the frequency increases conductivity increase either. In this way the majority of the radiofrequency energy gets stuck in the epidermis and dermis at lower frequencies, heating them up to such an extent that there is a risk of tissue damage. Moreover, as the radiofrequency energy remains close to the surface, it fails to reach the hypodermis where the fat cells are located, and whose membranes must be broken in order for the treatment to be effective.

Action on Adipocytes:

Once it reaches the subcutaneous layer, Coolwaves™ 2.45 GHz energy promotes the release of excess non-esterified free fatty acids through droplets or vesicles that gradually detach from the surface of the adipocyte towards the interstitium. The transport of such lipid droplets, clearly morphologically identifiable under the electron microscope^[8], towards the outside of the adipocyte, (i.e. towards the interstitial connective tissue), is called “BLEBBING”. This phenomenon either produces a metabolic stress in the fat cells and the increase of the catabolism induced by the Coolwaves™ in the mitochondria of the adipocytes and, additionally, it starts a situation of oxidative stress with production of Reactive Oxygen Species (ROS) and free radicals^[9]; in fact the metabolic cellular stress due to the blebbing generates the imbalance of the two chemical reactions which normally lead to the formation of ATP (oxidation prevails on the phosphorylation), thus determining

the production of ROS and free radicals. During blebbing initial phase, the adipocyte membrane remains intact (at this time the fat cells are empty and their size is reduced), but the continuous formation of molecular species such as ROS and free radicals and the involvement of adipocyte lipases^[10], (enzymes that act on constitutive triglycerides within the adipocytes) lead to the breakdown of cell membranes (plasma membrane, mitochondria and endoplasmic reticulum membranes).

In summary, the damaged adipocytes are those in which the “blebbing” phenomenon is stronger and more intense by the direct action of the Coolwaves™, thus provoking the interruption of the plasma membrane. In other adipocytes blebbing may require more time, but when it becomes more intense and extended, it leads to other membrane interruptions, with exposure of the lipid content towards the interstitium.

As a consequence of these structural and functional events, the cellular adipolysis process starts and the typical signs of this process are three: 1) dilated and swollen mitochondria, with few disordered and dilated ridges and with interruptions of the inner membrane, 2) rupture or interruptions of the plasma membrane, 3) dilatation of the endoplasmic reticulum. Furthermore, it must be considered that even if the adipose cell does not have an immediate rupture of the membrane, it can suffer irreparable damage in the following weeks; in fact the large quantity of small insoluble lipid drops released by the adipocytes constitutes an unfavorable environment such as to damage other adipocytes. During the processes that lead to cellular adipolysis, the recruitment of macrophages is stimulated with a receptor-type chemiotactic signals specifically called “FIND-ME” in which precisely the microparticles (or vesicles) released by the adipocytes recall cells of the monocyte-macrophage line^[11]. Most macrophages are located around damaged adipocytes, forming the characteristic structures called “CROWN LIKE

