

EUROPEAN USE OF **DERMOELECTROPORATION™:** ***a new frontier on aesthetic medicine***

by

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Abstract:

With the term “Biolifting” we understand a treatment procedure aimed to rejuvenating the face by non-surgical, “soft” and out-patient treatment means.

This procedure is suitable for acne subjects, initial stages of skin ageing without tissue yield cases, and upkeep of aesthetic surgery patients.

This procedure requires bi-monthly or monthly treatment – a total from four to eight – Each session consists of a superficial microdermabrasion performed with corundum crystals to remove the corneum layer and for vascularization enhancement. Then, a manual massage (gommage) will be performed to promote further mechanical smoothing of the skin. Immediately afterwards, active substances are introduced by means of the Dermoelectroporation™ methodology, a brand new one burst delivery this purpose, consisting in a controlled electrical pulses delivery that may cause “intercellular gates” in the dermis cells allowing the transdermal passage of molecules. A vibration features complete the Dermoelectroporation™ process stimulating the Merkel corpuscles to greater connective restructure of the tissue itself.

The session can be concluded with the application of pulsating light (IPL) so to introduce energy and to stimulate the regeneration properties of connective tissues.

A home treatment with moisturizing and re-generating creams complete the treatment.

This methodology is used, with outstanding results, also for the aesthetic treatment of stretch marks and hypertrophic scars.

Introduction :

Face rejuvenation is still one of the most requested treatment from customer for either Clinical health therapy and cure of aesthetic pathologies purposes. Both male and female patients desire to maintain a health-good looking and to correct, whenever possible, whatever skin problems such as acne, skin relaxation, irregularities, facial wrinkles, etc.

A number of treatments are suggested for this purpose; the integrated treatment with Dermoelectroporation™ is one more option available to the medical aesthetic specialist.

Anatomic and functional bases:

Dermo-epidermic tissue consists of various structures characterized by

- CORNEUS LAYER
- GRANULOUS LAYER
- “MALPIGHI” MUCOUS CORPUS

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- **BASAL LAYER**

Particularly there are various layers with different functional action:

- 1) Epidermis
- 2) Corneus layer
- 3) Derma
- 4) Papillary derma
- 5) Reticular derma
- 6) Hypoderma
- 7) Collagen fibers
- 8) Lobular collagen fibers
- 9) Adipose lobules
- 10) Adipose cells
- 11) Vessels
- 12) Sensorial nerves

With respect to innervations, a typical organization of the sense of touch exists, i.e.:

- 1) Mechanical stimulation

(characterized by corpuscles that are sensitive to Pressure, Vibration, Suction)

- 2) Thermal stimulation

(characterized by corpuscles that are sensitive to Cold and Hot variations)

- 3) Painful stimulation

(characterized by corpuscles that are sensitive to painful stimulation)

These corpuscles are connected to the central nervous system and they send back information at a local level through various receptors:

- **Peripheral receptors:**

- Sensitive to external alterations that are changed into nervous signals

- **Sensitive nervous fibers:**

- Conductive of information. Afferent or centripetal fibers, known as “dendritic” because they are “T” shaped, they convey signals to the cortex. The dendritic nervous terminations are the most numerous in the subcutaneous layer to supply the deep of the dermis and then the under-epidermal plexus.

- **Nervous centers:**

- Transforms the signal into perception, it is behind the *Roland scissoure*

Corpuscles:

The innervations system is extremely sensitive and complicated, characterized by innumerable corpuscles that are present in the dermo-epidermal and hypodermic system, and each aimed at a function. There are.

- 1) Free epidermal terminations
- 2) Free in derma terminations
- 3) Messner corpuscle
- 4) Vater Pacini corpuscle
- 5) Krause corpuscle
- 6) Ruffini corpuscle
- 7) Merkel corpuscle
- 8) Golgi corpuscle

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- 9) Surface nervous plexus
- 10) Deep nervous plexus
- 11) Keratinocytes
- 12) Merkel cells
- 13) Schwann cells

Touch organization:

There are various functions of receptor corpuscles:

- MECHANICAL RECEPTORS, sensitive to mechanical stimulation
- THERMO RECEPTOR, sensitive to thermal stimulation
- NOXIOUS RECEPTORS, sensitive to pain stimulation

Among mechanic receptors are the following:

MEISSNER corpuscles

- sensitive to light stimulation (typical in fingers and toes)

Vater-PACINI corpuscles

- present in deep derma and sensitive to deep pressure. They stimulate fibroblast activity and are extremely useful in defense and healing processes.

