*Istituto Dermopatico dell'Immacolata, IRCCS - IDI IRCCS*
**Dpt. Dermocosmetology and Skin Pathophysiology - Lab. Tissue Engineering and Skin Pathophysiology**

**FINAL REPORT**

**CLINICAL STUDY:**

# PHASE III, OPEN PHASE CLINICAL TRIAL FOR CLINICAL-INSTRUMENTAL ASSESSMENT OF THE EFFECTIVENESS ON GYNOID LIPODISTROPHY (CELLULITE) OF DEEP OSCILLATION®

**Short Title: DOSCI_STUDY_CLINICAL_CELLULITE**

**Applicant to the Ethical Committee IDI - SAN CARLO:**
**Provincia Italiana della Congregazione dei Figli dell'Immacolata Concezione – Istituto Dermopatico dell'Immacolata, IDI-IRCCS**
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## INTRODUCTION

Gynoid lipodystrophy *(cellulite),* or edematofibrosclerotic panniculitis (EFP), is a common condition in 85% of post-adolescent women (regardless of age and weight), for which treatment is frequently required.

The origin of cellulite is a combination of genetic, constitutional, hormonal and vascular disorders, often accelerated by a sedentary lifestyle, stress, liver disease, poor nutrition, intestinal disorders, or by concomitant pathologies characterized by a marked fluid retention.

According to most researchers in the field, *cellulite* it is a clear-cut disease, characterized by degeneration of the subcutaneous adipose tissue, increased fat cells, alteration of the venous capillary walls, and insufficient microcirculation in the leg, where intracellular accumulation in the tissues (edema) stimulates a tissue reaction that can trap the subcutaneous fat in the typical and unpleasant "orange peel". In fact, poor oxygenation leads progressively to the alteration of the structure and elasticity of connective tissue, with a proliferation of unregulated intracellular fibrils. Usually, it appears initially on the external side of the thigh and knee, then spreading on the inside of the thighs, hips, abdomen, buttocks and ankles.

Cellulite undergoes an evolution in time, passing through three stages. The first step is edematous, characterized by diffuse swelling, due to the accumulation of stagnant liquids, which can be felt to the touch, the skin being still soft. In the second fibrotic stage, the skin is hard to the touch and has disseminated nodules ("orange peel"). In the third and final sclerotic stage, i.e. tissue hardens, and assumes the typical "mattress" appearance, with very noticeable dips and bumps, resulting in pain in the legs, accentuated at pinching the affected part.

Addressing the complex issue of treatment of EFP, commonly denominated "cellulite", represents a so far unmet challenge for researchers and clinicians. Effective approaches must be directed primarily and generally at attenuating or removing the aggravating factors (obesity, unhealthy diet and general lifestyle, and the lack of physical exercise), and more specifically at inducing lipolysis or removing fat, disrupting altered fibrous septae, improving microcirculation, diminishing local inflammation. Current techniques include massage, pulsative suction, radiofrequencies, infrared heat, laser light, pharmacological agents applied topically or by intradermal injections. Serious concern has been raised about the safety and

efficacy of unreasonably expensive methods for the cellulite treatment, also based on the fact that, with the exception of surgical techniques, there are no entirely successful therapies presently available.

The purpose of this study was to evaluate the effectiveness of the bioresonance DEEP OSCILLATION®, performed by the Medical Device DEEP OSCILLATION® (PHYSIOMED ELEKTROMEDIZIN AG, Germany), in the treatment of cellulite. The effect of therapy with DEEP OSCILLATION®, was expected to be exerted on the connective tissue, by means of the induction of electrostatic fields. Through the pressure of therapist's hands or manual applicator, the device generates in fact an electrostatic field that causes the contraction of the affected tissues, which thereafter stretch again, in repeated cycles. This repeated action in rapid succession gives rise to a rhythmic deformation of the tissue. The electrostatic pulses lead to increased static friction, while tissue elasticity causes an adverse reaction to this process during the rest intervals between pulses. This way, the treated tissue is "pumped" in all its depth. DEEP OSCILLATION® is reported to act mainly on the intercellular circulation, in the interstitial connective tissue. Main treatment outcome is reported to be the restoration of interstitial flow traffic, especially the constant flow from the affected tissue and lymphatic blood vessels. For this reason, pain relief has traditionally been the main application for DEEP OSCILLATION® technique, and the main claimed benefit for edemato fibrosclerotic panniculitis.

The protocol adopted in this pilot study was expected to allow the patient suffering with cellulite to regain motor skills, and fluidity of the different tissue layers and fibers, as well as to enable better nourishment delivery to the affected tissues. Interstitial fluid would be hence redirected to the tissue, guaranteeing restored critical functions such as transport means, supply and storage of food, and debris removal.