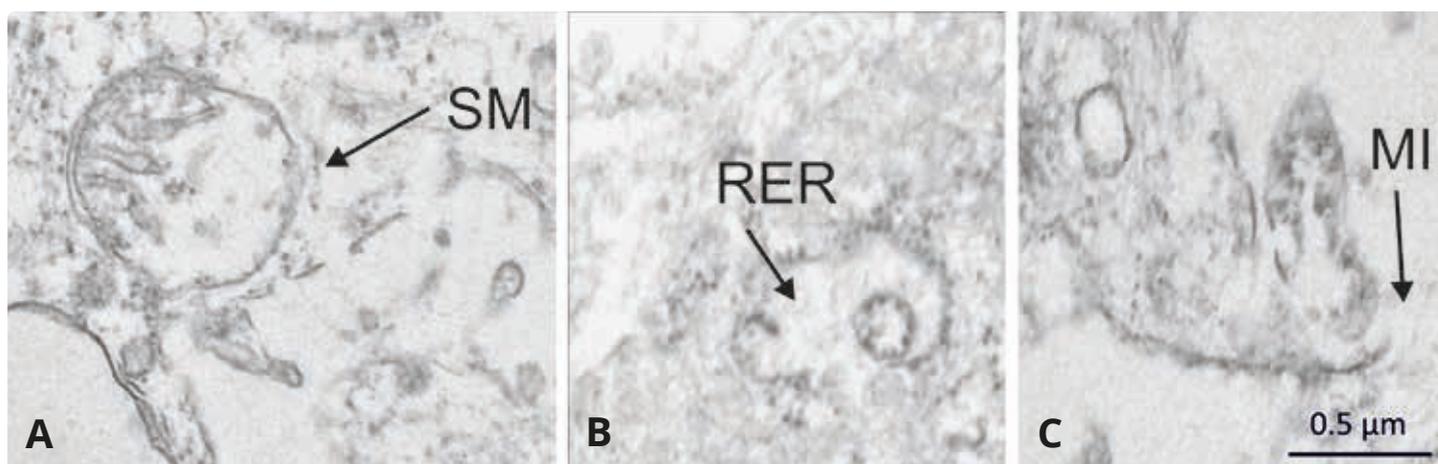


Figure 3. Signs of cellular stress 6 hours after one treatment with Onda - Coolwaves™. In the image A it is possible to observe a swollen mitochondria (SM). In the Image B the arrow shows the dilated Rough Endoplasmic Reticulum (RER). In the Image C it is visible a membrane interruption (MI)^[12].

STRUCTURES" (CLS)^[12] (precisely because of their arrangement to form a crown around damaged adipocytes). The macrophages are activated starting from single contacts and then form extensive multinucleated syncytia intervening in the removal not only of lipid droplets (free fatty acids, cholesterol, etc.) but also of cellular fragments of damaged adipocytes; this removal by macrophages represents a defense mechanism to restore the physiological homeostatic equilibrium.

Onda Body Contouring System

The Onda system generates a controlled microwave emission which preserves both upper dermal layer and deep muscle and organs. In fact the patent pending design of the applicators allows maximum safety during treatment and patient comfort. Thus Coolwaves™ are selectively driven to the subdermal fat layer through a deep and localised action on the hypoderma. The patent pending design allows limiting any possible electromagnetic field dispersion. The continuous cooling incorporated in the contact-handpieces, makes it possible to preserve the more superficial layers of the skin from unwanted overheating.

Onda body contouring system consists of a Shallow handpiece, specifically designed for skin tightening and superficial cellulite, and a Deep handpiece targeting fat and deep cellulite. Shallow handpiece, 5.6 cm large, induces a more concentrate and superficial heating up to 0.7 cm deep focalized heating. Together with the integrated cooling (till 5°C)^[13] this handpiece produces a controlled hyperthermia aimed to solubilizing the fibrous collagen and inducing the shrinkage of most superficial collagen fibers in order to get both tightening and remodeling effect on the superficial connective tissue. The deep handpiece, 6.6 cm large, induces a larger and deeper heating up to 1.2 cm depth, producing a controlled hyperthermia which causes a molecular oscillation on the adipocytes and solubilizing the deeper collagen fibers to induce the lipolysis of the fat cells and the remodeling of the collagen fibers by the fibroblasts activation. On both



Figure 4. Shallow and deep handpieces (patent pending).

the applicators a LED indicator system advises about the applicators coupling in order to support in the treatment execution.

Materials and Methods

Nineteen healthy patients, 10 women and 9 men (24 to 55, Avg 39) with visible abdominal adiposity, received 3 treatment sessions (4 weeks apart) with Coolwaves™ using the new Onda body shaping system (DEKA, Florence - Italy). This device utilizes a 2.45 GHz, internally cooled, microwave applicator to support patient comfort during the application. Appropriate protocol was set and the treatment was delivered in 1 pass for a duration of about 10 minutes each^[14]. The patients selection was made in regards of three groups discriminated one each other from the abdominal pinch size. Group 1 consisted of 4 patients with a pinch greater than 4.5 cm, Group 2 consisted of 10 patients with a pinch included between 2.5 cm and 4.5 cm and lastly Group 3 consisted of 5 patients with a pinch lower than 2.5 cm. All patients belonging to Group 1, 2 and 3 were suitably informed about the treatment procedure, the results that they might expect according to their single individual characteristic, the probable number of sessions necessary for achieving the desired results, the steps to follow before and after each treatment session and any possible side effects. Moreover, circumference measurement and photographic documentation were reported for each patient at time of the first visit (T0), after the first session 4 weeks apart from T0 (T1), after the second session 4 weeks apart from T1 (T2) and at the last treatment 4 weeks apart from T2 (T3) (Quantificare, Nice – France). A preliminary examination and anamnesis of all patients was made in order to carry on either a patients selection for the study and to determine the most appropriate protocol for it. To this aim, information on patient's anamnesis (with particular interest to hormonal imbalances, metabolic alterations, life style, use and abuse of alcohol, smoking etc.) and inspection (gynoid or