GOLGI corpuscles

- present in cells and sensitive to light pressure. They stimulate fibroblast and collagen connective regeneration, not in a cicatrization sense, but toward a functional anatomic restructuring.

MERKEL corpuscles

- they respond to vibration stimuli and propagate them to nervous plexi. They control metabolic activity and hydro-lipidic adjustment.

Among thermo-receptors there are:

KRAUSE corpuscles

- responding to the COLD stimulus

RUFFINI corpuscles

- responding to the HEAT stimulus
- Useful in defense and healing processes

Stimulation of the different receptors causes reactions at matrix and interstice levels that may be used in the different stages of the therapies.

The different reaction of Golgi or Vater Pacini corpuscles justifies the good results or complications obtained using wrong or in incorrect indications such active physiotherapeutic methods as *Endermologie®*.

The function of skin

Skin has various functions, including:

- 1) Protection
- 2) Exchange
- 3) Thermoregulation
- 4) Sensorial
- 5) Metabolism

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Also to be mentioned is the immunologic function due to the presence of the Langerhans cells with their immuno-qualified activity. After seizing the antigen, they abandon the epidermis and submit it to the T lymphocytes which react when necessary.

Exchange function

The skin also has an exchange function with the outside environment, which is also used as a means of pharmacological introduction.

Endermic diffusion is a passive phenomenon, in fact the skin behaves like a passive membrane. Penetration of the substances takes place in two stages characterized by:

- 1) Dormancy stage, in which the dermic layer is charged, usually electrically
- 2) Flow stage, in which the flow becomes constant

Dermaelectroporation™ Studies:

Biologically active drugs and macromolecules, such as peptide drugs, proteins, oligonucleotides and glycosaminoglycans, are characterized by short biological half-life and scarce bioavailability, such characteristics make it difficult to employ different therapeutic strategies other than parenteral ones and which very often are only practicable in hospital.

In this experimental study the Authors used a Dermaelectroporation™ technique that involves the Transderm® device, moreover the transdermal delivery of biologically active molecules *in vivo* has been analysed. The advantage of using controlled electric pulses Vs direct current application shows a significant reduction in the degradation of the molecules to be transdermally delivered as a result of electrolytic phenomena.

The study consists of three sections:

Section 1. Microscopic analysis of skin tissue after the application of the electric field;

Section 2. Qualitative analysis of transdermal delivery of a protein macromolecule (collagen type I);

Section 3. Quantitative analysis of transdermal delivery of lidocaine.

The study demonstrates that Dermaelectroporation™ can be used for transdermal delivery of biologically active molecules, in our case represented by a large-sized protein macromolecule (collagen) and by a general anaesthetic molecule (lidocaine).

Our protocol is suitable for subjects exhibiting the effects of acne, initial stages of skin ageing without tissue yield, and upkeep of aesthetic surgery, consisting first in a surface dermabrasion performed with corundum crystals, intended for the removal of the corneum layer and for vascularization. Immediately afterwards, active substances are introduced by means of the Dermaelectroporation™ methodology, a brand new one burst delivery this purpose, consisting in a controlled electrical pulses delivery that may cause “intercellular gates” in the dermis cells allowing the transdermal passage of molecules. A vibration features complete the Dermaelectroporation™ process stimulating the Merkel corpuscles to greater connective restructure of the tissue itself.

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When necessary, the autologous or cultured lipofilling, in particular session, provides us good aesthetic results enhancing harmony onto the patient's face.

Dermelectroporation Treatment:

Dermelectroporation treatment uses the skin endermic absorption capacities through controlled electrical pulsed delivered onto the skin. These pulses may open special “*electric gates* “ promoting the passage of substances of adequate size.

