

Evaluation Study

# Fat tissue reduction by depurative diet and compressive microvibration with spheres of variable density

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#### **ABSTRACT**

Society is characterised by a substantial increase in overweight and obesity, with progressive diseases such as diabetes, lipolymphedema and lipoedema. Many experiences have demonstrated the sensitivity of the subcutaneous adipose tissue utilising non-invasive mechanical treatments. This study aims to study the sensitivity of the subcutaneous adipose layer of the abdomen using compressive microvibration treatments with spheres of variable density. Thirty patients were followed between the period from 10th January to the 30th May 2022. Fifteen patients were treated with twelve compressive microvibration sessions with variable density spheres, and the other fifteen with the same treatment associated with a nutritional purification program. All patients were studied with clinical/instrumental examinations and evaluations in compliance with ethical and deontological standards. All patients showed improvements in the single treatment and the treatment associated with the nutritional program. The reduction of subcutaneous adipose tissue observed with the treatment of compressive microvibration with spheres of variable density indicates a direct stimulation of the biochemical and biophysical structures that regulate the cellular biology of adipose tissue, with metabolic action induced by the vibrations.

#### INTRODUCTION

As reported in the 4th Italian Obesity Barometer Report of 2022 (1), our society is characterised by a sharp increase in overweight and obesity, with a greater risk of heart disease, diabetes, oncological pathologies and chronic disabling diseases, such as painful lipodystrophy or lipedema.

The increase in adipose tissue in the abdomen is an expression of inflammatory and metabolic stimuli deriving from systemic alterations with progressive tissue alterations, both with subcutaneous adipose hypertrophy and venolymphatic stasis, as in lipolymphedema, and with painful fibro edematous gangue, such as in lipedema (2, 3).

Beyond the different etiological causes (such as lack of oxygen and nutrients with an excess of toxic elements, heavy metals, oxidising substances, sugars and macromolecules) or clinical classifications (4-6), early diagnosis is essential to reduce the progressive pathological evolutions of the adipose tissue and to allow non-invasive treatments to be used in the initial stages, therefore in preventive medicine.

This study is aimed at the clinical evaluation of a non-invasive treatment, possibly associated with depurative nutrition.

#### MATERIALS AND METHODS

In the Phlebology and Aesthetic Pathology Centre of Arezzo, in the period between January 10th to May 30th, 2022, 30 female patients were admitted, aged between 18 and 55 years (an average age of 32.65), of whom two smokers and twenty-eight non-smokers, ten patients on estrogen-progestogen pills and twenty without taking hormones. All the patients presented themselves spontaneously for a surgical examination to reduce the abdomen's subcutaneous adipose tissue (localised adiposity).

## Inclusion criteria:

- o BMI not less than 21.5 and more than 28.9;
- o subcutaneous fat hypertrophy ICD 729.3.

#### Exclusion criteria:

- o BMI below 21.5 and above 29;
- o Obesity;
- o systemic or unilateral lymphedema (positive Stemmer's test);
- o superficial varicose veins (CEAP-C2-C6);
- o subjects with other anti-cellulite or slimming treatments in progress;
- o patients with previous weight loss over 10 kg;
- o patients with orthopaedic prostheses or with metabolic pathologies in progress, especially Diabetes and Hashimoto syndrome. Lipedema (7, 8).

The 30 patients who met the inclusion criteria were enrolled and divided into two groups (Fig. 1, 2):

- <u>Group A</u>: 15 female patients with an average age of 32.12 years, an average height of 163 cm, an average weight of 66.93 kg and an average BMI of 25.35, of which none smokers and seven patients on estrogen-progestogen pills.
- <u>Group B:</u> 15 Female patients with an average age of 33.18 years, an average height of 164.6 cm, an average weight of 67.2 kg and an average BMI of 24.81, with two smokers and thirteen non-smokers, with three patients on estrogen-progestogen pills and twelve not taking hormones.