android morphotype, overweight or obesity, signs of venous insufficiency in the lower limbs, body asymmetries, motivations and expectations moving) were obtained. Some photographic documentation of each patient, before every treatment session, was obtained with the authorization of the patient. Blood test documentation of each patient, before the first treatment session (T0) and 24 hrs after the end of the protocol (T3) was obtained with the authorization of the patient. Inclusion criteria, instead embraces imperfections prevailing over other areas. Exclusion criteria, when treating localized adiposity, regarded: obese patient (defined as BMI >30); patients showing a largely diffused adiposity over the entire body; patients with limited thickness of the subdermal fat layer (< 1cm that means approximately pinch < 2cm). Moreover, for any kind of treatment were excluded: patients undergoing anticoagulant and antiaggregant treatments (possibility of persistent erythema) or getting systemic/oral steroids treatments (e.g., prednisone, dexamethasone); subjects with any body piercing/open wounds over the treatment area; under-age patients; breast feeding/pregnancy patients; patients with unrealistic expectations.

Before each treatment session, patients were requested to clean their abdomen and eliminate impurities (if any) that could interact with the Coolwaves™ or obstruct handpiece sources. Remove any make up, lotions, deodorants or ointments with a gentle soap, then rinse with plenty of water. For who needed, shave any dense hair on the area to be treated to improve the coupling between handpiece and skin. At this stage for each group, a general analysis of the physical state of the patient (standing position) was carried out to better identify either the areas to be treated and assess, for each of them, both the type and condition of the imperfection/pathology.

From a protocol stand point, Group 1 patients have been treated with 3 sessions 4 weeks spaced apart from each other, utilizing 140 W, 100,000

J energy dose and the Deep applicator. With the same criteria, Group 2 patients have been treated with 3 sessions 4 weeks spaced apart from each other, utilizing 130 W, 80,000 J energy dose and the Deep applicator. Finally Group 3 patients have been undergoing 3 sessions 4 weeks spaced apart from each other, utilizing 120 W, up to 70,000 J energy dose and the Shallow applicator. In all cases (G1, 2, and 3) cooling was kept at 5°C and the treatment

time per identified area was from about 7 to 10 mins with linear movement. Treatment time was approximately 20-40 mins per patient (avg).

Both qualitative and quantitative evaluations of the tissue have been performed (skinfold thicker than 2 cm and thinner than 5.5 cm) and no presence of nodules, fibrotic tissue or any anomaly was recorded during preliminary palpation screening so to allow the treatment with Onda to proceed ahead.

| ID Patient | Group 1 (P > 4.5 cm) | Group 2 (2.5 cm < P < 4.5 cm) | Group 3 (P < 2.5 cm) | Sex | Circumference Reduction @ T1 [cm] | Circumference Reduction @ T2 [cm] | Circumference Reduction @ T3 [cm] |
|------------|-------------------------|----------------------------------|-------------------------|-----|-----------------------------------|-----------------------------------|-----------------------------------|
| 1 | | | 3 | F | 0.50 | 1.00 | 2.00 |
| 2 | | 2 | | F | 2.00 | 3.00 | 3.50 |
| 3 | | 2 | | F | 1.50 | 2.50 | 2.50 |
| 4 | 1 | | | F | 2.00 | 3.50 | 5.00 |
| 5 | | 2 | | F | 1.00 | 1.50 | 3.00 |
| 6 | 1 | | | F | 1.50 | 3.00 | 4.00 |
| 7 | | 2 | | F | 1.50 | 2.00 | 3.50 |
| 8 | 1 | | | F | 0.50 | 1.50 | 5.00 |
| 9 | | 2 | | F | 1.00 | 2.50 | 4.00 |
| 10 | | 2 | | F | 2.00 | 3.00 | 3.50 |
| 11 | | 2 | | M | 3.50 | 6.00 | 7.00 |
| 12 | | | 3 | M | 0.50 | 2.50 | 3.00 |
| 13 | 1 | | | M | 1.00 | 2.50 | 4.00 |
| 14 | | | 3 | M | 1.00 | 2.00 | 3.00 |
| 15 | | 2 | | M | 2.00 | 3.00 | 4.00 |
| 16 | | | 3 | M | 0.50 | 1.50 | 2.50 |
| 17 | | 2 | | M | 1.00 | 2.50 | 4.50 |
| 18 | | | 3 | M | 0.50 | 1.50 | 2.50 |
| 19 | | 2 | | M | 2.00 | 3.50 | 4.50 |
| TOTALS | 4 | 10 | 5 | - | - | - | - |

