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Injective treatment of the so-called cellulite: a new approach aimed at restructuring extracellular matrix of deeper layers of the skin. Efficacy and safety of a new specific formula (part 1)

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SUMMARY

Background: An innovative injectable solution containing low molecular weight hyaluronic acid (HA), a specific Amino Acids mixture and a carbonate plus bicarbonate solution was formulated to counteract moderate edematous – fibrosclerotic lipodystrophy (PEFS) on the thighs.

Objective: The aim of this open clinical trial was to evaluate the efficacy and tolerance of the injectable product under study, on the main signs of cellulite. Methods: A single Italian center treated 25 female subjects aged 35-55 years, informed and consenting. The study treatment foresaw 6 injective sessions at intervals of 10 days, by blunt tip cannula. The study had to be interrupted prematurely because of the COVID-19 pandemic and auto-isolation procedure of participating subjects. A minimally representative number of clinical observations was reached even after only 2 injection sessions.

Results: data highlighted a reduction of cellulite visual aspect of at least 1 degree in 20% of subjects vs T0 (not statistically significant), according to reference photographic scales and a mean reduction of clinical degree of cellulite of 0,3. Interestingly, a statistically significant reduction of mean circumferences of the thighs occurred:-0,8 cm at T3i. While the injected product was tolerated very well, light bruises occurred in 45% of subjects.

Conclusions: Although two injection sessions represented only one third of the foreseen complete treatment, the data obtained already confirms the tolerance and a partial aesthetic performance of the injectable solution on the main signs of cellulite. In particular on the visual aspect and the circumferences of the treated areas. Nevertheless, too many light bruises occurred, because of the use of blunt tip cannula. The Author argues that improving the injection technique could result in better clinical results on P.E.F.S.

KEYWORDS
Cellulite, Hyaluronic Acid, Carbonates, Bicarbonates, Acidosis, Amino Acids

INTRODUCTION

Cellulite is a major concern for women at every age. This condition, better defined as panniculosis, or edhematous fibrosclerotic panniculosis (P.E.F.S.), leads progressively to a degenerative disease of adipose pannicula, also involving more superficial layers of the skin. The result is a profound structural and functional alteration of the skin in sites such as the buttocks, thighs, knees and even the inner surface of the arms. Basically, at the forefront of advanced research on extracellular

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matrix (ECM), injection treatments can exert a therapeutic effect. In spite of the techniques currently in use, which involve the destruction of the altered adipose panniculus and the fibrous shoots typical of the most advanced stages of cellulite, the proposed treatment represents an attempt to remodel the biochemical and architectural structure of the deep and superficial components of the skin. In recent years, scientific research has made it possible to develop a solution of low molecular weight hyaluronic acid (HA) and collagen and elastin amino acids (AA) capable of specifically stimulating the synthesis of the main components of the extracellular matrix. A previous version of this solution is currently used with success in skin rejuvenation and redensification protocols. The product "Sunekos Cell" (SC), proposed for the study, contains a patented platform of six structural amino acids fundamentally and specifically dosed for an optimal neo-synthesis of collagen and elastin in the dermis. It has already been demonstrated, in vitro, that its functional cluster of amino acids is suitable for promoting in loco the synthesis of collagen and elastin.

Local injection of this formulation can be a powerful tool in expert hands because chemotaxis induced by the presence in the dermis of specific amino acids for the production of collagen and elastin is known to be the strongest force in nature that drives life: living things are attracted to food. In fact, we are sending a very strong biological message to the fibroblasts. Feeding the fibroblasts with the right food (the right amino acids) can reactivate them and also restore a normal structure of the dermal architecture.

Moreover, the natural low molecular weight hyaluronic acid (HA) (200,000 daltons) synergistically present in the Sunekos Cell formula exerts a targeted stimulating action on the fibroblasts through the binding to the specific receptors for the HA fragments.

A bicarbonate/carbonate buffer has been added to the standard formula in order to have a pH 8.2 for specific use in panniculosis. The bicarbonate and carbonate solution buffers local acidosis due to the state of latent inflammation that characterizes both the early and late stages of the disease.

Materials and methods

Aim of this pilot study was to evaluate by clinical, morphometric and non invasive instrumental evaluations the efficacy of an injective treatment on cellulite sign and symptoms.

The tested product, a mixture of HA, aminoacids and carbonates solution, was administered by the injection technique, on healthy female volunteers with moderate oedematous – fibrosclerotic lipodystrophy (PEFS) on the thighs. An additional aim of this study was to evaluate the treatment tolerance. The treatment foresaw 6 injective sessions at intervals of 10 days according by blunt tip cannula (25G, 50mm).

The study had obtained the approval of an Independent Ethical Committee.