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DATA	middle age	YES smoke	NO smoke	YES hormones	NO Hormones
Group A	32,12	0	15	7	8
Group B	33,18	2	13	3	12
average value	32,65	total 2	total 28	total 10	total 20

**Fig. 1.** *General data of the patients enrolled in the two groups.* 

DATA	average height	Weight I	BMI I
Group A	163	66,9	25,3
Group B	164,6	67,2	24,81

**Fig. 2.** *Height, weight and BMI of the patients enrolled in the two groups.* 

#### Patients

All the clinical-instrumental evaluations were performed on each patient within 24 hours. The patients had not consumed coffee or smoked for the two hours before the testing.

The patients underwent a clinical and instrumental examination:

- a) the first and last measurements were taken 1 to 3 weeks after the end of the menstrual cycle;
- b) the clinical and instrumental examination aimed to study the patient's vascular, endocrine and adipose tissue:
- c) age, weight, height, Body Mass Index (BMI), and circumferences were recorded in the abdomen and the right thigh in all patients;
- d) the VAS test was performed to record the subjective judgments of the patients after the treatment.

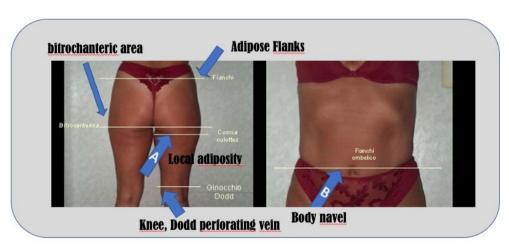
# Survey methodology

*BMI*: The parameters relating to body weight were treated with reference to the Lorenz formula, relating to the Body Mass Index (BMI) (9, 10), which defines the patient as "Underweight" with a value of less than 18.5%, "Normal" between 18.5 and 24.9%, "Overweight" between 25 and 29.9%. He defines "Obesity" as a BMI above 30%. Our study only included patients with a BMI between 21.5 and 28.9.

## Circumferences

The biometric tests of the circumferences, which for the sake of completeness we have detected both in the abdomen and in the right thigh, were acquired in centimeters according to the Lohmann-Roche-Martorell standards (11, 12), as detailed below (Fig. 3):

- Right Thigh (Point A): The patient is standing and carries the weight on the contralateral limb, the circumference is taken horizontally under the gluteal crease by placing the tape measure at the apex of the trochanteric adiposity.
- Abdomen (Point B): The measurement is taken at the end of the exhalation on the horizontal line passing through the navel centre.



**Fig. 3.** *Measurement of the circumferences in points A and B.* 

#### VAS test

At the end of the treatment cycle, each patient was given a self-assessment form to report judgment based on eight parameters, such as tolerance and efficacy of the treatment, evidence of subjective improvement, reduction in the visibility of cellulite and the sense of swelling, reduction of adipose tissue and lastly, general satisfaction.

The form required a judgment expressed with a vote from 1 to 10 (even decimal) for each item indicated, where 5 marks the difference between a pass and a fail, with four cut-off marks: from 1 to 2 worsening, from 3 to 5 no improvement, 6 to 8 significant improvement, 9 to 10 great improvement.

#### Treatment schemes

The 30 enrolled patients were divided into two groups with different treatments:

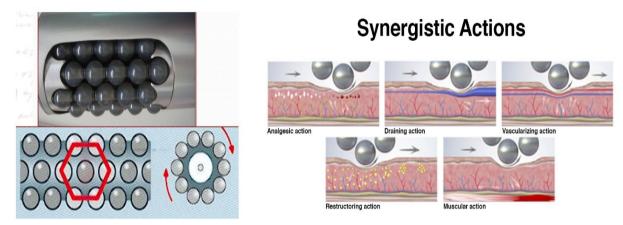
-group A (15 patients): Only non-invasive physical treatment with Compressive Microvibration Evolution, with two sessions a week for 5 weeks and then one session a week for 2 weeks, for 12 treatment sessions (approximately 2 months);

-group B (15 patients): The same physical treatment with Compressive Microvibration Evolution, for two sessions per week for five weeks and then one session a week for two weeks, for a total of twelve treatment sessions (about two months), associated with a purifying nutritional program (13).