## MATERIALS AND METHODS

Instrument

The physiotherapeutic method is based on the use of intermittent electrostatic fields of low intensity (U = 100-400V; I = 150μA) and extremely low frequency (F = 5-200Hz) which create deep oscillation in the underlying tissues (epidermis, derma, subcutaneous layer, and myofibrils). The instrumental tests were all performed at IDI Hospital in out-patient regime. The physiotherapic device was supplied by PHYSIOMED ELEKTROMEDIZIN AG, and its clinical use was officially authorized by IDI IRCCS Sanitary Direction, after technical/safety documents accreditation.

Patients and treatment protocol

No. 30 women aged between 18 and 50 years, affected with cellulite of I-III grade, were enrolled, after obtaining informed consent, in compliance to the following inclusion/exclusion criteria:

A. Inclusion Criteria

1. Female subjects aged between 18 and 50 years, in good general health conditions.
2. Subjects suffering from cellulite at stage I, stage II, or stage III.
3. Subjects having stopped any topical or systemic drug therapy for at least 15 days before inclusion in the study.
4. Subjects having agreed not to apply any cosmetic product or drug to the affected area.
5. Subjects having agreed not to undergo any specific other treatment to the affected area.
6. Subjects able and willing to follow the recommended protocol guidelines, and to undergo all surveys required in the course of the study.
7. Subjects informed verbally and in writing about the purpose and methods of treatment, and able to understand and sign the written informed consent elaborated by the investigators.

B. Exclusion Criteria

1. Women who are pregnant, or breastfeeding.
2. Subjects undergoing concomitant therapy, topical or systemic
3. Subjects suffering from systemic diseases, that would interfere with the evaluation of the treatment or increase risk of adverse events to the subject.
4. Subjects simultaneously engaged in another clinical trial.

All patients were subjected to a treatment protocol with DEEP OSCILLATION®, consisting of a two sessions-per-week schedule, for three months (the total duration of the treatment was 500-540 minutes).

At enrollment (T0), patients underwent clinical and anamnestic examination by a dermatology specialist, who carefully collected all relevant information regarding possible risk factors (sedentary lifestyle, intake of contraceptives, cardiovascular disease, etc.). Patient staging for cellulite was performed clinically, with a) measurement of circumferences - upper third of thigh, lower third of thigh, and upper third of leg b) clinical staging through the parameters of elasticity, mellowness, pain at palpation, skin surface appearance (visual numeric scale), presence of white-yellow striae and/or micronodules. Instrumental measurements adopted were impedance analysis, thermography, capillaroscopy, cutometry for the measurement of skin elasticity, skin ultrasound determination of microcirculation and fibrous tissue presence, doppler of lower extremities. The clinical / instrumental assessment was repeated at the end of treatment (T5, week 5). The clinical features were assessed by three independent dermatologists, using high resolution digital photographs.

The data obtained were statistically analyzed with the Wilcoxon nonparametric test for paired data values for the clinical evaluation, and Student's t-test for paired data, for instrumental values. The differences were considered statistically significant below a probability value $p < 0.05$.

## RESULTS AND CLINICAL CONCLUSION

Enrollment step resulted in a cohort of 30 female patients (age = 39.0±9,6y; weight = 58,0±6,1 kg; BMI =1,63±0,07), 14 patients suffering from edematous type (stage I), 12 were with fibrous-type cells (stage II), and 4 with severe sclerotic cellulite (stage III). Patients were recruited after their informed consent and approval of the local Ethical Committee.

Results of the pilot study confirmed:

a) the absolute safety of the treatment (there were no any immediate or remote adverse effects, or subjective complaints from the participants);
b) high efficacy of the treatment protocol, in terms of circumference reduction in 93% (n=28) of the patients, with circumferences reduction from 59,0 to 57,1 cm, upper thigh ($p<0.0002$); from 51.4 to 49.8 cm, lower thigh ($p<0.0001$); from 40.7 to 38.5 cm, upper leg ($p<0.003$) (FIG.1).