Inclusion criteria were: healthy female Caucasian subjects, age ranges: 35-65 yrs. with moderate oedematous – fibrosclerotic lipodystrophy on the thighs (3rd superior). Exclusion criteria were pregnancy, lactation, general or local disease, smoking, alcohol and drug abuse. Sample population: 25 volunteers to be included. The volunteers had to accept to respect the rules fixed in the list of recruitment criteria and not to deviate from their normal life habits; particular attention was paid to alimentary and drug assumption habits, as well as to cosmetic product(s) and cleansing for the body.

During the entire period of treatment, the exposure to strong UV irradiation (UV session, or sun bathing) was to be avoided. Evaluations were carried out mono-laterally on the right or left thigh (3rd superior), according to a subjects' randomization list defined by the investigator before the subjects' inclusion.

Clinical evaluations **(Fig.1)** was performed according to the following visual score:

➜ **Cellulitis visual aspect (clinical score according to a reference photographic scale)**

- no cellulitis **0**
- slight dimpling on skin surface **1**
- dimpling and skin depressions **2**
- dimpling and depressed striations **3**
- nodules and depressed striations **4**

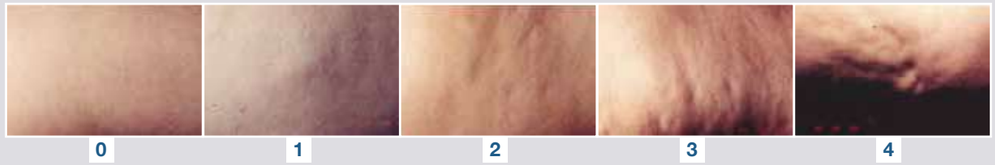
➜ **Product tolerance was evaluated considering:**

- local expected events/reactions induced by the injection procedure (tardive swelling, pain, erythema, bruise);
- any other adverse event/reaction, also of systemic source occurring during the study.

Morphometric evaluation
Circumference measurements

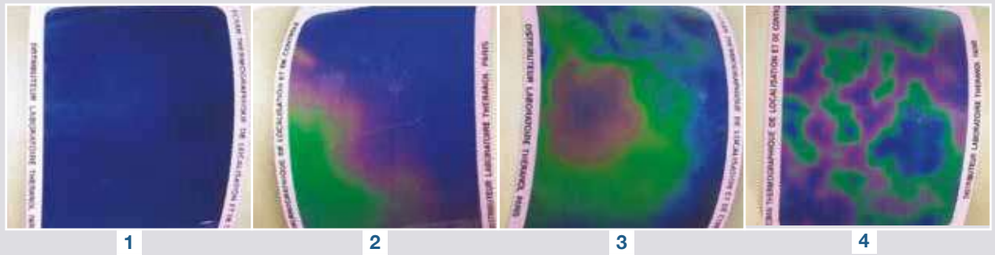
All the measures were performed in standard conditions at the thigh level (middle thigh and under gluteus), thanks to a specific electro-optical system able to fix the volunteer's position.

Fig. 1



Visual grading of cellulite

Fig. 2



Visual grading of contact thermography

Contact thermography

Contact thermography permits visualizing, through colors, the temperatures of the areas being examined by using encapsulated liquid crystals plates. It is therefore much helpful in pointing out skin temperature alterations. Each color of the liquid crystal corresponds to a different temperature following a standard chromatic scale from 21°C to 27°C: higher temperatures are shown by dark blue, while lower temperatures by green, yellow and black-red.

The thermography with liquid crystal allows to detect information about cutaneous microcirculation in normal conditions, after functional stimuli or vasoactive treatments: skin temperature grows in case of vasodilation, increase of blood vessels, increase local metabolism and reduced in case of vasoconstriction, pathological decrease of blood vessels, decrease of local metabolism, oedema and increase of adipose tissue. A characteristic thermography aspect of legs' oedematous – fibrosclerotic lipodystrophy is represented by the typical leopard skin with large hypothermic zones **(Fig.2)**.

➜ **Panniculopatia evaluation of the external thigh (3rd superior) follows next classification:**

- **0** = uniform hyperthermal image
- **1** = shaded spots thermal image (hyperthermal images)
- **2** = leopard spots (numerous hyperthermal images)
- **3** = hypothermal black holes
- **4** = uniform hypothermal image

Results

The study was started on 25 female healthy adult subjects, age range: 35-55 (mean age: 50 yrs.), whose written consent had been obtained. Unfortunately, the study had to be interrupted prematurely because of COVID-19 pandemic and auto-isolation procedure of participating subjects. A minimally representative number of clinical observations was only reached for T0, T2i, T3i. T2i is the time relating to the result of the first injection session (in fact the evaluation was performed immediately before the second injection session) and time T3i is relative to the result of the second.