# Compressive microvibration

A non-invasive physical method called "Compressive Microvibration" was used as therapy, characterised by equipment consisting of a cylinder controlled by a computerised system that houses a rotor of 50 biocompatible silicone spheres, with precise positioning, structure and dimension. By varying the rotation speed, frequencies ranging between 29 and 384 Hz are obtained (14).

The elastic response of the tissues to the micro-vibrations and micro-compressions sent by the spheres creates micro-upheavals and tissue translations which generate "vascular gymnastics" such as to favour a physiological thermal increase in the treated areas, expression of an improved vascularisation which activates the processes of tissue purification and cell regeneration. So, we can have five main actions: draining, vascularisation, analgesic, restructuring and tonic action (15, 16).



**Fig. 4.** Honeycomb position of the rotating microspheres in the handpiece. On the right, different actions that can be performed with different pressures and rotation frequencies of the spheres.

The heart of the treatment is both the design of the spheres, which are positioned in a honeycomb pattern (Fig. 4) to favor the transmission of micro-vibrations and the materials of the spheres themselves, which are studied and certified as polyvinyl chloride with 26% oxygen (ISO4589), with non-toxic and food approved plasticisers, stabilisers and processing aids, free of phthalates and bisphenol A as they meet the requirements of the Food and Drug Administration (FDA), Code of Federal Regulations (CFR) 21 CFR § 177.2600, comply with BfR recommendation XV for silicone.

Evolution technology "VD-tech" (variable density technology) has been used in this study, a particular device where 50 spheres with variable density alternate, most of them are very soft with internal gaps, some more rigid with a solid structure. At a specific working pressure, the soft spheres deform, enhancing the effect of the rigid spheres that generate a particular vibration defined as "Hyperwave", with the same frequency but with variable amplitude, which acts both on myofascial stimulation and on adipocytes, with a "positive/negative" pump effect (Fig. 5).



**Fig. 5**. *The structure with spheres of variable density creates a Hyperwave.* 

Enhancing the effect of this wave is associated with a band with a myofascial activator that emits a train of impulses that causes the rectus muscles to contract, thus creating a rigid working plane when the rigid spheres come into contact with the skin.

## The depurative diet

The adipose organ shows different adipocytes mixed for physiological and functional transdifferentiation, reversible depending on the need. White fat cells store lipids, while brown adipose tissue burns them (with an oxidation process) to produce metabolic heat: the body temperature. Brown adipose tissue can slow the evolution of adipose hypertrophy and obesity, while the increase in white deposit tissue, as in overweight cases, is always associated with systemic inflammation and insulin resistance (17-19).

We know that situations of overeating cause subcutaneous adipose hypertrophy, while the reduction of a load of carbohydrates and saturated fatty acids, even in a partial twelve-hour fast, determines the decrease in insulin and histamine levels, especially with the addition of Omega 3. The result is the improvement of insulin resistance with the activation of glucagon, a hormone capable of releasing glycogen and fatty acids from the liver and fat cells, thus reducing adipose tissue and oedema and mechanical compression of the lymphatic pathways, as in lipolymphedema.

In accordance with De Godoy's studies (20-22), which highlighted the correlations between subcutaneous abdominal fat, visceral fat and lipolymphedema of the lower limbs, and following the nutritional indications of the immunologist Mastandrea (23) to reduce the histamine and the consequent inflammation (24, 25), we used a nutritional scheme characterised by partial food rest for twelve hours for three days, followed by reduction of glucose, carbohydrates and white flour for ten days, in order to reduce the storage of sugar in the form of glycogen in the muscles with fluid recall and oedema, but also to increase the level of endothelial NO (nitric oxide) thanks to the reduction of oxidative inflammation, thus also favouring a physiological reduction of subcutaneous adipose tissue (26). In combination with the purifying diet, two 1200 mg Omega 3 pearls a day were recommended throughout this period.

- -Phase 1: Detox (3 days) (SuperDetox). It lasts for three days and is based on a temporary fast of twelve hours, with a good breakfast in the morning and a light dinner;
- -Phase 2: Purification (10 days) (Detox) The phase includes three daily meals with a good breakfast followed by lighter lunch and dinner, avoiding white flour (gluten), fresh dairy products and histamine foods;
- -Phase 3: Recovery (10/15 days) (Depur-food) It is the recovery phase where the body returns to regular food, eating everything but preferring eggs and vegetable food, with white flour and carbohydrates, especially in the morning.