In early 70’s a group of American dermatologists discovered a change in polarization of the cellular membrane which could be used to promote a kind of cellular “pulsation” by applying an intense electric impulse for a short time at an adequate wave length.

In fact, after the initial shock, the polarity conveyed is slowly reversed, production of electrolysis is avoided, and this opens inter-cellular channels in which substances can pass through.

This method was named “Electroporation treatment” and was used, with special techniques, in the transdermal treatment of melanoma.

To achieve Electroporation effect a trans-membrane voltage (0.5 to 1.5V) is generated through controlled electrical pulses delivery. These pulses cause the lipidic components in the cellular membrane to form water based channels and then to open skin pores.

These alterations give the membranes greater permeability to a large variety of hydrophilic molecules which otherwise could not enter the skin.

Once they are formed, these channels stay open for a relatively long time, about several seconds.

Over 4000 published scientific reports demonstrate the activity and possibilities of the method.

Mattioli Engineering developed a new concept of Dermelectroporation™ that follows the same rules as above stated someway.

Dermelectroporation™ though does not have either any injury action on the cells and any membrane alteration action.

Differently from Electroporation, Dermelectroporation™ ’s deliver lower electrical pulses with the same waveform so that not to have any electrolysis effect and to allow cells to open up and the active substance to penetrate into the skin.

Dermelectroporation™ device uses a pulsed delivery circuitry that allows to macromolecules such as Collagen and Elastine to be transdermally delivered into the dermis.

This Technology (patented by Mattioli Engineering) allows delivery of bursts of pulses with inversed polarity able to have no electrolysis effects at the electrodes and to keep unaltered the transdermal delivery effect using low powered voltages and current so that not to cause any undesired side effect.

Together with the pulses delivery a vibration is applied. The frequency goes up to 50Hz to 100Hz selectable and that determine a sinusoidal pressure on the skin.

The reason and the effect of the vibration is double:

Anesthetic effect: The electrical pulses frequency is equal or double the vibratory frequency, this cause an analgesic effect because vibration overcome the feeling of electrical pulses on the skin.

In addition to this vibration causes either a blood and lymphatic circulation improving together with a massage that promote the active substance penetration into the dermis.

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Studies from 2003 Nobel Prize for Chemical Professors Agree and Kinnon opened the pathway to prove the possibility to use one among the most fascinating characteristic of the human dermis : the

Hydroelectrophores”, that is, those water based channel that open up between cells due to Physical, Vibratory, Mechanical, chemical and nervous effects in a very spontaneous way and in such a manner to let the “external world” to be able to communicate with the interior universe.

These water-based gates could open up about 1,000,000,000,000,000,000.00 times per day.

We do believe that Dermoelectroporation™ can externally activate some hydroelectrophores to use them to transdermally deliver molecules with even big size and weight as experimental studies proved on rats made at University of Florence- Italy .

In this study some unaltered molecule of Fluorescent bovine type 1 collagen with 0.8 micron size have been transdermally delivered and monitored successfully.

Dermoelectroporation Treatment:

In aesthetic pathologies characterized by skin irregularities and dystrophies, such as acne, wrinkles, stretch marks, sagging of the skin, Dermoelectroporation™ treatment is preceded by a microdermabrasion treatment. This is carried out by means of corundum crystals (aluminum oxide in a sterile, disposable package) to exfoliate the stratum corneum with simultaneous vascularization of the tissue by mechanical stimulation (light suction – light pressure – dermabrasion)

When the dermabrasion treatment needs to be deeper and might cause pain, a session of Dermoelectroporation™ treatment is used first to introduce an anesthetic principle (0,5 % *lidocain* without adrenalin).

Removal of the corneous layer smooth the skin and facilitates Dermoelectroporation™ which is performed immediately after microdermabrasion applying substances containing elastine, collagen, and aminoacids. We’d rather to use the precursors of these substances instead.

Dermoelectroporation: Protocol of Treatment by Bacci:

Treatment ‘s purpose is to improve the outer appearance by stimulating the reconstitution of new collagenous and matrix tissue.