Data processing and statistical analysis were performed in accordance to our internal procedures (de-

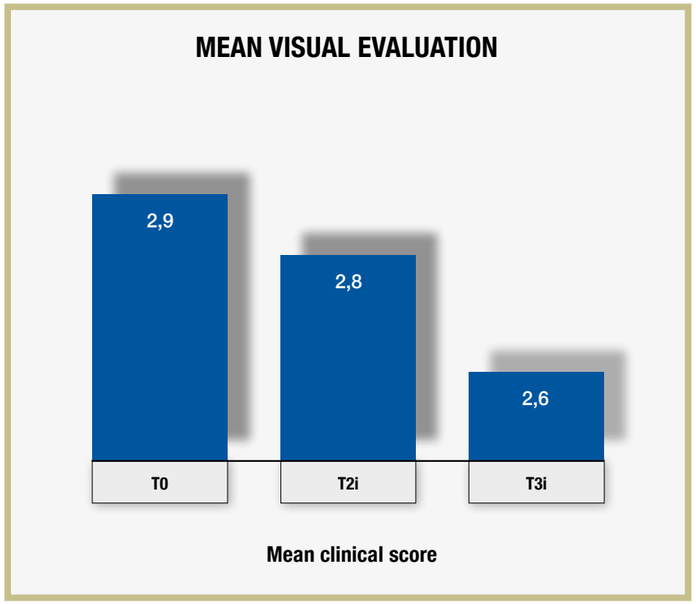


Fig. 3

scriptive and inferential analysis) as follows:

Friedman test followed, in case of statistically significant result, by Holm-Sidak Adjusted test.

Clinical assessment

Obtained results highlighted: a reduction of cellulite visual aspect of at least 1 degree in 20% of subjects vs T0 (not statistically significant), according to DERMING reference photographic scales and a mean reduction of clinical degree of cellulite of 0,2 at T2i and 0,3 at T3i **(Fig.3)**

Morphometric evaluation

All circumference measurements were performed in standard conditions thanks to a specific electro-optical system able to fix the volunteer's position.

At T2i the reduction corresponded to 0,4cm and at T3i to 0,8 cm. The last result was clinically/statistically significant, when compared to baseline **(Fig.4)** (Holm-Sidak Adjusted t test $p<0.05$ vs T0).

Tolerance evaluation

Although no important adverse event/reaction occurred during the trial, bruises occurred in 45% of cases. The average duration of the bruises was 12 days.

Contact thermography

Contact thermography mean score resulted reduced of 0.1 for both evaluation times, although this was not statistically significant (**Fig.5**).

Discussion and conclusions

Although the study was interrupted prematurely, some initial conclusions can be observed about the activity of injected formula and injection techniques. The formula in itself has demonstrated to exert a relevant restructuring activity on altered ECM at the level of P.E.F.S. In fact, already after only two injection sessions, a visible reduction of cellulite signs was obtained and, interestingly, a statistically significant reduction of thigh mean circumferences was obtained. In particular, this reduction was not expected, since the injected formula was not designed to have a slimming activity. Probably, mean circumference was due to a "panty" activity determined by an improvement of skin tone and consistency. On the contrary, while the formula itself was very well tolerated, the occurrence of bruises after the use of the blunt tip cannula was very high and probably not useful for a treatment aimed at reconstructing ECM of dermis and hypodermis. Based on this result, a less invasive needle technique should be designed. Previous studies on the use of the HA-6AA formula on the face demonstrated the superiority of Interstitial Fluid Technique (IFT) on intradermic random technique. In fact, IFT was demonstrated to combine injection and lymph-drainage by pushing interstitial fluids towards local lymph-nodes. Since in early stages of P.E.F.S. oedema and stasis are the main characteristics of the conditions, intradermal IFT towards inguino-crural lymphatic stations could be useful to reduce stasis at the level of thighs. On the other side, in advanced P.E.F.S. local fibrosis at the level hypodermis prevails.

In this case, a thin needle could reach deeper levels in order to put the product directly into the fibrosis. A new study for the evaluation of efficacy and tolerability of SC should therefore be designed in order to obtain the best from the treatment.