Table 1. Study patient's parameters allocation. Highlighted in yellow data of the three selected patients for the photographic documentation shown in figure 5, figure 6 and figure 7.

Then, some 15 cm x 15 cm areas are so identified over the abdomen of the patient in order to better assess the site of treatment once the patient will lay down on the bed.

Once laying on the bed a thin film of pure vaseline oil (pharmaceutical grade) was sprayed over the entire treatment area for proper contact of the handpiece with the skin, better coupling and greater fluidity of the movements.

After the treatment a lymphatic massage over the treated area was carried out. General indications for the patients are to follow an appropriate healthy diet and do a moderate physical activity.

Results

Clinically appreciable results in abdominal circumference, at the 3rd treatment was statistically detected and reported with clinical significance. Mean average loss of 3.7 cm was recorded for all groups at T3. At T1 follow up, mean loss was 1.2 cm for all patients. Further reduction of abdominal circumference was then recorded at second treatment (T2) as statistically significance as with 2.4 cm mean loss.

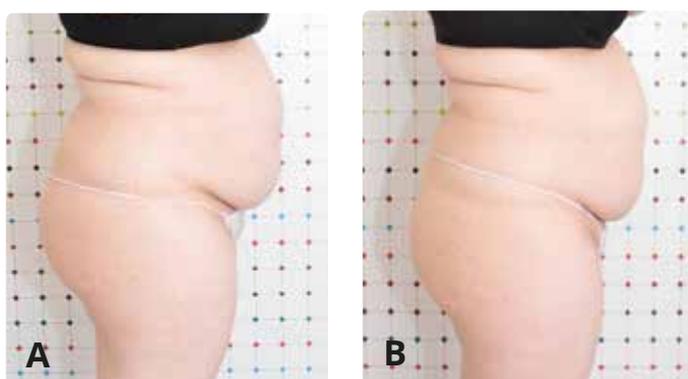


Figure 5. Before (A) and after (B) pictures of patient from Group 1 (age: 40; sex: F; weight: 85 Kg; treated area: abdomen; pre-treatment circumference size: 111 cm; post-treatment circumference size: 106 cm). She got an abdominal circumference reduction of 5.0 cm after 3 sessions against a Group AVG reduction of 4.5 cm. The protocol used in this case was: Power= 140 W; Energy= from 90-140000 J; Handpiece selected= Deep.

Table 1 reports circumference reduction (cm) after first (T1), second (T2) and third session (T3) for each Group:

Mean reduction of abdominal circumference after T3 was 4.5 cm (Group 1), 4 cm (Group 2) and 2,6 cm (Group 3). Mean reduction for sex was 1.3 cm (T1), 2.3 cm (T2) and 3.6 cm (T3) on females and 1.3 cm (T1), 2.8 cm (T2) and 2.4 cm (T3) on males. No particular red area were detected either during or after the treatment.

All 19 patients were checked through blood tests to ensure either no muscle damage was detected and the treatment was indeed selective for the subdermal fat layer. As it was possible to see, none of the tested patients showed significant changes in blood values (triglycerides and cholesterol) neither after a week from the first treatment (figure 8) nor after the last treatment T3 (figure 9). No significant increase in transaminases was recorded so hepatic function was preserved (figure 10). No muscular alteration was detected (figure 11), in addition renal functionality detection indexes remain stable throughout the whole treatment protocol (figure 12-1, 12-2 and 12-3)