Since the body always benefits from short periods of partial dietary rest (27, 28), in patients in group B this depurative nutritional scheme has been associated with the treatment of Compressive Microvibration Evolution with spheres of variable density.

## Objective of the study

- 1) Efficacy of the Compressive Microvibration Evolution in the chosen indications.
- 2) Treatment tolerance.
- 3) Advantage of combining the depurative nutritional scheme with the treatment used.

# Ethics of the study

The study included only volunteer patients who had explicitly requested to undergo these treatments.

All treatments were non-invasive, with long clinical trials and scientific publications. After informed consent, patients were expressly asked not to change their eating habits or lifestyle during the study period, apart from group B which had a dedicated nutritional program.

#### RESULTS

The 30 patients were included in two groups with different treatments:

- -Group A (No. 15 patients) Only non-invasive treatment of Compressive Microvibration Evolution.
- -Gruppo B (No. 15 patients) Treatment of Compressive Microvibration Evolution and depurative diet.

New measurements were taken at the end of all treatments, and the patients' judgments were recorded; no patient discontinued therapy or reported side effects.

# Weight and BMI

A modest but significant body weight reduction with BMI improvement was highlighted in all patients, which is more evident in Group B. These data lead us to believe that in Group B, there was also a metabolic effect on visceral adipose tissue, with reduced inflammation and subcutaneous fat tissue (Fig. 6).

DATA	Kg reduction	% BMI	average height	weight 1	weight 2	BMI 1	BMI 2
Group A	2,7	4	163	66,9	64,2	25,3	24,23
Group B	4	4,17	164,6	67,2	63,2	24,81	23,37

Fig. 6. Weight and BMI reduction, demonstrating metabolic improvement.

Group A - The fifteen patients treated had an average weight (before treatment) of 66.93 kg and an average BMI of 25.35. After treatment, there was an average weight of 64.2 kg and an average BMI of 24.23. with a reduction in average weight after only treatment with Compressive Microvibration Evolution of 2.7 kg (-4.09%) and an improvement in BMI of 3.98%.

Group B - The fifteen patients treated had an average weight (before treatment) of 67.2 kg and an average BMI of 24.81. After treatment, there was an average weight of 63.2 kg and an average BMI of 23.37, with reduction in average weight after treatment with Compressive Microvibration Evolution and purifying diet of 4.13 kg (-5.95%) and improvement in BMI of 4.17%.

These results are interesting, not so much for the absolute values but for the trend values that we interpret as a consequence of the improved microvascular function, as well as the activity of regulation and purification of the interstitial matrix with better fluidity of the cell membrane and consequent increase in cellular metabolism of the adipose tissue, which is noted in both groups, even if more so in Group B.

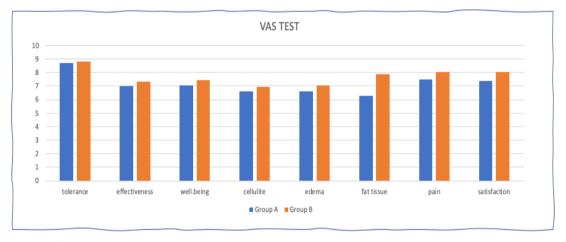
# Subjective evaluations (VAS test)

No complications were reported, and all patients performed the VAS test (Fig. 7, 8).

- -Group A Treatment tolerance (8.7), efficacy (7), subjective improvement (7.03), reduction of cellulite visibility (6.63), reduction of swelling (6.6), reduction of adipose tissue (6.3), reduction of pain symptom (7.5), general satisfaction (7.4).
- -Group B -Treatment tolerance (8.8), efficacy (7.3), subjective improvement (7.44), reduction of cellulite visibility (6.93), reduction of swelling (7.03), reduction of adipose tissue (7.86), reduction of pain symptom (8.06), general satisfaction (8.03).