There are several stages to get to the aim:

1. Lymphatic drainage and vascularization performed with Endermologie® Technique

We consider this part of the treatment very important for three reasons:

- a) *Lymphatic drainage with depuration of the tissues*
- b) *Vascularisation of the tissues*
- c) *Stimulation of the fibroblast preparing it to new production of collagen*

2. Skin smoothing performed by superficial microdermabrasion with corundum powder crystals (Ultrapeel® Transderm® System By Mattioli Engineering). After being made aseptic by means of non-alcoholic detergents, the skin is smoothed without being traumatized. Abrasion depth depends on the pathological case under scrutiny. At the end of the session, the crystals remaining on the skin are used to perform a final regularizing “gommage” with the fingers, and then the skin is washed with physiological solution.

3. Opening the “water-based gates” with Electric an Dermoelectroporation treatment with Tranderms®.

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Over the clean skin a sterile gauze pad is applied and on it is poured a sterile solution of the precursors of the elastine, collagene and aminoacid whose transdermic introduction is helped by the Dermoelectroporation treatment.

The products used on the face are officially products manufactured by an Italian company and studied by prof. Ceccarelli with action of biostimulation and biorecovering of the tissues.

The procedure usually lasts 5 minutes for any area, until the substances are absorbed. At this point the skin is washed with physiological solution and a soothing treatment is performed.

4. Energizing stimulation, performed, when required, using a low-power Intensive Pulse Light (532-695 nM).

Sometimes the Photoresurfacing session is performed after 5-6 days when the connecting tissue regeneration has a marked stimulating effect.

5. Soothing action, performed by applying compresses of cold water and soothing substances right after anti-herpetic cream (in our practice we use Zovirax® or Aciclin® as anti-herpetic and Biafin® or Biolenil Medestea® as soothing substances) application.

6. Cosmetic action. The patient may put on makeup to protect the skin from either cold and sun weather, using a fatty substance containing sun-screen.

7. Home treatment is recommended with a moisturizer containing Vitamin C and *Phytin acid* (in our experience Stand-by cream 5% MacPharma®) and sun screen.

The treatment is usually performed every 15-20 days twice or three times, and then a maintenance treatment every 2-3 months.

Indications:

The treatment is recommended for:

- Effects of Acne
- Start of skin sagging
- Skin stimulation
- Stretch marks
- Skin unevenness

Used topical products in our protocol of treatment

Biostimulation & Biorestitution (By Dr. Ceccarelli) (maurcec@tin.it)

Those Products are Classified as 3 Lvl. Medical Device and they are CE marked by The Italian Superior institute for Health (ISS)

Products are:

SKIN-B for biostimulation

SKIN-R for la biorestitution

Biostimulation product composition

Ialuronic Acid - fragments 22-38 monomer

- amminoacids 8.5%

- Glucosamine 1.2gr

- Sodium Bicarbonato 8.4%

- ph. 7.2

Osm: 450 mOsm/l

Product comes in a 5 ml sterile bottle according of the international laws

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Biorestitution product composition

Ialuronic Acid - fragments 22-38 monomer

-amminoacids 8.5%

ph. 5.8

Osm: 1100 mOsm/l

Product comes in a 5 ml sterile bottle according of the international laws

Conclusions.

Today, we believe Dermoelectroporation™ can be a new approved methodology to introduce the substances into the dermis. Surely, it is a new frontier on aesthetic medicine, representing a advanced methodology to treatment of acne, ageing and scars.