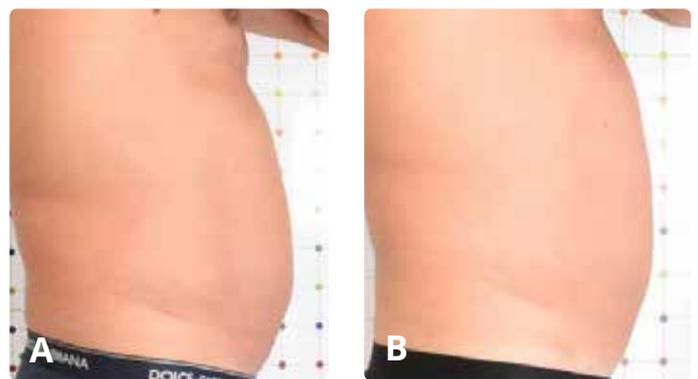


Figure 6. Before (A) and after (B) pictures of patient from Group 2 (age: 45; sex: M; weight: 80 Kg; treated area: abdomen; pre-treatment circumference size: 98 cm; post-treatment circumference size: 94.5 cm). He got an abdominal circumference reduction of 3.5 cm after 3 sessions against a Group AVG reduction of 4.0 cm. The protocol used in this case was: Power= 130W; Energy= from 80-120000J; Handpiece selected= Deep.



Figure 7. Before (A) and after (B) pictures of patient from Group 3 (age: 34; sex: F; weight: 40 Kg; treated area: abdomen; pre-treatment circumference size: 70 cm; post-treatment circumference size: 67 cm). She got an abdominal circumference reduction of 3 cm after 3 sessions against a Group AVG reduction of 2.6 cm. The protocol used in this case was: Power= 120 W; Energy= from 40-70000 J; Handpiece selected= Deep.

Conclusions

This initial clinical evaluation demonstrates, with statistical significance, sustainable reduction in circumference and improvement in appearance of treated abdomen once treated with Coolwaves™ by Onda microwave body contouring system, following the criteria literature reports for this type of application. Onda has been found to be a safe and effective tool for the reduction of adipose tissue volume on any treated skin type and with consideration with existing technologies^[15-23], no considerable pain nor noticeable discomfort were reported during each treatment session.

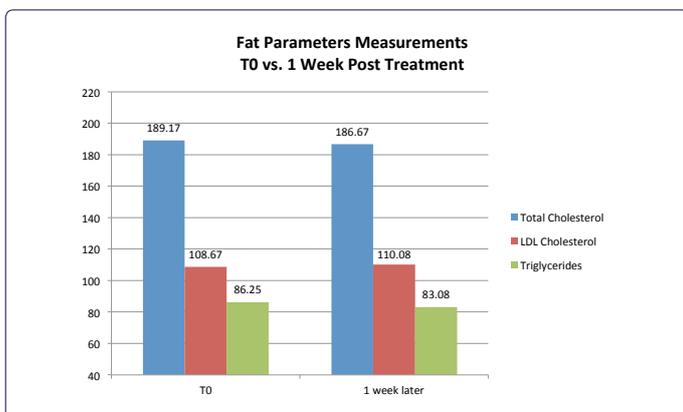


Figure 8. Blood test results before and after a week from the first treatment: no significant changes detected on LDL and total cholesterol as well as triglycerides.

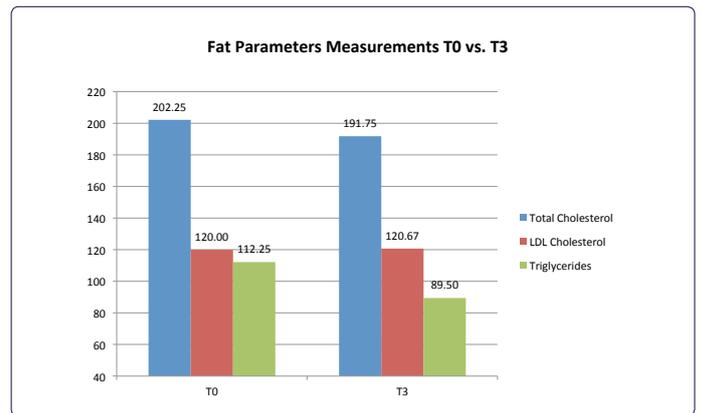


Figure 9. Total cholesterol, LDL cholesterol and triglycerides controlled at T0 and 24Hrs after T3 (before treatment -T0 and after the last treatment- T3) did not show statistically significant changes on average.



Figure 10. Transaminases examination 24Hrs after T3 Similar considerations as previously made for other parameters can be made for liver function indexes: no statistically significant variation was detected if we compare the values at T0 and 24Hrs after T3 treatment.