VAS test	tolerance	effectiveness	well.being	cellulite	edema	fat tissue	pain	satisfaction
Group A	8,7	7	7,03	6,63	6,6	6,3	7,5	7,4
Group B	8,8	7,33	7,44	6,93	7,03	7,86	8,06	8,03

**Fig. 7.** *VAS test with patient reviews.* 



**Fig. 8.** *VAS test with patient reviews.* 

# Abdominal circumference

The results show a significant reduction in the circumference of the abdomen, both in Group A (1.4 cm by 1.91%) and in Group B (3.2 cm by 4.13%), where the depurative diet was associated with the treatment of the Compression Microvibration Evolution (Fig. 9).

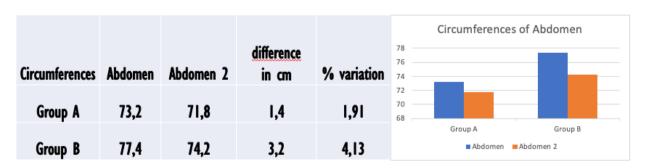
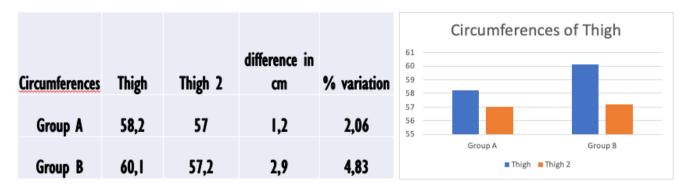


Fig. 9. Variations in the circumference of the abdomen.

# Thigh circumference

The thigh circumference was also significantly reduced, both in group A (1.2 cm by 2.06%) and in group B (2.9 cm by 4.83%) where the depurative diet is associated (Fig. 10).



**Fig. 10.** Changes in right thigh circumference.

From the observation of these results, the treatment has demonstrated efficacy on the metabolism of the subcutaneous fat in the abdomen and thigh, certainly more evident in the patients of Group B treated with integrated therapy.

These data also justify the feeling of well-being, less abdominal swelling and light legs declared by all the patients. The improvement in symptoms can be referred to the decrease in lymphatic stasis and the functional activation of the entire mesenchymal (adipoconnective) structure, not only as a direct effect on the vessel walls (phlebolymphotrophic/tonic action) but above all as a reactivation of the purifying, metabolic and regenerative activities of the cells (29).

#### **DISCUSSION**

As described by Bigs (30), Paul (31), Sanders (32) and Goldstein (33), repeated mechanical stress promotes tissue remodelling mediated by adipocyte-derived stem cells. These authors stated that neo-angiogenesis and extracellular matrix (ECM) remodelling are the main drivers of tissue renewal under mechanical stress, with moderate and repetitive mechanical input that can activate mitochondria by changing the appearance and structure of skin tissues.

Sbarbati (34, 35) also confirms that mechanical transduction stimuli applied externally to the skin surface cause changes in the physiological and functional structure of the tissues underlying the epidermis, including adipose tissue, with dilatation of the deep spaces of the dermis between the collagen fibres and with an increase in vascularisation associated with the activation of abundantly present stem cells.

Saggini (36) has demonstrated the action of micro-vibrations sent to the tissues by mechanical stimuli in a non-invasive way and with precise frequencies to have different actions on the microcirculatory and venouslymphatic system, on the adipose tissue, in the connective tissue and the fascio-muscular structure.

On this basis, we used the Compressive Microvibration Evolution for the reduction of subcutaneous adipose tissue in the abdomen and thigh, in consideration that such methodology allows to work directly on the deep subcutaneous adipose layer between the rectus muscles and Scarpa's fascia, where brown adipose tissue (BAT) is located, capable of generating working heat and rapidly intervening in fat metabolism, but also white fat cells "dSAT" are located in this area, which contain biologically active substances in energy metabolism (adipokines) and which are also helpful in reducing the surface adipose tissue "sSAT" and proinflammatory fat (WAT) (37-39).

Brown fat also contains a widespread innervation of the sympathetic nervous system which favours thermogenesis, which can also be activated with short, high-intensity stimulations which increase the bioavailability of nitric oxide with a vascularising action (40, 41). This bioavailability is lost in visceral overweight (VAT) and the increase of localised white adipose tissue, therefore in the typical abdominal adipose excess.