Fig. 4

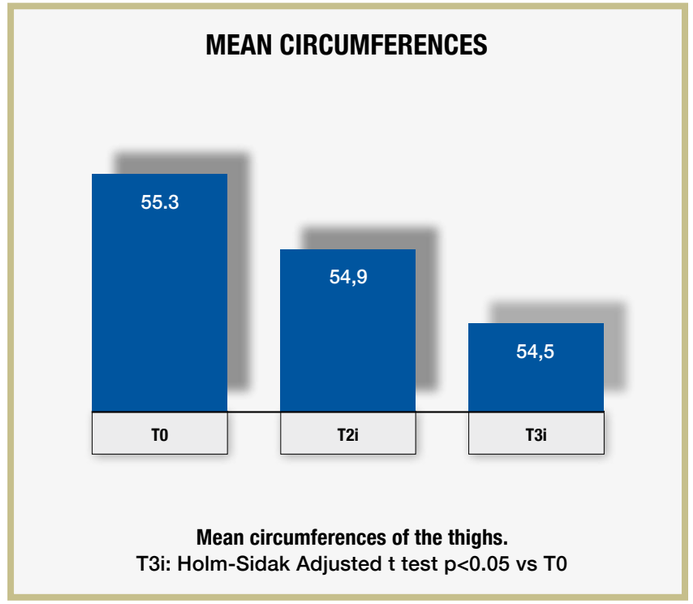
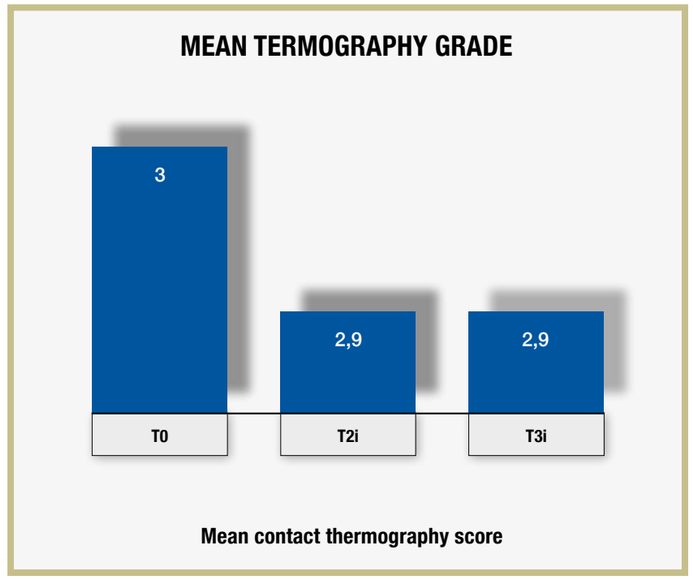


Fig.5



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Injective treatment of the so-called cellulite: a new approach aimed at restructuring extracellular matrix of deeper layers of the skin. Efficacy and safety of a new specific formula (part 2)

SUMMARY

Background: an innovative injectable solution containing low molecular weight hyaluronic acid (HA), a specific Amino Acids mixture and a carbonate plus bicarbonate solution was formulated to counteract moderate edematous – fibrosclerotic lipodystrophy (PEFS) on the thighs.

Objective: The aim of this open clinical trial was to evaluate efficacy and tolerance of the injectable product under study, on the main signs of cellulite. Methods: The study was conducted on 25 female adult subjects, age range: 33-60, whose written consent had been obtained. The patients were divided into 2 groups during the basal visit: - Group A (early stage): patients with grade 1-2 as per visual aspect grade : 11 patients

Group B (late stage): patients with grade 3-4 as per visual aspect grade: 14 patients

The study treatment foresaw 2 injective sessions at intervals of 10 days, according to a brand new injection method in the treatment of cellulite: IFT (for Group A) or Matelassé technique (for Group B) depending on the cellulite's stage. The study foresaw four observational visits over a four months period with the first and second injections at an interval of 10 days.

Results: data highlighted a reduction of cellulite visual aspect of at least 1 degree in 92% of all subjects (group A + group B) vs T0 (Holm-Sidak Adjusted Wilcoxon signed rank test p<0.05 T1M and T4M vs T0) according to reference photographic scales and a mean reduction of clinical degree of cellulite of of 0,88 at T1 and 0,95 at T4 for Group B and 0,9 at T1 and 0,6 at T4 per Group A 0,3. Interestingly, Morphometric evaluations underlined the "panty" activity of the treatment; in fact, already at T1M and at T4M the mean value of thigh and circumferences resulted clinically/ statistically reduced, when compared to baseline in both groups (-1,04 cm at T1 and -1,78 cm at T4 for Group B and –0,87 cm at T1 and -1,39 cm for Group A) (Holm-Sidak Adjusted t test p<0.05 vs T0). Obtained results were respectively of -4% for group A and -13,5% for group B at T1 and of -8,6% and -11,6% at T4, corresponding to a clinically and statistically significant reduction of the pannicula thickness vs T0, index of a lipo-reducing efficacy of the tested product

***Conclusions:** Sunekos Cell was able to counteract the dermal damage which seems to be the most important triggering of the condition and acidosis at local level. The injection techniques should be less invasive as possible and take into account the phase of the disease.*

INTRODUCTION

Injection therapy has always been considered one of the most viable solutions for the treatment of cellulite. Obviously, it is very important to identify the most suitable product for the case, having clearly in mind the mechanism of action and the expected results, but also the most suitable injection technique to be used. Treatment of the ECM is certainly the primary goal. As we have seen, the alterations at this level play a fundamental role in the genesis of the so-called cellulite.

It has been demonstrated that, on histological samples of animal models it was possible to evaluate that physiological elastinogenesis and collagenogenesis, induced in a specific dermal district, have been shown to be capable of reducing skin laxity, mainly correlated to the manifestations of cellulite.

The product "Sunekos Cell" (SC), proposed for the study ,contains a patented platform of six structural amino acids fundamentally and specially dosed for an optimal neo-synthesis of collagen and elastin in the dermis. It has already been demonstrated that a functional cluster of amino acids is suitable for promoting in loco the synthesis of collagen and elastin.