Bibliography

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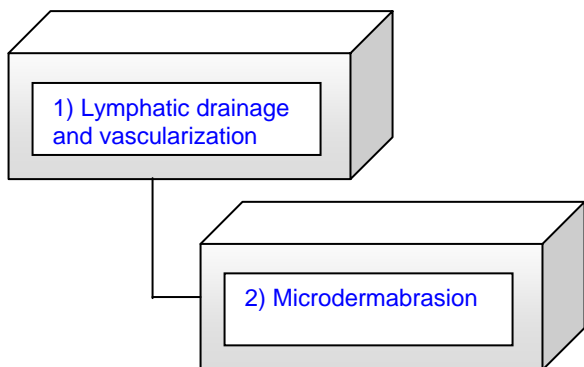
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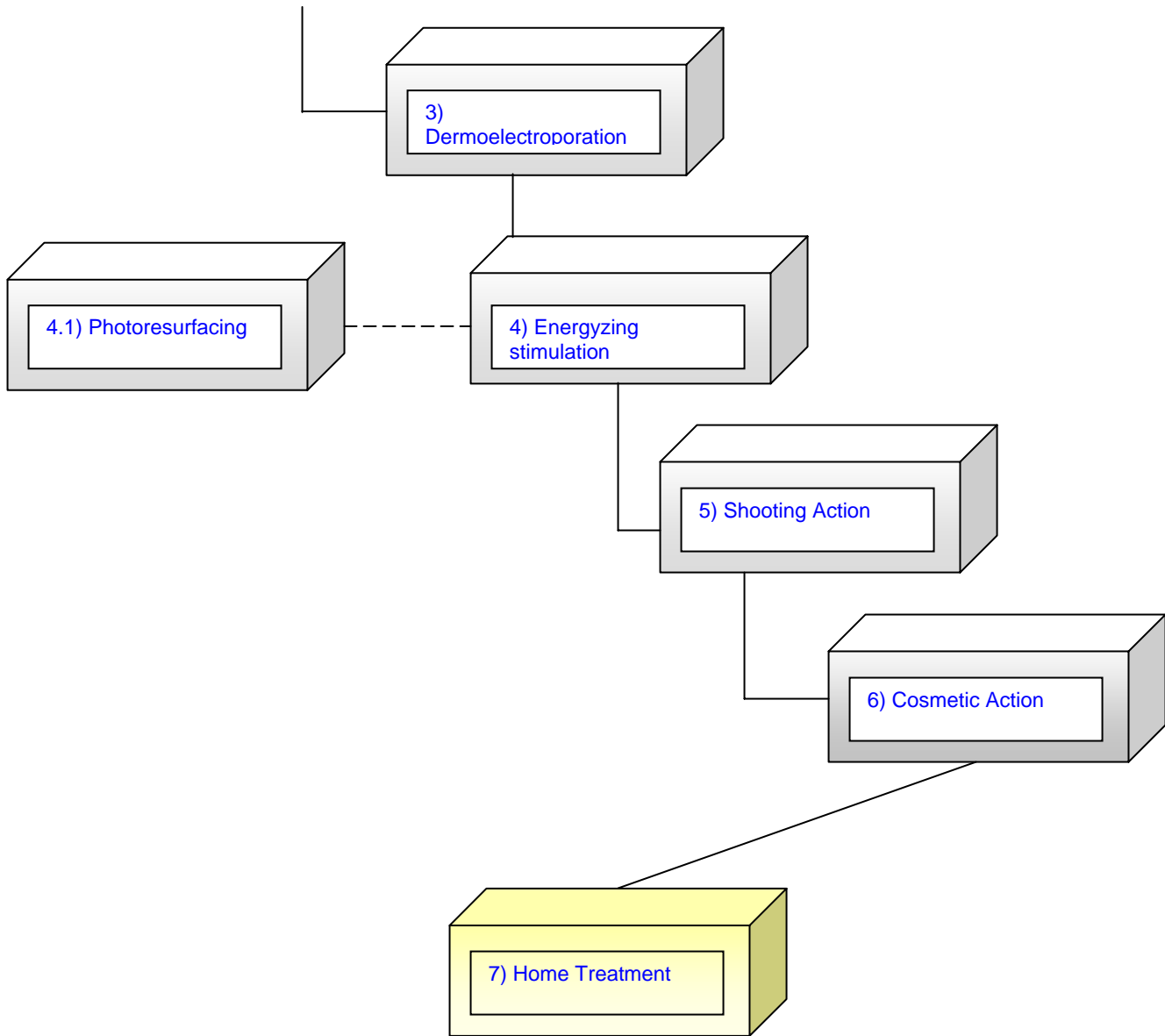
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European Dermoelectroporation™ Protocol – Flow chart





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