The results highlight the non-invasive treatment's effectiveness, especially when the physiotherapy methodology is associated with a nutritional purification scheme.

## Patient satisfaction

We must also reflect on the data relating to the subjective assessments of patients that include a judgment on the aesthetic appearance, in consideration that the evaluation of the aesthetic response of treatment is essential from the subjective final judgment of the patient herself since any "clinical/aesthetic" data takes on meaning only if related to the patient's satisfaction (42, 43).

The clinical, instrumental and laboratory studies do not report the sense of well-being and the change in the patient's quality of life in the social, psychological and emotional aspects since the subjective perception of one's condition does not always correspond to objective clinical data. Thus, a non-invasive treatment that improves the various instrumental parameters but is considered ineffective by the patient may finally not be indicated for that patient.

In the present study, all patients confirmed improved quality of life and subjective well-being, with a satisfactory reduction of adipose tissue localised in the abdomen and thigh, with data also confirmed by clinical and instrumental evaluations.

# **CONCLUSIONS**

This work certainly highlights the importance of individual food education and periodic depurative schemes that can also be used in association with non-invasive treatments for prevention and care, both for clinical and aesthetic purposes.

Adopting balanced nutrition with depurative cycles is useful for regulating hepatointestinal activities that reduce inflammatory processes and increase mitochondrial activities, detoxifying the tissues and regulating the proinflammatory adipose metabolism (44, 45).

The accumulation of ectopic adipose tissue generates intermediate lipotoxic molecules from triglycerides, with alteration of electron transport and cellular dysfunction that cause tissue inflammation, for which prevention assumes an important social role to reverse the vicious circle of dysfunctional adipose tissue.

The Compressive Microvibration Evolution with spheres of variable density has been shown to act on the subcutaneous adipose tissue thanks to its typical structural characteristics.

This study demonstrates that, in addition to the known vascularisatoion, draining, analgesic and restructuring actions, there is a further characteristic of local metabolic activation, which is undoubtedly helpful in reducing the superficial adipose tissue. However, above all, it can be an important non-invasive therapeutic aid in the prevention of overweight and complications of obesity, in addition to the prevention of aesthetic pathologies of adipose tissue, such as lipodystrophy and lipedema.

#### **Conflict of interest**

The authors had no conflicts of interest.