Local injection of this formulation can be a powerful tool in expert hands because chemotaxis induced by the presence in the dermis of specific amino acids for the production of collagen and elastin is known to be the strongest force in nature that drives life: living things are attracted to food. In fact, we are sending a very strong biological message to the fibroblasts. Feeding the fibroblasts with the right food (the right amino acids) also means restoring a normal structure of the dermal architecture.

Moreover, a natural low molecular weight hyaluronic acid (HA) (200,000 daltons) is also synergistically present in the Sunekos Cell formula, exerting a targeted stimulating action on the fibroblasts even through the binding the specific receptors for the HA fragments.

A bicarbonate/carbonate buffer was added to the standard formula of Sunekos to Sunekos Cell in order to have a pH 8.2 for specific use in panniculosis. The bicarbonate and carbonate solution buffers local acidosis due to the state of latent inflammation that characterizes both the early and late stages of the disease.

The disruption of the extracellular matrix of the dermis and hypodermis can be treated effectively, depending on the level and injection technique used. In the early stages, as we have seen, it is first of all important to treat the deep dermis, for an action on the interstitial fluids, in order to restore the physiological interstitial fluid movement towards the lymphatic circulation. In the advanced stage, the aim will be to rearrange the structural and architectural disorder of the fibrous septa of the hypodermis and injecting treatment with Sunekos Cell should therefore be exercised at a deeper level, in the fat adipose tissue. To summarize, when the process is initial and mainly involves the dermis, the injection technique will be at the level of the deep dermis, however taking into account the fact that the product, thanks to its low viscosity characteristics, will however spread optimally throughout the surrounding area. If, however, we are facing an advanced stage, the treatment will be at the level of the more superficial hypodermis, so as to exert a non-invasive action. Contrary to what is often stated by other authors, it is not necessary to violently disrupt fibrous branches, which is commonly done with large-caliber cannulas and often even with a "bayonet" cutting tip. The traumatic action of breaking the fibrous branches, in addition to systematically provoking at this level the formation of large bruises and hematomas (which often remain in unsightly hemosiderinic hyperpigmentations) greatly distances the objective of "restitutio ad integrum". Better then, reach the hypodermis with a smaller gauge needle and inject an adequate amount of the SC product, which will punctually manage to spread alone in a large surrounding area. In more detail, in the initial phase it will be possible to use the method we already know as Interstitial Fluid Technique (IFT), that is, making sure that the injecting treatment is at the same time able to push the movement of the interstitial fluids towards the local lymph node stations, realizing a real lymphatic drainage thanks to the push of the injected product. The injection is then followed by a light manual massage in the same direction. Since, in the early stages of panniculosis, the problem of stagnation of interstitial fluids, together with alterations of the micro-vascular-tissue exchange and the acidosis typical of the state of latent inflammation of the disease, is able to trigger the process of disruption of the 'ECM, it is very important to contrast the problem in its entirety, thanks to the specific formula SC, with a targeted injection technique. For IFT, it is advisable to use a 27-30G needle, 12 mm long, with an inclination of 45 ° with respect to the skin surface, made to penetrate for half of the length into the skin. Then inject 0.2-0.3 cc per point, with the

points arranged along radial lines converging from the lateral surface to the medial surface of the thigh, in the direction of the inguinal lymph nodes anteriorly and inguinal-crural posteriorly. The number of points (at a distance of about 2 cm from each other) and lines, will obviously vary depending on the extent of the edema and the orange peel skin **(Fig.1)**.

As for the more advanced stages, in order to obtain a rearrangement of the fibrous septae in the least traumatic way possible, the same type of needle will be used, 27-30G, mm12 in length, but this time inserted perpendicularly to the skin surface made to penetrate for its entire length and injecting 0.3-0.5 cc of product per point (Matelassé technique). Each point will be on lines drawn in the deepest depressions of the skin surface (mattress skin) at a distance of about 1.5 cm from each other **(Fig. 2)**.

To draw the areas to be treated, the patient must be examined in an orthostatic position, preferably in lighting conditions from above and slightly to the side, in order to accentuate the imperfections to be treated, tracing the lines most suitable for the case in question.

Study objective

The aim of this pilot study was to evaluate by clinical, morphometric and non invasive instrumental evaluations the efficacy of an injective treatment on "cellulite" signs and symptoms. A mixture of SUNEKOS® Cell a medical device composed of a small 10 ml bottle containing 210 mg of hyaluronic acid and 50 mg of aminoacids (glycine, proline, lysine ,leucine, valine and alanine) and 3 ml a solution of carbonates and bicarbonates was administered by injection technique, on healthy female volunteers with moderate oedematous – fibrosclerotic lipodystrophy (PEFS) on the thighs.

An additional aim of this study was to evaluate the treatment tolerance.

This study had obtained the approval of an Independent Ethical Committee on 16 January 2020.