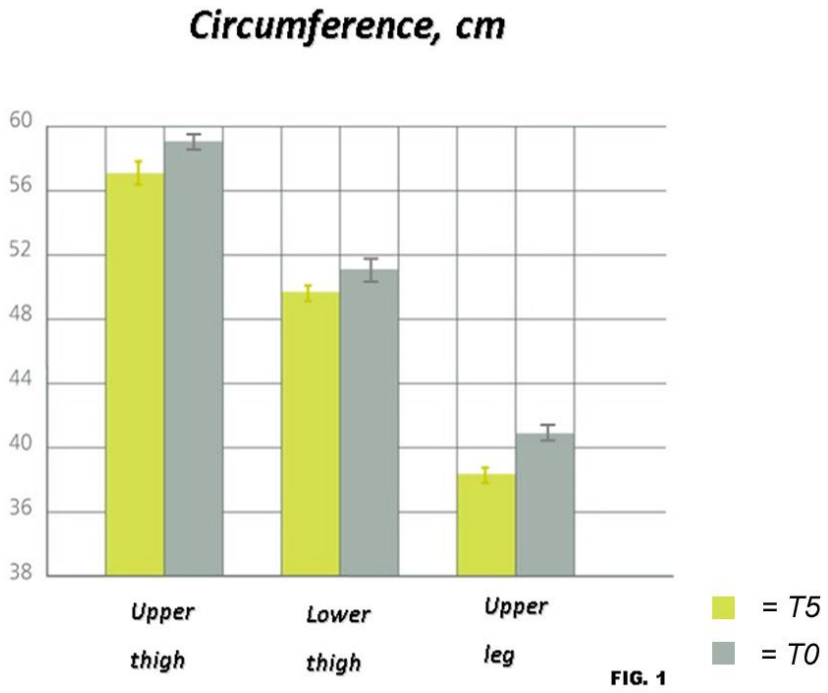
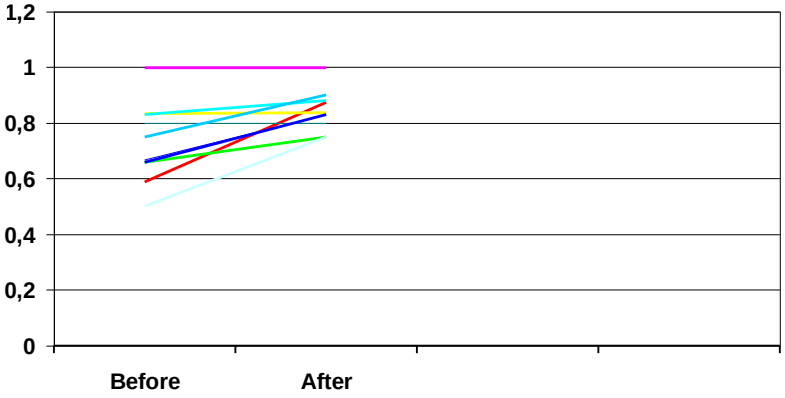


FIG. 1

c) high efficacy of the treatment protocol, in terms of skin elasticity characteristics, improved in 48% (n=14) of the patients, according to the two parameters of relaxation time and mechanical resistence (FIG. 2);

## *Skin Elasticity*




***R6***
***(Relaxation time)***

***R2***
***(Mechanical Resistance)***

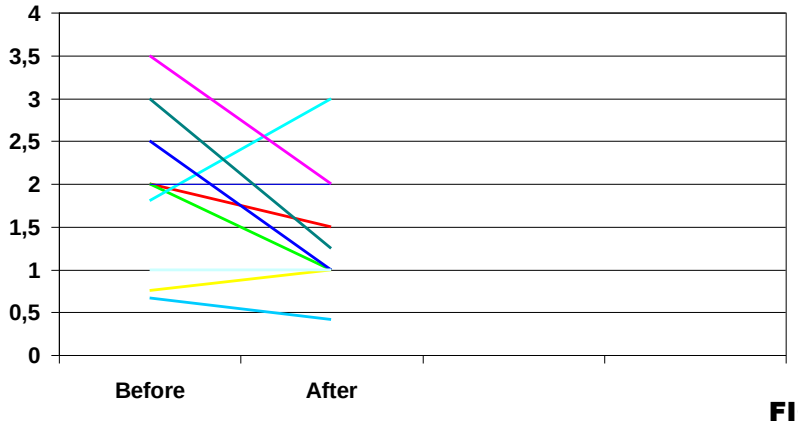



**FIG.**

d) edema, lymphostasis, and fibrous heterogeneity of subcutaneous layer were improved remarkably in 80% (n=24) of the patients.

The physiotherapy device DEEP OSCILLATION® (PHYSIOMED ELEKTROMEDIZIN AG, Germany), has been on the sanitary market since the 1980s, its safety and efficacy has been previously documented for different applications in traumatology, pain medicine, lymphatic drainage, physiotherapy.

The general conclusions of the expert clinicians responsible for the cellulite pilot study were that the DEEP OSCILLATION® method was efficient in more than 80% of the cases with

moderate (grade I-II) cellulite, inducing significant changes in the main bio-parameters of cellulite: (1) improved blood and lymph flow in the deep skin and subcutaneous layers; (2) diminished inflammation and edema; (3) disrupted or prevented formation of rough fibrous septae.

These outcomes provided effective treatment of cellulite (Grade I and II) in 80% of female subjects studied in this pilot study, where the average circumference of thigh and buttocks decreased, skin elasticity increased, and fibrosis was reduced.

## REFERENCES

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