## REFERENCES

- 1. Italian Obesity Barometer Report 2022.
- 2. Herbst KL. Subcutaneous Adipose Tissue Diseases: Dercum Disease, Lipedema, Familial Multiple Lipomatosis, and Madelung Disease 2019.
- 3. Cannon B and Nedergaard J. Brown adipose tissue: function and physiological significance. Physiological Reviews 2004; 84:277–359.
- 4. Callaghan DJ Rd, Robinson DM and Kaminer MS. Cellulite: a review of pathogenesis-directed therapy. Semin Cutan Med Surg 2017; 36(4):179-184. doi: 10.12788/j.sder.2017.031
- 5. Shavit E, Wollina U and Alavi A. Lipoedema is not lymphoedema: A review of current literature. Int Wound J 2018; 15(6):921-928.
- 6. Bass LS and Kaminer MS. Insights into the Pathophysiology of Cellulite: A Review. Dermatol Surg 2020; 46 Suppl 1(1):S77-S85. doi: 10.1097/DSS.0000000000002388.
- 7. Kröger K. Lymphoedema and lipoedema of the extremities. Vasa 2008; 37(1):39-51.
- 8. Zegarra TI and Tadi P. CEAP Classification of Venous Disorders 2022; 26.
- 9. Weir CB and Jan A. BMI Classification Percentile and Cut Off Points In Treasure Island (FL): StatPearls Publishing 2022; 27.
- 10. Alberto G, Novi RF, Maurino M, Trombetta A and Molinatti GM. Increased body mass index and insulin resistance parameters in dyslipidemia. Risk and positive correlation in essential obesity. Minerva Endocrinol 1998; 23(3):65-9.
- 11. Lohman TG, Roche AF and Martorell R. Anthropometric standardisation reference manual. Human Kinetics, Champaign 1988; pp:39-54.
- 12. Del Carmen Camano M, Garcia O & Coll, Simple anthropometric measurements to predict dyslipidemias in Mexican school-age children: a cross-sectional study, Open Journal of Preventive Medicine 2011; 1(3).
- 13. Bacci PA, "Nutrition" in Cellulite 2012, diagnosis and therapy of Female Evolutive Fibroedema 2012; pp:133-143.
- 14. Bacci PA, Bozzelli S, Leonardi S, Vannuccini S, Bellomo RG and Saggini R. Vascularising action of the compressive microvibrations, Journal of Applied Cosmetology 2021, 39(2):13-29.
- 15. Bacci PA, Leonardi S, Vannuccini S, Frappi S, Rampino G, Bellomo RG, Saggini R, Thermographic and clinical data (TCD Code) in the evaluation of cellulite treatment by Endosphères Therapy, Journal of Applied Cosmetology 2021; 39(2):60-80.
- 16. Bellomo RG, Buda R, Porreca AM, Virgili E, Postacchini G, Bacci PA, Saggini R and Barbato C, Treatment of lymphedema, two methods compared: ketogenic diet and endospheres, ketogenic diet and vodder lymphatic drainage, Journal of Applied Cosmetology 2022; 40(1):54-68.
- 17. Cinti S. Transdifferentiation properties of adipocytes in the adipose organ. Am J Physiol Endocrinol Metab 2009; 297(5):E977-86. doi: 10.1152/ajpendo.00183.2009
- 18. Hauck AK, Huang Y, Hertzel AV and Bernlohr DA. Adipose oxidative stress and protein carbonylation. J Biol Chem. 2019; 294(4):1083-1088. doi: 10.1074/jbc.R118.003214
- 19. Laboux T, Azar R. Dietary control of metabolic acidosis in chronic kidney disease. Nephrol Ther 2019; 15(7):491-497. doi: 10.1016/j.nephro.2018.12.001
- 20. De Godoy JMP. Systemic subclinical lymphedema due to obesity as the cause of clinical lymphedema: A new concept. Med Hypotheses 2019; 131:109312. doi: 10.1016/j.mehy.2019.109312
- 21. Pereira de Godoy JM, Pereira de Godoy LM, Pereira de Godoy AC, Guerreiro Godoy MF. Bariatric surgery and the evaluation of subclinical systemic lymphedema. J Surg Case Rep 2019; 2019(2):rjz028. doi: 10.1093/jscr/rjz028
- 22. Pereira de Godoy LM, Pereira de Godoy HJ, Pereira de Godoy Capeletto P, Guerreiro Godoy MF and Pereira de Godoy JM. Lipedema and the Evolution to Lymphedema with the Progression of Obesity. Cureus 2020; 12(12):e11854. doi: 10.7759/cureus.11854
- 23. Mastrandrea F. Immunotherapy in atopic dermatitis. Expert Opin Investig Drugs 2001; 10(1):49-63. doi: 10.1517/13543784.10.1.49