10 ml of SUNEKOS® Cell (1 small bottle of aminoacids and sodium hyaluronate in 7 ml of distilled water) and carbonates (3 ml ampoules) in solution was injected by needle (27-30G length 13mm); the needle was inserted into the medium-deep dermis (45°) at level of the trochanteric region, following the IFT pattern in case of light cellulite (orange peel appearance, following a fan shaped pattern across the thigh area converging towards inguinal lymph-nodes) and perpendicularly to the skin (90°) in the max deepness of furrows in case of moderate cellulite (mattress appearance). The distance between injection points was 1,5 cm.

Treatment

The study was conducted on 25 female adult subjects, age range: 33-60 (mean age: 48 yrs.), whose written consent had been obtained. The patients were divided into 2 groups during the basal visit:

Group A (early stage): patients with grade 1-2 as per visual aspect grade : 11 patients

Group B (late stage): patients with grade 3-4 as per visual aspect grade: 14 patients

The study treatment foresaw 2 injective sessions at intervals of 10 days according to IFT (for Group A) or Matelassé technique (for Group B) depending on the cellulite's stage.

4 visits were performed during the study (Fig. 3):

- T0+T1i: basal assessments, followed by the 1st injection procedure
- T2i: preliminary assessment and 2nd injection procedure
- T1M (1 month after the last injection procedure: evaluations foreseen by the study protocol (Follow-up phase)
- T4M (4 months after the last injection procedure)

Data processing and statistical analysis were performed as follows: Friedman test followed, in case of statistically significant result, by Holm-Sidak Adjusted test.

The inclusion criteria were the following: volunteers aged 35-65 years, with moderate oedematous – fibrosclerotic lipodystrophy on the thighs (3rd superior), with regular menstrual cycle (28-32 days), no Body Mass Index (BMI) variation (± 1) during the last month preceding the study inclusion, available and able to return to the study site for the treatment phase and post-procedural follow-up examinations, accepting not to change their habits regarding food, physical activity, cosmetic and cleansing products for the body, accepting not to expose their body to strong UV irradiation (UV session and/or sun bathes) during the entire duration of the study, accepting to sign the informed consent form.

The exclusion criteria were: pregnancy (only for female subjects not in menopause), lactation (only for female subjects not in menopause), smokers, alcohol abuse and/or drug use, female subjects not in menopause, who do not accept to perform the pregnancy test at T0 and T1M, female subjects not in menopause, who do not use adequate contraceptive precautions in order to avoid pregnancies during the study, oral contraceptive/replacement therapy started less than 1 year ago, change in the normal habits regarding food and physical activity during the month preceding the test and during the study period, use of any anti-cellulite/weight-loss treatment (manual or instrumental massage) on skin test areas during the three months, use of any drug able to cause a weight body variation, Body Mass Index (BMI) variation (± 1) during the study period, presence of clinically important vascular disorders, sensitivity to the test product or its ingredients, including delayed hypersensitivity to hyaluronic acid and granulomatous reactions (to be assessed by the investigator during the baseline), subjects whose insufficient adhesion to the study protocol was foreseeable, participation in a similar study currently or during the previous 6 months.

All evaluations were carried out mono-laterally on the right or left thigh (3rd superior), according to a subjects' randomization list defined by the investigator before the subjects' inclusion. At T2i, T1M and T3M clinical, morphometric and instrumental assessment were performed before the injection procedure.

Clinical evaluations were performed according to the following visual score:

➜ **Cellulite visual aspect (clinical score according to a reference photographic scale)**

• no cellulite	**0**
• slight dimpling on skin surface	**1**
• dimpling and skin depressions	**2**
• dimpling and depressed striations	**3**
• nodules and depressed striations	**4**