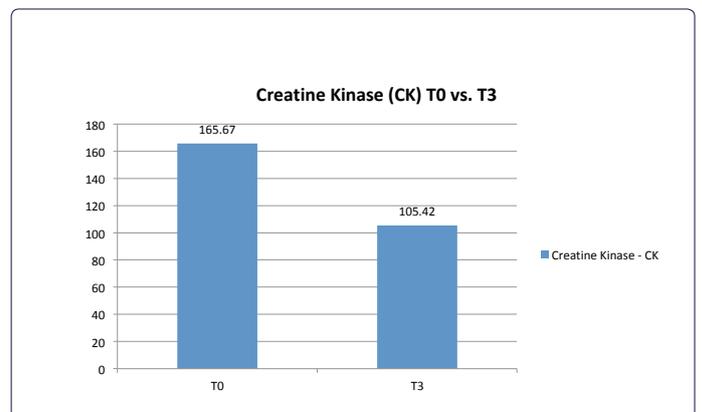


Figure 11. Creatine kinase (CK) did show an important decrease as a sign of safety of the method towards the selectivity of treated adipose tissue.

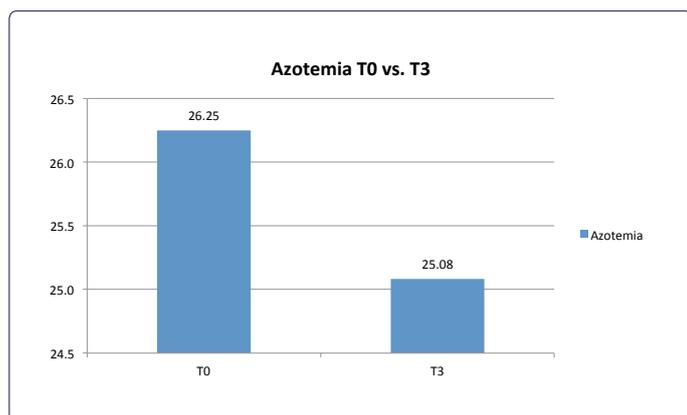


Figure 12 - 1. Renal functionality detection indexes: the diminishing of the Azotemia value indicates no implication of abnormal amount of urea in the blood.

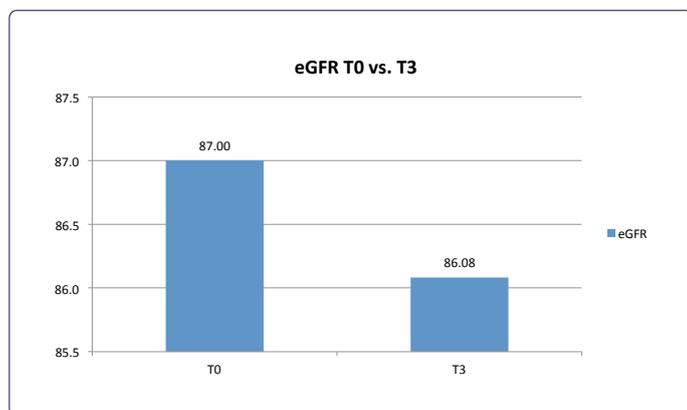


Figure 12 - 2. Renal functionality detection indexes: eGFR doesn't change significantly as to prove no increase in renal activity as a consequence of the treatment.

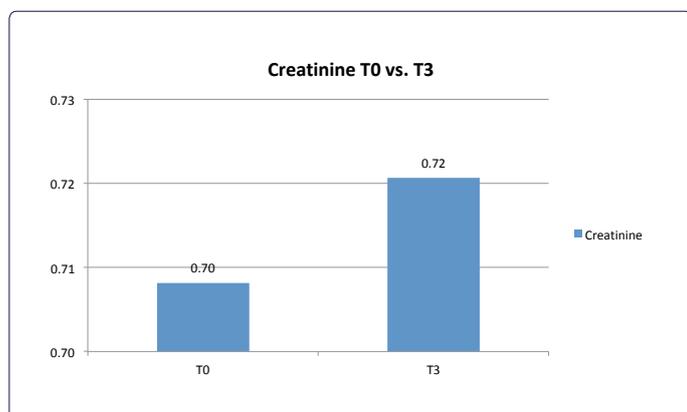


Figure 12 - 3. Renal functionality detection indexes: this slight and not particularly significant difference confirms what above detailed of all other parameters.

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