- 24. Branco ACCC, Yoshikawa FSY, Pietrobon AJ and Sato MN. Role of Histamine in Modulating the Immune Response and Inflammation. Mediators Inflamm 2018; 2018:9524075. doi: 10.1155/2018/9524075
- 25. Jørgensen EA, Knigge U, Warberg J and Kjaer A. Histamine and the regulation of body weight. Neuroendocrinology 2007; 86(3):210-4. doi: 10.1159/000108341
- 26. Gliozzi M, Scicchitano M, Bosco F, et al. Modulation of Nitric Oxide Synthases by Oxidized LDLs: Role in Vascular Inflammation and Atherosclerosis Development. Int J Mol Sci 2019; 20(13):3294. doi: 10.3390/ijms20133294
- 27. Fernando HA, Zibellini J, Harris RA, Seimon RV and Sainsbury A. Effect of Ramadan Fasting on Weight and Body Composition in Healthy Non-Athlete Adults: A Systematic Review and Meta-Analysis. Nutrients 2019; 11(2):478. doi: 10.3390/nu11020478
- 28. Hajek P, Myers K, Dhanji AR, West O and McRobbie H. Weight change during and after Ramadan fasting. J Public Health (Oxf) 2012; 34(3):377-81. doi: 10.1093/pubmed/fdr087
- 29. Distante F, Bacci PA and Carrera M. Efficacy of a multifunctional plant complex in the treatment of the so-called 'cellulite': clinical and instrumental evaluation. Int J Cosmet Sci 2006; 28(3):191-206. doi: 10.1111/j.1467-2494.2006.00319.x
- 30. Biggs LC, Kim CS, Miroshnikova YA and Wickström SA. Mechanical forces in the skin: Roles in tissue architecture, stability, and function. J Invest Dermatol 2020; 140(2):284-290. doi: 10.1016/j.jid.2019.06.137
- 31. Paul NE, Denecke B, Kim BS, Dreser A, Bernhagen J and Pallua N. The effect of mechanical stress on the proliferation, adipogenic differentiation and gene expression of human adipose-derived stem cells. J Tissue Eng Regen Med 2018; 12(1):276-284. doi: 10.1002/term.2411
- 32. Sanders JE, Goldstein BS and Leotta DF. Skin response to mechanical stress: Adaptation rather than breakdown-a review of the literature. J Rehabil Res Dev 1995; 32(3):214-226.
- 33. Goldstein B and Sanders J. Skin response to repetitive mechanical stress: A new experimental model in pig. Arch Phys Med Rehabil 1998; 79(3):265-272. doi: 10.1016/s0003-9993(98)90005-3
- 34. Segalla L, Chirumbolo S, Sbarbati A. Dermal white adipose tissue: Much more than a metabolic, lipid-storage organ? Tissue Cell. 2021; 71:101583. doi: 10.1016/j.tice.2021.101583
- 35. Rigotti G, Chirumbolo S, Cicala F, Parnigotto PP, Nicolato E, Calderan L, Conti G and Sbarbati A. Negative Pressure from an Internal Spiral Tissue Expander Generates New Subcutaneous Adipose Tissue in an In Vivo Animal Model. Aesthet Surg J. 2020; 40(4):448-459. doi: 10.1093/asj/sjz194
- 36. Bacci PA and Saggini R, Compressive Microvibration with Endosphères Therapy: Retrospective study, Journal of Applied Cosmetology 2022; 40(1): 69-90.
- 37. Lo Ka and Sun L. Turning WAT into BAT: a review on regulators controlling the browning of white adipocytes. Biosci. Rep 2013; 33(5):e00065.
- 38. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obes Rev 2010; 11(1):11-8. doi: 10.1111/j.1467-789X.2009.00623.x
- 39. Walker GE, Verti B, Marzullo P, Savia G, Mencarelli M, Zurleni F, Liuzzi A and Di Blasio AM. Deep subcutaneous adipose tissue: a distinct abdominal adipose depot. Obesity (Silver Spring) 2007; 15(8):1933-43. doi: 10.1038/oby.2007.231
- 40. Martinez-Sanchez N, Sweeney O, Sidarta-Oliveira D, Caron A, Stanley SA and Domingos AI. The sympathetic nervous system in the 21st century: Neuroimmune interactions in metabolic homeostasis and obesity. Neuron 2022; 110(21):3597-3626. doi: 10.1016/j.neuron.2022.10.017
- 41. Seydoux J and Girardier L. Control of brown fat thermogenesis by the sympathetic nervous system. Experientia 1977; 33(9):1128-30. doi: 10.1007/BF01922280
- 42. Barron F and Harrington DM. Creativity, intelligence and personality. Annual Review of Psychology 1981. 32: 439-476.
- 43. Perry-Smith JE and Shalley CE. The social side of creativity: a static and dynamic social network perspective. Academy of Management Review 2003; 28 (1):89-106.

- 44. Mastandrea F, Cadario G, Coradduzza G and coll. Safety and tolerability of the probiotic formula I-Prob. The Child. Journal of Pediatrics 2013; 1(2).
- 45. Mastandrea F. Probiotics and Regenerative Medecine. Eur Ann Allergy Clin Immunol 2016; 48(5):182-7.