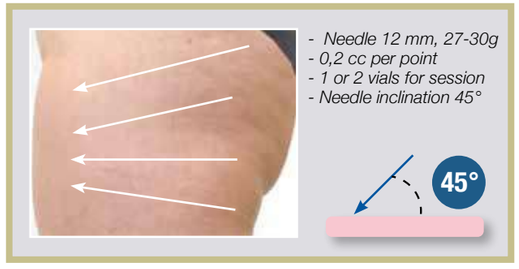


Fig. 1
IFT – Interstitial Fluid Technique

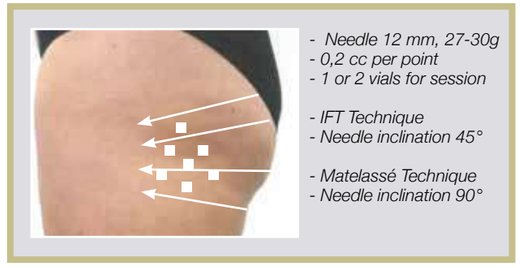
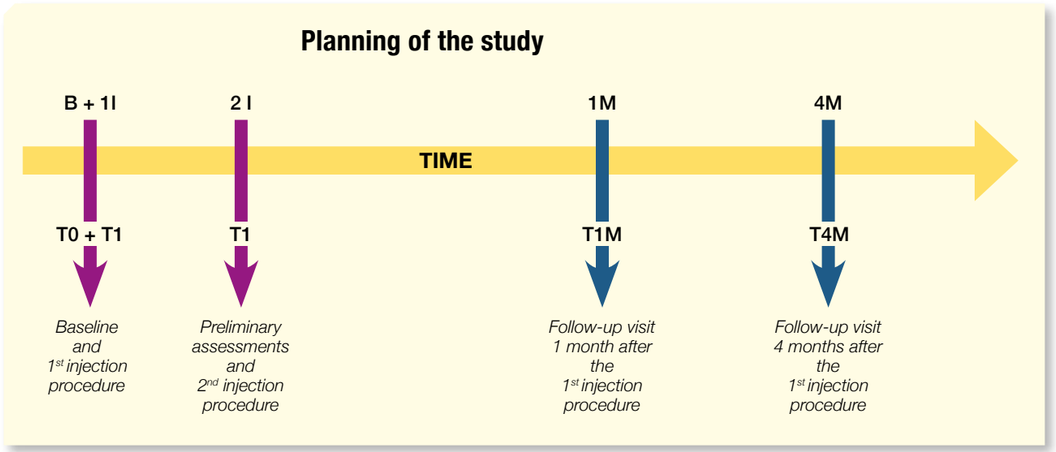


Fig. 2
Matelassé Technique

Fig. 3



Photographic documentation

At T0, T1M and T4M, 2D pictures of the thigh treated areas (left or right side randomly) for all included volunteers were taken.

Circumference measurements

All the measures were performed in standard conditions at the thigh level (middle thigh and under gluteus), thanks to a specific electro-optical system able to fix the volunteer's position.

To reduce the intra-individual variability, circumferences measurement were performed 3 times for each level.

Ultrasonographic evaluations

Ultrasonographic measurement of adipose panniculum thickness (mm) were performed at level of the 3rd superior (external side), through the instrument Body Metrix™ BX 2000 (Genex).

The BX 2000 generates an ultrasound signal (5 MHz) that propagates through tissue and then records the reflected signal.

Results

Clinical assessment

Obtained results highlighted a reduction of cellulite visual aspect of at least 1 degree in 92% of all subjects (group A + group B) vs T0 (Holm-Sidak Adjusted Wilcoxon signed rank test $p<0.05$ T1M and T4M vs T0), according to DERMING reference photographic scales and a mean reduction of clinical degree of cellulite of 0,88 at T1 and 0,95 at T4 for Group B and 0,9 at T1 and 0,6 at T4 per Group A **(Fig. 4)**.

Morphometric evaluation

All circumferences measurements were performed in standard conditions thanks to a specific electro-optical system able to fix the volunteer's position (see procedure).

Morphometric evaluations underlined the "panty" activity of the treatment; in fact, already at T1M and at T4M the mean value of thigh and circumferences resulted clinically/statistically reduced, when compared to baseline in both groups (-1,04 cm at T1 and -1,78 cm at T4 for Group B and –0,87 cm at T1 and -1,39 cm for Group A) (Holm-Sidak Adjusted t test $p<0.05$ vs T0) **(Fig. 5)**.

Ultrasound assessment

Ultrasonographic measurement of adipose pannicula was performed through the instrument Body Metrix™ BX 2000 (Genex). Obtained results were respectively of -4% for group A and -13,5% for group B at T1 and of -8,6% and -11,6% at T4, corresponding to a clinically and statistically significant reduction of the pannicula thickness vs T0, index of a lipo-reducing efficacy of the tested product **(Fig 6)**.

Tolerance evaluation

No adverse event/reaction (nor those expected, such as pain, discomfort and bruises) occurred during the trial. The very high tolerance (100%) was confirmed by the investigator at the end of the treatment period.

In order to highlight the results obtained not only numerically, the photographs of two patients, one of the early group and one of the late group, at time T0 and time T4M, are shown below **(Figg. 7 and 8)**

Discussion and conclusions

The so-called "cellulite" (needless to say, this term does not correspond to the exact medical definition of the condition) afflicts at least 90% of female population in the post-pubertal age almost all over the world and also male population is not entirely exempt from it. To date, there are scientific bases, now well documented, as they are based on histological, biochemical and ultrastructural observations that highlight the pathological aspects. Furthermore, the comorbidities (obesity, overweight, venous pathology of the lower limbs), the subjective symptomatology and the clinical signs that accompany its course, certify the clear deviation from the physiology of the skin. Certainly, the histological aspects that well represent the complexity of the pathogenesis of this disease are characterized by three essential events: alterations of the adipose tissue, hyper-polymerization of the connective tissue matrix and profound alterations of the microcirculation.

Female sex hormones play a significant role in the development of cellulite, in fact this pathology occurs almost exclusively in the female gender.

The main pathogenetic mechanism of cellulite is the altered capillary-venular permeability, with a slowing of the speed and volume of blood flow (vasomotion) at the local micro-circulatory level. The particular conformation of the micro-vascular-tissue unit justifies the fact that the defects in microcirculation of panniculopathy are often associated with alterations in the blood flow that extend to the skin and regional muscles, causing clinical effects such as hyperkeratosis (orange peel skin), tenderness and, in the more advanced stages, profound subversion of the loco-regional aesthetic (mattress skin). The presence of estrogen receptors in endothelial cells and smooth muscle explains the functional differences of female microcirculation, especially in relation to vascular tone and permeability and, therefore, the greater susceptibility of the female sex to the so-called cellulite.

The most recent studies inform us

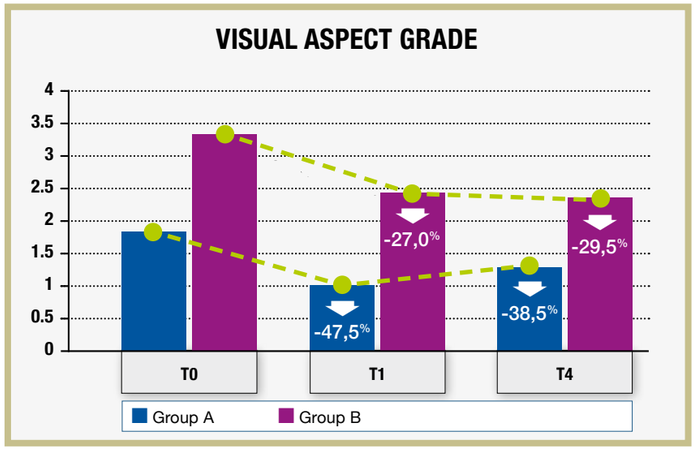


Fig. 4

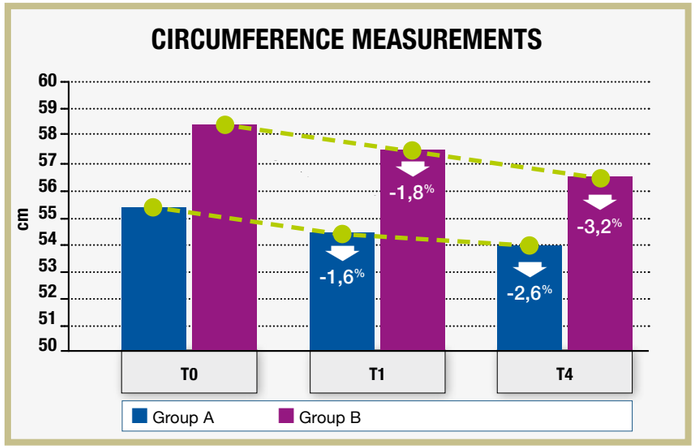


Fig. 5

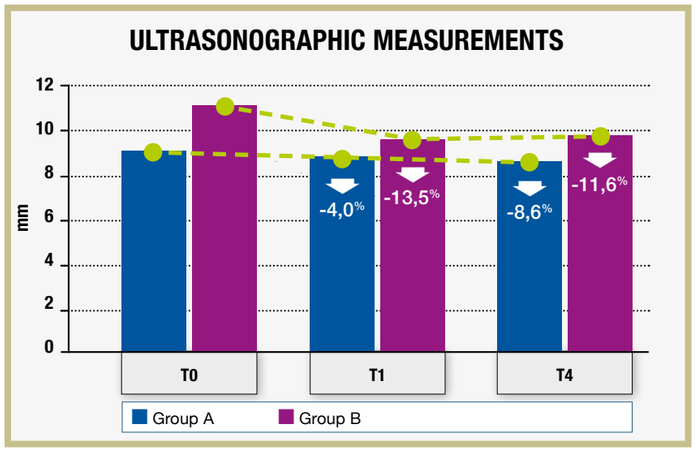


Fig. 6

Fig. 7
Early stage Cellulite

Fig.8
Late stage Cellulite

that, at the level of cellulite, among the functional alterations encountered by adipocytes, there is an increase in the release of phlogistic cytokines. Therefore, adiposity involves the activation, at regional level, of biochemical-cellular mechanisms of an inflammatory nature.

This notation is absolutely consistent with the estrogenic activity on the development of cellulite, which has been widely described and has been further ascertained with the observation of the tissue of women undergoing hormonal therapies and monitored by imaging techniques such as ultrasound and computerized axial tomography.

Once the process is triggered, over time it develops, due to the inflammatory processes described above, on the one hand the neo-synthesis of collagen that leads to the formation of fibrous branches, on the other the reduction of the compactness of the tissues around the fibrous branches. This increase in skin laxity seems in some ways similar to the manifestations of skin aging, also characterized by a degradation of the dermo-epidermal fibrous matrix. Sunekos Cell was able to counteract the dermal damage which seems to be the most important triggering of the condition and acidosis at local level. The injection techniques had an important influence on the results and was planned according to the phase of the disease: in early phases the Interstitial Fluid Technique was the most suitable in late stages the Matelassé Technique demonstrated to be amazingly effective.

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